Common Neurosurgical Conditions in the Pediatric Practice

Recognition and Management

Jeffrey P. Greenfield
Caroline B. Long
Editors

Springer

Common Neurosurgical Conditions in the Pediatric Practice

Jeffrey P. Greenfield • Caroline B. Long
Editors

Common Neurosurgical Conditions in the Pediatric Practice

Recognition and Management

Springer

Editors
Jeffrey P. Greenfield, MD, PhD
Associate Professor of Neurological Surgery
Weill Cornell Medical College
New York, NY, USA

Caroline B. Long, MD
Manhattan Pediatrics
New York, NY, USA

ISBN 978-1-4939-3805-6 ISBN 978-1-4939-3807-0 (eBook)
DOI 10.1007/978-1-4939-3807-0

Library of Congress Control Number: 2016945972

Printed on acid-free paper

This Springer imprint is published by Springer Nature
The registered company is Springer Science+Business Media LLC New York

Preface

Within medicine, increasing subspecialization has created an almost impossible task; primary care providers are now asked to triage their patients and provide appropriate referrals within a dizzying array of diverse medical fields. Pediatric neurosurgery remains one of a number of highly specialized fields within which most pediatric practitioners including physicians, physician's assistants, and nurse practitioners have never received any training. This fact, combined with the rarity of pediatric neurosurgical diseases, the acuity with which many of them present, the need for rapid triage and tertiary care, and parental anxiety when receiving a neurologic diagnosis, creates a challenging situation for providers caring for children with these conditions.

Several years ago, we hosted a CME event in New York City bearing the same name as this textbook. We solicited comments from attendees and were pleased that most participants felt we were filling a real deficiency in medical education—the cross-fertilization between subspecialties. In fact, a recent survey of pediatricians through an AAP initiative supports our suspicion that many primary care providers felt uncomfortable managing patients with neurosurgical conditions. This survey also suggested a number of neurosurgical topics that pediatricians felt they wanted more assistance in managing and triaging. All of these topics, and many others, are covered from both a neurosurgical and pediatric perspective in this textbook.

In fact, this textbook was designed around a central concept:

> Pediatricians and subspecialists need to have a closer working relationship to make childhood medicine work seamlessly in 2016 and beyond.

A pediatrician in a busy practice should not be expected to explain to a concerned parent what the differences in treatment options may be between different types of brain tumors; however all pediatric practitioners should be able to discern between benign and worrisome headaches and to decide when imaging, referral to neurology, or triage to an emergency department is warranted. The relationship between primary care physicians and subspecialists such as pediatric neurosurgeons is obviously at the crux of this book, but should also be at the forefront of mutual efforts to improve care of children. This textbook will never be able to replace the trust and confidence that is built through years of communication and shared patient experiences.

To highlight our belief in the strength of the relationship between primary care providers and subspecialists, this book was envisioned by and co-edited by a pediatric neurosurgeon and a pediatrician each providing the perspective

from within the lens through which they view these common neurosurgical conditions. We hope the vignettes provide real-life flavor to experiences many of you have had, or will have. We expect that the "red flags," "pediatrician's perspective," and references will serve as focused reviews on many of these topics. When reading a newly arrived imaging report, or caring for a child with an unfamiliar diagnosis, these chapters can serve as a medical refresher before calling a parent back with unexpected news or reviewing a finding in the office.

The book is organized into parts that loosely approximate the neurologic development of a child and address issues that are commonly encountered. The first part reviews neurologic development and birth-related trauma commonly seen in the neonatal intensive care unit including issues such as brain injury, brachial plexus injury, and hematomas. The second part addresses findings commonly encountered in the first month of life in the pediatrician's office. Lumps and bumps, manifestations of neurocutaneous diseases, or tethered cord stigmata are all reviewed in depth. The third part is a comprehensive review of hydrocephalus from birth-related intraventricular hemorrhage through the work-up of macrocephaly and headache management. Part 4 is an important group of chapters describing up to the date thoughts on imaging the central nervous system in children from prenatal ultrasound through MRI and CT including when these different modalities are important to select and the risks associated with each. The fifth grouping of chapters consists of explorations of common neurosurgical conditions that many pediatricians are uncomfortable dealing with, including brain tumors, spasticity, and vascular lesions to use as a reference tool when caring for a complex neurosurgical patient. Finally a series of chapters related to head trauma concludes the textbook, including sections on non-accidental trauma and concussion management.

Most importantly, we hope the topics we cover in the ensuing chapters provide you with some measure of confidence in dealing with conditions you may feel less comfortable with than others, and provide a framework within which you can direct subspecialized care.

We would very much like to take this opportunity to thank our mentors within medicine—Dan Cohen, Gary Edelstein, Sarah Long, Phil Stieg, and Mark Souweidane—for supporting and inspiring our careers and providing continual support and guidance through the years. Educating subsequent generations of pediatricians and neurosurgeons with the lessons you taught us is your greatest legacy and we are proud to be within your lineages.

To our parents and families who instilled within us the belief that education and academics can be at the center of a rich and meaningful life, thank you for supporting our endless training and sharing pride in our demanding but fulfilling careers. Everything we have learned began with your confidence in us and now allows us to begin to pass this on to the next generation of pediatric physicians.

Finally, we are forever indebted to Richard Lansing and Joni Fraser from Springer for seemingly unending patience as we tried to balance our busy medical careers and four young boys at home with an innocent foray into the editing and publishing world. We hope your confidence in us is rewarded in

the impact this book will have and the children benefiting from the shared knowledge going forward.

To our readers, best of luck caring for your patients with these neurologic conditions—there is often no greater challenge in medicine but also often no greater reward!

New York, NY, USA

Jeffrey P. Greenfield
Caroline B. Long

Contents

Contributors

Rick Abbott, M.D. Montefiore Medical Center, Bronx, NY, USA

Assem M. Abdel-Latif, M.D., M.Sc. Department of Neurological Surgery, Faculty of Medicine, Ain Shams University, Abbassia, Cairo, Egypt

Baxter B. Allen, M.D. New York Presbyterian Hospital—Weill Cornell Medical Center, New York, NY, USA

G. Rene Alvarez Berastegui, M.D. Department of Neurological Surgery, Weill Cornell Medical College, New York, NY, USA

Waleed A. Azab, M.D. Department of Neurological Surgery, Ibn Sina Hospital, Kuwait

Matei A. Banu, M.D. Department of Neurological Surgery, New York Presbyterian-Weill Cornell Medical Center, New York, NY, USA

Hediyeh Baradaran, M.D. Department of Radiology, New York Presbyterian Hospital—Weill Cornell Medical Center, New York, NY, USA

Charlotte A. Beam, M.S., C.G.C. Department of Neurological Surgery, Weill Cornell Medical College, New York, NY, USA

Imithri D. Bodhinayake, M.D. Department of Neurological Surgery, Weill Cornell Medical College, New York, NY, USA

Jason B. Carmel, M.D., Ph.D. Motor Recovery Laboratory, Mind and Brain Institute, Neurology, and Pediatrics, Weill Cornell Medical College, Burke Medical Research Institute, White Plains, NY, USA

Stephen T. Chasen, M.D. Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Weill Cornell Medical College, New York, NY, USA

Babacar Cisse, M.D., Ph.D. Department of Neurological Surgery, Weill Cornell Medical College, New York, NY, USA

Scott W. Connors, B.S. Department of Neurological Surgery, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY, USA

Katie Shayna Davis, M.S. Division of Child and Adolescent Psychiatry, New York State Psychiatric Institute, New York, NY, USA

Marc Dinkin, M.D. Department of Ophthalmology, Weill Cornell Medical College, New York Presbyterian Hospital, New York, NY, USA

Department of Neurology, Weill Cornell Medical College, New York Presbyterian Hospital, New York, NY, USA

Department of Neurosurgery, Weill Cornell Medical College, New York Presbyterian Hospital, New York, NY, USA

Zuhal Ergonul, M.D., Ph.D. Division of Child Neurology, Weill Cornell Medical College, New York, NY, USA

Emilie A. George, B.A. Weill Cornell Medical College, New York, NY, USA

Lara M. Gordon, M.D. Department of Pediatrics, New York Presbyterian Hospital—Weill Cornell Medical Center, New York, NY, USA

Jeffrey P. Greenfield, M.D., Ph.D. Associate Professor of Neurological Surgery, Weill Cornell Medical College, New York, NY, USA

Neil Haranhalli, M.D., B.S. Albert Einstein College of Medicine, Bronx, NY, USA

Linda A. Heier, M.D., F.R.C.P.(C) Department of Radiology, Division of Neuroradiology, Weill Cornell Medical College, New York, NY, USA

Caitlin E. Hoffman, M.D. Department of Neurological Surgery, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY, USA

Ibrahim Hussain, M.D. Department of Neurological Surgery, New York Presbyterian Hospital—Weill Cornell Medical College, New York, NY, USA

Sotirios T. Keros, M.D., Ph.D. Pediatric Neurology, Weill Cornell Medical College, New York, NY, USA

Sanford Children's Hospital, University of South Dakota Sanford School of Medicine, Sioux Falls, SD, USA

David Kimball, B.S. St. George's University School of Medicine, Great River, NY, USA

Caroline B. Long, M.D. Manhattan Pediatrics, New York, NY, USA

Konstantinos Margetis, M.D. Icahn School of Medicine at Mount Sinai, New York, NY, USA

Alison S. May, M.D. Department of Pediatrics, New York Presbyterian Hospital, New York, NY, USA

Matthew McCarthy, M.D. Department of Pediatrics, Division of Child Neurology, Weill Cornell Medical College, New York, NY, USA

Heather J. McCrea, M.D., Ph.D. Department of Neurological Surgery, New York Presbyterian Hospital—Weill Cornell Medical Center, New York, NY, USA

Peter F. Morgenstern, M.D. Department of Neurological Surgery, New York Presbyterian Hospital—Weill Cornell Medical Center, New York, NY, USA

Nelson Moussazadeh, M.D. Department of Neurological Surgery, New York Presbyterian—Weill Cornell Medical Center, New York, NY, USA

Memorial Sloan-Kettering Cancer Center, New York, NY, USA

Juliann M. Paolicchi, M.A., M.D., F.A.N.A. Pediatric Neurology, Komansky Center for Children's Health, Weill Cornell Medical Center, New York, NY, USA

Jeffrey M. Perlman, M.B., Ch.B. Department of Pediatrics, New York Presbyterian Hospital, Weill Cornell Medical College, New York, NY, USA

Kenneth R. Perrine, Ph.D. Department of Neurological Surgery, Weill Cornell Medical College, New York, NY, USA

Soniya N. Pinto, M.B.B.S. New York Presbyterian Hospital—Weill Cornell Medical Center, New York, NY, USA

Cathleen L. Raggio, M.D. Orthopedic Surgery, Hospital for Special Surgery, New York, NY, USA

Benjamin I. Rapoport, M.D., Ph.D. Department of Neurological Surgery, Weill Cornell Medical College, New York-Presbyterian Hospital, New York, NY, USA

Anil Sindhurakar, Ph.D. Motor Recovery Laboratory, Burke Medical Research Institute, White Plains, NY, USA

Vita Stagno, M.D. Department of Neurological Surgery, Weill Cornell Medical College, New York, NY, USA

Apostolos John Tsiouris, M.D. Neuroradiology Section, New York Presbyterian Hospital—Weill Cornell Medical Center, New York, NY, USA

María Teresa Alvarado Torres, M.D. Department of Neurological Surgery, New York Presbyterian Hospital, New York, NY, USA

Fundación Santa Fe de Bogotá, Bogotá, Colombia

Dara M. West, M.D. Department of Ophthalmology, USC Roski Eye Institute, Keck School of Medicine of USC, Los Angeles, CA, USA

Department of Neurology, Keck School of Medicine of USC, Los Angeles, CA, USA

Kaleb H. Yohay, M.D. Hassenfeld Children's Center for Cancer and Blood Disorders, New York, NY, USA

Part I

Development of the Brain and Spine

Normal Development of the Skull and Brain

1

Waleed A. Azab

Introduction

The cranial vault or neurocranium encloses the brain, meninges, and cerebrospinal fluid. *The single most important stimulus for head growth during infancy and childhood is brain growth*, and this will be a recurrent theme when trying to consider the driving forces behind many neurosurgical or central nervous system-related findings in your young patients. In the subsequent chapters, we will systematically introduce some pathologic conditions pertaining to the intersection of brain and skull development throughout adolescence. The abnormally large head, small head, and misshapen heads are all of concern to parents and medical care providers alike. In this chapter we will introduce a framework of thinking to use as a reference tool when evaluating your patients. In the subsequent chapter, we will provide a simple and yet comprehensive framework for the pediatric neurologic examination and then begin our journey through the various manifestations of normal, gone awry.

W.A. Azab, M.D. (✉)
Department of Neurosurgery,
Ibn Sina Hospital, Kuwait
e-mail: waleedazab@hotmail.com

In the newborn child, bones of the cranial vault are separated by intervening sutures. At points of multiple bony oppositions, sutures widen and assume the shape of fontanels. Sutures and fontanels close at quite wide age ranges (discussed more in Chap. 6). Sutures facilitate deformation of the head during delivery and allow uniform expansion of the calvarium during brain growth. The "cone-shaped" head that so many infants manifest after vaginal delivery should be an opportunity to tell anxious parents how well evolution and anatomy have conspired to allow babies with such large brains to develop intrauterinely for so long! In an otherwise normal (nonsyndromic) child, and the absence of a midsagittal ridge (Chap. 6), birth-related cranial deformity should not be cause for concern. Abnormal head shapes can of course be caused by craniosynostosis or deformational plagiocephaly. Premature closure of cranial sutures results in craniosynostosis, a condition that usually needs surgical treatment. Deformational (positional) plagiocephaly refers to the deformation of the head characterized by a persistent flattening on the side with an asymmetric head shape and misalignment of the ears. Plagiocephaly is a benign condition that should be differentiated from craniosynostosis and is usually treated conservatively. These conditions are very easily differentiated from the normal skull and are discussed in detail later.

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_1

Normal Skull Development

Enclosed within the skull bones, brain growth continues exponentially in the first 2 years of life. Postnatal growth of the skull is characterized by changing proportions of its components. In addition to the continued growth of the frontal and parietal bones, the squamous temporal bone increases in size so that it contributes a greater proportion of the skull vault in the adult than in the neonate [1]. The skull without the mandible is called the cranium (Fig. 1.1), and may be subdivided into two regions. The cranial vault or neurocranium encloses the brain, meninges, and cerebrospinal fluid, while the facial skeleton or viscerocranium hangs down from the front of the neurocranium and encloses the organs of special sense [2]. At birth, the skull is proportionally large, reflecting the importance of brain maturation. The volume of the neurocranium compared to that of the face is about 8:1 in the newly born infant. This ratio becomes 5:1 by 2 years, 3:1 at 6 years, and 2:1 in the adult [3]. The major part of the skull vault is formed by paired frontal and parietal bones and a single interparietal bone. The squamous part of the temporal bones and the membranous part of the greater wing of sphenoid contribute to the lateral walls of the skull [2].

The bones of the skull base are formed by endochondral ossification [1]. Bone formation of the skull vault takes place through a process of intramembranous ossification from a mesenchymal layer situated between the dermal mesenchyme and the meningeal membranes [4]. The mesenchymal cells condensate then differentiate into osteoblasts and deposit extracellular matrix. Ossification proceeds radially from these condensations to ultimately form the bones of the skull vault [5].

In the newborn, the membranous bones of the vault are separated by the intervening sutures. At the points of intersection, sutures widen and assume the shape of fontanels. The larger anterior fontanel is at the intersection of the sagittal, coronal, and metopic sutures, and the posterior fontanel is at the intersection of the sagittal and lambdoid sutures (Fig. 1.2). The most significant growth of the skull occurs along the sagittal and coronal sutures [6]. Sutures facilitate deformation of the head during delivery and allow uniform expansion of the calvarium during brain

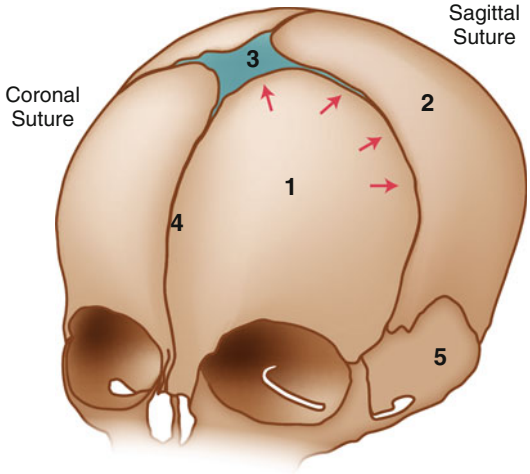


Fig. 1.1 Neonatal skull. Edge of the frontal bank of left coronal suture is marked with *arrows*. (*1*) Frontal bone, (*2*) parietal bone, (*3*) anterior fontanel, (*4*) metopic suture, (*5*) squamous temporal bone

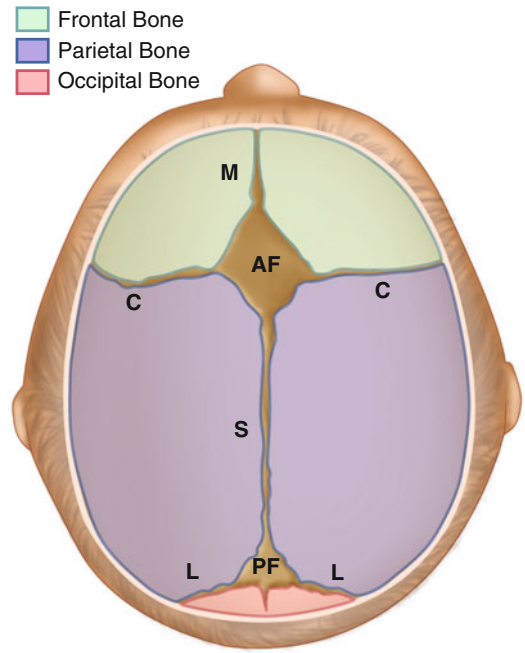


Fig. 1.2 Illustration of the vault of the skull in an infant viewed from above. *AF* anterior fontanel, *C* coronal suture, *L* lambdoid suture, *M* metopic suture, *PF* posterior fontanel, *S* sagittal suture

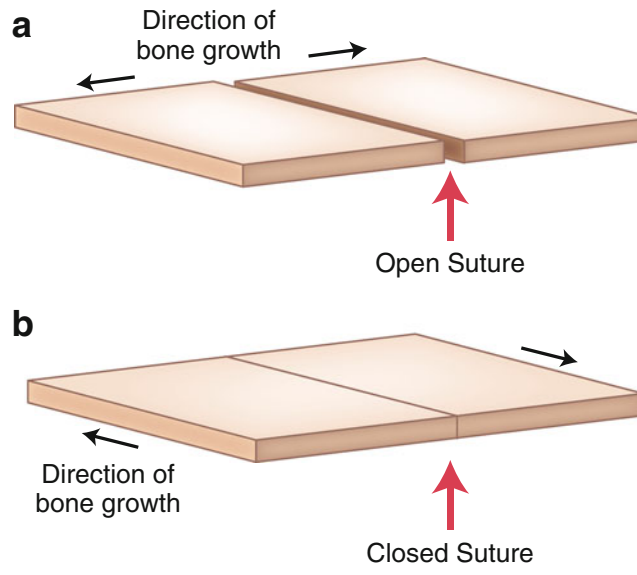


Fig. 1.3 Virchow's law

growth by its fibrous connective tissue content [7, 8]. Sutures regulate the balance between proliferation and differentiation of the osteogenic precursors through multiple molecular pathways and are the principal growth centers in the skull for the first few years of life [5, 9]. As a rule, the growth of the skull is perpendicular to the open suture lines and parallel to a fused suture (Virchow's law) (Fig. 1.3) [7]. Closure of the various fontanels and sutures takes place at specific age ranges, but it is rarely any cause for concern, in isolation, in a developmentally normal child with an otherwise normal cranial morphology when a fontanel closes earlier or later than expected (Table 1.1).

Table 1.1 Normal age ranges of closure for fontanels and cranial sutures

Fontanel or suture	Age of closure
• Anterior fontanel	12–18 months
• Posterior fontanel	3–6 months
• Posterolateral fontanel	24 months
• Anterolateral fontanel	3 months
• Metopic suture	3–8 months
• Coronal sutures	~35 years
• Lambdoid sutures	~35 years
• Sagittal suture	~35 years
• Squamosal sutures	~35 years

Modified from Pekçevik Y, Hasbay E, Pekçevik R. Three-dimensional CT imaging in pediatric calvarial pathologies. Diagn Interv Radiol. 2013 Nov–Dec;19(6):488–94

The base of the infant skull, on the other hand, contains multiple cartilaginous joints or synchondroses located between the sphenoid and ethmoid bones anteriorly and between the sphenoid and occipital bones posteriorly. Growth of the skull base and consequent cranial lengthening is largely independent of cerebral growth and takes place mostly at the synchondroses between the sphenoid and occipital bones. In the sphenoid region, three prominent synchondroses can be identified and are named the fronto-sphenoid, the inter-sphenoid, and the spheno-occipital. The first two usually close by age 2, but the spheno-occipital synchondrosis may be visible on lateral radiographs of the skull base until the age of 18 years [2, 10].

The single most important stimulus for head growth during infancy and childhood is brain growth [11]. Throughout the period of rapid development of the brain, pressure is exerted on the inner table of the skull, which accommodates to the increasing size of the brain. Such an adaptation is facilitated by the membranous fontanels, which remain open until maximal brain growth has been attained. Accurate assessment of head growth is therefore one of the most important aspects of the neurologic examination of infants and young children [11].

Normal Development of the Brain

The development of the nervous system occurs through the interaction of several synchronized processes, some of which are complete before birth, while others continue into adulthood [12]. The central nervous system begins to develop in the human fetus 2–3 weeks after fertilization of the oocyte. From 4 to 12 weeks of gestation, ectodermal tissues of the neural tube begin to differentiate into the precursors of the various structures of the nervous system. The forebrain and facial structures develop at one end and the spinal cord at the other. The hollow center of the tube in the region of the future brain eventually develops into the ventricles. Regions called proliferative or ventricular zones form in the vicinity of the ventricles and differentiate into the site for the division and origin of cortical and subcortical neurons [12, 13]. Between weeks 12 and 20 of gestation, neurons migrate from the ventricular and adjacent subventricular zones along a scaffolding of glial cells toward their determined final destinations in the cortex [12, 14].

Subsequently, a period of rapid programmed cell death occurs, reducing neuronal populations by half between 24 weeks of gestation and 4 weeks after birth. The cell bodies of the neurons are primarily found in the gray matter of the brain. Their myelinated axons form white matter. Myelination begins at the brain stem by 29 weeks and generally proceeds from inferior to superior and posterior to anterior. Proximal pathways tend to myelinate before distal, sensory before motor, and projection before association. Although most major tracts are significantly myelinated by early childhood, some axons continue to myelinate into the second and third decades of life [12].

Another major developmental process is the proliferation and organization of synapses, which begins around the 20th week of gestation [12]. The rate of synapse formation peaks after the 34th week of gestation reaching about 40,000 new synapses per second [13]. A rapid increase in synaptic density occurs after birth with a number estimate at the age of 2 years that is around 50 % greater than the typical number in adults [15]. Due to increasing cell and synaptic density, beginning at approximately 15 weeks of gestation, the surface of the growing brain begins to fold into sulci and gyri. The major sulci, except for the occipital lobe, are in place by 28 weeks of gestation, after which secondary and tertiary sulci are elaborated, with nearly all gyri present by birth. The sulcal and gyral patterns continue to increase in complexity after birth [12]. Rapid brain growth takes place in the first 2 years of life reaching 80–95 % of its adult size [16].

Abnormal Head Size

Evaluation of the Head Circumference

In 1968, Nellhaus compiled graphs of head circumference in children of both sexes from birth to 18 years of age [17]. Detailed tables and percentile charts based on measurements taken from a very large number of subjects have become available through the WHO Multicentre Growth Reference Study Group which established the WHO Child Growth Standards for head circumference for age. We have included these charts for easy accessibility inside the cover of this book. Detailed normative data and percentile charts for boys and girls, specific charts that account for prematurity, and specific chart for children with certain specific etiologies such as Down's syndrome can be accessed online at the WHO website (http://www.who.int/childgrowth/standards/hc_for_age/en/) [18]. A head circumference that is two standard deviations above or below the mean for age requires investigation and explanation [11].

Macrocephaly

Macrocephaly is defined as a head circumference more than two standard deviations for age and sex above the mean. It can be caused by various benign or pathological conditions (Table 1.2). Common causes of macrocephaly include familial megalencephaly (larger-than-normal brain mass), benign extracerebral collections of infancy (BECC), and hydrocephalus [21], the workup and treatment of which will be discussed in more detail in Chaps. 13 and 14.

Table 1.2 Causes of macrocephaly [11, 19–21]

• Familial megalencephaly (larger-than-normal brain mass)
• Benign extracerebral collections of infancy (BECC)
• Hydrocephalus
• Hydranencephaly
• Brain tumors
• Intracranial cysts
• Pseudotumor cerebri
• Subdural hematomas or hygroma
• Rebound or "catch-up" brain growth (after prematurity or serious illness)
• Genetic, metabolic, and dysplastic syndromes (e.g., neurofibromatosis, Soto syndrome, mucopolysaccharidoses, hemimegalencephaly, achondroplasia)
• Lipid storage disease, leukodystrophies, cranial dysplasias, and marrow hyperplasia (chronic hemolytic anemias)

Table 1.3 Causes of microcephaly [3, 11]

• Trisomies 13, 18, 21
• Lissencephaly, schizencephaly
• Rubenstein-Taybi, Cornelia de Lange, Angelman syndromes
• Fetal alcohol syndrome, anticonvulsants, maternal phenylketonuria (PKU)
• Intrauterine infections; TORCHS
• Radiation in the first and second trimesters
• Placental insufficiency
• Autosomal dominant and autosomal recessive familial microcephaly
• Hypoxic-ischemic injury, birth asphyxia
• Bacterial meningitis (especially group B streptococci), viral encephalitis (enterovirus, herpes simplex)
• Glut-1 deficiency, PKU, and maple syrup urine disease
• Tay-Sachs and Krabbe's diseases

Detailed history, neurological examination (especially for signs of high intracranial pressure), evaluation of developmental milestones, and assessment of head growth rate through serial head circumference measurements are important for differential diagnosis, urgency of imaging, and further management [19]. Macrocephaly with normal growth rate and normal neurological examination is reassuring and is characteristic of benign megalencephaly which is usually familial [21]. Rapid head growth rate with loss of developmental milestones or other neurologic findings, on the contrary, suggests an increased intracranial pressure, often caused by hydrocephalus or neoplasms [11].

Macrocephaly and accelerated head growth with normal neurological exam and absence of evidence of elevated intracranial pressure may occur as nonprogressive subarachnoid space dilatation with or without ventricular enlargement. This pattern is most commonly referred to as benign extracerebral collection of infancy (BECC). The cause is unknown, but it may be related to delayed development of parasagittal dural channels responsible for cerebrospinal fluid (CSF) resorption in young children (who have few arachnoid villi). Accelerated head growth may continue until 12–18 months of age and then usually stabilizes as a form of megalencephaly. Imaging features of BECC include normal to mildly enlarged lateral and third ventricles and symmetric enlargement of the frontal subarachnoid spaces, interhemispheric fissure, and Sylvian fissures [21].

Microcephaly

Microcephaly has fewer neurosurgical implications than macrocephaly. It is defined as a head circumference more than two standard deviations below the mean for age and sex which is by definition microcephaly [11]. Some causes of microcephaly are listed in Table 1.3 and has an expanded discussion dedicated to the topic within Chap. 6.

Abnormal Head Shape

Craniosynostosis

A detailed review of the various craniosynostoses and their management is beyond the scope of this chapter; Chap. 6 is dedicated entirely to this topic; however, a brief account on some features of this entity is presented here. Premature closure of cranial sutures results in craniosynostosis [22]. The incidence of craniosynostosis is approximately 1 in 2500 live births, and the condition is broadly classified into non-syndromic and syndromic craniosynostosis [23–25]. Unlike the syndromic

type, non-syndromic synostosis is not associated with other dysmorphisms of the face, trunk, or extremities. Furthermore, a non-syndromic craniosynostosis typically involves a single suture [26]. The most commonly affected sutures in descending order are the sagittal suture, followed by the unilateral coronal, bilateral coronal, metopic, and lambdoid sutures. Syndromic craniosynostosis is much less common and appears to be a more generalized disorder of mesenchymal development [25].

Sagittal synostosis is caused by fusion of the sagittal suture and results in a boat-shaped deformity of the skull or scaphocephaly, with growth restriction in width and compensatory excessive growth in calvarial length in the anteroposterior direction. This growth pattern leads to varying degrees of frontal bossing and occipital coning [26]. *Unicoronal synostosis* results in anterior plagiocephaly, with ipsilateral flattening of the forehead on the affected side and contralateral bulging of the frontoparietal calvaria. The growth restriction of the forehead in unicoronal synostosis results in a facial twist. It is believed that the compensatory pressure of the ipsilateral temporal lobe pushes the maxilla forward leading to forward displacement of the ipsilateral zygoma and rotation of the maxilla so that the nasal tip is deviated to the contralateral side. Bilateral coronal fusion produces brachycephaly or skull shortening in the anteroposterior diameter and skull lengthening in a cranio-caudal direction or turricephaly [27]. *Metopic synostosis* results in trigonocephaly or a triangular-shaped forehead with bifrontal and bitemporal narrowing and parietal and occipital prominence. Additionally, hypotelorism and a low nasal dorsum with epicanthal folds are present [25]. *Unilateral lambdoid synostosis* is characterized by abnormal shape of the occipital region and an ipsilateral mastoid bulge; the affected lambdoid suture is thickened and ridging with ipsilateral downward tilting of the occipital skull base. The external auditory canal and entire ear is displaced inferiorly, a clinical finding that is more reliable than inspecting for anterior or posterior displacement of the ear in differentiating positional plagiocephaly and lambdoidal synostosis. A compensatory bulge of the contralateral posterior parietal region gives the skull an oblique towering appearance when seen from the back [28–36].

References

1. Morris-Kay GM. Development of the head and neck. In: Standring S, editor. Gray's anatomy: the anatomical basis of clinical practice. New York: Churchill Livingstone/Elsevier; 2008. p. 595–614.
2. Black SM. External skull. In: Standring S, editor. Gray's anatomy: the anatomical basis of clinical practice. New York: Churchill Livingstone/Elsevier; 2008. p. 409–22.
3. Glass RB, Fernbach SK, Norton KI, Choi PS, Naidich TP. The infant skull: a vault of information. Radiographics. 2004;24(2):507–22.
4. Morriss-Kay GM, Wilkie AO. Growth of the normal skull vault and its alteration in craniosynostosis: insights from human genetics and experimental studies. J Anat. 2005;207(5):637–53.
5. Wilkie AO. Craniosynostosis: genes and mechanisms. Hum Mol Genet. 1997;6(10):1647–56.
6. Flores-Sarnat L. New insights into craniosynostosis. Semin Pediatr Neurol. 2002;9:274–91.
7. Pekçevik Y, Hasbay E, Pekçevik R. Three-dimensional CT imaging in pediatric calvarial pathologies. Diagn Interv Radiol. 2013;19(6):488–94.
8. Slater BJ, Lenton KA, Kwan MD, Gupta DM, Wan DC, Longaker MT. Cranial sutures: a brief review. Plast Reconstr Surg. 2008;121(4):170e–8.
9. Miura T, Perlyn CA, Kinboshi M, Ogihara N, Kobayashi-Miura M, Morriss-Kay GM, Shiota K. Mechanism of skull suture maintenance and interdigitation. J Anat. 2009;215(6):642–55.
10. Okamoto K, Ito J, Tokiguchi S, Furusawa T. High-resolution CT findings in the development of the sphenooccipital synchondrosis. AJNR Am J Neuroradiol. 1996;17(1):117–20.
11. Bernard TJ, Knupp K, Yang ML, Kedia S, Levisohn PM, Moe PG. Neurologic and muscular disorders. In: Hay WW Jr., Levin MJ, Deterding RR, Abzug MJ, Sondheimer JM, editors. Current diagnosis and treatment: pediatrics, 21e. McGraw-Hill Global Education Holding. [cited 2013August 16]. Available from: http://www.accessmedicine.com/content.aspx?aid=568 23534
12. Lenroot RN, Giedd JN. Brain development in children and adolescents: insights from anatomical magnetic resonance imaging. Neurosci Biobehav Rev. 2006;30(6):718–29.
13. Levitt P. Structural and functional maturation of the developing primate brain. J Pediatr. 2003;143(4 Suppl):S35–45.
14. Rakic P. Early developmental events: cell lineages, acquisition of neuronal positions, and areal and laminar development. Neurosci Res Program Bull. 1982;20(4):439–51.

15. Huttenlocher PR. Synaptic density in human frontal cortex—developmental changes and effects of aging. Brain Res. 1979;163:195–205.
16. Dekaban AS, Sadowsky D. Changes in brain weight during the span of human life: relation of brain weights to body heights and body weights. Ann Neurol. 1978;4:345–56.
17. Nellhaus G. Head circumference from birth to eighteen years. Practical composite international and interracial graphs. Pediatrics. 1968;41(1):106–14.
18. WHO.int. [Internet]. WHO Multicentre Growth Reference Study Group. WHO Child Growth Standards: Head circumference-for-age, arm circumference-for-age, triceps skinfold-for-age and subscapular skinfold-for-age: methods and development. Geneva: World Health Organization, 2007 [cited 2013 Aug 17]. Available from http://www.who.int/childgrowth/standards/second_set/technical_report_2/en/index.html
19. Dias MS, Li V. Pediatric neurosurgical disease. Pediatr Clin North Am. 1998;45:1539–78.
20. Ropper AH, Samuels MA. Developmental diseases of the nervous system. In: Ropper AH, Samuels MA, editors. Adams and Victor's neurology, 9e. McGraw-Hill Global Education Holding. [cited 2013 August 16]. Available from: http://www.accessmedicine.com/content.aspx?aID=3637070
21. Vertinsky AT, Barnes PD. Macrocephaly, increased intracranial pressure, and hydrocephalus in the infant and young child. Top Magn Reson Imaging. 2007;18(1):31–51.
22. Mehta VA, Bettegowda C, Jallo GI, Ahn ES. The evolution of surgical management for craniosynostosis. Neurosurg Focus. 2010;29(6):E5.
23. Lajeunie E, LeMerrer M, Bonaïti-Pellie C, Marchac D, Renier D. Genetic study of nonsyndromic coronal craniosynostosis. Am J Med Genet. 1995;55:500–4.
24. Lenton KA, Nacamuli RP, Wan DC, Helms JA, Longaker MT. Cranial suture biology. Curr Top Dev Biol. 2005;66:287–328.
25. Persing JA, Jane Sr JA, Piatt Jr JH. Craniosynostosis. In: Winn HR, editor. Youmans neurological surgery. Philadelphia: Saunders; 2011. p. 1940–54.
26. Garza RM, Khosla RK. Nonsyndromic craniosynostosis. Semin Plast Surg. 2012;26(2):53–63.
27. Marsh JM, Gurley JM, Kane AA. Nonsyndromic craniosynostosis. In: Mathes SJ, editor. Plastic surgery, Pediatric plastic surgery, vol. 4. Philadelphia: Saunders Elsevier; 2006. p. 135–64.
28. Ploplys EA, Hopper RA, Muzaffar AR, Starr JR, Avellino AM, Cunningham ML, Ellenbogen RG, Gruss JS. Comparison of computed tomographic imaging measurements with clinical findings in children with unilateral lambdoid synostosis. Plast Reconstr Surg. 2009;123(1):300–9.
29. Atmosukarto I, Shapiro LG, Cunningham ML, Speltz M. Automatic 3D shape severity quantification and localization for deformational plagiocephaly. Proc SPIE. 2009;7259(725952). pii:725952.
30. Cummings C. Positional plagiocephaly. Paediatr Child Health. 2011;16(8):493–6.
31. Drzymalski D, Proctor M. Genetics of craniosynostosis. In: Winn HR, editor. Youmans neurological surgery. Philadelphia: Saunders; 2011. p. 1936–9.
32. Marsh R, Gerber AJ, Peterson BS. Neuroimaging studies of normal brain development and their relevance for understanding childhood neuropsychiatric disorders. J Am Acad Child Adolesc Psychiatry. 2008;47(11):1233–51.
33. Moss SD. Plagiocephaly. In: Winn HR, editor. Youmans neurological surgery. Philadelphia: Saunders; 2011. p. 1976–81.
34. Seruya M, Oh AK, Taylor JH, Sauerhammer TM, Rogers GF. Helmet treatment of deformational plagiocephaly: the relationship between age at initiation and rate of correction. Plast Reconstr Surg. 2013;131(1):55e–61.
35. van Vlimmeren LA, van der Graaf Y, Boere-Boonekamp MM, L'Hoir MP, Helders PJ, Engelbert RH. Effect of pediatric physical therapy on deformational plagiocephaly in children with positional preference: a randomized controlled trial. Arch Pediatr Adolesc Med. 2008;162(8):712–8.
36. Yoo HS, Rah DK, Kim YO. Outcome analysis of cranial molding therapy in nonsynostotic plagiocephaly. Arch Plast Surg. 2012;39(4):338–44.

The Neurologic Exam in Neonates and Toddlers

2

Alison S. May and Sotirios T. Keros

Introduction

Performing a comprehensive neurological examination in children is sometimes considered a challenge by non-neurologists. A neurologic exam which tests all aspects of all neurologic modalities can quite literally take several hours to perform. On the other hand, a very good, thorough neurologic exam which yields substantial relevant information can be performed in under 5 min. Adherence to a systematic framework or approach to the examination, appropriate for the age and abilities of the child, can be extremely helpful in simplifying the basic questions: Is this child normal, and if not, why not, and how do I describe it? This chapter will focus on how to perform some of the routine elements of the neurologic examination with tips on how to tailor the exam for various age groups.

A.S. May, M.D.
Department of Pediatrics, New York Presbyterian Hospital, 525 E. 68TH ST BOX 91, New York, NY 10021, USA

S.T. Keros, M.D., Ph.D. (✉)
Pediatric Neurology, Weill Cornell Medical College, 525 E. 68th St, Box 91, New York, NY 10021, USA

Sanford Children's Hospital, University of South Dakota Sanford School of Medicine, Sioux Falls, SD 57105, USA
e-mail: Sok2005@med.cornell.edu

The History

As always, obtaining a solid history of present illness is essential for directing the physical exam and establishing a diagnosis, and one is often able to narrow the differential diagnosis substantially based on history alone. As most people who work with children have already learned, simple observation of the child while obtaining the history can also influence one's approach toward obtaining information.

Birth History

It is likely not necessary to remind anyone with a background in pediatrics that any history in children should include details of the pregnancy and birth. Many neurologic disorders, whether genetic or acquired, can begin in pregnancy. Complications in pregnancy, such as growth restriction, failure to progress, fetal distress, or prolonged labor, may indicate antenatal disorders rather than any process which began as a result of the actual birth process itself. One should evaluate for maternal antenatal factors such as illnesses and teratogenic exposures. Of course, the gestational age at which the child was born will also help establish a developmentally appropriate norm. If known, Apgar scores may also be informative and give a general clue as to the onset or timing of childhood disorders.

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_2

Developmental History

Typically, developmental milestones are divided into three broad domains—motor, language, and social. Assessing the current developmental milestones achieved is essential in evaluating mental status and cognition. Knowing when some key milestones, such as first words or first steps, were reached will help to classify the severity of any delays. Determining the pattern and timing of any developmental problem is necessary to classify it as static (such as might be seen in cerebral palsy), progressive (as might be seen in some mitochondrial disorders), or regressive (as seen in Rett syndrome, some leukodystrophies and Landau-Kleffner syndrome, to list a few examples). Additional considerations in assessing developmental norms are discussed in the "Mental Status" section.

The General Exam

Although clichéd, it bears repeating that the majority of the neurological examination can be performed simply by paying careful attention to a child's affect, behaviors, and natural or spontaneous movements. Of course, this does not obviate the need for a systematic, methodical approach to a complete neurologic exam when the situation warrants. There are many neurologic disorders that have systemic "non-neurologic" involvement which are evident during the general physical exam. This chapter will first point out a few key considerations to note while performing a general exam, which are relevant to neurologic disorders, and then proceed to address the conventional neurologic examination.

The Head

The first assessment of the head is to determine its size. This measurement is a way to evaluate the status of the central nervous system in the newborn and early childhood period, because head size is a proxy for the overall volume of the brain and the cerebrospinal fluid. To measure the head circumference, a tape measure is placed on the occiput posteriorly and placed above the eyebrows anteriorly or along the largest protrusion of the forehead. Ideally this measurement is taken a few times and averaged, as it is can be difficult to accurately measure the head circumference, and there is often variation between measurements. Circumference measurements should be plotted on an appropriate growth chart. Macrocephaly is typically defined as an occipitofrontal head circumference greater than the 97th percentile for age, while microcephaly refers to measurements less than the 2nd or 3rd percentile.

It is critical to remember that any rapid changes or progressive trends in percentile are likely more important than any absolute value at a single point in time.

Rapid increases in head circumference may be the first indication of hydrocephalus. On the other hand, rates of head growth which do not keep pace with weight or length may represent a brain which is not growing as expected. In cases of systemic disease such as malnourishment, head size is relatively preserved compared to length and weight. Please refer to Chap. 14 for a full discussion of the evaluation of a large head.

Next, the anterior and posterior fontanelles should be assessed. The anterior fontanelles should be evaluated with the child in an upright position. An anterior fontanelle which is bulging or firm can be a sign of increased intracranial pressure. The anterior fontanelle typically closes between 7 to 19 months of age, and several conditions are associated with early or delayed closure. However, early or late fontanelle closure without other abnormalities in the exam is rarely a cause of concern. The posterior fontanelle can be closed as early as birth and otherwise closes by 2 months of age.

The cranial sutures, the edges of the bone plates that form the skull, should also be assessed while examining the head. Craniosynostosis, the premature closure of these sutures, will affect the size and shape of the head. Plagiocephaly (literally means "oblique head") refers to a flattening of a portion of the skull. The most commonly

seen form is positional plagiocephaly, where the occipital region is flattened (usually toward the lateral side) and the ipsilateral frontal area is prominent due to forward protrusion. The incidence of positional plagiocephaly has increased as a result of the "back-to-sleep" campaign. Positional plagiocephaly is primarily a cosmetic issue, which does not affect brain development. Craniosynostosis and plagiocephaly are discussed in more detail in Chap. 6.

The Face

The presence of dysmorphic facial features, if any, may be suggestive of genetic syndromes. While 15 % of normal newborns may have one dysmorphic feature, the presence of two or more of such features is much less common and is associated with increased risk of a clinically significant anomaly. Some constellations of facial features are readily identified by most people (e.g., the classic facies in Down syndrome), but many abnormal facial features can be subtle and not easily recognized. It is helpful to systematically examine and even measure several facial features, as there are well-established norms for comparison. Typically, this type of detailed facial analysis is performed by geneticists. Interestingly, computer automated-dysmorphometry is a growing field of research, and there are case reports where this technique has revealed a genetic diagnosis.

The Neck

The neck should be examined to assess for full range of motion and absence of rigidity or asymmetry, particularly if there are abnormalities of the head or head shape. Infant torticollis, which results in twisting of the head due to a shortened sternocleidomastoid muscle, is a common cause of positional plagiocephaly. Nuchal rigidity is of course a concerning sign which may signify meningeal irritation due to infection or other causes and should be assessed for in any ill appearing child, keeping in mind that nuchal rigidity is often not present in cases of meningitis, particularly in children.

Cardiovascular and Abdomen

Auscultation of the heart or other large vessels such as the carotid arteries, descending aorta, or renal arteries can reveal murmurs or bruits which may be a risk factor for stoke from causes such as embolism, renovascular hypertension arising from fibromuscular dysplasia, or Takayasu arteritis. Organomegaly, specifically hepatosplenomegaly, can be present in many storage diseases.

The Skin

The skin and the central nervous system both develop from the ectoderm during embryogenesis, and many neurologic diseases are associated with dermatologic findings. There are several classic neurocutaneous disorders where the diagnosis can often be made simply from skin findings. Café au lait spots, axillary or inguinal freckling, and neurofibromas are markers of neurofibromatosis Type 1. Ash leaf spots or hypopigmented patches, adenoma sebaceum, and shagreen patches are lesions seen in children with tuberous sclerosis. Cutaneous vascular lesions, such as capillary malformations involving the ophthalmic region of the trigeminal nerve, are associated with Sturge-Weber syndrome. Additional information on neurocutaneous disorders is provided in Chap. 7.

The Spine and Back

Abnormalities noted in the back or spine, such as discolorations, dimples, or tufts, may be clues to an underlying problem with the spinal cord. Alternately, purely bony problems with the spine, such as hemivertebrae, can cause secondary spinal cord injuries through severe scoliosis or narrowing of the spine. Please see Chaps. 8, 9, and 19 for more thorough discussion of the back, spine, and spinal cord disorders.

The Neurologic Exam

The neurological exam is often presented in a "head to toe" format. With infants and children, of course, the examiner does not always have the luxury of focused patient cooperation as he or she marches down a preset list of areas and functions to be examined. As always, first perform whichever parts of the examination the patient will readily allow. One strategy is to initially assess for tone, range of motion, and deep tendon reflexes, while a child is resting or otherwise calm. If at any point there is crying or screaming, this is a good time to assess the cranial nerves by observing for facial strength and symmetry and palate elevation, for example. Also, an uncooperative child's limb strength is usually easily assessed by the vigorousness with which the child attempts to evade or terminate the exam.

Mental Status

The mental status and its examination are obviously dependent on the child's age. By about age 6, one can generally assess mental status and cognition using a similar approach as used in adults. For completeness, a brief review of the mental status for older children will be described. The key components of mental status include the level of arousal, orientation, attention, memory, language, and higher cognitive functions. The level of arousal is typically graded or classified (from best to worst) as awake and alert, drowsy, confused, lethargic, obtunded, stuporous, or comatose. Orientation states range from fully oriented (knowing the date, location, the people in the room) to complete confusion. Standard definitions of orientation do not apply to infants and toddlers, of course. Memory, which includes both short-term and long-term memory, can be assessed with a standard test of recall of named objects after a few minutes or asking about activities performed the day before or perhaps the previous summer. Attention is commonly assessed with a digit span test. Give the child a list of digits to repeat verbally or to dial on a telephone number pad. Many 4- or 5-year-old children can remember and instantly repeat at least four digits. Basic language skills should also be evaluated, including investigation of receptive language, for example, understanding and following commands, and expressive language, such as spontaneous and provoked speech, naming, repetition, etc. Reading and writing skills are other components of a language examination which can be tested in school-age children.

In neonates and premature babies, the mental status exam is essentially restricted to evaluating for gestational-age-appropriate level of alertness and "general movements," which describe the highly stereotypical patterns of motions which neonates will do while awake. Before 28 weeks' gestational age, it is very difficult to note discrete times of wakefulness. By about 28 weeks, one can observe that a gentle movement will cause arousals in the infant. At 32 weeks, eyes begin to open spontaneously and may stay open for extended periods of time. Around 36 weeks one begins to see progressively increased periods of wakefulness and alertness, with vigorous crying. By term, there should be clear attention to visual and auditory stimuli.

In infants between 1 and 6 months of age, the mental status is still primarily an evaluation of alertness and attentiveness, but which now can be also assessed with the motor behaviors which make up the traditional milestones commonly assessed in children. For example, facial tracking requires sustained wakefulness and sustained attention, in addition to an intact visual system and functioning cranial nerves. Thus, in the younger children, the developmental milestones do not neatly fit into any one category of a neurologic exam and blur the lines between mental status, cognition, and motor component.

Cranial Nerves

Although the 12 cranial nerves can be individually evaluated in an order child upon request, in younger children these are often evaluated with observation of spontaneous or provoked responses.

I: Olfactory Nerve

This nerve mediates the sense of smell. This nerve is rarely tested even in adults and has little utility for testing in a child unless a deficit is somehow otherwise suspected.

II: The Optic Nerve

CN II transmits visual inputs from the retina to the areas of the brain which control reflexive movements and unconscious perception (i.e., pupillary light reflexes, blink to threat, tracking and pursuit mechanisms) as well as the conscious perception of light.

The most direct evaluation of the optic nerve is to assess for pupillary light reflex, which requires the proper functioning of the optic nerve to transmit the light information which hits the retina and cranial nerve III which mediates the pupillary constriction. The direct response describes ipsilateral constriction of the pupil, while the consensual response is the constriction which also occurs in the contralateral eye. Pupillary light reflexes should be apparent by 32–35 weeks' gestational age but can be difficult to assess in infants because the pupils are relatively small relative to the size of the iris at this age.

By term, infants should be able to fixate and follow with their eyes, and this tracking response strengthens in the first 2–3 months of life.

The ideal subject to test for tracking is a human face held 8–12 in from the child. An easy way to test for tracking is to hold the child in your outstretched arms, facing you, as you rotate him or her around. It is important to note that tracking at this age is likely due to involuntary responses and deep brain structures and does not necessarily involve higher cortical areas such as primary visual cortex.

Visual field evaluation is not classically a test of optic nerve integrity, although it is reasonable to include a discussion of visual fields in this section. Visual field testing may identify focal retinal deficits as well as brain lesions involving any part of the visual pathway. In cooperative children (and adults), the best method is to position yourself at arms' length away from the patient and place your palms with fingers extended toward the patient in the area of the visual field you wish to test. Ask the child to look at your nose and to point or look if he or she sees the movement when you briefly flex or wiggle just your index finger a few times. This method of visual field testing is preferred to finger counting or bringing in wiggling fingers from the periphery, as many children will reflexively look toward the end of any outstretched arm and thus requires repeated attempts and urging not to look to the sides and anticipate the stimulus. Testing four quadrants in each eye is usually sufficient, remembering that visual field deficits are not necessarily peripheral and can also be patchy.

In younger children who cannot participate in confrontational visual field testing, an effective method is to hold an interesting object, such as a colorful toy, with both hands behind the examiners head. Then, simultaneously bring the object out into one quadrant of the visual fiend and an empty hand in the opposing quadrant. If the child can see the object, then he or she will look toward the more interesting stimulus, in this case the toy. In the youngest children, a "blink-to-threat" technique can be used. To do this the examiner brings an object such as a fist rapidly toward the eye. This is repeated, coming from different directions while looking for a blink response. Note that this test can frequently be unreliable, as air movements from an approaching hand or other object may stimulate a blink response. In addition, failure to blink is not necessarily an indication of lack of sight, so one must use caution in over-interpreting the results of blink-to-threat testing.

Finally, the fundoscopic exam is a method which directly visualizes the retinal portion of the optic nerve. This can be very challenging in children and a discussion of fundoscopy is beyond the scope of this chapter. If any visual deficits are suspected in a child, a referral to a pediatric ophthalmologist or neuro-ophthalmologist is suggested for a detailed examination and dilated fundoscopy. Chapter 12 will give an in-depth description of the ophthalmologic exam in children.

III/IV/VI: The Oculomotor Nerve, the Trochlear Nerve, and the Abducens Nerve

The oculomotor nerve, the trochlear nerve, and the abducens nerve are responsible for the movement of the eyes. The oculomotor nerve contains the fibers which mediate the efferent papillary reflex and elevate the eyelid, in addition to being the nerve which innervates most of the muscles which control eye movements (the superior rectus, inferior rectus, medial rectus, and inferior oblique). The trochlear nerve controls the superior oblique muscle, which has a complicated function which varies depending on the direction of gaze, but is essentially responsible for intorting and depressing the eye, while the abducens nerve controls the lateral rectus which abducts the eye for lateral movements.

To formally test for the integrity of these nerves and the associated muscles, assess for full range of motion in the horizontal and vertical directions. Testing the "diagonals" increases the sensitivity of noting any deficits, because the extraocular muscles do not attach to the globe at perfect right angles. If limited range of motion or disconjugate gaze is noted in any direction, each eye can then be evaluated separately in an attempt to determine which eye is the abnormal one. In older children, inquiring about diplopia is important, as patient self-reporting can be more sensitive than directional testing. In infants, use a strong stimulus such as a toy or your own face in an attempt to have them follow, while you assess eye movements. In newborns, using the "doll's eye" reflex can be used to assess horizontal eye movements. To perform this test, also known as the oculocephalic reflex, the head is turned somewhat quickly but gently to one side. The movement should result in a temporary deviation of both eyes in a direction opposite to the direction of turning. The doll's reflex is typically present as early as 25 weeks of gestation.

There are several clinically important eye abnormalities that are worth noting. Weakness of the superior oblique muscle or trochlear nerve will result in a compensatory head tilt in many children, in order to prevent the diplopia which results from the abnormal elevation (hypertropia) of the affected eye. The most common cause of trochlear nerve damage is head trauma. Incomplete abduction of an eye is usually due to weakness of the lateral rectus which is innervated by the abducens nerve. One cause of abducens injury is increased intracranial pressure due to brain edema or hydrocephalus. Also, Duane syndrome is a form of congenital abducens nerve malfunction (occasionally also involving other cranial nerves), which limits eye mobility but is typically benign and does not result in overt visual deficits. Horner's syndrome is a constellation of findings, which include miosis (pupillary constriction), ptosis, and anhidrosis on the same side of the face, and is frequently caused by disruption of sympathetic innervation which ascends along the carotid artery. However, Horner's syndrome can also arise from a central brain or spinal disorder.

Parinaud syndrome results in an impairment of upward gaze, often accompanied by eyelid retraction and pupillary abnormalities. Parinaud syndrome is the result of a lesion or compression of the pretectal area in the dorsal midbrain, which is a common location for pediatric neoplasms. Other causes of this syndrome include obstructive hydrocephalus or direct injury due to ischemia or hemorrhage.

V: The Trigeminal Nerve

The trigeminal nerve controls sensation of the face as well as the muscles of mastication. Facial sensation in older children can be tested by applying a stimulus such as light touch to each division of the trigeminal nerve: the ophthalmic branch of the forehead, the maxillary branchor (the cheek), and the mandibular branch (the chin). In infants, tickling or stroking the face, for example, with a cotton swab on one side of the nose, cheek, or lip, should elicit a rooting-like motor response toward the side of the face that was stimulated. The trigeminal nerve can also be tested by eliciting the corneal reflex. A very light touch to the cornea, such as with a wisp of cotton, should trigger a bilateral blink reflex. The sensation is mediated by the ophthalmic branch, while the motor response arrives via the facial nerve.

Chewing movements are mediated by the muscles of mastication which are innervated by

the mandibular branch of V. Opening the jaw is due to the action of the external pterygoids while closing the jaw is due to the masseter and temporalis. In neonates the muscles of mastication can be tested indirectly by evaluation of sucking strength and control and more directly by allowing the infant to bite on your fingers.

VII: The Facial Nerve

The facial nerve controls the muscles of facial expression and also mediates taste on the anterior two thirds of the tongue. In cooperative children, facial nerve integrity can be demonstrated by noting strong eye closure, wrinkling of the eyebrows, smiling, and strong puffing out of the cheeks. The face at rest can also be examined to evaluate for any asymmetry such as widening of the palpebral fissure or flattening of the nasolabial fold which might suggest weakness, keeping in mind of course that some slight asymmetries may be normal.

In infants and neonates, evaluating for facial symmetry at rest and while crying or smiling is usually sufficient. Taste in older children can be tested by using a concentrated solution of salt or sugar, placed on the tongue with a cotton swab, and should be reported before putting the tongue back in the mouth to avoid detection with cranial nerve IX. Testing taste is usually done in order to help determine if a facial nerve deficit is due to problems with the nerve (i.e., a "peripheral 7th" such as due to a Bell's palsy, in which case taste will be impaired) from a "central 7th," where taste would be expected to be preserved.

VIII: The Vestibulocochlear Nerve

The vestibulocochlear nerve mediates hearing and vestibular function. Finger rubs or whispers can test for hearing acuity. If a deficit is observed, use a tuning fork (256 Hz) to perform the Weber and Rinne tests. In the Weber test, the tuning fork is placed at the vertex of the head. The sound should appear to come from the midline if hearing in intact. However, if one ear is abnormal, the sound will lateralize to the side of decreased hearing in cases of conductive hearing loss (i.e., a problem with the outer ear, eardrum, or ossicles) but will lateralize to the normal ear in cases of sensorineural hearing loss arising from damage to the cochlea or eighth nerve. The Rinne test is performed by holding the base of the vibrating tuning fork against the mastoid process of the abnormal ear. When the subject no longer perceives sound, the vibrating end of the tuning fork is then placed just outside the ear canal. If the tuning fork can now be heard, this signifies a "positive test" and suggests sensorineural hearing loss. If the tuning fork cannot be heard after removing it from the mastoid, the test is negative and suggests a conductive hearing loss. Note that in normal ears without hearing loss, the normal result is "positive."

Children begin to clearly localize sound at about 6 months. Use a noisy toy or loud voice while observing patient reaction to evaluate hearing. In younger infants and newborns, a startle response or eye blink to loud or sudden sounds can evaluate for basic hearing ability. This reflex is present as early as 28 weeks. Vestibular dysfunction can manifest with diverse symptoms such as vertigo, nystagmus, emesis, and ataxic movements. Direct tests of vestibular function are beyond the scope of the basic neurological exam and this chapter.

IX and X: The Glossopharyngeal Nerve and Vagus Nerves

The glossopharyngeal nerve and vagus nerves are often tested together. The glossopharyngeal nerve mediates taste and sensation to the pharynx, and the vagus nerve is responsible for many functions, among which is pharyngeal constriction, palate elevation, and vocal cord movement. Symmetric palate elevation while saying "ahh" tests the integrity of the vagus nerve, while the gag reflex tests both the sensory function of the glossopharyngeal nerve and motor aspects of the vagus. Normal swallowing suggests that these nerves are intact, as they must work together for the proper coordination needed to swallow.

XI: The Spinal Accessory Nerve

The spinal accessory nerve innervates the sternocleidomastoid and the trapezius muscles. Head turning against resistance tests the sternocleidomastoid, and a strong shoulder shrug tests the

trapezius muscles. In newborns, observe for proper neck strength with turning of the head. Isolated spinal accessory nerve lesions are rare, however, and routine testing in infants is rarely helpful unless there are other neurologic signs.

XII: The Hypoglossal Nerve

The hypoglossal nerve innervates the tongue, and a deficit will produce deviation to the abnormal side upon tongue protrusion. Tongue strength can also be tested by asking the child to move the tongue from side to side and also to push against the interior of the cheek with resistance applied from the outside the mouth. In any case of suspected nerve or muscle disease, or in infants with generalized weakness (e.g., in suspected spinal muscular atrophy), the tongue should be examined at rest while in the mouth for fasciculations. Tongue fasciculation can be an early indicator of neuromuscular disease. Be careful, however, as a protruding tongue will often have a normal tremor or movement that can be mistaken for fasciculations. In newborns the sucking reflex can be utilized to evaluate lingual tone and strength.

Motor Examination

There are several elements to the motor or strength portion of the neurological exam. First, a simple observation of positioning at rest may show atypical postures or asymmetries which may suggest weakness or abnormalities of tone. The preterm infant, for example, keeps the limbs in an extended position but the normal full-term infant has flexed extremities at rest. Some characteristic poses, such as "frog-leg posturing," or external rotation of the legs suggests a systemic weakness. Scissoring of the legs, where the legs tend to cross at the feet or ankles, is one sign of possibly increased tone of the hip adductors and is often seen in children with spasticity from upper motor neuron injuries such as corticospinal track injuries. Fisting of the hand or holding the thumb adducted across the palm is a position which also suggests corticospinal tract involvement. Observation at rest will also usually reveal adventitious movements such as tremors, tics, and myoclonus.

Another component of the motor exam is tone, which describes the basic resting resistance of a muscle or group of muscles.

Tone is best examined by assessing resistance to passive movement with the subject at rest.

Low tone or hypotonia can be focal, axial (i.e., central or truncal), appendicular (in the limbs), or generalized. Increased tone or hypertonia is generally either focal or generalized.

Hypertonia can be classified as spastic, where the greater the velocity of passive movement the higher the observed tone, or rigid, where the tone is uniform and not velocity dependent.

The assessment of tone can be somewhat subjective and can be influenced by the state of the patient. A resting or sleeping child can have lower tone than while awake. In general, the normal flexed posture of a newborn and relatively increased tone decreases with age until about 6 months and then plateaus.

In newborns, there are certain generalities which can help to describe or indicate abnormal tone. For example, when pulling a newborn's arm gently across the chest toward the opposite shoulder, there should be increasing resistance felt as the elbow approaches the midline. If the elbow crosses the midline without excessive force, this is an indication of decreased tone, and this is sometimes referred to as a positive "scarf sign." In infants, axial tone can be evaluated by holding the patient in a ventral suspension and observing the position of the child draped over the arm. Infants with normal tone should make some attempt to lift the head and keep the back arched. Additionally, one can raise the infant from supine to sitting by pulling on the arms and observing for any abnormal head lag (no lag by 6 months of age), a sign of axial hypotonia and neck weakness.

Formal strength testing usually involves testing for strength in an isolated muscle group. Both muscle bulk and strength should be graded. The most common grading system ranges from 0 to 5, where zero corresponds to no movement, 1 represents a flicker of movement or muscle contraction which does not result in limb motion, 2 indicates

movement but not against gravity (i.e., in the plane of the bed), 3 is movement against gravity but without resistance, 4 is movement against resistance, and 5 is full power or movement against strong external resistance.

In infants and young children, strength testing is typically performed while observing functional movements. For example, symmetric and age appropriate reaching, crawling, or cruising suggest normal strength. Of note, asymmetry in reaching or demonstration of a hand preference before about 1 year of age may be a sign of pathologic weakness in the non-preferred arm or hand.

Sensory Examination

The sensory examination includes evaluation of the primary modalities of pain, temperature, touch, proprioception, and vibration sense. Formal sensory testing can be done typically after 5–6 years of age. A complete sensory examination can take a long time to perform in a healthy subject. *In reality, the sensory exam is usually tailored to a specific area of concern where a deficit is already suspected, as it will seldom reveal an abnormality which has not been previously self-reported.* Pain sensation can be tested with a sterilized pin, being careful to apply the same pressure in all areas. However, it is quite difficult to apply consistent, nontraumatic pressure with each application. Furthermore, certain areas of the skin are naturally more sensitive than others. Thus, variations in the exam are to be expected, and mild sensory deficits or asymmetries should be treated suspiciously and placed in context of the overall history and other examination findings. In general, asking the subject if the pin feels sharp is acceptable, as opposed to attempting to quantify the degree of pain or sharpness. Temperature sensation is transmitted together with pain by the spinothalamic tract and can be tested by placing a cool metal object against the skin. Touch is evaluated by using a cotton swab or the examiners finger and gently pressing, not wiping, against the skin. With eyes closed, the subject should be able to identify the location of the stimulus. Proprioception, or joint position sense, can be tested by holding the sides of a joint (e.g., the lateral aspects of the big toe) and moving the distal aspect of the joint gently and briefly in an up or down direction. A healthy person should be able to detect even very small movements and specify the direction. Vibration sense, which is transmitted together with proprioception in the dorsal column system of the spinal cord, is best tested by placing a 128 Hz tuning fork on a bony portion of a finger, toe, or other joint.

Sensory testing in newborns and infants is usually limited to basic testing while assessing for motor output as a potential response to a stimulus. For example, an infant will usually withdraw a limb in response to a tuning fork. This procedure also provides temperature and touch stimulation and trial-to-trial variability in infant testing is common. Noxious stimuli such as nail bed pressure, pinching of the skin, or pinprick should also elicit a cry or withdrawal. Light touch or tickling will also usually precipitate a withdrawal of the foot, for example. Again, a sensory exam is most sensitive when there is a specific area of concern for neurologic injury.

Reflex Examination

In neurology, reflexes can refer to either the deep tendon reflexes mediated by stretch receptors in the joints and muscles or to developmental and behavioral reflexes. Deep tendon reflexes test the sensory integrity of the stretch receptors and associated sensory nerves and also require a functioning muscle to produce the motor response. Most reflexes are mediated by only one or two spinal nerve roots and are very helpful when attempting to localize an injury. Upper motor neuron injuries (those arising in the cortex of corticospinal track) will lead to a condition where deep tendon reflexes (and overall tone) are elevated, while lower motor neuron injuries (i.e., the cell bodies of the motor neurons in the spinal cord and their associated nerve fibers) or muscular injury will cause depressed or absent reflexes. When testing the tendon reflexes at a joint such

as the elbow or knee, the joint should be relaxed and bent approximately 90°. A brisk tap with a reflex hammer provides the stretch response and the reaction is a contraction of the muscle. The magnitude of tendon reflexes is dependent on the location as well as strength of the tap with the hammer. Tendon reflexes are most commonly tested in the arms at the biceps (mediated by C5 and C6) just anterior to the elbow, the brachioradialis (also C5/6) above the wrist on the radial aspect of the forearm, and the triceps (C6/7) just posterior to the elbow. In the legs these include the patellar reflex (L2/L3/L4) elicited by a strike just below the patella and the ankle reflex (L5/S1/S2) produced by tapping the Achilles tendon, usually while maximally flexed. The adductor reflex (L2–4) is tested by tapping the adductor tendon near the medial epicondyle of the distal femur. The most common grading system ranges from 0 to "4+" where 0 refers to no reflex, 1+ is a weak reflex, 2+ is a normal reflex, 3+ is hyperactive, and 4+ generally indicates some clonus or spreading. A "crossed adductor response" is one of the more common examples of a reflex spreading and occurs when a tap of one thigh adductor leads to bilateral adductor muscle contraction. Clonus is most easily assessed at the ankle, elicited with a rapid jerk of the ankle into a dorsiflexed position. If present, clonus will appear as a repeated movement or beating of the dorsiflexed foot into plantar flexion. Some beats of clonus can be normal in newborns and young infants as well as teenagers and some adults, but many beats of clonus or sustained clonus should prompt a more thorough examination of possible upper motor nerve injury.

Although deep tendon reflexes can be tested at any age, the triceps reflex is particularly difficult to elicit in neonates. Tendon reflexes can also be difficult to achieve in babies because of their constant motion and light weight, and thus nonspecific movements as well as movement due to the hammer itself can be interpreted as a reflex response. In addition, their small size makes for a small target; the biceps tendon and patellar tendon require a precise hit from the hammer, which can take practice or repeated trials. With children, it is often sufficient to simply use "low" or "brisk" and then allow the examiner to classify the reflexes as abnormal or normal depending on the rest of the exam.

There are also some reflexes known as "non-stretch" or superficial reflexes. Among these is the abdominal reflex which is elicited by stroking or lightly scratching one side of the abdomen. This should trigger a small ipsilateral contraction of the abdominal muscles and is one way to test for sensation and motor integrity of the thoracic roots 8 through 12, which may be damaged in a spinal cord injury, but does not otherwise have large associated muscle groups for easy testing. The cremasteric reflex causes elevation of the ipsilateral testicle upon upward stimulation of the inner thigh. This reflex is mediated by L1 and L2. Anal tone and the anal "wink" reflex are mediated by S2–S4.

One of the most widely tested superficial reflexes is the plantar reflex.

In children aged 1 or older, a normal plantar reflex produces a plantar flexion of the large toe, while an upward or extensor response is considered abnormal. An extensor response of the toe in non-infant is evidence that this otherwise spinally mediated reflex is not suppressed by information from the cortex.

Thus, an extensor response is another sign of upper motor neuron injury. There are nearly a dozen methods which can be used to test for the plantar response, but the most often used is Babinski test. The Babinski test involves stroking the lateral side of the bottom of the foot up toward the ball of the foot and then curving in toward the toes. An initial upward movement of the big toe is considered a "positive" Babinski sign. A downward movement or no movement is considered the normal situation. The plantar reflex is mediated by the L4-S2 spinal roots. In some cases, a plantar or extensor response is unequivocal. However, testing can be variable from trial to trial, particularly because it is sometimes difficult not to elicit a tickle or withdrawal response upon testing. Note that infants will have a normally positive Babinski sign, as a result of an immature brain. However, a lack of a Babinski sign in an otherwise healthy infant does not have particular neurologic significance.

Developmental Reflexes

These are the final group of reflexes which are commonly tested as part of the neurologic exam. These are reflexes typically present early in life that extinguish with progressive maturation of cortical inhibitory function. These reflexes have two useful functions in neurology. First, their persistence past a certain age may be a clue of a systemic problem. Secondly, and somewhat more commonly, is that these reflexes can be used to elicit a motor response which an infant would otherwise not do voluntarily.

For example, the Moro reflex can be valuable in trying to determine whether there is asymmetric weakness or injury such as might occur in a clavicular fracture or perhaps a brachial plexus injury during birth. The Moro reflex refers to the abduction and subsequent adduction of the arms elicited by a sudden loss of head or truck support, which creates a sensation of falling. This reflex is readily elicited in a newborn and disappears by 5 or so months of age. *A grasp response is the well-known curling of the fingers or toes when a finger or other object is placed in the palm of the hands or against the balls or soles of the feet.* The sucking reflex and rooting reflexes are also examples of common developmental reflexes and can be used to stimulate motor activity for neurologic testing. The stepping reflex is present during the first 6 weeks of life. This reflex is stimulated by holding an infant upright and resting the feet against a surface with the knees slightly bent. The typical response is for the infant to raise a leg and move it forward, as if taking a step. The Landau response is triggered with ventral suspension of the child or placement in the prone position, which should result in an extension of both the head and legs. This reflex begins around 3 months and persists through infancy. The tonic neck response describes a flexion of the limbs of the contralateral side and extension of the limbs on the ipsilateral side in response to a force head turn. This usually diminishes by 4–5 months, which is the age many babies begin to roll over. Of note, a normal tonic neck reflex can provoke asymmetries in tone and position, and thus it is important to make sure the head is midline during a neurologic examination. Refer to Table 2.1 for a list of some developmental reflexes and their expected age resolution.

Coordination

Although coordination is commonly thought of as cerebellar-mediated process, coordination is the integration of many different pathways which are all necessary to produce accurate movements. As a result, impaired coordination can be seen in disorders of the cerebellum and basal ganglia as well as various other sensory and motor systems. Finger-to-nose testing is an easy way to assess coordination and simply requires the subject to move his or her finger from the nose to an examiner's finger or other object, which should be placed as far from the subject while still being reachable, as this distance adds some sensitivity

Table 2.1 Developmental reflexes and their expected age of resolution

Reflex	Stimulus	Response	Resolution
Rooting	Stroke cheek or lip	Head turns and mouth opens toward stimulus	2–3 months
Stepping	Hold upright with feet touching surface	Moves feet as if taking steps	3–4 months
Tonic neck	Placed on back, turn head to side	Ipsilateral arm extension and contralateral flexion	4–5 months
Moro	Sudden falling motion or loud noise	Arms extend and abduct, then adduct	5–6 months
Palmar grasp	Press palm surface	Finger curl	5–6 months
Plantar grasp	Press sole of foot	Toes curling	9–10 months
Landau response	Place on stomach	Back arches and head raises	Starts at 3 months, resolves at 12 months

to the test. The subject should be asked to go from finger to nose and back somewhat briskly, but excessive speed is not necessary to evaluate coordination. Rather, the subject should be able to accurately and very precisely touch the fingertip to the examiner's fingertip. During this test, observe for any dysmetria, which can take the form of missing the target laterally or "pass pointing." Beware of any vision abnormality or impaired depth perception which will confound the results. Finger-to-nose testing is also a good way to evaluate for an intention tremor. An analogous test in the lower extremities involves having the patient place the heel of one foot on the knee of the opposing leg and carefully sliding the heel down the shin toward the ankle and back again. Another test of coordination is the rapid alternating movements test, which when abnormal is called dysdiadokinesis. One way to perform this test is to have the subject rapidly tap the index finger to the thumb or alternately to tap a thigh or other surface with the dorsum of the hand and then the palm of the hand as quickly as possible. Rapid foot tapping is an analogous test in the lower extremities. Note that mild weakness will tend to slow any rapid alternating movements, and thus this is a good test for evaluating subtle unilateral weakness in a hand or foot, by comparing speed of movements to the other side.

Testing coordination is not feasible in newborns and infants, due to lack of established circuitry, in addition to the obvious inability to follow commands. By several months of age, however, simply testing for abnormal movements upon reaching for objects will give some sense of coordination and must of course be compared to the abilities of other children at that age. Midline or truncal ataxia, which can arise from lesions in the vermis of the cerebellum such as might be seen in a meduloblastoma, will affect the ability to sit normally or will affect the balance of a walking child.

Gait

A gait exam is an essential part of any neurological examination, and a normal gait requires the normal functioning of all components of the nervous system. To some degree, if a child can successfully walk or run down a hallway, stop, and return when asked, the majority of the neurologic exam is surely normal, as they have demonstrated relatively intact hearing, cognitive, motor, visual, and sensory pathways. It is best to evaluate gait by observing the child while barefoot. Note the station or the stance of the patient, their steps, the speed, and the steadiness of the gait. Steadiness varies with age and should be considered in the context of the patient's age. Cooperative children should be asked to walk regularly, then on their toes and heels, and finally with one foot directly in front of the other. This ability to tandem walk is usually present by 5 years of age. For many abnormalities, the gait will be affected in predictable or stereotypical ways. For example, focal weakness in one leg may make toe walking difficult on that foot or result in a limp or other noted asymmetry. Truncal ataxia or ataxia of a leg will result in a state of imbalance and appear clumsy and staggered, with a wide-based gait. Arm weakness or tone may be seen as a decreased arm swing. Other characteristic gait abnormalities are somewhat less intuitive to use in pinpointing the abnormality. Circumduction, for example, is a lateral swinging movement of the foot with excessive lifting at the hip while bringing the foot to the front, which is seen in cases of foot drop or distal weakness. A spastic gait due to increased tone, such as might be seen in cerebral palsy, will appear shuffling, with the legs adducted and the child somewhat on the toes or front of the foot. An antalgic gait describes the traditional limping pattern seen with maneuvers to limit bearing weight on a painful leg.

Obviously, gait can only be tested once a child begins walking. However, an evaluation of crawling, standing, or cruising can be relatively effective proxies for the information provided by independent walking.

Conclusion

The neurologic examination as presented in this chapter is intended to be a brief reminder or summary of various ways to identify and describe

suspected neurologic abnormalities in children. There is of course tremendous variation among clinicians in their overall approach and examining techniques. However, the examination and its components as described represent a solid framework which should help any pediatric health-care provider when trying to determine whether a particular set of complaints, symptoms, or signs are abnormal and whether they may warrant additional work-up and neurological or neurosurgical consultation.

Clinical Pearls and Red Flags

- While a systematic and complete neurologic exam is occasionally needed, observation alone of a child at rest and play can elucidate a tremendous amount about both normal and abnormal neurologic findings.
- To some degree, if a child can successfully walk or run down a hallway, stop, and return when asked, the majority of the neurologic exam is surely normal, as they have demonstrated relatively intact hearing, cognitive, motor, visual, and sensory pathways.
- Understanding and interpreting the neurologic exam in children requires in-depth knowledge of normal development.
- Handedness in infants under 1 year of age may indicate a relative weakness or neurologic problem in the nondominant side.

Suggested Reading[1]

Aminoff MJ, Simon RR, Greenberg D. Clinical neurology. Europe: McGraw-Hill Education; 2015.

Fenichel GM. Clinical pediatric neurology: a signs and symptoms approach. 3rd ed. Philadelphia: WB Saunders; 1997.

Newman SA, Ropper AH, Brown RH. Adams and Victor's principles of neurology. 8th ed. New York: McGraw-Hill Medical; 2005.

[1]There are many excellent basic neurology textbooks which contain extensive discussions about the various aspects of the neurologic exam presented in this chapter. Several are listed here in lieu of a specific reference list.

Part II

Newborn Through Infancy

Birth Trauma to the Scalp and Skull

3

Babacar Cisse, Ibrahim Hussain,
Jeffrey P. Greenfield, and Caroline B. Long

Vignette #1

A healthy, 30 year old G1P1 woman gives birth to a full-term, 8-lb boy. Her labor is complicated by shoulder dystocia, requiring vacuum-assisted extraction.

Six hours later, the infant is noted to have an asymmetric swelling on the left side of the scalp without associated ecchymosis. Vital signs are stable and the infant has a normal neurologic exam. Laboratory studies demonstrate marked anemia and indirect hyperbilirubinemia. Plain films (Fig. 3.1) demonstrate an extracranial fluid collection extending across suture lines.

Figure** 3.1 **represents an example of a/an

(a) ***Cephalohematoma***
(b) ***Subgaleal hematoma***
(c) ***Epidural hematoma***
(d) ***Caput succedaneum***

Answer: (b) Subgaleal hematoma

Introduction

Scalp and skull injuries account for nearly two-thirds of all birth traumas [1]. Most of these minor injuries can be treated conservatively; however, early identification of those complications that may require surgical intervention is critical. When evaluating patients during visits in the first week or while still in the nursery, it is important to remember that the greatest risk factor for skull or scalp trauma is instrumented delivery with forceps or vacuum devices. Macrosomia and primiparous mothers are other risk factors for injury to the newborn skull during delivery. These injuries can be grouped into three categories: extracranial hematoma, intracranial hematomas, and skull fractures without hemorrhage. Surgical intervention is predicated on the severity of the trauma and potential for worsening or neurologic injury.

B. Cisse, M.D., Ph.D. (✉)
Department of Neurological Surgery, Weill Cornell Medical College, 68th Street, New York, NY 10065, USA
e-mail: bac7002@nyp.org

I. Hussain, M.D.
Department of Neurological Surgery, New York Presbyterian Hospital—Weill Cornell Medical College, 525 East 68th Street, Box 99, New York, NY 10065, USA

J.P. Greenfield, M.D., Ph.D.
Associate Professor of Neurological Surgery, Weill Cornell Medical College, 525 East 68th Street, Box 99, New York, NY 10065, USA

C.B. Long, M.D.
Manhattan Pediatrics, New York, NY, USA

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_3

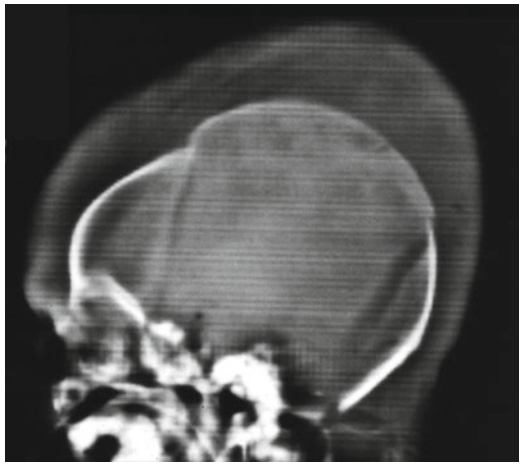


Fig. 3.1 Lateral skull radiograph in an infant

Extracranial (Scalp) Hematoma

To understand extracranial hematomas, it is important to review the layers of the scalp. From superficial to deep, the layers of the scalp include the skin, dense subcutaneous tissue, galea aponeurosis, loose subaponeurotic (connective) tissue, and the pericranium (also referred to as periosteum) (Fig. 3.2). Venous drainage from the scalp is primarily through emissary veins that traverse the skull and drain into the intracranial dural venous sinuses. Likewise, diploic veins drain the diploic space, which is the area of cancellous bone between the outer and inner tables of the skull.

Infants with scalp hemorrhages typically present with focal swelling, abnormally enlarging head circumference, anemia, indirect hyperbilirubinemia, and in severe cases, hypotension secondary to severe intravascular volume loss. A 50 cc hematoma can represent a significant portion of the intravascular volume of a normal 3.5 kg newborn. Plain films or noncontrast computed tomography (CT) scans of the skull can be obtained to exclude an underlying skull fracture and intracranial hematoma. Certainly in the hospital setting, signs such as a full fontanel or lethargic behavior such as failure to feed will prompt an urgent imaging evaluation; however, in the office setting, a well-appearing baby with a scalp swelling might very justifiably be managed with observation alone. Extracranial hematomas are generally treated conservatively with volume resuscitation, blood transfusions, phototherapy, and observation.

Caput Succedaneum

Caput succedaneum refers to a hematoma that forms beneath the subcutaneous tissue and above the galea (Fig. 3.2). These collections are not considered pathologic in all cases, as most occur spontaneously to a mild degree during normal vaginal delivery. During birth, pressure around the presenting part of the scalp against the cervix prevents venous drainage from that area. In this regard, prolonged vaginal and vacuum-assisted deliveries are the biggest risk factors for developing *caput succedaneum*. They are present immediately following birth and can have varying degrees of ecchymosis and associated skin color changes. The swelling usually has ill-defined margins, which cross cranial sutures. Management consists primarily of observation, as *caput succedaneum* often resolves within a few days [1] without any long-term neurologic or cosmetic sequelae following resolution.

Subgaleal Hemamtoma

The subgaleal space extends anteriorly from the orbital ridge to the nape of the neck posteriorly, and laterally to the ears (Fig. 3.2) [2]. Subgaleal hematomas form in the potential space between the galea and the periosteum, therefore can cross suture lines. Rupture of the emissary veins caused by vacuum-assisted delivery is the most common cause, although they can also be seen with head trauma in young children beyond the infancy. Skin bruising and a boggy fluid collection can be noted on physical exam. The time frame for development is typically between 6 and 72 h after delivery. In addition to anemia and hyperbilirubinemia, hypovolemic shock can ensue as 50 % of a newborn's blood volume can fill up this potential space [3]. These children should be screened for coagulopathies that need rapid and prompt correction. Management is primarily conservative, with observation, blood transfusion, and phototherapy as needed.

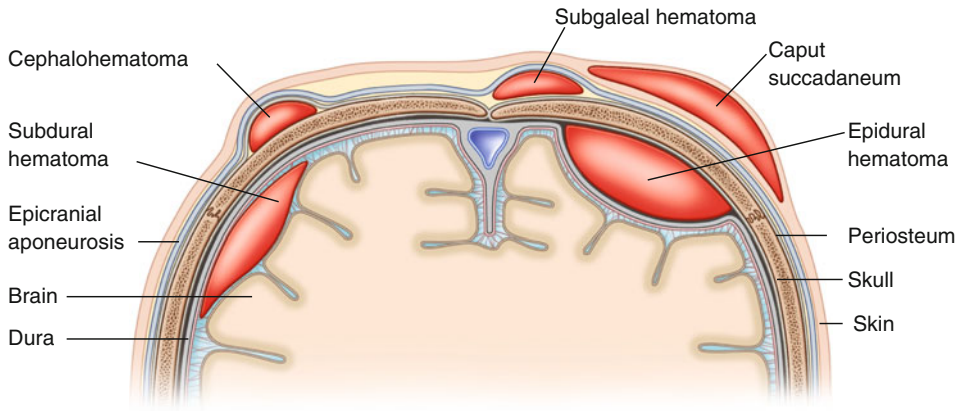


Fig. 3.2 Anatomic layers between the brain and the skull define specific injury planes

Cephalohematoma

Cephalohematomas, also referred to as subperiosteal hematomas, are scalp masses seen in infants following delivery, and are most commonly associated with vacuum-assisted deliveries [4]. The blood sources of these hematomas are the diploic veins of the skull which communicate superficially with veins in the periosteum. In this regard, hematomas form in the space between the periosteum and the outer table of the skull (Fig. 3.2). Given that the bleeding source is from the respective skull bone, these hematomas *do not cross the cranial suture lines*, distinguishing them from caput succedaneum and subgaleal hematomas. Plain films and CT imaging may be obtained to rule out an underlying fracture. Aspiration of these collections is not advised due to the risk of infection, which has the potential to spread and result in osteomyelitis. As with other scalp hematomas, these collections are primarily observed clinically while correcting anemia and lab abnormalities. Imaging of these resolving collections (not routinely recommended) will reveal a calcification pattern that forms from the periphery to the center.

Intracranial Hematomas

Intracranial hematomas are exceedingly rare complications of birth trauma. However, such hematomas have the potential to cause rapid deterioration due to the small intravascular reserve of the newborn baby and fairly expansile intracranial space within which blood can asymptomatically collect, before presentation with hemodynamic collapse. While intracranial hemotomas can also present with scalp swelling or enlarging head circumference, they are more likely to present with acute neurologic deterioration or alteration in consciousness. Failure to recognize these hematomas early may lead to significant brain damage and ensuing herniation that can be fatal. It is paramount for neurosurgeons to be alerted early for the proper management of these hematomas and for them to assess the need for any intervention that may include drainage through a burr hole or a craniotomy for evacuation of hematoma.

Epidural hematomas (EDH) (Fig. 3.3) occur between the inner table of the skull and the dura. They usually result from injury to the middle meningeal artery secondary to an overlying skull fracture. Given the pliability of the skull in infants, EDH can simulate the presentation of scalp swelling. While these hemorrhages are true emergencies, not all require surgical decompression. Spontaneous resolution of infant EDH has been seen as the blood products escape extracranially through the fracture, rather than compressing the underlying brain. These can still result in significant and rapid hemodynamic compromise.

Subdural hematomas (SDH) (Fig. 3.3) result from rupture of the bridging veins traversing the space between the dura and the outer surface of

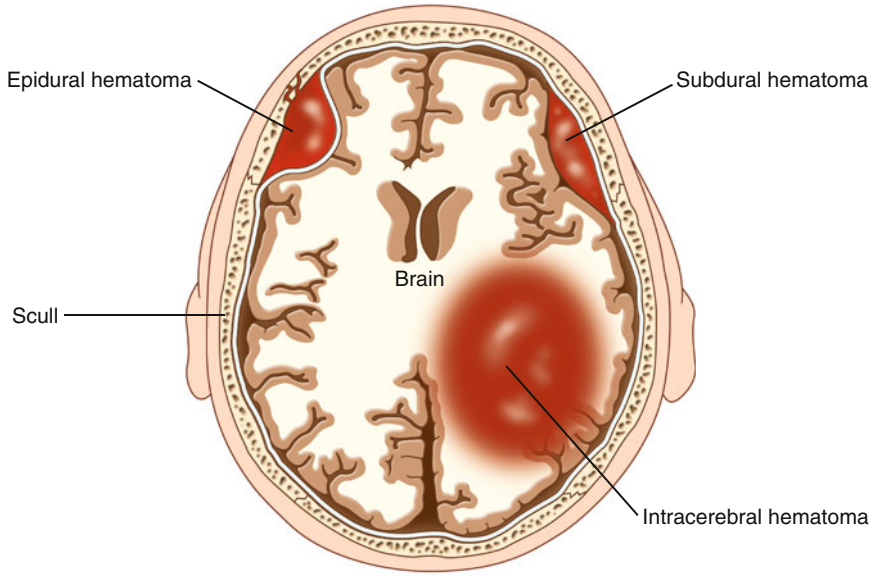


Fig. 3.3 Epidural and subdural hematomas

the brain. SDH are more commonly associated with high-impact traumas and rapid deceleration injuries (e.g., shaken baby syndrome), and are rarely seen as a complication of birth. For a more complete description of the findings associated with non-accidental trauma please refer to Chap. 27.

Subarachnoid hemorrhages (SAH) similarly are rarely seen in neonates and are more commonly associated with high-impact traumas. These hemorrhages occur in the subarachnoid space, which is between the more superficial arachnoid layer and the inner pia mater layer that apposes the brain parenchyma. This space contains CSF and blood vessels. In spontaneous cases, further angiographic imaging may be required to rule out an underlying vascular lesion (e.g., arteriovenous malformation, aneurysm).

On noncontrast CT imaging, EDH appears as lens-shaped, in contrast to crescent-shaped subdural hemorrhages. Subarachnoid hemorrhages

Vignette #2

A 4500 g boy is delivered by spontaneous vaginal delivery at 37.5 weeks. The delivery was prolonged requiring the assistance of forceps. 10 days following birth, the patient is noted to have an asymmetric swelling on the left side of his scalp. The mass is attributed to cephalohematoma and is observed. Plain films demonstrate normal diastatic sutures without evidence of fracture. No further imaging is pursued. By 3 weeks of age, the mother reports that swelling has gotten worse, and she notes that it transiently grows during crying and is pulsatile at other times. The patient has stable vitals with a normal neurologic exam. The scalp mass is soft, ballotable, evenly shaped contours that cross over suture lines and is not associated with ecchymosis. MRI shows an intracranial porencephalic cyst with CSF contents communicating with an extracranial cyst through a bony discontinuity.

This is an example of a/an?

(a) *Growing skull fracture*
(b) *Epidural hematoma*
(c) *Subderma hematoma*
(d) *Cephalohematoma*

Answer: Growing skull fracture with leptomeningeal cyst

will appear within the sulci of the brain, and depending on the extent, it may also be seen in the major cisterns and/or extend into the ventricles.

Skull Fractures

Skull fractures can occur during the birthing process by direct pressure from forceps and vacuum-assisting devices, or by pressure from the sacral promontory in a narrow birth canal. Linear fractures (Fig. 3.4) occur in 10 % of births and are associated with cephalohematomas. Noncontrast CT imaging is not required, but can be obtained to better characterize these fractures and rule out any associated intracranial hematomas [5]. These fractures do not require surgical intervention and usually resolve within 4–6 weeks.

Depressed skull fractures (also referred to as ping-pong fractures) (Fig. 3.5) are rarer than linear fractures, but carry a greater potential for harm. All infants with evidence of a depressed skull fracture on plain film should under go noncontrast CT imaging to rule out any intracranial hematoma.

In cases with a greater than 1 cm displacement from the donor site, concern for dural tear, a focal neurologic deficit, or bony fragments embedded in the brain parenchyma, surgery may be required for exploration and elevation. In asymptomatic infants, however, observation with spontaneous elevation and union of the fracture has been reported [6].

A growing skull fracture is a rare but serious complication of fracture healing. Usually seen with linear skull fractures, there is diastatic enlargement of the fracture caused by the development of a leptomeningeal cyst (Fig. 3.6).

The etiology usually stems from an underlying dural tear that pulses out cerebrospinal fluid over time. Treatment is aimed at preventing further cranial deformation and potential infection. In this respect, craniotomy with duroplasty and in extensive cases, cranioplasty, is the preferred surgical approach [7, 8]. CSF diversion through

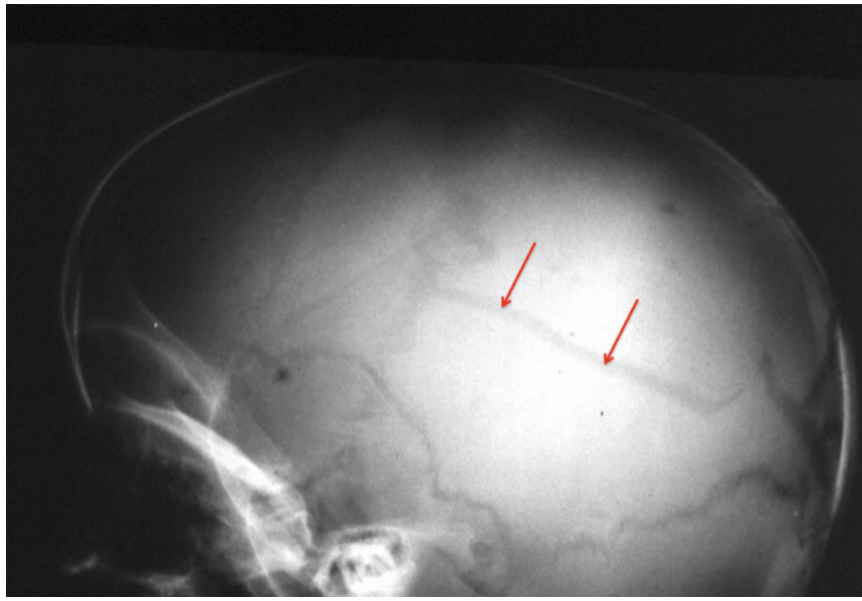


Fig. 3.4 Linear skull fracture without significant diastasis

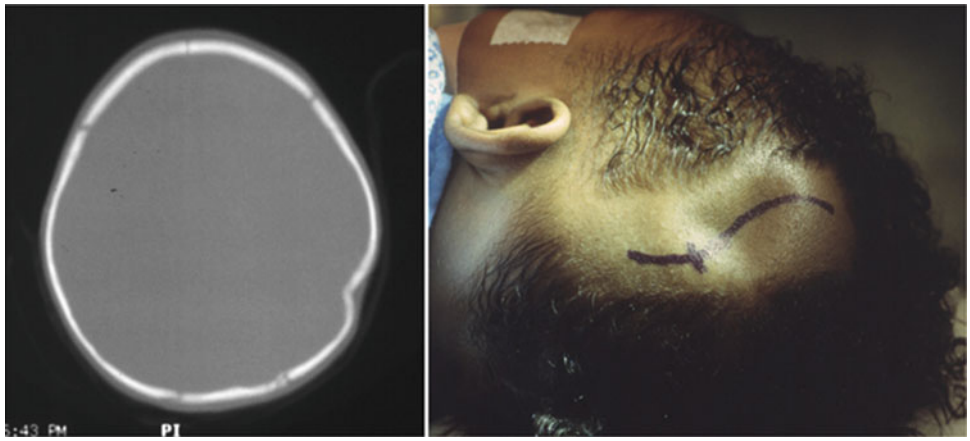


Fig. 3.5 Depressed, "ping-pong" fracture requiring surgical correction

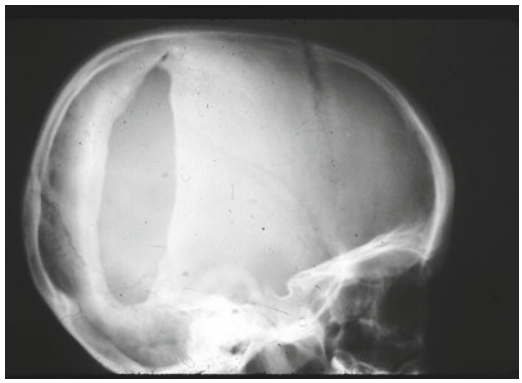


Fig. 3.6 Leptomeningeal cyst or "growing skull fracture." A pulsatile or continuously enlarging fluid collection should raise concerns for communication with the cerebrospinal fluid system

ventriculoperitoneal shunting may be required in some cases to prevent recurrence. By 3 months following surgery, reduction in the size of the cranial defect and bone growth at the previous fracture site can be seen [9].

Conclusion

- Scalp and skull trauma during birth are commonly encountered, especially given that a large number of cases occur during otherwise normal deliveries. As the use of vacuum-assisted devices has become more widespread, the risk of scalp hemorrhages in any of the various potential spaces has increased. In contrast, the decreased use of forceps has led to a reduction in the number of skull fractures, though this can be seen in non-instrumented deliveries through maternal-fetal bone-on-bone interaction. While the vast majority can be treated conservatively, being able to differentiate potentially morbid complications from scalp and skull trauma can prevent acute decline secondary to blood loss, increased intracranial pressure, and infection.

Pediatrician's Perspective

Most scalp swellings can be observed without radiologic or neurosurgical intervention. The following infants should be referred urgently for evaluation and imaging

- Rapidly enlarging mass on the order of hours
- Continuously growing mass despite 2–3 days of observation
- A collection that varies with exertion or crying
- A mass that changes from fluctuant to hard/calcified.

- Concern for infection (usually periorbital edema or swelling in mastoid region)
- Change in level of arousal
- Focal neurologic deficit
- Any initially discovered skull fracture without obvious etiology (Chap. 27).

References

1. Linder N, Linder I, Fridman E, Kouadio F, Lubin D, Merlob P, et al. Birth trauma—risk factors and short-term neonatal outcome. J Matern Fetal Neonatal Med. 2013;26:1491–5.
2. King SJ, Boothroyd AE. Cranial trauma following birth in term infants. Br J Radiol. 1998;71:233–8.
3. Swanson AE, Veldman A, Wallace EM, Malhotra A. Subgaleal hemorrhage: risk factors and outcomes. Acta Obstet Gynecol Scand. 2012;91:260–3.
4. Hughes CA, Harley EH, Milmoe G, Bala R, Martorella A. Birth trauma in the head and neck. Arch Otolaryngol Head Neck Surg. 1999;125:193–9.
5. Kim HM, Kwon SH, Park SH, Kim YS, Oh KW. Intracranial hemorrhage in infants with cephalohematoma. Pediatr Int. 2014;56:378–81.
6. Sorar M, Fesli R, Gurer B, Kertmen H, Sekerci Z. Spontaneous elevation of a ping-pong fracture: case report and review of the literature. Pediatr Neurosurg. 2012;48:324–6.
7. Liu XS, You C, Lu M, Liu JG. Growing skull fracture stages and treatment strategy. J Neurosurg Pediatr. 2012;9:670–5.
8. Rinehart GC, Pittman T. Growing skull fractures: strategies for repair and reconstruction. J Craniofac Surg. 1998;9:65–72.
9. Naim Ur R, Jamjoom Z, Jamjoom A, Murshid WR. Growing skull fractures: classification and management. Br J Neurosurg. 1994;8:667–79.

Evidence-Based Medicine Resources

American Academy of Pediatrics Committee on Fetus and Newborn: Controversies concerning vitamin K and the newborn. Pediatrics. 2003;112:191–2.

Gupta SN, Kechli AM, Kanamalla US. Intracranial hemorrhage in term newborns: management and outcomes. Pediatr Neurol. 2009;40(1):1–12.

Ou-Yang MC, Huang CB, Huang HC, Chung MY, Chen CC, Chen FS, et al. Clinical manifestations of symptomatic intracranial hemorrhage in term neonates: 18 years of experience in a medical center. Pediatr Neonatol. 2010;51:208–13.

Tung GA, Kumar M, Richardson RC, Jenny C, Brown WD. Comparison of accidental and nonaccidental traumatic head injury in children on noncontrast computed tomography. Pediatrics. 2006;118(2):626–33.

Volpe J. Editorial: Neonatal intracranial hemorrhage—iatrogenic etiology? N Engl J Med. 1974;291:43–5.

Brachial Plexus Injuries During Birth

4

Peter F. Morgenstern

Case 1
A healthy gravida 4 para 3 mother gave birth after an uneventful pregnancy to a male infant. The delivery was complicated by shoulder dystocia requiring episiotomy and multiple maneuvers including grasping of the left arm during delivery. In the deliver room, the infant was noted to be 4600 g and on initial examination had no movement in the left arm. He was also visibly uncomfortable on palpation of the left clavicle, where a fracture was discovered on subsequent X-ray. On follow-up neurologic exam the patient was noted to have asymmetric pupils, smaller on the left, as well as a slight ptosis on the left side.

Case 2
A diabetic gravida 3 para 1 mother delivered a healthy female infant by Caesarian section after a pregnancy complicated by prenatal identification of fetal macrosomia. At birth, the child weighed 4300 g and was taken to the nursery without incident. On day-of-life one, a pediatric resident noted a pronounced asymmetry in the movements of the child's arms. On further examination, she made several observations—the left arm remained internally rotated and abducted at the shoulder with the elbow extended while the right arm flexed normally with spontaneous activity. She also noticed that the fingers and wrist remained flexed.

Brachial plexus birth palsy (BPBP) is an uncommon but critically important complication of the delivery process that must be identified early. These cases demonstrate a range of presenting severity of neonatal brachial plexus injury and highlight some of the resulting deficits. Understanding this pathology demands an understanding of the relevant gross and functional anatomy, as well as the factors one must consider in approaching its management.

Anatomy and Mechanisms of Injury

The brachial plexus is a network of nerves arising from the nerve roots of C5–T1 and innervating the muscles and skin of the upper back, chest, and arm (Fig. 4.1). Most proximally, the ventral rami of C5–T1 form the roots after giving off branches to the muscles of the neck. The roots converge to form three trunks. The upper (C5–6), middle (C7), and lower (C8–T1) trunks each split into two divisions, anterior and posterior, which subsequently converge into three cords. The posterior cord forms from the three posterior divisions (C5–T1). The lateral cord comprises the anterior divisions of the middle and upper trunks (C5–7), while the medial cord is the continuation

P.F. Morgenstern, M.D. (✉)
Department of Neurological Surgery,
New York Presbyterian Hospital—Weill Cornell Medical Center, 520 East 70th Street, Starr 651,
New York, NY 10065, USA
e-mail: pfm2001@nyp.org

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_4

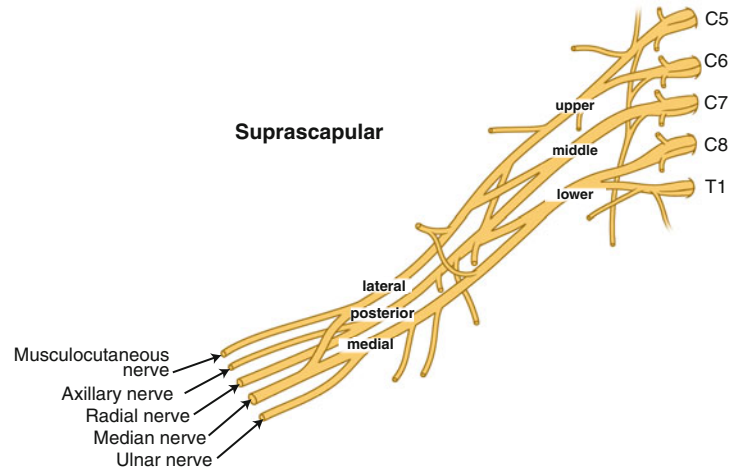


Fig. 4.1 Simplified schematic of brachial plexus anatomy (reprinted with permission from [1])

of the anterior division of the lower trunk (C8–T1). The plexus ends in terminal branches, which provide motor and sensory innervation to the arm and are summarized in Table 4.1.

Its anatomy and the mechanics of the delivery process make the brachial plexus particularly vulnerable to birth injury. The importance of identifying and characterizing injury early on cannot be overemphasized, as children who do not receive adequate care and follow-up may be relegated to a lifetime of disability and sometimes deformity of the affected arm. The role of the pediatrician is to recognize these injuries early in order to facilitate evaluation, therapy, and potentially surgery for those who do not recover.

Injury to the brachial plexus can occur anywhere along its span from the cervical spine into the upper arm, but there are regions that are more likely to be injured in neonates. Injuries most frequently arise from traction on the arm while the following shoulder is impacted within the birth canal, resulting in stretch injury or avulsion of the roots of the plexus. The most severe injuries may involve many or all of the proximal components of the plexus, leading to complete paralysis of the affected arm.

The mechanisms of injury to the brachial plexus in neonates at first seem straightforward but have proven to be more complex with further study. The above example, injury in the presence of shoulder dystocia that requires obstetric maneuvers to deliver the arm, was initially thought to be the clear explanation for the pattern of injury seen in the neonates [1]. However, some authors have suggested that it is not so simple. Comparisons of infants with brachial plexus injuries, both with and without dystocia, as well as studies identifying infants with injury to the posterior shoulder, have shown that the forces involved in delivery are more complex than previously understood. One interesting point that remains to be fully explained is the observation that infants with injuries that are not associated with shoulder dystocia frequently have more severe injuries that take longer to resolve and are more often associated with fractures of the clavicle [2], which occur concurrently in approximately 3 % of injuries [3].

Four types of injury have classically been described. Neuropraxia, the most benign, is a temporary conduction block. Axonotmesis is the disruption of the axon without significant damage to the surrounding neuronal elements. These two injuries typically recover spontaneously with time and supportive care. Neurotmesis and avulsion are injuries that often require surgical management to achieve more complete recovery. They are complete disruptions of the nerve, and differ in that neurotmesis is a post-ganglionic injury and avulsion is pre-ganglionic [4, 5].

Epidemiology

The incidence of brachial plexus birth injuries has been largely stable over the last decade despite improvements in the safety of obstetric

Table 4.1 Terminal nerves of the brachial plexus and their functions

Nerve	Root origin	Branch point	Termination
Phrenic nerve	C3–5	Roots	Diaphragm
Dorsal scapular nerve	C4–5	Roots	Rhomboids and levator scapulae
Long thoracic nerve	C5–7	Roots	Serratus anterior
Nerve to subclavius	C5–6	Upper trunk	Subclavius
Suprascapular nerve	C5–6	Upper trunk	Supra- and infraspinatus
Lateral pectoral nerve	C5–7	Lateral cord	Pectoralis major and minor
Musculocutaneous nerve	C5–7	Lateral cord	Coracobrachialis, Brachialis and Biceps Brachii; sensation to lateral forearm
Median nerve	C5–T1	Lateral and medial cords	Forearm flexors (except flexor carpi ulnaris and medial half of flexor digitorum profundus), thenar muscles, 1st and 2nd lumbricals; sensation to palmar aspect of thumb, 2nd, 3rd, and half of 4th digits including nailbeds
Upper subscapular nerve	C5–6	Posterior cord	Subscapularis
Thoracodorsal nerve	C6–8	Posterior cord	Latissimus Dorsi
Lower subscapular nerve	C5–6	Posterior cord	Subscapularis and Teres Major
Axillary nerve	C5–6	Posterior cord	Deltoid, Teres Minor; sensation to lateral arm
Radial nerve	C5–T1	Posterior cord	Triceps Brachii, Supinator, Anconeus, Extensors of forearm, Brachioradialis; sensation to posterior arm, dorsal aspect of thumb, 1st and half of 2nd digits
Medial pectoral nerve	C8–T1	Medial cord	Pectoralis Major and Minor
Medial cutaneous nerve of the arm	C8–T1	Medial cord	Sensation to anterior and medial arm
Medial cutaneous nerve of the arm	C8–T1	Medial cord	Sensation to medial forearm
Ulnar nerve	C8–T1	Medial cord	Flexor carpi ulnaris, medial half of flexor digitorum profundus, intrinsic hand muscles except thenar and lateral two lumbricals; sensation to medial hand, palmar aspect of medial 5th and half of 4th digits, dorsal aspect of medial 5th, 4th, and half of 3rd digits

practice and training. Large cohort studies over the years have noted an incidence of 0.4–2.5/1000 live births, with little change over time despite changes in obstetric practice designed to reduce perinatal complications [6–9]. Some have proposed that this is the result of a concurrent rise in average birth weight [5].

A 2008 study of children in the United States utilized the Kid's Inpatient Database to produce an incidence of 1.5/1000 births by identifying injuries in three separate years over the period from 1997 to 2003. There were no significant associations in ethnic or socioeconomic factors that could be ascertained. Furthermore, this observational cohort study was more optimistic about a decreasing rate of injury over time, from 1.7 to 1.3 per 1000 live births over the 6-year period [10].

We have seen that a number of fetal and maternal characteristics are associated with the presence of injuries of the neonatal brachial plexus. Maternal diabetes, fetal macrosomia, prolonged labor, forceps delivery, primiparity, increasing maternal age, and shoulder dystocia have all been identified as risk factors for injury. Of these, shoulder dystocia and fetal macrosomia have been singled out as the higher risk conditions. Twin gestation and Caesarian delivery have been associated with a lower rate of brachial plexus palsy [10]. Some centers have attempted the use of elective Caesarian section to reduce the incidence of brachial plexus injury in the setting of multiple prenatal risk factors. One group noted a decreased risk of brachial plexus injury and clavicular fracture with Caesarian section compared with vaginal delivery. However, the category "other birth trauma" saw an increase in risk with Caesarian delivery [11]. A head-to-head study investigating elective Caesarian delivery demonstrated no significant decrease in the incidence of brachial plexus injury [9].

Fig. 4.2 Infant with Erb palsy. The arm is internally rotated and abducted at the shoulder, the elbow is extended, and the forearm is pronated with flexed wrist and fingers

Presentation and Natural History

In the delivery room, identification of the injury is the first step. Localizing the nerve injury may require further study, as the evaluation of a newborn infant will be limited early on by pain. It should be noted, however, that the pain is typically not the result of the nerve injury itself [12] but rather the corresponding fractures and muscular trauma. Neonates affected by brachial plexus palsies have also frequently been noted to suffer from other injuries. Clavicular fractures, facial nerve palsies, cephalohematomas, and arm ecchymoses have all been notably associated with brachial plexus palsies and are the typical stigmata of a traumatic delivery [6, 9].

The most common presenting finding in the neonate is the classic Erb's Palsy, which arises from a lesion of the C5–6 roots. The arm is internally rotated and abducted at the shoulder, the elbow extended, and the forearm is pronated with flexed wrist and fingers (Fig. 4.2). Injuries may involve C4, causing respiratory distress as a result of phrenic nerve disruption. With C7 involvement, the triceps may be impaired as well. In the most severe cases, the entire plexus may be involved, causing complete paralysis of the arm (Fig. 4.3).

More proximal injuries can sometimes be identified by findings related to loss of function of nerves branching early from cervical roots or in close association with the roots themselves. A Horner's syndrome may occur due to sympathetic chain injury where it is adjacent to the roots of C8 and T1. Winged scapula deformities result from injuries to the C5–7 roots proximal to the takeoff of the long thoracic nerve. Babies with brachial plexus injury often preferentially turn their heads away from the affected side, resulting in torticollis and/or positional plagiocephaly [5]. Furthermore, patients with residual deficits have sometimes been noted to have differences in upper extremity length when compared to the non-injured side, potentially compounding the degree of disability [13].

Recovery rates have generally been reported as favorable. Early studies of recovery rates of children after injury identified flaccid paralysis, Horner's syndrome, and diaphragmatic dysfunction

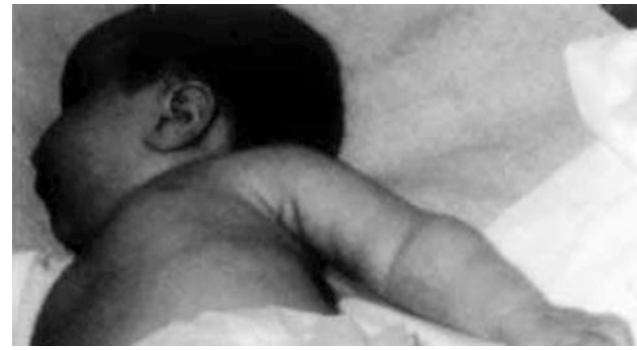


Fig. 4.3 Infant with complete paralysis of the arm, demonstrating an extensive brachial plexus injury

as poor prognostic indicators, as well as the absence of shoulder dystocia at delivery [2]. Large prospectively collected cohorts from the 1980s reported high overall rates of recovery, ranging from 77.8 % to as high as 95.7 % [6, 7]. However, more recent discussions of the rate of spontaneous recovery have somewhat tempered the optimism of some practitioners. Earlier reports may have overstated the likelihood of improvement without intervention [10] and newer data suggest that 30 % or more of the infants injured will not achieve a satisfactory outcome without intervention [14, 15]. Injuries involving more roots—i.e., C5–7 rather than only C5–6—portend a worse prognosis. In a study of 168 infants with brachial plexus palsy between 1990 and 2005, it was noted that infants with C5–6 lesions recovered completely 86 % of the time [16]. Those with C5–7 lesions, however, recovered only 38 % of the time while those with lesions of the entire plexus did not recover fully. These observations, among others, have resulted in changes to practice patterns with respect to timing of surgical evaluation and intervention for brachial plexus birth injury.

Evaluation

Discussions of the natural history of brachial plexus birth injuries are inextricably linked to the consideration of surgical repair. Identifying infants who are destined for a poor functional outcome is critical, and is largely in the hands of the child's primary healthcare providers. Defining a satisfactory outcome is critical to the consideration of recovery rates. This has led to the development of multiple rating scales and tools for evaluators to characterize injuries to the infant brachial plexus.

The simplest observations reported by studies of infant recovery after injuries to the brachial plexus have hinged on evaluations of upper arm strength. For example, it has been demonstrated that infants who recovered fully had reached greater-than-antigravity strength in the deltoid, biceps, and triceps muscles by the age of 4.5 months. All others had persistent varying degrees of weakness [14].

Most instances of BPBP are identified immediately following delivery and require several important initial steps. Care should be taken to avoid exacerbating injury or causing pain on the affected side, and plan X-rays of the upper extremity and shoulder should be completed to avoid missing associated fractures and dislocations. The infant should also be thoroughly examined to identify ptosis or miosis, which may herald the presence of a Horner's syndrome [1]. The next steps include evaluation by pediatric physical and occupational therapists, as well as regular follow-up to identify signs of recovery and, conversely, the infants who do not recover and may warrant referral for surgical management.

Multiple classification systems have been proposed to characterize brachial plexus injury in attempts to standardize the evaluation and monitoring of clinical progress in these children. The most widely recognized of these was published by the British Medical Research Council (BMRC) in [17] and evaluates infants using limb positioning, establishing a grading system from 0 to 5 to describe a

range of muscle strength. The challenges of grading resistance in infants were observed over time, and a modified BMRC scale was introduced to accommodate this. The adjustment limited the grades to M0 to M3, thus reducing the gradations used to measure different degrees of manual resistance in the infant. This scale has been used widely as an outcome score for motor recovery [18].

The Score of 10 is a scoring system that was introduced in 1997 in order to characterize children with persistent deficits after birth injuries. It is performed at an age at which the child can follow verbal prompts to complete a range of active movements and assigns greater weight to movements that are particularly important to function. The total comprises Erb and Klumpke scores, representing evaluations of the upper and lower plexus (Table 4.2). The authors proposed that high scores indicated children with good function, mid-range scores defined children who had some degree of impairment but sufficiently good function to benefit from surgery, and those with low scores would be unlikely to achieve sufficient benefit from intervention [19]. As this score can only reliably be applied to older children, it is not helpful in the early evaluation and referral of infants with injuries.

The Toronto Test Score was developed to predict recovery in infants. Patients are prompted to actively flex and extend the shoulder, thumb, fingers, wrist, and elbow. Their movements are rated from 0 (no movement) to 2 (normal motion) and summed to a maximum 10 points each for flexion and extension. Each parameter has been studied for its ability to predict recovery, demonstrating that several permutations had a high rate of accuracy in predicting infants' recovery when first tested at 3 months of age. The simplest of these was the use of elbow flexion and wrist extension, though there were several other similarly accurate combinations [20]. This scale is useful in that the examiner can take whichever movements can be elicited from the infant and cobble together a score that may have some predictive value. For example, one group used only elbow flexion with reasonable results [21, 22].

The Mallet Classification (Fig. 4.4) is used to evaluate shoulder function specifically in children who have sustained neonatal brachial plexus injuries. Five different shoulder functions are graded from no function (Grade I) to full function (Grade V) [24]. This system recognizes the importance of the shoulder and elbow flexors in ability of a child to make use of the affected arm in the absence of complete recovery, but can only be used in older children because of the degree of active cooperation and complex movements that are required.

The Hospital for Sick Children Active Movement Scale (Table 4.3) is a measure of

Table 4.2 Score of 10 (adapted with permission from [19])

Erb score		
Shoulder abduction	>120°	2
	90–120°	1
	<90°	0
Shoulder external rotation	>60°	1
	<60°	0
Elbow flexion	Hand-to-mouth	2
	Cannot reach hand-to-mouth	0
Elbow extension	Full shoulder abduction without elbow flexion	2
	Shoulder abduction with some elbow flexion	1
	Unable to extend elbow with shoulder abducted	0
Trumpet sign	Negative	1
Forearm supination	>40°	1
Forearm pronation	>40°	1
Klumpke Score		
Wrist extension		1
Wrist flexion		2 1
Metacarpophalangeal extension		1 0.5
Interphalangeal extension		2 1 0
Finger flexion		2 1
Thumb adduction		1
Thumb abduction		1

strength with and without the effect of gravity on the infant's entire arm [21, 22]. It was developed to document recovery in upper extremity function in injured children, and can be used from infancy into later childhood. It evaluates overall joint movements, rather than individual muscle groups, with an eye toward function. It has been shown to have both excellent inter- and intra-rater reliability, as well as consistent results when used by practitioners with a range of experience [18, 23].

Bae et al. [23] evaluated the Mallet Classification, Toronto Test Score, and Active Movement Scales on the measures of inter- and intra-rater reliability. When tested in isolation, the individual components of these scales were generally reliable, though some components of the Mallet Classification were less consistent. In the aggregate scores, all three scales demonstrated excellent inter- and intra-rater reliability, validating their use throughout the literature and clinical practice in attempts to monitor patient outcomes and predict their recoveries.

In an attempt to simplify the evaluation process, some clinicians have looked for more straightfor-

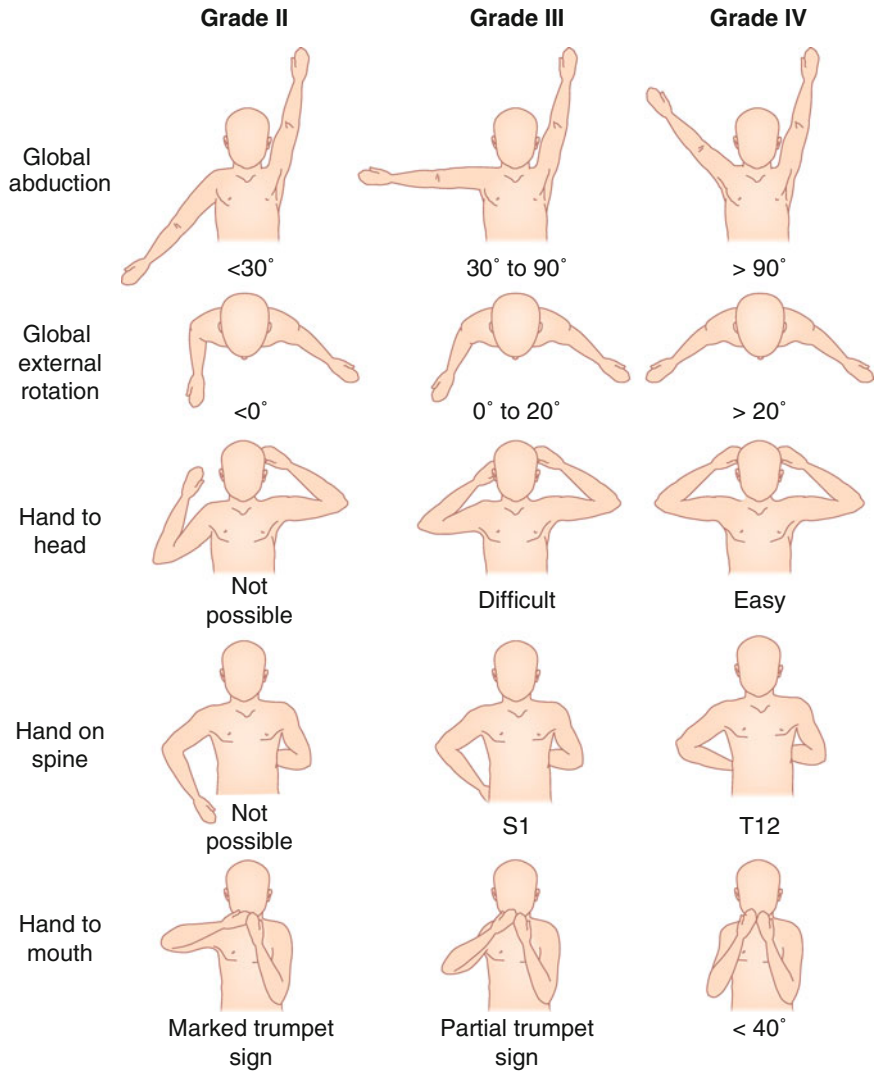


Fig. 4.4 Modified Mallet Classification (reprinted with permission from [23])

Table 4.3 Hospital for sick children active movement scale (adapted with permission from [18])

Observation	Grade
Gravity eliminated	
No contraction	0
Contraction, no motion	1
Motion ≤ half range	2
Motion > half range	3
Full motion	4
Against gravity	
Motion ≤ half range	5
Motion > half range	6
Full motion	7

ward predictors on outcome. For example, one group studied thumb pain sensation as an easy and rapid evaluation of the injured infant. This group demonstrated a sensitivity of 66 % and specificity of 96 % for nail bed compression applied at less than 2 months of age in order to predict poor functional outcome defined by the evaluation of elbow flexion at 6 months of age [25]. This simple test can be performed in the general practitioner's office, and may aid in the early identification of at-risk infants. It should not be used in isolation though, given the low sensitivity.

Perhaps, the most helpful and comprehensive grading scale for the general practitioner was introduced in 1987 and is called the Narakas Classification (Table 4.4), which has undergone various modifications [26, 27]. Infants are graded from 1 to 4 based ranging from mild dysfunction of C5 and C6 roots only to complete paralysis of the arm with Horner's syndrome. Grade I injuries spontaneously recover greater than 90 % of the time, while Grade II and above recover 65 % of the time or less. While it is not adequate alone to guide surgical decision-making [26], this straightforward evaluation method can aid in the determination of which infants should be referred to more specialized care.

Beyond clinical evaluation and classification of injuries, some authors have attempted more objective laboratory methods to evaluate the extent of injury and ascertain prognosis. Electromyography (EMG), for example, is commonly used in adults with peripheral nerve injuries and may be valuable in the evaluation of the infant [28]. Infants evaluated at 1 month of age by needle EMG were observed in one study for signs of clinical improvement over time. The absence of motor unit potentials in the deltoid or biceps at that time point was highly sensitive for persistent paralysis at 3 months, potentially allowing for early referral of affected infants. A high false-positive rate in this study, however, should give the evaluator pause when considering surgical management prior to 3 months of age [29].

In addition to EMG, some have considered quantitative ultrasound to evaluate the muscle in the injured arm in comparison to the uninjured one. This group evaluated infants using the Active Movement Scale and found that muscle backscatter and thickness varied between injured and uninjured arms depending on the degree of impairment. Muscle thickness increased with clinical improvement, but it was not clear whether these evaluations could predict future antigravity strength in the infant's affected arm [21, 22]. This tool requires further study, but may prove useful.

Other radiographic studies have limited value in the evaluation of BPBP, but can contribute

Table 4.4 Narakas classification (adapted with permission from [5])

Group	Roots affected	Clinical findings	Spontaneous recovery
1	C5–6	Limited shoulder abduction/external rotation and elbow flexion	>80 %
2	C5–7	Above + wrist drop	~60 %
3	C5–T1	Flaccid paralysis	30–50 %
4	C5–T1	Flaccid paralysis + Horner's syndrome	Low probability

some information. Myelography under general anesthesia has been useful for identifying children with pseudomeningoceles that occur more commonly with avulsion injuries, thus aiding in surgical decision-making by identifying more severe injuries and are unlikely to recover. However, pseudomeningocele can also occur without a root avulsion, so interpreting the results of a myelogram can be challenging [30, 31]. Magnetic resonance imaging of the spine can also demonstrate pseudomeningocele associated with root avulsion, but has limited sensitivity and resolution in the identification and localization of other types of injuries [30, 32, 33]. Ultrasound of the brachial plexus has been used to identify a range of peripheral nerve pathologies, and may be more sensitive than MRI with equivalent specificity in identifying injury [21, 22]. MRI of the shoulder is useful in identifying secondary injuries, such as early secondary joint deformities. In recent years, advances magnetic resonance neurography have demonstrated improved sensitivity in identifying pathology of the brachial plexus in infants, as well as correlation with EMG and physical findings [34]. This imaging modality may become increasingly useful in the coming years as an adjunct to existing evaluation methods.

Management

Once the initial diagnostic work-up has been completed, the first step in management for infants with BPBP is physical and occupational therapy. This should begin early, with most recommending initiation on or about the third week of life [5]. This consists of passive range-of-motion exercise to minimize the onset of contractures. Medial rotation contracture of the shoulder is the most common of these [35]. Deformities of flexion and pronation at the elbow are also common and often occur in tandem with contracture at the shoulder [36]. Exercises are age-dependent. In young children, they are aimed at encouraging two-handed play and, later, self-care. In the absence of improvement within 2 months of age, patients are referred for further evaluation including surgical consultation [5].

Neonatal plexus injuries lend themselves to surgical repair for a variety of reasons, but perhaps the most important is an accident of anatomical development. The superior roots adhere to the periosteal lining of the transverse process of their corresponding vertebrae, making them particularly prone to rupture rather than avulsion, as the traction forces are not transmitted into the spinal canal. The roots of C8 and T1 are more likely to avulse because they lack this association with the bone [1]. Nerve ruptures are more reparable because there is a proximal stump available for reconstruction, while avulsions leave no stump. Neonatal injuries occur much more commonly in the upper components of the plexus. Approximately 50 % of patients with brachial plexus lesions at birth have lesions of the upper roots or trunks alone (C5–6) while another 25 % have injuries of C5–7. The most severe neonatal injuries, those that do not exhibit signs of early recovery as discussed above, are more frequently amenable to surgical repair than their adult counterparts. However, there is no definitive guideline for the role of surgical intervention in these children, nor is it perfectly clear when any proposed intervention should be performed [37]. Some have attempted to answer these questions over the last half-century.

While imaging modalities and EMG have been helpful in the diagnostic process for infants with BPBP, the decision to explore and repair or reconstruct the infant brachial plexus is still largely clinical [1]. Infants without return of biceps function in the first 3–4 months have clearly documented decreased likelihood of full recovery, and should be evaluated for possible surgical intervention [5, 35, 38]. A review of the literature on the timing of intervention reveals differing opinions, but the more recent consensus has erred on the side of earlier exploration of the plexus, ranging between the ages of 3 and 9 months in infants without improvement or with signs of severe injury—complete paralysis or presence of Horner's syndrome [5, 35, 38, 39]. Furthermore, some have warned that infants in whom surgery has been postponed are at a higher risk of developing glenohumeral joint deformities and have suggested a combined surgical approach for infants with BPBP complicated by such deformity [40].

While current research supports intervention for patients with severe injury—Narakas Group 4, for example—or non-recovering injury at a relatively early age, the evidence for or against surgical intervention in children with more moderate injuries is limited. A "gray zone" has been described for infants whose optimal management is unclear. This concept was proposed to help guide clinicians in the absence of level I evidence for surgical management. Patients with intermediate AMS scores are repeatedly evaluated over months until 5–6 months of age. At that time, the recommendation is that surgery be performed on infants without continued meaningful recovery, while it should be deferred for those with recovering function suggestive of a reversible injury [13].

The outcomes of surgery are difficult to assess, as there has been no randomized controlled trial comparing operative and nonoperative management of these infants. However, multiple authors have demonstrated the safety and potential for good outcomes with surgery [37, 41]. Additionally, others have suggested that, based on existing data, surgical correction alters the natural history of BPBP for the better [5, 36, 42, 43]. This and other data, past and present, point to surgery as a viable option to improve function and reduce long-term disability in infants who do not recover spontaneously. However, one must consider that the goals of surgery vary by degree of injury. Not all infants who reach the operating room have a chance of returning to full functional capacity in the injured arm. For lesions of the upper plexus only, the intention is to ameliorate the deficits caused by shoulder and elbow dysfunction. While this is also important for total plexus injuries, the primary objective for these infants is to restore function to the hand [5]. When complete recovery is not an attainable goal, the surgeon must seek to improve critical movements that provide the patient with as much opportunity as possible to use the arm effectively.

Conclusion

Injuries to the infant brachial plexus are uncommon complications of the delivery process that can cause a high degree of long-term morbidity. With early identification and management, many infants can be spared long-term severe disability with noninvasive interventions such as physical rehabilitation. A small percentage of injured infants will ultimately require surgery, but surgical evaluation is necessary at an early age for those who do not begin to recover in order to achieve the maximal benefit of intervention. A multidisciplinary approach to these injuries will ensure that each child receives the appropriate treatment for any given deficit.

References

1. Piatt Jr JH. Birth injuries of the brachial plexus. Clin Perinatol. 2005;32:39–59.
2. Gherman RB, Ouzounian JG, Miller DA, Kwok L, Goodwin TM. Spontaneous vaginal delivery: a risk factor for Erb's palsy? Am J Obstet Gynecol. 1998;178(3):423–7.
3. Walle T, Hartikainen-Sorri AL. Obstetric shoulder injury. Associated risk factors, prediction and prognosis. Acta Obstet Gynecol Scand. 1993;72(6):450–4.
4. Sunderland S. Nerves and nerve injuries. London: Churchill Livingstone; 1978.
5. Van Ouwerkerk WJR, van der Sluijs JA, Nollet F, Barkhof F, Sloof ACJ. Management of obstetric brachial plexus lesions: state of the art and future developments. Childs Nerv Syst. 2000;16:638–44.
6. Greenwald AG, Schute PC, Shiveley JL. Brachial plexus birth palsy: a 10-year report on the incidence and prognosis. J Pediatr Orthop. 1984;4(6):689–92.
7. Hardy AE. Birth injuries of the brachial plexus: incidence and prognosis. J Bone Joint Surg Am. 1981;63B(1):98–101.
8. Jackson ST, Hoffer MM, Parrish N. Brachial-plexus palsy in the newborn. J Bone Joint Surg Am. 1988;70-A(8):1217–20.
9. Walsh JM, Kandamany N, Ni Shuibhne N, Power H, Murphy JF, O'Herlihy C. Neonatal brachial plexus injury: comparison of incidence and antecedents between 2 decades. Am J Obstet Gynecol. 2011;204(4):324.
10. Foad SL, Mehlman CT, Ying J. The epidemiology of neonatal brachial plexus palsy in the United States. J Bone Joint Surg Am. 2008;90:1258–64.
11. Moczygemba CK, Paramsothy P, Meikle S, Kourtis AP, Barfield WD, Kuklina E, Posner SF, Whiteman MK, Jamieson DJ. Route of delivery and neonatal birth trauma. Am J Obstet Gynecol. 2010;202(4):361e1–6.
12. Kline D, Hudson A. Nerve injuries. Philadelphia: WB Saunders; 1995.
13. Bain JR, DeMatteo C, Giertsen D, Hollenberg RD. Navigating the gray zone: a guideline for surgical decision making in obstetrical brachial plexus injuries. J Neurosurg Pediatr. 2009;3:173–80.
14. Noetzel MJ, Park TS, Robinson S, Kaufman B. Prospective study of recovery following neonatal brachial plexus injury. J Child Neurol. 2001;16(7):488–92.

15. Okby R, Sheiner E. Risk factors for neonatal brachial plexus paralysis. Arch Gynecol Obstet. 2012; 286:333–6.
16. Lindqvist PG, Erichs K, Molnar C, Gudmundsson S, Dahlin LB. Characteristics and outcome of brachial plexus birth palsy in neonates. Acta Pediatr. 2012; 101:579–82.
17. Medical Research Council: Nerve Injuries Committee. Aids to the investigation of peripheral nerve injuries. London: His Majesty's Stationary Office; 1942. p. 48.
18. Curtis C, Stephens D, Clarke HM, Andrews D. The active movement scale: an evaluative tool for infants with obstetrical brachial plexus palsy. J Hand Surg. 2002;27A(3):470–8.
19. Chuang DCC, Ma HS, Wei FC. A new evaluation system to predict the sequelae of late obstetric brachial plexus palsy. Plast Reconstr Surg. 1998;101:673–85.
20. Michelow BJ, Clarke HM, Curtis CG, Zuker RM, Seifu Y, Andrews DF. The natural history of obstetrical brachial plexus palsy. Plast Reconstr Surg. 1994;93:675–81.
21. Zaidman GM, Holland MR, Noetzel MJ, Park TS, Pestronk A. Newborn brachial plexus palsy: evaluation of severity using quantitative ultrasound of muscle. Muscle Nerve. 2013;47(2):246–54.
22. Zaidman CM, Seelig MJ, Baker JC, Mackinnon SE, Pestronk A. Detection of peripheral nerve pathology: comparison of ultrasound and MRI. Neurology. 2013;80(18):1634–40.
23. Bae DS, Waters PM, Zurakowski D. Reliability of three classification systems measuring active motion in brachial plexus birth palsy. J Bone Joint Surg Am. 2003;85A(9):1733–8.
24. Mallet J. [Obstetrical paralysis of the brachial plexus. II. Therapeutics. Treatment of sequelae. Priority for the treatment of the shoulder]. Rev Chir Orthop Reparatrice Appar Mot. 1972;58 Suppl 1:166–8. French.
25. Heise CO, Martins RS, Foroni LH, Siqueira MG. Prognostic value of thumb pain sensation in birth brachial plexopathy. Arq Neuropsiquiatr. 2012;70(8): 590–2.
26. Al-Qattan MM, El-Sayed AAF, Al-Zahrani AY, Al-Mutairi SA, Al-Harbi MS, Al-Mutairi AM, Al-Kahtani FS. Narakas classification of obstetric brachial plexus palsy revisited. Hand Surg Eur. 2009;34:788–91.
27. Narakas AO. Obstetric brachial plexus injuries. In: Lamb DW, editor. The paralysed hand. Edinburgh: Churchill Livingstone; 1987. p. 116–35.
28. Malessy MJA, Pondaag W, van Dijk JG. Electromyography, nerve action potential and compound motor action potentials in obstetric brachial plexus lesions: validation in the absence of a "Gold Standard". Neurosurgery. 2009;65(4):A153–9.
29. Van Dijk JG, Pondaag W, Buitenhuis SM, van Zwet EW, Malessy MJA. Needle electromyography at 1 month predicts paralysis of elbow flexion at 3 months in obstetric brachial plexus lesions. Dev Med Child Neurol. 2012;54:753–8.
30. Carvalho GA, Nikkhah G, Matthies C, Penkert G, Samii M. Diagnosis of root avulsions in traumatic brachial plexus injuries: value of computerized tomography myelography and magnetic resonance imaging. J Neurosurg. 1997;86:69–76.
31. Hashimoto T, Mitomo M, Hirbuki N, Miura T, Kawai R, Nakamura H, Kawai H, Ono K, Kozuka T. Nerve root avulsion of birth palsy: comparison of myelography with CT myelography and somatosensory evoked potentials. Radiology. 1991;178:841–5.
32. Medina LS, Yaylali I, Zurakowski D, Ruiz J, Altman NR, Grossman JA. Diagnostic performance of MRI and MR myelography in infants with a brachial plexus birth injury. Pediatr Radiol. 2006;36(12):1295–9.
33. Miller SF, Glasier CM, Griebel ML, Boop FA. Brachial plexopathy in infants after traumatic delivery: evaluation with MR imaging. Radiology. 1993; 189(2):481–4.
34. Smith AB, Gupta N, Strober J, Chin C. Magnetic resonance neurography in children with birth-related brachial plexus injury. Pediatr Radiol. 2008;38(2): 159–63.
35. Waters PM. Comparison of the natural history, the outcome of microsurgical repair, and the outcome of operative reconstruction in brachial plexus birth palsy. J Bone Joint Surg Am. 1999;81-A(5):649–59.
36. Birch R, Bonney G, Wynn Parry CB. Birth lesions of the brachial plexus. Surgical disorders of the peripheral nerves. London: Churchill Livingstone; 1998. p. 209–33.
37. Belzberg AJ, Dorsi MJ, Storm PB, Moriarity JL. Surgical repair of brachial plexus injury: a multinational survey of experienced peripheral nerve surgeons. J Neurosurg. 2004;101(3):365–76.
38. Laurent JP, Lee R, Shenaq S, Parke JT, Solis IS, Kowalik L. Neurosurgical correction of upper brachial plexus birth injuries. J Neurosurg. 1993;79:197–203.
39. Hale HB, Bae DS, Waters PM. Current concepts in the management of brachial plexus birth palsy. J Hand Surg. 2010;35A:322–31.
40. Palti R, Horwitz MD, Smith NC, Tonkin MA. Early combined neurosurgery and orthopedic surgery in neonatal brachial plexus palsy. Hand Surg. 2011;16(2): 155–9.
41. Badr Y, O'Leary S, Kline DG. Management of one hundred seventy-one operative and non-operative obstetrical birth palsies at Louisiana State University Health Sciences Center. Neurosurgery. 2009;65(4 Suppl):A67–73.
42. Clarke HM, Curtis CG. An approach to obstetrical brachial plexus injuries. Hand Clin. 1995;11: 563–81.
43. Gilbert A. Long term evaluation of brachial plexus surgery in obstetrical plexus surgery. Hand Clin. 1995;11:583–94.

Neonatal Brain Injury

5

Anil Sindhurakar and Jason B. Carmel

In the course of 1 year, the human brain develops from a "primitive streak" in the embryo to the world's most complex biological system. Human brain development represents a crowning achievement of both evolutionary biology and developmental neuroscience. This period, which includes development both in utero and in the neonatal period, is filled with both tremendous opportunity and significant vulnerability. While tremendous neurological function is gained during typical development, injury to the developing brain can cause lifelong impairments. This chapter discusses the types of injuries that commonly occur during this critical period of development, their diagnosis and management, and the sequelae of brain injuries that occur early in life.

Before we address the particularities of common injuries to the developing brain, we should consider some of the rules. One common idea is that the developing brain is capable of more significant recovery from injury than at later points. This idea is commonly described as the Kennard doctrine, after Margaret Kennard, an experimental psychologist whose work in the 1920s and 1930s compared long-term neurological outcomes of experimental brain injuries in primates performed at various developmental stages. Her conclusion was that for circumscribed cerebral lesions, recovery was better after injury early in development compared to later. The empirical evidence that Kennard created is supported by studies of brain plasticity, the ability to make new neuronal connection, which is greatest early in life. While called the Kennard "doctrine," this is really a hypothesis with some experimental evidence, but far from a fact or rule.

The reason why the Kennard doctrine cannot be considered a fact is that while brain plasticity is high, early in development, the developing nervous system also is more vulnerable to injury during this period. Studies of premature birth reveal this vulnerability. Infants born premature are susceptible to two kinds of brain injury: bleeds in the brain (intraventricular hemorrhage) and damage to brain white matter (periventricular leukomalacia). The susceptibility of this population to these complications can be explained by the demands of the growing brain: in the case of bleeds by friable blood vessels in the area of the brain where new neurons are formed, and in the case of white matter disease by the fragility of the cells that create myelin, the fatty membrane that wraps axons and causes white matter to

A. Sindhurakar, Ph.D.
Motor Recovery Laboratory, Burke Medical Research Institute, 785 Mamaroneck Avenue, White Plains, NY 10605, USA

J.B. Carmel, M.D., Ph.D. (✉)
Motor Recovery Laboratory, Mind and Brain Institute, Neurology, and Pediatrics, Weill Cornell Medical College, Burke Medical Research Institute, 785 Mamaroneck Avenue, White Plains, NY 10605, USA
e-mail: Jason.carmel@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_5

appear white. Thus, the brains of infants born prematurely are at high risk. This calls into question the idea that earlier is better when it comes to brain injury and recovery.

We have organized this chapter by the common types of brain injuries that affect babies in the neonatal period. Because infants born prematurely have selective vulnerabilities, we have split the major maladies by those that affect term and preterm infants alike and those that predominantly affect preterm infants. For those etiologies affecting both term and preterm infants, we begin with a discussion of generalized hypoxia and ischemia and then consider arterial ischemic stroke. We then discuss the two major causes of brain injury in preterm infants—intraventricular hemorrhage and periventricular leukomalacia. For each of these diseases we discuss the etiology, clinical presentation, diagnosis, management, and outcomes. The goal is to inform the reader about the major causes of neonatal brain injury, how to approach them clinically, and how to optimize outcomes.

Brain Injuries Affecting Term and Preterm Infants

Neonatal brain injuries can occur from many different conditions and infants under 1 year of age are at the highest risk of acquiring these injuries. Given the complexity of the sources of injuries to neonatal brain this section focuses on the two most important neurological conditions in term infants that are acquired at or near the time of birth: Hypoxic-ischemic encephalopathy and neonatal stroke. Despite advances in neonatal care techniques these neurological conditions continue to be major contributors to infant mortality. In order to improve the outcomes of these disease states, being able to diagnose and treat them early might significantly improve long-term outcomes.

Hypoxic-Ischemic Encephalopathy

Hypoxic-Ischemic Encephalopathy (HIE) occurs when there is insufficient substrate delivery to the brain to meet its metabolic demands. Either hypoxia, which is reduced oxygen delivery, or ischemia, which is reduced cerebral blood flow, can contribute. HIE occurs in 4 out of 1000 term babies. Although there have been tremendous improvements in neonatal care in recent years, hypoxic-ischemic cerebral injuries continue to be significant cause of infant mortality as well as long-term medical conditions such as cerebral palsy, mental retardation, visual impairment, and epilepsy.

Clinical Presentation

Symptoms displayed by infants suffering from HIE vary depending upon severity of injury. However, few symptoms such as abnormal levels of consciousness and reflexes as well as seizures are present at all levels of severity. In order to better understand clinical presentation of this type of brain injury, it has been useful to classify the encephalopathy as mild, moderate and severe, according to the original system developed by Sarnat. In severe cases of HIE, within first 12 h of birth infants generally present with reduced levels of consciousness and preserved spontaneous breathing but patterns of breathing frequently become irregular. This is followed by onset of seizures and hypotonia. As the brain injury leads to cerebral edema, the brain swells, and this manifests as a bulging fontanelle. Brainstem abnormalities such as irregular eye movements, motor responses and apnea often worsen within next 12 h and may result in respiratory arrest and death by 72 h of life. Clinical outcomes of HIE with different degrees of severity are summarized in Table 5.1. Symptoms of mild HIE usually resolve within 72 h. With more severe injury, abnormal levels of consciousness, disturbance in feeding behavior and generalized hypotonia often persist. Improvements in these neurological signs are difficult to predict but infants that show fastest improvements within the first week have the best chance for normal outcome in the long-term.

Diagnosis

An accurate diagnosis of HIE requires evidence for both hypoxia and ischemia, in the form of history and laboratory findings, as well as encephalopathy, based on clinical signs. The specific

Table 5.1 HIE severity and clinical outcomes

	HIE severity		
Clinical symptoms	Mild	Moderate	Severe
Level of consciousness	Hyperalert	Lethargy	Coma
Seizures	–	+/–	+
Tone	Normal or increased	Decreased or increased	Decreased
Tendon reflexes	Increased	Increased or decreased	Decreased or absent
Primitive reflex	Exaggerated	Depressed	–
Brainstem dysfunction	–	+/–	+
Other features	Jitteriness, sympathetic over-activity	+/–	Elevated intracranial pressure, automatic dysfunction
Outcome	Normal	20–40 % abnormal	100 % abnormal or death

+: Present, –: Absent, +/–: Present or absent
Table adapted from Swaiman KF, Ashwal S, Ferriero DM. Pediatric neurology: Principles and practice, 4th ed. Philadelphia Elsevier Mosby, 2006

etiology can be made only after careful review of the pregnancy, delivery, and neurological examination of the affected infant. In order for an acute neurological injury to be designated as HIE the American Academy of Pediatrics and the American College of Obstetrics and Gynecology put forth specific criteria for HIE in its 1996 guidelines. These include following conditions:

- Apgar scores of 0–3 for longer than 5 min
- Acidosis in umblical artery blood (pH <7)
- Neonatal neurologic sequelae such as hypotonia, seizures and coma
- Injury to multiple organs like kidney, lungs, liver, heart and intestines

Among these criteria, one of the most powerful predictor of the extent of brain injury is the amount of dysfunction in other organs susceptible to hypoxia and ischemia, including the kidneys, liver, and heart. These organs have the advantage of being able to assay function and dysfunction directly, including blood biomarkers of cell injury. Biomarkers of brain injury have not yet been validated for HIE.

Clinical experience suggests that type of hypoxic-ischemic injury and its duration can be highly predictive of the pattern of injury to the brain. Acute and total injury for just 10–11 min can result in irreversible brain injuries. These injuries tend to be predominantly localized into the deep gray matter structures of the brain such as basal ganglia and thalamus while leaving much of the cerebral cortex intact. On the other hand, partial and prolonged events (over an hour or longer) results in injury to the cerebral cortex and subcortical white matter but tends to spare deep gray matter structures. In addition, advances in neuroimaging allow clinicians to better define the brain structures that are affected. Some of the most frequently used imaging modalities are ultrasonography, CT, and MRI. EEG, when applied broadly over the scalp can also help localize damage, at least within cortical structures. Of these imaging techniques, MRI gives the greatest amount of information about area of brain affected, ischemic components, and evidence of blood in the tissue. The utility of various imaging modalities is summarized in Table 5.2. The advantages of different imaging techniques must be balanced with practical considerations of the time, expense, and availability of the various imaging modalities as well as how medically stable the patient is to travel to an imaging facility, in the case of CT or MRI as opposed to being able to do ultrasound in the neonatal unit.

Management

The mainstay of management for HIE is to ensure adequate substrate delivery in order to match

Table 5.2 Diagnostic tools for different neuropathological conditions

Neuropathological condition	Diagnostic tool		
	MRI	CT	US
Selective neuronal necrosis: cerebral cortex	++	+	−
Selective neuronal necrosis: basal ganglia and thalamus	++	+	+
Selective neuronal necrosis: brain stem	++	+/−	−
Parasagittal cerebral injury	++	+	−
Focal and multifocal ischemic injury	++	++	+
Periventricular Leukomalacia	++	+	++[a]

MRI magnetic resonance imaging, *CT* computed tomography, *US* ultrasound
++: Very useful, +: Useful, +/− Questionably useful, −: Not useful
[a]Very useful for focal component but not useful for diffuse component or non-cystic PVL
Table adapted from Volpe JJ. Neurology of the newborn, 5th ed. Philadelphia: Saunders, 2008

brain metabolic demands. This includes adequate ventilation and perfusion, as well as correction of acidosis or other metabolic derangements caused by the original hypoxia or ischemia. Correction of metabolic disturbances addresses brain metabolic needs directly. It also helps to restore proper cerebral autoregulation of blood flow. Proper care for any infant suffering from HIE requires attention to disturbance to other systems besides neurological functions. From the perspective of brain health, addressing other end organ dysfunction helps to support uninjured brain tissue as well as repair of damaged areas.

Two aspects of management help to lower the metabolic demands of the brain. First is the treatment of seizures. Seizures are common after HIE, and they place an extra metabolic demand on the brain. Barbiturates, particularly phenobarbital, as well as benzodiazepines for acute management, have been the mainstays of drug therapy. Ongoing studies of newer antiepileptics are ongoing and may expand treatment options, particularly in refractory seizures that often accompany severe HIE. However, given the potential side effects of antiepileptic drugs, treatment options must take into consideration minimizing the number and duration of pharmacological therapy.

The second intervention that helps lower brain metabolic demands is hypothermia. Several multicenter clinical trials have demonstrated a beneficial role of either selectively cooling the head or whole body cooling. Benefits have been reported when cooling was maintained for 72 h. This method of neuroprotection appears to provide beneficial effects through mechanisms such as decrease in energy consumption, reducing accumulation of extracellular glutamate and reactive oxygen species as well as inhibition of deleterious inflammatory events and apoptotic cell death pathways. Such neuroprotection strategy that impacts multiple mechanisms not only directly improves odds of positive outcome in long term but it might widen the window for opportunities to make other therapeutic options to be effective for a longer period of time as well. Other interventions aimed at protecting the brain during this time are also under active investigation, including preventing excitotoxicity and oxidative damage.

Long-Term Outcomes

Like prognostication for many injuries or illnesses, making a definitive prognosis for any individual is difficult. However, large groups of data have been collected on children with HIE that allow guidance of clinical decisions and prognosis for patients and their families. The most helpful clinical markers are: Apgar scores, and particularly the 'extended' Apgar scores that are recorded after 5 min of birth. Research suggests that infants with depressed Apgar scores of 3 or less (out of 10) after 15 min or longer have mortality rate as high as 60 % within a year and a similar rate of Cerebral Palsy (CP) in the survivors. Also, certain specific aspects of neurological syndrome such as severity of the neonatal encephalopathy, presence of seizures and the duration of hypotonia are all negative prognostic signs. In case of injury severity, it has been reported that when infants are diagnosed with the most severe form of HIE, their mortality rate is as high as 80 % but when they are diagnosed with less severe forms of the disease, the likelihood decrease precipitously. On the other hand, presence of seizures can increase the risk of neuro-

logical sequelae by as much as 40-fold. While seizures themselves can harm the brain, their negative prognostic significance is more likely related to them being a marker of a very substantial initial injury.

Neuroimaging tools such as ultrasound and magnetic resonance imaging (MRI) are also routinely used to predict long-term outlooks. Ultrasound images are most useful in predicting outcomes from injury to deeper cortical structures such as basal ganglia and thalamus in term infants. However, MRI scans have been the most valuable imaging modality for outcome prediction. Using MRI it has been shown that term infants with injury to the basal ganglia and thalamus associated with severe HIE have the worst neurological outcomes compared to injury to watershed areas of brain associated with longer and less severe HIE.

Neonatal Stroke

Another common form of neonatal brain injury is stroke. In newborn infants, incidence of neonatal stroke is 1 in 4000 live births. While stroke can refer to both ischemia and hemorrhage of either arterial or venous origin, for the majority of neonates, stroke is arterial ischemic event, as determined by the pattern of injury. While the cause for arterial ischemic stroke in newborns is most often unknown, the presumed mechanism is thromboembolic, as opposed to local clots associated with atherosclerotic disease, for example. There is a male predominance in neonatal strokes and also a tendency of left-sided MCA occlusion. The predilection for the left side is likely due to hemodynamics that favors passage of emboli to this side. Why boys have more strokes than girls is unknown.

Clinical Presentation

Stroke in newborns usually do not show clinical symptoms similar to adult stroke and the injury often remains unrecognized until infants are older. Many children with neonatal stroke develop hemiparesis and present with early hand preference within the first year. Of the infants that do show symptoms, the most recognizable sign of the newborns with both arterial and venous stroke is seizure. However, unlike the seizures in most of the neonatal encephalopathies, which tend to be multifocal and myoclonic, seizures associated with stroke are mostly focal, involving only one side of the body or one limb.

Diagnosis

Diagnosis of stroke often begins with recognition of an early hand preference, neglect of one side of the body, or other focal neurological signs. Determination of the etiology is usually performed with brain imaging, with MRI being the preferred modality. Often, ultrasound may not show any abnormalities acutely in case of ischemic strokes. CT scans may also show only subtle signs because the brain has relatively low attenuation (e.g., is dark) in the neonate. MRI and MR angiography and venography are more useful tools to precisely locate the site of injury if occlusions or venous thrombosis are suspected. Effectiveness of different imaging modalities for detecting ischemic injuries in neonates is summarized in Table 5.3.

An important clinical question is whether neonatal stroke requires a diagnostic workup of the etiology, as it would for adult stroke. The International Pediatric Stroke Study has found few cases of embolic sources or hypercoagulability. However, while the yield for investigations of arterial ischemic stroke is low, the determination of whether to pursue a workup must be made

Table 5.3 Effectiveness of different imaging modalities for ischemic injuries

Imaging tool	Findings	Timing
Ultrasound	Increased echogenicity	2–10 days
CT	Low attenuation	1–7 days
MRS	Increased lactate Decreased NAA	1–15 days After 3 days
DWI	Reduced diffusion	1–5 days
Anatomic MRI	T2 prolongation	24 h

CT computed tomography, *MRS* proton magnetic resonance spectroscopy, *DWI* diffusion weighted imaging, *MRI* magnetic resonance imaging

Table adapted from Barkovich AJ. Pediatric neuroimaging, 4th ed. Philadelphia: Lippincott Williams and Wilkins, 2005

based on an individual case, including family history and clinical suspicion of emboli. An echocardiogram is recommended if the neuroimaging indicates presence of embolism. A hypercoagulable workup is indicated in children with family history of clotting disorders or multiple events.

Neuroimaging studies using MRI and CT scans have recognized distinctive topography and vascular distribution in case of arterial strokes and venous thrombosis. Almost 75 % of term neonates with arterial stroke tend to have unilateral stroke and all unilateral lesions involve middle cerebral artery. Further, of all the cases involving middle cerebral artery almost 65 % tend to be left artery. Distribution of topography and vascular distribution from a large clinical study of 244 infants using CT and MRI scans is summarized in Table 5.4. In case of venous thrombosis, most cases are best recognized using MRI. Majority of thrombosis cases involve superior sagittal sinus (>65 %) and infarction is present in 40–60 % of the time. The infarcts are usually hemorrhagic and intraventricular hemorrhage is present in 20–35 % of the cases. When infarction is not present, brain edema is the principal finding.

Management

Acute management of stroke starts with a workup to identify the etiology and treatment of the same if a source is found. Hypercoagulable states are treated according to their specific derangement.

Table 5.4 Topography and vascular distribution of ischemic stroke

Infarct topography	Percentage
Laterality	
Unilateral	75
Bilateral	25
Vascular distribution	
Left MCA	55
Right MCA	30
Bilateral MCA	10
Other arteries	5

MCA middle cerebral artery
Table adapted from Volpe JJ. Neurology of the newborn, 5th ed. Philadelphia: Saunders, 2008

If an embolic source is found, treatment is targeted to removing or dissolving the clot. The treatment of sinovenous thrombosis is controversial; anticoagulants can be administered, but controlled studies comparing intervention with natural history are lacking. Children with known prothrombotic risks are given prophylactic therapy, such as aspirin or anticoagulants.

Long-Term Outcomes and Rehabilitation

Human brain at neonatal stage is very "plastic" meaning it is much more capable of adapting to changes in the environment, behavior and neural processes. Hence, infants are capable of recovering from injuries such as neonatal stroke lot better than adult human beings. Neural connections are still forming in a brain of a newborn and this makes it possible for transferring important functions from one part of brain to another in case of an injury. For example, while stroke most often affects the left hemisphere, neonatal stroke does not produce aphasia, the loss of language production or understanding, as it would in adult stroke. Instead, children with left hemisphere lesions develop control of language from the right hemisphere. Because of such plasticity, neonates with large stroke can develop with mild to moderate impairments in the long-term.

Having said this, there are still many neonates that do not recover fully after neonatal stroke. One of the most common outcomes after neonatal stroke is cerebral palsy, which is a disorder of movement and posture due to a non-progressive injury to the developing brain. For stroke, the most common lasting deficit is hand and arm dysfunction on the side of the body opposite the stroke hemisphere. Impairment of motor function is more common following arterial strokes than sinovenous thrombosis. Besides motor dysfunction, children with neonatal stroke can develop sensory deficits like numbness, visual impairments as well as difficulty in facial recognition. Other long-term morbidities associated with stroke include cognitive impairments like learning disability, mental retardation and behavioral disorders as well as epilepsy that usually originate from cortex adjacent to the infarction.

In the case of chronic stroke, there are two effective rehabilitation strategies for hand and arm hemiparesis. The first is use of constraint-induced movement therapy, in which the less involved arm and hand are immobilized (by a sling or cast), and the hemiparetic arm and hand are used for training of dexterity. Alternatively, the hands can be trained together, with the hemiparetic hand used as a helper for bimanual tasks. These strategies both produce lasting gains in dexterity of the hemiparetic hand. They also improve measures of bimanual skill, tasks that require the two hands be used together. Ongoing studies are addressing which type of therapy is most effective for different severity and different etiologies of hemiparesis, such as stroke, periventricular white matter injury, and bleeds. In addition, brain stimulation and other forms of neuromodulation are being investigated for hemiparesis, with promising early results.

Brain Injuries Affecting Preterm Infants

Preterm infants are born vulnerable to brain injury due to fragility of the developing brain itself, the blood vessels that supply brain cell proliferation, and other organ systems that provide crucial support of brain development. The fully developed brain can maintain adequate blood and oxygen delivery within a large range of systemic blood pressure. Cerebral arteries respond to high pressure by constricting to limit arterial pressure in the brain. Conversely, when systemic blood pressure is low, cerebral arteries dilate to maintain cerebral perfusion. Immature cerebral autoregulation predisposes premature infants to excess cerebral perfusion, leading to hemorrhage, and hypoperfusion, leading to injury of the white matter, which is most susceptible to ischemic injury. We discuss both hemorrhage and white matter injury in detail, below. In addition, preterm infants have greater incidence of neurodevelopmental problems even without overt brain injury. This indicates that even in infants afforded all of the nutritional, respiratory, and metabolic support of the newborn intensive care unit, prematurity can have direct deleterious effects on brain development. Hence, a separate section addresses complications in infants due to prematurity itself as a factor contributing to lasting neurological impairments.

Hemorrhagic Injuries

Recent advances in neonatal intensive care have made it possible for preterm infants to survive the neonatal period. However, a significant portion surviving infants go on to develop neurodevelopmental disabilities later in life. Hemorrhagic injuries represent a major cause of these disabilities in preterm infants. Among different types of hemorrhagic insults, germinal matrix intraventricular hemorrhage (IVH) is the most common in preterm infants. The reason that this area is more susceptible to hemorrhages is because the blood vessels that make up its vasculature are very thin walled. This attribute, which likely accommodates the large metabolic demands of the rapidly growing brain, also creates vulnerability. In utero, oxygen is supplied through the placenta, and the lungs are not highly perfused. When a baby is born, hemodynamics shift to perfuse the lungs in order to oxygenate blood. The increase in right heart pressures is accompanied by a rise in venous pressure. This explains why most intraventricular hemorrhage occurs in the first week of life outside the uterus. As cerebral autoregulation matures and the fragile blood vessels of the germinal matrix become more robust, the risk of bleeding drops; IVH after 34 weeks of gestation is unusual.

Clinical Presentation

The most significant clinical findings in infants with IVH are respiratory disturbances that become severe enough to warrant mechanical ventilation. Depending on the severity of the injury, clinical syndromes are categorized into three stages: catastrophic deterioration, saltatory deterioration, and clinically silent syndrome. Of the three, clinically silent syndrome is the most common with over 75 % of the IVH cases unrecognizable clinically. Catastrophic deterioration

involves dramatic display of multiple symptoms such as sharp decline in peripheral hematocrit, deep stupor, respiratory disturbances, generalized tonic seizures, dilated and unresponsive pupils along with flaccid quadriparesis. Saltatory syndrome is more difficult to recognize. It involves altered levels of consciousness, hypotonia and abnormal reflexes that come and go in an unpredictable pattern. Some commonly recognized symptoms of catastrophic deterioration are shown in Table 5.5 along with their incidence.

Diagnosis

Two factors have led to surveillance of IVH in the preterm population: its high incidence and the lack of clinical signs in the majority of those affected. Cranial ultrasounds are routinely performed in the first week of life for babies born before 34 weeks. Based on the ultrasound results, clinicians have categorized IVH into four basic categories: Grade I–IV. Grading system and criteria for the different categories are shown in Table 5.6. Grades I–III are ranges of severity for germinal matrix hemorrhage. Grade IV IVH is considered to be a result of infarction of the brain tissue adjacent to the germinal matrix with subsequent bleed into the infarct. Due to the echogenic nature of blood, ultrasound detects IVH effectively for all grades.

The echogenic region of the injury is usually located in the frontal and parietal regions. CT scans are also useful in detecting the lesion but the necessity of exposing sick children to ionizing radiation has made it less preferred compared to ultrasonography. Similarly, MRI is also capable of detecting the lesions with excellent resolution. However, high cost and time involved in producing results with MRI has precluded its use in detecting hemorrhagic injuries. The management of neonates with IVH is discussed in depth in Chap. 11.

Management

In the acute care of infants with IVH, a major challenge is maintaining proper cerebral perfusion. Arterial blood pressure can drop due to loss of blood in the circulation. Increased intracerebral pressure can further lower cerebral perfusion. On the other hand, increased blood pressure increases the risk of expanding the hemorrhage. Other factors that might lead to progression of hemorrhage and thus need to be carefully monitored are hypercarbia, acidosis and seizures.

Posthemorrhagic hydrocephalus is the major neurosurgical complication of IVH. Clotted blood obstructs cerebrospinal fluid flow, either at the foramen between ventricles or at the uptake in the arachnoid villi near the dural venous sinuses leading to buildup of cerebrospinal fluid

Table 5.5 Symptoms of catastrophic syndrome IVH

Symptom	Incidence (%)
Decrease in hematocrit	75
Seizures	10–15
Changes in tone	75–90
Abnormal eye signs	33–95
Apnea/bradycardia	50–75
Hyperglycemia	>50
Hyponatremia	>50
Metabolic acidosis	>75

Table adapted from Swaiman KF, Ashwal S, Ferriero DM. Pediatric neurology: Principles and practice, 4th ed. Philadelphia Elsevier Mosby, 2006
Data from Cepeda et al., 1978, Dubowitz et al., 1981, Moylan et al., 1978; Ment unpublished data, NS27116 Randomized Indomethacin IVH Prevention Trial, 1997

Table 5.6 Grading system for intraventricular germinal matrix hemorrhage

Grade	Criteria
I	Germinal matrix hemorrhage with no or minimal intraventricular hemorrhage
II	Intraventricular hemorrhage (10–50 % of ventricular area)
III	Intraventricular hemorrhage (>50 % of ventricular area; ventricles enlarged due to parenchymal injury)
IV	Grade III IVH with periventricular hemorrhagic infarction

Table adapted from Swaiman KF, Ashwal S, Ferriero DM. Pediatric neurology: Principles and practice, 4th ed. Philadelphia Elsevier Mosby, 2006
Data from Papile LS, Burstein R. Incidence and evolution of the subependymal intraventricular hemorrhage: A study of infants with weights less than 1500 grams. J Pediatr 1978; 92:529

within the ventricles. To monitor for this complication, the head circumference is measured serially; the head of an infant with unfused skull plates will expand to accommodate the enlarged ventricles. Serial ultrasound scans at intervals of 4–7 days can directly measure ventricle size.

For the purpose of managing preterm neonates with risk for hydrocephalus, they are classified into four basic groups depending on their ventricular dilation. The first is slowly progressive ventricular dilation group that exhibits moderate dilation and appropriate head growth rate that only requires close surveillance. The second is persistent slowly progressive ventricle dilation group that presents with moderate-to-severe dilation with clearly excessive head growth rate. Children in this category must be put under close surveillance and serial lumbar punctures may be performed to remove excess CSF buildup. The third is persistent rapidly progressive dilation group that presents with severe dilation and rapid head growth rate. These children must be treated by lumbar punctures as well as more invasive ventricular drainage techniques or even ventriculoperitoneal shunts when needed. The fourth category is arrested progression group that has spontaneous arrest of ventricular dilation or arrest after lumbar puncture. These children can develop late-onset hydrocephalus and thus need to be closely monitored for many months.

Outcomes

Outcomes in preterm infants with IVH depend upon the severity of the IVH as well as the degree of prematurity. Infants with grade I IVH have low mortality rate and progression to ventricular dilation is also low. Mortality rate in grade II hemorrhagic injury is higher only in those infants that weigh less than 750 g and up to 15 % of survivors develop progressive ventricular dilation. Children with grade III injury have much higher mortality when they weigh less than 750 g but it is less than 10 % if the infant is 1000–1500 g. Almost 75 % of these infants go on to develop progressive ventricular dilation. Infants with grade IV IVH have the highest mortality rate particularly if they weigh less than 750 g and most of these children go on to develop progressive ventricular dilation.

Grade IV IVH has a poorer prognosis, likely related to the fact that it involves infarction of the area adjacent to the choroid plexus, including the basal ganglia and the corticospinal tract. Given the location of the injury, it is not surprising that motor deficits are the most severe and persistent of the impairments. Motor deficits that are most common are spastic hemiparesis or asymmetrical spastic quadriparesis. There is also evidence suggesting unilateral lesions have more favorable outcomes compared to bilateral ones. Grade III and IV IVH are also associated with cerebral palsy and negative cognitive outcomes. Long-term outcomes as a function of severity of IVH are summarized in Table 5.7.

White Matter Injuries

Preterm infants are at increased risk of white matter injury particularly in the periventricular regions of the brain, a condition known as periventricular leukomalacia. These regions of the brain represent vascular end zones that are most susceptible to hypoxic-ischemic injuries. Besides the immature vasculature during prematurity, intrinsic vulnerability of immature oligodendrocytes, the cells that myelinate axons in the brain, makes these infants more vulnerable to ischemia and inflammation. PVL by definition refers to loss of white matter in the dorsal and lateral areas surrounding the ventricles. However, it can be composed of two distinctive components: cystic

Table 5.7 Long-term outcomes in preterm infants with germinal matrix hemorrhage

Severity of IVH[a]	Incidence of neurological sequelae (%)
Grade I	15
Grade II	25
Grade III	50
Grade IV (IVH with PVHI)	75

IVH intraventricular hemorrhage, *PVHI* periventricular hemorrhagic infarction

[a]Refer Table 5.6 for grading system

Table adapted from Volpe JJ. Neurology of the newborn, 5th ed. Philadelphia: Saunders, 2008

and non-cystic. Cystic PVL consists of macroscopic focal necroses that evolve into cysts, and non-cystic PVL consists of microscopic lesions that give rise to glial scars. Animal studies indicate that inflammation contributes strongly to PVL, and clinical studies corroborate these findings as infants born with mothers with chorioamnionitis have higher incidence of PVL.

Clinical Presentation

PVL rarely presents clinically in the neonatal period. Rather, it presents with failure to meet developmental milestones or other sequelae in later childhood. When PVL is the predominant injury, clinical presentation includes abnormal tone and muscle power in the legs. This pattern, known as spastic diplegia, reflects the involvement of corticospinal fibers that control leg movement. In severe injury, the optic radiations may become involved, and affected infants can have visual field deficits. On the other hand, if the injury is diffuse it usually involves more cortical and subcortical areas and will subsequently present with more widespread neurologic signs such as behavioral and cognitive disorders.

Diagnosis

Diagnosis of PVL in the neonatal period is usually based on ultrasound imaging used for screening IVH. Initially within first few days of injury, increased echogenicity is observed in the dorsolateral regions of the lateral ventricles. Hyperechogenecity is most distinguishable in PVL from normally observed hyperechoic periventricular brain in preterm infants if ultrasound is performed on the posterior end of the fontanelle. Echogenicity is apparent from all approaches in case of PVL but normally observed echogenicity is less prominent from posterior view. However, conclusive diagnosis is made after cystic lesions become apparent within 2–4 weeks or using MRI. CT and MRI scans for PVL have not proven to be effective in diagnosis of this disease at earlier stages. Late stage PVL is best recognized using MRI scans as it can detect more diffuse lesions of the white matter that are difficult to recognize with CT or ultrasound.

Management

Preterm infants are under heightened risk of hypoxic-ischemic injuries. Immature cerebrovascular autoregulation and prevalence of respiratory illnesses adds further complications that make the premature newborns more susceptible to white matter injuries. Hence, first line of defense during acute care must focus on adequate ventilation and maintaining proper cerebral blood flow. Precautions in using 100 % oxygen, risks for hypercarbia and hypocarbia discussed in management for term-infants with hypoxic-ischemic injuries apply to caring for preterm infants as well. Another important aspect of acute care for preterm infants is maintenance of metabolic homeostasis. Blood glucose and oxygen levels must be more carefully monitored in preterm infants. Any indication of acidosis or hypoglycemia must be immediately corrected upon detection. Seizures and brain swelling may also accompany white matter injuries. These morbidities can worsen the condition of already vulnerable preterm infants. Hence, clinicians must take appropriate measures to control the seizure and edema soon as their symptoms become apparent. In the context of PVL, many premature infants have oculomotor dysfunction so care must be taken in looking for signs for such neurological outcome as well. Further, PVL has been associated with inflammation and excitotoxicity thus neuroprotective strategies such as administering drugs that inhibit excitatory amino acids like magnesium sulfate and oxygen free radical inhibitors such as allupurinol and oxypurinol must be considered when warranted.

Outcomes

Preterm infants with PVL have several long-term outcomes such as spastic diplegia, cognitive deficits, visual impairments and behavioral disorders. Major long-term motor sequelae of PVL is spastic diplegia, which is also the major motor deficit in preterm infants in general. When lesions are more severe, arm function may also be affected. Visual deficits are common in PVL as are cognitive impairments. Low birth weight is another risk factor for PVL. Twenty-five to 50 % of infants who weigh less than 1500 g have PVL

manifesting as cognitive, behavioral, visual disorders and motor deficits

Prematurity

An infant may be designated preterm if gestation period is less than 37 weeks. However, those infants that are born before 32 weeks and have birth weight below 1500 g are at the highest risk of neurological impairments. By definition a preterm infant is immature and has to face postnatal environmental changes with underdeveloped organ systems. Preterm infants born before 34 weeks of gestation have difficulty with even the most basic necessities of survival such as feeding and breathing. In addition to these basic problems, many of these infants are at heightened risk of hypoxic-ischemic injuries and hemorrhagic injuries that were discussed in earlier sections. But even the infants that escape these insults still present with significant cognitive and behavioral disorders in the long-term. Hence, a careful assessment of prematurity as an important contributor to neurological outcomes in neonates will be discussed in this section.

Clinical Presentation

Neurological symptoms present in a preterm infant can vary by their gestational age and birth weight. Hence, clinicians first must determine gestational age of the preterm infant. The Ballard Scoring System, which includes the criteria for extremely low birth weight infants, is the main tool used to determine the age. This scoring system based on physical examination of different parts of the body including ear cartilage, sole creases, breast tissue, and genitalia offers an accurate estimate of gestational age. Infants are designated extremely low birth when they weigh less 1000 g at birth and very low birth when they weigh less than 1500 g at birth. Neurological examination must also take into consideration muscle tone and joint mobility of the limbs. Preterm infants are usually hypotonic. They present with poor sucking, crying, and respiratory effort and fewer spontaneous limb movements than term infants.

Diagnosis

Without overt signs of brain injury, the neurological consequences of prematurity are a game of wait and see. Children are often followed closely, not only to care for their ongoing medical needs, but also as close surveillance of neurodevelopment.

Management

Given that preterm birth is associated with significant infant mortality and morbidity, focus in management and treatment of this condition should be upon early detection and prevention of preterm birth. Risk scoring system, uterine contraction monitoring and fetal fibronectin testing are some of the methods of early detection of preterm birth. Among these risk scoring system and uterine contraction monitoring have not been found to be as sensitive in predicting preterm birth as fibronectin levels, particularly if it is tested in conjunction with measuring the cervical length. Preterm contractions are treated with tocolytic therapy using pharmacological agents such as magnesium sulfate and corticosteroids. Although few studies conclude that antenatal corticosteroid use in management of high-risk preterm birth reduces morbidity and mortality in newborn infants with improvements in lung maturity, there are also evidence pointing towards its negative outcome on brain development and cardiovascular system. Hence, such therapies must be prescribed only after weighing in all the associated risks.

The evidence is convincing that magnesium sulfate can protect the brain of the neonate. Babies of mothers given magnesium sulfate as tocolysis but who were delivered prematurely have a lower risk of developing cerebral palsy. They also have a lower risk of substantial gross motor dysfunction. Thus, what was first administered solely to prevent preterm birth was found also to protect the brain against the consequences of prematurity.

Outcomes

Major indicators of neurologic outcome in premature infants are birth weight and gestation age. Extremely low birth weight infants that are

usually born at 28 weeks or less and weigh less than 1000 g are at highest risk of infant mortality and morbidities. These children have the highest rate for development of neurological outcomes such as cerebral palsy, visual, hearing and cognitive impairments. Infants that are born weighing less than 1500 g are categorized as very low birth infants and they are usually born between 28 and 32 weeks. These children are at also at high risk of developing many neurodevelopmental abnormalities. Almost 50 % of these children have one or more neurological disorder by 5 years of age. Neurological, behavioral, and motor deficits are frequently present and care must be taken for social and environmental factors that begin to play major role in impacting quality of life in these children with age.

Injuries to the brain and changes in brain volume as identified by neuroimaging tools are also another reliable indicators of negative long-term outcomes in preterm infants. Functional aspects of the injury are closely related to the location and severity of the brain injury. Similarly, smaller brain volume, ventriculomegaly, altered fiber tracts and intercallosal connections are also prognosticators of poor neurological outcome. Further, reduced gray and white matter volumes have been associated with cognitive impairments. Specific injury to white matter in preterms like PVL, as discussed in previous section, indicate motor and cognitive impairments as well as development of cerebral palsy.

Conclusion

As advances in medicine allow us to sustain babies born prematurely, we have also created a large class of vulnerable children. A great challenge for medicine will be how to bring these children to maturity with preserved brain function. Drawing on developmental neuroscience and advances in clinical care, we must create for the brain what the neonatal ICU incubator is for a premature baby—a haven for growth and development.

Bibliography

American Academy of Pediatrics. Relation between perinatal factors and neurological outcome. In: Poland RL, Freeman RK, editors. Guidelines for perinatal care. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 1992. p. 221.

Barkovich AJ. Pediatric neuroimaging. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2005.

Cepeda EE, Heibronner DM, et al. Glucose tolerance in premature infants with massive intracranial hemorrhage (ICH). Pediatr Res. 1978;12:521.

Colvin M, McGuire W, Fowlie PW. ABC of preterm birth: neurodevelopmental outcomes after preterm birth. BMJ. 2004;329:1390.

Committee on Fetus and Newborn, American Academy of Pediatrics and Committee on Obstetric Practice, American College of Obstetrics and Gynecology. Use and abuse of the APGAR score. Pediatr. 1996;98:141.

Dubowitz LM, Levene MI, Morante A, et al. Neurologic signs in neonatal intraventricular hemorrhage: a correlation with real-time ultrasound. J Pediatr. 1981;99:127.

Gillick BT, Krach LE, Feyma T, et al. Primed low-frequency repetitive transcranial magnetic stimulation and constraint-induced movement therapy in pediatric hemiparesis: a randomized controlled trial. Dev Med Child Neurol. 2014;56(1):44.

Golomb MR, Cvijanovich NZ, Ferriero DM. Neonatal brain injury. In: Swaiman KF, Ashwal S, Ferriero DM, editors. Pediatric neurology: principles and practice. 4th ed. Philadelphia: Elsevier Mosby; 2006.

Hill A. Hypoxic-ischemic cerebral injury in the newborn. In: Swaiman KF, Ashwal S, Ferriero DM, editors. Pediatric neurology: principles and practice. 4th ed. Philadelphia: Elsevier Mosby; 2006.

Kirton A, Chen R, Friefeld S, et al. Contralesional repetitive transcranial magnetic stimulation for chronic hemiparesis in subcortical paediatric stroke: a randomised trial. Lancet Neurol. 2008;7(6):507.

Kirton A, Armstrong-Wells J, Chang T, et al. Symptomatic neonatal arterial ischemic stroke: the international pediatric stroke study. Pediatrics. 2011; 128:e1402.

Ment LM. Intraventricular hemorrhage of the preterm neonate. In: Swaiman KF, Ashwal S, Ferriero DM, editors. Pediatric neurology: principles and practice. 4th ed. Philadelphia: Elsevier Mosby; 2006.

Moylan FM, Herrin JT, Krishnamoorthy KS, et al. Inappropriate antidiuretic hormone secretion in premature infants with cerebral injury. Am J Dis Child. 1978;132:399.

Papile LS, Burstein R. Incidence and evolution of the subependymal intraventricular hemorrhage: a study of infants with weights less than 1500 grams. J Pediatr. 1978;92:529.

Sarnat HB, Sarnat MS. Neonatal encephalopathy following fetal distress: a clinical and electroencephalographic study. Arch Neurol. 1976;33:969.

Staudt M, Lidzba K, Grodd W, et al. Right-hemispheric organization of language following early left-sided brain lesions: functional MRI topography. Neuroimage. 2002;16(4):954.

Swaiman KF, Wu Y. Cerebral palsy. In: Swaiman KF, Ashwal S, Ferriero DM, editors. Pediatric neurology: principles and practice. 4th ed. Philadelphia: Elsevier Mosby; 2006.

Volpe JJ. Cerebral white matter injury of the premature infant—more common than you think. Pediatrics. 2003;112:176.

Volpe JJ. Neurology of the newborn. 5th ed. Philadelphia: Saunders; 2008.

Wen SW, Smith G, Yang Q, et al. Epidemiology of preterm birth and neonatal outcome. Semin Fetal Neonatal Med. 2004;9:429.

Xiong T, Gonzalez F, Mu S. An overview of risk factors for poor neurodevelopmental outcome. World J Pediatr. 2012;8(4):293.

6 Evaluation of Head Shape in the Pediatric Practice: Plagiocephaly vs. Craniosynostosis

Charlotte A. Beam, G. Rene Alvarez Berastegui, and Jeffrey P. Greenfield

Clinical Vignette

An 8-week-old infant presents to your office for his 2-month well visit. His parents are first time parents and explain to you that they think their child has a "funny shaped head." The child was the product of a naturally conceived, full term, unremarkable pregnancy with a natural spontaneous vaginal delivery without medical complication. He had a normal hospital stay and newborn screening was within normal limits. His developmental progress thus far is age appropriate. On examination, you are unable to palpate an anterior fontanel and you feel ridging along the top of his head. You also notice that the child's head shape seems narrow and elongated. As a practitioner, what are you thinking and how should you best proceed?

(a) The child looks like his mom, offer reassurance
(b) Send for CT scan to evaluate for sagittal synostosis
(c) Obtain an ultrasound to look for hydrocephalus
(d) Diagnosis sagittal synostosis clinically, refer for neurosurgical consultation without imaging.

C.A. Beam, M.S., C.G.C. (✉)
G.R.A. Berastegui, M.D.
Department of Neurological Surgery, Weill Cornell Medical College, 525 E. 68th Street, New York, NY 10065, USA
e-mail: Chp2027@med.cornell.edu

J.P. Greenfield, M.D., Ph.D.
Associate Professor of Neurological Surgery, Weill Cornell Medical College, 525 East 68th Street, Box 99, New York, NY 10065, USA

Answer: (d). Most forms of craniosynostosis do not require any more than an understanding of cranial morphology to diagnose. Sagittal ridging and an elongated shape are very diagnostic for sagittal suture synostosis.

Anatomy of the Infant Skull

Understanding the anatomy of the infant skull and learning some of the key physical features that distinguish plagiocephaly from craniosynostosis can aid practitioners in making accurate diagnoses and timely referrals to pediatric neurosurgeons when appropriate.

The cranial vault is composed of multiple bones (Fig. 6.1). The frontal and occipital bones make up the front and back of the skull, while paired parietal, temporal, sphenoid, and ethmoid bones compose either side. All of the bones are separated by narrow seams of fibrous connective tissue known as sutures, which remain open until the majority of brain growth is reached at age 2 [1].

The fontanels are fibrous connective tissues located between multiple cranial bones (Fig. 6.1). Newborns have six fontanels: the anterior and posterior fontanels and paired mastoid and sphenoid fontanels. The anterior fontanel, located between the frontal and parietal bones, is the most prominent of the fontanels and the one most commonly palpated when conducting pediatric physical examinations.

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_6

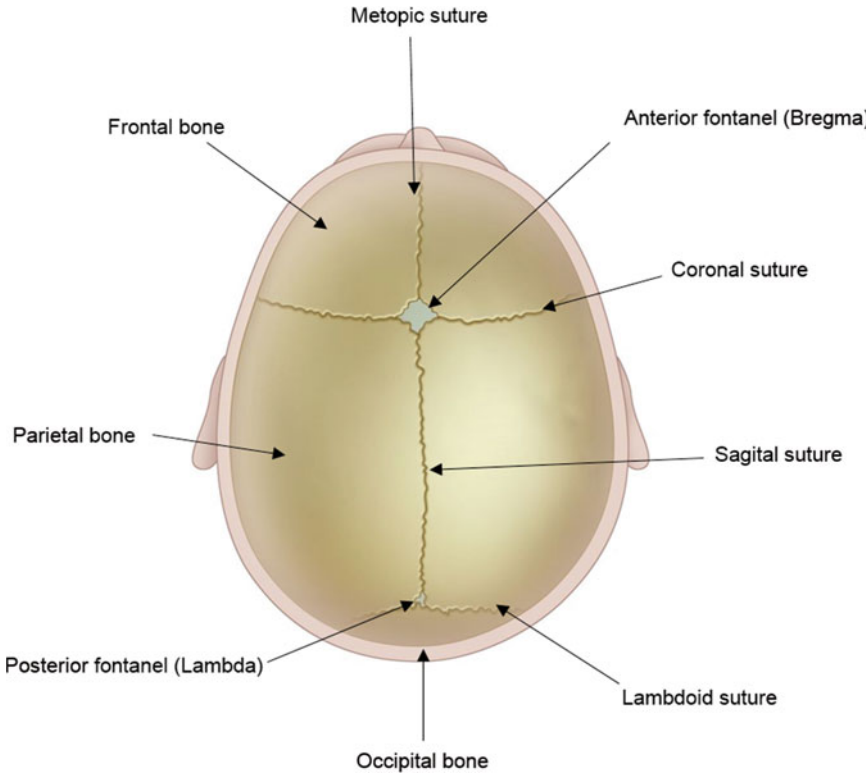


Fig. 6.1 Superior view of normal skull including the major bones, sutures, and fontanels

When examining an infant in your office, first locate the anterior fontanel to serve as a landmark to feel for the surrounding sutures. The lateral axes of the anterior fontanel make up the coronal sutures, the sagittal suture is located posterior to the anterior fontanel and the metopic suture extends anteriorly from the anterior fontanel dividing the frontal bone of the forehead. The lambdoid sutures are located in the posterior portion of the skull lateral to the posterior fontanel connecting the parietal bones with the occipital bone (Fig. 6.1).

The Anterior Fontanel

A common referral to pediatric neurosurgeons from primary care providers is for evaluation of a child's anterior fontanel. It is easy to become fixated on the fontanel being either larger or smaller than you expect, however, the anterior fontanel can vary greatly in size and time of closure. An infant's gender and race can also influence the size and closure rate of the anterior fontanel. At birth, fontanel size can range from 0.6 to 3.6 cm, with most averaging approximately 2.1 cm in size [2, 3]. Infants of African descent tend to have larger fontanels ranging from 1.4 to 4.7 cm [4]. While preterm infants can have smaller fontanels, the size is comparable to full-term infants once preterm infants reach term [5].

It is not uncommon for fontanels to increase in size after birth and this should not raise concern if developmental progress and head circumference is normal [6].

On average, the anterior fontanel closes by 13.8 months of age. Only about 1 % of infants have a closed anterior fontanel by 3 months of age and this percentage increases to 38 % by 12 months of age. Ninety-six percent of anterior

fontanels are closed by 24 months [2]. Fontanels typically close sooner in boys than in girls [5]. While early fontanel closure is most often be a normal variation, it can be associated with craniosynostosis and abnormal brain development; therefore, it is imperative that morphology is appreciated and precise head circumference measurements are obtained to exclude a pathological development [2].

Referrals to pediatric neurosurgery are also seen for the opposite finding—for the delayed closure of the anterior fontanel. While this can be a normal variant, there are a few true medical conditions associated with an enlarged or delayed closure of the anterior fontanel including achondroplasia, congenital hypothyroidism, Down syndrome, increased intracranial pressure, familial macrocephaly, and rickets.

The most common causes of raised intracranial pressure associated with bulging anterior fontanels are meningitis, encephalitis, hydrocephalus, hypoxic-ischemic injury, trauma, and intracranial hemorrhage [2]. If any of these conditions are suspected, it is important that immediate referral be made so infants can receive proper care and begin treatment if necessary.

The Posterior Fontanel

The posterior fontanel, located at the junction of the occipital and parietal bones, is usually completely closed by 2 months of age, taking the name bregma. Its normal measurement ranges from 0.5 to 1 cm, but as with the anterior fontanel, it tends to be slightly larger in infants of African ancestry with an average size of 0.7 cm compared to an average size of 0.5 cm in Caucasian infants [2].

Plagiocephaly

The term plagiocephaly is derived from the Greek word *plagios*, meaning oblique and *kephale*, meaning head.

Deformational Plagiocephaly

Also known as positional molding, deformational plagiocephaly is a common cranial deformity in children and is by far, ***the most common cause of misshapen skull in infants***. It is a term used to describe flattening on one side of the head (Fig. 6.2) [7].

When the American Academy of Pediatrics introduced the *Back to Sleep Program* in 1992 to reduce the number of infant fatalities caused by sudden infant death syndrome (SIDS), the number of referrals to pediatric neurosurgeons for deformational plagiocephaly dramatically increased. While this program has been successful at reducing the number of infant deaths attributed to SIDS by 40 % in the United States, as a result, there has been an exponential rise in asymmetric (plagiocephaly) and symmetric (brachycephaly) occipital flattening [8]. Recent studies estimate the prevalence of deformational posterior cranial flattening to be as high as 18–19.7 % in healthy infants [7, 9],

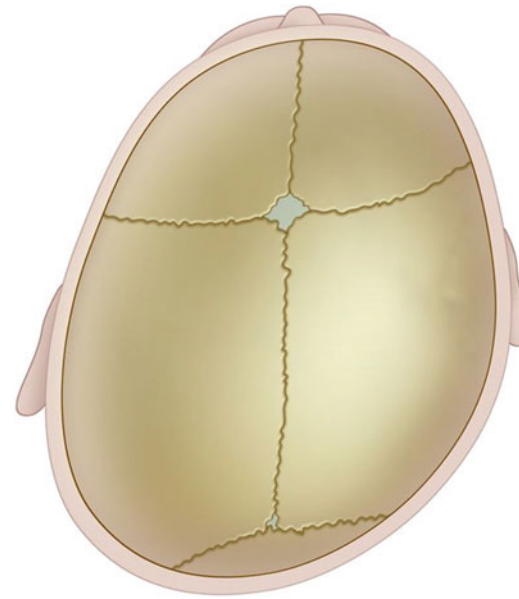


Fig. 6.2 Right posterior deformational plagiocephaly. Anterior bossing of the forehead and displacement of the ear on the ipsilateral side are consistent with a deformation rather than synostotic condition

but these calculations can vary, depending on how this entity is defined [7, 10].

Most cases of deformational plagiocephaly are caused by applied pressure to the back of the skull while an infant is sleeping in the supine position. Other predisposing factors of deformational plagiocephaly include muscular torticollis, prematurity, developmental delay, and intrauterine constraint due to multiple gestation pregnancies [7].

Diagnosis: Clinical Signs

The classic findings associated with deformational plagiocephaly include occipital flattening and contralateral occipital bulging with anterior shifting of the ipsilateral forehead (frontal bossing), ear, and cheek [7]. The shape that the skull creates from this molding, when evaluated from a vertex view, resembles a parallelogram [11, 12]. A more severe form of plagiocephaly is known as brachycephaly. The shape of a brachycephalic skull differs from plagiocephaly in that brachycephaly involves bilateral occipital flattening. This presentation does not involve ipsilateral frontal bossing or anterior displacement of the auricle.

Treatment for deformational plagiocephaly mostly relies upon behavior modification. A timely evaluation is optimal because interventions are time dependent; however, evaluation for plagiocephaly is usually not recommended before 3–4 months of age since many cases self-correct by this age [13]. After an infant receives a diagnosis of plagiocephaly, parents should be encouraged to have their child spend as little time as possible on the flattened side of the skull. This can be achieved by alternating the child's sleeping position and repositioning the crib so the infant must turn toward the non-flattened side of the skull to look toward the room. Supervised "tummy-time" is also a way to improve a flattened skull [14]. Additionally, the use of baby carriers as opposed to car seats and strollers can aid in improving the flattened part of an infant skull. An infant's skull is soft and malleable within the first 6 months; therefore, any type of repetitive positioning can influence the skull shape and ultimately result in plagiocephaly. Infants with muscular torticollis may benefit from physical therapy to address the cervical muscular contracture [10].

Helmet therapy is also a treatment option for plagiocephaly. It is not always warranted, but could be considered when the deformity is a serious cosmetic concern of the parents. However, there is minimal evidence to support the effectiveness of this method for treatment [15, 16]. There are no risks associated with helmet therapy, but mild transient skin irritation has been described as an adverse event [17].

The challenge for the pediatric primary care provider is to identify the child manifesting signs of a true cranial deformity due to premature suture fusion from amongst the majority of children being evaluated for positional plagiocephaly.

Scaphocephaly: Sagittal Synostosis

Sagittal synostosis is the most common synostosis identified in the pediatrician's office and can even be identified in the nursery by observant practitioners. It is associated with frontal bossing, bilateral occipital/parietal narrowing posterior to the anterior fontanel and decreased vertical height of the posterior cranium: a long narrow head (Fig. 6.3). Head circumferences greater than the 90th percentile can also be associated with sagittal synostosis [7].

Trigonocephaly: Metopic Synostosis

A less common but important synostosis to recognize in the office is metopic synostosis or trigonocephaly. Metopic synostosis presents with frontal narrowing, parietal widening and

Fig. 6.3 (continued) sagittal synostosis with cranial vault remodeling. Significant reduction in frontal and occipital bossing can be appreciated. In (**f**) and (**g**), pre- and post-op portrait views of a second child demonstrate how release of the sagittal suture results in a return to natural morphology and cranial balance

Fig. 6.3 Sagittal synostosis. In (**a**) the long narrow head referred to as scaphocephaly, is due to compensatory growth along the long axis of the skull secondary to restricted lateral growth. (**b**–**e**) Demonstrate before the surgery and postoperative images of a child who had a strip craniectomy for repair of sagittal synostosis. (**b**) Pre-op sagittal, (**c**) pre-op axial, (**d**) post-op sagittal, (**e**) post-op axial views of a child diagnosed and treated for

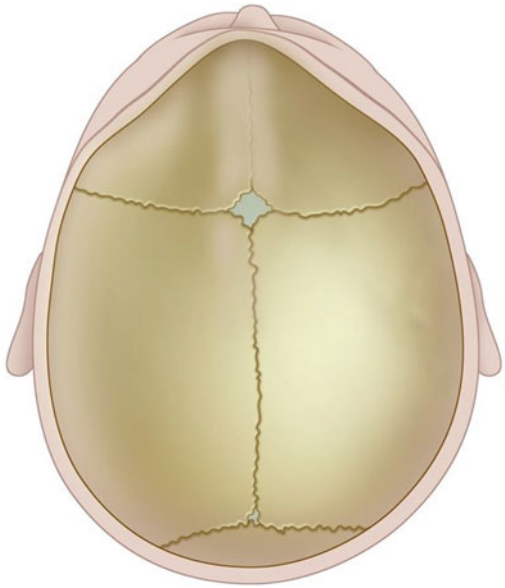


Fig. 6.4 Trigonocephaly. The pointed configuration of trigonocephaly from the vertex view is easily distinguished from metopic ridging which presents with a normally contoured forehead albeit with a distinct ridge down the center

hypotelorism, resulting in a head shape known as trigonocephaly. When evaluating infants from a vertex view, it is usually easy to examine midline pointedness of the forehead as a result of the metopic suture being fused (Fig. 6.4). While metopic synostosis is a less common form of craniosynostosis, *metopic ridging is very common*. The metopic suture can begin to fuse as early as 2 months of age and it is not uncommon for the ridging to be visible along the midline of the forehead. It is paramount to correctly distinguish metopic synostosis from metopic ridging because metopic ridging in the absence of frontal narrowing, parietal widening and hypotelorism, does not require surgical correction.

Unilateral Coronal Synostosis (UCS): Premature Closure of the Coronal Suture

This entity is characterized by flattening of the forehead and superior orbital rim with the eye protruding beyond these structures. Nasal root and midfacial angulation as well as anterior displacement of the ipsilateral ear are also physical features seen in unilateral coronal synostosis. The asymmetry in the palpebral fissures can be seen in deformational plagiocephaly as well, but the main difference is that the more open-appearing eye in deformational plagiocephaly is on the same side of increased forehead bossing, whereas in unilateral coronal synostosis, it is on the flattened forehead side The side opposite the fused and ridged coronal suture will demonstrate compensatory forehead bossing (Fig. 6.5).

Lambdoid Synostosis: Premature Closure of the Lambdoid Suture

At first glance, lambdoid synostosis may be difficult to differentiate from deformational plagiocephaly; however, in lambdoid synostosis, the cranial height is shorter on the flattened side. It is usually associated with mastoid bulging on the affected side [7], This is a rare entity and is best identified by standing behind the child and identifying the ear on the affected side as lower and more posteriorly displaced than the ear on the unaffected side. This diagnosis often requires a CT scan for verification.

Deformational Brachycephaly

Deformational brachycephaly refers to symmetrical occipital flattening and compensatory parietal widening. It is associated with little or no rounding of the back of the head and patients appear to have a disproportionately wide head when evaluated from the front. The posterior vertex may be taller than in the front with a sloped appearance of the head [7, 10].

Synostotic Brachycephaly: Bilateral Coronal Synostosis

Bilateral coronal synostosis is characterized by severe forehead retrusion, making the eyes seem more prominent. The shape the head takes in this form of synostosis is known as anterior

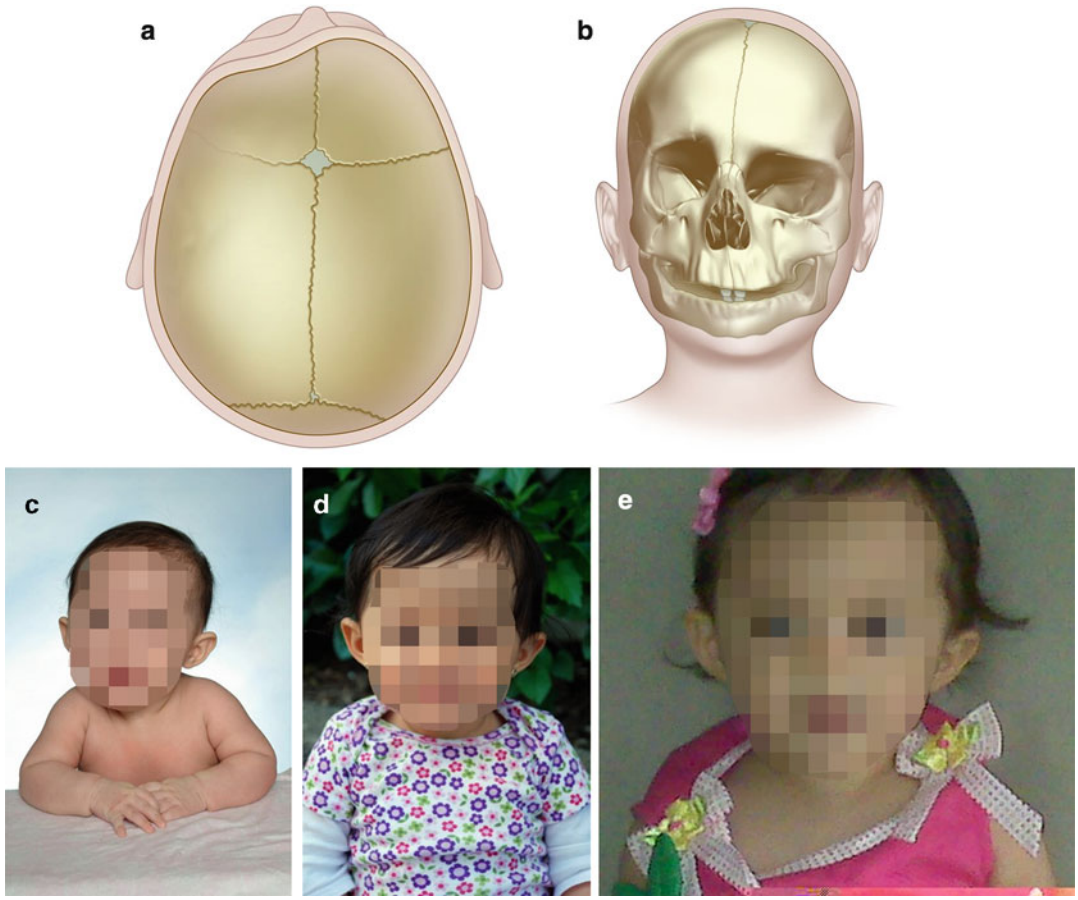


Fig. 6.5 Left unilateral coronal synostosis. (**a** and **b**) Orbital asymmetries are often the first feature noted by parents or primary care providers. Restricted growth perpendicular to the coronal sutures results in asymmetries of the facial, orbital and frontal fossa structures. Four months old (**c**), 6 months old (**d**), 1 year old (**e**). Surgery was performed at 9 months to correct the unilateral right coronal synostosis. Orbital and frontal bone symmetry has been restored by releasing the fused suture and advancing the orbit on plane with the contralateral orbital bar

turricephaly. Bilateral coronal synostosis is often associated with syndromic forms of craniosynostosis such as Crouzon disease or Apert syndrome. These children are invariably identified at birth and have multiple medical co-morbidities, thus making this diagnosis in the office would be unusual. Children with syndromes causing bilateral coronal synostosis receive urgent medical and surgical care in the first months of life and need to be followed by a comprehensive craniofacial clinic for life.

Deformational Scaphocephaly (DS)

Deformational scaphocephaly is a rare type of plagiocephaly characterized by flattening of one side of the head and a compensatory expansion at the anterior and posterior cranium. The usual shape of the head in this entity is a narrow head and sometimes associated with pronounced facial asymmetry. This head shape can sometimes be seen in premature infants secondary to undergoing shunting for hydrocephalus (Fig. 6.6).

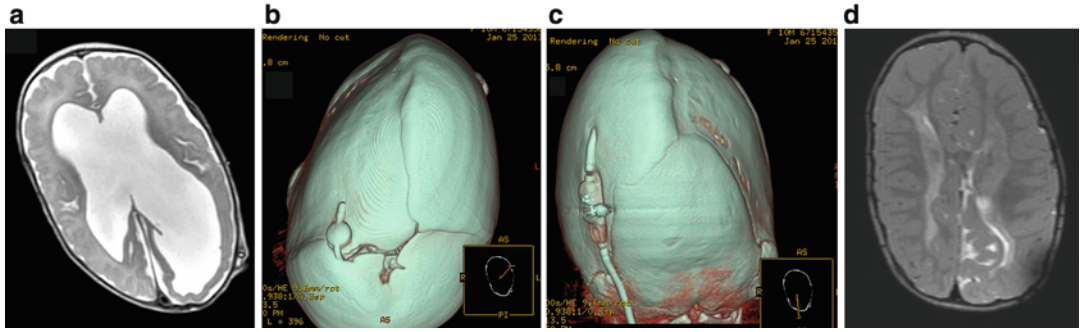


Fig. 6.6 Deformational scaphocephaly. Congenital hydrocephalus (**a**) often requires ventriculoperitoneal shunting. This can result in collapse of the calvarium and secondary deformational scaphocephaly (**b** and **c**). This can be corrected by calvarial reconstruction at an early age, resulting in both a re-expanding cortical mantle (**d**) for optimized neuro-developmental potential, plus an acceptable cosmetic result

Imaging

It is not necessary to order imaging to confirm or rule out a diagnosis of craniosynostosis. If there is still a concern of premature cranial suture fusion or cranial dysmorphology after completing a physical examination, the next step is to refer the child to a pediatric neurosurgeon. The accuracy of plain radiography to diagnose suture fusion is questionable. Computed tomography is costly, often requires sedation, and involves low-dose ionizing radiation. It is impractical to have every child with cranial flattening undergo imaging because the majority of infants with cranial asymmetry will have deformational plagiocephaly and not synostosis. A neurosurgeon can usually distinguish these processes by history and physical examination and should make the decision whether radiologic imaging is necessary in rare cases [7].

Pediatrician's Perspective

The majority of infant with cranial asymmetry have deformational plagiocephaly and not synostosis. For this increasingly common and conservatively managed condition, the diagnosis and subsequent anticipatory guidance can be provided in the pediatrician's office. Of course for concerning head shapes or those requiring another evaluation, referral to a pediatric neurosurgeon is always warranted.

Imaging should rarely be ordered by the primary care provider as the utility is usually minimal and in the cases where CT may be required, specific radiation dose-reduction protocols to allow for 3D reconstruction and appreciation of cranial morphology should be ordered by the surgeon. Of course there are symptoms requiring an *urgent* evaluation (same day office or ED), including a bulging anterior fontanel with associated signs of raised intracranial pressure such as lethargy, emesis or up-gaze paresis.

The majority of synostotic cases however, when detected in the office, warrant an *elective* referral (within days to weeks): Signs of craniosynostosis such as asymmetric orbital balance with ipsilateral flattened forehead (coronal synostosis), or a long narrow skull with bossing of the forehead or occipital region (sagittal synostosis) will make up >90 % of the craniosynostosis and require surgical evaluation from a pediatric neurosurgeon.

References

1. Wexler A. Craniofacial anatomy. In: Thaler SR, Bradley JP, Garri JI, editors. Craniofacial surgery. New York: Informa Healthcare; 2008. p. 7–40.
2. Kiesler J, Ricer R. The abnormal fontanel. Am Fam Physician. 2003;67(12):2547–52.
3. Popich GA, Smith DW. Fontanels: range of normal size. J Pediatr. 1972;80(5):749–52.
4. Faix RG. Fontanel size in black and white term newborn infants. J Pediatr. 1982;100(2):304–6.
5. Duc G, Largo RH. Anterior fontanel: size and closure in term and preterm infants. Pediatrics. 1986;78(5):904–8.

6. Pedroso FS, Rotta N, Quintal A, Giordani G. Evolution of anterior fontanel size in normal infants in the first year of life. J Child Neurol. 2008;23(12):1419–23.
7. Rogers GF. Deformational plagiocephaly, brachycephaly, and scaphocephaly. Part I: terminology, diagnosis, and etiopathogenesis. J Craniofac Surg. 2011;22(1):9–16.
8. Changing concepts of sudden infant death syndrome: implications for infant sleeping environment and sleep position. American Academy of Pediatrics. Task Force on Infant Sleep Position and Sudden Infant Death Syndrome. Pediatrics. 2000;105(3 pt 1): 650–6.
9. Hutchison BL, Hutchison LAD, Thompson JMD, Mitchell EA. Plagiocephaly and brachycephaly in the first two years of life: a prospective cohort study. Pediatrics. 2004;114(4):970–80.
10. Robinson S, Proctor M. Diagnosis and management of deformational plagiocephaly. J Neurosurg Pediatr. 2009;3(4):284–95.
11. Kalra R, Walker ML. Posterior plagiocephaly. Childs Nerv Syst. 2012;28(9):1389–93.
12. Knight SJ, Anderson VA, Meara JG, Da Costa AC. Early neurodevelopment in infants with deformational plagiocephaly. J Craniofac Surg. 2013;24(4): 1225–8.
13. Sze RW, Parisi MT, Sidhu M, Paladin AM, Ngo A-V, Seidel KD, et al. Ultrasound screening of the lambdoid suture in the child with posterior plagiocephaly. Pediatr Radiol. 2003;33(9):630–6.
14. Rogers GF. Deformational plagiocephaly, brachycephaly, and scaphocephaly. Part II: Prevention and treatment. J Craniofac Surg. 2011;22(1):17–23.
15. Goh JL, Bauer DF, Durham SR, Stotland MA. Orthotic (helmet) therapy in the treatment of plagiocephaly. Neurosurg Focus. 2013;35(4):E2.
16. Couture DE, Crantford JC, Somasundaram A, Sanger C, Argenta AE, David LR. Efficacy of passive helmet therapy for deformational plagiocephaly: report of 1050 cases. Neurosurg Focus. 2013;35(4):E4.
17. Gump WC, Mutchnick IS, Moriarty TM. Complications associated with molding helmet therapy for positional plagiocephaly: a review. Neurosurg Focus. 2013;35(4):E3.

Neurocutaneous Disorders

7

Kaleb H. Yohay and Matthew McCarthy

Abbreviations

AT	Ataxia-Telangiectasia
AVF	Arteriovenous fistula
AVM	Arteriovenous malformations
CNS	Central nervous system
CT	Computed tomography
HI	Hypomelanosis of Ito
IP	Incontinentia pigmenti
JMML	Juvenile myelomonocytic leukemia
KTS	Klippel-Trenaunay syndrome
KTW	Klippel-Trenaunay-Weber syndrome
MPNST	Malignant peripheral nerve sheath tumor
NF1	Neurofibromatosis type 1
NF2	Neurofibromatosis type 2
NF-kB	Nuclear factor kappa B
NM	Neurocutaneous melanosis
PGD	Pre-implantation genetic diagnosis
SGCT	Subependymal giant cell tumor
SWS	Sturge-Weber Syndrome
TSC	Tuberous sclerosis complex
UBO	Unidentified bright object
VHL	Von Hippel-Lindau
VS	Vestibular schwannomas

Vignette

A 2 year old boy recently moved to your city and establishes care with you. He has a reddish birthmark on his forehead and a sporadic history of seizures over his early childhood. What does this child likely have, and to what type of sub specialists should you consider referring the family?

(a) Tuberous sclerosis
(b) Neurofibromatosis Type II
(c) Neurofibromatosis Type I
(d) Sturge-Weber Syndrome

Answer: (d) SWS. Any child with a port-wine stain of the upper face (V1 or V2) should have an MRI of the brain with contrast to look for leptomeningeal angiomatosis. They should also be referred to an ophthalmologist to screen for elevated intraocular pressure or other ocular abnormalities. Established patients with SWS should be followed regularly by a neurologist and also an ophthalmologist.

Introduction

The term neurocutaneous disorders describes a broad group of diseases affecting both the nervous system and skin. While this encompasses a variety of disorders, they are classified together because of their common involvement of tissues

K.H. Yohay, M.D. (✉)
Hassenfeld Children's Center for Cancer and Blood Disorders, New York, NY 10016, USA
e-mail: Kay2003@med.cornell.edu

M. McCarthy, M.D.
Department of Pediatrics, Division of Child Neurology, Weill Cornell Medical College, 525 East 68th Street, Box 91, New York, NY 10065, USA
e-mail: Kay2003@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_7

of ectodermal origin, especially the nervous system, skin, and eyes. Most of these disorders are inherited life-long conditions that can affect many other organ systems in addition to cutaneous and neurologic manifestations. In the following sections, several neurocutaneous disorders will be discussed, with a focus on helping the practitioner recognize the clinical features of each disorder, and discussing the key aspects of their diagnosis and management. Although there are many other neurocutaneous syndromes that are not discussed in this chapter, we have focused on the more common disorders presenting in children, specifically those that often necessitate neurosurgical management.

Neurofibromatosis Type 1

Overview

Neurofibromatosis type 1 (NF1) is a common neurocutaneous disorder that affects approximately 1 in 3000 people. It is inherited in an autosomal dominant genetic pattern approximately half of the time, with the remainder of cases arising spontaneously from de novo mutations. The disorder is caused by a mutation in the NF1 gene that is located on the long arm of chromosome 17 (17q11.2) which encodes the tumor suppressor neurofibromin. NF1 is characterized by certain cutaneous findings (café-au-lait macules, freckling, cutaneous, and subcutaneous neurofibromas), but many other organ systems can be affected and, despite essentially 100 % penetrance, the clinical phenotype for the disorder is variable. Overall, though morbidity and mortality studies on people with NF1 are scant, it appears that lifespan is probably reduced by about 10–15 years compared to the general population. The most common cause of death in NF1 is malignancy.

Diagnosis

The diagnosis of NF1 is made clinically based on certain physical findings. It most commonly presents during childhood, and nearly all (97 %) of people affected with NF1 will meet the criteria for diagnosis based on clinical manifestations by 8 years of age. The diagnosis of NF1 can be made using a set of clinical criteria developed by the National Institutes of Health (see Table 7.1).

Table 7.1 NIH diagnostic criteria for neurofibromatosis type 1

An individual with 2 or more of the following signs is considered to have NF1:
1. 6 or more café-au-lait macules (must be greater than 5 mm in greatest diameter in prepubertal children and greater than 15 mm in greatest diameter after puberty)
2. 2 or more neurofibromas of any type or 1 plexiform neurofibroma
3. Freckling in the axillary or inguinal regions
4. A tumor of the optic pathway (optic glioma)
5. 2 or more Lisch nodules (iris hamartomas)
6. A distinctive osseous lesion, such as sphenoid wing dysplasia or thinning of the cortex of long bones (with or without pseudoarthrosis)
7. A first-degree relative (parent, sibling, child) diagnosed with NF1 by the above criteria

Currently, the diagnosis of NF1 is based on clinical grounds alone. Additional diagnostic testing with NF1 genetic testing is available, but of limited clinical utility. The current genetic tests are over 95 % sensitive and essentially 100 % specific. There are some exceptions where genetic testing can be helpful. For instance, in children with café-au-lait macules and characteristic freckling only, genetic testing for NF1 and SPRED1 can be useful to differentiate Legius syndrome from NF1. Genetic tests can also be useful for family planning purposes for persons with NF1 considering pre-implantation genetic diagnosis (PGD).

Clinical Manifestations

Cutaneous

Café-au-lait macules are typically the first manifestation of NF1. Nearly all patients with NF1 tend to have enough café-au-lait macules for diagnosis (99 %) by the age of 1 year. These flat, well circumscribed, evenly hyperpigmented macules are usually oval in shape with smooth borders and measure between 10 and 40 mm in diameter (see Fig. 7.1). Café-au-lait macules can

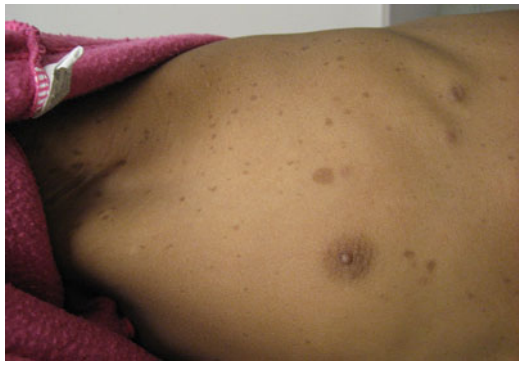


Fig. 7.1 Axillary freckling and a café-au-lait macule in a patient with NF1

be present at birth and in individuals with NF1 they tend to appear predominantly on the torso, buttocks, and legs, but can appear almost anywhere. They can increase in number and size with age, but may fade later in life. In the general population, as many as 25 % of people will have one or more café-au-lait macules without any associated disorder. Several other disorders, including neurofibromatosis type 2 (NF2), McCune-Albright syndrome, and Legius syndrome, are also known to be associated with the presence of café-au-lait spots. In particular, Legius syndrome may meet clinical criteria for NF1 with multiple café-au-lait macules and characteristic freckling. However, they do not develop other manifestations of NF1 and there is an association with a mutation in the SPRED1 gene.

Freckling is also a common cutaneous finding in NF1 with about 90 % of patients exhibiting this feature by age 7. Freckles tend to appear later than café-au-lait macules and are most commonly are found in the axillary, inguinal, or other intertriginous regions (see Fig. 7.1).

Nerve Sheath Tumors

Neurofibromas are benign nerve sheath tumors primarily composed of Schwann cells, fibroblasts, perineural cells, and mast cells. They can be classified as cutaneous, subcutaneous, or plexiform. Neurofibromas are present in about half of individuals with NF1 by 10 years of age and >80 % of people with NF1 by the age of 20. Cutaneous neurofibromas are soft, flesh-like, exophytic papules and nodules in the skin that usually present during childhood and adolescence. They can cause cosmetic disfigurement or pruritis, but are usually otherwise asymptomatic and are not known to have malignant potential. Subcutaneous neurofibromas are firm, rubbery subcutaneous nodules that can be painful or tender. Both cutaneous and subcutaneous neurofibromas are rarely present at birth and tend to appear in mid or late childhood with an increase in number and, slowly in size, as individuals age.

Plexiform neurofibromas are typically present at birth, but often do not manifest symptomatically until later in childhood or adulthood. This type of neurofibroma can be classified as either nodular or diffuse. Nodular neurofibromas can present along any peripheral nerve, including the brachial or sacral plexus and spinal nerve roots. They are typically asymptomatic, but can be painful and have the potential to cause symptoms of spinal cord compression when they involve proximal nerve roots via extension through foramina into the spinal canal. Most often they are discovered in adulthood and on neuroimaging have a typical "dumbbell" appearance. Diffuse plexiform neurofibromas tend to be found earlier in childhood. They most often appear as a soft mass under the skin and can give the overlying skin a dark or thickened appearance. These neurofibromas tend to grow with age and can become disfiguring, limit range of motion, or impair organ function. Unlike other neurofibromas, they are not limited by perineurium and can have projections into surrounding normal tissues. This, in addition to the fact that they are often highly vascular and have extensive nerve involvement, makes complete surgical resection impossible without sacrificing adjacent healthy tissue or resulting in significant loss of function.

Unlike cutaneous and subcutaneous neurofibromas, plexiform neurofibromas may undergo transformation to become malignant peripheral nerve sheath tumors (MPNSTs). MPNSTs are aggressive sarcomas that are reported to occur in around 10 % of individuals with NF1. They carry a poor prognosis and are often fatal. Malignant transformation is seen more often in deep nodular or diffuse plexiform neurofibromas. The transformation to a MPNST is often heralded by new onset of rapid or asymmetric growth of the mass

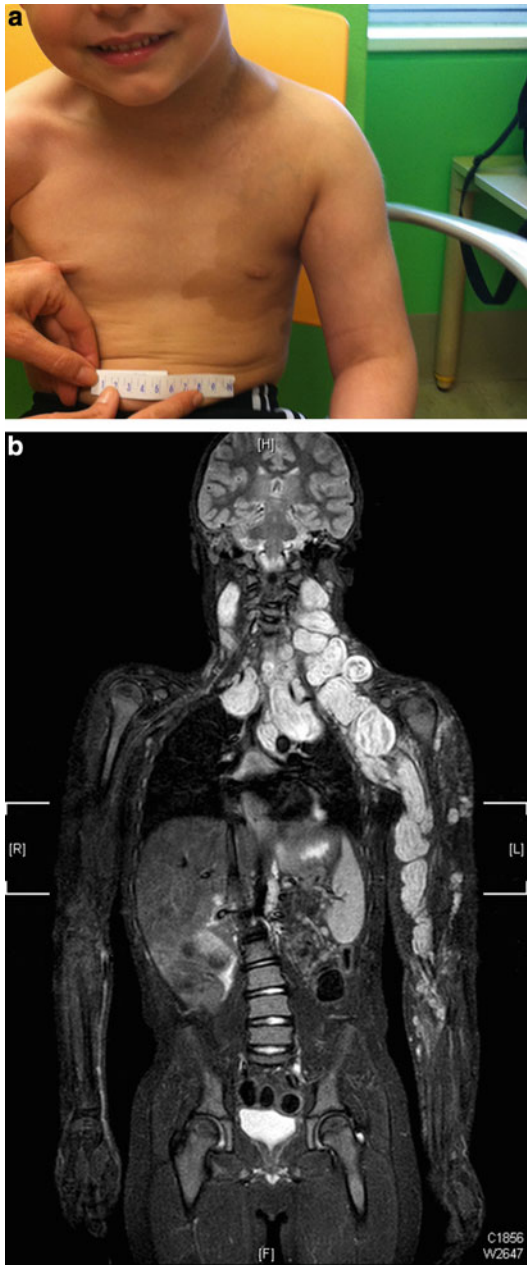


Fig. 7.2 NF1 patient with a malignant peripheral nerve sheath tumor of the left arm (**a**) with accompanying MRI (**b**)

or new onset of severe pain. Malignant transformation can be determined in part with MRI and PET imaging, though biopsy is often required (see Fig. 7.2a, b).

Currently, there are no proven medical therapies for nerve sheath tumors, and generally, surgical excision is the only treatment option despite carrying a high risk of nerve injury, bleeding, and recurrence of tumor.

Central Nervous System (CNS) Tumors

CNS gliomas are the second most common tumor seen in NF1 after neurofibromas. In contrast to sporadically occurring CNS gliomas, the gliomas seen in NF1 often behave more indolently. While most gliomas in NF1 are low-grade pilocytic astrocytomas, some people will develop high-grade tumors. Most of the CNS gliomas seen occur in the optic pathway and can be present in about 15% of individuals with NF1 (see Fig. 7.3a, b). These optic gliomas are usually asymptomatic (roughly 2/3). This benign behavior differs from optic gliomas that are unrelated to NF1. They tend to arise prior to age 4, usually in the intraorbital portion of the optic nerve, and often bilaterally. These tumors can also involve the optic chiasm and can cause precocious puberty due to their proximity to the suprasellar region. Symptomatically, optic gliomas in NF1 can cause vision loss or proptosis.

Since optic gliomas in NF1 tend to cause symptoms or progress in the first decade of life, the current recommendation is for annual ophthalmologic examination until age 6, as well as serial neuroimaging. Surgery is considered in instances of significant proptosis or visual loss, particularly in unilateral gliomas anterior to the chiasm. Chemotherapy has been effective and is most commonly used in symptomatic optic gliomas.

Brainstem tumors associated with NF1 are similarly more indolent than sporadic equivalents and often do not require any treatment. Most often they are asymptomatic, but can cause headache, ataxia, cranial neuropathies, and increased intracranial pressure that may require shunting.

Other CNS Manifestations

Unidentified bright objects (UBOs) are focal areas of T2 hyperintensity on MRI that are characteristic radiographic findings in NF1. They are not contrast enhancing and not associated with any edema or mass effect. Likewise, they are not known to be associated with any neurologic deficits. Most often they are noted in the brainstem, cerebellum, basal ganglia, or subcortical white matter. It is thought

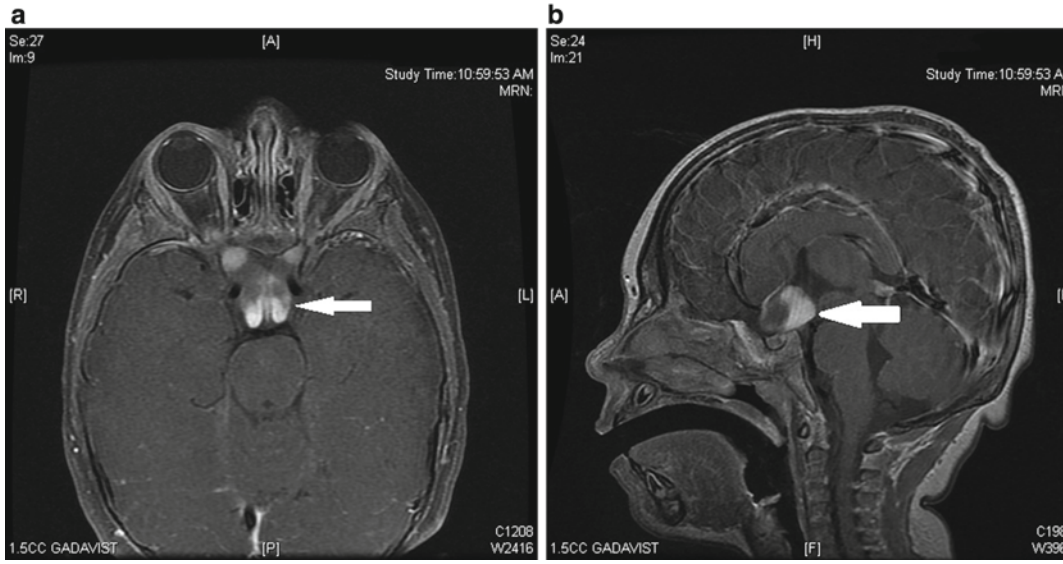


Fig. 7.3 MRI with optic glioma shown in axial (**a**) and sagittal (**b**) views

that they represent increased fluid within myelin in areas of dysplastic glial proliferation.

It has also been recognized that many people with NF1 (30–60 %) have mild cognitive deficits, particularly attention deficit hyperactivity disorder (ADHD) and learning disabilities. IQ in patients with NF1 tends to be 5–10 points lower when compared to the general population or unaffected siblings. While seizures are not a common finding in NF1, the lifetime risk of seizure is approximately twice that of the general population with an overall prevalence of 4 %. The onset of seizures varies and they can be focal or generalized. Macrocephaly also occurs in up to half of children with NF1. On occasion, it is the result of hydrocephalus from aqueductal stenosis, but more commonly it is caused by increased brain size and cerebral white matter volume.

Other Malignancies

In addition to intracranial gliomas and astrocytomas and the potential for transformation of plexiform neurofibromas to MPNSTs, there are some other malignancies associated with NF1. These include pheochromocytomas, rhabdomyosarcomas, gastrointestinal stromal tumors, and juvenile myelomonocytic leukemia (JMML). Children with NF1 have an up to 500-fold increased risk of JMML in particular.

Ophthalmologic

Lisch nodules are benign, asymptomatic iris hamartomas that present in greater than >70 % of people with NF1 by age 10. Typically, they are only visualized under slit lamp examination as raised, usually pigmented bumps on the iris. Another rare ophthalmologic complication of NF1 is congenital glaucoma.

Skeletal

NF1 has several characteristic osseous lesions that are usually apparent within the first year of life and are found in about 14 % of patients. Around 5 % of people with NF1 will have sphenoid wing dysplasia that is most commonly found incidentally on imaging of the skull with computed tomography (CT) or X-ray. Sphenoid wing dysplasia in NF1 tends to be unilateral, may or may not be associated with an overlying neurofibroma, and can be associated with compromised integrity of the bony orbit leading to proptosis or globe displacement.

Pseudoarthrosis can also be seen as a result of cortical thinning of long bone, most often causing tibial bowing (see Fig. 7.4). This occurs in up to

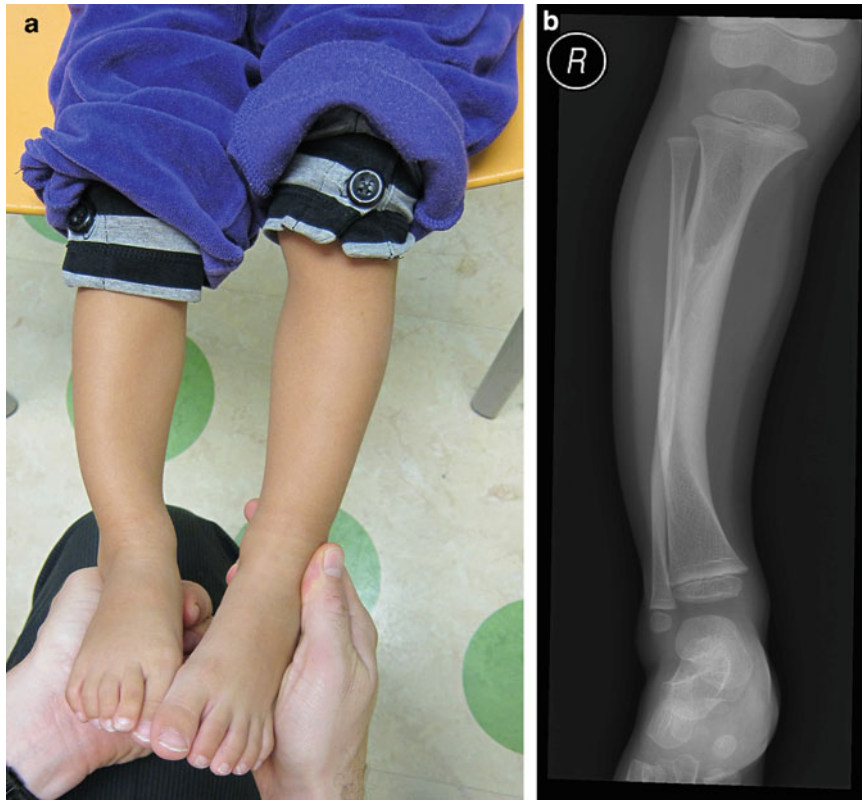


Fig. 7.4 Tibial bowing in a patient with NF1 (**a**) with accompanying radiograph (**b**)

5 % of individuals with NF1 with most cases occurring before 2 years of age. Depending on the severity, treatment can involve bracing, surgical correction, or amputation.

Scoliosis is seen up to 50 % of individuals with NF1. Cervical or upper thoracic kyphosis is most commonly seen. Most often, scoliosis is caused by distortion of vertebral bodies by neurofibromas in neural foramina or from vertebral dysplasia. Generally, scoliosis in NF1 is divided into dystrophic and non-dystrophic forms. The less common dystrophic form can be accompanied by scalloping of vertebrae, rib spindling, paravertebral soft tissue masses, foraminal enlargement, a short curve with severe apical rotation, or subluxation of a vertebral body. Dystrophic scoliosis is more likely to progress rapidly and can produce spinal cord compression causing chronic or acute neurologic symptoms. Therefore, early and aggressive surgical management is often needed. Non-dystrophic scoliosis requires management similar to idiopathic scoliosis, with close observation, bracing, and surgical fusion when indicated.

Another skeletal manifestation seen in around 30 % of NF1 patients is short stature. Children with NF1 are often vitamin D deficient and can have precocious or delayed puberty.

Cardiovascular

Patients with NF1 are at increased risk of cardiovascular abnormalities, including vasculopathy, hypertension, and congenital heart defects. Symptomatic vasculopathy is fairly uncommon, but can involve large or small vessels and result in stenosis, occlusion, aneurysm formation, or arteriovenous fistulae. The most common vascular dysplasia is renal artery stenosis, often with resultant hypertension. Renal angiography should be considered in any child with NF1 who has per-

sistently elevated blood pressure. In adults with NF1, hypertension can also be caused by pheochromocytoma or primary hypertension. Cerebrovascular abnormalities can also be seen, especially stenosis of the internal carotid arteries and the middle or anterior cerebral arteries. This can sometimes be accompanied by Moyamoya disease and present with signs and symptoms of stroke, hypoperfusion, or seizures.

Management Considerations

Due to the complex array of manifestations in NF1, it is important that patients are evaluated and managed at a center with familiarity and expertise in neurofibromatosis. Effective care requires a multidisciplinary approach that includes genetics, neurology, neurosurgery, radiology, ophthalmology, orthopedics, dermatology, plastic surgery, neuropsychology, oncology, and radiation oncology. Current recommendations for screening include biannual physicals through childhood. These exams should pay special attention to screening for hypertension, macrocephaly, scoliosis, evidence of orthopedic abnormalities, and new or changing cutaneous lesions. They should also undergo yearly neurologic and ophthalmologic examinations. Close monitoring for neuro-developmental problems is warranted and a referral should be made for formal neuropsychiatric evaluation if there are any concerns. Routine screening with imaging is not indicated and should only be performed for specific indications on history or exam. This includes focal neurologic signs or symptoms, progressive or severe headaches, visual changes, proptosis, precocious or delayed puberty, new onset of seizures, and plexiform neurofibromas of the neck or face. Baseline imaging of neurofibromas is not necessary, though MRI or PET scans should be obtained if there is any concern for transformation to an MPNST. Additionally, because of the high incidence of Vitamin D deficiency and increased risk of osteopenia, daily Vitamin D supplementation may be considered.

Neurofibromatosis Type 2

Overview

NF2 is far less common than NF1 with a prevalence of about 1:40,000. Unlike NF1, NF2 usually presents in young adults and is restricted almost entirely to tumors of the central and peripheral nervous systems (see Table 7.2). The average age of symptom onset in NF2 is around 20 years, while the average age of diagnosis is about 28. Most people present with hearing loss secondary to vestibular schwannomas or with other symptoms caused by meningiomas or spinal schwannomas. Patients presenting in childhood tend to present with signs or symptoms from tumors other than vestibular schwannomas (cranial meningiomas or spinal tumors) and tend to have a more severe phenotype.

The hallmark feature of NF2 is the development of bilateral vestibular schwannomas, often leading to deafness. Other features include meningiomas, schwannomas of cranial, spinal, or peripheral nerves, café-au-lait macules, lens opacities, and peripheral neuropathy. NF2 is also inherited in an autosomal dominant genetic pattern due to a mutation encoding the protein merlin on the long arm of chromosome 22 (22q11.2), which is thought to act as a tumor suppressor. Like NF1, as many as 50% of individuals present with NF2 as the result of a sporadic mutation. It also has nearly 100% penetrance with high phenotypic variability.

Data on the morbidity and mortality in NF2 is limited and studies are prone to sampling bias. Most patients eventually lose hearing and a third will have some degree of visual impairment. Many develop facial weakness due to tumor growth or complications of treatment and some patients also develop weakness or sensory dysfunction secondary to myelopathy, neuropathy, or brain tumor growth.

Diagnosis

The diagnosis of NF2 is made using a set diagnostic guidelines based on specific clinical findings (see Table 7.3).

Table 7.2 Features of NF1 and NF2

	NF1	NF2
Inheritance	Autosomal dominant	Autosomal dominant
Spontaneous mutations	50 %	50 %
Incidence	1:3000	1:40,000
Chromosome	17q11.2	22q12.2
Gene Product	Neurofibromin	Merlin
Typical presentation	Café-au-lait macules during infancy or early childhood	Hearing loss or vestibular dysfunction in young adulthood or cataracts
Nerve sheath tumors	Neurofibroma, plexiform neurofibroma, MPNSTs	Schwannoma
Intracranial tumors	Optic pathway gliomas, other astrocytomas/gliomas	Vestibular schwannomas, meningiomas
Spinal tumors	Nodular plexiform neurofibromas (roots)	Schwannomas (roots), ependymomas (intramedullary)
Cutaneous features	Café-au-lait macules, axillary/inguinal freckling, cutaneous neurofibromas, subcutaneous neurofibromas	Cutaneous schwannomas
Cognitive	LD and ADHD common, IQ mildly decreased	Normal
Skeletal	Scoliosis, short stature, pseudoarthrosis, sphenoid dysplasia	None
Ophthalmologic	Lisch nodules, congenital glaucoma	Juvenile subcapsular lenticular opacities, cataracts, corneal scarring, retinal hamartomas
Other tumors	CML, pheochromocytoma	None
Other neuro manifestations	UBOs, macroencephaly	Neuropathy, areflexia
Other	Vascular abnormalities, GI bleeding, constipation	

MPNST malignant peripheral nerve sheath tumor, *LD* learning disability, *ADHD* attention deficit and hyperactivity disorder, *CML* chronic myelogenous leukemia, *UBOs* unidentified bright objects
From Yohay K. Neurofibromatosis types 1 and 2. Neurologist 2006; 12(2):86–93

Table 7.3 Diagnostic criteria for neurofibromatosis type 2

NF2 can be diagnosed in individuals with one of the following:
1. Bilateral vestibular schwannomas
OR
2. First-degree relative (parent, sibling, child) with NF2 AND
(a) A unilateral vestibular schwannoma before age 30 OR
(b) Any 2 of the following: meningioma, schwannoma, glioma, neurofibroma, posterior subcapsular lenticular opacity
Presumptive or probable NF2 is diagnosed in individuals with the following:
1. Unilateral vestibular schwannomas before age 30 AND at least 1 of the following: meningioma, schwannoma, glioma, posterior subcapsular lenticular opacity
OR
2. Multiple meningiomas (2 or more) AND unilateral vestibular schwannoma before the age of 30 OR 1 of the following: schwannoma, glioma, posterior subcapsular lenticular opacity

Current testing of lymphocyte DNA from non-founder (familial) NF2 patients is about 92 % sensitive, but only about 70 % sensitive in founder (sporadic) NF2 patients. The lack of sensitivity in nonfamilial cases is likely due to the high prevalence of genetic mosaicism. As such, a positive genetic test can be helpful in confirming the diagnosis, screening family members, and possibly

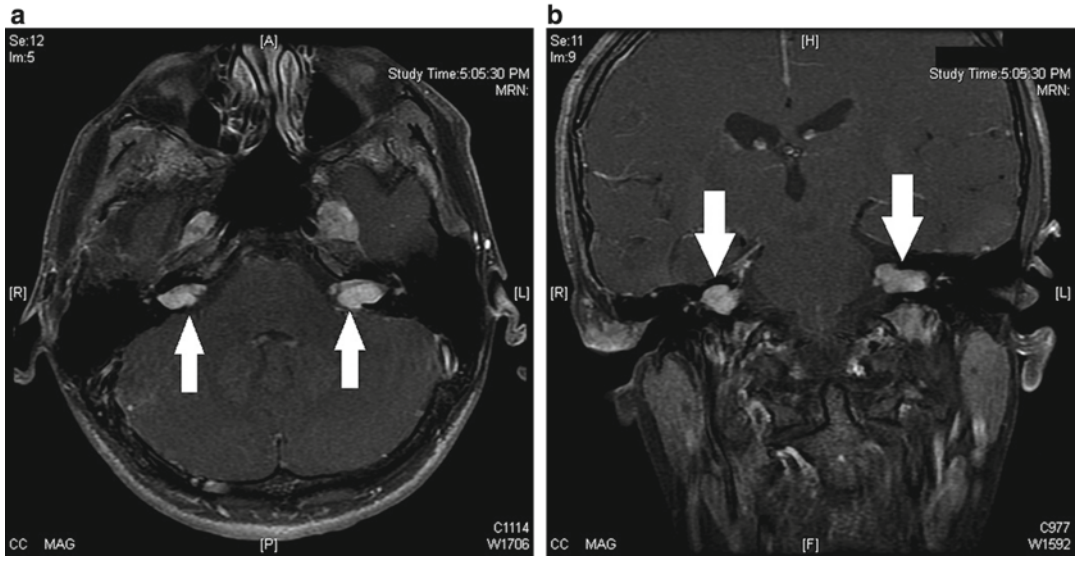


Fig. 7.5 Bilateral vestibular schwannomas in a patient with NF2 shown on MRI in axial (**a**) and coronal (**b**) views

for PGD. A negative test result does not rule out NF2 and the diagnosis must be made on the basis of the above clinical diagnostic criteria.

Clinical Manifestations

Cutaneous

While café-au-lait macules can be seen in 30–40 % of people with NF2, they are usually fewer in number compared to NF1. Additional cutaneous findings in NF2 are usually associated with underlying superficial schwannomas or cutaneous schwannomas and, less commonly, neurofibromas.

Schwannomas

Schwannomas are the cardinal feature of NF2. They are benign, encapsulated tumors that arise from Schwann cells of cranial nerves III–XII, spinal nerves, or peripheral nerves. Malignant transformation is rare for a schwannoma. While they can arise from any cranial nerve, they most commonly arise from the vestibular portion of cranial nerve VIII and are referred to as vestibular schwannomas (VS). VS can be bilateral and are present in essentially all individuals with NF2 They arise at the cerebellopontine angle and are typically slow growing, causing gradual loss of hearing (see Fig. 7.5a, b). Balance and other cranial nerve functions may become impaired and brainstem compression and obstructive hydrocephalus can occur as well.

Schwannomas arising from the dorsal spinal roots (spinal schwannomas) are present in more than 80 % of patients with NF2. Spinal schwannomas are typically small and asymptomatic, though they can become large and cause compression of the spinal cord or adjacent organs. These tumors are radiographically indistinguishable from neurofibromas arising from spinal roots in NF1 patients, frequently taking on the same "dumbbell" appearance.

Peripheral schwannomas can arise from any nerve, superficial or deep, and can cause pain or impaired motor or sensory function. Superficial peripheral schwannomas can manifest as subcutaneous nodules or as raised, well-circumscribed cutaneous lesions, often with some associated skin and hair changes. Though cutaneous schwannomas are seen in up to half of NF2 patients, they are generally a relatively minor component of the disorder.

Other Nervous System Tumors

Approximately half of patients with NF2 develop meningiomas. They are typically slow growing and can occur in the meninges of the brain, spine,

or optic nerve. Many of these meningiomas are asymptomatic, though pain and neurologic dysfunction may occur based on tumor size, location, and extent of associated edema. Ependymomas and other low-grade gliomas, including astrocytomas, are also more prevalent in patients with NF2, with an estimated incidence as high as one in three patients. The vast majority of glial neoplasms seen in NF2 patients are ependymomas. These are most often intramedullary spinal or cauda equina tumors but rarely can be intracranial.

Ophthalmologic

Visual impairment is common in the NF2 population. Juvenile posterior subcapsular lenticular opacities are common (60–80 %), though are not always symptomatic. Retinal abnormalities, particularly hamartomas are also frequently seen. Corneal injury may occur in patients with facial weakness. Optic nerve and/or orbital meningiomas are also seen in some patients with NF2 and can cause visual impairment.

Other Nervous System Manifestations

Patients with NF2 develop few neurologic manifestations other than the direct result of their tumor burden. Patients with NF2 may develop a peripheral neuropathy and hyporeflexia that is not necessarily directly related to the growth of schwannomas. Foot drop is one of the most common findings.

Management Considerations

The initial evaluation of a person with NF2 should include thorough neurologic and ophthalmologic examinations, and audiologic testing, in addition to a gadolinium-enhanced MRI of the brain with thin cuts through the internal auditory canals for most patients. Individuals with any signs or symptoms that are concerning for myelopathy should also have a spinal MRI. Genetic counseling covering genetic and/or radiologic screening for any at risk relatives should be provided. Follow-up evaluation should be done yearly with a thorough clinical/neurologic exam, audiologic testing, and brain MRI. Serial spinal MRI is only needed for patients with known symptomatic or large spinal tumors.

Treatment decisions for VS in NF2 should be made on an individual basis, taking into consideration degree of hearing loss, size and growth of the tumor, contralateral hearing function, impact on other cranial nerves and the brainstem. The primary treatment for VS is surgical resection and it carries a high risk of nerve injury, bleeding, and tumor recurrence. VS in NF2 tend to be more difficult to treat than sporadic VS because they are often multifocal along the vestibular nerve and can be associated with facial nerve schwannomas. Small (less than 1.5 cm) VS can often be resected without loss of hearing or other cranial nerve function. However, larger tumors are usually monitored and resected or debulked only with evidence of progression (clinically or radiographically) due to the higher risk of functional loss (hearing loss and facial weakness). Many centers offer cochlear implantation and auditory brainstem implants, as well as auditory rehabilitation with instruction in lip reading and signing. Stereotactic radiosurgery may be used in some cases; however, there have been mixed outcomes and concern that people with NF2 have increased risk of secondary malignancies following radiation. There has been some recent interest in using molecularly targeted therapies to treat people with NF2. A retrospective analysis of ten NF2 patients treated with bevacizumab showed that the majority of these patients showed radiographic and symptomatic improvement, and additional clinical trials are ongoing.

The treatment of other tumors in NF2 (peripheral/spinal schwannomas, ependymomas, meningiomas) is limited to progressive or symptomatic tumors. Treatment of these tumors also includes surgical resection or debulking.

Tuberous Sclerosis Complex

Overview

Tuberous sclerosis complex (TSC) is an autosomal dominant genetic disorder that affects multiple organ systems and is primarily characterized

by the development of benign neoplasms of the brain, skin, and kidneys. The incidence of TSC has been reported to be as high as 1 in 5800. TSC is only inherited in 30 % of cases and results from a spontaneous mutation in the remaining 70 %. Two distinct genes have been identified as causative of TSC: TSC1 located on chromosome 9q34 and TSC2 located on chromosome 16p33.3. TSC1 encodes for a protein called hamartin while TSC2 encodes for a protein called tuberin. These two proteins interact to form a complex that has been shown to be integral in multiple intracellular signaling pathways. TSC has near 100 % penetrance but with wide phenotypic variability. Patients with mutations in TSC1 may have a milder phenotype compared to those with mutations in TSC2. Neurologic disease, particularly subependymal giant cell tumors (SGCTs), status epilepticus, and renal disease including renal cell carcinoma and hemorrhage into angiomyolipomas, are the most common causes of premature death in TSC.

Diagnosis

TSC is generally diagnosed based on clinical findings (see Table 7.4). While genetic testing is available, it has a limited clinical utility due to poor sensitivity.

Table 7.4 Clinical criteria for diagnosing tuberous sclerosis complex

TSC can be diagnosed based on the following clinical criteria:
1. To be diagnosed with definite TSC, a patient must have 2 major features AND 2 minor features
2. To be diagnosed with probable TSC, a patient must have 1 major feature AND 1 minor feature
3. To be diagnosed with possible TSC, a patient must have 1 major feature OR >1 minor features
Major features:
• Facial angiofibromas or forehead plaque
• Nontraumatic ungual or periungual fibroma
• Hypomelanotic macules (3 or more)
• Shagreen patch (connective tissue nevus)
• Multiple retinal nodular hamartomas
• Cortical tuber[a]
• Subependymal nodule
• Subependymal giant cell astrocytoma
• Cardiac rhabdomyoma, single or multiple
• Lymphangiomyomatosis[b]
• Renal angiomyolipoma[b]
Minor features
• Multiple randomly distributed pits in dental enamel
• Hamartomatous rectal polyps[c]
• Bone cysts[d]
• Cerebral white matter radial migration lines[a]
• Gingival fibromas
• Nonrenal hamartoma[c]
• Retinal achromic patch
• "Confetti" skin lesions
• Multiple renal cysts[c]

[a]When cerebral cortical dysplasia and cerebral white matter migration tracts occur together, they should be counted as one rather than two features of tuberous sclerosis
[b]When both lymphangiomyomatosis and renal angiomyolipomas are present, other features of tuberous sclerosis should be present before a definite diagnosis is assigned
[c]Histologic confirmation is suggested
[d]Radiographic confirmation is sufficient

Clinical Manifestations

Cutaneous

Cutaneous lesions are very common and often the initial manifestation that leads to an eventual diagnosis of TSC. The most common skin lesions are hypomelanotic macules, previously known as Ash Leaf lesions. Despite occurring in nearly all individuals with TSC (up to 97 %), these hypomelanotic macules are not specific to TSC. They are often present from birth and can increase in number with age. While they can appear anywhere on the skin, they tend to be more commonly seen on the trunk and buttocks.

Facial angiofibromas (previously termed adenoma sebaceum) are pink or reddish papular lesions involving the cheeks and naso-labial folds, typically in a malar distribution and sparing the upper lip. Up to 75 % of people with TSC will have facial angiofibromas, often appearing in childhood and becoming more prominent with age. As many as 20 % of patients with TSC will have forehead fibrous plaques, which are raised brown or flesh-colored plaques comprised of coalesced nodules.

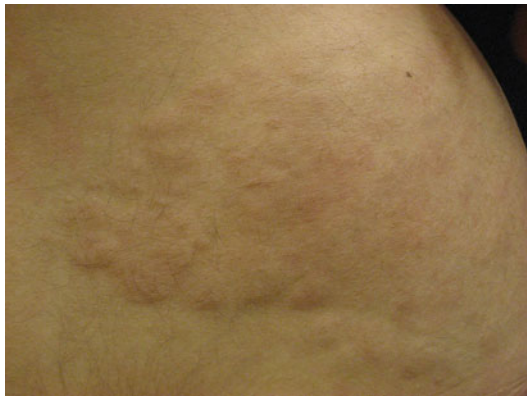


Fig. 7.6 Shagreen patch in a patient with TSC

Shagreen patches are irregular areas of raised, rough skin that has been described as having the texture of an orange peel (see Fig. 7.6). About half of people with TSC will have this finding, usually becoming evident around puberty. The most common location for a Shagreen patch is in the lumbosacral region.

Periungual or subungual fibromas are pink or flesh-colored nodules that grow in the finger or toe nail beds in patients with TSC. They are seen in about 20 % of patients with TSC and are more commonly found in adolescents or adults.

CNS Tumors

Neurologic complications of TSC are very common and are one of the main causes of morbidity and mortality. Cortical tubers are seen in up to 95 % of patients with TSC. They are composed of disorganized neurons and dysmorphic giant astrocytes. The typical six-layered lamination pattern of neurons in the cortex is lost and the bordering zone between gray and white matter becomes indistinct. In patients with TSC, the number of cortical tubers correlates with the severity of seizures and cerebral dysfunction.

Individuals with TSC also commonly have white matter lesions. These lesions may represent areas of demyelination, dysmyelination, hypomyelination, and/or heterotopic neurons or glia along cortical migration paths.

Subependymal nodules are present in the majority of patients with TSC. They are hamartomatous growths comprised of dysplastic astrocytes and auroral cells located in the subependymal region along the walls of the lateral ventricles.

Subependymal giant cell tumors (SGCTs, formerly called subependymal giant cell astrocytomas or SEGAs) are low-grade glioneuronal tumors seen in approximately 15 % of patients with TSC. They tend to originate near the foramen of Monroe, and as a result, often cause obstructive hydrocephalus and may require surgical resection or medical therapy with everolimus.

Other Nervous System Manifestations

Seizures are a very common cause of morbidity in TSC. The incidence of epilepsy and seizures probably exceeds 95 %. They typically begin during infancy or early childhood, with the incidence decreasing with increasing age. The seizures seen in TSC can be generalized or partial in onset. Infantile spasms are present in approximately 1/3 of patients with TSC.

Behavioral and cognitive impairments are common in TSC with a majority of patients showing some amount of intellectual impairment and greater than 60 % being diagnosed with behavioral problems including autism spectrum disorders, ADHD, or obsessive compulsive disorder. In TSC, the incidence of autism spectrum disorders is likely greater than 25 % with a higher incidence in patients with global intellectual impairment compared to those with normal intelligence. Roughly half of patients with TSC meet diagnostic criteria for ADHD.

Ophthalmologic

Retinal abnormalities can be seen in patients with TSC that are most often asymptomatic and only rarely cause loss of vision. Retinal hamartomas are seen in about 50 % of patients with TSC. Punched out areas of retinal depigmentation, angiofibromas of the eyelid, strabismus, or colobomas can also be seen.

Cardiac

The most common cardiac manifestation of TSC is cardiac rhabdomyoma. These can be found in 1/2 to 2/3 of newborns with TSC. Although most do not cause any significant medical problems

and regress spontaneously with age, they can cause symptoms of heart failure, arrhythmia, or murmurs.

Renal

The most common renal complication of TSC is the growth of angiomyolipomas which are seen in up to 80 % of patients. Angiomyolipomas are benign tumors composed of immature smooth muscle and fat cells and abnormal blood vessels. They most often remain asymptomatic, despite being multiple and bilateral in many cases. Angiomyolipomas can cause renal failure or hypertension by disruption of normal kidney tissue or hemorrhage from aneurysm formation. Hemorrhage can be a life-threatening complication seen more often in angiomyolipomas larger than 4 cm and so they are often treated with embolization. Renal cysts are also common in TSC, and like angiomyolipomas can present bilaterally and cause renal insufficiency or hypertension. A relationship between TSC and renal carcinoma has been postulated but not yet clearly established.

Pulmonary

Lymphangioleiomyomatosis is characterized by proliferation of atypical smooth muscle-like cells in the lungs and progressive cystic destruction of lung tissue. It presents with dyspnea, hemoptysis, chest pain, chylothorax, and/or pneumothorax. Lymphangioleiomyomatosis is a chronic, sometimes progressive illness most commonly seen in young adult women with TSC.

Management Considerations

At diagnosis, an MRI of the brain with and without gadolinium is indicated to evaluate for cortical tubers, subependymal nodules, SGCTs, white matter abnormalities, and hydrocephalus. For children and adolescents diagnosed with TSC, a follow-up MRI should be obtained every 1–3 years. In cases where an SGCT is identified, consideration should be given to increasing monitoring frequency.

Renal ultrasound is the initial study that should be performed at diagnosis to evaluate for renal cysts and/or angiomyolipomas. Repeat ultrasounds should be performed every 1–3 years, with the frequency varying based on the presence or absence of lesions. For larger lesions or concern about malignancy, CT or MRI can be considered. Cardiac ultrasound to evaluate for rhabdomyomas should be considered for infants with TSC who have a heart murmur, arrhythmia, or signs of heart failure.

Because TSC can have a very complex presentation involving multiple organ systems, it is important to ensure that patients have access to multiple medical specialties, preferably in a multidisciplinary clinic with familiarity and expertise in the care of patients with TSC. Coordinated multidisciplinary care should include specialists from genetics, neurology, neurosurgery, radiology, ophthalmology, dermatology, plastic surgery, neuropsychology, and oncology. In addition to the radiographic screening already discussed, patients with TSC should be followed with annual general, neurologic, skin, and ophthalmologic examinations, as well as academic and developmental screening.

Specific treatment for TSC is dependent on the particular manifestations in an individual patient. Seizures can be one of the more challenging aspects to treat in TSC. The particular therapy is dependent on multiple factors, including seizure type, severity, age, and EEG findings. For children with TSC and infantile spasms, Vigabatrin is the treatment of choice, though ACTH may be nearly as effective. Many individuals will require multi-drug regimens and the medication should be tailored to the specific type of seizure present. For patients with medically intractable seizures, the initiation of the ketogenic diet, implantation of a vagal nerve stimulator, or surgery may be indicated. Surgery is increasingly becoming an option, particularly for patients with an identifiable epileptogenic focus.

SGCTs causing focal neurologic deficits, obstructive hydrocephalus, or growth on serial imaging should be considered for treatment. For many years, surgical resection or radiation was the only available option. Radiation has fallen out of favor due to the increased risk of secondary malignancy in TSC (similar to other tumor predisposi-

tion syndromes, like NF1 and NF2). Recently, everolimus, an mTOR inhibitor, was approved as medical therapy for SGCTs in TSC for whom surgical resection is not desired. Other mTOR inhibitors are currently being investigated.

Due to the risk of hemorrhage, it is recommended that patients with angiomyolipomas larger than 3–4 cm be considered for embolization, or partial or total nephrectomy. Initial studies also suggest that mTOR inhibitors may decrease the size of angiomyolipomas, and trials are in progress. Hormonal manipulation, bronchodilator therapy, and alpha-interferon are all used for the treatment of Lymphangioleiomyomatosis with uncertain benefit. Asymptomatic cardiac rhabdomyomas do not require any treatment and will all undergo spontaneous regression. Rarely, surgical resection is required in symptomatic infants.

Sturge-Weber Syndrome

Overview

Sturge-Weber Syndrome (SWS) is a congenital neurocutaneous disorder that occurs in about 1 in 50,000 people that is characterized by several clinical findings, including a "port-wine stain" of the upper face or forehead, leptomeningeal angiomatosis, and vascular abnormalities of the eye. The most common problems for patients with SWS are seizures, glaucoma, hemiparesis, visual field deficits, stroke-like episodes, headaches, and cognitive or behavioral issues. SWS is a sporadic disease without any well-established genetic or environmental risk factors. Recently, it was shown that SWS and port-wine stains are associated with a somatic activating mutation in the GNAQ gene. While port-wine stains are a hallmark feature of SWS, they are one of the most common occurring vascular malformations (around 3 in 1000) and most children with a port-wine stain do not have SWS. The long-term clinical outcome and prognosis for SWS varies greatly, as does the range of severity of symptoms. In general, individuals with more extensive involvement of the brain, bilateral disease, higher seizure frequency, and larger areas of leptomeningeal angiomatosis will have worse outcomes.

Diagnosis

The diagnosis of SWS must be confirmed radiographically with evidence of leptomeningeal angiomatosis on an MRI of the brain with gadolinium. The presence of port-wine stains on the upper face is not specific for SWS and the diagnosis cannot be made until leptomeningeal angiomatosis has been confirmed. There are currently no standardized guidelines for testing asymptomatic children with port-wine stains. The risk of significant neurologic or ocular findings in a child with any port-win stain is approximately 8–10 %. However, the risk increases to almost 75 % if the port-wine stain involves the entire V1 distribution of the trigeminal nerve. Rarely, patients will be diagnosed with SWS without a port-wine stain (presence of leptomeningeal angiomatosis on MRI). These cases tend to present later in life and are often less severe. Currently, there are no laboratory tests that are useful for diagnosing SWS.

Clinical Manifestations

Cutaneous

Port-wine stains (or nevus flammeus) are red or purple-colored blanching lesions that represent deoxygenated blood in underlying dilated veins. They can be present anywhere on the body, but only port-wine stains presenting in the V1 and V2 dermatomal distribution of the trigeminal nerve are associated with SWS. Involvement of the upper or lower eyelid also increases the risk of SWS. In SWS, the port-wine stain is usually unilateral, but can be bilateral as well. Port-wine stains are always present at birth, even though many of the symptoms of SWS do not appear until much later. Port-wine stains do not directly cause any of the neurologic symptoms seen in SWS.

Nervous System

Leptomeningeal angiomatosis describes capillary-venous malformations of the pia and arachnoid mater. The presence of this finding on MRI is essential to make the diagnosis of SWS. It can occur in any area of the brain ipsilateral to the port-wine stain and most often is present over

the occipital area. It is seen best on T1-weighted MRI imaging with gadolinium as enhancement of the meninges. Associated findings on MRI include atrophy of the ipsilateral brain, white matter changes, and enlargement of the choroid plexus. It is important to note that the brain findings in SWS typically evolve and worsen over time, and therefore, imaging studies can be negative early on.

Epilepsy is diagnosed at some point in up to 75 % of people with SWS and unilateral port-wine stain and up to 90 % of people with SWS and bilateral port-wine stain. The seizures seen in SWS are usually focal motor or complex partial seizures, but generalized seizures can also occur. Focal seizures are usually the earliest symptom seen in SWS and can begin as early as infancy. However, seizures may not present until later in childhood or even adulthood in some cases.

Other symptoms commonly seen in infancy include other features representing unilateral brain dysfunction, including hemiparesis, gaze preference, or early handedness. Fifty percent of patients with SWS will at some point experience hemiparesis or a visual field deficit. People with SWS can also have stroke-like symptoms with an acute onset of functional deficits, which may slowly recover and do not return to the previous baseline.

Headache is a common complaint (almost 50 %) in individuals with SWS, especially migraines. While the treatment of headaches in SWS does not differ from the standard treatment of headaches in children, there is some thought that headaches in SWS may precede seizures or stroke-like episodes. Therefore, aggressive treatment and prevention is often recommended.

Cognitive and behavioral problems in SWS include language delays, mood problems, anxiety, hyperactivity, and inattention. It is important to screen children with SWS for developmental and behavioral issues, using formal neuropsychological testing when indicated.

Ophthalmologic

Vascular malformations of the eye can be seen in SWS, including choroid hemangiomas. The incidence of glaucoma in SWS is reported as high as 70 %. It always involves the side of the port-wine stain in unilateral disease, but can be unilateral or bilateral when seen in conjunction with bilateral port-wine stains. It often presents in early childhood (60 %) or later in childhood or adulthood. The presence of a port-wine stain involving the upper and lower lid and the presence of episcleral hemangioma are independently associated with a higher risk for developing glaucoma.

Management Considerations

Any child with a port-wine stain of the upper face (V1 or V2) should have an MRI of the brain with contrast to look for leptomeningeal angiomatosis. They should also be referred to an ophthalmologist to screen for elevated intraocular pressure or other ocular abnormalities. Established patients with SWS should be followed regularly by a neurologist and also an ophthalmologist. There is no known treatment for the underlying cause of SWS, which is abnormal vasculature and associated leptomeningeal angiomatosis. Therefore, treatment should be targeted at treating specific manifestations of the disease.

Children with asymptomatic SWS or suspicious port-wine stains should be counseled on the signs and symptoms of seizures due to the high risk of epilepsy. Because of this high risk, a long-term anti-epileptic drug should be started with the first seizure episode. Medications like carbamazepine or oxcarbazepine that are effective treatments for partial seizures should be considered as first-line treatment. Other medications, including topiramate, levetiracetam, phenobarbital, and valproate are also often used. Individuals with SWS can develop status epilepticus and prescribing rectal diazepam should be considered. In cases of medically refractory epilepsy, respective brain surgery should be considered. Despite significant morbidity associated with surgery, there is some evidence that patients with SWS can become seizure free after hemispherectomy. Aspirin therapy has been used to treat SWS, as one of the proposed mechanisms of injury is venous stasis causing microthrombi and ischemia. Low dose aspirin use may reduce the number of seizures, though studies are lacking. Glaucoma should be treated with topical medications first. Surgical intervention with trabeculectomy is an

option after failed medical treatment. Port-wine stains are not thought to cause any symptoms in SWS, but are often treated for cosmetic purposes. While the lesions do not typically grow with age, they can become thickened and more rough-textured. Laser therapy can be used to reduce the discoloration and make the lesion less noticeable.

Von Hippel-Lindau

Overview

Von Hippel-Lindau (VHL) is an inherited disease occurring in about 1 in 36,000 people that is characterized by neoplasms in several organ systems. The neoplasms are caused by inactivation of the tumor suppressor VHL located on chromosome 3p25. Although the cancers seen in VHL most commonly are discovered in adulthood, they can first manifest in adolescence. VHL is an autosomal dominant disorder, but can be caused by a sporadic mutation in 20 % of affected individuals. Clinical outcomes vary widely in VHL and depend on the clinical presentation in each individual. The most common cause of death is renal cell carcinoma. However, significant morbidity can be seen from neurologic impairment secondary to CNS hemangioblastomas or visual impairment from retinal angiomas.

Diagnosis

While diagnosis of VHL may be suspected based on the clinical presentation with certain neoplasms, the diagnosis can be made definitively via molecular testing for the VHL gene. Any person found to have one of the tumors characteristic for VHL or any individual with an affected parent should undergo testing. Genetic testing is almost 100 % sensitive and specific for VHL. In persons with no family history of VHL, the diagnosis can be made clinically based on having either (a) two or more hemangioblastomas of the CNS or (b) one retinal or brain hemangioblastoma in addition to any one of: pheochromocytoma, renal cell carcinoma, serous cystadenoma or neuroendocrine tumor of the pancreas, papillary cystadenoma of the epididymis, or broad ligament. With a family history of VHL, the diagnosis can be made clinically with any one of renal cell carcinoma (before age 60), CNS hemangioblastoma, retinal angioma, pancreatic cysts, and cystadenomas of the epididymis or broad ligament. It is possible to test for a VHL mutation in a fetus with amniocentesis or chorionic villus sampling and PGD is available.

Clinical Manifestations

The cancers commonly seen in VHL include hemangioblastomas of the brain or spinal cord (40–70 %), clear cell renal cell carcinoma (70 %), retinal angiomas (also called retinal hemangioblastomas) (60 %), serous cystadenomas (70 %) or neuroendocrine tumors of the pancreas (15 %), papillary cystadenomas of the epididymis (40 %), endolymphatic sac tumors of the ear (15 %), and pheochromocytomas (10 %). CNS hemangioblastoma is the most common tumor seen in VHL. They are highly vascular, often multifocal along the craniospinal axis. They can cause symptoms based on mass effect, including headache, emesis, hyperreflexia, ataxia, dysmetria, or ataxia depending on the specific location of the tumor.

Management Considerations

Currently, there are no formally assessed guidelines for screening asymptomatic patients with VHL. Expert opinion suggests that individuals with VHL should undergo annual screening physical exams, urine screening with cytology for renal cell carcinoma, renal ultrasound, ophthalmologic examination (including fluorescein angiography), 24 h urine collection of vanillylmandelic acid levels, and abdominal ultrasound. Every 3 years, MRI of the brain and spine (up until age 50, then every 5 years after) and abdominal CT should be done as well.

Therapies for VHL should be directed at the specific presentation and does not differ from the treatments used for isolated instances of each problem.

Neurocutaneous Melanosis

Overview

Neurocutaneous melanosis (NM) is a rare sporadic disorder characterized by the presence of large congenital nevi in addition to leptomeningeal melanosis. NM is thought to be caused by an abnormal differentiation of neural crest cells during embryologic development leading to increased numbers of melanocytes in the leptomeninges, in addition to cutaneous melanosis. NM has a highly variable presentation, and therefore, prognosis can differ greatly between individuals.

Diagnosis

The diagnosis of NM is often made in infants and can be made using clinical criteria (see Table 7.5). This set of criteria helps distinguish NM from malignant melanoma unrelated to NM which can often metastasize to the CNS. Skin biopsy can be done to confirm the diagnosis of cutaneous nevus and also rule out malignant melanoma. MRI with contrast can show CNS lesions consistent with leptomeningeal melanosis.

Clinical Manifestations

Cutaneous

Congenital nevi are benign melanocytic lesions that can be seen in as many as 2 % of newborns. A congenital nevus is considered large or giant when it measures greater than 20 cm in adults or 9 cm on the head or 6 cm on the trunk of an infant. Giant nevi are usually bilateral and most frequently occur in a "bathing trunk" or "garment" pattern over the lumbar and sacral areas. While metastatic melanoma is a distinct entity from NM, there is an increased risk of melanoma in individuals with NM.

Table 7.5 Diagnostic criteria for neurocutaneous melanosis

1. One large congenital nevus (20 cm or greater in adults; 9 cm or greater on the head or 6 cm or greater on the trunk of an infant) OR 3 smaller congenital nevi, together with either leptomeningeal melanosis or melanoma
2. No cutaneous melanoma except when examined areas of meningeal lesions are histologically benign
3. No melanoma of the meninges except when examined areas of the cutaneous lesions are histologically benign

Nervous System

Leptomeningeal melanosis can often be asymptomatic and is often only seen on imaging done as a screen. Neurological manifestations are variable and depend on the extent and location of CNS melanosis. Neurologic manifestations will often arise in the first year of life and are most commonly increased intracranial pressure or hydrocephalus. Children with NM can also have seizures. The extent of cutaneous nevi does not seem to correlate with the extent of CNS involvement.

Another common CNS abnormality seen in approximately 10 % of children with NM is Dandy-Walker malformation (enlarged posterior fossa, complete or partial absence of cerebellar vermis, enlarged cystic fourth ventricle, and hydrocephalus). Patients with NM and Dandy-Walker malformation have a poor overall prognosis and often die during the first decade of life.

Management Considerations

Treatment of the cutaneous manifestations of NM is pursued for both cosmetic reasons and because of the high risk of malignant transformation. Some advocate for complete resection, though this is controversial due to the extent of surgical resection often required. Regular dermatologic assessments should be done as well. Resection of cutaneous nevi does not affect the risk of malignant transformation in the CNS.

Treatment of neurological manifestations in NM is directed at specific causes. Surgical resection can alleviate symptoms depending on the size and location of CNS melanosis. Also, ventriculoperitoneal shunt may be required for treatment of hydrocephalus. If no symptoms are present, regular imaging is necessary to monitor for progression and malignant transformation.

Incontinentia Pigmenti

Overview

Incontinentia pigmenti (IP) is an X-linked dominant disorder caused by a mutation in the gene for nuclear factor kappa B (NF-kB) essential modulator. IP affects the skin, central nervous system, teeth, eyes, and sometimes other organ systems. IP has a highly variable clinical presentation and is almost exclusively found in females as nearly all males die in utero. It is important to note that infants with IP often have many findings that suggest non-accidental trauma, including retinal hemorrhage, brain ischemia, and cutaneous findings that can be interpreted as evidence of abuse. It is important to ask about a family history of other females with similar findings in infancy.

Diagnosis

The diagnosis of IP is suspected based on clinical findings as well as family history. Nearly, all patients with IP will have stage 3 skin lesions and most will also have stage 1 and 2 findings (see section below). These cutaneous findings in association with tooth, eye, and nervous system manifestations suggest the diagnosis of IP. Genetic testing is available to confirm the diagnosis.

Clinical Manifestations

Cutaneous

Skin findings in IP are generally described in four stages. Stage 1 is usually apparent in the first 2 weeks of life and is known as the vesiculobullous, vesicular, or inflammatory stage. It consists of erythematous vesicles or blisters, often in a linear pattern on the limbs and trunk and sparing the face. Stage 2 is the verrucous stage, which is characterized by wart-like lesions replacing the stage 1 vesicles or arising in new areas usually starting around 2 months of life. Stage 3 is characterized by brown or gray hyperpigmented areas with a pattern of "whorls and streaks" following Blaschko's lines located on the body and limbs, especially in the groin, axillae, and nipples. Stage 3 typically begins between 3 and 6 months of age and persists for many years. Stage 4 is the atrophic stage, during which mildly hypopigmented and hairless patches of skin are seen, most often on the posterior of the calves.

Nervous System

CNS abnormalities are not universally seen in IP, but can account for significant morbidity. Approximately 25 % of people with IP will have seizures, which is associated with a worse neurologic outcome. In 10 % of patients there will be cerebral palsy and/or intellectual disability. Other symptoms that have been reported include hemiparesis, cerebellar ataxia, microcephaly, and abnormalities seen on imaging, including heterotopias, atrophy, ischemic processes, hemorrhagic necrosis, and abnormalities of the corpus callosum.

Other Organ Systems

The teeth are affected in 70–90 % of people with IP. Dental abnormalities can include delayed dentition, missing or extra teeth, and conical or peg shaped teeth. Ophthalmologic complications are seen in about one third of people with IP. These can include vascular retinopathy, retinal detachment, optic atrophy, eye misalignment, nystagmus, and microphthalmia. Ocular manifestations are closely linked to CNS disease in IP. The hair and nails of individuals with IP are often affected and they can have alopecia and ridging or pitting of the nails.

Management Considerations

There is no specific treatment for IP and therefore treatment is directed by symptom presentation. Skin findings typically do not require treatment, but should be followed by a dermatologist. Dressings should be applied to vesicular stage lesions in order to prevent infection. Full eye examination and close follow-up with an ophthalmologist are required to monitor of ocular manifestations. Neurologic complications, such as seizures, spasticity, and developmental delay, should be treated with conventional methods.

Hypomelanosis of Ito

Overview

Hypomelanosis of Ito (HI) describes the characteristic skin and nervous system findings caused by underlying genetic mosaicism and chimerism. The typical skin findings in HI are usually present at birth (50 %) or become evident during infancy. HI is not a distinct disease entity, but rather represents a broad range of overlapping clinical phenotypes and has an estimated incidence of about 1 in 8000.

Diagnosis

The diagnosis of HI is based on clinical findings. The diagnosis can be supported by finding chromosomal alterations or mosaicism on a karyotype, but this is typically not necessary.

Clinical Manifestations

Cutaneous

The characteristic skin findings in HI are unilateral or bilateral hypopigmented areas often described as whorls, streaks, and patches that generally, but not always, follow the lines of Blaschko. The lesions are more easily visualized in darker skinned infants and can be made more visible using ultraviolet light for light skinned individuals. These lesions can be mistaken for stage 3 skin findings in IP. However, HI lacks the preceding inflammatory skin stages seen in IP.

Nervous System

Nervous system involvement is common and estimated to occur in anywhere from 30 to 90 % of patients with HI. Developmental delay and mental retardation are the most common neurological complications. In addition, various types of seizures can be present. Other neurologic manifestations include gray and white matter changes in MRI, macrocephaly, megalencephaly, hemimegalencephaly, craniofacial abnormalities, and neuronal migration disorders.

Other Organ Systems

Other findings in HI include musculoskeletal abnormalities (short stature, scoliosis, abnormal digit formation, and joint contractures), ocular abnormalities of the retina, optic nerve, iris, lens, and extraocular muscles, and abnormalities of the hair, nails, and teeth. There are also reports of cardiac and urogenital abnormalities in HI as well as an association with some malignancies.

Management Considerations

HI has no cure and no specific treatment. Screening imaging is not necessary for asymptomatic individuals, but should be pursued to evaluate for causes of individual complaints, such as seizures, developmental delay, or other focal neurologic deficits. Treatments in HI should be directed at specific manifestations of the disease on an individual basis.

Ataxia-Telangiectasia

Overview

Ataxia-telangiectasia (AT) is a rare autosomal recessive disorder caused by mutations in the ATM gene leading to chromosome instability, radiosensitivity, immunodeficiency, and a predisposition to cancer. The ATM gene encodes a protein that is involved in recognizing DNA damage and initiating repair mechanisms. It has an incidence of 1 in 40,000–100,000 births. Children with AT are often normal at birth and then begin to show signs of ataxia and motor coordination problems by the age of 2 or 3. It affects multiple organ systems including the nervous system, skin and hair, eyes, immune system, musculoskeletal system, and endocrine pathways. The life expectancy for a person with AT is in the 20–30 year range with the most common causes of mortality being infection and malignancy.

Diagnosis

The diagnosis of AT is suspected based on clinical presentation. In terms of laboratory testing,

children with AT will have elevated levels of serum alpha-fetoprotein in more than 95 % of cases. While elevated alpha-fetoprotein is not specific to AT, a molecular diagnosis made by looking for absence of the ATM protein is more than 99 % accurate. Neuroimaging with MRI will often showing thinning of the molecular layer of the cerebellum and cerebellar atrophy by around age 10.

Clinical Manifestations

Cutaneous

Telangiectasias are chronic dilatations of capillaries near the surface of the skin or mucous membranes that lead to the appearance of dark red blotches. They often manifest several years after the onset of ataxia, typically between the ages of 3 and 6. They are most commonly found on the bulbar conjunctiva, face, antecubital and popliteal fossae, and knuckles, but can be seen anywhere. Another cardinal feature of AT is progeric changes to hair and skin, with graying hair and atrophy of skin on the face making people with AT appear prematurely aged.

Nervous System

Childhood onset ataxia and dysarthria is seen in 100 % of children with AT. Approximately 90 % will also have diminished or absent deep tendon reflexes, choreoathetosis or dystonia, characteristic facies and posture, and drooling. One third of children with AT will have apparent cognitive arrest and many will have mental retardation. People with AT are also frequently described as having an equable disposition. Later, neurologic progression includes further loss of deep tendon reflexes, diminished sensation, neutral or up-going plantar response, and eventually diffuse weakness, atrophy, and fasciculations.

Other Organ Systems

Ocular symptoms are common in AT and include jerky eye movements and oculomotor apraxia (~85 %). Additionally, more than 60 % of children will have clinical immunodeficiency with frequent sinopulmonary infections as a result. Various malignancies, most often lymphoid, occur at an increased frequency in AT, with one third of patients developing a malignancy at some point. There is also an increased sensitivity to radiation in upwards of 90 % of people with AT. Endocrine and growth abnormalities are commonly seen in AT as well.

Management Considerations

At this time, there is no known specific treatment or cure for AT. Symptomatic and rehabilitative treatment can be used to improve quality of life and prolong life expectancy. Treatment approaches should be aimed at specific disease manifestations.

Pediatricians' Perspective

The majority of neurocutaneous disorders is inherited in an autosomal dominant pattern or arise de novo.

Genetic testing is available for most of these disorders, although often not required for diagnosis which is typically based on clinical criteria.

Management of patients with suspected or confirmed neurocutaneous disorders requires a team approach, including several subspecialists.

Bibliography

Alkonyi B, Chugani HT, Karia S, Behen ME, Juhász C. Clinical outcomes in bilateral Sturge-Weber syndrome. Pediatr Neurol. 2011;44(6):443–9.

Assogba K, Ferlazzo E, Striano P, Calarese T, Villeneuve N, Ivanov I, et al. Heterogeneous seizure manifestations in Hypomelanosis of Ito: report of four new cases and review of the literature. Neurol Sci. 2010;31(1):9–16. Epub 2009 Nov 10.

Au KS, Williams AT, Gambello MJ, et al. Molecular genetic basis of tuberous sclerosis complex: from bench to bedside. J Child Neurol. 2004;19:699–709.

Baser ME, Friedman JM, Wallace AJ, Ramsden RT, Joe H, Evans DG. Evaluation of clinical diagnostic criteria for neurofibromatosis 2. Neurology. 2002;59(11):1759–65.

Bay MJ, Kossoff EH, Lehmann CU, Zabel TA, Comi AM. Survey of aspirin use in Sturge-Weber syndrome. J Child Neurol. 2011;26(6):692–702.

Berlin AL, Paller AS, Chan LS. Incontinentia pigmenti: a review and update on the molecular basis of pathophysiology. J Am Acad Dermatol. 2002;47(2):169–87. quiz 188–90.

Bodemer C. Incontinentia pigmenti and hypomelanosis of Ito. Handb Clin Neurol. 2013;111:341–7. doi:10.1016/B978-0-444-52891-9.00040-3.

Bourgeois M, Crimmins DW, de Oliveira RS, Arzimanoglou A, Garnett M, Roujeau T, et al. Surgical treatment of epilepsy in Sturge-Weber syndrome in children. J Neurosurg. 2007;106(1 Suppl):20–8.

Carson BS, Javedan SP, Freeman JM, Vining EP, Zuckerberg AL, Lauer JA, et al. Hemispherectomy: a hemidecortication approach and review of 52 cases. J Neurosurg. 1996;84(6):903–11.

Ch'ng S, Tan ST. Facial port-wine stains—clinical stratification and risks of neuro-ocular involvement. J Plast Reconstr Aesthet Surg. 2008;61(8):889–93.

Comi AM. Presentation, diagnosis, pathophysiology, and treatment of the neurological features of Sturge-Weber syndrome. Neurologist. 2011;17(4):179–84.

DeBella K, Szudek J, Friedman JM. Use of the National Institutes of Health Criteria for diagnosis of neurofibromatosis 1 in children. Pediatrics. 2000;105(3):608–14.

DeLucia TA, Yohay K, Widmann RF. Orthopaedic aspects of neurofibromatosis: update. Curr Opin Pediatr. 2011;23(1):46–52.

Evans DG, Huson SM, Donnai D, Neary W, Blair V, Teare D, et al. A genetic study of type 2 neurofibromatosis in the United Kingdom. I. Prevalence, mutation rate, fitness, and confirmation of maternal transmission effect on severity. J Med Genet. 1992;29(12):841–6.

Evans DG, Baser ME, O'Reilly B, Rowe J, Gleeson M, Saeed S, et al. Management of the patient and family with neurofibromatosis 2: a consensus conference statement. Br J Neurosurg. 2005;19(1):5–12.

Friedman JM. Review article: Neurofibromatosis 1: Clinical manifestations and diagnostic criteria. J Child Neurol. 2002;17:548.

Kadonaga JN, Frieden IJ. Neurocutaneous melanosis: definition and review of the literature. J Am Acad Dermatol. 1991;24(5 Pt 1):747–55.

Kaelin WG. Von Hippel-Lindau disease. Annu Rev Pathol. 2007;2:145–73.

Khaier A, Nischal KK, Espinosa M, Manoj B. Periocular port wine stain: the Great Ormond Street Hospital experience. Ophthalmology. 2011;118(11):2274–2278.e1.

Kim JJ, Rini BI, Hansel DE. Von Hippel Lindau syndrome. Adv Exp Med Biol. 2010;685:228–49.

Kossoff EH, Buck C, Freeman JM. Outcomes of 32 hemispherectomies for Sturge-Weber syndrome worldwide. Neurology. 2002;59(11):1735–8.

Krueger DA, Franz DN. Current management of tuberous sclerosis complex. Paediatr Drugs. 2008;10:299–313.

Krueger DA, Care MM, Holland K, et al. Everolimus for subependymal giant-cell astrocytomas in tuberous sclerosis. N Engl J Med. 2010;363:1801–11.

Lee A, Driscoll D, Gloviczki P, Clay R, Shaughnessy W, Stans A. Evaluation and management of pain in patients with Klippel-Trenaunay syndrome: a review. Pediatrics. 2005;115(3):744–9.

Listernick R, Louis DN, Packer RJ, Gutmann DH. Optic pathway gliomas in children with neurofibromatosis 1: consensus statement from the NF1 optic pathway glioma task force. Ann Neurol. 1997;41(2):143–9.

Listernick R, Ferner RE, Liu GT, Gutmann DH. Optic pathway gliomas in neurofibromatosis-1: controversies and recommendations. Ann Neurol. 2007;61(3):189–98.

Mavrou A, Tsangaris GT, Roma E, Kolialexi A. The ATM gene and ataxia telangiectasia. Anticancer Res. 2008;28(1B):401–5.

McClatchey AI, Giovannini M. Membrane organization and tumorigenesis—the NF2 tumor suppressor, Merlin. Genes Dev. 2005;19:2265–77.

Minić S, Trpinac D, Obradović M. Incontinentia pigmenti diagnostic criteria update. Clin Genet. 2013. doi:10.1111/cge.12223 [Epub ahead of print].

Oduber CE, van der Horst CM, Hennekam RC. Klippel-Trenaunay syndrome: diagnostic criteria and hypothesis on etiology. Ann Plast Surg. 2008;60(2):217–23.

Oduber CE, van der Horst CM, Sillevis Smitt JH, Smeulders MJ, Mendiratta V, Harper JI, et al. A proposal for classification of entities combining vascular malformations and deregulated growth. Eur J Med Genet. 2011;54(3):262–71.

Parsa CF. Sturge-Weber syndrome: a unified pathophysiologic mechanism. Curr Treat Options Neurol. 2008;10(1):47–54.

Perlman SL, Boder Deceased E, Sedgewick RP, Gatti RA. Ataxia-telangiectasia. Handb Clin Neurol. 2012;103:307–32. doi:10.1016/B978-0-444-51892-7.00019-X.

Plotkin SR, Stemmer-Rachamimov AO, Barker FG, Halpin C, Padera TP, Tyrrell A, et al. Hearing improvement after bevacizumab in patients with neurofibromatosis type 2. N Engl J Med. 2009;361:358–67.

Price HN, Schaffer JV. Congenital melanocytic nevi-when to worry and how to treat: facts and controversies. Clin Dermatol. 2010;28(3):293–302.

Quan SY, Comi AM, Parsa CF, Irving ND, Krakowski AC, Cohen BA. Effect of a single application of pulsed dye laser treatment of port-wine birthmarks on intraocular pressure. Arch Dermatol. 2010;146(9):1015–8.

Roach ES, DiMario FJ, Kandt RS, Northrup H. Tuberous sclerosis consensus conference: recommendations for diagnostic evaluation. J Child Neurol. 1999;14:401–6.

Ruggieri M, Pavone L. Hypomelanosis of Ito: clinical syndrome or just phenotype? J Child Neurol. 2000;15(10):635–44.

Seashore MR, Cho SC, Desposito F, Sherman J, Wappner RS, Wilson MG, et al. Health supervision for children with neurofibromatosis. Pediatrics. 1995;96(2):368–72.

Shah KN. The diagnostic and clinical significance of café-au-lait macules. Pediatr Clin North Am. 2010;57(5):1131–53.

Shirley MD, Tang H, Gallione CJ, Baugher JD, Frelin LP, Cohen B, et al. Sturge-Weber syndrome and port-wine stains caused by somatic mutation in GNAQ.

N Engl J Med. 2013;368(21):1971–9. doi:10.1056/NEJMoa1213507. Epub 2013 May 8.

Tanaka K, Kambe N, Fujita M, Ando Y, Takashima S, Yuasa I. Incontinentia pigmenti in identical twins with separate skin and neurological disorders. Acta Derm Venereol. 1990;70(3):267–8.

Thomas IT, Frias JL, Cantu ES, Lafer CZ, Flannery DB, Graham Jr JG. Association of pigmentary anomalies with chromosomal and genetic mosaicism and chimerism. Am J Hum Genet. 1989;45(2):193–205.

Turin E, Grados MA, Tierney E, Ferenc LM, Zabel A, Comi AM. Behavioral and psychiatric features of Sturge-Weber syndrome. J Nerv Ment Dis. 2010;198(12):905–13.

Yates JR, Maclean C, Higgins JN, Humphrey A, le Maréchal K, Clifford M, et al. The tuberous sclerosis 2000 study: presentation, initial assessments and implications for diagnosis and management. Arch Dis Child. 2011;96(11):1020–5.

Yohay K. Neurofibromatosis types 1 and 2. Neurologist. 2006;12(2):86–93.

Yohay K. Neurofibromatosis type 1 and associated malignancies. Curr Neurol Neurosci Rep. 2009;9(3):247–53.

Cutaneous Markers of Spinal Dysraphism

8

Assem M. Abdel-Latif

Vignette A 5-year-old boy in your general practice has been having occasional urinary incontinence both at school and at home. He has also been complaining of numbness in his feet for the past few months to his father. He has no weakness and normal reflexes on physical examination. Upon inspection of his skin, a very discreet and thick patch of dark hair is noticed on the lumbo-sacral spine near the midline. Mom confirms that it has always been present but the providers in your practice had reassured her that it was nothing to be worried about. This patient has:

(a) Myelomeningocele
(b) Hypermelanosis
(c) Hypertrichosis and likely diastematomyelia
(d) Elevated testosterone

Answer: (c) Localized hypertrichosis is significantly associated with the *occult* spinal dysraphic state known as split cord malformations or diastematomyelia. Given the new onset of symptoms, it is likely that the boy is experiencing some symptoms attributable to tethering secondary to the split cord malformation.

A.M. Abdel-Latif, M.D., M.Sc. (✉)
Department of Neurological Surgery, Faculty of Medicine, Ain Shams University, Abbassia, Cairo 11566, Egypt
e-mail: Assem_mounir@hotmail.com

Definition

Spinal dysraphism is a spectrum of diseases characterized by incomplete fusion of the midline mesenchymal, bony, or neural elements of the spine which can be either occult (closed) or open [1–3]. As the skin and the neural structures share the same ectodermal origin, anomalies across the spectrum simply represent inappropriate dysjunction of the two embryologic levels.

Epidemiology

The general incidence for meningoceles and myelomeningoceles is approximately 1–2/1000 live births, regardless the ethnic and geographic variability [4]. It is difficult to ascertain reliable figures for occult dysraphism; yet 5–30 % was a reported debatable rate [5] and there is a significant female preponderance. There is clearly a role that genetic and environmental factors play in the development of spinal dysraphism since geographic, racial, and socioeconomic differences have been revealed [6]. For example, a high incidence has been reported in Northern Ireland and South Wales and a higher incidence in eastern than western North America. These conditions are most prevalent among Hispanics, intermediate in non-Hispanic Caucasians, and lowest in blacks and Asians populations.

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_8

Risk Factors

The discovery that relative folate deficiency causes open neural tube defects is one of the most important dietary discoveries in fetal-maternal medicine. Mothers of affected children display normal blood folic acid levels; however, they are significantly lower than those of the mothers with babies without neural tube defects. It has been estimated that up to 70 % of nonsyndromic open neural tube defects can be prevented by folate supplementation [7]. Maternal diabetes is thought to create a 20 times increased risk of neural tube defects, and certain antiepileptics, especially carbamazepine and valproic acid, are recommended to be avoided during fetal development due to the risk of NTD.

Classification of Spinal Dysraphism [8, 9]

- *Type I*: Open spinal dysraphism; includes myelomeningoceles and myeloceles
- *Type II*: Closed spinal dysraphism; includes lipomyelomeningoceles, lipomyeloceles, posterior meningoceles, and myelocystoceles
- *Type III*: Occult spinal dysraphism without spinal contents as a mass effect, but associated with cutaneous markers in the lumbosacral region

Clinical Presentation

Clinical manifestations largely depend on the location: about 70 % of the myelomeningoceles are in the lumbar or lumbosacral region. Meningoceles are often covered by intact skin. Antenatal diagnosis of open neural tube defects is often made through ultrasonography or MRI and obviously upon birth within the delivery room or nursery (Fig. 8.1). Neurologic deficits are more frequent in children with myelomeningoceles as a result of damage to exposed neural structures to the amniotic fluid. Other skeletal physical findings that may be appreciated include foot deformities, dislocated hips, or knee/hip contractures. In cases of occult spinal dysraphism, the manifestations will vary according to the malformation present, but quite frequently the children are completely neurologically intact without discernable deficit. Hydrocephalus is associated with 85–90 % of cases of open neural tube defects (associated with Chiari type II malformations) even though it may not be evident at birth. Rarely are closed defects associated with hydrocephalus.

Cutaneous Manifestations

For the open neural tube defects (Fig. 8.1), the lesion is readily visible whether it was covered by intact skin or not. The challenge for primary care providers occurs with the occult or hidden/closed neural tube defects. *Cutaneous manifestations represent minor aberrations in the development of surface ectoderm due to abnormalities in the dorsal endomesenchymal tract* [10–12]. We will include the various skin manifestation of occult tethered cord below for easy identification.

Tuft of hair (or localized hypertrichosis) sometimes referred to as a "faun tail" [13] (Fig. 8.2).

Skin dimples [14, 15] (Fig. 8.3)

These can be classified into *simple dimple/coccygeal pit*, which are usually ≤5 mm in diameter and are 2.5 cm or less from the anus. They are localized just above the gluteal furrow and **usually not associated** with underlying dysraphism. *Atypical dimples* on the other hand are usually >5 mm in diameter and >2.5 cm from the anus (i.e., higher up in the back) and are highly associated with spinal dysraphism.

If you have to split the glutei to see the dimple, then this is low-lying and less suspicious for dysraphism. If it is readily visible on the back, above the upper gluteal limit, then the dimple is suspicious.

Asymmetric or malformed Gluteal cleft. These are referred to as duplicated or asymmetric or Y-shaped clefts or creases (Fig. 8.4).

Subcutaneous lipomas

Usually occur in combination of other masses, e.g., hemangiomas/vascular malformations,

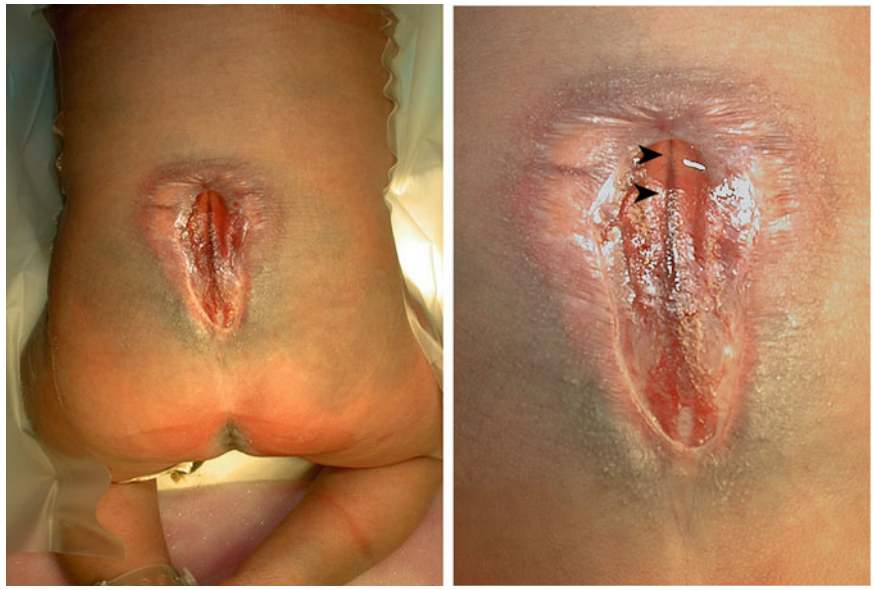


Fig. 8.1 A 1-day-old infant diagnosed prenatally with open neural tube defect and ventriculomegaly. The lesion is located at the lumbosacral junction and a closer look depicts split placode (*arrow heads*) and covered by glistening layer of arachnoid. This appearance is typical for open neural tube defects or spina bifida aperta

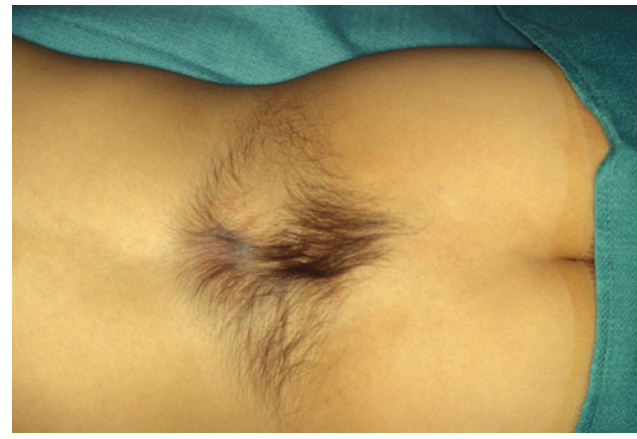


Fig. 8.2 Localized hypertrichosis or hair tuft in the lumbosacral area. Typical appearance and considered highly suggestive of underlying spinal dysraphism, especially split cord malformations

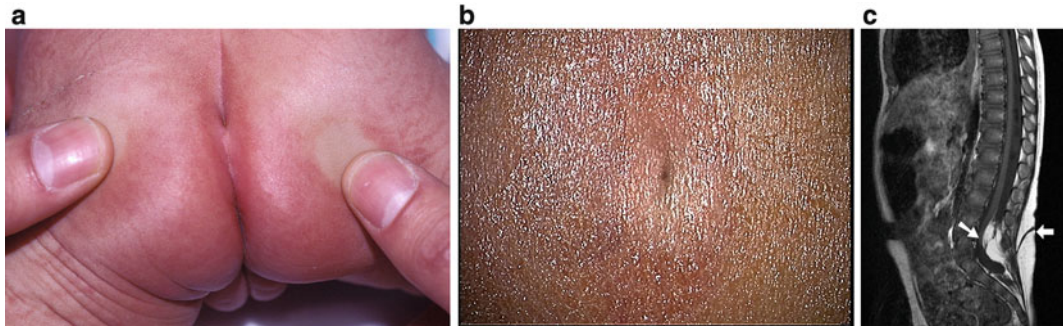


Fig. 8.3 Typical/simple skin dimple seen by spreading the glutei and notably close to the anal verge (**a**). An atypical skin dimple seen higher up in the back (**b**). This can be associated with an underlying dermal sinus track that leads to intradural lipoma as seen in MRI (**c**) (*white arrowheads*)

hyrpertrichosis. There is a well-established association with intra-dural lipomas and spinal cord tethering so that the finding warrants further work up (Fig. 8.5).

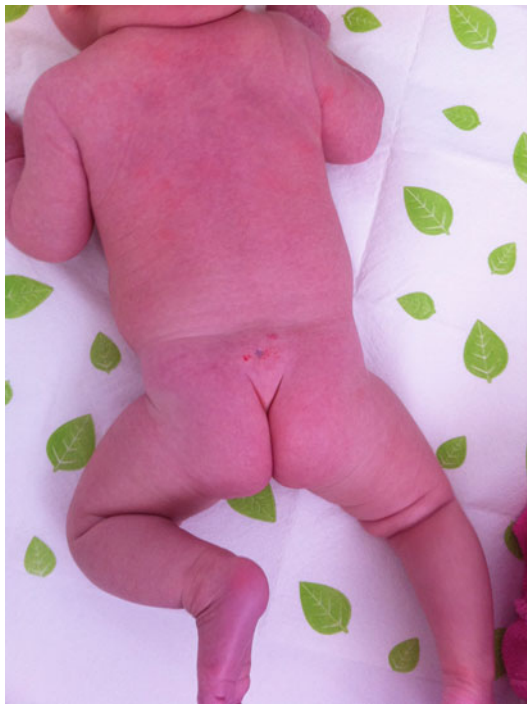


Fig. 8.4 Asymmetric Y-shaped gluteal cleft that is moderately associated with spinal dysraphism except if present with other lesions

Hemangiomas and capillary vascular malformations

The use of nonuniform classification of the vascular skin lesions makes it difficult to draw conclusions about sensitivity and specificity of these midline lesions as markers of dysraphism. Incidence ranges from 2.6 to 12% and are thought to represent angioblastic tissue that fails to unite formally with the developing vasculature of the body [16].

They usually occur in combination with other masses, e.g., subcutaneous lipoma or hypertrichosis. The isolated occurrence of vascular malformations designated as flat capillary hemangiomas is considered to have the lowest association with underlying intradural pathologies (Fig. 8.6) [17, 18]. Reports are evolving of retrospective [19] and prospective [14] studies showing a higher and significant association with occult spinal dysraphism when isolated flat capillary vascular malformation is found in a usual lumbosacral location.

Tails or skin appendages

Tails are essentially vestigial remnants of the primitive coccyx that are supposed to undergo regression, while skin appendages may represent sometimes atretic meningoceles [20], a soft pedunculated skin tag or fibroma pendulum [21] (Fig. 8.7).

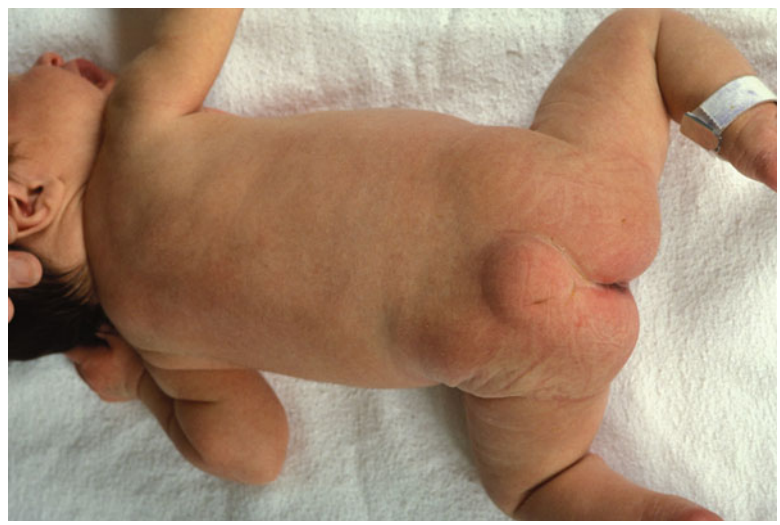


Fig. 8.5 Subcutaneous lipoma with typical association with an asymmetric/deviated gluteal furrow. This association is considered highly suggestive of underlying spinal dysraphism

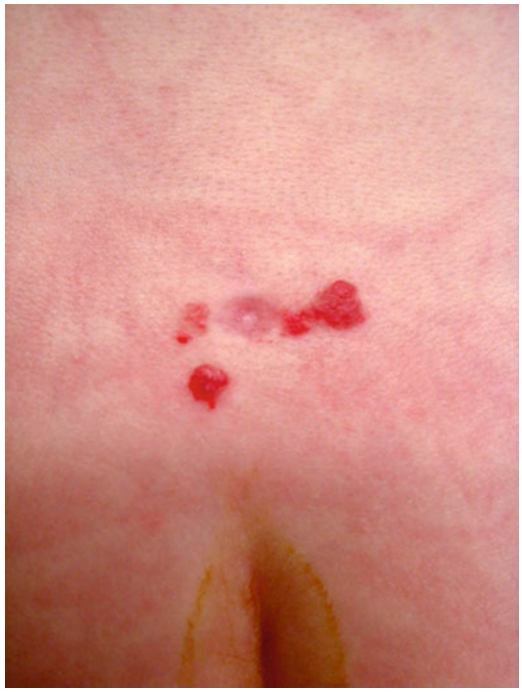


Fig. 8.6 Typical appearance of a cutaneous hemangioma. This appearance along with other cutaneous vascular malformation is increasingly recognized as a marker for occult spinal dysraphism in some studies and reports

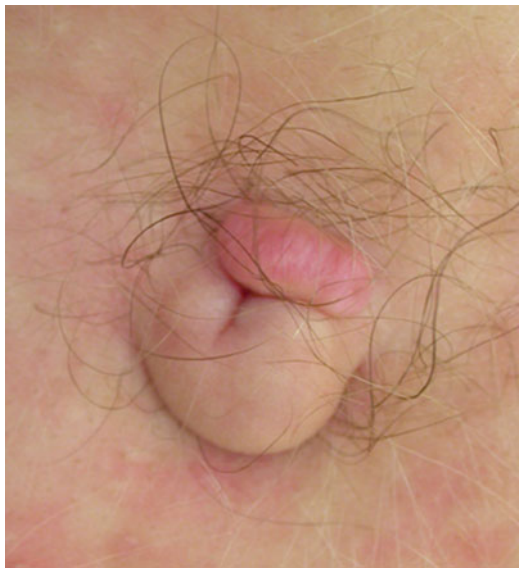


Fig. 8.7 Typical appearance of tail or vestigial appendage. This is considered also a highly suggestive cutaneous maker of an underlying spinal cord abnormality

The Predictive Value of the Skin Lesions

For clinicians, deciding when to order further imaging is predicated upon the simple question: What is the likelihood that this lesion represents a cutaneous manifestation of an underlying dystrophic state? While these lesions can never be perfectly predictive, Table 8.1 gives a guideline as to when various cutaneous manifestations should lead the pediatrician towards considering an imaging study under the correct clinical scenario. In a large prospective study of cutaneous markers of possible spinal dysraphism conducted in tertiary dermatology centers, atypical dimples were the most common skin manifestation of occult spinal dysraphism with a 55 % predictive value in accordance with previous reports [15]. Followed by lipomas and vascular anomalies are also demonstrating increasing correlation with spinal dysraphism [14]. Another retrospective study [1] found the port-wine stain (or flat capillary vascular malformation) and deviated gluteal furrow (DGF) to be the most commonly occurring skin markers either isolated or in combination, again followed by a subcutaneous lipoma. In sum, the results suggest that the occurrence of two or more lesions (especially with lipoma being one of them) was the strongest predictor of occult dysraphism, still in accordance with the earlier [22, 23] and later published literature [14]. Yet isolated vascular lesions in that study were not indicative of underlying spinal pathology.

Table 8.1 Risk of association of skin lesion

Cutaneous marker	Risk/likelihood of dysraphism
Simple dimple	Very low
Blue spot/nevus	Very low
Flat vascular malformation/ port-wine stain	Very low
Atypical dimple	Moderate risk
Deviated gluteal furrow	Moderate risk
Subcutaneous lipoma	Moderate to high risk
Hypertrichosis	High risk (split cord)
Dermal sinus track, tail	High risk
Two lesions or more	Confirmed risk

As for the dermal sinus tracks, significant association with spinal dysraphism has been described in retrospective studies reviewing operated patients for dermal sinuses [24, 25]. Association with neurologic deficit and the high risk of intradural infections was also documented which drives the recommendation for thorough investigation upon noticing the cutaneous marks in such patients. The high association can still be explained by the retrospective nature of the study and possible referral bias of the more complex cases to that center.

Localized hypertrichosis has been reported to be significantly associated with spinal dysraphism with split cord malformations (or diastematomyelia) being the particular pathology [26, 27].

Deviated gluteal furrow found in isolation wasn't associated with dysraphism, although the risk rises when it's found in association with other lesions.

Is Radiological Screening Warranted in Presence of Skin Lesions?

Screening for typical skin dimples is not advisable especially if they are isolated [28], in contrast to the atypical dimples that should be screened [1, 15, 22, 23].

Subcutaneous lipomas, isolated or in combination of other skin lesions, are suggestive and thus need to be investigated.

One publication [1] has suggested a management algorithm based on their results and divided the patients into three groups:

Highly suggestive group, with ≥2 skin lesion or a single suggestive lesion (lipoma, hypertrichosis, tail, dermal sinus tract, and more recently vascular malformation) or 1 skin lesion with evidence of spinal cord dysfunction (abnormal arching of the foot, gait troubles, or urinary/rectal problems). These patients should be investigated with MRI regardless of the age. *Moderately suggestive group*, with 1 skin lesion (atypical dimple, unclassified hamartoma, and deviation of the gluteal furrow). Those patients are investigated with MRI if >6 months of age or if <6 months and the ultrasound was suspicious. *Low-risk group*, with 1 skin lesion (Mongolian blue spot, nevus, and simple dimple). Those patients are not screened as long as they are not symptomatic.

Which Method to Use for Screening?

The use of ultrasound in screening for spinal dysraphism is very helpful especially in children younger than 6 months of age where the bony density of the posterior spinal elements doesn't preclude adequate visualization. However, MRI is the best method of detection of the underlying spinal lesions cited in most published studies. The availability, cost, and the need for sedation may preclude its immediate use and many practitioners rely on ultrasound as a screening test to see if an MRI is warranted. In summary, in the presence of lesions known to be highly associated with spinal dysraphism, multiple lesions, skin lesions in upper cervical or thoracic spine, suspicious findings on the ultrasonography, or suspicion by the radiologist OR, in all children older than 6 months of age, MRI is the screening modality of choice. Otherwise ultrasonography can be a good alternative with the understanding that diagnostic accuracy may be undermined.

Concerted effort is being directed towards addressing some of the issues of diagnostic screening as this remains a confusing topic for many primary care practitioners, particularly with respect to vascular skin lesions [29]. Any concern on the part of a pediatrician would be absolutely enough to warrant a visit to the pediatric neurosurgeon and a direct inspection of the region of concern and to obtain a focused neurological examination.

References

1. Guggisberg D, Viney C, Bodemer C, Brunelle F, Zerah M, Pierre-kahn A, et al. Skin markers of occult spinal dysraphism in children. Arch Dermatol. 2004;140:1109–15.
2. Schropp C, Sorensen N, Collman H, et al. Cutaneous lesions in occult spinal dysraphism - correlation with

intraspinal findings. Childs Nerv Syst. 2006;22: 125–31.
3. Pierre-kahn A, Lacombe J, Pichon J, et al. Intraspinal lipomas with spina bifida: prognosis and treatment in 73 cases. J Neurosurg. 1986;65:756–61.
4. Akalan N. Spinal dysraphism. In: Akbarina BA, Yazici M, Thompson GH, editors. The growing spine management of spinal disorders in young children. Berlin: Springer; 2011. p. 269–79.
5. Greenberg MS. Spinal dysraphism (spina bifida). In: Greenberg MS, editor. Handbook of neurosurgery. 7th ed. New York, NY: Thieme Medical Publishers; 2010. p. 247–56.
6. Burton BK. Spina bifida. In: Kumar P, Burton BK, editors. Congenital malformations evidence-based evaluation and management. New York, NY: McGraw Hill, Medical; 2008. p. 41–9.
7. Czeizel A, Dudas I. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. N Engl J Med. 1992;327:1832–5.
8. Assaad A, Mansy A, Kotb M, Hafez M. Spinal dysraphism: experience with 250 cases operated upon. Childs Nerv Syst. 1989;5:324–9.
9. Deeg K, Lode H, Gassner I. Spinal sonography in newborns and infants - Part II: spinal dysraphism and tethered cord. Ultraschall Med. 2008;29:77–88.
10. Drolet B. When good is not good enough: the predictive value of cutaneous lesions of the lumbosacral region for occult spinal dysraphism. Arch Dermatol. 2004;140:1153–5.
11. Pang D, Dias M, Ahab-barmada M. Split cord malformation: Part I; unified theory of embryogenesis for double spinal cord malformation. Neurosurgery. 1992;31:3.
12. Kumar R, Singh S. Spinal dysraphism: trends in northern India. Pediatr Neurosurg. 2003;38:133–45.
13. Laurent I, Leaute-Labreze C, Maleville J, Taieb A. Faun tail and sacral hemangioma associated with occult spinal dysraphism. Ann Dermatol Venereol. 1998;125:414–6.
14. Sardana K, Gupta R, Garg VK, Mishra D, Mishra P, Grover C, et al. A prospective study of cutaneous manifestations of spinal dysraphism from India. Pediatr Dermatol. 2009;26(6):688–95. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20199442.
15. Kriss V, Desai N. Occult spina dysraphism in neonates: assessment of high-risk cutaneous stigmata on sonography. Am J Roentgenol. 1998;171(6):1687–92.
16. Burns A, Kaplan L, Mulliken J. Is there an association between hemangioma and syndromes with dysmorphic features? Pediatrics. 1991;88: 1257–67.
17. Selden N, Allen R, Sandquist M, et al. Isolated lumbosacral strawberry nevi do not indicate the presence of occult spinal dysraphism. Scottsdale, AZ: AANS/CNS section on Pediatric Neurological surgery; 2002.
18. Allen R, Sandquist M, Piatt JJ, et al. Ultrasonographic screening in infants with isolated spinal strawberry nevi. J Neurosurg Spine. 2003;98(3):247–50.
19. Tubbs RS, Wellons III JC, Iskandar BJ, Oakes WJ. Isolated flat capillary midline lumbosacral hemangiomas as indicators of occult spinal dysraphism. J Neurosurg Pediatr. 2004;100(2):86–9.
20. Rauzzino M, Iskandar BJ, Oakes WJ. Occult spinal dysraphism. Contemp Neurosurg. 1998;20:1–6.
21. Vincent A, Farley M, Chan E, James W. Birt-Hogg-Dube syndrome: a review of the literature and the differential diagnosis of firm facial papules. J Am Acad Dermatol. 2003;49:698–705.
22. McAtee-Smith J, Herbert A, Rapini R, Goldberg N. Skin lesions of the spinal axis and spinal dysraphism: fifteen cases and a review of literature. Arch Pediatr Adolesc Med. 1994;148:740–8.
23. Chen C, Lin K, Wang H, Lui T. Dermoid cyst with dermal sinus tract complicated with spinal subdural abscess. Pediatr Neurol. 1999;20:157–60.
24. Ackermann L, Menezes A. Spinal congenital dermal sinuses: a 30-year experience. Pediatrics. 2003;112: 641–7.
25. Soonawala N, Overweg-plandsoen WCG, Brouwer OF. Early clinical signs and symptoms in occult spinal dysraphism: a retrospective case study of 47 patients. Clin Neurol Neurosurg. 1999;101:11–4.
26. Keim H, Greene A. Diastematomyelia and scoliosis. J Bone Joint Surg Am. 1973;55:1425–35.
27. Miller A, Guille J, Bowen J. Evaluation and treatment of Diastematomyelia. J Bone Joint Surg Am. 1993; 75:1308–16.
28. Gibson P, Britton J, Hall D, Hill C. Lumbosacral skin markers and identification of occult spinal dysraphism in neonates. Acta Pediatr. 1995;84(2):208–9.
29. Enjolras O, Mulliken J. Vascular tumors and vascular malformations (new issues). Adv Dermatol. 1997; 13:375–423.

Tethered Cord

9

María Teresa Alvarado Torres

Vignette A 3-year-old boy who started walking at 18 months was in your clinic for his 3-year routine visit. His parent suggested that he seemed fine except when he became tired. As he tired, his left leg started to drag slightly. His mother did not notice that he complained of any pain after exercising but the fatigue was reproducible. She felt that the cosmetic appearance of his back looked normal but upon closer inspection, a subtle gluteal asymmetry was detected. Neurologically the child was completely normal except for decreased proprioception and light touch on the left.

(a) Order an ultrasound of the lumbar spine
(b) Order a CT of the lumbar spine
(c) Order an MRI of the lumbar spine
(d) No imaging is necessary

Answer (c). On the MRI, a fatty filum terminale (tethered cord) was found distal to the spinal cord with a low *conus medullaris*. Urodynamics were suggestive of incomplete emptying and EMGs showed subtle asymmetry in distal muscle groups. The patient went to surgery to detheter his spinal cord without complication.

M.T.A. Torres, M.D. (✉)
Department of Neurological Surgery,
New York Presbyterian Hospital, 525 E 68th St,
New York, NY 10065, USA

Fundación Santa Fe de Bogotá,
Av Calle 116, Bogotá 110111, Colombia
e-mail: Maa2102@med.cornell.edu;
mateato@gmail.com

Introduction

As with other pathologies of the spinal cord, tethered spinal cords (TSC) may be due to a congenital malformation or secondary to scar from a infection or trauma. Broadly, tethered cord is defined as an abnormal attachment of the spinal cord to the tissues that surround it, and usually is associated with a low *conus medullaris* and a thickened *filum terminale*. In severe cases, it is associated with conditions including lipomyelomeningoceles, meningoceles, myelomeningoceles, diastematomyelia, and other dysraphic conditions. TSC may occur as a consequence after reparative surgery for *spina bifida aperta*, trauma, infections, or any condition that may cause arachnoiditis. It is important to differentiate between the radiological diagnosis and the clinical syndrome; many patients have radiographic tethered cord without any clinical manifestations; TSC may can be an incidental radiographic finding [1, 4].

The clinical manifestations of TSC are variable; however symptoms when linked to the imaging should be directly attributable to the location of the neural structures involved. Most tethered cords are physically tethered in the lumbosacral region, which makes some combination of lumbosacral pain, bowel and bladder dysfunction, and motor or sensory changes in the legs the most common constellation of symptoms upon presentation [1–4]. Surgery is the treatment of choice in symptomatic patients.

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_9

History

One of the first reports of TSC in the literature was made by Johnson in 1857. He performed surgery on a child with progressive weakness in the lower extremities, and discovered a lipoma in the lumbar region associated with an abnormal lower and frankly tethered cord [5]. Similarly, Jones reported a surgery where he untethered the spinal cord in a patient with lower limb atrophy, difficulty in micturition, and back pain, who after surgery demonstrated improvement in motor and urinary symptoms [6]. Since the mid-twentieth century TSC has been definitively established as the major link between the anatomy and the symptoms in many congenital pathologies including diastematomyelia, spinal lipomas, thickened filum terminale, lipomyelomeningoceles, meningoceles, myelomeningoceles, and dermal sinus tracts. Fuchs introduced the term myelodysplasia to refer to patients with deep tendon reflexes and sensorial alterations associated with foot deformities who also had spina bifida occulta [1, 4–6, 8, 9]. In 1953 Garceau described a neurological syndrome associated with spinal deformity that he called *filum terminale syndrome* [26]. It was not long before the relationship between activities and the exacerbation of symptoms was established [7], the mechanism that fully explains TSC symptoms as a result of tension throughout the spinal cord: caudal cord ischemia resulting from mechanical tension [10–12].

Pathophysiology

At the level of the conus medularis, the spinal cord is attached to the filum terminale, which is a pia mater band that extends to the lower level of the spinal canal. Normally, the length of this band is enough to allow movements without producing any tension over the length of the spinal cord. In addition, the spinal roots are free inside the spinal canal and are not tethered to any structure in the intra- or extraforaminal space. When the filum terminale or the nerve roots are attached or *tethered* to some structure, range of motion is reduced and an increase occurs in the mechanical tension applied on the nervous structures [1, 13, 14]. It has been shown that this traction associated with movement causes disturbances in blood flow and oxidative metabolism that can produce ischemia and worsening neurologic function [10–12]. This is thought to explain why the release of the filum and roots produces significant improvement of symptoms. In addition to this traction, we also know that in some patients an intrinsic defect in the spinal cord or spinal nerves may produce an alteration in nerve transmission that cannot be remedied by surgery [1, 15].

Thickened Filum or Fatty Filum Terminale

The filum terminale and the lower spinal roots are formed from the caudal eminence around the 24th day (secondary neurulation) of gestation. In this process, the neural tube canal is formed at the level of S2. Any disturbance during secondary neurulation may cause a tethered cord below this level [16, 17]. On the other hand at postovulatory days 43–48, the *conus medullaris* starts losing its thickness and begins its ascension within the canal, a process that is completed around postmenstrual 40 weeks [18]. Normally at the end of pregnancy the position of the conus is at level of L1–2 [19]. A caudally displaced *conus medullaris* (at L3 or below) should be considered for evaluation of tethered cord syndrome. The thick filum terminale is a condition considered as the simplest form of tethered cord, a filum terminale of 2 or more millimeter is considered like abnormally thick [2], and in some patients it is intimately associated with fatty infiltration of the ligament and is therefore referred to as a *fatty filum terminale* [20]. Other forms of lipomatous accumulations are lipomyelomeningocele and intradural lipoma, the first one related with defects in the lumbosacral fascia and lamina and the second one without cutaneous or bone abnormities and more frequently located within the thoracic spine [24].

Other pathologies derived as a result of abnormal gastrulation or primary and secondary neurulation include conditions with incomplete formation of caudal elements such as split cord

malformations including diastematomyelia and diplomyelia [21, 24], dermal sinus which is a track coursing from the skin to the dura, subarachnoid space or to the spinal cord, and the open spinal dysraphisms already discussed.

Clinical Presentation and Diagnosis

An important percentage of patients with TCS may have skin stigmata (see Chap. 8) raising the suspicion of a closed spinal dysraphism and tethered cord. Those findings are localized in the midline, can be cutaneous lipomas, tails, dermal sinuses, atypical dimples, deviations of gluteal crease, hamartomas, hemangiomas, port-wine stains, hypertrichosis, and pigmentary nevus, among others [22]. Some studies support a higher risk of TSC with the presence of more than one of those [23].

Besides skin stigmata, it is necessary to be aware that depending on the level of the tethered cord as well as the grade of tension on neural elements, the underlying etiology, and age of patient, the clinical presentation may be different. Simple reflex abnormities or foot atrophy can be the first manifestation of this condition in infants. Each alteration or asymmetry in the motor or sensory examination should be noted in your examination. In older children disturbances of gait and sphincter control may be a red flag. In patients older than 12 years the most frequent symptom is leg or back pain exacerbated with flexion and exercise, and in young adults the most typical presentations are pain and motor disturbances along with sensory dysfunction.

In adults the clinical presentation is similar to adolescents; the main symptoms are pain and bladder dysfunction exacerbated with movement. Spine deformations are also common and can worsen the pain. In patients with a known history of spina bifida the diagnosis of TSC may only be arrived after years of sexual dysfunction [27], mild weakness, or subtle urological symptoms. In some cases, the clinical presentation may occur after mild trauma [27–29]. There may also be orthopedic and urologic abnormalities that are part of the tethered cord syndrome; some authors have suggested the name of neuro-uro-orthopedic syndrome. Disturbances in bladder and bowel control can be explained by the compromise of the sacral roots that innervate these organ systems. Among the urinary disturbances are uncoordinated bladder or sphincter function, or incomplete bladder emptying. The discovery of the urologic symptoms is challenging particularly in infants who may not yet be potty-trained and can present with mild bladder dysfunction. In older children urinary incontinence is more obvious [25].

One of the most common alterations of the urinary function is detrusor hyperreflexia but other disturbances like decreases in bladder compliance, dyssynergia, and decreased sensation can be found. In order to rule out any additional urologic compromise, urodynamic tests are generally required particularly to assess intra-bladder pressure, leak point pressure, compliance, contractions, electromyelogram activity, and sensation. Depending on the affected spinal level, the urologic outcomes can be variable after detethering procedures. There are some studies that report success rates between 29 and 75 % [29, 30].

Imaging

While MRI is the most useful and widely utilized radiological exam for surgical planning and diagnosis of this pathology, there are additional exams that can be useful for screening specially in the youngest children. Ultrasonography can show the level of the *conus medullaris* and can identify fat or other obvious abnormalities suggestive of dysraphism [31]. Lack of motion of the cord can also be visualized by a trained ultrasonographer or radiologist. Plain film radiography is used to see bone abnormalities that can be associated with tethered cord. Open posterior arches, defects in lamina, vertebral bodies, disc spaces, or pedicles such as widening of the spinal canal evidenced by increased interpeduncular distance or scalloping would necessitate additional studies in order to rule out spinal cord abnormalities and TSC. Radiographs may also be useful to identify the spinal curvature to measure the degree of kyphosis, lordosis, and scoliosis of the spinal column [21]. CT obviously has a much

higher resolution than plain radiographs and allows more detailed views of bony abnormalities that may be found with tethered cord but also presents a significantly increased exposure to ionizing radiation. CT myelography can be useful when an MRI is unobtainable, and may show a thickened filum, fat, and the relation between lipomas, subarachnoid space, and nervous structures. Despite all these options, MRI remains the gold standard. MRI beautifully demonstrates associated pathologies and abnormalities besides the level and morphology of conus medullaris. MRI also allows the identification of other related conditions such as anorectal malformations. Supine and prone MRI can demonstrate lack of motion of the spinal cord, which is suggestive of tethered cord. Some studies have tried to compare the efficacy between prone and supine positioned MRIs to demonstrate the presence or absence of movement of the *conus medullaris*. Supine MRI can show the level of the conus as well as the filum and fat but it is not always enough to define movement within the spinal canal. In some patients supine imaging can be normal but prone imaging can show a loss of movement suggestive of TSC [32]. Egelhoff and colleagues found that the *conus* level had the highest diagnostic accuracy with a sensitivity of 69–77 % with a specificity of 94 %, a positive predictive value of 82–83 %, and a negative predictive value of 89–92 %; however prone and cine MRI did not increase the accuracy of the supine imaging. We do not routinely advocate for this type of imaging. Fetal MRI may detect complex anomalies of neural tube but can have low specificity [33].

Pediatrician's Perspective

1. Most tethered cords are physically tethered in the lumbosacral region, which makes some combination of lumbosacral pain, bowel and bladder dysfunction, and motor or sensory changes in the legs the most common constellation of symptoms upon presentation.
2. Midline findings such as cutaneous lipomas, tails, dermal sinuses, atypical dimples, deviations of gluteal crease, hemangiomas, and hypertrichosis should make you wary of identifying signs and symptoms of TSC. More than one of these signs is very suggestive.
3. There may also be orthopedic and urologic abnormalities that are part of the tethered cord syndrome. Urologic and orthopedic care are essential to the preoperative evaluation of TCS and part of postoperative monitoring.
4. MRI is the most useful and widely utilized radiological exam for surgical planning and diagnosis of this pathology.

References

1. Agarwalla PK, Dunn IK, Scott RM, Smith ER. Tethered cord syndrome. Neurosurg Clin N Am. 2007;18:531–47.
2. Hoffman HJ, Hendrick EB, Humphreys RP. The tethered spinal cord: its protean manifestations, diagnosis and surgical correction. Childs Brain. 1976;2(3):145–55.
3. Yamada S, Iacono RP. Tethered cord syndrome. In: Pang D, editor. Disorders of the pediatric spine. New York, NY: Raven; 1995. p. 159–73.
4. Daszkiewicz P, Barszcz S, Roszkowski M, Maryniak A. Tethered cord syndrome in children - impact of surgical treatment on functional neurological and urological outcome. Neurol Neurochir Pol. 2007;41:427–35.
5. Johnson A. Fatty tumour from the sacrum of a child, connected with the spinal membranes. Trans Pathologic Soc Lond. 1857;8:16–8.
6. Jones WL. Spina bifida occulta: no paralytic symptoms until seventeen years of age: spine trephined to relieve pressure on the cauda equina: recovery. Br Med J. 1891;1:173–4.
7. Spiller WG. Congenital and acquired enuresis from spinal lesion: a) myelodysplasia; b) stretching of the cauda equina. Am J Med Sci. 1916;151:469–75.
8. Brickner WM. Spina bifida occulta: (1) with external signs, with symptoms; (2) with external signs, without symptoms; (3) without external signs, with symptoms; (4) without external signs; without symptoms. Am J Med Sci. 1918;155(4):473–502.
9. Warf BC. Pathophysiology of tethered cord syndrome. In: McLone DG, editor. Pediatric neurosurgery: surgery of the developing nervous system. 4th ed. Philadelphia, PA: Saunders; 2001. p. 282–8.
10. Yamada S, Iacono RP, Androde T, Mandybur G, Yamada BS. Pathophysiology of tethered cord syndrome. Neurosurg Clin N Am. 1995;6:311–23.
11. Yamada S. Tethered cord syndrome in adults and children. Neurol Res. 2004;26:717–8.
12. Yamada S, Won DJ. What is the true tethered cord syndrome? Childs Nerv Syst. 2007;23:371–5.

13. Herman JM, McLone DG, Storrs BB, et al. Analysis of 153 patients with myelomeningocele or spinal lipoma reoperated upon for a tethered cord. Presentation, management and outcome. Pediatr Neurosurg. 1993;19(5):243–9.
14. Schoenmakers MA, Gooskens RH, Gulmans VA, et al. Long-term outcome of neurosurgical untethering on neurosegmental motor and ambulation levels. Dev Med Child Neurol. 2003;45(8):551–5.
15. Hervey-Jumper SL, Garton HJ, Wetjen NM, Maher CO. Neurosurgical management of congenital malformations and inherited disease of the spine. Neuroimaging Clin N Am. 2011;21:719–31.
16. Muller F, O'Rahilly R. The development of the human brain, the closure of the caudal neuropore, and the beginning of secondary neurulation at stage 12. Anat Embryol (Berl). 1987;176(4):413–30.
17. Muller F, O'Rahilly R. The primitive streak, the caudal eminence and related structures in staged human embryos. Cells Tissues Organs. 2004;177(1):2–20.
18. Dias MS, McLone DG. Normal and abnormal early development of the nervous system. In: McLone DG, editor. Pediatric neurosurgery: surgery of the developing nervous system. 4th ed. Philadelphia, PA: Saunders; 2001. p. 31–71.
19. Wolf S, Schneble F, Troger J. The conus medullaris: time of ascendence to normal level. Pediatr Radiol. 1992;22(8):590–2.
20. Emans PJ, van Aalst J, van Heurn EL, et al. The Currarino triad: neurosurgical considerations. Neurosurgery. 2006;58(5):924–9.
21. Iskander BJ, Oakes WJ. Anomalies of the spine and spinal cord. In: McLone DG, editor. Pediatric neurosurgery: surgery of the developing nervous system. 4th ed. Philadelphia, PA: Saunders; 2001. p. 307–23.
22. Guggisberg D, Hadj-Rabia S, Viney C, et al. Skin markers of occult spinal dysraphism in children: a review of 54 cases. Arch Dermatol. 2004;140(9):1109–15.
23. McLone DG, Thompson DNP. Lipomas of the spine. In: McLone DG, editor. Pediatric neurosurgery: surgery of the developing nervous system. 4th ed. Philadelphia, PA: Saunders; 2001. p. 289–301.
24. Sweet J, Kalhorn CG. Spinal dysraphism: a review of clinical manifestations and surgical treatment options. Semin Spine Surg. 2005;17:23–9.
25. Thompson DNP. Spinal dysraphic anomalies; classification, presentation and management. J Pediatr Child Health. 2010;20:9.
26. Bowman RM, Mohan A, Ito J, Seibly JM, McLone DG. Tethered cord release: a long-term study in 114 patients. J Neurosurg Pediatr. 2009;3:181–7.
27. Rajpal S, Tubbs RS, George T, Oakes WJ, Fuchs HE, Hadley MN, et al. Tethered cord due to spina bifida occulta presenting in adulthood: a tricenter review of 61 patients. J Neurosurg Spine. 2007;6:210–5.
28. Hudgins RJ, Gilreath CL. Tethered spinal cord following re- pair of myelomeningocele. Neurosurg Focus. 2004;16(2):E7.
29. Giddens JL, Radomski SB, Hirshberg ED, Hassouna M, Fehlings M. Urodynamic findings in adults with the tethered cord syndrome. J Urol. 1999;161:1249–54.
30. Guerra LA, Pike J, Milks J, Barrowman N, Leonard M. Outcome in patients who underwent tethered cord release for occult spinal dysraphism. J Urol. 2006;176:1729–32.
31. Naidich TP, McLone DG. Neuroradiology: ultrasonography versus computed tomography. In: Holtzman RNN, Stein BM, editors. The tethered spinal cord. New York, NY: Theime-Stratton; 1985. p. 47–58.
32. Singh S, Kline-Fath B, Bierbrauer K, Racadio JM, Salisbury S, Macaluso M, Jackson EC, Egelhoff JC. Comparison of standard, prone and cine MRI in the evaluation of tethered cord. Pediatr Radiol. 2012;42:685–91. doi:10.1007/s00247-011-2308-8.
33. Zugazaga Cortazar A, Martinez M, Feliubadalo D, Bella Cueto MR, Serra L. Magnetic resonance imaging in the prenatal diagnosis of neural tube defects. Insights Imaging. 2013;4:225.

Lumps and Bumps: Scalp and Skull Lesions

10

Nelson Moussazadeh and Matei A. Banu

Vignette A 2-year-old boy who you have followed in your practice since birth has had 2 weeks of subtle enlargement of a 1 cm round mass at the nasion. His parents were concerned because it seemed to get larger the previous night when he was crying and this morning a large dark hair extruded from a pore in the center. He had unexplained bacterial meningitis when he was 7 months old. This child has:

(a) An infected sebaceous cyst
(b) An encephocoele
(c) A dermoid cyst with dermal sinus tract
(d) A skull fracture with leptomeningeal cyst

Answer: (c) Dermoid cysts are commonly located along the midline, at the glabella, anterior fontanelle, nasion, and vertex. Dermoid cysts and tracts, containing a wider variety of dermal components than epidermoid counterparts, mostly present to clinical attention in infancy and early childhood and intracranial extension has been reported in approximately 36 % of cases, with intradural extension in 16 %.

Scalp and skull lesions are manifestations of a wide variety of processes and pathologies, with a corresponding variance in treatment and prognosis. When encountered in children, these lesions should be evaluated with an understanding of their potential significance in this unique demographic group, and with a low threshold for specialty referral and potential imaging as appropriate. While most frequently benign, many lesions are nonetheless of sufficient cosmetic concern or are diagnostically ambiguous; pediatric neurosurgeons are uniquely qualified and equipped for the evaluation and management of these lesions, for craniofacial reconstruction as needed with the assistance of colleagues with expertise in plastic surgery, dermatology, or otolaryngology, and for further referral for any adjuvant treatment modalities.

Clinical Presentation and Evaluation

While visual and tactile features of masses may be similar across disparate etiologies (Table 10.1), historical and clinical features of scalp and skull lesions frequently inform their ultimate diagnoses to a large degree. At the most extreme end of the spectrum, congenital lesions including neural tube defects such as meningocele/meningoencephalocele are clearly apparent at birth. Other congenital processes such as aplasia cutis and dermoid tracts are noticed in the earliest weeks of life once birth-related scalp edema has subsided.

N. Moussazadeh, M.D. (✉) • M.A. Banu, M.D.
Department of Neurological Surgery, New York Presbyterian-Weill Cornell Medical Center, 525 East 68th Street, New York, NY 10065, USA
e-mail: moussazn@mskcc.org

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_10

Table 10.1 Differential diagnosis of scalp and skull lesions in children

Pathologic category	Disorders
Congenital	Aplasia cutis
	Atretic encephalocele
	Dermoid/epidermoid cyst
	Enlarged biparietal foramina
	Sinus pericranii
Traumatic	Caput succedaneum
	Cephalohematoma
	Growing skull fracture (leptomeningeal cyst)
Vascular	Hemangioma
	Sinus pericranii
	Arteriovenous fistula/cirsoid aneurysm
Neoplastic—benign	Aneurysmal bone cyst
	Fibrous dysplasia
	Giant cell tumor
	Infantile myofibroma
	Neurofibroma
	Osteoblastoma
	Osteoid osteoma
	Osteoma
	Ossifying fibroma
Neoplastic—malignant	Osteogenic sarcoma
	Ewing's sarcoma
	Chordoma, chondrosarcoma
	Metastases including neuroblastoma
Inflammatory	Cranial fasciitis
	Necrobiotic nodule
	Langerhans cell histiocytosis
	Lymphadenopathy

Neurologic examination, while essential to the evaluation of any patient with a suspected intracranial process, is both difficult and poorly sensitive in this age group; meticulous fontanel examination and trending of head circumference remains critical. Among older infants and children, tenderness or pain is not specific for any particular pathology.

For all pediatric patients with suspected neurologic pathology, particular emphasis should be placed on family history (e.g., for neurocutaneous disorders), and age-appropriate neurologic symptoms including seizures, divergent macrocephaly, and endocrinopathies (e.g., diabetes insipidus, precocious puberty) should be ruled out. Clinical examinations should include head circumference and fontanel palpation (in those younger than 2 years of age) and include cutaneous, systemic and inflammatory evaluations. Examination of the scalp and skull lesions themselves should note superficial integrity, location relative to midline, coloration, and appreciation for potential venous sinus or other vascular involvement.

Imaging

Radiographic evaluation of scalp and particularly skull lesions is frequently helpful. Fine-cut CT, MRI or MR angiography/venography can aid in the differential diagnosis. In some instances, however, (e.g., dermoid cysts), radiology may not be needed. Plain radiographs often suffice for scalp and skull lesions in combination with a thorough physical examination, while avoiding the need for the radiation exposure associated with CT; however these or MR imaging are frequently necessary for narrowing of the differential or surgical planning. Useful adjuncts include ultrasound in patients with open fontanels and invasive angiography in cases of vascular pathology.

Scalp Lesions

In the first year of life, the most common encountered processes are congenital, developmental, and traumatic perinatal anomalies. These include atretic cephaloceles, cephalohematomas, dermoid cysts, hemangiomas, and sinus pericranii. In toddlers and children under 5–10 years of age, dermoids and posttraumatic masses are frequent. In older children, neurofibromas and occasional angiomas enter the differential diagnosis [1].

Surgery is frequently required for scalp lesions, either for cosmesis, neurological decompression, pathological diagnosis or to prevent hemorrhagic or hyperemic sequelae of vascular lesions.

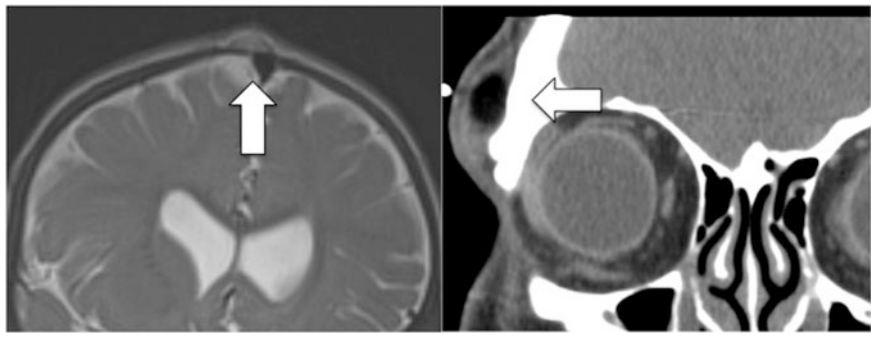


Fig. 10.1 Dermoids: Anterior fontanel dermoid on coronal T2-weighted MRI (*left*) and periorbital dermoid on coronal-reformat computed tomography scan (*right*)

Certain lesions are extensive and can erode into the calvarium, necessitating complex reconstruction techniques and meticulous perioperative planning.

Congenital Lesions

The most common congenital scalp lesions encountered in the pediatric patient are encephaloceles, aplasia cutis congenita, and dermoid or epidermoid cysts. The most frequent location for each of these lesions is the midline, and generally in the anterior face and scalp from the nasomaxillary complex to the vertex. Some of these lesions are associated with intracranial components or syndromic disorders and thus require a thorough diagnostic workup.

Dermoid and Epidermoid Cysts

Dermoid and epidermoid cysts are the most common scalp lesions in the pediatric population, comprising over 20 % of all scalp lesions [2]. Both are subcutaneous thin-walled sacs lined with stratified squamous epithelium, formed by entrapment of ectodermal elements during embryologic development partitioning ectodermal inclusion cysts in areas of suture closure, neural tube closure and division of cerebral hemispheres [3, 4]. They are thus commonly located along the midline, such as glabella, anterior fontanelle, nasion, and vertex, whereas epidermoid cysts are located more off-midline (Fig. 10.1). Both are more commonly located in the anterior scalp (e.g., in the periorbital area, over the anterior fontanelle, or frontotemporal region) than the posterior parietal and occipital regions [4]. Dermoid cysts and tracts, containing a wider variety of dermal components than epidermoid counterparts, mostly present to clinical attention in infancy and early childhood while epidermoid cysts more frequently do not become symptomatic until adolescence or adulthood; there is no clear gender predilection [4]. Intracranial extension has been reported in approximately 36 % of cases, with intradural extension in 16 % [5].

Dermoid and epidermoid cysts present as well-circumscribed non-tender slowly growing masses of with intact overlying skin. Growth occurs due to epithelial desquamation and keratin accumulation. Focal alopecia has also been described. Embryologically, dermoid cysts contain both dermal and epidermal elements whereas epidermoid cysts only contain epidermal elements. Although they are commonly isolated to the skin and subcutaneous tissue, they may have intracranial extension with a dermal sinus, and may present with meningitis.

Radiographically, dermoid cysts are nonenhancing soft-tissue masses that may result in scalloping of the adjacent bone on CT, while

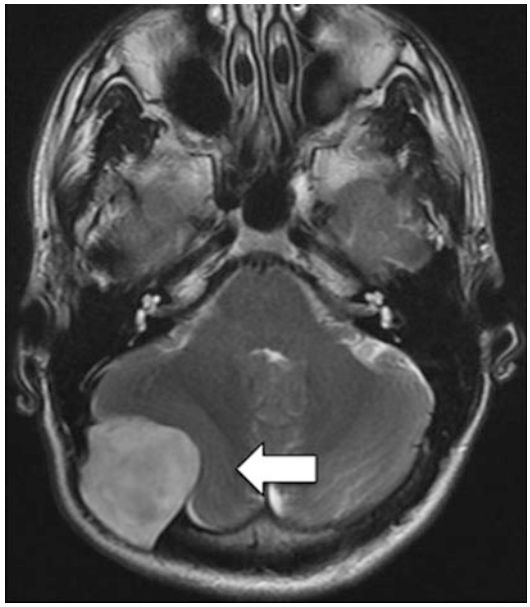


Fig. 10.2 Occipital dermoid as demonstrated on axial T2-weighted MRI with posterior fossa intracranial extension

MRI may evaluate the presence of intracranial extension. Epidermoid cysts are typically lytic on CT, and T2 bright and diffusion restricting on MRI; they can have a heterogeneous appearance depending on the heterogeneity of their contents [1]. In many cases the signal characteristics on imaging alone can distinguish between these two processes (with dermoid cysts often similar to fat on CT/MRI and with epidermoid cysts with characteristics more similar to simple fluid), this distinction frequently does not alter the decision of how to manage these lesions [6].

While dermoid cysts are most commonly painless and otherwise asymptomatic, surgical removal is usually recommended given their potential to enlarge and penetrate the skull (Fig. 10.2). In cases of dermal sinus tract, the feared complication of meningitis makes exploration a necessity. Preoperative MRI scans are frequently unnecessary but may be recommended for surgical planning to rule out, for example, sagittal sinus involvement. Most lesions can be removed in a surgical procedure lasting less than an hour. Recurrence has been reported both intracranially and extracranially [7].

Encephaloceles and Atretic cephaloceles

Cephaloceles are defects of the cranial vault and leptomeninges (Fig. 10.3). Based on the type of tissue herniating through the defect, cephaloceles are classified as either meningoceles, if they solely contain meninges and cerebrospinal fluid or as encephaloceles, if brain tissue is also herniated. Atretic encephaloceles, comprising approximately 37.5–50 % of encephaloceles contain a small nodule of fibro-fatty neural rests that are attached to the dura through a connective tissue stalk [6, 8, 9]. Reported incidence of encephaloceles varies widely in the literature, from 1 in every 40,000 live births to 7 % depending on the geographical and demographic characteristics of the studied population [10–13].

Cephaloceles occur either due to incomplete closure of the calvarium, such as defective induction of bone formation or due to bone erosion caused by an intracranial mass or cyst. The latter is the mechanism for acquired encephaloceles. The meningeal sac most commonly protrudes with or without brain tissue in the occipital or parietal regions (75 %), with only 15 % of cases presenting with protrusions in the frontoethmoidal area and 10 % in the skull base region, specifically the naso-pharynx [13]. Moreover, frontoethmoidal encephaloceles are more common in patients of southeastern Asian descent.

Occipital cephaloceles are more common in girls [10]. While most are sporadic, some cases are syndromic, for example as seen in Meckel syndrome, and with Chiari III and Dandy-Walker malformations as well as with severe callosal abnormalities [10, 11]. For syndromic etiologies, *MKS1*, *TMEM67*, *TMEM216*, *RPGRIP1L*, and *CEP290* aberrancies have been associated with cephalocele formation [10].

MR and ultrasound are capable of evaluating the extent of brain and CSF extrusion; ultrasound has the advantage of allowing rapid prenatal or postnatal visualization of the sac and its likely contributory compartments, while MRI provides the precise intracranial anatomic definition necessary for the thorough work-up required for these patients. Evaluating occipital encephaloceles for

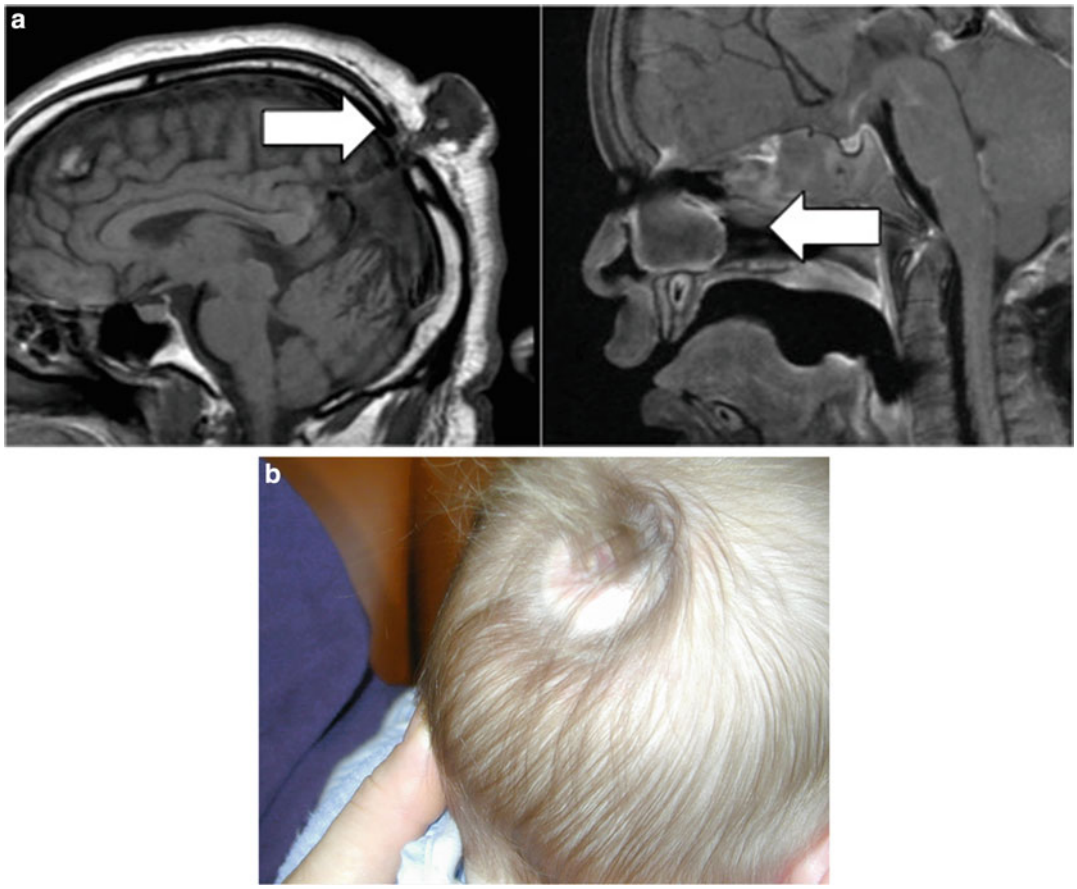


Fig. 10.3 (**a**) Encephaloceles: Atretic parietal encephalocele (*left*), and foramen cecum encephalocele (*right*) on sagittal T1-weighted magnetic resonance imaging. (**b**) The hair collar sign: A ring of dark, coarse long hair around a midline scalp nodule is associated with atretic encephalocele and warrants MR imaging

cerebellar and venous sinus involvement is essential prior to surgery [14]. CT may be used to assist with defining bony boundaries preoperatively.

The surgical management of cephaloceles involves resection of the sac with ligature of the base and closure of the defect, for example with pericranial grafts, and is associated with good cosmetic outcomes [15]. Careful dissection of the herniated sac is of utmost importance, as the dura is thin and very adherent to the bone in pediatric patients. For skull base and fronto-ethmoidal encephaloceles, endonasal endoscopic repair is a viable option [16, 17]. Fronto-ethmoidal encephaloceles frequently require complex combined craniofacial approaches. Common complications of the surgical procedure are CSF leaks, meningitis and wound compromise.

Aplasia Cutis Congenita of the Scalp

Aplasia cutis congenita (ACC) is a rare congenital syndrome characterized by the focal absence of cutaneous tissue, frequently affecting all layers of the skin and adjacent tissue (Fig. 10.4) [18]. Furthermore, in 15–30 % of patients, defects of the skull bone and/or dura can also occur, exposing the brain and sagittal sinus and thereby increasing the risk of infection, thrombosis and hemorrhage [19]. Dural and skull defects can also lead to associated encephaloceles, further complicating the differential diagnosis. The most common location is the vertex, accounting for over 70 % of cases [19]. The lesion is usually solitary, although multiple lesions have also been reported [20]. Its incidence is 1 in 10,000, with a

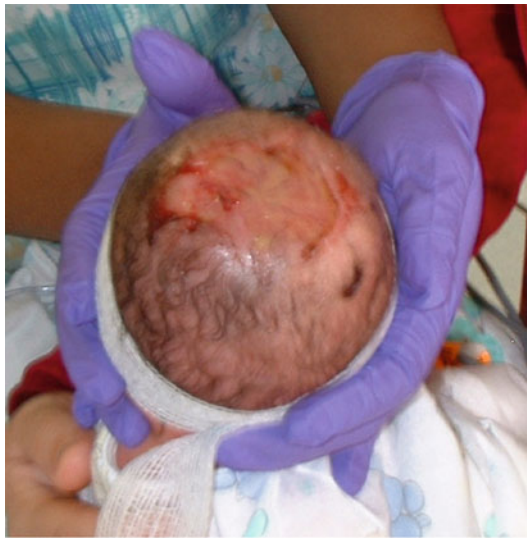


Fig. 10.4 Aplasia cutis congenita

slight female predominance (7:5) [19, 21]. Although the exact etiology is unknown, autosomal dominant inheritance has been demonstrated in 25 % of cases [4]. Associations with other syndromes have also been described such as the Adams-Oliver syndrome with absence of lower extremities below calf region, absence of all upper extremity digits, cutis marmorata telangiectatica, cortical fissure, and/or bilateral clubfoot [22].

Untreated ACC can lead to meningitis, hemorrhage with exsanguination, sagittal sinus thrombosis, and seizures. Mortality rates in these cases are as high as 20–50 %, and are higher in patients with complex lesions affecting the bone and dura [18, 23]. Management is guided by the extent of the lesion, location and the affected structures. Treatment of small lesions may consist of careful wound dressing, regular wound inspection and prophylactic antibiotics, followed by delayed scar excision as needed. Newer dressing modalities, such as Omiderm, Xeroform, Acticoat, and Elasto-Gel, have decreased the need for cumbersome frequent dressing changes. These dressing techniques also decrease inflammation and infection therefore promoting wound healing. The purpose of wound dressing is to maintain a moist healing environment and prevent eschar formation [18]. Bacteriostatic dressings further decrease the risk of infection and should be considered as the treatment of choice. Conservative measures have been proven beneficial even in large defects though very frequently result in local alopecia. Several reports suggest conservative management to be the preferred method of choice in the neonatal period in order to avoid surgical complications [18, 20]. Frequently, lesions involving the vertex and therefore underlying the posterior fontanel close spontaneously at 6–8 weeks, together with the normal closure of the fontanel [18]. However, for lesions exposing the dura or brain, prompt early surgical management is imperative. Surgical reconstruction techniques have varied from full-thickness skin grafts to local scalp flaps, pericranial flaps, autologous bone grafts, tissue expansion, and free flaps. Local flaps can provide immediate coverage of exposed neural structures and therefore reduce the risk of infection. Cranioplasty using the split-rib technique or using autologous pericranium has been proven beneficial in lesions involving the skull. In certain cases, staged tissue expansion and skull reconstruction might be necessary. In such cases, tissue expanders are used to construct a well-vascularized space for the cranioplasty. Graft failure and necrosis are potential complications of the reconstruction surgery along with sagittal sinus thrombosis, mostly due to abnormal vascular supply and vascular anastomoses of the region.

Traumatic Lesions

Cephalohematoma, Caput Succedaneum, Subgaleal Hematoma

In the newborn, a variety of birth trauma-related lesions may be manifest in the scalp depending on the compartment injured and occur in 1–2 % of spontaneous vaginal deliveries and 3–4 % in forceps assisted deliveries A full description of the various manifestations of bleeding in and around the skull layers is available in Chap. 3, but a figure is included here summarizing the various traumatic lesions as they are important to keep in mind within the first few years of life when formulating a differential diagnosis in a child with a skull mass (Fig. 10.5) [24].

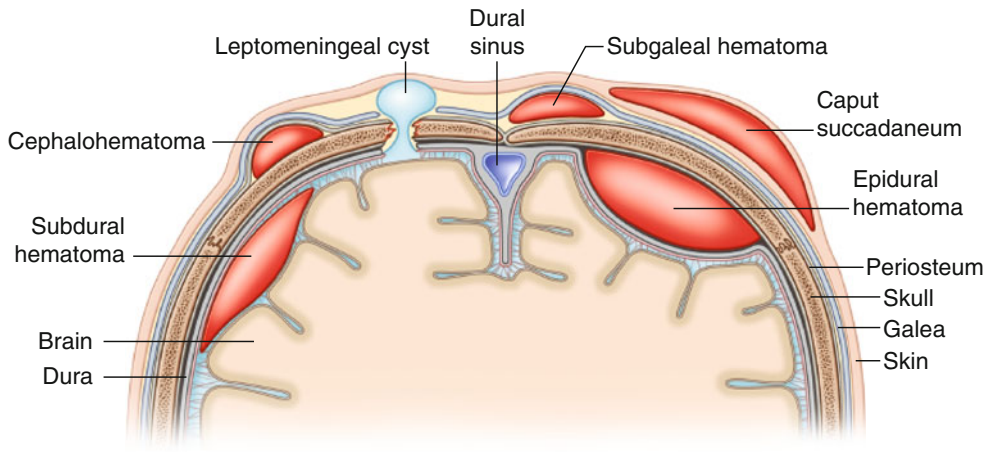


Fig. 10.5 Pediatric intra- and extracranial traumatic masses. Note that caput succadaneum is superficial to the galea, subgaleal hemorrhages remain superficial to the periosteum, and that cephalohematomas are subperiosteal. Epidural hemorrhages are typically related to laceration of dural arteries (especially the middle meningeal artery) and are distinguished radiographically by their lentiform shape and dural constraint, unlike subdural hemorrhages which cross suture lines. Growing skull fractures or leptomeningeal cysts are rare and late masses caused by cystic cerebrospinal fluid dilatations and bony diastasis associated skull fractures lacerating the dura in infants and toddlers

Vascular Lesions

Sinus Pericranii

Sinus pericranii is a rare slow-flow vascular anomaly involving extracranial and intracranial veins. It is a collection of congenital scalp veins that communicate with intracranial venous sinuses through numerous dilated diploic veins. Typically congenital, cases of posttraumatic sinus pericranii have also been reported [25]. It typically presents as a soft, bulging but compressible mass of 1.5 cm or smaller diameter over or paramedian to the sagittal midline, mostly over the central or posterior third of the superior sagittal sinus. Parietal (34 %), occipital (23 %), and temporal (4 %) locations are also possible [26]. The lesion enlarges with the Valsalva maneuver, crying, neck flexion, or other maneuvers increasing intracranial pressure and reduces with elevation or direct pressure. It is mostly asymptomatic and pulsations or bruits are not observed [27]. Contrast-enhanced CT or MR imaging demonstrates significant extracranial venous flow and frequently can pinpoint the connecting venous channel; an evaluation of previse venous anatomy are essential to rule out additional vascular abnormalities which may include aneurysmal malformations of the internal veins, cavernous hemangiomas, and venous angiomas. CT typically also demonstrates scalloping of the inner or outer table of the cranial vault owing to erosion.

Surgical management is generally not required unless the lesion causes discomfort, as the natural history of these involves involution following puberty, while thrombosis is also possible [28]. If resection is desired for cosmetic concerns, careful resection of the vascular lesions with or without preoperative embolization is curative, and large bony defects can be repaired. Preoperative vascular imaging is essential to rule out communication with the superior sagittal sinus. It has been suggested that the role of the vascular anomaly in normal venous drainage of the brain should be carefully evaluated prior to resection [26]. Therefore, a rare complication is thrombosis of the sagittal sinus and should be avoided.

Hemangiomas

Scalp hemangiomas are relatively common benign endothelial proliferations that rapidly increase in size in the first years of life and gradually involute in late childhood or after puberty.

They are seen in some 1–2 % of infants (3:1 female:male ratio and with 60 % in the head and neck), and are associated with prematurity and a variety of syndromes [13, 29]. Depending on the depth of vascular proliferation, the hemangioma appears either as a bright red maculopapular lesion if superficial, or blue if deep. These may involve the skull or intracranial compartment primarily or by erosion, while primary calvarial hemangiomas are most commonly seen externally given the relatively thin scalp of children [30]. Multiple in 15 % of cases, hemangiomas are usually asymptomatic, classically compress with dependency or external pressure given their low intrinsic pressure, and rarely bleed or ulcerate [31]. Rare cases of infection and painful thrombosis have been reported [32]. Depending on location, hemangiomas can also lead to facial paralysis and hearing loss via compression of the associated peripheral nerves or external ear structures. When located within the calvarial bone, hemangiomas can lead to headaches, scalp pain, and palpable masses.

Hemangiomas of the scalp are generally benign with involution and/or complete regression by 10 years and rarely require treatment. Prognosis is excellent even without therapy [32]. However, giant hemangiomas, rarely reported in the literature, are more prone to complications such as high-output heart failure, or thrombocytopenia with associated hemorrhagic complications as part of the Kasabach Merritt syndrome, and should therefore be closely monitored [33]. Intralesional or systemic steroids, embolization, interferon alfa-2a, or cryosurgery as well as surgical resection are part of the therapeutic armamentarium for these lesions. Location and depth of the hemangioma as well as the potential for complications are indications for aggressive surgical management. Esthetically incapacitating lesions, lesions that have recurrent hemorrhage or ulcerations along with giant hemangiomas require prompt surgical intervention. Most lesion regress by late childhood and are more adequately managed with conservative measures [32].

The port-wine stain is the most common syndromic face and scalp hemangioma and is associated with Sturge-Weber syndrome. This "port-wine" stain is a pink or red macule located on the forehead, face and nuchal area of newborns, and is associated with a 5 % rate of underlying intracranial malformations. Similarly, diffuse hemangiomas demand further workup for the PHACES syndrome (posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of the aorta, eye anomalies, sternal cleftin, or supraumbilical raphe). Peri-orbital hemangiomas require imagistic workup in order to assess intracranial extension. MR imaging is sufficient to assess intracranial extension and to rule out potential intracranial malformations. Typical MRI findings include homogenous T2 brightness with associated small flow voids [13].

AVMs and Venous Malformations of the Scalp

Arterio-venous malformations are rare congenital or posttraumatic aberrant vascular lesions that are have been encountered in the scalp as pulsatile masses with palpable thrills in infants with high-output cardiac physiology [34]. These children also have dilated scalp, facial and neck veins owing to the venous hypertension related to their malformation. These lesions typically are progressive and are diagnosed on MRI in the setting of a tangle of flow voids. Angiography is an important diagnostic tool in AVMs, and should be considered prior to treatment especially given the potential existence of associated aneurysms or of communication with large dural sinuses which are relevant surgically [35]. Treatment generally consists of embolization or surgical resection of the nidus or and may require a combination of these techniques. Preoperative embolization should be considered if excessive blood loss is possible and may pose a risk, especially in infants and young children. Potential postoperative complications are scalp necrosis and venous thrombosis due to communications of the vascular malformation with the normal scalp circulation.

In contrast, venous malformations are congenital dysmorphic venous lesions that occur in

the head and neck area in up to 40 % of cases, and are not associated with high pressure or high flow. They are grossly bluish and nonpulsatile; on MRI they are typically T2-bright with septations and heterogenous enhancement, do not demonstrate flow voids, and commonly have associated small venous calcifications (phleboliths) [13]. Venous malformations are typically treated with sclerotherapy.

Subcutaneous Nodules

Necrobiotic Granulomas and Subcutaneous Granuloma Annulare

Subcutaneous necrobiotic granulomas are painless immobile scalp masses that are usually fixed to the fascia. While their precise cause is unknown, they are thought to be primarily inflammatory lesions given microscopic findings of necrosis and chronic inflammatory changes with palisading histiocytes and giant cells in the upper dermis. Given that lesion(s) of varying sizes are found commonly on the frontal and occipital scalp, regions which are most commonly exposed to minor trauma, posttraumatic etiologies have been proposed [36]. While asymptomatic nodules have significant histopathological similarities to rheumatoid nodules, given that isolated necrobiotic granulomas are not associated with systemic rheumatic symptoms they are considered a separate benign entity [37].

Different clinical patterns have been described, ranging from asymptomatic nodules to groups superficial flesh-colored papules to large areas of scarring alopecia with ulcerations. Biopsy is typically advocated for diagnosis (with the exception of known juvenile rheumatoid arthritis), while surgical excision is usually otherwise not required given their propensity for spontaneous resolution without complication [36].

Subcutaneous granuloma annulare (SGA) is a rare, related disorder of unclear etiology with deep dermal nodules that may adhere to the periosteum. Various treatment modalities have been attempted thus far with poor efficacy including topical corticosteroids, potassium iodide, dapsone, niacinamide, chlorambucil, and isotretinoin. Surgical excision has been shown to have a poor efficiency as well, with high rates of recurrence [38].

Neurofibromas

Neurofibromas are locally aggressive benign nerve sheath tumors of neuroectodermal origin that are most commonly associated with neurofibromatosis type I (NF1; 1:3000 incidence at birth) in up to 10 % of patients [39]. They are the most common tumors of the peripheral nerve sheath and represent 5 % of all benign soft tissue tumors. These tumors diffusely infiltrate the dermis and subcutaneous tissue, and occasionally enter the orbit or cranium, but normal structures are usually spared [40]. Malignant transformation has been reported and should be considered if pain or rapid enlargement is described, and in NF1 patients (who are most likely to develop the plexiform subtype of this lesion) [40]. In isolated lesions a complete NF1 work-up is thus required, as these lesions may be the initial manifestation of the disease. Localized neurofibromas are isolated, flesh-colored dome shaped or pedunculated papules, displaying a characteristic buttonhole sign [39]. Plexiform neurofibromas on the other hand involve multiple nerve branches and have a worm-like feel upon palpation [39]. Diffuse neurofibromas of the scalp have been reported as well and involve extensive areas of alopecia [40]. These are single lesions with a rapidly infiltrative growth pattern. Ultrasound and MRI are well suited to assess the size and neurovascular relations of deep neck lesions. Lesions producing pain or functional impairment require surgical excision. These tumors frequently entail a rich vascular supply and preoperative angiography and embolization have been suggested to be beneficial in reducing the risk of hemorrhage [39, 41]. Recurrence is possible even after gross total resection. Due to the high recurrence rates and potential for malignant transformation, close follow-up is recommended.

Infantile Myofibroma and Primary Fibrosarcomas of the Scalp

Infantile myofibroma is a benign mesenchymal proliferation and an indolent form of sarcoma. It is one of the more common benign fibrous tumors of infancy that can involve both the scalp and the skull, and sometimes even the dura. Lesions are usually solitary but if multiple lesions are present it is termed infantile myofibromatosis. It presents as an asymptomatic enlarging soft tissue mass of various sizes, ranging from several millimeters to several centimeters, in the neck or frontal scalp. Pathologic diagnosis is important to exclude the more aggressive form of spindle cell sarcoma and a variety of more aggressive sarcomas [8]. Surgery is typically advocated but in select patients observation may be warranted given their benign behavior; they can, however, rapidly enlarge with resultant compressive symptoms necessitating surgical excision [42].

Fibrosarcomas of the scalp can develop after local irradiation, burns and trauma, and are more common in neurofibromatosis patients [43]. Approximately 5 % of all fibrosarcomas occur in the head and neck area, the majority (25–40 %) in children under 5 years of age [13]. There is a slight male predominance (3:2 gender ratio). These are highly vascular fibroblastic tumors with large areas of hemorrhage and necrosis. Gross total resection is the standard therapy for such lesions and is frequently possible given their rare intracranial extension. Fibrosarcomas have been shown to be radiosensitive and radiation therapy should be used for recurrences or advanced cases [43]. On CT, fibrosarcomas are of homogenous attenuation, enhance variably, and demonstrate surrounding areas of bony remodeling, and MRI may be useful preoperatively [28].

Cranial Fasciitis

This is a rare, non-neoplastic, firm, painless, rapidly expanding mass limited to children <6 years of age [44]. It is more common in males and is usually found in the parietotemporal region [44]. Etiology is unknown but it has been linked to previous craniotomies and other forms of head trauma [45, 46] and may be a process originating in the periosteum or galea with secondary skull reaction. While cranial fasciitis has the potential to rapidly expand to a large size with erosion through the skull's outer external table, intracranial expansion is unusual. Symptoms may arise due to local compression and infiltration of immature bone. Resection is required (and curative) in such cases, while biopsy is important in all cases given the clinical and radiographic similarities with more aggressive processes including infantile myofibromas and various other sarcomas and histocytoma. X-rays frequently demonstrate a single lytic skull defect with an associated soft-tissue mass while MRI will demonstrate a T2 bright, non-contrast enhancing epicenter [44].

Skull Lesions

A similarly wide variety of skull processes present in the pediatric population, ranging from congenital and developmental, neoplastic, inflammatory, and infectious. In addition to the largely expansile lesions described below, the spectrum of craniosynostoses, plagiocephaly, and parietal foramina (covered in later chapters) may also result in abnormal calvarial conformations. The most common lesions are presented below.

Langerhans Cell Histiocytosis

Langerhans cell histiocytosis (LCH) is a blanket term for focal clonal proliferations of immature dendritic cells thought to be neoplastic in origin. The range of LCH disorders frequently involves bone and most commonly the skull, but may range from unisystem LCH (eosinophilic granuloma) to the multifocal multisystem Letterer-Siwe disease. An intermediate chronic multifocal form resulting in diabetes insipidus (from hypothalamic/pituitary involvement), calvarial and orbital involvement with proptosis is described in older classifications as Hand-Schüller-Christian disease [47].

Eosinophilic granuloma (EG) of the skull presents as a painful, enlarging swelling felt

through the scalp, most frequently in children aged 5–15. These lesions have a classic "punched-out" appearance on X-rays reflecting their lack of sclerotic margins (Fig. 10.6). Computed tomography demonstrates the extent of diploic involvement and, most commonly, only minimal intracranial mass effect. EG less commonly affects other organs including skin, lungs, and stomach.

Letterer-Siwe disease is an acute, fulminant disease typically affecting infants and children younger than 2 years of age, and commonly results in seborrheic-like cutaneous eruptions on the scalp and trunk, hepatosplenomegaly, lymphadenopathy, pulmonary lesions, and lytic osseous lesions. Resultant infiltrative myelosuppression contribute to the poor prognosis of this disease, which has a reported 50 % rate of survival at 5 years even with chemotherapy [48].

Historical management paradigms for solitary EG have focused on ruling out systemic involvement given that some 20–30 % may be multifocal. This is typically achieved via (X-ray) skeletal survey; radionucleotide bone scan may be complementary. The natural history of these lesions is unclear, with some reports of spontaneous regression. However, the preponderance of literature advocates for treatment via surgical curettage/resection with craniectomy; reconstruction options include split-thickness cranioplasty grafted from adjacent bone [49, 50]. As local and distant recurrences have been reported in up to 30 % of patients, respectively, these patients should undergo radiographic surveillance postoperatively [51].

Enlarged Parietal Foramina

Enlarged parietal foramina (EPF) is a condition of symmetric biparietal skull depressions due to defects of intramembranous ossification in the bilateral parietal bones. Normally, the majority of the skull, including the parietal bones, is ossified by the fifth month of gestation [52]. Insufficient ossification of the vascularized membranes around the parietal notch leads to permanent skull defects located near the intersection of the sagittal and lambdoid sutures ranging from several millimeters to several centimeters in size. Importantly, these lesions should be distinguished from the normal variant small (1–2 mm) parietal foramina, which transmit parietal emissary veins to the superior sagittal sinus (Fig. 10.7), and cranium bifidum or the Catlin mark, an EPF variant with a single large central parietal defect [53]. EPF has been reported in 1:15,000–1:50,000 live

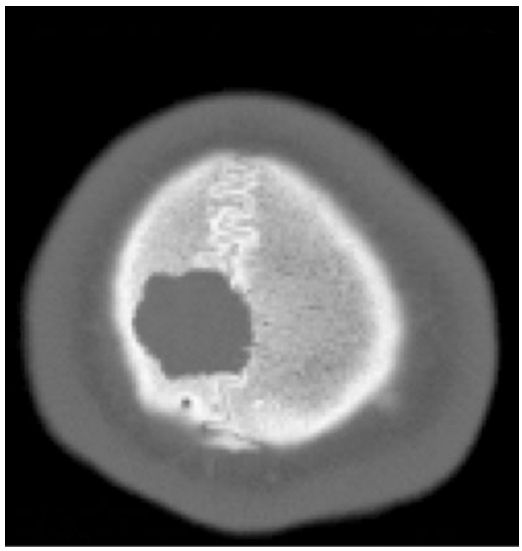


Fig. 10.6 Eosinophilic granuloma. Note the lesion's "punched-out" appearance reflecting a lack of a sclerotic margin

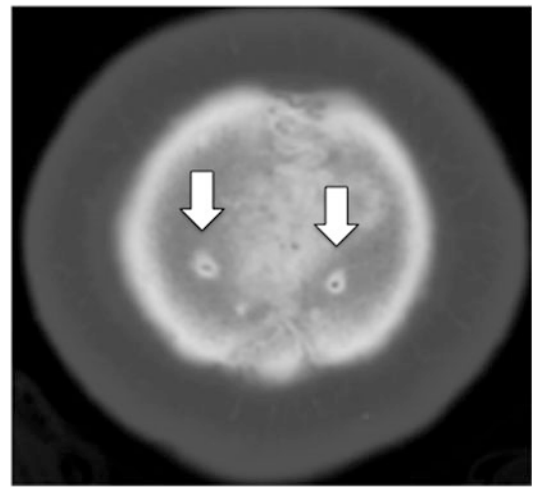


Fig. 10.7 Normal parietal foramina. Axial CT through the vertex demonstrating small persistent biparietal foramina in an adult

births [54], and is heritable in an autosomal dominant fashion with incomplete penetrance and associated with mutations in the MSX2 and ALX4 genes; some 16% of cases are sporadic [55]. Associations with craniofacial anomalies such as cleft palate, myelomeningocele/encephalocele, and cortical/vascular malformations of the posterior fossa have been reported. The size of the EPF does not correlate with the risk of associated brain abnormalities.

Clinically, EPF are identified as flattened symmetric divots upon palpation, and may be associated with enlarged posterior fontanels. Associated neurologic symptoms are rare in isolated EPF and may include seizures; gratuitous palpation and contact sports in patients with larger lesions should be avoided given the risk of inducing intracranial hypertension or direct injury [56]. On skull X-rays they manifest as oval symmetric radiolucencies resembling a pair of spectacles [52]. MR imaging is helpful in ruling out associated cortical abnormalities especially in those with epilepsy, and CT with three-dimensional reconstruction allows for better bony anatomy delineation than X-rays; vascular imaging is also frequently advocated to rule out associated vascular malformations prior to any surgical intervention [52]. Genetic counseling and testing may play a role in suspected familial or syndromic cases, including when there exists suspicion for the Potocki-Shaffer syndrome or ALX4-related frontonasal dysplasia [52]. EPF is generally treated conservatively, but large defects may require operative management, which is typically recommended at age 4: while progressive reduction of the defect has been described, spontaneous closure is generally incomplete. Cranioplasty is also frequently recommended for children with associated seizure disorders. Closure is generally achieved with autologous calvarial bone grafts or synthetic materials such as mesh plating with hydroxyapatite [57, 58].

Primary Bone Tumors

Primary bone tumors of the skull are all rare, and include osteoblastoma, osteoma, and osteoid osteoma. Osteoblastoma is the most common of these but remains rare in the calvarium accounting for some 3% of all osteoblastomas [59]. Typically presenting in the second decade of life as enlarging painful masses, on X-rays these lesions demonstrate osteolysis with surrounding sclerosis. CT is variable but usually reflects an expansile, non-enhancing intrinsic bone lesion often involving the outer table and rarely eroding the inner table, and may demonstrate calcification. Treatment is surgical, as while most are pathologically benign, lesions in older patients have a higher likelihood of demonstrating features of low-grade osteosarcoma.

Osteoid osteoma presents with pain masses; classically this pain is worst at night and responsive to aspirin. These demonstrate a lytic expansile lesion with sclerotic margins radiographically with a central calcified nidus of osteoid and woven bone pathologically. Like osteoblastoma, these lesions are more commonly encountered in the appendicular (especially lower extremity) skeleton and the posterior elements of the lumbar spine. Osteoma is exceedingly rare in the skull; it has been reported as a benign expansion of mature cortical bone without associated bony destruction and is hyperdense on CT. While these may be observed in the absence of symptoms or cosmetic deformity, or simply drilled down, the natural history and recurrence rates of these approaches is not clear. Osteomas are commonly resected with split-thickness cranioplasty grafting from adjacent skull.

Intraosseous Hemangioma

The most common primary osseous mass of the orbitozygomatic region is intraosseous (cavernous) hemangioma (IOH), and has been reported in children. These slowly-growing hamartomatous lesions are proliferations of endothelial-lined channels within normal bone. Typically affecting females, IOH presents with proptosis, extraocular disturbance/diplopia, or focal extraorbital bony swelling in the zygoma or frontal bone. CT has a classic "sunburst" pattern. Preoperative embolization has been advocated to reduce the risk of significant intraoperative hemorrhage given their vascularity.

Aneurysmal Bone Cyst

Aneurysmal bone cysts (ABC) are painful expanding non-neoplastic masses comprised of blood-filled cysts encountered in the first two decades of life, most often in long-bone metaphyses and in the cervicothoracic posterior elements. Predominantly encountered cranially in the facial bones, these may result in cranial neuropathies. Radiographically, ABCs are lytic, multiloculated expansile lesions of the inner and outer calvarial tables reflecting hemorrhagic products without proper blood vessels surrounded by thinned rims of expanded cortical bone. Treatment is surgical following embolization to mitigate a significant risk of intraoperative hemorrhage. Recurrence has been reported in the appendicular literature, which can be treated with radiotherapy. Given that a significant proportion of ABC are secondary to primary bone tumors (predominantly chondroblastoma, osteoblastoma, and giant cell tumor in the non-skull literature), an ABC diagnosis should prompt a close pathologic examination for elements of these tumors.

Fibrous Dysplasia

Fibrous dysplasia (FD) is a benign expansile process in which medullary bone is replaced with fibrosis. It presents as benign monostotic or polyostotic forms, with craniofacial involvement in up to half of cases. Presentation may include pain, cosmetic calvarial deformity, cranial neuropathies and potential pathologic fracture; in the common setting of sphenoid involvement and optic compression, visual loss and proptosis may be seen. McCune-Albright syndrome describes the constellation of polyostotic FD, hypersecretory endocrinopathies (most commonly precocious puberty), and unilateral café-au-lait spots. CT demonstrates a ground-glass appearance. Treatment for lesions only resulting in pain is aimed at symptomatic relief, while those resulting in neurologic deficit may be aimed at preserving function.

Metastases

Metastases should be routinely considered in the differential for those with extracranial malignancies, the most common solid form of which in children is neuroblastoma. Radiographically, osseous neuroblastoma metastases demonstrate the classic periosteal "hair-on-end" appearance on CT. Given the chemosensitivity of this disease, it frequently remains nonsurgical; however staging (including via MRI) and vigilant surveillance are required. Calvarial lymphoma has been described and remains rare in the pediatric population; like neuroblastoma, treatment is usually nonsurgical and requires diligent systemic treatment and follow-up.

Pediatrician's Perspective

1. Dermoid and epidermoid cysts are the most common scalp lesions in the pediatric population, comprising over 20 % of all scalp lesions. Think benign first.
2. Leaking cerebrospinal fluid, even if a pore or tract cannot be identified, necessitates a referral to a neurosurgeon who will evaluate for dermal sinus tract extending from skin to dura. Midline structures from the tip of the nose to the sacrum should be examined closely for enlarged pore or aberrant hair. This is an urgent consultation.
3. Hemangiomas of the scalp are generally benign with involution and/or complete regression by 10 years and rarely require treatment.
4. Primary bone tumors of the skull are all rare, and include osteoblastoma, osteoma, and osteoid osteoma, but the classical presentation is nighttime or early morning pain responsive to aspirin suggesting a biologic, or cortisol-sensitive, etiology. X-ray or CT will demonstrate a lytic expansile lesion with sclerotic margins.

Acknowledgements Many thanks to Apostolos J. Tsiouris, Associate Professor of Clinical Radiology at NewYork Presbyterian-Weill Cornell Medical College, for contribution of radiographic examples.

References

1. Willatt JM, Quaghebeur G. Calvarial masses of infants and children. A radiological approach. Clin Radiol. 2004;59:474–86.
2. Pannell BW, Hendrick EB, Hoffman HJ, Humphreys RP. Dermoid cysts of the anterior fontanelle. Neurosurgery. 1982;10:317–23.
3. Sorenson EP, Powel JE, Rozzelle CJ, Tubbs RS, Loukas M. Scalp dermoids: a review of their anatomy, diagnosis, and treatment. Childs Nerv Syst. 2013; 29:375–80.
4. Wood J, Couture D, David LR. Midline dermoid cyst resulting in frontal bone erosion. J Craniofac Surg. 2012;23:131–4.
5. Crawford R. Dermoid cyst of the scalp: intracranial extension. J Pediatr Surg. 1990;25:294–5.
6. Annet L, Duprez T, Grandin C, Dooms G, Collard A, Cosnard G. Apparent diffusion coefficient measurements within intracranial epidermoid cysts in six patients. Neuroradiology. 2002;44:326–8.
7. Rahbar R, Shah P, Mulliken JB, Robson CD, Perez-Atayde AR, Proctor MR, et al. The presentation and management of nasal dermoid: a 30-year experience. Arch Otolaryngol Head Neck Surg. 2003;129:464–71.
8. Asadi Amoli F, Sina AH, Kasai A, Ayan Z. A well-known lesion in an unusual location: infantile myofibroma of the eyelid: a case report and review of literature. Acta Med Iran. 2010;48:412–6.
9. Martinez-Lage JF, Sola J, Casas C, Poza M, Almagro MJ, Girona DG. Atretic cephalocele: the tip of the iceberg. J Neurosurg. 1992;77:230–5.
10. Copp AJ, Stanier P, Greene ND. Neural tube defects: recent advances, unsolved questions, and controversies. Lancet Neurol. 2013;12:799–810.
11. Mahapatra AK, Suri A. Anterior encephaloceles: a study of 92 cases. Pediatr Neurosurg. 2002;36:113–8.
12. Oucheng N, Lauwers F, Gollogly J, Draper L, Joly B, Roux FE. Frontoethmoidal meningoencephalocele: appraisal of 200 operated cases. J Neurosurg Pediatr. 2010;6:541–9.
13. Moron FE, Morriss MC, Jones JJ, Hunter JV. Lumps and bumps on the head in children: use of CT and MR imaging in solving the clinical diagnostic dilemma. Radiographics. 2004;24:1655–74.
14. Morioka T, Hashiguchi K, Samura K, Yoshida F, Miyagi Y, Yoshiura T, et al. Detailed anatomy of intracranial venous anomalies associated with atretic parietal cephaloceles revealed by high-resolution 3D-CISS and high-field T2-weighted reversed MR images. Childs Nerv Syst. 2009;25:309–15.
15. Hervey-Jumper SL, Cohen-Gadol AA, Maher CO. Neurosurgical management of congenital malformations of the brain. Neuroimaging Clin N Am. 2011;21:705–17. ix.
16. Komotar RJ, Starke RM, Raper DM, Anand VK, Schwartz TH. Endoscopic endonasal versus open repair of anterior skull base CSF leak, meningocele, and encephalocele: a systematic review of outcomes. J Neurol Surg A Cent Eur Neurosurg. 2013; 74:239–50.
17. Nyquist GG, Anand VK, Mehra S, Kacker A, Schwartz TH. Endoscopic endonasal repair of anterior skull base non-traumatic cerebrospinal fluid leaks, meningoceles, and encephaloceles. J Neurosurg. 2010; 113:961–6.
18. Harvey G, Solanki NS, Anderson PJ, Carney B, Snell BJ. Management of aplasia cutis congenita of the scalp. J Craniofac Surg. 2012;23:1662–4.
19. Bharti G, Groves L, David LR, Sanger C, Argenta LC. Aplasia cutis congenita: clinical management of a rare congenital anomaly. J Craniofac Surg. 2011;22:159–65.
20. Suarez O, Lopez-Gutierrez JC, Andres A, Barrena S, Encinas JL, Luis A, et al. Aplasia cutis congenita: surgical treatment and results in 36 cases. Cir Pediatr. 2007;20:151–5.
21. Kim CS, Tatum SA, Rodziewicz G. Scalp aplasia cutis congenita presenting with sagittal sinus hemorrhage. Arch Otolaryngol Head Neck Surg. 2001;127:71–4.
22. Bilginer B, Onal MB, Bahadir S, Akalan N. Aplasia cutis congenita of the scalp, skull and dura associated with Adams-Oliver syndrome. Turk Neurosurg. 2008;18:191–3.
23. Santos de Oliveira R, Barros Juca CE, Lopes Lins-Neto A, Aparecida do Carmo Rego M, Farina J, Machado HR. Aplasia cutis congenita of the scalp: is there a better treatment strategy? Childs Nerv Syst. 2006;22:1072–9.
24. Gandolfo C, Krings T, Alvarez H, Ozanne A, Schaaf M, Baccin CE, et al. Sinus pericranii: diagnostic and therapeutic considerations in 15 patients. Neuroradiology. 2007;49:505–14.
25. Bollar A, Allut AG, Prieto A, Gelabert M, Becerra E. Sinus pericranii: radiological and etiopathological considerations. Case report. J Neurosurg. 1992;77:469–72.
26. Akram H, Prezerakos G, Haliasos N, O'Donovan D, Low H. Sinus pericranii: an overview and literature review of a rare cranial venous anomaly (a review of the existing literature with case examples). Neurosurg Rev. 2012;35:15–26.
27. Ota T, Waga S, Handa H, Nishimura S, Mitani T. Sinus pericranii. J Neurosurg. 1975;42:704–12.
28. Carpenter JS, Rosen CL, Bailes JE, Gailloud P. Sinus pericranii: clinical and imaging findings in two cases of spontaneous partial thrombosis. AJNR Am J Neuroradiol. 2004;25:121–5.
29. Burns AJ, Navarro JA, Cooner RD. Classification of vascular anomalies and the comprehensive treatment of hemangiomas. Plast Reconstr Surg. 2009; 124:69e–81.
30. Wyke BD. Primary hemangioma of the skull; a rare cranial tumor; review of the literature and report of a case, with special reference to the roentgenographic appearances. Am J Roentgenol Radium Ther. 1949;61:302–16.

31. Sargent EN, Reilly EB, Posnikoff J. Primary hemangioma of the skull. Case report of an unusual tumor. Am J Roentgenol Radium Ther Nucl Med. 1965; 95:874–9.
32. Spector JA, Blei F, Zide BM. Early surgical intervention for proliferating hemangiomas of the scalp: indications and outcomes. Plast Reconstr Surg. 2008;122: 457–62.
33. Little KE, Cywes S, Davies MR, Louw JH. Complicated giant hemangioma: excision using cardiopulmonary bypass and deep hypothermia. J Pediatr Surg. 1976;11:533–6.
34. Massimi L, De Bonis P, Esposito G, Novegno F, Pettorini B, Tamburrini G, et al. Vertex scalp mass as presenting sign of a complex intracranial vascular malformation. J Neurosurg Pediatr. 2009;3:307–10.
35. Matsushige T, Kiya K, Satoh H, Mizoue T, Kagawa K, Araki H. Arteriovenous malformation of the scalp: case report and review of the literature. Surg Neurol. 2004;62:253–9.
36. Medlock MD, McComb JG, Raffel C, Gonzalez-Gomez I. Subcutaneous palisading granuloma of the scalp in childhood. Pediatr Neurosurg. 1994;21:113–6.
37. Hata N, Inamura T, Imayama S, Morioka T, Nishio S, Miyazono M, et al. Multiple palisading granulomas in the scalp of an infant: a case report. Surg Neurol. 2001;56:396–9.
38. Jankowski PP, Krishna PH, Rutledge JC, Waldhausen J, Avellino AM. Surgical management and outcome of scalp subcutaneous granuloma annulare in children: case report. Neurosurgery. 2008;63:E1002. discussion E1002.
39. Macias VC, Rafael M, Fernandes C, Rosa JC. Diffuse neurofibroma--an uncommon cause of alopecia. An Bras Dermatol. 2013;88:166–9.
40. Yoo KH, Kim BJ, Rho YK, Lee JW, Kim YJ, Kim MN, et al. A case of diffuse neurofibroma of the scalp. Ann Dermatol. 2009;21:46–8.
41. Ergun SS, Emel E, Karabekir S, Buyukbabani N. Extracranial diffuse neurofibroma with intracranial extension. Plast Reconstr Surg. 2000;105:801–3.
42. Engel M, Thiele O, Mechtersheimer G, Hoffmann J, Freudlsperger C, Freier K, Castrillon-Oberndorfer G. Solitary infantile myofibroma of the skull. J Craniofac Surg. 2011;22(6):e66–8.
43. Muzumdar D, Michaud J, Ventureyra EC. Primary giant congential infantile fibrosarcoma of the scalp: case report and review of literature. Childs Nerv Syst. 2006;22:300–4.
44. Johnson KK, Dannenbaum MJ, Bhattacharjee MB, Illner A, Dauser RC, Whitehead WE, et al. Diagnosing cranial fasciitis based on distinguishing radiological features. J Neurosurg Pediatr. 2008;2:370–4.
45. Pagenstecher A, Emmerich B, van Velthoven V, Korinthenberg R, Volk B. Exclusively intracranial cranial fasciitis in a child. Case report. J Neurosurg. 1995;83:744–7.
46. Summers LE, Florez L, Berberian ZJ, Bhattacharjee M, Walsh JW. Postoperative cranial fasciitis. Report of two cases and review of the literature. J Neurosurg. 2007;106:1080–5.
47. Kaul R, Gupta N, Gupta S, Gupta M. Eosinophilic granuloma of skull bone. J Cytol. 2009;26(4):156–7.
48. Aster JC. Diseases of white blood cells, lymph nodes, spleen and thymus. In: Kumar V, Abbas AK, Fausto N, editors. Robbins and cotran pathologic basis of disease. 7th ed. Philadelphia, PA: Elsevier Saunders; 2005.
49. Rawlings 3rd CE, Wilkins RH. Solitary eosinophilic granuloma of the skull. Neurosurgery. 1984;15(2): 155–61.
50. Martinez-Lage JF, Poza M, Cartagena J, Vicente JP, Biec F, de las Heras M. Solitary eosinophilic granuloma of the pediatric skull and spine. The role of surgery. Childs Nerv Syst. 1991;7(8):448–51.
51. Oliveira M, Steinbok P, Wu J, Heran N, Cochrane D. Spontaneous resolution of calvarial eosinophilic granuloma in children. Pediatr Neurosurg. 2003;38(5):247–52.
52. Griessenauer CJ, Veith P, Mortazavi MM, Stewart C, Grochowsky A, Loukas M, et al. Enlarged parietal foramina: a review of genetics, prognosis, radiology, and treatment. Childs Nerv Syst. 2013;29:543–7.
53. Mupparapu M, Binder RE, Duarte F. Hereditary cranium bifidum persisting as enlarged parietal foramina (Catlin marks) on cephalometric radiographs. Am J Orthod Dentofacial Orthop. 2006;129:825–8.
54. Reddy AT, Hedlund GL, Percy AK. Enlarged parietal foramina: association with cerebral venous and cortical anomalies. Neurology. 2000;54:1175–8.
55. Mavrogiannis LA, Taylor IB, Davies SJ, Ramos FJ, Olivares JL, Wilkie AO. Enlarged parietal foramina caused by mutations in the homeobox genes ALX4 and MSX2: from genotype to phenotype. Eur J Hum Genet. 2006;14:151–8.
56. Lodge T. Developmental defects in the cranial vault. Br J Radiol. 1975;48:421–34.
57. Perlyn CA, Schmelzer R, Govier D, Marsh JL. Congenital scalp and calvarial deficiencies: principles for classification and surgical management. Plast Reconstr Surg. 2005;115:1129–41.
58. Kortesis B, Richards T, David L, Glazier S, Argenta L. Surgical management of foramina parietalia permagna. J Craniofac Surg. 2003;14:538–44.
59. Gibson SE, Prayson RA. Primary skull lesions in the pediatric population: a 25-year experience. Arch Pathol Lab Med. 2007;131(5):761–6.

Part III

Hydrocephalus Primer

Intraventricular Hemorrhage in the Premature Infant

11

Jeffrey M. Perlman

Case Vignette BE, a 1080 g, 26 weeks appropriate for gestational age, white male was born to a 27-year-old primigravida mother following an uncomplicated pregnancy except for premature onset of labor. Upon arrival in Labor and Delivery, the mother was fully dilated with the infant in the breech position. An immediate Cesarean section was performed. The infant was delivered flaccid with a heart rate of 70 beats per minute. Resuscitation included bag and mask ventilation followed by intubation. The Apgar scores were 4 at 1 min and 7 at 5 min, respectively. The infant was transferred to the neonatal intensive care unit where his clinical course was consistent with moderate-to-severe hyaline membrane disease and he received a dose of surfactant replacement therapy within the first 60 min of life. The ventilator support and oxygen requirements were lowered in response to improved pulmonary compliance, Over the initial 24 h, the infant continued to exhibit moderate costal retractions, and the FiO_2 requirement gradually increased. A second dose of surfactant was administered at 18 h of age. Over the course of the day, the infant was noted to exhibit increasing irritability; however, he received no medication for sedation. Additional ancillary information revealed the following: the weight was now 970 g; the urine output for the initial 24 h was 0.9 ml/kg/h; a serum K^+ was 6.3 meq/l with a serum bicarbonate of 20 meq/l. The hematocrit had fallen from 45 to 35 %. A cranial ultrasound scan was obtained at 30 h of age, because of the irritability and fall in hematocrit. The scan revealed a large amount of blood in the germinal matrix region that had extended into the left lateral ventricle, which was dilated and filled with blood—consistent with a grade 3 IVH. In addition there were increased echogenicity within the left fronto-parietal white matter (Fig. 11.1).

This case raises several important questions:

1. Why did this premature infant develop a significant hemorrhage?
2. Could the bleeding have been prevented?
3. How should the infant be managed and evaluated over the next several days to weeks?

Background

The overall incidence of PV-IVH has declined over the past three decades; however the occurrence of severe hemorrhage remains substantial, particularly in the tiniest of the very-low-birth-weight population [1–3] (Table 11.1). Thus, approximately 26 % of infants of a gestational age between 23 and 25 weeks and 12 % between 26 and 27 weeks still develop the most severe

J.M. Perlman, M.B., Ch.B. (✉)
Department of Pediatrics, New York Presbyterian Hospital, Weill Cornell Medical College, 525 East 68th Street,New York, NY 10065, USA
e-mail: Jmp2007@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_11

forms of hemorrhage [3]. This is highly relevant because as survival of infants born at the cutting edge of viability continues to increase, severe hemorrhage rates are likely to increase, and with them long-term neurodevelopmental deficits.

Neuropathology

The primary lesion is bleeding from vessels within the periventricular subependymal germinal matrix located between the caudate nucleus and thalamus at the level of the foramen of Monro [2] (Fig. 11.2). The matrix is a transient gelatinous region that provides poor support for a large, immature network of blood vessels primarily supplied by Heubner's artery, a branch of the anterior cerebral artery [4]. The venous drainage also appears to be important with regard to the risk for bleeding. Thus the drainage includes the terminal, choroidal, and thalamo-striate veins that lead to the internal cerebral vein. The blood flow then makes a "U-turn" in the subependymal region at the level of the foramen of Monro, where most of hemorrhage originates [2]. This creates the potential for obstruction of the venous drainage resulting in venous distention with obstruction of the terminal and medullary veins, with subsequent rupture. The primary vascular source of PV-IVH has not been clearly established. Thus the initial descriptions suggested a venous origin of hemorrhage [2] while subsequent pathologic studies described it as emanating from capillary or arterial vessels [4]. Based on studies conducted over the years it is most likely, that PV-IVH results from forces acting upon both the arterial and venous circulations [1, 2].

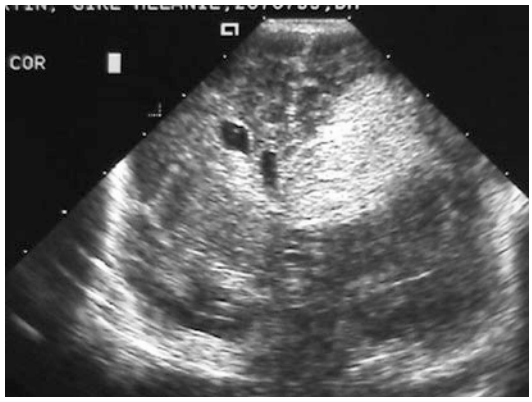


Fig. 11.1 Coronally oriented head ultrasound scan. Note the blood in the left germinal matrix region, within the frontal horn of the left lateral ventricle and within the left fronto-parietal white matter

Importance of the Germinal Matrix

The germinal matrix is an active site of active cellular proliferation, and is a source of both neuronal precursors early in gestation as well as glial elements that become oligodendroglia and astrocytes in the third trimester [2]. The matrix involutes after approximately 32 weeks and by term gestation, this region is essentially absent. Destruction of the matrix as a result of hemorrhage may result in impairment of myelination, brain growth, and subsequent cortical development [2].

Grading the Hemorrhage

The hemorrhage may be confined to the germinal matrix region (grade 1 IVH) or it may extend and rupture into the adjacent ventricular system (grade II or III IVH) depending on the extent of blood, or may extend into the adjacent white matter (termed a grade IV IVH or intraparenchymal

Table 11.1 Intraventricular hemorrhage

	23 weeks	24 weeks	25 weeks	26 weeks	27 weeks	28 weeks
Gestational age	*N* = 496	*N* = 1223	*N* = 1426	*N* = 1530	*N* = 1811	*N* = 1967
Grade of IVH						
Grade 3	15 %	9 %	8 %	5 %	4 %	6 %
Grade 4	21 %	14 %	13 %	7 %	5 %	9 %

Adapted from Stoll BJ, Hansen NE, Bell EF, et al. Neonatal Outcomes of Extremely Premature Infants From the NICHD Neonatal Research Network. Pediatrics 2010; 126: 443–456

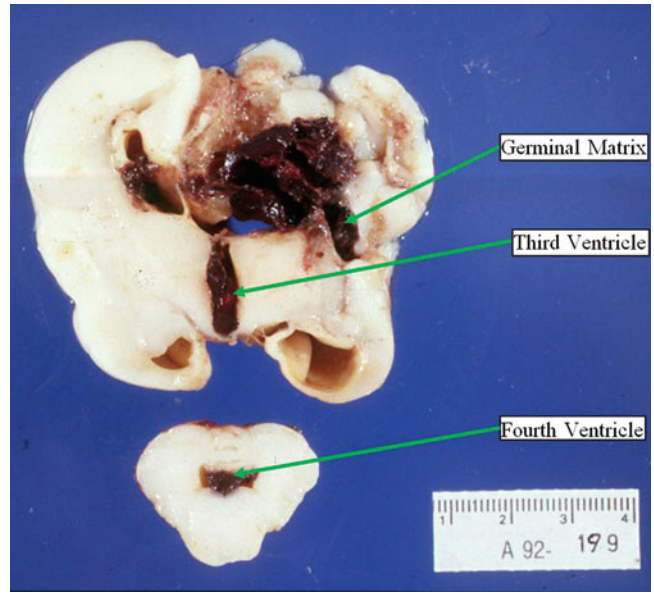


Fig. 11.2 Pathologic specimen from a premature infant demonstrating blood within the germinal matric, left lateral ventricle, third and fourth ventricles

echogenicity (IPE)) [2, 5, 6] (Fig. 11.1). The latter lesion, which is often unilateral, represents an area of hemorrhagic necrosis of varying size within periventricular white matter, dorsal and lateral to the external angle of the lateral ventricle [2, 6, 7].

Pathogenesis of IVH

In general terms, three factors appear to be central to the genesis of hemorrhage. The first relates to inherent vulnerability of the germinal matrix, with immature vessels and poorly supportive gelatinous matrix as described above [2]. The second relates to the concept of a pressure passive circulation often referred to as loss of autoregulation, and the third relates to perturbations in cerebral blood which are common in the sick premature infant.

Cerebral Autoregulation and Pressure-Passive Circulation

Autoregulation is defined as a state whereby CBF remains constant as cerebral perfusion pressure varies over a certain range [8]. The mean arterial pressure at which CBF decreases during hypotension is termed the lower limit, and the arterial pressure at which CBF increases is called the upper limit of autoregulation. In newborn animals, the range of blood pressures at which CBF remains constant is lower than in adult animals [9, 10]. More importantly, in fetal lambs, the resting blood pressure is only slightly higher than the lower limit of the autoregulatory curve [10]. If a similar situation exists in newborn infants, moderate hypotension could result in reduced CBF and create the potential for ischemic brain injury. Evidence has indicated that the autoregulatory response remains intact in human neonates with mild asphyxiation or who have minimal respiratory distress [2]. By contrast seminal data of Lou and colleagues [11] derived from 19 newborn infants with varying degrees of respiratory distress studied in the first hours of life were the first to indicate that CBF varied considerably with spontaneous variations in blood pressure, suggesting that autoregulation was, in fact, lacking. Subsequent studies over the subsequent years utilizing different methods to assess CBF or cerebral blood flow velocity including Doppler, near-infrared spectroscopy, and xenon have supported the concept of a pressure passive cerebral circulation in the sick infant; that is, CBF varies directly with changes in systemic blood pressure [12–15].

To summarize, although intact cerebral autoregulation has been documented in the premature infant, it appears to function within a limited blood pressure range, and is likely to be absent particularly in the sick hypotensive preterm infant [12–15]. This clinical state places the developing brain at great risk for injury during times of hypotension and or elevated blood pressures.

Intravascular Perturbations

Evidence has pointed to a critical role for intravascular factors and specifically perturbations in ABP as a major mechanism of capillary rupture and hemorrhage. First, the cerebral circulation of the sick infant was considered pressure passive (see above) [12–15]. Second, experimental studies indicated that germinal matrix hemorrhage could be produced by systemic hypertension with or without prior hypotension [16, 17]. Third, infants with lower mean ABP in the first postnatal days and infants who received rapid volume expansion to correct hypotension were more likely to develop IVH [18–20].

In the original pathologic description of IVH, elevations in venous pressure were proposed as an important source of hemorrhage, based in part on the previously described venous drainage of germinal matrix and white matter [2]. Indeed simultaneous increases in venous pressure were observed in infants who exhibit variability in ABP, such as with respiratory distress syndrome (RDS) and associated complications, e.g., pneumothorax or pulmonary interstitial emphysema, or with mechanical or high-frequency ventilation [21–23].

To summarize, the cumulative data suggested that there is a significant contribution from both arterial and venous perturbations to the development of IVH. Over the years, studies have indicated that these intravascular responses can be modulated by additional factors, i.e., inflammation associated with chorioamnionitis (negative influence) [24] or the administration of glucocorticoids to the mother (positive influence) [25, 26].

Periventricular White Matter Injury (WMI) Associated with IVH

The cause of the WMI associated with hemorrhage still remains unclear. The original hypothesis was that the intraparenchymal lesion represented an "extension" of hemorrhage from the germinal matrix or lateral ventricle into previously normal periventricular white matter. However subsequent neuropathologic data indicate that the intraparenchymal lesion represents an area of hemorrhagic necrosis [2, 5, 7]. The WMI appears to be closely linked to the adjacent hemorrhage and two potential pathways have been proposed to explain this intricate relationship. The first suggests a direct relationship to the hemorrhage based on several clinical observations. First, the WMI is always noted concurrent with or following a large GM and/or IVH, and is rarely if ever observed prior to the hemorrhage, and second the WMI is always observed ipsilateral to the side of the larger hemorrhage with bilateral bleeding [1, 2]. This consistent relationship between the GM and WMI may in part be explained by the venous drainage of the deep white matter as described previously. A second explanation is that the WMI evolves de novo and the IVH and WMI occur concurrently. Since both the GM and the periventricular white matter are border zone regions, the risk for ischemic injury increases during periods of systemic hypotension, particularly in the face of a pressure passive cerebral circulation [1, 2]. Hemorrhage in these regions may then occur as a secondary phenomenon i.e. reperfusion injury. In support of this theory is the fairly consistent observation of the simultaneous detection of PV-IVH and WMI by cranial ultrasound imaging. Moreover elevated hypoxanthine and uric acid levels, perhaps as markers of reperfusion injury, have been observed on the first postnatal day in infants who subsequently developed WMI [27, 28].

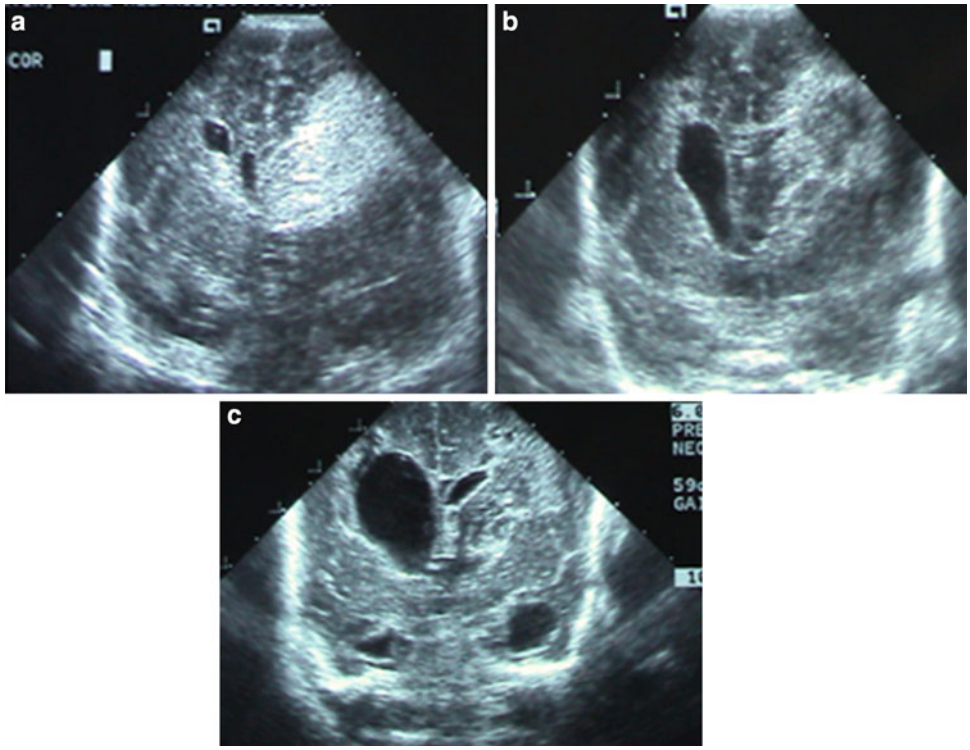


Fig. 11.3 Coronal sections demonstrating the large left-sided intraventricular hemorrhage with involvement of the ipsilateral white matter (**a**); followed by cystic evolution and dilation of the lateral ventricles (**b**) and further dilation (**c**)

Case Continued

The infant continued to exhibit moderate respiratory distress and developed a left sided pneumothorax requiring chest tube placement. The arterial blood gases showed moderate hypercarbia (pCO_2 55 to 58 mmHg and mild acidosis—pH 7.20–7.26). The hematocrit continued to fall to 22 % on DOL 4. A repeat cranial sonogram revealed more prominent "echoes" within the left fronto-parietal white matter, and the lateral ventricles were more distended as a result of increased hemorrhage. Serial sonograms over the first 6 weeks demonstrated progressive enlargement of the lateral, third, and fourth ventricles (Fig. 11.3).

Question

1. Why did the hemorrhage progress?
2. What is the cause of the progressive ventriculomegaly?

Linking Systemic and Cerebral Vascular Perturbations in Infants with Respiratory Distress Syndrome (RDS) to PV-IVH

Perturbations on the Arterial Side

Numerous studies established an association between RDS its complications, i.e., pneumothorax and IVH [22, 23]. The mechanisms linking the two conditions appear to be mediated via systemic perturbations including fluctuations or rapid increases in blood pressure in large part related to respiratory mechanics often precipitated by the infant breathing out of synchrony with the ventilator and/or in associations with complications such as a pneumothorax [23, 29]. Simultaneous perturbations on the venous side were noted with resultant increases in venous pressure [21]. In a series of studies conducted in

sick intubated and ventilated premature infants, these striking systemic changes with parallel changes in the cerebral circulation were associated with the subsequent development of IVH, and could be prevented by eliminating the fluctuations [23, 30]. Importantly over time, the advent of newer ventilators that work in tandem with the infants own respiratory efforts coupled with the antenatal use of steroids perhaps by stabilizing the germinal matrix vessels has made this association less prominent [25, 26]. However in a susceptible infant (no exposure to antenatal steroids) close attention to fluctuations in blood pressure should be a priority, and when present should be minimized.

Perturbations in Venous Pressure

Fluctuations in venous pressure simultaneous with the ABP perturbations in preterm infants with RDS who developed PV-IVH have also been observed [21]. The fluctuations or increases in venous pressure can be exacerbated by the use of higher mean airway pressures such as may be observed with high-frequency oscillatory ventilation, or pneumothorax. The potential importance of these venous fluctuations in the genesis of hemorrhage is intertwined with the venous drainage of the deep white matter and in particular the peculiar U-shaped turn ending at the terminal vein in the region of the germinal matrix. Increases in venous pressure in this region raise the likelihood of venous distension and resultant obstruction of the terminal and medullary veins resulting in a venous infarction.

Hypercarbia and Intraventricular Hemorrhage

The potential contribution of hypercarbia has only in recent years been clearly delineated in premature infants [31]. Thus in a study undertaken in the first week of life in VLBW infants, increasing $PaCO_2$ resulted in an increase in CBF and progressive impairment of cerebral autoregulation [31]. Hypercapnia defined by a maximum $PaCO_2$ recorded during the first 3 days of life has also been associated with severe IVH. In a retrospective cohort study of 574 VLBW infants, as the maximum $PaCO_2$ increased from 40 to 100 mmHg, the probability of severe IVH increased from 8 to 21 % [32]. In a single-center retrospective review of 849 infants weighing <1250 g extremes in $PaCO_2$, both low and high, as well as fluctuations in $PaCO_2$ during the first 4 days of life increased the risk of severe IVH [33]. These cumulative observations indicate that extremes in $PaCO_2$ should be avoided during the period in which infants are at high risk of IVH. This is highly relevant since permissive hypercapnia has been advocated as a ventilator strategy to minimize barotrauma to the lungs of preterm infants, and thus prevent the evolution to chronic lung disease [34] (Fig. 11.4).

Surfactant Administration and PV-IVH

The introduction of surfactant administration to reduce the severity of RDS in the late 1980s was the most important development in the management of sick premature infants. Since surfactant reduced the severity of RDS as well as the rate of pneumothorax, it was postulated that it would also lead to a decrease in the rates of IVH. However, this was not borne out in the many surfactant trials [35]. This lack of effect has been attributed to the impact of surfactant administration on fluctuations of CBF in sick preterm infants who have pressure passive circulation and the rapid changes of $PaCO_2$ and PaO_2 that may subsequently lead to brain injury [36, 37].

Post-hemorrhagic Hydrocephalus (PHH)

PHH complicates approximately 40–50 % of severe IVH [2]. The progression of PHH may be rapid, i.e., days, and in such cases, it is usually associated with

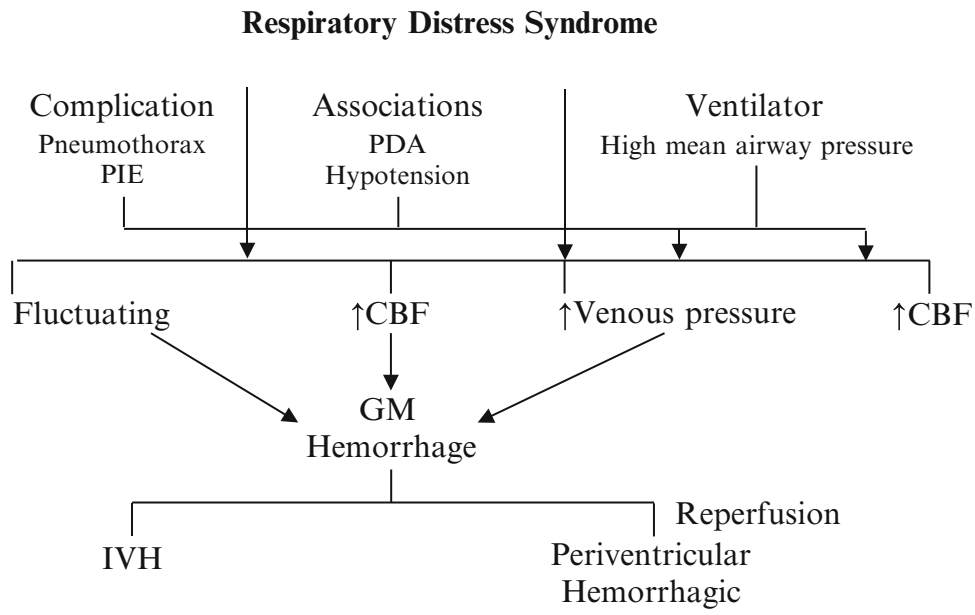


Fig. 11.4 Schematic representation depicting the association of vascular and venous perturbations in an infant with respiratory distress syndrome and the relationship to subsequent intraventricular hemorrhage

raised intracranial pressure. The obstruction under such circumstances appears to be secondary to an impairment of cerebrospinal fluid absorption caused by particulate clot usually demonstrated by ultrasound scan. This may be at the foramen of Monroe or the aqueduct of Sylvius. Treatment is usually immediate, via external drainage above the site of obstruction. More commonly, a communicating hydrocephalus evolves from 1 to 4 weeks following the diagnosis of hemorrhage. The hydrocephalus is commonly secondary to an obliterative arachnoiditis distal to the outflow of the fourth ventricle. The clinical criteria of evolving hydrocephalus, i.e., full anterior fontanel and rapid head growth, do not appear for days or weeks after ventricular dilation has already been present. Possible explanations for this discrepancy include the relative excess of water in the centrum semiovale and the relatively large subarachnoid space. Thus, serial scans are critical to follow for the evolution of PHH.

Understanding the natural history of PHH is important to consider when deciding upon management strategy. The natural tendency is to immediately intervene. However, in most cases, the ventricular dilation is under normal pressure and slowly progresses [38]. In approximately half the cases, the progression ceases usually within the first month without intervention. In the remaining 50 % the hydrocephalus is progressive and under increased pressure, and intervention becomes mandatory [38].

The management of PHH will depend on the size of the infant, the amount of blood in the ventricles, and the intracranial pressure. Many neurosurgeons prefer not to place a ventriculoperitoneal shunt until the infant's weight is at least >1500 g. In the smallest premature infants, temporizing diversion techniques to control ventricular size have evolved and include the placement of an external ventricular drain or subgaleal shunt, serial lumbar punctures, and/or the use of drugs, namely acetazolamide [38–40].

Clinical Manifestations of Hemorrhage

The time to initial diagnosis hemorrhage has shifted to a later onset in recent years [41]. Thus, in the initial descriptions of PV-IVH, the majority of cases, i.e., 90 %, evolved within the first 72 h of postnatal life [42]. However, in a subsequent

report, the onset of IVH was delayed beyond the first week of life in a substantial number of cases [41]. Thus, for neonates <28 weeks or less than 1000 g, IVH was diagnosed by days 3–5 in approximately 80 % of infants, with the remaining cases noted beyond the tenth postnatal day. This changing pattern likely reflects the complexity of disease in the tiniest infants and the extent of supportive medical care, i.e., prolonged use of high-frequency ventilation. Most cases (up to 70 %) continue to remain clinically occult, and are only detected by screening cranial ultrasound imaging [2]. Those infants with severe IVH frequently exhibit clinical signs including a bulging fontanel, seizures, fall in hematocrit, hyperglycemia, metabolic acidosis, and pulmonary hemorrhage.

Strategies to Prevent Severe IVH

General Considerations

Based on accumulating data over the years, several fundamental factors should be considered when assessing the risk for IVH. The development of IVH appears to be strongly influenced in part by the administration of antenatal glucocorticoids [25, 42–44] and/or the presence of histologic chorioamnionitis/fetal vasculitis [45] (Table 11.2). Postnatal markers of infants at high risk for IVH include extreme prematurity, i.e., <1000 g, male gender, and intubated with RDS [1–3, 38]. For infants with RDS, the risk for IVH is even greater when there are associated perturbations in arterial and venous pressures [29, 30]. The perturbations can be minimized with careful ventilator management including the use of synchronized mechanical or assist control ventilation, sedation, or in more difficult cases with paralysis [30]. By contrast the risk for severe IVH in the non-intubated infant is low, i.e., <10 % [38].

Perinatal Glucocorticoid Administration

The single most important "intervention" shown to significantly reduce the development of IVH has been a short course of antenatal glucocorticoid steroids administered to augment pulmonary maturation [25, 42, 43]. An effect that is dose dependent (Table 11.3). The relative risk (RR) for

Table 11.2 Dose-dependent effect of antenatal glucocorticoids on total and severe intraventricular hemorrhage

	Antenatal steroid doses		
Outcome	None *n* (%)	Partial *n* (%)	Complete *n* (%)
HMD	37 (79)	18 (58)	18 (39)
Surfactant	34 (72)	20 (64)	16 (35)
PDA	28 (60)	18 (58)	15 (33)
Total IVH*	27 (64)	16 (52)	11 (25)
IVH (3 or 4)*	18 (43)	8 (26)	5 (11)
Death	18 (38)	5 (16)	6 (13)
CLD [8]	14 (48)	9 (35)	11 (28)
CLD or death	32 (68)	14 (45)	17 (37)
Steroids for CLD	18 (38)	14 (45)	12 (26)
Intubation days	22 (10–32)	18 (4–31)	14 (1–22)

HMD hyaline membrane disease, *PDA* patent ductus arteriosus, *IVH* intraventricular hemorrhage, *CLD* chronic lung disease

Adapted from Salhab W, Hyman L, Perlman JM. Partial or Complete Antenatal Steroids Treatment and Neonatal Outcome in Extremely Low Birth Weight Infants Less Than or Equal to 1000 g: Is There a Dose Dependent Effect? J Perinatol 2004; 23:668–672

Table 11.3 Short- and long-term neurologic outcome in infants who received indomethacin and infants who received a placebo

Outcome	Indomethacin group (*n* = 574) (%)	Placebo group (*n* = 569) (%)	Adjusted odds ratio (95%CI)	*P* value
Severe IVH	9	13	0.6 (0.4–0.9)	0.02
Cerebral palsy	12	12	1.1 (0.7–1.6)	0.64
Cognitive delay MDI < 70	27	26	1.0 (0.8–1.4)	0.86

CI confidence interval, *IVH* intraventricular hemorrhage, *MDI* mental development index

Adapted from Schmidt B, Davis P, Moddemann D, Ohlsson A, Roberts RS, Saigal S, et al. Long-term effects of indomethacin prophylaxis in extremely-low-birth-weight infants. N Engl J Med 2001;344(26): 1966–72

severe IVH following any antenatal glucocorticoid exposure 0.54 (95 % CI 0.43–0.69) [25]. In a recent review the number of mothers needed to treat with antenatal steroids to prevent one case of IVH was 9 (95 % confidence interval 6–19) [46]. The mechanisms whereby glucocorticoids reduce severe IVH remain unclear, but may relate to less severe RDS, or higher resting ABP [25, 47]. The type of glucocorticoid also appears be important with antenatal exposure of dexamethasone, but not betamethasone associated with an increased risk of WMI in premature infants [48].

Postnatal Strategies

Postnatal medications used to prevent hemorrhage have included phenobarbital [49, 50], vitamin E [51], and indomethacin [52, 53]. While there was initial enthusiasm for the use of the first two medications, significantly different outcomes have not been described. Noteworthy, in one large randomized study, infants who received phenobarbital exhibited a higher incidence of severe IVH when compared to controls [50]. The early postnatal administration of indomethacin has been associated with a significant reduction in severe IVH; however the neurocognitive deficits were comparable between groups [53] (Table 11.3).

Outcomes

The infant with severe IVH is at highest risk for adverse motor and cognitive deficits. This is related in part to the extent of the white matter involvement noted by cranial ultrasound imaging or MRI [54]. Thus with a large IPE (>1 cm in diameter) the outcome is invariably poor with major motor and cognitive defects consistently noted at follow-up [1, 2, 5, 6]. With smaller lesions (<1 cm in diameter), the outcome is less precise and a small percentage (approximately 20 %) may even have a normal outcome [2, 5]. However, as noted previously, the issue is more complicated and even infants with a normal ultrasound scan as well as those with lesser grades of hemorrhage are at risk for motor as well as cognitive deficits. Thus major neurologic disability was noted in 5–10 % of infants and a MDI < 70 and in 25 % of cases infants with a normal cranial sonograms and major neurologic disability noted in 13 %, and a mental developmental index < 70 noted in 45 % of infants with lesser grades of hemorrhage (grade 1 and 2) [55, 56]. However, the comparable neurodevelopmental outcome for infants with and without IVH in the indomethacin study (Table 11.3) clearly indicates that the genesis of brain injury in the sick premature infant is much more complex than can be deduced from the neonatal neurosonographic appearance.

Future Directions

In recent years, white matter injury often in the absence of IVH is the predominant finding observed on MRI in very-low-birth-weight infants [1, 2]. Since antenatal glucocorticoids significantly reduce IVH, the target population should be those VLBW who deliver rapidly or emergently with minimum intrapartum care. In addition close attention to blood pressure should be a priority so as to avoid hypotension and/or perturbations. It is this group of infants who may derive benefit from early indomethacin administration. Understanding the mechanisms of white matter injury remains an important avenue for future research.

Pediatrician's Perspective

1. The management of children with very low birth weights and resultant intraventricular hemorrhage is almost entirely within the domain of neonatal intensivists. However, delayed appearance of hydrocephalus may occur within the general pediatrician's window of post-PICU surveillance.
2. Close surveillance of head circumference and assessment of sutures and fontanel's remain as the single most important feature of the clinical examination when concerned about IVH and its immediate consequences.
3. Delayed consequences of IVH are quite varied. Development of cerebral palsy for example,

can occur many years after the child has been discharged from NICU follow-up clinics and becomes the responsibility of the pediatrician to recognize and help triage.

4. Referrals to neurosurgical care should occur with divergent macrocephaly, splayed sutures, bulging fontanels, irritability of uncertain etiology, increased tone/spasticity, and asymmetric neurologic examination. Often head ultrasound is a simple and accessible route of imaging these children to begin the process of establishing an urgency to the referral.

References

1. Shalak L, Perlman M. Hemorrhagic-ischemic cerebral injury in the preterm infant: current concepts. Clin Perinatol. 2002;29:745–63.
2. Volpe J. Neurology of the newborn. 5th ed. Philadelphia, PA: Saunders/Elsevier; 2008.
3. Stoll BJ, Hansen NE, Bell EF, et al. Neonatal outcomes of extremely premature infants from the NICHD neonatal research network. Pediatrics. 2010; 126:443–56.
4. Hambleton G, Wiggelsworth JS. Origin of intraventricular hemorrhage in the preterm infant. Arch Dis Child. 1976;57:651–5.
5. Guzzetta F, Schackelford GD, Volpe S, et al. Periventricular intraparenchymal echodensities in the premature newborn: critical determinant of neurologic outcome. Pediatrics. 1986;78:945–1006.
6. Perlman JM, Rollins N, Burns D, et al. Relationship between periventricular intraparenchymal echodensities and germinal matrix-intraventricular hemorrhage in the very low birth weight neonate. Pediatrics. 1993;91:474–80.
7. Gould SJ, Howard S, Hope PL, Reynold EO. Periventricular intraparenchymal cerebral hemorrhage in preterm infants: the role of venous infarction. J Pathol. 1987;151:197–202.
8. Harper AM. Autoregulation of cerebral blood flow influence of the arterial blood pressure on the blood flow through the cerebral cortex. J Neurol Neurosurg Psychiatry. 1966;29:398.
9. Hernandez MJ, et al. Autoregulation of cerebral blood flow in the newborn dog. Brain Res. 1980;184:199.
10. Papile LA, et al. Autoregulation of cerebral blood flow in the preterm fetal lamb. Pediatr Res. 1985;19:159.
11. Lou HC, et al. Impaired autoregulation of cerebral blood flow in the distressed newborn infant. J Pediatr. 1979;94:118–25.
12. Pryds O, et al. Heterogeneity of cerebral vasoreactivity in preterm infants supported by mechanical ventilation. J Pediatr. 1989;115:638–45.
13. Pryds O, et al. Cerebral blood flow reactivity in spontaneously breathing preterm infants shortly after birth. Acta Paediatr Scand. 1990;79:391.
14. Tsuji M, et al. Cerebral intravascular oxygenation correlates with mean arterial pressure in critically ill premature infants. Pediatrics. 2000;106:625.
15. Kaiser JR, Gauss CH, Williams DK. Surfactant acutely affects cerebral and systemic hemodynamics and gas exchange in very low birth weight infants. J Pediatr. 2005;144:809–14.
16. Goddard-Finegold J, Armstrong D, Zeller RS. Intraventricular hemorrhage following volume expansion after hypovolemic hypotension in the newborn beagle. J Pediatr. 1982;100:796–9.
17. Ment LR, Stewart WB, Duncan CC, et al. Beagle puppy model of intraventricular hemorrhage. J Neurosurg. 1982;57:219–23.
18. Bada HS, Korones SB, Perry EH, et al. Mean arterial blood pressure changes in premature infants and those at risk for intraventricular hemorrhage. J Pediatr. 1990;117:607–14.
19. Goldberg RN, Chung D, Goldman SL, et al. The associations of rapid volume expansion and intraventricular hemorrhage in the preterm infant. J Pediatr. 1980;96:1060–3.
20. Miall-Allen VM, De Vries LS, Whitelaw AG. Mean arterial blood pressure and neonatal cerebral lesions. Arch Dis Child. 1987;62:1068–9.
21. Perlman JM, Volpe JJ. Are venous circulatory changes important in the pathogenesis of hemorrhagic and/or ischemic cerebral injury? Pediatrics. 1987;80:705–11.
22. Hill A, Perlman JM, Volpe JJ. Relationship of pneumothorax to the occurrence of intraventricular hemorrhage in the premature newborn. Pediatrics. 1982;69:144–9.
23. Perlman JM, McMenamin JB, Volpe JJ. Fluctuating cerebral blood flow velocity in respiratory distress syndrome. Relation to the development of intraventricular hemorrhage. N Engl J Med. 1983;309:204–9.
24. Yanowitz TD, Potter DM, Bowen A, Baker RW, Roberts JM. Variability in cerebral oxygen delivery is reduced in premature neonates exposed to chorioamnionitis. Pediatr Res. 2006;59:299–304.
25. Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. Cochrane Database Syst Rev 2006; (3): CD004454.
26. Salhab W, Hyman L, Perlman JM. Partial or complete antenatal steroids treatment and neonatal outcome in extremely low birth weight infants less than or equal to 1000 grams: is there a dose dependent effect? J Perinatol. 2004;23:668–72.
27. Russell GAB, Jeffers G, Cook RWI. Plasma hypoxanthine: a marker for hypoxic-ischemic induced periventricular leukomalacia? Arch Dis Child. 1992; 67:388–92.
28. Perlman JM, Risser R. Relationship of uric acid concentrations and severe intraventricular hemorrhage/leukomalacia in the premature infant. J Pediatr. 1998;132:436–9.

29. Perlman JM, Thach BT. Respiratory origin of fluctuations in arterial blood pressure in premature infants with respiratory distress syndrome. Pediatrics. 1988;81:399–403.
30. Perlman JM, Goodman S, Kreusser KL, et al. Reduction of intraventricular hemorrhage by elimination of fluctuating cerebral blood flow velocity in preterm infants with respiratory distress syndrome. N Engl J Med. 1985;312:1253–7.
31. Kaiser JR, Gauss CH, Williams DK. The effects of hypercapnia on cerebral autoregulation in ventilated very low birth weight infants. Pediatr Res. 2005; 58(5):931–5.
32. Kaiser JR, Gauss CH, Pont MM, Williams DK. Hypercapnia during the first 3 days of life is associated with severe intraventricular hemorrhage in very low birth weight infants. J Perinatol. 2006;26(5):279–85.
33. Fabres J, Carlo WA, Phillips V, Howard G, Ambalavanan N. Both extremes of arterial carbon dioxide pressure and the magnitude of fluctuations in arterial carbon dioxide pressure are associated with severe intraventricular hemorrhage in preterm infants. Pediatrics. 2007;119(2):299–305.
34. Woodgate P. G., Davies M. W. Permissive hypercapnia for the prevention of morbidity and mortality in mechanically ventilated newborn infants. Cochrane Database Syst Rev 2001; (2): CD002061.
35. Jobe AH. Pulmonary surfactant therapy. N Engl J Med. 1993;328:861–8.
36. Nuntnarumit P, Bada HS, Yang W, Korones SB. Cerebral blood flow velocity changes after bovine natural surfactant instillation. J Perinatol. 2000;20(4):240–3.
37. Kaiser JR, Gauss CH, Williams DK. Surfactant administration acutely affects cerebral and systemic hemodynamics and gas exchange in very-low-birth-weight infants. J Pediatr. 2004;144(6):809–14.
38. Hill A, Volpe JJ. Normal pressure hydrocephalus in the newborn. Pediatrics. 1981;68:623–9.
39. Ventriculomegaly Trial Group. Randomized trial of early tapping in neonatal post-hemorrhagic ventricular dilation. Arch Dis Child. 1990;114:611.
40. Shinnar S, Gammar K, Bergman EW, et al. Management of hydrocephalus, use of acetazolamide and furosemide to avoid cerebrospinal fluid shunts. J Pediatr. 1985;107:31–5.
41. Perlman JM, Rollins N. Surveillance protocol for the detection of intracranial abnormalities in premature neonates. Arch Pediatr Adolesc Med. 2000;154(8):822–6.
42. Perlman JM, Volpe JJ. Intraventricular hemorrhage in the extremely small premature infant. Am J Dis Child. 1986;140:1122–4.
43. Kari MA, Eronen M, Virtanen M, Hallman M, Teramo K, Koivisto M, et al. Prenatal dexamethasone treatment in conjunction with rescue therapy of human surfactant: a randomized placebo-controlled multicenter study. Pediatrics. 1994;93:730–6.
44. Leviton A, Dammann O, Allred EN, Kuban K, Pagano M, Van Marter L, et al. Antenatal corticosteroids and cranial ultrasonographic abnormalities. Am J Obstet Gynecol. 1999;181(4):1007–17.
45. Hansen A, Leviton A. Labor and delivery characteristics and risks of cranial ultrasonographic abnormalities among very-low-birth-weight infants. The Developmental Epidemiology Network Investigators. Am J Obstet Gynecol. 1999;181(4):997–1006.
46. Halliday H. Use of steroids in the perinatal period. Paediatr Respir Rev. 2004;5:s321–7.
47. Garland JS, Buck R, Leviton A. Effect of maternal glucocorticoid exposure on risk of severe intraventricular hemorrhage in surfactant-treated preterm infants. J Pediatr. 1995;126:272–9.
48. Baud O, Foix-L'Helias L, Kaminski M, Audibert F, Jarreau P, Papiernik E, et al. Antenatal glucocorticoid treatment and cystic periventricular leukomalacia in very premature infants. N Engl J Med. 1999; 341(16):1190–6.
49. Donn S, Roloff DW, Goldstein GW. Prevention of intraventricular hemorrhage in preterm infants by phenobarbitone: a controlled trial. Lancet. 1981;2: 215–7.
50. Kuban KC, Leviton A, Krishnamoorthy KS, Brown E, Littlewood-Teele R, Baglivo JA, et al. Neonatal intracranial hemorrhage and phenobarbital. Pediatrics. 1986;77:443–50.
51. Sinha S, Davis J, Toner N, Bogle S, Chiswick M. Vitamin E supplementation reduces frequency of periventricular hemorrhage in very preterm infants. Lancet. 1987;11:466–71.
52. Ment LR, Ehrenkranz RA, Duncan CC, Scot DT, Taylor KJW, Katz K, et al. Low-dose indomethacin and prevention of intraventricular hemorrhage: a multicenter randomized trial. Pediatrics. 1994;94:543–50.
53. Schmidt B, Davis P, Moddemann D, Ohlsson A, Roberts RS, Saigal S, et al. Long-term effects of indomethacin prophylaxis in extremely-low-birth-weight infants. N Engl J Med. 2001;344(26):1966–72.
54. Woodward LJ, Anderson PJ, Austin NC, et al. Neonatal MRI to predict neurodevelopment outcome in preterm infants. N Engl J Med. 2006;355:685–94.
55. Laptook AR, O'Shea TM, Shankaran S, Bhaskar B. Adverse neurodevelopmental outcomes among extremely low birth weight infants with a normal head ultrasound: prevalence and antecedents. Pediatrics. 2005;115:673–80.
56. Patra K, Wilson-Costello D, Taylor HG. Grades I-II intraventricular hemorrhage in extremely low birth weight infants: effects on neurodevelopment. J Pediatr. 2006;149:169–73.

Neuro-Ophthalmic Presentation of Neurosurgical Disease in Children

12

Dara M. West and Marc Dinkin

Vignette 1
An 18-month-old child who reached all milestones appropriately in her first year is in your office for her routine 18-month visit. Her head circumference, which was always on the large side, has not plateaued at the year point and she continued to acquire milestones. Her fontanel which was always previously open is now fused and not palpable. Her father suggests to you that she has been taking longer and longer naps and is harder to arouse in the morning. The neurologic exam is normal and she will not cooperate for a fundoscopic exam in your office. You should

(a) Send her for a formal neuro-ophthalmologic examination
(b) Refer her for an evaluation at a pediatric neurosurgeon's office
(c) Begin a discussion about potentially imaging her brain
(d) All of the above

Answer (d) The pediatric neurosurgeon often considers an ophthalmologic evaluation to be the single most accurate representation of a child's intracranial dynamics and thus will perform and refer for fundoscopic examination with a very low threshold, often before imaging. Due to the difficulty in examining young, fussy children, pediatric ophthalmologists and neuro-ophthalmologists both play an important role in the comprehensive assessment of children with suspected intracranial pathology.

Assessment of Visual Function

Visual Acuity

The evaluation of visual function begins with a measurement of visual acuity, the vital sign of vision. Visual acuity should be tested separately in each eye, and with the child's glasses, if they have any. Assessment may be conducted with a wall chart at the appropriate distance or with a near card. In both cases, it is helpful to place

D.M. West, M.D.
Department of Ophthalmology, USC Roski Eye Institute, Keck School of Medicine of USC, 1450 San Pablo Street, 4th Floor, Los Angeles, CA 90033, USA

Department of Neurology, Keck School of Medicine of USC, 1520 San Pablo Street, Suite 3000, Los Angeles, CA 90033, USA

M. Dinkin, M.D. (✉)
Department of Ophthalmology, Weill Cornell Medical College, New York Presbyterian Hospital, 1305 York Avenue, 11th Floor, New York, NY 10021, USA

Department of Neurology, Weill Cornell Medical College, New York Presbyterian Hospital, 520 E 70th St, 6th Floor, New York, NY 10021, USA

Department of Neurosurgery, Weill Cornell Medical College, New York Presbyterian Hospital, 520 E 70th St, 6th Floor, New York, NY 10021, USA
e-mail: mjd2004@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_12

a pinhole in front of the tested eye if the patient cannot reach 20/20, to reduce the effect of angled light rays through the refractive elements of the cornea and lens in a patient who does not have the ideal glasses correction. Visual acuity may be decreased by media opacities (cataracts or vitreous hemorrhage, for example), conditions of the fovea or central macula (such as macular edema, detachment, or degeneration), optic neuropathies and bilaeral disease of the occipital cortex.

Color Testing

In any child complaining of vision loss, color testing is essential. While the neuro-ophthalmologist will typically quantify color loss using a set of standardized color plates, one may obtain good information about the relative color sensitivity of each eye by testing for red desaturation. A small red object is shown to each eye individually. If one eye has dyschromatopsia (decreased color vision), the red object will generally look desaturated or orange. Dyschromatopsia occurs in cases of macular and optic nerve disease, but in cases of the latter, it is typically more severe and out of proportion to the degree of acuity loss.

Visual Field Testing

While formal testing of the peripheral and central visual field may be done with an automated or manual perimeter, much can be learned from a simple bed-side confrontational examination. Each eye should be tested individually, either by checking when the patient sees a small red object moving slowly in from the periphery, or by counting fingers in each quadrant. Monocular central scotomas tend to reflect macular or optic nerve disease, with extension toward the physiologic blind spot in the latter case, resulting in the cecocentral scotoma.

Pupillary Testing

Differentiating an optic nerve injury from other ocular causes of vision loss can be difficult, even with observation of the optic nerve head, since retrobulbar lesions do not cause any changes in the optic nerve head appearance for many weeks. For this reason, evaluation of the pupils for a relative afferent pupillary defect (RAPD or Marcus Gunn pupil) is essential. Light stimulation into either eye will send a signal through the ipsilateral optic nerve, through both optic tracts and through a collection of fibers that peel off and enter the dorsal midbrain where they synapse with both the ipsilateral and contralateral (decussating through the posterior commissure) pretectal nuclei. Each pretectal nucleus synapses with the corresponding Edinger-Westphal nucleus of the oculomotor nucleus, which in turn sends fibers through the third cranial nerve to the ciliary ganglion and finally to the constrictor pupillae governing pupillary constriction. In this way, light into either eye will cause both pupils to constrict. If one optic nerve is damaged but still intact, then light stimulation will still cause the consensual pupillary response. However, if the normal eye is stimulated first and then the light is swung over to the eye with the optic neuropathy, the ensuing level of stimulation of the pupillary response will be less, leading to a resetting of the pupils to a less constricted state. Both pupils will thus dilate just as the practitioner shines the light into the eye with the optic neuropathy. In addition to reflecting optic neuropathies, the RAPD may also be present in the setting of central retinal artery occlusions (CRAO) and contralateral optic tract injury (see below).

Funduscopy

Although ophthalmologists typically utilize the slit lamp along with a 78 or 90 diopter lens to visualize the fundus stereoscopically, one may obtain a great deal of information using only a small direct ophthalmoscope. With such a device, one may screen for papilledema, which is bilateral disc edema reflecting elevated intracranial pressure, or cupping or pallor of the optic nerve (reflecting chronic glaucomatous or non-glaucomatous optic neuropathies, respectively). Indeed, the presence of unilateral optic nerve pallor may be the presenting sign of chronic neoplastic compression of the optic nerve. Some

macular conditions, including large retinal detachments, hemorrhages, and pigmentary retinopathy, may be detected using the simple direct ophthalmoscope. The advent of the non-mydriatic fundus camera, which allows detailed photography of the fundus even in the absence of dilating drops, may lead to increased sensitivity for optic nerve and retinal disease in emergency rooms and other clinical settings [1].

Efferent Testing

To understand a patient's eye movements, one begins looking at the motility of each eye. In small children, an attractive object should be used to earn the child's attention so that an accurate impression of their excursions can be made. In some cases, even though there is little or no limitation of motility, there remains a misalignment of the two eyes, in which case it is termed a *tropia*. Examples include an exotropia (eyes deviated outward), esotropia (eyes deviated inward), hypertropia (eye deviated above the other eye), and hypotropia (eye deviated below the other eye). If this misalignment only becomes obvious on examination when one eye is no longer needed (i.e., it is covered by an occluder), then it is termed a *phoria*. In such cases, it is useful to perform a cross cover test, where each eye is covered for a second and then the occluder is switched to the other eye. When an eye is uncovered, it will tend to move back to midline (to be used again for vision) from where it was. Thus in the case of a left hypertropia, the left eye would move back down closer to fixation when it is uncovered. The pediatric ophthalmologist or neuro-ophthalmologist will place prisms of varied strengths over an eye until the cross cover movements are eradicated, and in this way, the proper prism for home use can be determined.

Papilledema and Disorders of Elevated Intracranial Pressure

Fundoscopy is the most important component of the physical examination when increased intracranial pressure (ICP) is suspected. Patients complaining of headache, transient or persistent visual field loss, diplopia, pulsatile whooshing, or presenting with focal neurologic findings should always undergo a fundoscopic examination for visualization of the optic nerve head to rule out papilledema. Papilledema refers to optic disc swelling resulting from elevated ICP, and is typically bilateral. When intracranial pressure is transmitted to the optic nerve sheath, axoplasmic flow is disrupted and water, protein, and cellular waste products spill into the extracellular space around the lamina cribosa, leading to optic disc edema [2, 3]. On fundoscopic examination, the margins of the optic nerve head appear blurred, blood vessels on or around the disc may be obscured, and there are often flame or splinter hemorrhages and cotton wool spots (small infarcts of the retinal nerve fiber layer that feeds into the nerve) on or surrounding the disc [4]. In equivocal cases, it is useful to look for spontaneous venous pulsations, which when present suggest normal ICP, although with imperfect specificity [5]. Papilledema has been classified according to the Frisén scale, which is reviewed in Fig. 12.1. A scale-based simply on severity of papilledema may be more reproducible [6].

Any patient with papilledema is at risk for vision loss and requires urgent evaluation. Often, papilledema is a sign of dangerous intracranial pathology that may require urgent neurosurgical intervention. Therefore, patients with papilledema should undergo urgent imaging of the brain and evaluation by an ophthalmologist or neuro-ophthalmologist. If the patient has other neurologic deficits associated with the papilledema, they should be referred to the emergency department for emergent imaging and evaluation. Those patients with mass lesions on neuroimaging should undergo neurosurgical evaluation on an urgent or emergent basis depending on location of the lesion, relationship to surrounding structures, and patient presentation.

Visual Function in Papilledema

Although most optic neuropathies lead to decreased acuity and color vision, these functions remain relatively spared in papilledema,

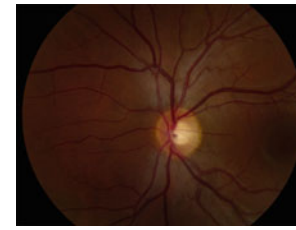
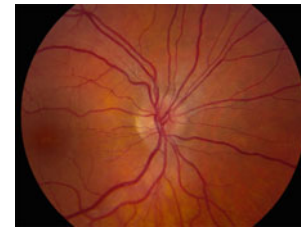
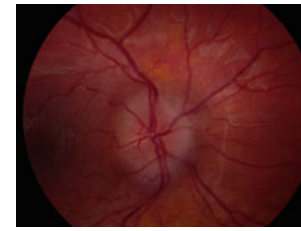
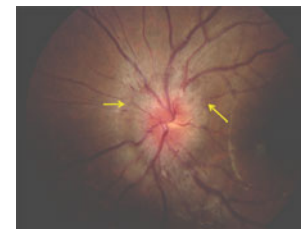
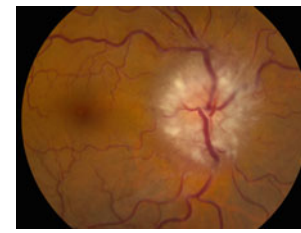
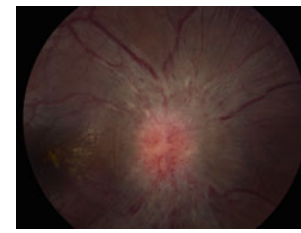
GRADE 0 Normal. No halo or vessel obscuration	
GRADE I C-shaped halo of blue retinal nerve fiber thickening (spares temporally)	
GRADE II Full halo of blue retinal nerve fiber thickening (no temporal sparing)	
GRADE III Major vessel obscuration at borders. (arrows)	
GRADE IV Major vessel obscuration on disc. Note veins are present but no arterioles.	
GRADE V All vessel lost on disc.	

Fig. 12.1 The Frisén scale illustrating increasing grades of papilledema

as the maculopapillary bundle that carries central acuity and color data from the center of the retina, the fovea, remains relatively unharmed. Instead, papilledema typically leads to peripheral visual field defects. The earliest defect tends to be an enlargement of the physiologic blind spot, a small scotoma located approximately 15° temporal to fixation, which reflects the absence of the light-sensitive retinal cells (the rods and cones) at the location of the optic nerve head. Since papilledema results in separation of the retinal layers, and therefore retinal dysfunction in the region around the nerve head, the blind spot is enlarged. The superior disc is prone to edema in early papilledema, which may explain why field defects in the inferior nasal visual field also occur frequently in papilledema.

While early papilledema typically spares central vision, with time, peripheral field loss can progress, resulting in severe tunnel vision, and ultimately acuity and color vision can be lost. In rare cases of fulminant papilledema, acuity and color may be lost at presentation, signifying a neuro-ophthalmic injury that regardless of cause requires urgent reduction in ICP to try and prevent permanent injury to the optic nerve and central vision loss. Furthermore, some cases of papilledema are accompanied by the tracking of fluid to the fovea, in which case acuity is also reduced at presentation [7].

Causes of Papilledema in Children

Intracranial hypertension from any cause may result in papilledema. The differential diagnosis includes mass lesions, venous sinus thrombosis (VST), craniosynostosis (premature closure of the skull sutures), aqueductal stenosis, and idiopathic intracranial hypertension. The presence of papilledema indicates only elevated ICP but there are no features of the disc appearance that can differentiate one cause from another. If papilledema is visualized, imaging of the brain with a contrast-enhanced MRI or CT scan is indicated to rule out a structural lesion or venous sinus thrombosis as the etiology, and evaluation by a neurologist and ophthalmologist is encouraged.

Aqueductal Stenosis

A common etiology of increased intracranial pressure in children is aqueductal stenosis, which refers to prevention of CSF outflow by a blockage at the level of the cerebral aqueduct. It may be associated with hydrocephalus, enlarged ventricles above the obstruction, and or periaqueductal edema within the midbrain. Aqueductal stenosis can be treated effectively with a ventriculoperitoneal shunt (VPS) allowing CSF to be redirected to the peritoneal cavity and relieving the pressure on the brain. Less commonly, a ventriculoatrial shunt is used. Endoscopic third ventriculostomy (ETV) is now the preferred treatment option [8] for pure aqueductal stenosis. ETV is a minimally invasive technique which obviates the need for placement of an indwelling shunt, minimizing risks including shunt infection, blockage, and breakage.

Mass Lesions

Pediatric papilledema may be the first or only sign of a mass lesion, such as a tumor, abscess, or hemorrhage. In children, most brain tumors are located in the posterior fossa, within the cerebellum or brainstem, [9] placing children at high risk for obstruction of the fourth ventricle and for elevated ICP. These include pilocytic astrocytomas, medulloblastomas, and brainstem gliomas.

Vignette 2

A 15-year-old boy presented to the emergency department with fever, headache, neck pain, and vomiting. Headaches were worse at night and when lying flat. The patient also noted binocular horizontal diplopia, and altered respirations. Neuro-ophthalmic examination revealed that he was unable to fully abduct his right eye. Intermittent episodes of apnea during sleep, bradycardia, and hypertension were observed. Dexamethasone and acetazolamide were started in an attempt to reduce intracranial pressure. MRI brain with and without gadolinium revealed a heterogeneously enhancing mass arising dorsal to the fourth ventricle with minimal surround-

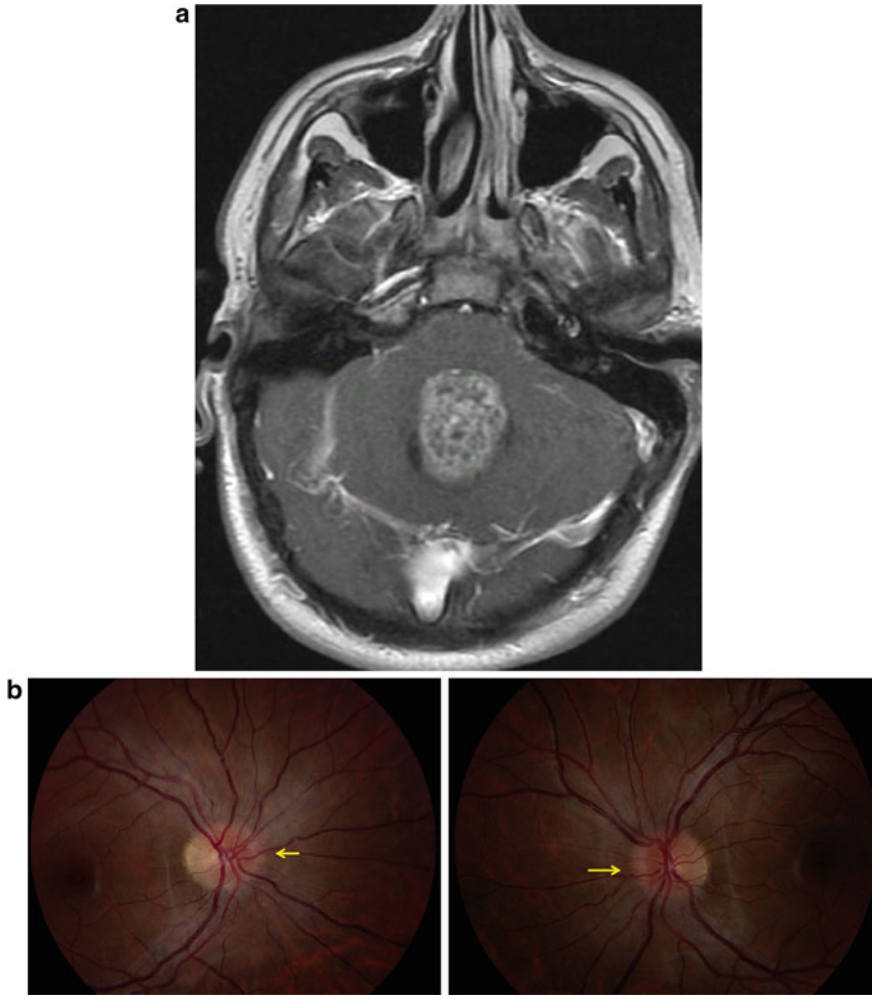


Fig. 12.2 Posterior fossa astrocytoma. (**a**) T1 weighted MRI brain with and without gadolinium reveals a heterogeneously enhancing mass arising dorsal to the fourth ventricle, partially obliterating the fourth ventricle. The patient's exam revealed Frisén grade I papilledema (**b**). *Arrows* identify a blue halo associated with retinal nerve fiber layer thickening

ing vasogenic edema, partially obliterating the fourth ventricle, as seen in Fig. 12.2a. The tumor was resected and pathology was consistent with pilocytic astrocytoma, WHO grade I. Postoperatively, an external ventricular drain was placed and measured a mildly elevated intracranial pressure to the low 20s. Despite the mildly elevated pressures, the patient remained asymptomatic so his drain was clamped. Three weeks later, headaches, nausea, and vomiting recurred. He was referred to neuro-ophthalmology where a dilated fundoscopic examination revealed Frisén grade I papilledema and a mild abduction deficit in his left eye. The Frisén grade I papilledema is pictured in Fig. 12.2b, where arrows identify a blue halo associated with retinal nerve fiber layer thickening. The patient was monitored conservatively and 8 weeks later he was without headache, and the abducens palsy resolved. The decision to undergo shunt placement was deferred and he continued to improve clinically.

As demonstrated above, papilledema is often accompanied by headache, nausea, or vomiting, and may be accompanied by other signs of elevated ICP including abducens palsies. The abducens or sixth cranial nerve is particularly

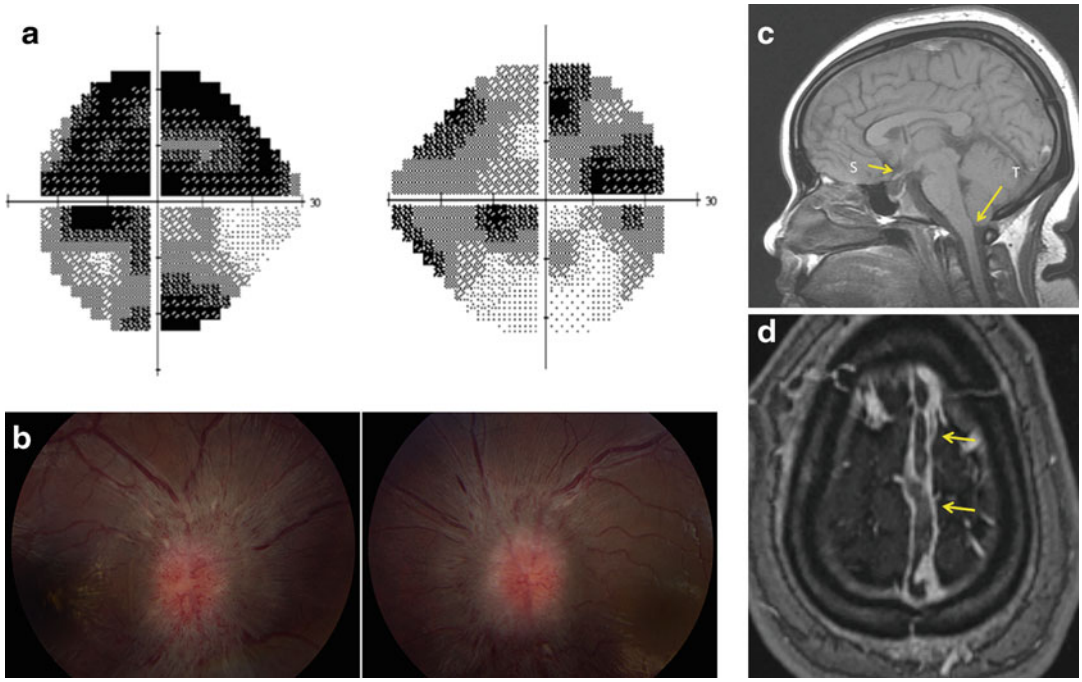


Fig. 12.3 Papilledema and visual field loss in the setting of IIH and venous sinus thrombosis. (**a**) Humphrey visual fields demonstrate severely restricted fields, bilaterally. (**b**) Fundus photos illustrate Frisén grade 5 papilledema with loss of vasculature on the disc. (**c**) Sagittal MRI brain reveals signs indicative of elevated ICP. *Yellow arrows* illustrate the empty sella (S) as well as the downward tonsillar herniation (T) found in conjunction with elevated intracranial pressure. (**d**) Axial MRI with and without gadolinium with *arrows* identifying the thrombus in the superior sagittal sinus

vulnerable to injury by elevated ICP as it must ascend along the clivus bone before coursing above the clinoid process to enter Dorello's canal and the cavernous sinus. With elevations in ICP, downward movement of the brainstem stretches the abducens nerve which is then compressed against the clinoid process. In this setting, the abducens palsy is a false localizing sign and may point the practitioner erroneously to the brainstem. This particular patient showed signs of Cushing's triad of hypertension, bradycardia, and apnea, indicating a neurologic and neurosurgical emergency as it suggests imminent herniation.

MRI Findings Associated with Papilledema

While the funduscopic examination remains the gold standard to diagnosing papilledema, there are several associated MRI findings that may help confirm the finding or even indicate that a funduscopic examination is necessary. Radiographic papilledema is defined as flattening of the posterior sclera and enlargement of the perineural subarachnoid space, best seen on coronal T2 orbital MRI [10]. Increased ICP may also compress the pituitary gland inferiorly, leading to the appearance of an empty sella, and in some cases, the cerebellar tonsils may herniate a few millimeters below the foramen magnum. Figure 12.3c illustrates MRI findings typically found in association with papilledema.

Idiopathic Intracranial Hypertension

Idiopathic intracranial hypertension (IIH), previously called pseudotumor cerebri, is a disease of elevated ICP in the absence of any structural cause that typically presents in obese woman of childbearing age. It is of particular importance to the neurosurgeon since severe cases may be

treated with neurosurgical procedures. Children with IIH are often not obese. Typical presenting symptoms include a positional headache worse when supine and in the morning, neck pain, horizontal diplopia from abducens nerve palsies, nausea, retrobulbar pain, pulsatile tinnitus, and visual loss when more severe [11]. Ophthalmologic examination usually reveals papilledema, and in many cases, an abducens nerve palsy. Visual field testing will usually reveal some degree of visual field constriction, typically an enlarged blind spot or inferior nasal defect. It is diagnosed only after excluding all other etiologies of increased intracranial pressure, such as mass lesions, aqueductal stenosis, and venous sinus thrombosis [10]. The modified Dandy criteria require the absence of localizing neurological findings (excluding abducens nerve palsies) and an elevated opening pressure in the absence of alternate causes on MRI [12]. Patients generally feel a dramatic but temporary relief of their headache after a large volume lumbar puncture.

As its name suggests, the etiology of IIH remains unclear, but its association with obesity in women suggests that weight-related elevation in intrathoracic venous pressure may play a role or that increased estrogen conversion by adipose tissue may lead to changes in the competence of the arachnoid granulations that absorb the CSF [13–15]. There is increasing evidence of a high frequency of non-thrombotic stenosis at the level of the transverse sinus-sigmoid sinus junction in patients with IIH. Whether this stenosis is a primary cause of IIH or is simply a consequence of secondary venous compression remains controversial [16].

Treatment of IIH

Management of these patients depends on the severity of symptoms, and most importantly, the degree of visual loss. Patients with spared vision, or with only mild deficits, can be managed medically with acetazolamide, topiramate, or furosemide in combination with an emphasis on weight loss. However, those patients who do not respond to medical therapy and those who have more severe disease sometimes need surgical intervention [11] to address vision-threatening increased ICP. Conventional options in such cases include the placement of a ventriculoperitoneal or lumboperitoneal shunt, optic nerve fenestration, or repeated lumbar punctures if surgical treatment is unavailable [10] or deemed too risky due to comorbidities. The high frequency of venous sinus stenosis in patients with IIH has resulted in the practice of stent placement within the venous sinus in some centers when conventional venography confirms the stenosis and shows an abnormally high pressure gradient across the stenosis. Retrospective series indicate improvement in IIH symptoms and papilledema in a majority of patients, and appear to remain patent for over 2 years [17] but prospective trials are lacking and this remains an experimental procedure [17, 18]. Experience in the pediatric population in particular remains quite limited.

Venous Sinus Thrombosis

Venous sinus thrombosis (VST) is relatively rare in children, but may present with a syndrome of elevated ICP mimicking IIH. Important precipitants in children include meningitis, genetic thrombophilias, the use of oral contraception in teenagers, and prior manipulation of the venous sinuses. Patients with papilledema should always be evaluated for venous sinus thrombosis as it is a treatable condition with potentially severe effects on the brain and visual system.

Vignette 3

A 16-year-old young woman with increased body mass index presented to her local emergency department with severe holocephalic headaches that would wake her up from sleep. Head CT was unremarkable and she was discharged home. She presented to the ER 3 weeks later when blurry vision developed and she was evaluated by neuro-ophthalmology. Examination revealed visual acuity of 20/200 in the right eye

and only the ability to count fingers in the left eye. She was unable to see any color plates and had severely restricted fields bilaterally (Fig. 12.3a), as well as Frisén grade 5 papilledema bilaterally. Figure 12.3b illustrates the Frisén grade 5 papilledema with loss of vasculature on the disc. An MRI of her brain revealed a partial empty sella and radiographic papilledema while MR venogram (MRV) ruled out VST. The patient's MRI is shown in Fig. 12.3c, with yellow arrows illustrating the empty sella (S) as well as the downward tonsillar herniation (T) found in conjunction with elevated intracranial pressure. Lumbar puncture showed normal contents but an opening pressure >55 cm H_2O. She was diagnosed with fulminant IIH and because of the profound vision loss, underwent VP shunt placement and treatment with acetazolamide. At discharge her vision had improved to 20/30 OD and 20/400 OS. One month later, severe headache and vomiting recurred. Examination revealed no improvement in visual fields or papilledema. MRV showed extensive thrombus of the superior sagittal sinus and bilateral transverse sinuses. In Fig. 12.3d, arrows identify thrombus in the superior sagittal sinus. She was started on therapeutic enoxaparin. Out of concern for infection, she underwent a repeat lumbar puncture which remained notable for elevated ICP, and cultures grew staphylococcus epidermidis. She was treated with antibiotics and her shunt was externalized and eventually revised. Despite improvement in headaches, a follow-up exam showed no visual improvement and the development of optic nerve atrophy. An optic nerve fenestration was performed on her right eye with improvement in her papilledema and some improvement in her visual field on the right. She subsequently underwent optic nerve sheath fenestration to the left eye.

This case demonstrates the potential of IIH to cause severe visual loss in critical cases, and the importance of early surgical intervention when acuity or serious visual field loss is present. Although the patient was left with significant acuity loss in her left eye, the placement of a VPS upon presentation may have avoided a similar fate to the right eye. Also highlighted is the potential for papilledema in cases of VST, as discussed above. This case is unique in that a VST appeared to supervene in a case of IIH. It remains unclear whether the VST was present all along but missed by the initial MRV or whether a secondary infection led to a septic VST. In any case of IIH where papilledema does not improve with placement of a VPS, the shunt should be interrogated and replaced if necessary, and repeat venous imaging should be considered to rule out an occult VST.

Craniosynostosis

Craniosynostosis refers to the aberrant fusion of cranial bones with loss of the normal sutures. This occasionally results in a small cranial vault. The etiologies for this are reviewed in detail in Chap. 6. In addition to varied types of cranial morphological complications already discussed in Chap. 6, craniosynostosis may also result in elevated ICP and thus papilledema. Any child with a history of rickets and papilledema should be investigated for hypophosphatemic rickets, which can lead to craniosynostosis due to abnormal suture formation [19]. Studies have shown that craniofacial surgery for craniosynostosis reduces preoperative papilledema [20].

Unilateral Papillitis

It should be noted that disc swelling may also be found in cases of inflammation, whether from autoimmune disease or infection, and more rarely, neoplastic infiltration. In such cases, there is typically acuity and color vision loss and the disc edema is often unilateral, helping to differentiate them from papilledema. Optic neuritis, a demyelinating inflammatory condition of the optic nerve, may cause disc edema in a minority of cases, but disc hemorrhages and cotton wool spots are absent, and the presentation is frequently associated with pain with eye movements.

Visual Field Defects

The early identification of visual field deficits can help the practitioner properly localize lesions of the central nervous system that may be amenable to neurosurgical resection. In many cases, timely management may help prevent further visual field loss or even reverse existing deficits. Monocular visual field defects suggest a lesion of the optic nerve or retina or a media opacity within the ocular structures. There are several patterns of visual field loss that suggest an optic neuropathy as the cause. First, a cecocentral scotoma, which stretches from the central region to the physiologic blind spot, tends to occur in cases where acuity is decreased, and reflects dysfunction of the highly metabolic fibers of the maculopapillary bundle which links the optic nerve to the fovea, the central region of the macula containing the highest density of cones. This is differentiated from the central scotoma of maculopathies that may have an irregular border. Ischemic causes of optic neuropathies typically cause altitudinal defects, meaning that either the superior half or inferior half of the visual field is lost. Arcuate scotomas are most often linked with glaucoma, but may occur in any optic neuropathy, and reflect injury to fibers temporal to the optic nerve that must arc around the fovea and maculopapillary bundle to reach the optic nerve head.

Chiasmal lesions tend to cause bitemporal hemianopsias, due to disruption of the nasal fibers as they cross within its body. Pituitary compression of the chiasm tends to cause a superior bitemporal hemianopsia early on, since the compression is from below, while superior tumors compressing the superior aspect of the chiasm (such as craniopharyngiomas) typically cause inferior bitemporal hemianopsias at first.

Retrochiasmatic lesions lead to contralateral homonymous (same side in both eyes), hemianopsias, or quadrantanopsias. This includes lesions of the optic tract, lateral geniculate nucleus of the thalamus, optic radiations of the parietal lobe (leading to an inferior homonymous field defect), Meyer's loop of the temporal lobe (leading to a superior homonymous defect), and occipital lobe.

Vignette 4

A 9-year-old girl presented with ataxia and was noted to have left-sided hemi-atrophy. MRI revealed a right thalamic and midbrain tumor, pictured in Fig. 12.4a with arrows illustrating compression of the optic tract (OT) and the fourth cranial nerve (IV). Biopsy was consistent with a WHO grade I juvenile pilocytic astrocytoma (JPA). Neuro-ophthalmology was consulted because of vertical diplopia. On examination, she was found to have an incongruous left inferior quadrantanopia, pictured on humphrey visual fields in Fig. 12.4b, as well as a left relative afferent pupillary defect. Motility examination revealed a right hypertropia that was worse in left gaze and right head tilt, consistent with left fourth nerve palsy. Dilated funduscopy revealed temporal pallor of the right optic nerve and bowtie atrophy of the left. The bowtie atrophy is illustrated in Fig. 12.4c with arrows identifying the atrophied fibers.

This case demonstrates several important neuro-ophthalmological examination findings. A left inferior quadrantanopia could reflect either a right superior occipital lobe lesion, a right parietal lobe lesion or right optic tract lesion, but multiple findings confirmed that the field loss localized to the optic tract. First, as can be seen in A, the defects are incongruous, meaning that the exact shape is different in the right and left eyes. This is more common in optic tract lesions since the fibers from the two eyes have not completely intermingled yet, although this point has been debated [21]. Second, cortical lesions causing a homonymous field defect would not cause any optic atrophy over time, since the nerve fibers of the optic nerve continue through the optic chiasm and tracts to synapse in the thalamus, but do not continue into the cortex. The type of atrophy seen in the eye contralateral to the lesion is in fact classic for optic tract lesions in that the temporal and nasal sides are pale, but the superior and inferior aspects of the nerve are relatively spared. This finding, referred to as "bowtie" or "band" atrophy, results from the fact that the retinal fibers destined to become part of the contralateral optic tract enter the optic nerve head from the nasal and temporal sides. As they atrophy, the

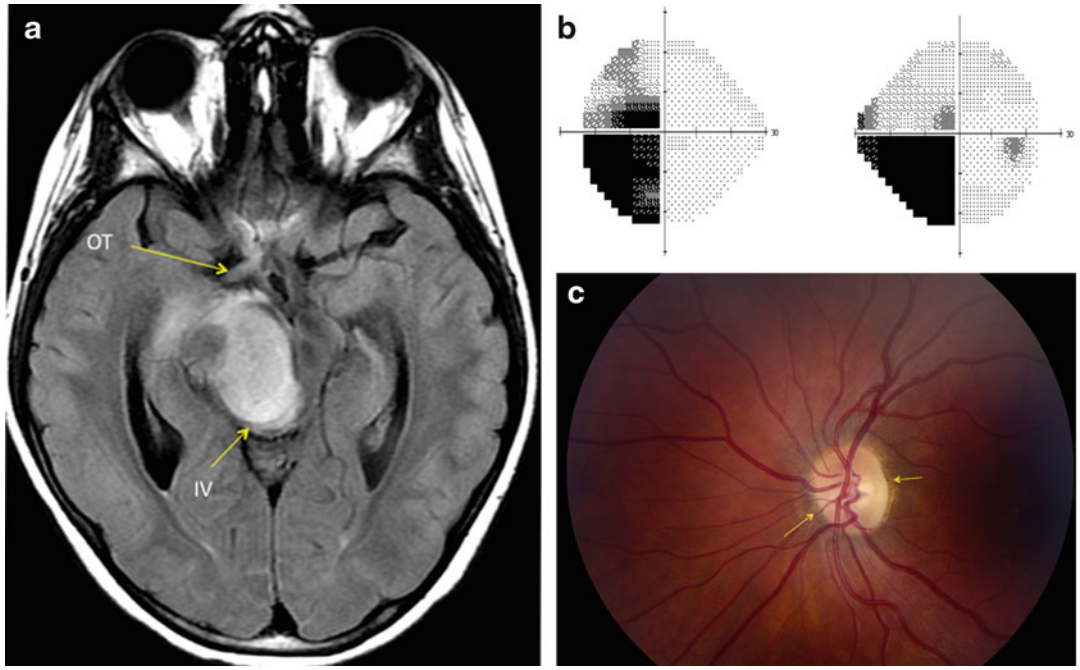


Fig. 12.4 Compression of optic tract and fourth cranial nerve. (**a**) T1 weighted axial MRI reveal a right thalamic and midbrain tumor with *arrows* illustrating compression of the optic tract (OT) and the fourth cranial nerve (IV). (**b**) Humphrey visual fields demonstrate an incongruous left inferior quandrantanopia. (**c**) Fundus photography illustrates bowtie atrophy with *arrows* identifying the atrophied fibers

corresponding parts of the disc become pale. Finally, the presence of left-sided RAPD implies a right optic tract lesion in the setting of the left homonymous defect. This finding occurs because of a slightly uneven splitting of each optic nerve at the chiasm so that the right optic tract actually contains more left optic nerve fibers than right. Its injury therefore will have a similar effect as a left optic nerve injury on the pupillary response.

Whenever a new homonymous visual field deficit is detected on examination, the patient should undergo urgent imaging with an MRI brain, and possibly an MR angiogram if this is unrevealing. Often, a mass lesion will be discovered which may require neurosurgical intervention.

Please see Fig. 12.5 for a review of pattern of field defects.

Vignette 5

A 13-year-old boy with a history of Wolff-Parkinson-White syndrome treated with catheter ablation and amblyopia OD was noted by his pediatrician to have growth deceleration. Growth hormone stimulation testing was consistent with growth hormone deficiency. Gadolinium-enhanced brain MRI revealed a suprasellar mass involving the optic chiasm and hypothalamus, extending along the right optic nerve and into the right optic foramen, most consistent with a hypothalamic/chiasmatic glioma. In Fig. 12.6c, a sagittal contrast-enhanced MRI shows the suprasellar mass lesion. Figure 12.6d demonstrates coronal cuts of the sella, illustrating compression of the right optic nerve. He was referred to neuro-ophthalmology where formal visual field testing revealed a bitemporal hemianopsia, as seen in Fig. 12.6a. Funduscopic examination revealed optic nerve pallor and temporal atrophy bilaterally as visualized in Fig. 12.6b. He continues to be observed with serial MRIs and visual field testing and over the course of 1 year has shown no progression of his disease.

While most suprasellar tumors causing chiasmal compression are amenable to neurosurgical

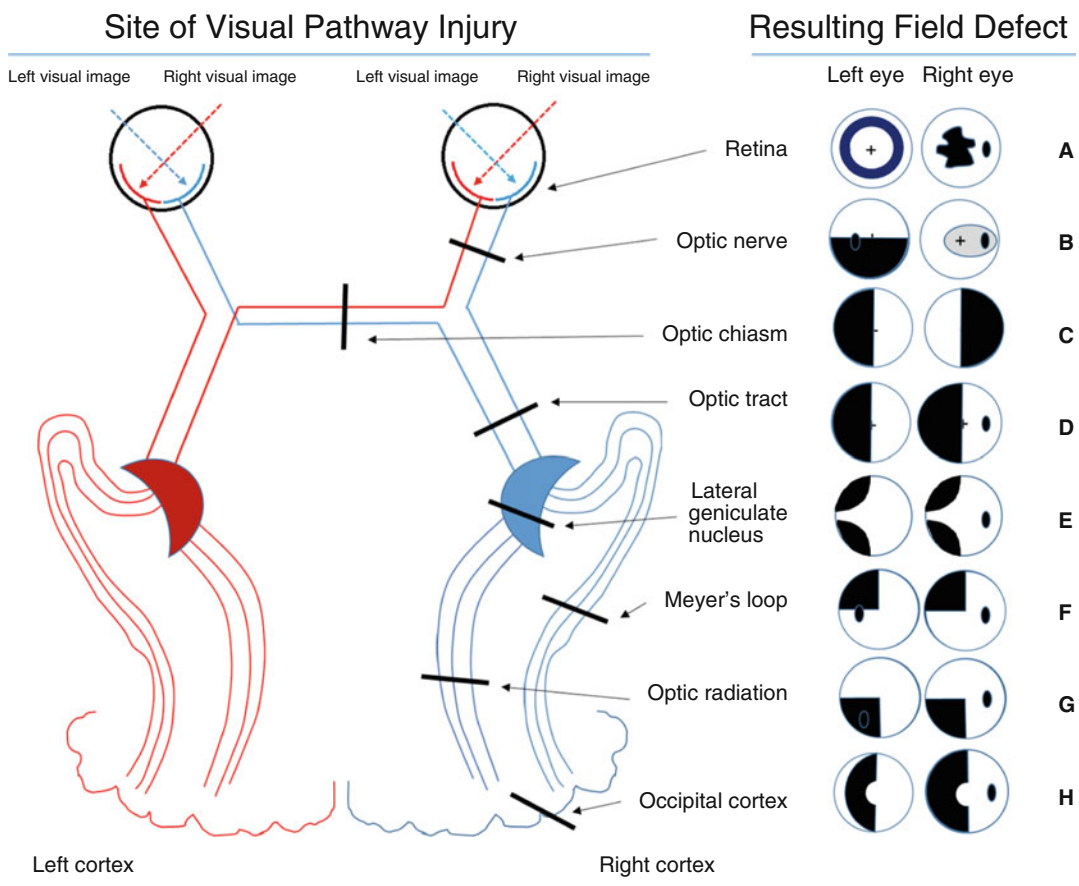


Fig. 12.5 Review of the afferent visual pathways and field defects corresponding to injury at each level. *Red lines* represent the pathways carrying right visual field information to the left occipital cortex and *blue lines* represent pathways carrying left visual field information to the right visual cortex. *Dashed lines* represent light rays landing on the retina. *Thick black lines* represent sites of injury corresponding to the visual field loss shown on the *right*. (*A*) Retinal disease affecting the macula tends to cause central scotomas, often in a geographic pattern, as seen in the right eye's field, while peripheral retinal disease such as retinitis pigmentosa, typically causes a ring scotoma as seen in the left eye. (*B*) Optic neuropathies may cause altitudinal defects (seen in the left eye's field) or cecocentral scotomas which are ovoid areas of blindness encompassing central fixation (*plus sign*) and the physiologic blind spot (this cecocentral scotoma is shown in *gray* to allow visualization of the physiological blind spot). (*C*) Disease of the optic chiasm typically causes a bitemporal hemianopsia. (*D*) Optic tract injury causes a contralateral homonymous hemianopsia, classically incongruous, meaning that the exact shape of the field defect is different in each eye. (*E*) A stroke to the lateral geniculate nucleus causes a contralateral sectoranopia, leading to loss either of the contralateral central third (posterior choroidal artery infarct, not shown) or the contralateral upper and lower thirds sparing the central third (anterior choroidal artery infarct, shown here). (*F*) Damage to Meyer's loop, which travels in the temporal lobe, leads to a contralateral homonymous superior quadrantanopia. (*G*) Damage to the optic radiation, which travels in the parietal lobe, causes a contralateral homonymous inferior quadrantanopia. (*H*) Occipital lobe injury causes a contralateral homonymous hemianopsia which is typically congruous (meaning that the exact shape of the field loss is equal in each eye). In cases of occipital lobe stroke due to posterior cerebral artery occlusion, there may be "macular sparing" as shown here, due to redundant perfusion of the occipital pole by branches of the middle cerebral artery. If the anterior extent of the occipital cortex is spared, then there may be a spared temporal crescent in the eye ipsilateral to the field loss, as shown here, reflecting a region of cortex which receives monocular visual information from a crescent of vision seen only by the contralateral eye

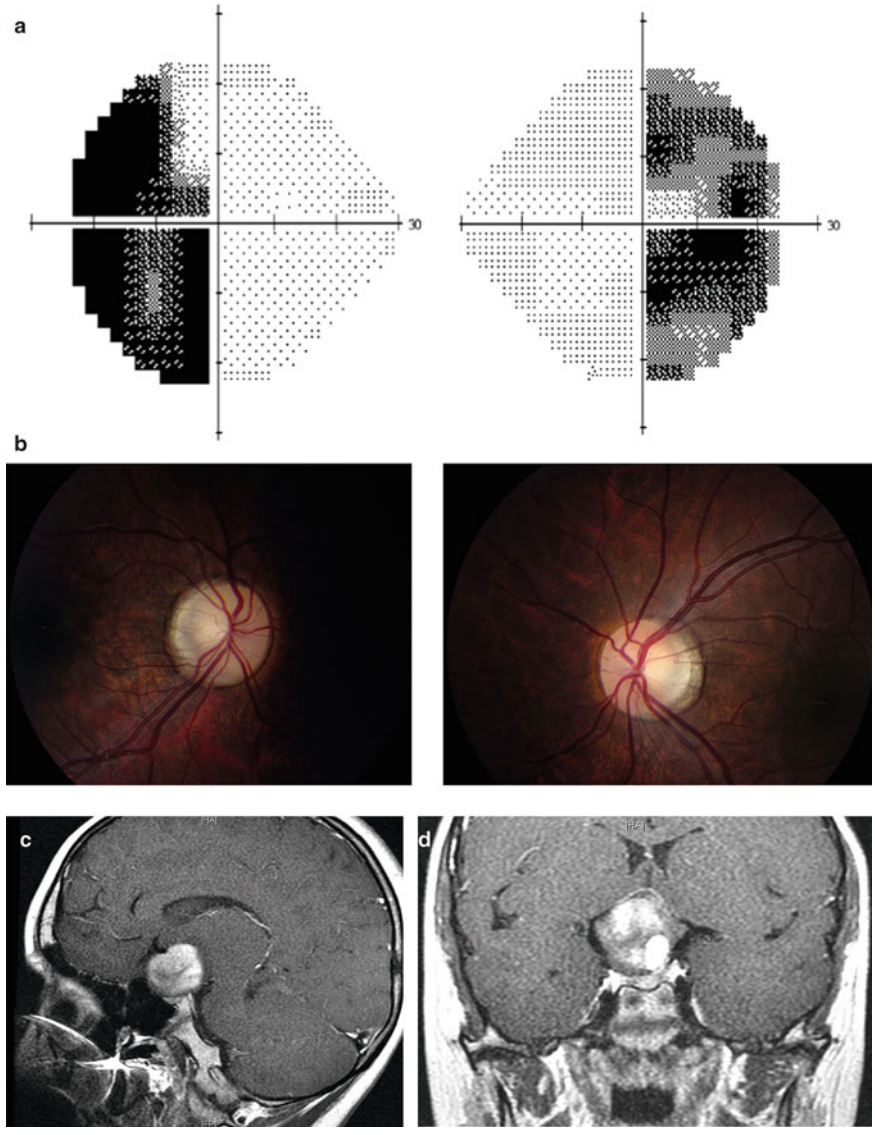


Fig. 12.6 Visual field loss and optic atrophy from optic chiasm glioma. (**a**) Humphrey visual field testing demonstrates bitemporal hemianopsia. (**b**) Fundoscopic examination reveals optic nerve pallor and temporal atrophy bilaterally. (**c**) Sagittal contrast-enhanced MRI illustrates a suprasellar contrast enhancing mass lesion. (**d**) Coronal MRI cuts of the sella illustrate compression of the right optic nerve

resection and should be referred for neurosurgical evaluation, it is crucial that optic chiasmal gliomas are recognized to avoid ill-advised attempts at potentially vision-threatening resection. Often, limited biopsies or tumor-associated cyst fenestrations can be offered to aid in oncologic decision making and optic apparatus decompression can be preformed when appropriate.

Dorsal Midbrain (Parinaud) Syndrome

Vignette 6

A 6-month-old boy was noted by his pediatrician to have increasing head circumference from the seventieth to 95th percentile over a short period

of time. On examination, there was increased head circumference with frontal bossing and a full, pulsatile fontanel. CT scan of the head revealed external hydrocephalus with only mildly dilated ventricles. He was referred to neuro-ophthalmology from a neurosurgeon to assess for papilledema. Neuro-ophthalmological examination revealed only mild bluish changes around the right optic nerve and mild nasal elevation of the left optic nerve, consistent with Frisén grade I papilledema. In addition, there was impaired upgaze and lid retraction in the right more than left. He had close interval follow-up for a year and a half with stable fundus examination, and resolution of lid retraction. He did not need surgical intervention.

As demonstrated above, young children who have not yet experienced fusion of their cranial sutures may not develop significant papilledema. Instead, they may develop macrocephaly as their predominant sign of an underlying pathologic intracranial process, emphasizing the importance of serial head circumference measurements. In some cases, as demonstrated, patients with elevated ICP due to ventricular outflow obstruction may present with some or all of the features of a dorsal midbrain (or Parinaud) syndrome, reflecting the flow of high-pressured CSF into the dorsal mesencephalon surrounding the aqueduct. The four primary findings of this syndrome all affect the neuro-ophthalmological examination:

- *Light-Pupil Dissociation*: The bulk of fibers of the optic tract carry visual information from the contralateral visual field to the ipsilateral thalamus, which relays the information to the occipital cortex. However, some fibers peel off the optic tract and head to the dorsal midbrain where they synapse in the pretectal nucleus. This nucleus sends axons to the ipsilateral Edinger-Westphal (EW) subnucleus of the oculomotor (third cranial nerve) nucleus, and the contralateral EW by way of the posterior commissure, a band of fibers that cross the dorsal midbrain right behind the aqueduct. From each EW, a message is sent to the ipsilateral constrictor pupillary to govern pupillary constriction in the presence of light [22, 23]. Compression of the posterior commissure by a mass lesion or aqueductal fluid results in damage to this process and pupillary constriction due to light is dampened. Constriction of the pupils due to a near stimulus (accommodation) is spared, as its pathway is governed by a greater number of fibers whose input comes from higher cortical areas. Thus, the term light-near dissociation is used.
- *Upgaze paresis*: This results from dysfunction of the rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) and interstitial nucleus of Cajal (INC), both of which are involved in vertical eye movements, or their outputs through the posterior commissure [24].
- *Convergence-retraction "nystagmus"*: In the presence of upgaze paresis, attempts at upgaze may instead result in a compensatory activation of alternate extraocular muscles, resulting in repeated retraction of the globes into the orbit. A simultaneous adduction of each eye with the retraction may reflect the relative strength of the medial recti muscles.
- *Lid retraction (Collier's sign)*: The central caudal subnucleus (CCS) of the oculomotor nucleus governs lid elevation bilaterally. It is tonically activated during wake periods but receives inhibitory input from the contralateral nucleus of the posterior commissure to allow intermittent blinking to protect the cornea. This input, predictably, travels through the posterior commissure so that compression of the commissure may result in a disinhibited CCS, and over-activation of the levator palpebrae causing lid retraction. This should be differentiated from the lid retraction of thyroid eye disease, which is often associated with proptosis as well.

Diplopia and Gaze Palsies

Double vision is a relatively common neuro-ophthalmological complaint in children and may be the first sign of serious neurological disease. Monocular double vision (that is, the second image is present even with only one eye open) is generally the result of ocular pathology, whereas

binocular diplopia results from a true inter-ocular misalignment. This misalignment, or strabismus, may be the result of dysfunction of one of the cranial nerves innervating the extraocular muscles, the third, fourth, or sixth cranial nerves, or of the muscles they innervate due to orbital disease. The pathology may lie within the brainstem affecting the coordination of ocular movements in the horizontal or vertical planes, or at the level of the neuromuscular junction in cases of myasthenia gravis. Determining which patients require urgent neuroimaging and referral to the neurosurgeon is of utmost importance.

Most commonly, children with ocular misalignment have a congenital strabismus, which will either correct with time or will require ophthalmologic surgery for correction and prevention of long-term suppression of the visual input of one eye by the visual cortex (amblyopia). However, in other cases, the misalignment can be indicative of more dangerous intracranial pathology.

Abducens Palsies

The abducens nerve, which controls the lateral rectus muscle and governs abduction of the ipsilateral eye, emerges from the abducens nucleus in the pons. It may be affected by pontine lesions, disease of the subarachnoid space through which it subsequently courses, bony tumors of the clivus bone over which it ascends (such as chordomas), lesions of the medial cavernous sinus, and orbital lesions. As mentioned briefly in the papilledema section, abducens palsies may result from increased intracranial pressure. In this case, patients usually suffer from abducens palsies from compression of the sixth cranial nerves against the clivus on one or both sides. In fact, a sixth nerve palsy may be the first sign of a neoplastic process in the brain, even in the absence of papilledema or other neurologic findings. One study found 5 out of 16 patients with isolated six nerve palsy without papilledema to have an intracranial neoplasm, suggesting the importance of neuroimaging in such patients [25]. Other studies, however, have had less dramatic findings and suggest that while intracranial neoplasm is associated with sixth nerve palsy, there are usually other neurologic symptoms [26]. *The variation in data, however, suggests that pediatricians should have a low threshold to image patients with sixth cranial nerve palsies, especially if the clinical examination does not improve with close follow-up*. If imaging is not pursued at the initial presentation, parents should be cautioned about the importance of close follow-up, but reassurance can be given if there are no other associated signs or symptoms.

Vignette 7

A 4-year-old girl presented to her pediatrician with a 1-week history of falls, spasticity in her left leg, and left ptosis, 2 days of headache and ear pain. On exam in the office, she was noted to have a right gaze palsy. She was sent from her pediatrician's office to the emergency department where an MRI of the brain showed a lesion in the pons. A cut through the pons on T2 weighted MRI brain is shown if Fig. 12.7, where cystic elements of the tumor can be visualized and the mass can be seen compressing the fourth ventricle. A right suboccipital stereotactic-guided biopsy of the lesion was consistent with primitive

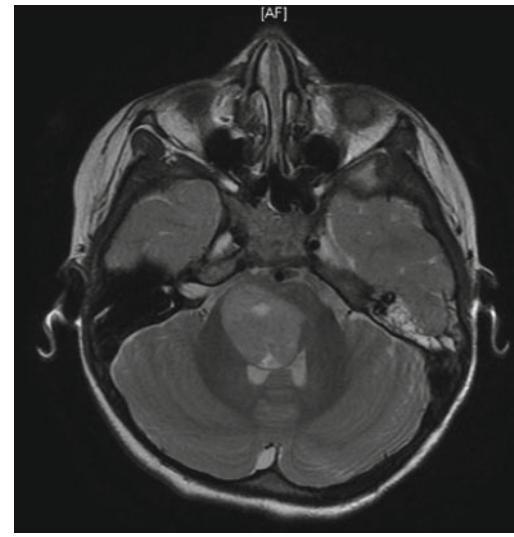


Fig. 12.7 Neuroectodermal tumor, grade IV, of the pons. T2 weighted MRI brain demonstrating a mass lesion with cystic elements and compression of the fourth ventricle

neuroectodermal tumor, WHO grade IV. She subsequently underwent a suboccipital craniotomy for resection of the tumor, followed by radiation therapy. Post-operatively, the patient developed diplopia. Examination revealed a right abducens palsy, left-beating nystagmus on left gaze, and incomplete eyelid closure.

In this particular case, the tumor led to dysfunction of right gaze due to involvement of the right abducens nucleus, which controls right gaze of both eyes. The incomplete eye closure was the result of involvement of the facial nerve. Spasticity of the left leg reflected concomitant right corticospinal tract involvement. The necessary resection of the tumor caused injury to the right abducens nerve and thus limited abduction of the right eye. The involvement of the right medial vestibular nucleus resulted in a left-beating nystagmus. Nystagmus will be discussed in more detail in a subsequent section.

Trochlear (Fourth Cranial) Nerve Palsies

The fourth cranial nerve, or the trochlear nerve, which controls the superior oblique muscle (SOM) is particularly susceptible to injury in the setting of closed head trauma, in which case there is often bilateral injury. It is the only cranial nerve to exit the dorsal brainstem, after which it crosses behind the lower midbrain and courses anteriorly to the contralateral superior oblique muscle. Much of its course parallels the rigid tentorium, against which it may be compressed in the setting of trauma. It may also be affected by tumors of the midbrain or within the lateral cavernous sinus.

Patients with trochlear nerve palsies typically present with vertical diplopia worse in downgaze, reflecting the elevation of the affected eye due to SOM dysfunction. Since depression of the globe is limited, typical complaints include trouble reading or walking downstairs, both of which require downgaze. There may also be a torsional diplopia (the second image is tilted relative to the first) reflecting the SOM-mediated intorsion (rotation so that the top of the eye moves nasally). Patients typically compensate with a contralateral head tilt to reduce diplopia. This may be the presenting sign in pediatric patients who do not complain of diplopia.

On examination, the affected eye is higher than the other eye, but the deviation may be subtle and difficult to confirm with simple testing of ocular motility. A simple test to determine the side of a trochlear nerve palsy is the pencil test: place a pencil in front of the child and if the child sees two pencils, one on top of another, ask the child to imagine that the pencils continue to infinity. The side on which the two pencils will cross is the side of the trochlear nerve palsy.

Since the trochlear nerve decussates, damage to the inferior dorsal midbrain where its nucleus resides will cause a contralateral palsy. This was the situation in vignette 4 above, where the tumor was present in precisely that location.

Vignette 8

A 15-year-old boy with a history of amblyopia OS was struck by a car as a pedestrian. He lost consciousness and was rushed to a local emergency department where CT scan of the head demonstrated multiple skull fractures and an epidural hematoma that was subsequently evacuated by neurosurgery. During his recovery, he noticed binocular double vision, initially oblique in orientation indicating a combination of vertical diplopia from his trochlear palsy, and a horizontal component from decompensation of his congenital strabismus.

Oculomotor Nerve Palsies

The oculomotor nerve innervates the superior rectus (elevation), inferior rectus (depression), inferior oblique (extorsion and elevation), and medial rectus (adduction) muscles. The classical pattern of injury therefore results in an eye that is down and out from residual trochlear nerve and abducens nerve function respectively. Additionally, ptosis is typically present as the third nerve innervates the levator palpebrae

muscle, and the pupil may be dilated or even nonreactive, owing to compression of the axons to the constrictor pupillae [27]. If the pupil is involved, then aneurysmal compression of the third nerve as it passes near the posterior communicating artery must be suspected. This is much more common in adults than in children. Other etiologies of a pupil-involving third nerve palsy include pituitary apoplexy, cavernous sinus lesions, meningitis, or skull-based lesions [27]. If a third nerve palsy is found on examination, the patient should undergo work-up with an MRI brain and MRA head. If the pupil is involved, an emergent work-up is indicated, to rule out those rare cases of aneurysmal compression.

Cavernous Sinus Syndrome and Orbital Apex Syndrome

Vignette 9

A 10-month-old infant with a history of neuroblastoma presented with progressive proptosis, ophthalmoplegia in all directions, ptosis, and an enlarged pupil in his left eye. The examination is illustrated in Fig. 12.8a. CT scan revealed metastatic disease within the left cavernous sinus extending toward the orbit and pushing the globe forward. There was no relative afferent pupillary defect. Figure 12.8b is a CT scan showing a mass lesion in the left cavernous sinus. In Fig. 12.8c, axial cuts through the orbit illustrate compression of the globe on the left.

The cavernous sinus is a paired, retro-orbital venous structure that surrounds the pituitary gland and carries within it the oculomotor nerve, trochlear nerve, first and second branches of the trigeminal nerve (V_1 and V_2, responsible for sensation over the top two-thirds of the face), abducens nerve, and sympathetic fibers responsible for pupillary mydriasis and lid elevation. Cavernous sinus disease therefore can lead to any combination of dysfunction of the aforementioned structures. A Horner syndrome in association with an ipsilateral abducens palsy is a cavernous sinus lesion until proven otherwise, since the sympathetic fibers travel adjacent to the abducens nerve within the sinus. Additionally, since the eye's venous drainage through the superior ophthalmic vein is into the cavernous sinus, venous hypertension and therefore intraocular hypertension may ensue.

Lesions located at the orbital apex affect most of the same structures as they enter the orbit, except only a branch of V_1 enters the orbit so sensory loss, if present, is limited to the cornea and immediate periorbital region. Furthermore, orbital apex lesions may also affect the optic nerve which enters the orbit through the optic canal. In case 9 above, there was a complete ophthalmoplegia and proptosis suggestive of a cavernous sinus lesion. The lack of any clear optic nerve involvement suggested compression at the level of the cavernous sinus as opposed to the orbital apex.

Skew Deviation

A pure vertical diplopia may not always reflect a trochlear nerve palsy, but instead may result from a skew deviation, a central cause of non-paralytic vertical strabismus. Skew deviations cause a vertical misalignment of the eyes despite full vertical excursion of each eye on motility testing. The utricle, which is part of the labyrinth of the inner ear, detects tilting of the body that might occur in the course of movement. In response, it sends a message through the vestibular (eighth cranial nerve) to the vestibular nucleus, which then sends fibers to the riMLF and INC of the midbrain to make corrective torsional and vertical movements of the eyes. If the body tilts to the right for example, this system will lead to extorsion of the left eye and intorsion of the right eye to lessen the effect of viewing the world at a tilt. Additionally, since body tilting to the right lowers the right eye relative to the left, the utricular-vestibular system will lead to an elevation of the right eye relative to the left. If one utricle or its afferent signal which courses from the medulla up to the midbrain is disrupted by a lesion, then the contralateral utricular-vestibular signal is relatively overactive; in other words, the brain thinks that the body has tilted to the side opposite the utricle whose signal is injured. The ipsilateral eye will

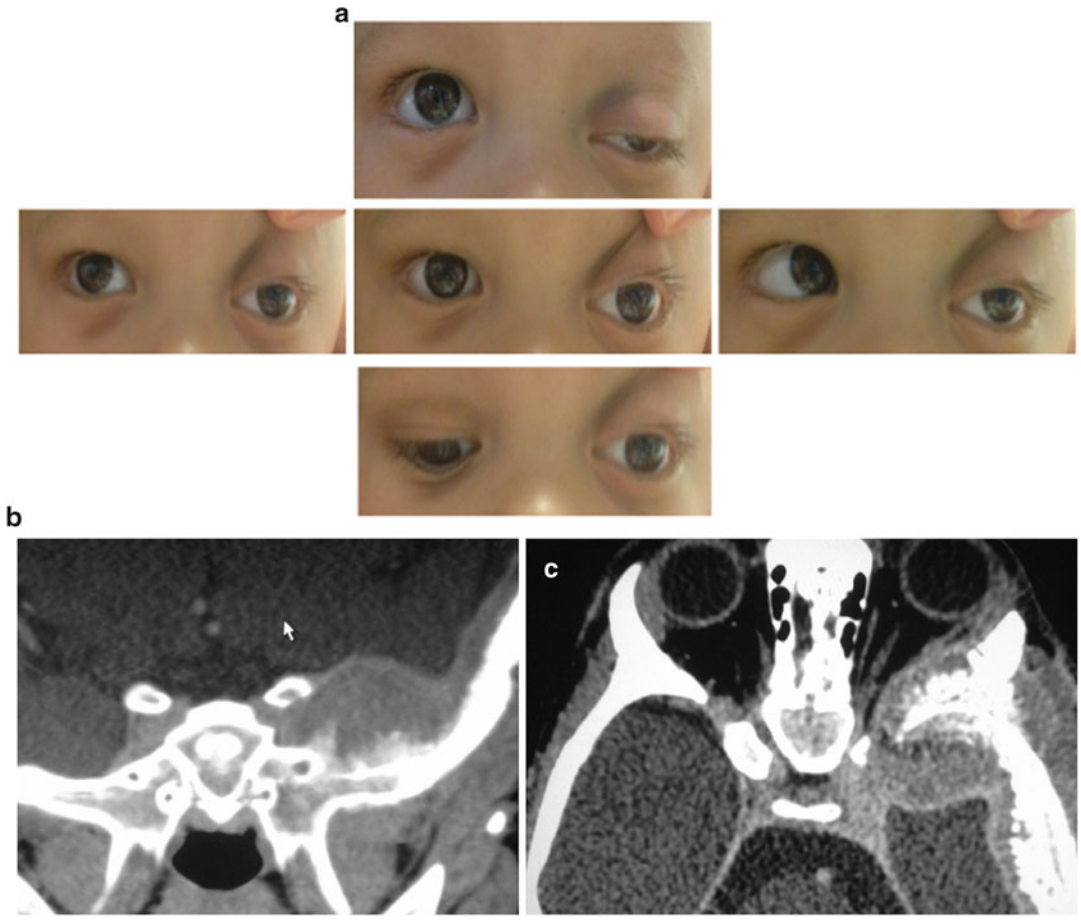


Fig. 12.8 Metastatic neuroblastoma to the left cavernous sinus. (**a**) Examination of a patient with a mass in the left cavernous sinus reveals ptosis and ophthalmoplegia in all directions. (**b**) Coronal CT imaging shows a mass lesion in the left cavernous sinus. (**c**) Axial CT cuts through the orbit illustrate compression of the globe on the left

therefore find itself lower than the contralateral eye even though no actual tilting has occurred. The patient will experience a vertical diplopia. The pattern of diplopia in various gazes may vary, but typically it can be differentiated from a trochlear nerve palsy in that motility is spared and the degree of misalignment is significantly decreased when the patient is tested in the supine position [28].

It is important that the primary care physician seeing children with diplopia be aware of the entity of skew, since its presence suggests disease of the vestibular nerve or more commonly the brainstem or cerebellum, and in children, it may be one of the first signs of a tumor within the posterior fossa. Any child with a suspected skew deviation should undergo neuroimaging.

Nystagmus and Saccadic Intrusions

Nystagmus

Nystagmus is a to-and-fro motion of the eyes, where the initial movement is slow and is considered to be the pathologic component. It can be classified according to direction, timing (fast phase and slow phase), amplitude and whether it is conjugate (similar direction in both eyes) or not. It may be present on primary gaze or induced

with eye movements in a particular direction. When the second phase is a corrective fast saccade, it is termed jerk nystagmus, and when it is also a slow movement, it is termed pendular nystagmus. In jerk nystagmus, the direction of the nystagmus is defined by the fast phase. There are a myriad of subtypes, but the salient point is that many of them localize to the brainstem or cerebellum and therefore are of potential neurosurgical significance. Below, we will introduce a few subtypes important in children. For a more comprehensive review of nystagmus in children, please see the review by Dinkin and Rizzo [29].

Vestibular Nystagmus

Relevant Anatomy

The vestibular ocular reflex (VOR) is responsible for horizontal or vertical eye movements contralateral to those of the head, in order to maintain fixation on targets of interest. The VOR system depends on the sensation of rotational movement by the semicircular canals, lateral movement by the utricle and movement along the *z*-axis by the saccule. Information is then transferred along the vestibular nerve to the medial vestibular nucleus (MVN) in the medulla, and from there to the nuclei relevant to the opposed ocular motion. With a lateral head movement, the signal from the horizontal semicircular canal feeds to the MVN which then sends fibers that cross and stimulate the contralateral abducens nucleus, thus mediating contralateral gaze. The anterior and posterior semicircular canals are situated so that they pick up head rotation in the vertical and torsional planes. This signal also travels along the eighth nerve to the MVN and then communicates with the midbrain INC to mediate opposite eye movements in the vertical and torsional planes. Damage to any point in this system can lead to a relative imbalance in the VOR signal, thus producing an inappropriate slow drift of the eyes, as if the head has moved. This is typically followed by a cortically mediated corrective saccade, resulting in a jerk nystagmus. When a jerk nystagmus is due to vestibular dysfunction, it is typically accompanied by vertigo or imbalance.

The most important step for a primary care physician faced with a vestibular nystagmus is differentiating between nystagmus as a result of damage to the inner ear or vestibular nerve (peripheral nystagmus) as opposed to brainstem pathways (central nystagmus). This is because causes of peripheral nystagmus tend to be relatively benign (viral labyrinthitis, vestibular neuronitis, benign paroxysmal positional vertigo) while central nystagmus may reflect brainstem demyelination, stroke, or most relevant to this review, tumors that require biopsy or resection. There are exceptions to this, since peripheral nystagmus may also reflect vestibular tumors such as schwannomas (seen in most every patient with neurofibromatosis II), and central nystagmus may simply reflect the central dysfunction that accompanies use of anti-epileptic drugs such as phenytoin or phenobarbital.

Patterns of Peripheral Vestibular Nystagmus

Injury to a horizontal semicircular canal leads to a purely horizontal conjugate jerk nystagmus with the fast phase in the opposite direction. Because the anterior and posterior semicircular canals lie along the vertical and torsional planes, their dysfunction tends to cause a compensatory mixed vertical-torsional nystagmus. If all three canals are injured (as in toxicity), then the vertical drifts of the anterior and posterior canals cancel each other, and the patient displays a mixed horizontal–torsional nystagmus. Peripheral nystagmus is typically worse in the direction of the fast phase and is dampened by convergence. Associated symptoms suggestive of peripheral disease include tinnitus and hearing loss, and there is typically more intense vertigo, nausea and vomiting as compared to central. Neuroimaging performed for peripheral nystagmus tends to be less emergent and should include thin cuts along the internal auditory canal.

Patterns of Central Vestibular Nystagmus

Central vestibular pathways tend to be subdivided according to plane of movements. Therefore, as a rule, the presence of pure ver-

tical (upbeat or downbeat) nystagmus without any concurrent torsional component reflects a central etiology. A pure torsional nystagmus (without any vertical movement) also reflects a central cause. Typically, the patient displays nystagmus that changes direction depending on gaze (upbeat in upgaze, right beat in right gaze, etc.). Vertigo tends to be less prominent. Central nystagmus should prompt urgent neuroimaging to rule out lesions affecting the brainstem or cerebellum.

Vignette 10

A patient presented at the age of 9 years with several weeks of right posterior headache, dizziness, nausea, vomiting, and some gait instability. She underwent a CT scan of the head, which revealed a posterior fossa mass with associated hydrocephalus. She was taken to the operating room for biopsy and resection, and pathology was consistent with a juvenile pilocytic astrocytoma, WHO grade I. Postoperatively, the patient complained of horizontal diplopia and oscillopsia. In addition to bilateral abducens nerve palsies, the neuro-ophthalmic examination revealed a counterclockwise torsional nystagmus in both eyes, with upbeat nystagmus in upgaze, left-beating nystagmus in left gaze, and right beating nystagmus in right gaze.

This is an example of direction-changing central vestibular nystagmus. In this particular patient, there was a prominent upgaze component of her nystagmus, suggesting involvement of the pathways of the interstitial nucleus of Cajal, which is the center in the midbrain that maintains vertical gaze. The bilateral abducens palsies were most likely from increased intracranial pressure causing compression of the sixth cranial nerves.

Downbeat Nystagmus

Downbeat nystagmus results from dysfunction of the vestibulocerebellar pathways, most commonly in the setting of lesions affecting the flocculus and paraflocculus of the cerebellum [30]. When downbeat nystagmus is found on exam, lesions of the cervicomedullary junction such as an Arnold-Chiari malformation should be suspected and the patient should undergo neuroimaging [31].

See-Saw Nystagmus

In see-saw nystagmus, there are disconjugate vertical oscillations of the eyes as well as conjugate torsional movements such that the elevated eye intorts while the depressed eye extorts. This type of nystagmus is most commonly seen in lesions of the optic chiasm and hypothalamus and, therefore can be seen with parasellar masses, often associated with a bitemporal hemianopsia [32]. Rarely, children can be born with absence of chiasmal crossing, an entity referred to as "nondecussating retinal-fugal fiber syndrome," which can result in see-saw nystagmus [33, 34]. The identification of such a nystagmus should prompt the acquisition of an MRI with thin slices through the sellar and suprasellar region.

Vignette 11

A 12-year-old girl was found to have a juvenile pilocytic astrocytoma on head CT after she fainted in gym class. The lesion compressed the optic chiasm, and required resection. One year later, she required VP shunt placement for hydrocephalus. She followed with neuro-ophthalmology for visual field monitoring. Examination revealed a bitemporal hemianopsia, as illustrated by the Humphrey visual fields seen in Fig. 12.9a. A pendular mixed torsional and vertical nystagmus was seen in the right eye, as well as a right optic neuropathy from compression. Five years after her original operation, the patent developed worsening of her visual fields as well as bilateral optic nerve pallor as seen in Fig. 12.9b. MRI showed enlargement of the tumor necessitating re-resection, after which the amplitude and frequency of the nystagmus worsened. Coronal and sagittal MRI cuts are shown in Fig. 12.9c, which illustrate a large T2 hyperintense lesion compressing the optic chiasm.

In this case, a suprasellar lesion with chiasmal and right optic nerve damage resulted in an acquired, monocular pendular nystagmus. Such a finding typically suggests the presence of a chiasmal or suprachiasmal lesion, or may occur in the setting of vision loss in the ipsilateral eye [35].

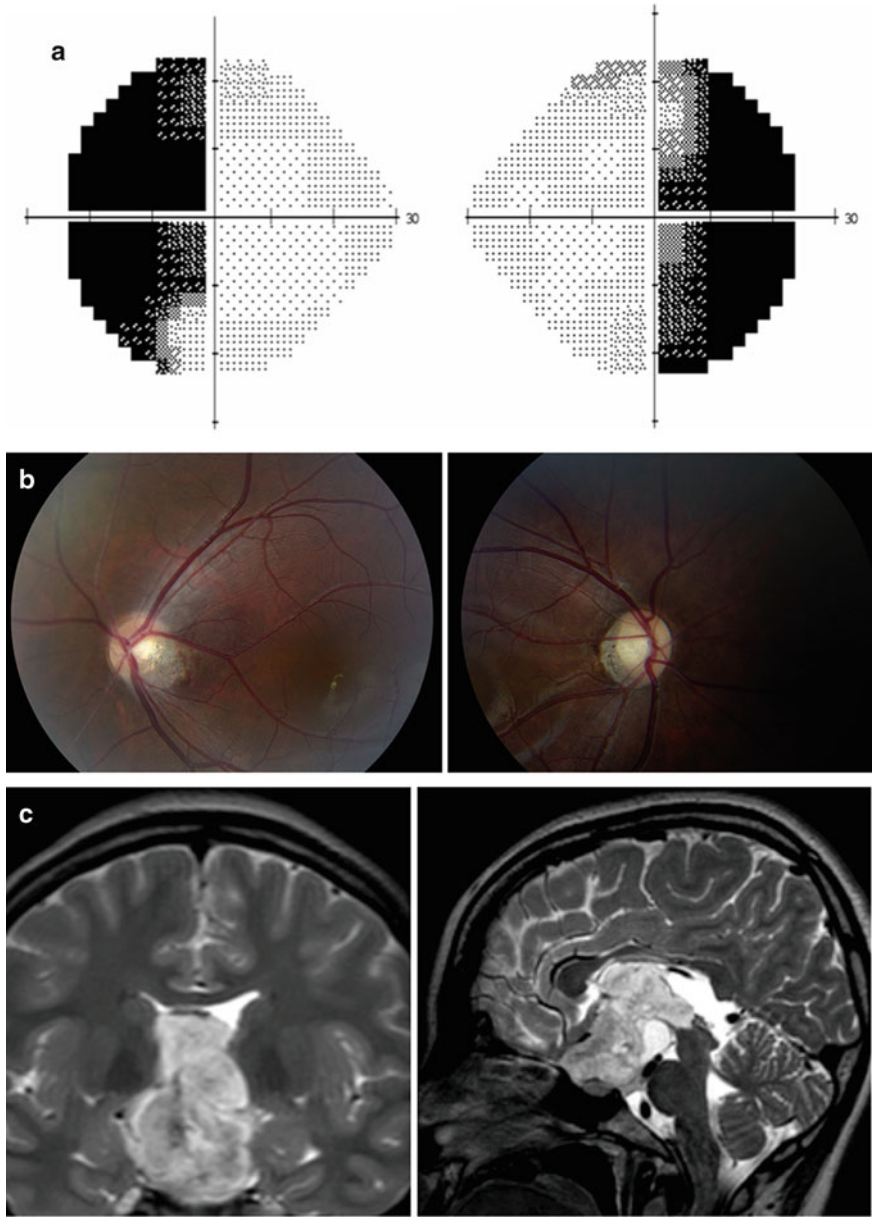


Fig. 12.9 Compression of optic chiasm from JPA. (**a**) Humphrey visual fields reveal a bitemporal hemianopsia. (**b**) Fundus photos demonstrate bilateral optic nerve pallor from compression of the optic chiasm. (**c**) Coronal and sagittal MRI images, illustrate a large T2 hyperintense lesion compressing the optic chiasm

Ocular Flutter and Opsoclonus

Saccadic intrusions refer to involuntary movements of the eyes in which there is no slow phase, and all the movements are saccades. There are many subtypes of saccadic intrusions, but the most clinically relevant in children are ocular flutter and opsoclonus. In ocular flutter, there are back-to-back horizontal saccades, without an inter-saccadic interval. Opsoclonus is similar except that the movements are omnidirectional and of higher amplitude so that they eyes appear to dance around

in all directions. In both cases, one must rule out a cerebellar lesion, and paraneoplastic disease must be considered, especially in cases of opsoclonus. In cases of paraneoplastic disease, there may be an antibody-mediated attack on the omnipause neurons in the brainstem that inhibit the burst neurons responsible for saccade initiation, thus leading to uncontrolled saccadic movements [36, 37]. In approximately 50 % of children with opsoclonus, the underlying neoplasm is a neuroblastoma or other neural crest tumor [37, 38].

Anisocoria

Vignette 12

A 16-year-old boy with no prior past medical history other than gastroesophageal reflux presented to his local emergency department with a headache followed by a generalized seizure. Upon arrival, he was found to be extensor posturing with his left arm, and he had an unreactive right pupil at 5 mm, with a sluggishly reactive left pupil at 3 mm. He underwent CT scan of the head, which demonstrated a 10×6×5 cm intraparenchymal hemorrhage with 2 mm of midline shift and uncal herniation. He was taken to the operating room for an emergent right craniotomy where he was found to have a large right temporal arteriovenous malformation (AVM). He subsequently underwent two embolizations and ultimately an open AVM resection. At outpatient follow-up, he was noted to have a complete left homonymous hemianopsia, as demonstrated by the patient's Humphrey visual fields (Fig. 12.10a), the resulting damage from the intracranial hemorrhage on the right side of his brain. The patient's AVM is pictured by CTA in Fig. 12.10b and by angiogram in Fig. 12.10c.

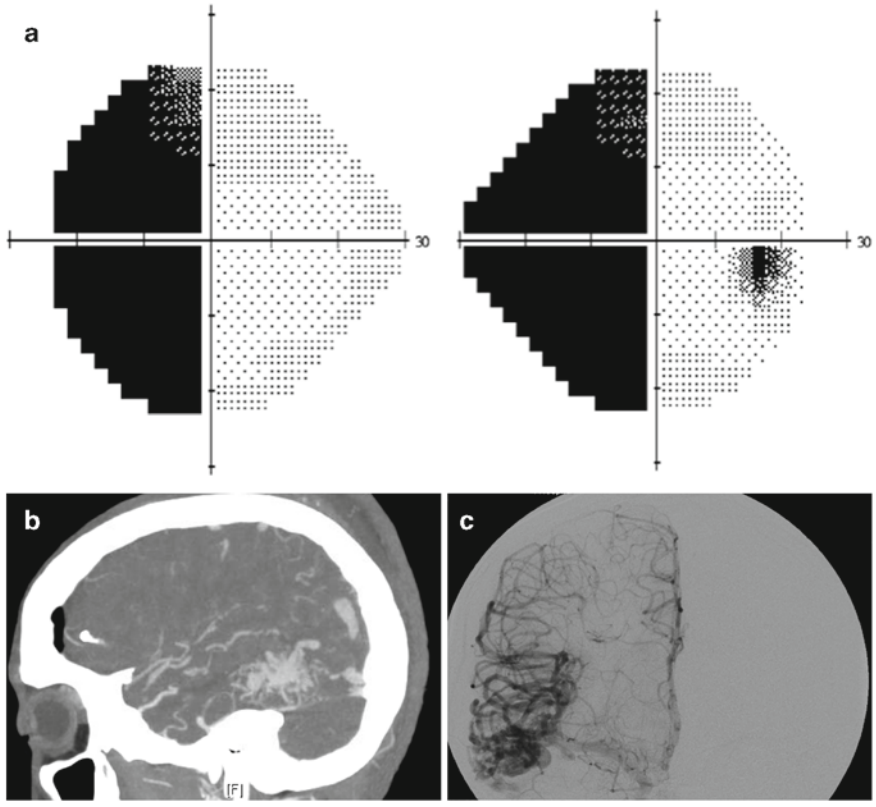


Fig. 12.10 Right temporal arteriovenous malformation causing hemorrhage and visual field loss. (**a**) Humphrey visual fields reveal a complete left homonymous hemianopsia. CT angiogram (**b**) and formal angiogram (**c**) reveal an arteriovenous malformation in the right temporal lobe

Anisocoria can be a normal physiologic variant, or can be an indication of underlying life-threatening pathology. It is important when examining a patient with anisocoria to determine which pupil is abnormal, the larger or smaller one. Examination is best done in both light and dark conditions, with the patient focusing on a distant object to prevent miosis from accommodation [39]. When anisocoria is greater in light conditions, this indicates that the large pupil is abnormal, and that there is dysfunction of pupillary constriction, either from an oculomotor nerve palsy, a degeneration of the ciliary ganglion (Adie's pupil), or pharmacological dilation. In contrast, when anisocoria is more notable in dark conditions, this indicates that there is a dysfunction of the sympathetic pathways that govern dilation, which is typically accompanied by ipsilateral ptosis, and is termed a Horner syndrome.

In physiologic anisocoria, the difference in the size of the pupils is generally 1 mm or less and there is no associated abnormal eye movement or ptosis. The degree of anisocoria is typically the same in light and dark. This is the most common etiology of anisocoria and can be present in up to 20 % of healthy normal children [39].

Horner Syndrome

Horner syndrome (HS) results from damage to the sympathetic pathways that govern the pupillary constriction, lid elevation, and sweating that accompany the fight or flight reaction. It may be either congenital or acquired. Congenital HS usually presents within the first 4 weeks of life and is related to stretching of the oculosympathetic fibers around the brachial plexus during birth. Axons from the first neuron in the pathway descend from the hypothalamus to the ipsilateral lateral thoracic spinal cord where they synapse. The second-order fibers ascend from the thoracic cord over the apex of the lung and up through the sympathetic plexus alongside the cord to synapse in the superior cervical ganglion. From there, the final third order fibers travel within a plexus around the common carotid artery. Fibers destined for the eye proceed along the internal carotid artery, through the cavernous sinus and alongside the abducens nerve to finally enter the orbit where they innervate the dilator pupillae and Müller's muscles that govern lid elevation related to sympathetic drive.

Acquired HS could therefore be secondary to brainstem disease, spinal cord lesions, apical lung lesions (rare in children), lesions of the sympathetic chain, carotid artery lesions in the neck, cavernous sinus lesions, or orbital disease. Cocaine eye drops can confirm that the anisocoria is the result of a Horner syndrome, as cocaine will cause dilation of eyes with intact sympathetic responses. After cocaine eye drops are given, the degree of anisocoria will increase if it is a Horner syndrome [40]. Apraclonidine eye drops are an alternative to cocaine. Apraclonidine is an alpha-2-receptor agonist used for the treatment of increased intraocular pressure. However, it also has weak alpha-1 activity, so that only an eye with a HS, which develops upregulation of the norepinephrine receptors in the iris, will react with dilation. Therefore, patients with Horner syndrome will have reversal of anisocoria after instillation of apraclonidine eye drops [41]. However, apraclonidine should be avoided in the pediatric population as it has been documented to cause severe peripheral vasoconstriction, hypertension, and pulmonary edema [42]. Work-up of Horner syndrome in children should include palpation of neck, axilla and abdomen, urine catecholamine testing, and MRI scan of the head, neck, and chest [27]. Abnormal imaging is an indication for surgical referral.

Pediatrician's Perspective

1. A careful history and neurological examination is essential in the assessment of any child complaining of unexplained neurological or visual symptoms.
2. While a neuro-ophthalmological consultation utilizing formal visual fields, a slit lamp examination, and dilated funduscopy can be of great value, the essential neuro-ophthalmic examination can be conducted at the bed-side or within the pediatrician's office, with just an

acuity card, pen light, moving target and hand-held ophthalmoscope, and can yield significant clinical clues about the underlying pathology.

3. By mastering basic neuro-ophthalmic examination skills, the general pediatrician will be able to make important ocular, neurological, and neurosurgical diagnoses that would otherwise be missed and make the timely referrals necessary to permit more detailed evaluations when appropriate.
4. Any patient with papilledema is at risk for vision loss and requires urgent evaluation. Often, papilledema is a sign of dangerous intracranial pathology that may require urgent neurosurgical intervention.
5. Craniosynostosis occasionally results in increased ICP and papilledema.
6. Abducens (sixth nerve) palsy may be the first sign of a mass lesion even prior to papilledema.
7. Pure vertical (upbeat or downbeat) nystagmus reflects a central etiology and therefore warrants referral for urgent imaging.
8. Up to 20 % of healthy children will have physiologic anisocoria. This can be distinguished from pathologic anisocoria in that the degree of anisocoria remains the same in both dim and bright light in the case of physiologic anisocoria.

References

1. Bruce B, Lamirel C, Wright D, et al. Nonmydriatic ocular fundus photography in the emergency department. N Engl J Med. 2011;364:387–9.
2. Hayreh S. Optic disc edema in raised intracranial pressure. V. Pathogenesis. Arch Ophthalmol. 1977;95:1553–65.
3. Tso MOM, Hayreh SS. Optic disc edema in raised intracranial pressure IV. Axoplasmic transport in experimental papilledema. Arch Ophthalmol. 1977; 95:1458–62.
4. Donohoe CD. The role of the physical examination in the evaluation of headache. Med Clin N Am. 2013;97:197–216.
5. Wong SH, White RP. The clinical validity of the spontaneous retinal venous pulsation. J Neuroophthalmol. 2013;33:17–20.
6. Sinclair AJ, Burdon MA, Nightingale PG, et al. Rating papilloedema: an evaluation of the Frisen classification in idiopathic intracranial hypertension. J Neurol. 2012;259:1406–12.
7. Hoye III VJ, Berrocal AM, Hedges III TR, Amaro-Quireza ML. Optical coherence tomography demonstrates subretinal macular edema from papilledema. Arch Ophthalmol. 2001;119:1287–90.
8. Stagno V, Navarrete EA, Mirone G, Esposito F. Management of hydrocephalus around the world. World Neurosurg. 2013;79:e17–20.
9. Dolecek TA, Propp JM, Stroup NE, Kruchko C. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2005–2009. Neuro Oncol. 2012;14:v1–49.
10. Gordon NS. Idiopathic intracranial hypertension. Eur J Paediatr Neurol. 2006;10:1–4.
11. Wall M. Idiopathic intracranial hypertension. Neurol Clin. 2010;28:593–617.
12. Smith JL. Whence pseudotumor cerebri? J Clin Neuroophthalmol. 1985;5(1):55–6.
13. Sinclair AJ, Walker EA, Burdon MA, et al. Cerebrospinal fluid corticosteroid levels and cortisol metabolism in patients with idiopathic intracranial hypertension: a link between 11β-HSD1 and intracranial pressure regulation? J Clin Endocrinol Metabol. 2010;95(12):5348–56.
14. Donaldson JO. Pathogenesis of pseudotumor cerebri syndromes. Neurology. 1981;31(7):877–80.
15. Donaldson JO, Horak E. Cerebrospinal fluid oestrone in pseudotumor cerebri. J Neurol Neurosurg Psychiatry. 1982;45(8):734–6.
16. Ahmed R, Friedman DI, Halmagyi GM. Stenting of the transverse sinuses in idiopathic intracranial hypertension. J Neuroophthalmol. 2011;31(4):374–80.
17. Ducruet AF, Crowley RW, McDougall CG, Albuquerque FC. Long-term patency of venous sinus stents for idiopathic intracranial hypertension. J Neurointerv Surg. 2014;6(3):238–42.
18. Ahmed RM, Wilkinson M, Parker GD, et al. Transverse sinus stenting for idiopathic intracranial hypertension: a review of 52 patients and of model predictions. Am J Neuroradiol. 2011;32:1408–14.
19. Glass LR, Dagi TF, Dagi LR. Papilledema in the setting of x-linked hypophosphatemic rickets with craniosynostosis. Case Rep Ophthalmol. 2011;2: 376–81.
20. Florrison JMG, Van Veelen M-LC, Bannink N, et al. Papilledema in isolated single-suture craniosynostosis: prevalence and predictive factors. J Craniofac Surg. 2010;21:20–4.
21. Kedar S, Zhang X, Lynn MJ, Newman NJ, Biousse V. Congruency in homonymous hemianopia. Am J Ophthalmol. 2007;143:772–80.
22. Dacso CC, Bortz DL. Significance of the Argyll Robertson pupil in clinical medicine. Am J Med. 1989;86(2):199–202.
23. Trimarchi F. Neuro-ophthalmology. Curr Opin Neurol Neurosurg. 1992;5(5):740–3.

24. Pierrot-Deseilligny CH, Chain F, Gray F, Seradaru M, Escourolle R, Lhermitte F. Parinaud's syndrome: electro-oculographic and anatomical analyses of six vascular cases with deductions about vertical gaze organization in the premotor structures. Brain. 1982;105:667–96.
25. Dotan G, Rosengeld E, Stolovich C, Kessler A. The role of neuroimaging in the evaluation process of children with isolated sixth nerve palsy. Childs Nerv Syst. 2012;29:89–92.
26. Merino P, Gomez de Liano P, Villalovo JMC, Franco G, Gomez de Liano R. Etiology and treatment of pediatric sixth nerve palsy. J AAPOS. 2010;14:502–5.
27. Kaeser P-F, Kawasaki A. Disorders of pupillary structure and function. Neurol Clin. 2010;28:657–77.
28. Wong AMF. Understanding skew deviation and a new clinical test to differentiate it from trochlear nerve palsy. J AAPOS. 2010;14:61–7.
29. Dinkin MJ, Rizzo III JF. Abnormal eye movements in children. Int Ophthalmol Clin. 2008;48:95–134.
30. Pierrot-Deseilligny C, Milea D. Vertical nystagmus: clinical facts and hypotheses. Brain. 2005;128: 1237–46.
31. Yeow YK, Tija TL. The localizing value of downbeat nystagmus. Singapore Med J. 1989;30:273–6.
32. Druckman R, Ellis P, Kleinfeld J, Waldman M. Seesaw nystagmus. Arch Ophthalmol. 1966;76:668.
33. Sami DA, Saunders D, Thompson DA, et al. The achiasmia spectrum: congenitally reduced chiasmal decussation. Br J Ophthalmol. 2005;89:1311–7.
34. Apkarian P, Bour LJ. See-saw nystagmus and congenital nystagmus identified in the non-decussating retinalfugal fiber syndrome. Strabismus. 2001;9:143–63.
35. Shaw FS, Kriss A, Russel-Eggit I, Taylor D, Harris C. Diagnosing children presenting with asymmetric pendular nystagmus. Dev Med Child Neurol. 2001;43:622–7.
36. Zee DS, Robinson DA. A hypothetical explanation of saccadic oscillations. Ann Neurol. 1979;5(5):405–14.
37. Averbuch-Heller L, Remler B. Opsoclonus. Semin Neurol. 1996;16(1):21–6.
38. Pranzatelli MR. The neurobiology of the opsoclonus-myoclonus syndrome. Clin Neuropharmacol. 1992; 15(3):186–228.
39. Ettinger ER, Wyatt HJ. Variation and clinical observation with different conditions of illumination and accommodation. Investig Ophthalmol Vis Sci. 1991;32:501–9.
40. Van der Wiel HL, Van Gijn J. The diagnosis of Horner's syndrome. J Neurol Sci. 1986;73(3):311–6.
41. Morales J, Brown SM, Abdul-Rahim AS, Crosson CE. Ocular effects of apraclonidine in Horner syndrome. JAMA Ophthalmol. 2000;118:951–4.
42. Yarwood J, Bartholomew K. Systemic effects of topical ophthalmic agents. Br J Anesth. 2010;105:238–9.

Hydrocephalus and Ventriculomegaly

13

Assem M. Abdel-Latif and Jeffrey P. Greenfield

Clinical Vignette An 18-month-old child presented to the emergency department with repeated vomiting. The child's mother relayed that the vomiting occurred a few hours after having eaten. She didn't report any diarrhea or abdominal cramping. On examination, the child was pale. He was afebrile but tachypneic; his pulse was 90 beats/min. Neurologically, the child was obeying commands and was alert but restless. His pupils were normal and reactive. The abdominal exam was normal with no tenderness, guarding, or rigidity. The preliminary diagnosis was food poisoning with resultant gastritis, and the decision in the emergency room was to obtain blood samples for chemistry, keep him under observation, and initiate IV hydration.

During 3 h of observation, he vomited again and became less alert. Progressive dehydration was diagnosed and more IV fluids were pushed. An hour later, he was noted to be unarousable even with painful stimuli. He had midsize pupils that were sluggishly reactive. Emergency head CT was ordered but he arrested on his way out of the CT machine and was intubated for resuscitation. His CT showed a posterior fossa tumor with tense obstructive supratentorial hydrocephalus. He was immediately taken to the operating room for placement of an external ventricular drain.

A.M. Abdel-Latif, M.D., M.Sc. (✉)
Department of Neurological Surgery, Faculty of Medicine, Ain Shams University, Abbassia, Cairo 11566, Egypt
e-mail: Assem_mounir@hotmail.com

J.P. Greenfield, M.D., Ph.D.
Associate Professor of Neurological Surgery, Weill Cornell Medical College, 525 East 68th Street, Box 99, New York, NY 10065, USA

Introduction

Hydrocephalus, as a clinical term, is often used to describe a large or an enlarging head size in an infant with a bulging fontanel; in other settings it may be used to suggest increased intracranial pressure (ICP) or brain edema and obliterated basal cisterns on imaging [1]. Neurosurgeons use the word hydrocephalus more precisely to describe a *dilated ventricular system with an increase in the intra-axial CSF volume*. An increase in the CSF volume may cause ventricular dilatation, which accounts for most cases of hydrocephalus. Secondary causes, such as brain atrophy with resultant ventricular dilation, are referred to as *hydrocephalus ex vacuo*. Hydrocephalus isn't a single disease but rather a symptom or sign that relates to CSF dynamics [2, 3].

A technical definition of hydrocephalus is "an active distension of the ventricular system of the brain resulting from inadequate passage of CSF from its point of production within the cerebral ventricles to its point of absorption into the systemic circulation" [4]. This definition excludes brain atrophy, idiopathic intracranial hypertension, and normal volume hydrocephalus since

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_13

these conditions don't require ventricular dilatation. Moreover, it doesn't require increased ICP so that idiopathic and secondary normal pressure ventriculomegaly (NPH) can be included.

In 2010, the International Hydrocephalus Workshop endorsed the consensus definitions settled upon the by International Society of Pediatric Neurosurgery [5]. Their definitions are:

1. Hydrocephalus is a condition characterized by a dynamic imbalance between the formation (production) and absorption of spinal fluid resulting in an increase in the size of the fluid cavities (ventricles) within the brain. (*This definition would serve for general use of all readers.*)
2. Hydrocephalus is a condition characterized by a dynamic imbalance between the formation (production) and absorption of spinal fluid that results in an increase in the size of the fluid cavities within the brain and, in some situations, in an expansion of the spaces outside the brain, with or without an increase in the size of the ventricles.

It is important to emphasize that while ventriculomegaly can be readily diagnosed by various imaging modalities, *findings must be interpreted in the context of the clinical symptoms and signs in order to permit a firm diagnosis of active hydrocephalus* [6]. In the presence of a working definition of hydrocephalus, a classification scheme may help in understanding the etiology, pathophysiology, and subsequent treatment options for this most common pediatric neurosurgical condition.

Classification of Hydrocephalus

Hydrocephalus can be generally classified according to many perspectives:

1. Age, childhood, and adult hydrocephalus
2. Communicating or noncommunicating
3. Primary (or idiopathic) vs. secondary
4. Genetic or hereditary vs. sporadic
5. Anatomical classification (biventricular, triventricular, and tetraventricular hydrocephalus, even multiloculated or asymmetric hydrocephalus)

A classification was presented by Dandy and Blackfan in the early twentieth century to describe hydrocephalus. In their work, Dandy and Blackfan [7] classified hydrocephalus as either communicating or noncommunicating hydrocephalus based on the presence or absence of communication (detected by dye) between the cranial CSF compartment and the spinal CSF compartment. Today hydrocephalus is variably regarded by experts in flow dynamics as nearly entirely obstructive with only the site of obstruction (intraventricular vs. extraventricular, defining a difference) [8].

Another way of defining hydrocephalus is as a dynamic imbalance between the formation (production) and absorption of spinal fluid that results in an increase in the size of the fluid cavities within the brain and, in some situations, in an expansion of the spaces outside the brain, with or without an increase in the size of the ventricles. The pathophysiology can be regarded as obstructive at one or more of critical transit points that subsequently affects the resultant pattern of ventricular enlargement [4]. Figure 13.1 shows the interrelated compartments of cerebrospinal fluid production, circulation, and absorption.

Special forms of hydrocephalus that can be encountered in a typical pediatric neurosurgical practice will be discussed below including a brief discussion of the etiologies, diagnoses and related conditions, and the treatment options that your patients may be encountering when facing these diagnoses:

- External hydrocephalus
- Hydranencephaly
- Trapped fourth ventricle
- Posthemorrhagic hydrocephalus
- Normal volume hydrocephalus

External Hydrocephalus

Definition. Enlargement of the subarachnoid spaces over the frontal poles and their cortical sulci with rapid increase of the head circum-

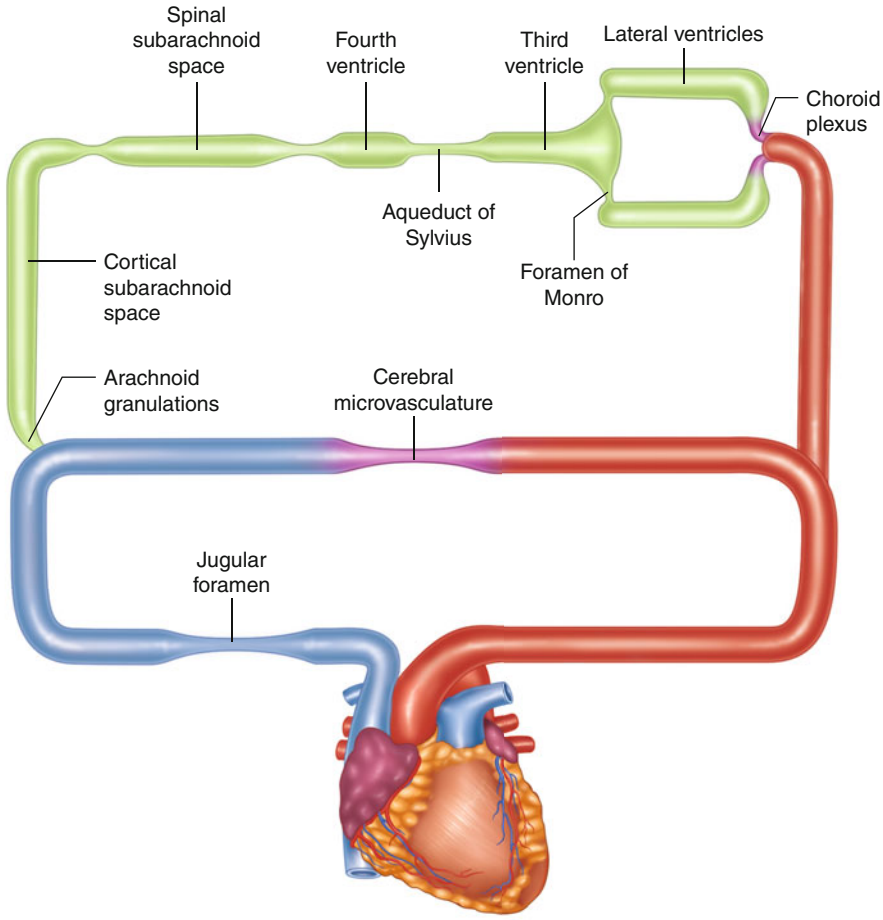


Fig. 13.1 A schematic representing the interconnected circulations of cerebrospinal fluid and intravascular blood. Arterial blood (*red*) forms CSF (*teal*) through an ultrafiltration process at the level of the choroid plexus. The CSF circulation can be interrupted at any of the compartments within the flow chart. The final absorption of CSF into the venous circulation returning to the heart (*purple*) occurs at the level of the arachnoid granulations, a common site of pathology for many communicating forms of hydrocephalus [5]

ference [9–11]. Also worth noting is the absence of radiological or clinical features of increased ICP such as periventricular lucency or a tense anterior fontanel [12].

Radiological findings. Normal or mildly dilated ventricles are noted with enlarged basal cisterns and widening of the interhemispheric fissure. CT demonstrates extra-axial fluid collections that usually share the density of CSF, while MRI or cranial U/S demonstrates veins coursing through the fluid collection from the surface to the inner table of the skull (known as the cortical vein sign).

Presentation. Typically infants are asymptomatic and present with an enlarging head that starts to appear in the first year of life and usually compensates by 12–18 months without treatment [12]. Frontal bossing may be seen and, occasionally, slight motor developmental delay is noted. This is likely due to the large head causing neuromuscular issues with balance and walking rather than an intrinsic effect upon brain development.

Etiology. The pathophysiology is not fully understood, but a defect in CSF absorption has been postulated secondary to delayed maturation of the arachnoid villi [13, 14]. An association of

widened SAS has also been reported in some children with craniosynostosis [15]. The fact that it may follow intraventricular or subarachnoid hemorrhage [16, 17] or superior vena cava obstruction [18] also suggests a common distal transient defect in CSF absorption.

Management. This etiology is sometimes referred to as "benign external hydrocephalus" because it's commonly viewed as a self-limiting condition of infancy that resolves spontaneously during childhood [19, 20]; therefore, conservative follow-up is mandated. As pediatricians and pediatric neurosurgeons, it is crucial to emphasize to the parents that children with this diagnosis have normal neurologic development [10]. Shunting may be required in rare instances of manifestations of increased ICP, bulging fontanel, considerable macrocrania, or frontal bossing, but this is a rare necessity in this etiology [17, 21]. A few reports exist of the use of acetazolamide or even transient mannitol treatment with good outcomes [22], but this is not common practice.

Differential diagnosis: The etiology to distinguish from benign subdural collections of infancy is symptomatic chronic extra-axial fluid collections.

Benign Subdural Collections of Infancy

Definition. Fluid collections over the frontal convexities associated with prominent cortical sulci and interhemispheric fissure, with normal or slightly enlarged ventricles, suggest benign subdural collections of infancy [23].

Etiology. Most of the cases are attributed to perinatal trauma, but an etiology is not always identified.

Presentation. Infants usually come to medical attention around 4 months of age with accelerated head growth rate, often demonstrating a tense fontanel and poor head control.

Radiological findings. A hypodense fluid collection is seen over the frontal lobes and interhemispheric fissure on CT scan. This entity shares the radiologic and clinical features of external hydrocephalus, yet on diagnostic tap, fluid is usually clear yellow (xanthochromic) with high protein content, whereas in external hydrocephalus, fluid is clear CSF. MRI and cranial ultrasound fail to show "cortical vein sign," the fluid intensity on MRI is mostly slightly different from CSF, and CSF flow studies will not show flow into the collection continuous with the intraventricular CSF.

Management. This radiologic entity gradually resolves spontaneously within several months. A single subdural tap may speed this up, but surgical management is rarely indicated except in cases of significant neurologic decline. Head growth curves and any developmental delay usually normalize.

Symptomatic Extra-Axial Fluid Collections in Children

Various terms are used to describe this condition: "chronic subdural hematoma" "effusions," "hygromas," and "extra-axial fluid collections" [10, 23].

Etiology. In a study of 103 patients, 36 % were believed to be due to head trauma (including non-accidental head trauma), 22 % were post-meningitic, and 19 % post-shunting [24]. Other reported causes include hypoxic brain damage and coagulation defects [25].

Presentation. The following manifestations are more common to find: seizures, irritability, lethargy, signs of increased ICP, macrocrania, focal deficit, and developmental delay.

Radiological findings. Collections of varying signal characters cause obliteration of the cortical sulci and often some degree of ventricular compression.

Management. Serial subdural taps (to exclude infection and to help drainage), Burr hole drainage, and subdural shunting may all be considered [26].

Differential diagnosis. The differential diagnosis of extra-axial fluid collections in children includes normal variants of enlarged subarachnoid space and interhemispheric fissure, external hydrocephalus, benign subdural collections of infancy, cerebral atrophy, or craniocerebral disproportion.

Hydranencephaly

Definition. Total or near total absence of the cerebral tissue to be replaced by CSF and covered by intact meninges and cranial vault (post-neurulation defect) [27, 28].

Etiology. Bilateral ICA occlusion causing territorial infarcts and subsequent loss of the cerebral tissue supplied by the ICAs [29]. Perinatal infections also implicated and association with maternal smoking has been described [30].

Presentation. The child's head size is usually normal at birth but quickly becomes progressively larger. Irritability, hemodynamic instability, signs of increased ICP, marked developmental delay, and seizures.

Radiological findings. Complete absence of the cortical mantle (small bands of cerebrum are still consistent with diagnosis), an intact falx, and brain tissue supplied by the PCAs (posterior fossa structures, brainstem, thalamus, and hypothalamus).

Prognosis and treatment. As there is no possibility of cerebral cortical recovery, shunting is only done to control the head size to facilitate general palliative care for the child.

Differential diagnosis. One must consider the diagnosis of maximal hydrocephalus, in which there is progressive dilatation of CSF spaces with a minimal amount of cortical tissue. This tissue can actually demonstrate a remarkable degree of re-expansion with shunting. Children with maximal hydrocephalus may just show subtle neurodevelopmental delay in contrast to hydranencephaly patients who are profoundly abnormal neurologically [28].

Trapped Fourth Ventricle and Multiloculated Hydrocephalus

Uniloculated hydrocephalus is dilatation of one segment of the ventricular system due to obstruction at the foramen of Monroe causing unilateral ventricular dilatation. Alternatively, obstruction at the cerebral aqueduct and fourth ventricular outlet may cause dilatation of the fourth ventricle [31].

Various forms of isolated ventricular compartments have been described [32, 33]:

- Multiple intraventricular septations
- An isolated lateral ventricle/unilateral hydrocephalus
- Entrapped temporal horn
- Isolated fourth ventricle
- Expanding septi pellucidum/cavum vergae

Etiology. Compartmentalization of the ventricular system increases following infection (meningitis, ventriculitis, and shunt infection) or intraventricular hemorrhage.

Pathophysiology. Formation of septations from microglial membranes extending through denuded ependyma from underlying glial tufts or post-inflammatory debris obstructing the ventricular foramina is believed to result in the development of loculations [34, 35].

Presentation. The presentation is diverse due to the varied subtypes. It usually presents with manifestations of mass effect, and cerebellar, brain stem, and cranial nerve manifestations are commonly reported. Alternatively, increased ICP or seizures from a very large compartmentalization may also occur.

Treatment. Most children will require multiple procedures, often utilizing a combination of endoscopic membrane fenestrations with shunts. Endoscopic techniques are used to communicate the loculated regions together to allow for simplified shunting [36–38].

Dandy-Walker Malformation (DWM)

Definition. DWM is defined as agenesis of the cerebellar vermis with cystic dilatation of the fourth ventricle and hydrocephalus. Other associated pathological changes include elevation of the transverse sinus, enlargement of the posterior fossa, and occlusion of the foramina of Luschka and Magendie [7, 39, 40]. The condition can be detected antenatally by fetal sonography as early as the 14 week of gestation [41].

Presentation. The presentation is highly variable according to the degree of hydrocephalus and associated anomalies. Children less than a year of age usually come to medical attention with signs and symptoms of hydrocephalus. They often have a characteristic head shape with large prominent occiput. Older children may present differently with neurocognitive and developmental delay, problems with coordination, or spastic paraparesis.

Radiological findings. Due to variability of pathological features, a set of radiological abnormalities have been proposed [42, 43]. Hydrocephalus is not always present especially at birth but it occurs in 75–80 % of cases by 3 months of age.

Other findings of DWM include:

1. Large median posterior fossa cyst widely communicating with the fourth ventricle
2. Absence of the lower portion of the vermis
3. Hypoplasia, anterior rotation, and upward displacement of the vermian remnant
4. Absence or flattening of the angle of the fastigium
5. Large bossing posterior fossa with elevation of the torcula
6. Anterolateral displacement of normal or hypoplastic cerebellar hemispheres

Pathophysiology of DWM-Associated Hydrocephalus

Hydrocephalus was thought initially to result from occlusion of the fourth ventricular outlet foramina; however, other causes are believed to include maldevelopment of the subarachnoid space or aqueductal stenosis from upward herniation of the posterior fossa cyst. A contribution of venous anatomy has also been suggested as a cause due to abnormal location of the torcula.

Treatment. Debate exists as to within which compartment to first place a shunt: the lateral ventricle or the posterior fossa cyst, or both, simultaneously. A common approach is to shunt the infratentorial cyst first and then perform an endoscopic third ventriculostomy if the ventricles fail to decompress with follow-up.

Differential diagnosis. Due to marked variability of pathological features of DWM, the following conditions are commonly regarded within the differential diagnosis:

Dandy-Walker variant is a DWM differentiated by a slightly less abnormal cerebellar vermis, a smaller cystic cavity, and a posterior fossa that is not markedly dilated [44–47]. Recently it has been considered as a separate entity from the DWM and given the name of "vermian-cerebellar hypoplasia."

Persistent Blake's pouch cyst is a persistence of a congenital dorsal appendage of the fourth ventricle, which then forms a posterior fossa cyst widely communicating with the fourth ventricle.

Mega cisterna magna is an enlarged cisterna magna combined with vermian dysgenesis but with vermian tissue remaining between a normal fourth ventricle and the cistern [47].

Posterior fossa arachnoid cyst/retrocerebellar arachnoid cysts are true cysts that do not communicate with the fourth ventricle and are not accompanied by cerebellar hypoplasia. The radiological appearance may give the impression of communication because the cyst compresses the cerebellar tissue.

Neonatal Posthemorrhagic Hydrocephalus

Neurodevelopmental Pathophysiology

In the developing brain, the periventricular germinal matrix between the thalamus and the caudate nucleus provides the source for neuronal and glial elements to both cerebral hemispheres. It's a highly vascular structure whose vessels have immature connective tissue architecture and lack auto regulatory properties of mature cerebral vasculature.

Risk factors for the development of neonatal hemorrhage include early gestational age at delivery (25–30 % of preterm babies) [48], any cause of large fluctuations in cerebral blood flow due to vigorous resuscitation, pneumothorax, respiratory distress syndrome or seizures, or neonatal sepsis, which may cause cerebral vasculitis.

A major concern in children with neonatal IVH is the development of hydrocephalus, which may subsequently adversely affect the neurocognitive development of the child. Chapter 11 contains a complete discussion of neonatal IVH for more details. Briefly, progressive posthemorrhagic ventricular dilatation (PPHVD) has been estimated to occur in 25–50 % of preterm infants diagnosed with IVH. This is believed to cause a three- to fourfold increased risk of cognitive and psychomotor delay [49]. Hydrocephalus in these children is attributed to blood and its breakdown products in the CSF that may excite an ependymal reaction causing obstruction at critical passages such as the cerebral aqueduct. Alternatively, the blood may cause scarring of the subarachnoid space and villi and impair CSF absorption. Comprehensive management is discussed in Chap. 12, but a general classification is presented here for easy reference.

Papile et al. Classification of Germinal Matrix Hemorrhage [50]

1. Grade I: hemorrhage restricted to subependymal parenchyma or minimally involves the ventricle (<10 %).
2. Grade II: hemorrhage extends into the ventricle but doesn't expand it or occupy >50 % of the ventricle.
3. Grade III: hemorrhage occupies >50 % of the ventricle and often distends it.
4. Grade IV: classically refers to the extensive IVH with parenchymal involvement but recently referred to as periventricular hemorrhagic infarction (PVHI) because it mostly results from venous occlusion with subsequent hemorrhage [51–53].

Normal Volume Hydrocephalus

This is a term that generates considerable debate and is often referred to as "slit ventricle syndrome" since the condition is usually described with shunted children who develop manifestations of increased intracranial pressure without ventriculomegaly [54, 55].

Children may be classified within several different groups:

- Children with functioning shunts with very low ICP [56, 57]
- Children with intermittent malfunction of the shunt with impaired drainage. This group can show some ventriculomegaly in the transitory phase of increased ICP
- Children with definite shunt malfunction who have rigid ventricular walls [58, 59]
- Children with functioning shunts but manifesting increased ICP due to increased venous pressures which occur within pseudotumor cerebri
- Children with functioning shunts and high ICP due to craniocerebral disproportion [60]

Normal pressure hydrocephalus is a well-described clinical and radiographic entity usually diagnosed in elderly adults with ventriculomegaly, but only normal or upper edge of normal ICP is less commonly found in pediatric patients [61]. Another commonly used term is arrested hydrocephalus, which refers to the condition of non-shunted persistent ventriculomegaly with normal ICP and no obvious clinical manifestations. These children also pose a management challenge but usually only require observation.

Post-traumatic Hydrocephalus

Definition. A fairly high risk of ventricular dilatation (7–29 %) may occur within variable periods after trauma ranging from 2 weeks to several years [62].

Pathophysiology. Obstruction due to intraventricular hemorrhage, small clots, or contusions, compressing the narrow ventricular passages, or a decrease in CSF absorption due to subarachnoid hemorrhage, infections, or early surgical procedures resulting in significant subarachnoid scarring are among the proximal causes of post-traumatic hydrocephalus [63].

Clinical presentation. The acute presentation is with overt manifestations of increased ICP. These may be headache, bradycardia, or changes in the neurologic exam, typically recognized within the intensive care setting. It should also be suspected in cases of CSF leakage or increasing CSF collections following a trauma-related craniotomy. In the chronic setting, which can be days to weeks post-injury, this entity may present with a more insidious progressive cognitive decline, behavioral changes, or failure to attain functional improvement after the initial head trauma [64–66].

Treatment. Post-traumatic hydrocephalus, with either acute or chronic presentations, is likely to benefit from CSF diversion.

Differential diagnosis. Post-traumatic brain atrophy may be very difficult to differentiate from a normal pressure variant of the posttraumatic hydrocephalus sharing clinical and radiological characters. Invasive ICP monitoring can help distinguish the two, as can ophthalmologic evaluation for papilledema and comparison of serial imaging.

Radiologic Recognition and Definition of Hydrocephalus

Various modalities can be used to detect and follow hydrocephalus, depending on the age of the patient and the acuity of the presentation. Ultrasound is the modality of choice for neonates with open fontanels as it visualizes the supratentorial compartment with excellent resolution. It is widely utilized in neonates with IVH for diagnosis and surveillance imaging because it is safe, routinely available and cost-effective. It cannot always visualize the entire intracranial space but is an excellent first choice for very young children, particularly in NICU and outpatient settings. CT and MRI, discussed in significant detail in Chaps. 18 and 20, offer far more detailed evaluations of the entire ventricular system and a better visualization of possible underlying etiologies. Relative risks and benefits of these tests are also fully covered in other dedicated portions of this textbook. With respect to the radiologic *definition* of hydrocephalus, there is no single radiological parameter that can be totally relied upon, but some criteria do exist:

1. An obvious appearance of the temporal horns, especially if both are ≥2 mm
2. A frontal horn/internal diameter ratio (FH/ID) >0.5, which is the ratio between the largest width of the frontal horns to the internal skull diameter on the same slice
3. An Evan's ratio >0.3, which is the ratio between frontal horn largest width (FH) and the maximum biparietal diameter in the same CT slice
4. FOH ratio ≥0.37, which is the ratio of the sum of the largest diameter of the frontal and the occipital horns (FH + OH) to twice the maximum biparietal diameter [67]

5. A sagittal MRI showing upward bowing and thinning of the corpus callosum or bulging and prominence of third ventricular recesses
6. Reduction of the frontal horn caudate angle or increased frontal horn radius
7. Periventricular white matter hypodensity on CT, hypointensity on T1WI, or hyperintensity on T2WI and FLAIR sequences. These all indicate trans-ependymal egress of CSF into the surrounding parenchyma

Clinical Presentation of Hydrocephalus

Clinical manifestations of hydrocephalus differ according to the age group of diagnosis between neonates and infants, children, and young adults. Much of this difference is due to the presence of an open fontanel as patent cranial sutures alter the pathophysiology of hydrocephalus. Open sutures permit a compensatory cranial expansion to balance an increase in the ICP. The development of clinical manifestations also depends upon the rate of ICP increase. Mechanisms such as suture diastasis are better able to compensate in a subacute or the chronic form than in the acute presentation [68–70].

Neonates and Infants

Symptoms:
- Irritability.
- Poor suckling/poor feeding.
- Delayed milestones, especially poor head control.
- Repeated vomiting and clinical status deterioration can still occur even with open sutures.

Signs:
- Progressive increase in the head circumference may be the earliest and the most sensitive sign in this age group.
- A bulging anterior fontanel, splaying of the cranial sutures, engorged scalp veins, and "sunset" appearance of the eyes.
- Apneic spells.

Children and Young Adults

Symptoms:
- Manifestations of increased ICP are often more pronounced.
- Headache, nausea, and vomiting.

Signs:
- Bradycardia
- Papilledema
- Behavioral or cognitive changes
- Deteriorating level of consciousness

Hydrocephalus Associated with Chiari Malformations

Hydrocephalus is present in 85–90 % of children with Chiari II malformations. The etiology is directly related to the presence of spinal dysraphism acting as a CSF reservoir shifting cranial CSF to the spine resulting in the absence of the distending forces in the cranial compartment during fetal development. This leads to the constellation of features of Chiari II including hydrocephalus [71]. In these children hydrocephalus is thought to occur secondary to compromised CSF flow at multiple points including the cerebral aqueduct, the outflow of the fourth ventricle, and basal cisterns surrounding the brainstem.

Clinical presentation. Hydrocephalus usually presents in first year of life often at birth and frequently in the week following the repair of the spinal dysraphism. The clinical presentation is similar to the manifestations described under the section of symptoms and signs in neonates and infants; however, it also includes CSF fistula with the newly repaired spinal defect as a pseudomeningocele or direct CSF leak [72].

Management. Endoscopic third ventriculostomy is far less effective in neonates with hydrocephalus even in cases where aqueductal stenosis is found; thus, ventriculoperitoneal shunting still serves as the mainstay of treatment for this population.

Aqueductal Stenosis

Description. Tri-ventricular hydrocephalus describes a common neuroanatomical variant in which the fourth ventricle does not share the same degree of dilatation as the remaining ventricular compartments. It's the most classic form of obstructive hydrocephalus.

Etiology. Either defined as intrinsic due to narrowing or blockage of the aqueduct, which is usually secondary to causes such as post-inflammatory gliosis from infection or hemorrhage or extrinsic occurring due to compression from outside, which can be due to congenital causes including Chiari type II or Dandy-Walker malformations tectal plate gliomas or pineal region masses.

Management. Aqueductal stenosis represents an excellent opportunity for endoscopic third ventriculostomy because the etiology is believed to be purely obstructive without a communicating component. Failure of ETV is likely due to a contribution of an absorptive defect due to hemorrhage or infection [73].

X-Linked Hydrocephalus

Description. This genetic form of hydrocephalus affects only males due to transmission via phenotypically normal mothers. X-linked hydrocephalus represents ~2 % of cases of hydrocephalus with incidence of 1/25,000–1/60,000.

Pathophysiology. A genetic locus on Xq28 [74] results in abnormal expression of the L1CAM membrane-bound protein that plays an important role in axonal migration and CNS development.

Radiologic criteria. These children have MRIs demonstrating symmetric hydrocephalus with predominant enlargement of the occipital horns [75], hypoplastic or aplastic corpus callosum, a large massa intermedia, an enlarged quadrigeminal plate, and a hypoplastic cerebellar vermis.

Management. Treatment is no different than other forms of congenital hydrocephalus; however, the neurocognitive prognosis is more uniformly dismal.

Idiopathic Intracranial Hypertension

IIH is a condition much more commonly described in adults than in children yet appears to be increasing in frequency with increasing pediatric obesity. It is often described as a stand-alone clinical entity but can be understood also as a subtype of slit ventricles syndrome [76, 77].

Etiology. IIH is not fully understood but venous hypertension is the most likely cause. Often patients are overweight or obese, and significant stenosis of the venous outflow is commonly identified.

Clinical presentation. Children will present with a combination of worsening headaches and visual manifestations. Blurry vision or field cuts are often described, and papilledema may be seen, depending on the time frame of symptom evolution. IIH is diagnosed clinically and ophthalmologically and is confirmed with a high opening pressure on lumbar puncture.

Management. The main clinical concern in the acute setting is vision preservation, through different treatment modalities according to the clinical severity.

- Medical: acetazolamide and diuretics.
- Weight loss.
- Repeated lumbar punctures.
- CSF drainage by lumboperitoneal shunts, falling out favor due to associated complications or ventriculoperitoneal shunts utilizing stereotactic guidance.
- Optic nerve sheath fenestration.
- More recently, interventional neuroradiology has developed venous sinus stents to address commonly found venous sinus stenosis. These stents have been used with success in limited trials to date.

Hydrocephalus with Brain Tumors

With reference to the case scenario presented at the beginning of the chapter. hydrocephalus presenting in association with brain tumors is nearly always obstructive in nature. Notable exceptions to this include communicating forms due to increased CSF secretion from choroid plexus papilloma and carcinoma or disseminated leptomeningeal disease at later stages of malignant disease. Hydrocephalus is identified in about 50 % of brain tumors [78].

Common pathologies associated tumors of the fourth ventricle including ependymoma, and medulloblastoma, tumors of the cerebellar vermis or hemisphere such as juvenile pilocytic astrocytoma, or tumors of the pineal region or tectal plate (e.g., benign tectal gliomas).

Clinical presentation. Children with brain tumors and hydrocephalus very frequently come to medical attention for the symptoms attributable to the hydrocephalus rather than the tumor directly. A slow progression of the tumor may result in a more acute change in the ICP after a compliance curve has been maximally stressed. This typically results in children with inconstant headache and vomiting that may occur in isolation of other manifestations, particularly upon awakening in the morning.

Management. Persistent post-tumor resection hydrocephalus rates of 10–30 % have been consistent. Estimation scores have also been formulated and tested also for validation [79] to settle on the optimal treatment choice, are widely debated, and include:

- Direct tumor resection alone with expectant resolution of obstructive hydrocephalus
- Temporary perioperative ventricular decompression with the use of and external ventricular drain
- A preoperative endoscopic third ventriculostomy
- Ventriculoperitoneal shunting prior to or following tumor resection

Pediatrician's Perspective

- Hydrocephalus is a heterogeneous disease encompassing many etiologies and pathologies. The presence of large ventricles on imaging study reports that you may receive is not synonymous to hydrocephalus. The clinical presentation of hydrocephalus varies according to age and rate of the development of increase in the ICP.
- Clinical findings should always guide management, but clearly in nearly all circumstances, children will need to be evaluated and followed closely by pediatric neurosurgeons.
- A very common diagnosis you may encounter in your neonatal population is external hydrocephalus. Remember that this doesn't mean there is symptomatic hydrocephalus or brain atrophy; it's usually a developmentally transient phenomenon in which the frontal subarachnoid spaces are more prominent resulting in large heads. These children should be seen by a pediatric neurosurgeon, simply for reassurance, as surgery is usually not indicated.
- Another very common diagnosis your patients may carry secondary to prematurity is intraventricular hemorrhage resulting in hydrocephalus. These children often have a difficult first year of life and may require one or more operations to address their hydrocephalus.
- Just as large ventricles shouldn't always mean surgery is needed, likewise, small ventricles don't mean that surgery isn't needed! Slit ventricle syndrome and idiopathic intracranial hypertension (formally called pseudotumor cerebri) is a broad and challenging category of hydrocephalus. Using scientific classification is crucial to reach optimal management options. These children and their families require very intense neurosurgical counseling and often frequent intervention, and close communication with their pediatric neurosurgeon is suggested for optimization of surgical and nonsurgical care of their intracranial condition.

References

1. Raimondi A. A unifying theory for the definition and classification of hydrocephalus. Childs Nerv Syst. 1994;10:2–12.
2. Mori K. Hydrocephalus: revision of its definition and classification with special reference to "intractable infantile hydrocephalus". Childs Nerv Syst. 1990; 6:198–204.
3. Mori K, Shimada J, Kurisaka M, Sato K, Watanabe K. Classification of hydrocephalus and outcome of treatment. Brain Dev. 1995;17:338–48.
4. Rekate HL. The definition and classification of hydrocephalus: a personal recommendation to stimulate debate. Cerebrospinal Fluid Res. 2008;7:1–7.
5. Rekate HL, Aygok GA, Kouzelis K, Petra MK, Michael P. Fifth International Hydrocephalus Workshop, Crete, Greece, May 20–23, 2010: Themes and Highlights. Hydrocephalus, Selected papers from the International Workshop in Crete 2010. New York, NY: Springer, 2012. p. 17–20.
6. Moore AJ, Newell DW. Hydrocephalus. In: Neurosurgery, Principles and practice. London: Springer; 2005. p. 425–44.
7. Dandy W, Blackfan K. Internal hydrocephalus, an experimental, pathological and clinical study. Am J Dis Child. 1914;8:406–82.
8. Ransohoff J, Shulman K, Fishman R. Hydrocephalus: A review of etiology and treatment. J Pediatr. 1960;56:499–511.
9. Greenberg MS. Hydrocephalus. In: Handbook of Neurosurgery. 7th ed. New York, NY: Thieme Publishers; 2010. p. 307–8.
10. Zahl SM, Egge A, Helseth E, Wester K. Benign external hydrocephalus: a review, with emphasis on management. Neurosurg Rev. 2011;34(4):417–32. Available from: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=3171652andtool=pmcentrezandrendertype=abstract.
11. Alvarez L, Maytal J, Shinnar S. Idiopathic external hydrocephalus: natural history and relationship to benign familial macrocephaly. Pediatrics. 1986;77:901–7.
12. Kumar R. External hydrocephalus in small children. Childs Nerv Syst. 2006;22:1237–41.
13. Barlow C. CSF dynamics in hydrocephalus-with special attention to external hydrocephalus. Brain Dev. 1984;6:119–27.
14. Maytal J, Alvarez L, Elkin C, Shinnar S. External hydrocephalus: radiologic spectrum and differentiation from cerebral atrophy. Am J Roentgenol. 1987; 148:1223–30.
15. Chadduck WM, Chadduck JB, Boop FA. The subarachnoid spaces in craniosynostosis. Neurosurgery. 1992;30(6):867–71.
16. Kendall B, Holland I. Benign communicating hydrocephalus in children. Neuroradiology. 1981;21:93–6.
17. Hellbusch L. Benign extracerebral fluid collections in infancy: clinical presentation and long term follow-up. J Neurosurg. 2007;107:119–25.
18. Karmazyn B, Dagan O, Vidne B, Horev G, Kornreich L. Neuroimaging findings in neonates and infants from superior vena cava obstruction after cardiac operation. Pediatr Radiol. 2002;32:806–10.
19. Papasian N, Frim D. A theoretical model of benign external hydrocephalus that predicts a predisposition towards extra-axial hemorrhage after minor head trauma. Pediatr Neurosurg. 2000;33:188–93.
20. Odita J. The widened frontal subarachnoid space. A CT comparative study between macrocephalic, microcephalic, and normocephalic infants and children. Childs Nerv Syst. 1992;8:36–9.
21. Gout A, Gautier I, Bellaiche M, Pinard J, Tremon M, Rodriguez D, et al. Idiopathic peri-cerebral enlargement in infants: simple anatomical variant or hemorrhagic risk factor? Arch Pediatr. 1997;4:983–7.
22. Roshan K, Elizabeth C, Chacko A, Rajendra J, Gururaj A, Dilip S. External hydrocephalus-a report of 16 cases from Oman. J Trop Pediatr. 1998; 44:153–6.
23. Greenberg MS. Head trauma. In: Handbook of Neurosurgery. New York, NY: Thieme Publishers; 2010. p. 904–5.
24. Litofsky N, Raffel C, McComb J. Management of symptomatic chronic extra-axial fluid collections in pediatric patients. Neurosurgery. 1992;31:445–50.
25. Strassburg H. Macrocephaly is not always due to hydrocephalus. J Child Neurol. 1989;4(Suppl):S32–40.
26. Johnson D. Comment on Litofsky N S et al.: Management of symptomatic chronic extra-axial fluid collections in pediatric patients. Neurosurgery. 1992;31:450.
27. Greenberg MS. Neural tube defects. In: Handbook of Neurosurgery. 7th ed. New York, NY: Thieme Publishers; 2010. p. 244.
28. Sutton LN, Bruce DA, Schut L. Hydranencephaly versus maximal hydrocephalus: an important clinical distinction. Neurosurgery. 1990;6(1):35–8.
29. Iannetti P, Galletti F, Emanuelli O, Sturniolo M, Benedetti P. Severe outcome of brain perfusion failure: A pre-hydranencephalic state? Brain Dev. 1991;13:447–51.
30. William WK, Tang MHY. The association between maternal smoking and fetal hydranencephaly. J Obstet Gynaecol Res. 1999;25(1):39–42.
31. Andresen M, Juhler M. Multiloculated hydrocephalus: a review of current problems in classification and treatment. Childs Nerv Syst. 2012;28:357–62.
32. Spennato P, Cinalli G, Carannante G, Ruggiero C, Basso D, De Caro M. Multiloculated hydrocephalus. In: Cinalli G, Maxner W, Sainte-Rose C, editors. Pediatric hydrocephalus. Milan: Springer; 2004. p. 219–44.
33. Spennato P, Cinalli G, Ruggiero C, Aliberti F, Trischitta V, Cianciullli E, et al. Neuroendoscopic treatment of multiloculated hydrcephalus in children. J Neurosurg. 2007;106:29–35.
34. Schultz P, Leeds N. Intraventricular septations complicating neonatal meningitis. J Neurosurg. 1973;52: 547–52.

35. Oi S, Abbott R. Loculated ventricles and isolated compartments in hydrocephalus: their pathophysiology and efficacy of neuroendoscopic surgery. Neurosurg Clin N Am. 2004;15:77–87.
36. Teo C, Burson T, Misra S. Endoscopic treatment of trapped fourth ventricle. Neurosurgery. 1999;44: 1261–2.
37. Masahiro S, Morita A, Asano S, Ueki K, Kirino T. Neuroendoscopic aqueductal stent placement procedure for isolated fourth ventricle after ventricular shunt placement. J Neurosurg. 2000;92:1036–9.
38. Torres-Corzo J, Vecchia RR, Rangel-Castilla L. Trapped fourth ventricle treated with shunt placement in the fourth ventricle by direct visualization with flexible neuroendoscope. Minim Invasive Neurosurg. 2004;47:86–9.
39. Spennato P, Mirone G, Nastro A, Consiglio Buonocore M, Ruggiero C, Trischitta V, et al. Hydrocephalus in Dandy – Walker malformation. Childs Nerv Syst. 2011;27:1665–81.
40. Brown J. The Dandy-Walker syndrome. In: Vinken P, Bruyn G, editors. Handbook of clinical neurology. Amsterdam: North Holland; 1977. p. 623.
41. Tsao K, Chuang NA, Filly RA, Barkovich AJ, Goldstein RB. Entrapped fourth ventricle: another pitfall in the prenatal diagnosis of Dandy-Walker malformations. J Ultrasound Med. 2002;21:91–6.
42. Klein O, Pierre Khan A, Boddaert N, Parisot D, Brunelle F. Dandy-Walker malformation: prenatal diagnosis and prognosis. Childs Nerv Syst. 2003;19:484–9.
43. Cinalli G, Spennato P, Del Basso De Caro M, Buonocore M. Hydrocephalus and Dandy-Walker malformation. In: Cinalli C, Maixner W, Sainte-Rose C, editors. Pediatric hydrocephalus. Milan: Springer; 2004. p. 259–77.
44. Harwood-Nash D, Fitz C. Neuroradiology in infants and children, vol. 3. St Louis, MO: Mosby; 1976. p. 104–9.
45. Raybaud C. Cystic malformations of the posterior fossa. Abnormalities associated with the development of the roof of the fourth ventricle and adjacent meningeal structures. J Neuroradiol. 1982;9:103–33.
46. Sesaki-Adams D, Elbabaa S, Jewells V, Carter L, Campbell J, Ritter A. The Dandy-Walker variant: a case series of 24 pediatric patients and evaluation of the associated anomalies, incidence of hydrocephalus, and developmental outcomes. J Neurosurg Pediatr. 2008;2:194–9.
47. Barkovich A, Kjos B, Norman D, Edwards M. Revised classification of posterior fossa cysts and cyst-like malformations based on the results of multiplanar MR imaging. AJNR Am J Neuroradiol. 1989;10:977–88.
48. Lemons J, Bauer C, Oh W, Korones S, Papile L, Stoll B, et al. Very low birth weight outcomes of the National Institute of Child health and human development neonatal research network, January 1995 through 1996 December. Pediatrics. 2001;107:E1.
49. O'Shea T, Kuban K, Allred E, Paneth N, Pagano M, Dammann O, et al. Neonatal cranial ultrasound lesions and developmental delays at 2 years of age among extremely low gestational age children. Pediatrics. 2008;122:e662–9.
50. Papile L, Burnstein J, Burnstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr. 1978; 92:529–34.
51. Babies R. Neonatal posthemorrhagic hydrocephalus from prematurity: pathophysiology and current treatment concepts. J Neurosurg Pediatr. 2012; 9(March):242–58.
52. El-Dib M, Massaro A, Bulas D, Aly H. Neuroimaging and neurodevelopmental outcome of premature infants. Am J Perinatol. 2010;27:803–18.
53. Limbrick DDJ, Mathur A, Johnston JM, Munro R, Sagar J, Inder T, et al. Neurosurgical treatment of progressive posthemorrhagic ventricular dilation in preterm infants: a 10-year single-institution study. J Neurosurg Pediatr. 2010;6(September):224–30.
54. Di Rocco C. Is the slit ventricle syndrome always a slit ventricle syndrome? Childs Nerv Syst. 1994;10:49–58.
55. Roth J, Biyani N, Udayakumaran S, Xiao X, Friedman O, Beni-Adani L, et al. Modified bilateral subtemporal decompression for resistant slit ventricle syndrome. Childs Nerv Syst. 2011;27(1):101–10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/20617320.
56. Rekate HL. Classification of slit ventricle syndrome using intracranial pressure monitoring. Pediatr Neurosurg. 1993;19:15–20.
57. Rekate HL. Shunt related headaches: the slit ventricle syndromes. Childs Nerv Syst. 2008; 24:423–30.
58. Engel M, Carmel PW, Chutorian AM. Normal volume hydrocephalus. Neurosurgery. 1979;5(5):549–52.
59. Collman H, Mauersberger W, Mohr G. Clinical observations and CSF absorption studies in the slit ventricle syndrome. Adv Neurosurg. 1980;8:183–5.
60. Miller JP, Cohen AR. Slit ventricle syndrome. In: Jallo GI, Kothbauer KF, Pradilla G, editors. Controversies in neurosurgery. New York, NY: Thieme Medical Publishers; 2010. p. 51–62.
61. Maixner W, Morgan M, Besser M, Johnston I. Ventricular volume in infantile hydrocephalus and its relationship to intracranial pressure and cerebrospinal fluid clearance before and after treatment. Pediatr Neurosurg. 1990;16:191–6.
62. Licata C, Cristofori L, Gambin R, Vivenza C, Turazzi S. Post-traumatic hydrocephalus. J Neurosurg Sci. 2001;45(3):141–9.
63. Choi I, Park H-K, Chang J-C, Cho S-J, Choi S-K, Byun B-J. Clinical factors for the development of posttraumatic hydrocephalus after. J Korean Neurosurg Soc. 2008;43:227–31.
64. Long D. Diagnosis and management of intracranial complications in traumatic brain injury rehabilitation. In: Horn L, Zasler N, editors. Medical rehabilitation of traumatic brain injury. Philadelphia, PA: Hanley and Belfus; 1996. p. 333–62.

65. Paoletti P, Pezzotta S, Spanu G. Diagnosis and treatment of post-traumatic hydrocephalus. J Neurosurg Sci. 1983;27(3):171–5.
66. Guyot L, Michael D. Post-traumatic hydrocephalus. Neurol Res. 2000;22(1):25–8.
67. O'Hayon BB, Drake JM, Ossip MG, Tuli S, Clarke M. Frontal and occipital horn ratio: A linear estimate of ventricular size for multiple imaging modalities in pediatric hydrocephalus. Pediatr Neurosurg. 1998;29(5):245–9. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9917541.
68. Kaye AH. Raised intracranial pressure and hydrocephalus. In: Essential neurosurgery. 3rd ed. Oxford: Blackwell Publishing; 2005. p. 27–39.
69. Brent K, Milsom S, Furneaux C. Chronic hydrocephalus: a treatable cause of primary amenorrhoea. Br J Obstet Gynaecol. 2007;114:901–3.
70. Touraine P, Plu-Bureau G, Beressi N, Decq P, Thalabard J-C, Kuttenn F. Resumption of luteinizing hormone pulsatility and hypogonadotropic hypogonadism after endoscopic ventriculocisternostomy in a hydrocephalic patient. Fertil Steril. 2001;76(2):390.
71. McLone D, Knepper P. The cause of Chiari II malformation: a unified theory. Pediatr Neurosurg. 1989;15:1–12.
72. Warf BC. Hydrocephalus associated with neural tube defects: characteristics, management, and outcome in sub-Saharan Africa. Childs Nerv Syst. 2011;27:1589–94.
73. Cinalli G, Spennato P, Nastro A, Alberti F, Ruggiero C, Mirone G, et al. Hydrocephalus in aqueductal stenosis. Childs Nerv Syst. 2011;27:1621–42.
74. Izumoto S, Yamasaki M, Arita N, Hiraga S, Ohnishi T, Fujitani K, et al. A new mutation of the L1CAM gene in an X-linked hydrocephalus family. Childs Nerv Syst. 1996;12(12):742–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/9118141.
75. Kanemura Y, Okamoto N, Sakamoto H, et al. Molecular mechanisms and neuroimaging criteria for severe L1 syndrome with X-linked hydrocephalus. J Neurosurg. 2006;105(5 Suppl):403–12.
76. Collmann H, Sörensen N, Krauss J. Hydrocephalus in craniosynostosis: a review. Childs Nerv Syst. 2005;21(10):902–12. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15864600.
77. Cinalli G, Spennato P, Sainte-Rose C, Arnaud E, Aliberti F, Brunelle F, et al. Chiari malformation in craniosynostosis. Childs Nerv Syst. 2005;21(10):889–901. Available from: http://www.ncbi.nlm.nih.gov/pubmed/15875201.
78. Wong T, Liang M, Chen H. Hydrocephalus with brain tumors in children. Childs Nerv Syst. 2011;27:1723–34.
79. Riva-Cambrin J, Detsky AS, Lamberti-Pasculli M, Sargent MA, Armstrong D, Moineddin R, et al. Predicting postresection hydrocephalus in pediatric patients with posterior fossa tumors. J Neurosurg Pediatr. 2009;3(5):378–85. Available from: http://www.ncbi.nlm.nih.gov/pubmed/19409016.

Neurosurgical Considerations in Macrocephaly

14

Imithri D. Bodhinayake and Heather J. McCrea

Clinical Vignette An 8-month-old baby boy was brought to your office over parental concerns that their child's head seemed much bigger than other babies. He had been seen in your office at his routine 6-month visit and exhibited a HC that placed him above the 90th percentile.

On examination today, he remains well appearing, meeting all developmental milestones and raises no clinical concerns with respect to eating, sleeping or activity levels. His HC did in fact jump and his curve now places him above the 95th percentile. His AF is sunken and he exhibits no other signs of raised intracranial pressure.

You initiate a conversation with his mother regarding family history, and she indicates that the child's father and in fact all the males on his side of the family, have large heads and she wondered if the tendency to have a large head could be genetic. You discuss the likely etiologies of benign familial macrocephaly or enlarged subarachnoid spaces of infancy and assure them that no imaging is required to evaluate the child.

I.D. Bodhinayake, M.D.
Department of Neurological Surgery, Weill Cornell Medical College, 525 E 68th Street, Box #99, New York, NY 10021, USA

H.J. McCrea, M.D., Ph.D. (✉)
Department of Neurological Surgery, New York Presbyterian Hospital – Weill Cornell Medical Center, 525 E 68th Street, Box #99, New York, NY 10021, USA
e-mail: Hjm9003@nyp.org

Epidemiology

A true global incidence or prevalence of macrocephaly is difficult to ascertain as it results from a variety of conditions. As mentioned previously, hydrocephalus is the most common pathologic cause of macrocephaly. Hydrocephalus occurs in approximately 1 out of every 1000 live births [1–3]. However, not all of these children develop macrocephaly. Many of these cases worldwide are associated with meningomyelocele/spina bifida, which may be treated prior to having an affect on HC. Most megalencephalic conditions are considered rare disorders [4, 5] affecting less than 1 in 125,000 people. Males are affected more frequently than females, possibly because many of the megalencephalic conditions are X-linked genetic disorders [4, 6]. Bone dysplasias that lead to macrocephaly such as achondroplasia have a low incidence and prevalence. For example, achondroplasia affects about 250,000 people worldwide and occurs in about 1 in 10,000 to 1 in 30,000 live births [7, 8], but not all patients with this disease have HC that is consistent with macrocephaly.

Etiology

It is useful to consider abnormalities in the hypothetical compartments of the head in order to understand the development of macrocephaly.

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_14

Increased volume of CSF, blood, bone, or brain parenchyma, including the presence of mass lesions, prior to suture or fontanel fusion contribute towards increased HC and macrocephaly. Table 14.1 provides an overview of the abnormalities commonly associated with each compartment. Within each compartment, congenital defects, genetic and metabolic syndromes, and neoplastic causes may play a role in the development of macrocephaly.

The expansion of the CSF compartment, or hydrocephalus, is the most common etiology of macrocephaly and comprises a large portion of pediatric neurosurgical patient volume. Hydrocephalus may result from overproduction of CSF from choroid plexus tumors, obstruction of CSF outflow from masses or congenital malformations, or decreased CSF reabsorption as a result of inflamed ependymal surfaces, breakdown products of hemorrhage, or infection [9] (Table 14.2). The resulting ventricular enlargement compresses the brain against the skull, reduces subarachnoid space and increases venous pressure in the dural sinuses. If left untreated, fluid crosses the ependymal lining of the ventricular system (trans-ependymal flow) leading to cerebral edema, ischemia of white matter tracts, and atrophy. In children whose cranial sutures have not yet fused, the cranium compensates for the expanding ventricles and increased ICP by enlarging. Thus, increased HC or crossing of HC percentiles is often one of the first signs of hydrocephalus.

Certain groups are at increased risk of hydrocephalus secondary to hemorrhage or infection.

Table 14.1 Etiology of macrocephaly utilizing a cranial compartment-based algorithm

CSF based	Blood based	Bone based	Parenchyma based
Hydrocephalus from	Hemorrhage	Marrow expansion (thalassemia)	Megalencephaly (true parenchymal expansion)
– Neoplasm	– Trauma	Hyperphosphatasia	– Metabolic dysregulation of storage and degradation
– Cysts	– Intraventricular hemorrhage (IVH) in preterm infants	Achondroplasia	– Dysregulated neuronal proliferation
– Infection	– Subdural, epidural, subarachnoid hemorrhage (SDH, EDH, SAH)	Osteogenesis imperfecta	Mass effect (other tissue)
– Inflammation			
– Intraventricular hemorrhage (IVH)			– Neoplasm
Choroid plexus papilloma	Arteriovenous malformations		– Abscess
Benign enlargement of subarachnoid space			– Cysts

Table 14.2 Etiology of hydrocephalus

Overproduction	Intracerebral obstruction	Decreased absorption
Rare	Common	Common
All ventricles equally dilated	Dilation of ventricles dependent on level of obstruction	All ventricles equally dilated
Choroid plexus tumor	Stenosis at foramen of Monro, aqueductal stenosis, or fourth ventricular outlet obstruction from:	Continuous communication between ventricles and subarachnoid space but poor reabsorption
	– Congenital causes: neural tube deficits, CNS malformations, Chiari II, Dandy-Walker, IVH	Early childhood hemorrhage or infections leading to meningitis and inflammation of ependymal lining
	– Acquired causes: posterior fossa tumors, hemorrhage, abscesses	

Premature infants are at significant risk of intraventricular hemorrhage (IVH) as a result of their underdeveloped vascular germinal matrix [10]. The breakdown products of hemorrhage and resulting inflammation obstruct CSF absorption and lead to hydrocephalus. Similarly, traumatic or neoplastic causes of intraparenchymal or intraventricular hemorrhage can lead to hydrocephalus and macrocephaly when they occur during early development. Additionally, CSF flow and/or absorption may be impaired when infections cause inflammation in the meninges and ependymal linings of the ventricles [11]. Intrauterine infections with a propensity for this type of inflammation include syphilis [12], rubella, toxoplasmosis [13], and lymphocytic choriomeningitis [14]. Neonatal and early childhood (typically 6 months to 2 years) infections include bacterial meningitis [15] and mumps [16, 17].

During infancy, brain growth itself is the primary determinant of head growth. After hydrocephalus, megalencephaly is the next most frequent cause of macrocephaly. Megalencephalic conditions have traditionally been categorized broadly into anatomic and metabolic etiologies (Fig. 14.1). Many of these conditions are associated with genetic mutations. However, the exact reason that megalencephaly develops from these mutations is often unknown. Some mutations lead to abnormal regulation of neuronal proliferation and overgrowth of brain parenchyma that is apparent at birth. Other mutations result in metabolic abnormalities in storage or degradation, leading to an increase in cell size from accumulated metabolic products. Children with metabolic etiologies, such as leukodystrophy, develop postnatal megalencephaly due to a gradual accumulation of metabolic products [18].

As our understanding of genetic conditions broadens, the classification of megalencephalic conditions may be altered. Some have moved away from a traditional anatomic and metabolic subgrouping instead grouping megalencephalic conditions as syndromes with associated conditions such as polymicrogyria (the radiographic presence of several small gyri, particularly in the peri-sylvian area), hydrocephalus, polydactyly, cutaneous manifestations, and capillary malformations [5]. These syndromes include megalencephaly, polymicrogyria, polydactyly,

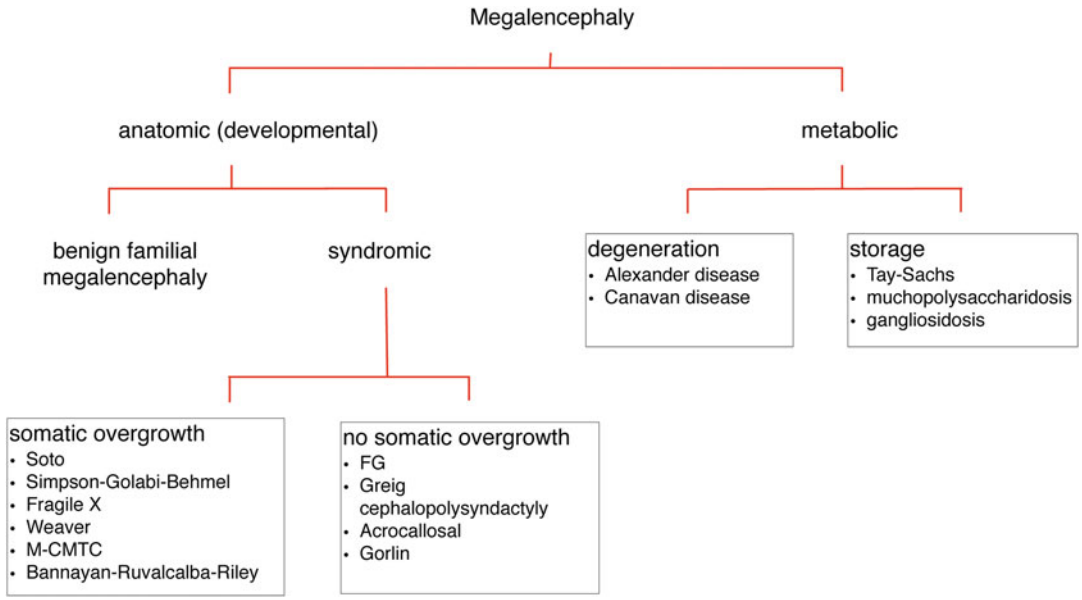


Fig. 14.1 Megalencephalic conditions associated with macrocephaly. Abbreviations: Macrocephaly-cutis marmorata telangiectatica congenita (M-CMTC); FG syndrome (FG)

hydrocephalus (MPPH) [19], macrocephaly-cutis marmorata telangiectatica congenita (M-CMTC), and macrocephaly capillary malformation (MCAP) [5].

Although megalencephalic conditions account for a substantial portion of the genetic causes of macrocephaly, an important non-megalencephalic cause of genetic macrocephaly is benign familial macrocephaly. In this autosomal dominant condition, there is benign enlargement of the subarachnoid spaces without megalencephaly [20, 21]. The enlargement of the subarachnoid spaces in turn causes macrocephaly. Affected children often have a first-degree relative with benign familial macrocephaly.

Presentation

Initial presentation to a pediatrician or pediatric neurologist depends on the etiology of the underlying condition leading to macrocephaly. In many cases, an increased HC may be first the presenting sign of the underlying condition. Therefore, it is important to track postnatal HC and HC throughout the child's early development [2]. When evaluating premature infants, age should be adjusted for the degree of prematurity. Many computer-based electronic records now perform this adjustment automatically, but it is crucial to check that this has been compensated for; a 4–6-week error in age may significantly skew the HC chart of a neonate. Any significant increase or decrease in HC between percentiles should be a cause for further evaluation. A HC percentile that is markedly different from the length and weight percentiles should also be considered carefully. When evaluating a child's HC, it is also important to note the HC of both parents because benign enlargement of the subarachnoid space runs in families [6, 21]. Though work-up may still be indicated to confirm such a diagnosis, a child with a large head whose parents have large heads is certainly less concerning than a child with a large head whose parents have small- to mid-sized heads.

Signs and symptoms associated with hydrocephalus may include full anterior fontanels, prominent scalp veins, failure to thrive, decreased appetite, failure to achieve developmental milestones, irritability, or loss of interest due to increased pressure on the frontal lobe [9]. In more severe cases, patients may have papilledema, impaired upward gaze due to compression of the midbrain including Parinaud syndrome, seizures, altered mental status, or even loss of consciousness. In late stages, Cushing's reflex—the triad of widened pulse pressure, irregular breathing and bradycardia due to increased ICP—and spasticity from stretching of motor fibers over dilated ventricles, may be present [22]. A patient's presentation depends on the age of onset (corresponding to the degree of suture fusion) and the duration and rate of development of elevated ICP. Children who develop hydrocephalus when they are younger than 2 years of age usually present with macrocephaly while children who develop hydrocephalus when they are older typically present with signs of increased ICP [9, 22].

Conditions associated with megalencephaly are broadly associated with seizures, developmental delay and/or mental retardation. Depending on the etiology of megalencephaly, macrocephaly may be present at birth or develop during early childhood [5]. Some children may show stigmata of the underlying disease. For example, those with neurofibromatosis typically have café au lait spots and axillary freckling while those with Sotos syndrome would present with characteristic features such as a high-prominent forehead and down-slanting palpebral fissures [4, 6].

Mass lesions typically present with signs of increased ICP including altered mental status. The presentation would include macrocephaly only if the lesion or resulting hydrocephalus is left untreated. As the name implies, infants with macrocephaly from benign enlargement of subarachnoid spaces are typically asymptomatic apart from the increased HC. Occasionally they may present with subdural hematoma caused by the larger head size and increased tautness of bridging vessels in the extra-axial fluid spaces [23]. In rare cases, they may present with transient language or motor deficits [21, 24].

Evaluation

Initial evaluation for any child should include a medical history and family history, HC measurements, and a complete physical exam, including neurologic and developmental exams. Hydrocephalus and/or macrocephaly should be suspected in infants with HC crossing percentiles. Imaging studies can determine the presence or absence of megalencephaly, bone proliferative conditions, hemorrhage, or hydrocephalus [25]. Additionally, imaging studies can help identify the cause of hydrocephalus, including aqueductal stenosis and mass lesions.

Infants, including premature infants being screened for IVH, are evaluated by ultrasound. Screening is typically first done 5 days after birth and repeated several weeks later [25]. Computed tomography (CT) or preferably magnetic resonance imaging (MRI) may be used in the evaluation of older children. CT studies have the advantage of requiring no sedation but expose the child to radiation [26] and have poorer resolution. In contrast, MRI studies have better resolution and do not expose the child to radiation, but they typically require sedation.

A widely used alternative to CT is "quick-brain MRI" to assess for hydrocephalus and/or shunt function. Unlike MRI, the single-shot fast-spin echo (SSFSE) MRI or quick-brain MRI requires no sedation due to the short amount of time required for this imaging. Images acquired through this protocol allow assessment of abnormal fluid collections, ventriculomegaly, and shunt positioning [27, 28], sparing children unnecessary exposure to radiation. However, short MRI sequences can produce movement artifacts that can be mistaken for intraventricular hemorrhage [29]. A full discussion of how to image children may be found in Chap. 20.

If infectious causes are suspected, and there is no evidence of hydrocephalus or mass lesion on imaging, a lumbar puncture should be performed. Additional genetic testing or metabolic testing may be indicated to diagnose specific megalencephalic conditions.

Treatment and Management

The underlying cause of macrocephaly will dictate the treatment plan. If abnormal bone proliferation or megalencephaly is noted on initial evaluation and imaging studies, appropriate referrals to specialists including pediatric neurologists and geneticists should be made. For many of the megalencephalic conditions, no specific treatment exists. However, specialist management may be required to manage underlying metabolic and/or seizure disorders.

Pediatric neurosurgery should be consulted if hydrocephalus, hemorrhage, and/or a mass lesion are diagnosed. Mass lesions may be resected or biopsied, and depending on the pathologic diagnosis may require additional chemotherapy or radiation therapy. Intracranial bleeds or hematomas may be monitored for resolution with close radiographic follow-up or evacuated depending on the severity of the bleed and symptoms.

As illustrated in Fig. 14.2, the lateral ventricles communicate with the third ventricle through the foramen of Monro while the third ventricle communicates with the fourth ventricle through the aqueduct of Sylvius. Any intraventricular obstruction or obstruction at the level of the foramen or the aqueduct may result in hydrocephalus. In the treatment of hydrocephalus, the primary objective is to drain excess CSF, relieve increased intracranial pressure, and prevent further neurological deterioration. In many cases, hydrocephalus resulting from mass lesions may be cured by resection of the lesion without the need to treat the resulting hydrocephalus. However, hydrocephalus resulting from other etiologies and those with a tumor who are inappropriate candidates for resection or do not resolve their hydrocephalus after tumor resection typically require treatment of hydrocephalus rather than the underlying cause [30].

Shunting

Despite considerable advancements in hydrocephalus management, a main treatment remains cerebrospinal fluid shunting. The most frequently

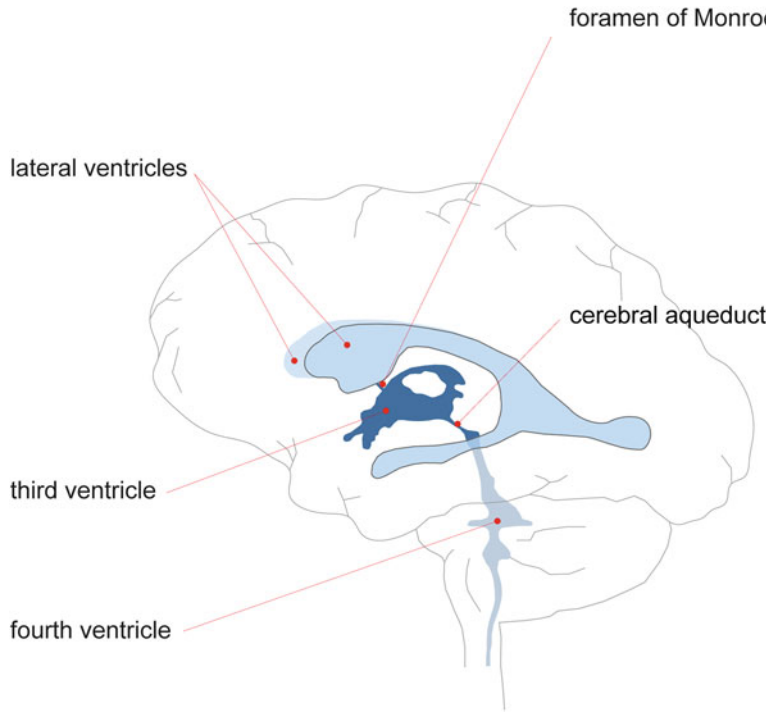


Fig. 14.2 Left lateral view of ventricular system

used type of shunt is the ventriculoperitoneal (VP) shunt. As illustrated in Fig. 14.3, a catheter is inserted into the lateral ventricle and connected to a one-way valve just outside the skull. This valve is then connected to a second catheter that is tunneled subcutaneously into the abdomen and placed into the peritoneal space. The body reabsorbs this fluid through the peritoneal lining. The one-way valve ensures both the direction and rate of CSF flow. Valves may be programmable (i.e., adjustable to different pressures) or non-programmable (set at a predetermined pressure).

It is important for the family and pediatrician to know which type of valve their child has. MRI scans may lead to accidental adjustment of programmable shunts. Thus, for any MRI scan done on a child with a programmable shunt (with the exception of MRI compatible programmable valves), the setting must be known prior to the MRI scan, the setting must be checked after the MRI scan to be sure that the valve has not reset, and the valve must be reset to the original pre-MRI value if a change has occurred. Some newer generation programmable valves are MRI compatible and should not reset with the MRI magnet, but the majority of programmable valves are set via magnet and thus susceptible to reprogramming during MRI.

If conditions such as peritonitis preclude the placement of a VP shunt, a ventriculoatrial shunt that drains into the heart or a ventriculopleural shunt that drains CSF into the pleural space can be used. While shunting converts hydrocephalus into a chronic, manageable condition, patients with shunts may be subject to considerable morbidity. This includes infection, which may occur in 5–15 % of procedures [31], and additional surgery for shunt malfunction or obstruction.

Endoscopic Third Ventriculostomy (ETV)

ETV may be utilized in situations where hydrocephalus results from an obstruction in CSF flow beyond the level of the third ventricle [30, 32]. This level of obstruction is found in patients

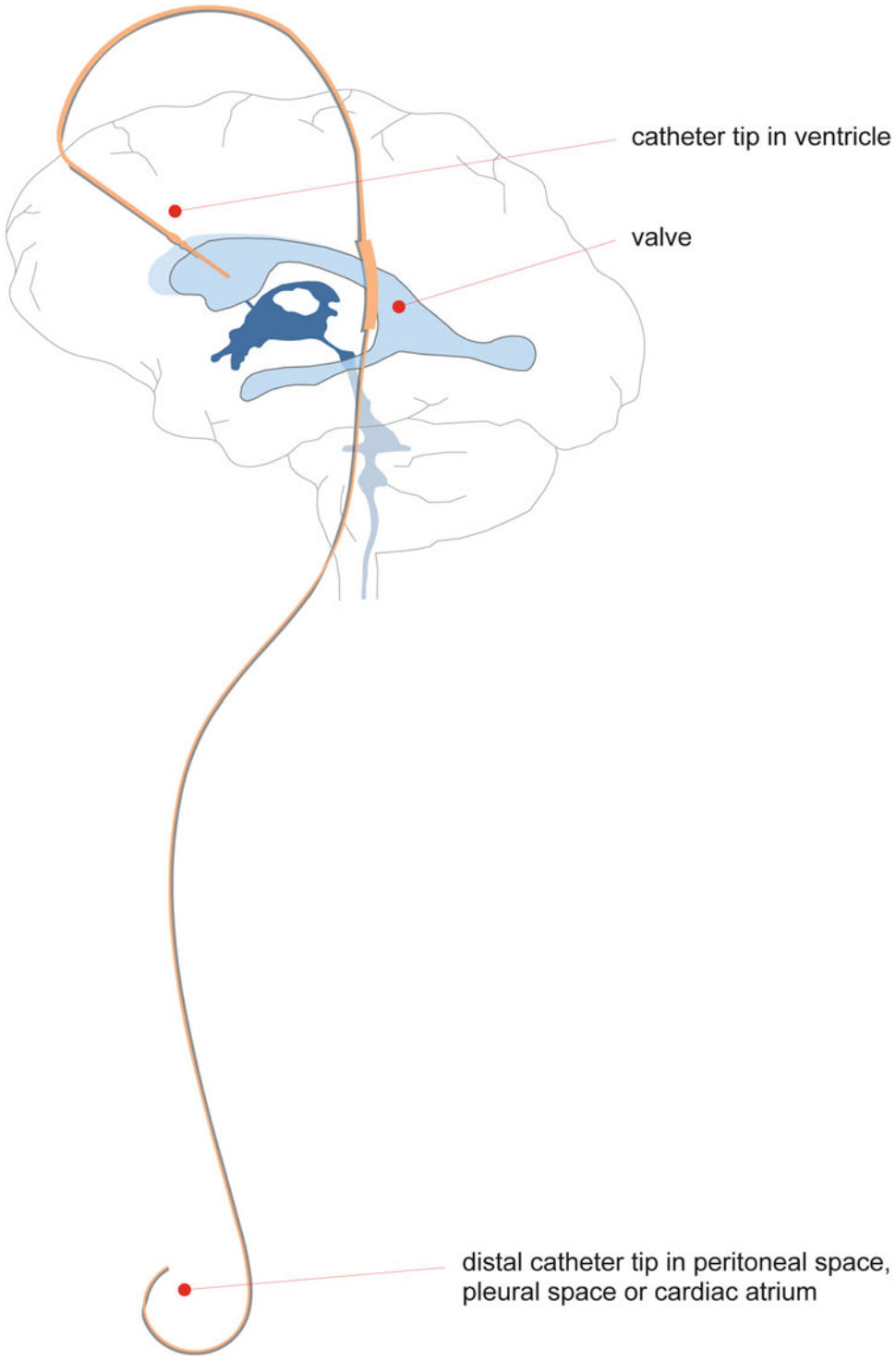


Fig. 14.3 Diversion of CSF away from dilated ventricles

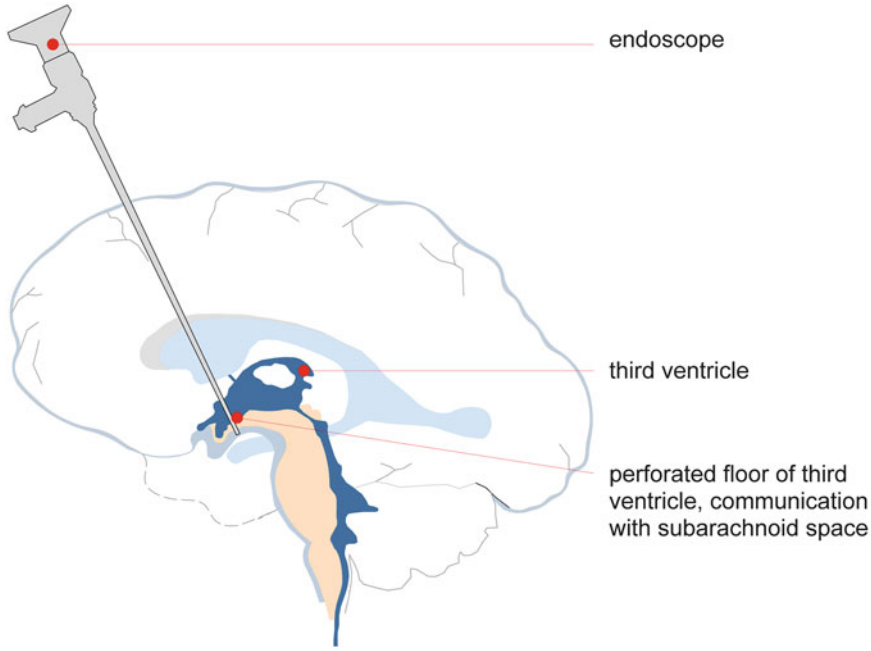


Fig. 14.4 Endoscopic third ventriculostomy

with aqueductal stenosis as well as in those with posterior fossa tumors. During an ETV, an endoscope is passed into the third ventricle and a small perforation is made in the floor of the third ventricle, connecting the third ventricle directly with the subarachnoid space (Fig. 14.4) and allowing for an alternate route of CSF drainage [33]. In the correct population, this is an effective form of surgical management for hydrocephalus. As shown in Table 14.3, ideal candidates for this procedure include patients older than 1 year and those that have lesions at or below the level of the aqueduct [34, 35].

The decision for ETV versus shunt is based on etiology of hydrocephalus, patient age, and surgeon preference. Although no randomized controlled data on the ideal candidates for ETV are available, the indications for ETV are well established in neurosurgical practice (Table 14.3). An international cohort study of 489 patients with ETV versus 720 patients with shunts [36] suggests that among patients with characteristics that favor ETV, the risk of ETV failure is lower than that of shunt failure in the immediate postoperative period. Furthermore, the ETV failure risk for these patients continues to be less than the risk of shunt failure with increasing time after surgery [36, 37].

Table 14.3 Favorable patient characteristics for endoscopic third ventriculostomy

• Obstructing lesion at or below aqueduct (posterior fossa tumors/malformations, aqueductal stenosis)
• Age greater than 1 year
• Absence of a previous shunt
• Absence of previous infections or intraventricular hemorrhage (IVH)

Although ETV carries risks of intraoperative morbidity including hemorrhage, cerebral infarction, infection such as meningitis, diabetes insipidus (DI), and syndrome of inappropriate antidiuretic hormone secretion (SIADH) [38], the procedure is typically well tolerated. As a result, some surgeons may consider trying an ETV even in patients who would not be classical ETV candidates. In these cases, the lower likelihood of success is explained to the parents so that they understand that a shunt may still be necessary. If the procedure is successful, the child avoids the lifetime risk of morbidity associated with repeated shunt-related procedures.

Goals of Treatment

- Reduction in shunt burden
- Reduction in infection rates
- Decrease in the number of reoperations
- Reduction of loculated fluid collections wherever possible to ensure the above principles

Medical Management

In general, medical management of hydrocephalus is not thought to be an effective alternative to surgery. The main medical forms of therapy include diuretics, fibrinolysis, and serial lumbar punctures (LP) [9]. Diuretics such as furosemide and carbonic anhydrase inhibitors such as acetazolamide decrease CSF production. Acetazolamide blocks the carbonic anhydrase-dependent active transport of the choroidal epithelial cells, decreasing CSF production. Fibrinolysis is used post-hemorrhage to reduce the burden of blood products on surrounding parenchyma. Serial LPs may be utilized in preterm infants in order to temporize the child until they are older and better able to tolerate a procedure [9]. Additionally, a small percentage of neonates will not require permanent diversion after temporizing CSF diversion procedures such as a ventricular reservoir [39]. Therefore delaying shunt placement may avoid a small number of permanent shunting procedures. The decision to tap should be guided by examination of the fontanel, cardiovascular examination, and ultrasound studies. Of note, LPs are contraindicated when space-occupying lesions are suspected due to the possibility of cerebral herniation post LP.

Follow-Up and Indications for Re-evaluation

It is important for physicians and caregivers of patients who have undergone shunt and/or ETV procedures to monitor patients for signs and symptoms of elevated ICP (Table 14.4) as these may indicate a failure in adequate CSF diversion. Early recognition and effective triage requires collaboration between pediatricians, emergency department physicians, and radiologists as well as hospital-wide policy implementations [40]. At the onset of these signs and/or symptoms, pediatric neurosurgery re-evaluation should be initiated. Neurosurgeons may then recommend additional radiographic studies and/or proceed with intraoperative shunt repositioning and/or replacement.

Table 14.4 Signs and symptoms of elevated ICP

Infants and young children	Older children
• Decreased activity	• Nausea and emesis
• Decreased appetite	• Severe dehydration from emesis
• Irritability	• Headache
• Altered mental status	• Blurry vision
• Emesis	• Altered mental status and personality changes
• Seizures	• Seizures
• Cushing's triad	• Cushing's triad

Conclusion

- HC is an important indicator of brain growth and normal development in infants
- HC measurements and tracking on gender-appropriate charts should be part of all well-child visits
- Crossing HC percentiles should be a cause for concern
- Macrocephaly, defined as HC>2 SDs above normal, is caused by an abnormal volume expansion in any of the hypothetical compartments of the head: CSF, blood, parenchyma, or bone.
- A complete family and medical history and physical, neurological, and developmental exam along with appropriate imaging studies, metabolic tests, and genetic tests helps determine etiology of macrocephaly
- Hydrocephalus and/or mass lesions should prompt pediatric neurosurgery referral
- Primary treatment for hydrocephalus includes shunting procedures and ETV

- ETV is better suited for older children (>1 year) and those with posterior fossa lesions or aqueductal stenosis with no prior history of shunting.
- Long-term follow-up and management includes interval imaging and referral to pediatric neurosurgery for signs and symptoms of increased ICP

Pediatrician's Perspective

The evaluation of the head is an integral part of pediatric well-patient visits for the first several years of life, and raises significant parental consternation, particularly in the first year. Unusual head *shape*, discussed in Chap. 6, may be more cosmetically obvious and immediately concerning to parents, but close tracking of head *size* is far more likely to yield an important finding necessitating a referral to pediatric neurosurgery.

From an urgency perspective, the key to being able to triage children with the right degree of haste to neurosurgery simply requires a good sense of three things: their fontanel, their exam, and the rate at which their HC has changed percentiles. A normal exam and slack fontanel should reassure you that a non-urgent referral to a pediatric neurosurgeon or neurologist (if at all) could be considered even in the face of an HC chart with a curve crossing percentiles. In contrast, a bulging fontanel or abnormal neurologic exam should prompt urgent referral to neurosurgery.

If you believe the increasing HC percentage is due to benign familial macrocephaly or enlarged subarachnoid spaces of infancy and continue to follow these children in your office without imaging or referral, you will typically see a leveling off of the HC curve by approximately 12–16 months of age. These children will always have 95th percentile HC so while their head may look disproportionally large early on, there is rarely a cosmetic or neuromuscular issue with being on the high end of the bell curve once their body catches up.

References

1. Fernell E, Hagberg B, Hagberg G, von Wendt L. Epidemiology of infantile hydrocephalus in Sweden. I. Birth prevalence and general data. Acta Paediatr Scand. 1986;75:975–81.
2. Zahl SM, Wester K. Routine measurement of head circumference as a tool for detecting intracranial expansion in infants: what is the gain? A nationwide survey. Pediatrics. 2008;121:e416–20.
3. Jeng S, Gupta N, Wrensch M, Zhao S, Wu YW. Prevalence of congenital hydrocephalus in California, 1991-2000. Pediatr Neurol. 2011;45:67–71.
4. Olney AH. Macrocephaly syndromes. Semin Pediatr Neurol. 2007;14:128–35.
5. Barkovich AJ, Guerrini R, Kuzniecky RI, Jackson GD, Dobyns WB. A developmental and genetic classification for malformations of cortical development: update 2012. Brain. 2012;135:1348–69.
6. Williams CA, Dagli A, Battaglia A. Genetic disorders associated with macrocephaly. Am J Med Genet A. 2008;146A:2023–37.
7. Baujat G, Legeai-Mallet L, Finidori G, Cormier-Daire V, Le Merrer M. Achondroplasia. Best practice and research. Clin Rheumatol. 2008;22:3–18.
8. Waller DK, Correa A, Vo TM, et al. The population-based prevalence of achondroplasia and thanatophoric dysplasia in selected regions of the US. Am J Med Genet A. 2008;146A:2385–9.
9. Ullrich NJ. Hydrocephalus and pseudotumor cerebri. In: Rudolph CD, Rudolph AM, Lister GE, First L, Gershon A, editors. Rudolph's pediatrics. 22nd ed. New York, NY: McGraw-Hill; 2011.
10. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. J Pediatr. 1978;92:529–34.
11. Barichello T, Generoso JS, Milioli G, Elias SG, Teixeira AL. Pathophysiology of bacterial infection of the central nervous system and its putative role in the pathogenesis of behavioral changes. Rev Bras Psiquiatr. 2013;35:81–7.
12. Arnold SR, Ford-Jones EL. Congenital syphilis: a guide to diagnosis and management. Paediatr Child Health. 2000;5:463–9.
13. Olariu TR, Remington JS, McLeod R, Alam A, Montoya JG. Severe congenital toxoplasmosis in the United States: clinical and serologic findings in untreated infants. Pediatr Infect Dis J. 2011;30:1056–61.

14. Barton LL, Mets MB. Congenital lymphocytic choriomeningitis virus infection: decade of rediscovery. Clin Infect Dis. 2001;33:370–4.
15. Barichello T, Fagundes GD, Generoso JS, Elias SG, Simoes LR, Teixeira AL. Pathophysiology of neonatal acute bacterial meningitis. J Med Microbiol. 2013;62:1781.
16. Aydemir C, Eldes N, Kolsal E, Ustundag G, Gul S, Erdem Z. Acute tetraventricular hydrocephalus caused by mumps meningoencephalitis in a child. Pediatr Neurosurg. 2009;45:419–21.
17. Kanra G, Ozen M, Kara A, et al. Mumps hydrocephalus ameliorated with external drainage. Turk J Pediatr. 2005;47:397–9.
18. Renaud DL. Leukoencephalopathies associated with macrocephaly. Semin Neurol. 2012;32:34–41.
19. Mirzaa G, Dodge NN, Glass I, et al. Megalencephaly and perisylvian polymicrogyria with postaxial polydactyly and hydrocephalus: a rare brain malformation syndrome associated with mental retardation and seizures. Neuropediatrics. 2004;35:353–9.
20. Day RE, Schutt WH. Normal children with large heads--benign familial megalencephaly. Arch Dis Child. 1979;54:512–7.
21. Zahl SM, Egge A, Helseth E, Wester K. Benign external hydrocephalus: a review, with emphasis on management. Neurosurg Rev. 2011;34:417–32.
22. Losowska-Kaniewska D, Oles A. Imaging examinations in children with hydrocephalus. Adv Med Sci. 2007;52 Suppl 1:176–9.
23. Miller R, Miller M. Overrepresentation of males in traumatic brain injury of infancy and in infants with macrocephaly: further evidence that questions the existence of shaken baby syndrome. Am J Forensic Med Pathol. 2010;31:165–73.
24. Alvarez LA, Maytal J, Shinnar S. Idiopathic external hydrocephalus: natural history and relationship to benign familial macrocephaly. Pediatrics. 1986;77:901–7.
25. Vertinsky AT, Barnes PD. Macrocephaly, increased intracranial pressure, and hydrocephalus in the infant and young child. Top Magn Reson Imaging. 2007;18:31–51.
26. Smyth MD, Narayan P, Tubbs RS, et al. Cumulative diagnostic radiation exposure in children with ventriculoperitoneal shunts: a review. Childs Nerv Syst. 2008;24:493–7.
27. Iskandar BJ, Sansone JM, Medow J, Rowley HA. The use of quick-brain magnetic resonance imaging in the evaluation of shunt-treated hydrocephalus. J Neurosurg. 2004;101:147–51.
28. Rozovsky K, Ventureyra EC, Miller E. Fast-brain MRI in children is quick, without sedation, and radiation-free, but beware of limitations. J Clin Neurosci. 2013;20:400–5.
29. Cianfoni A, Martin MG, Du J, et al. Artifact simulating subarachnoid and intraventricular hemorrhage on single-shot, fast spin-echo fluid-attenuated inversion recovery images caused by head movement: a trap for the unwary. AJNR Am J Neuroradiol. 2006;27:843–9.
30. Drake JM. The surgical management of pediatric hydrocephalus. Neurosurgery. 2008;62 Suppl 2:633–40. discussion 40-2.
31. Drake JM, Kestle JR, Milner R, et al. Randomized trial of cerebrospinal fluid shunt valve design in pediatric hydrocephalus. Neurosurgery. 1998;43:294–303. discussion 5.
32. Weaver M, Proctor MR. Minimally invasive pediatric neurosugery. Totowa, NJ: Humana Press Inc.; 2005.
33. Jimenez DF. Third ventriculostomy. In: Jimenez DF, editor. Intracranial endoscopic neurosurgery. Park Ridge, IL: The American Association of Neurological Surgeons; 1998.
34. Gangemi M, Mascari C, Maiuri F, Godano U, Donati P, Longatti PL. Long-term outcome of endoscopic third ventriculostomy in obstructive hydrocephalus. Minim Invas Neurosurg. 2007;50:265–9.
35. Ray P, Jallo GI, Kim RY, et al. Endoscopic third ventriculostomy for tumor-related hydrocephalus in a pediatric population. Neurosurg Focus. 2005;19:E8.
36. Kulkarni AV, Drake JM, Kestle JR, et al. Predicting who will benefit from endoscopic third ventriculostomy compared with shunt insertion in childhood hydrocephalus using the ETV Success Score. J Neurosurg Pediatr. 2010;6:310–5.
37. Kulkarni AV, Drake JM, Kestle JR, et al. Endoscopic third ventriculostomy vs cerebrospinal fluid shunt in the treatment of hydrocephalus in children: a propensity score-adjusted analysis. Neurosurgery. 2010;67:588–93.
38. Bouras T, Sgouros S. Complications of endoscopic third ventriculostomy: a systematic review. Acta Neurochir Suppl. 2012;113:149–53.
39. Wellons JC, Shannon CN, Kulkarni AV, et al. A multicenter retrospective comparison of conversion from temporary to permanent cerebrospinal fluid diversion in very low birth weight infants with posthemorrhagic hydrocephalus. J Neurosurg Pediatr. 2009;4:50–5.
40. Chern JJ, Macias CG, Jea A, Curry DJ, Luerssen TG, Whitehead WE. Effectiveness of a clinical pathway for patients with cerebrospinal fluid shunt malfunction. J Neurosurg Pediatr. 2010;6:318–24.

Evaluation and Classification of Pediatric Headache

15

Zuhal Ergonul

Clinical Vignette 1 A 15-year-old overweight girl was referred to the emergency room for complaints of double vision for 2 days, and worsening headache for 2 weeks. The headache started several weeks ago and has gotten worse last 2 weeks. She describes it as a constant, pounding headache all over the head. She does not have a prior history of migraines. Headache is getting worse with strong lights. Two days ago she also developed double vision and it is worse when she looks to the right.

Headache in children and adolescents is most often due to a benign process such as an acute viral illness or migraine but it remains one of the most common reasons for pediatric neurology referrals resulting in distress for both patients and their families. It is important to remember that when parents bring their child to the primary care provider with a "headache," there is a specific question that they usually want answered: Is there a life-threatening cause? Do they have a brain tumor? However, after the evaluation for secondary causes of headache is completed, most children with a primary headache syndrome are left untreated or undertreated [1]. This chapter reviews a systematic evaluation and comprehensive management of headaches in children.

Z. Ergonul, M.D., Ph.D. (✉)
Division of Child Neurology, Weill Cornell Medical College, 505 East 70th Street 3rd Floor, Box 91, New York, NY 10021, USA
e-mail: zuhalergonul@hotmail.com

Identification and Classification of Headache

Primary Versus Secondary Headache

Classification helps us better diagnose headache disorders and ultimately treat them properly. The International Headache Society classification designates three distinct classes: primary headache, secondary headaches, and cranial neuralgias. Primary headaches are those in which the headache itself is the disorder. Secondary headaches are caused by structural, inflammatory or metabolic problems. Cranial neuralgias are head pains caused or behaving as if they were due to compression, or distortion of a nerve of the head.

In children, the ability to describe the headache may be limited by the child's development stage. To reassure yourself, approach the complaint of headache utilizing a structured questionnaire for headache history, followed by a structured neurological examination [2].

Headache History

A headache evaluation should rely less upon diagnostic testing than upon history. A simple but structured questionnaire will help elicit the pertinent features of the headache to help establish a differential diagnosis. One needs to ask what effect the headache has on the patient's life and

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_15

any resultant disability. Give the patient and family enough time to consider the question and answer thoughtfully before moving on. Adult neurologists are often anxious when confronted with a child presenting with a headache. However, the key components of the evaluation as in any neurological complaint remain unchanged: clinical history, physical and neurological exam including vital signs, and ancillary testing if indicated.

Secondary causes will be less likely in patients who have experienced headache for several years, most secondary causes of headache evolve over a few weeks to months. Keep in mind that even patients with a primary headache disorder including migraine may develop a secondary headache (increased intracranial pressure, brain tumor, etc.). Even patients with a longstanding history of headache with a recent change in pattern must be re-evaluated [3].

Headache Questions

1. Describe the pattern of your headache [4]

   Acute single episode (sudden first headache): Infectious (meningitis, systemic viral/bacterial illness), vascular (stroke, intracranial hemorrhage), trauma

   Acute recurrent episodes of headache: Episodic migraine, tension-type headache, trigeminal autonomic cephalalgias

   Chronic non-progressive (chronic daily headaches): Chronic migraine, new daily persistent headache, chronic tension-type headache

   Chronic/subacute progressive (gradually worsening headache): Space-occupying lesion, hydrocephalus, pseudotumor cerebri, Chiari malformations

   Acute on chronic (a mixture, more than one type of headache): Primary headache disorder such as chronic migraine with a superimposed secondary cause
2. How and when did your headache begin?

   Exploring the triggering events (head trauma for post-concussion headache, prior viral illness for new daily headache, etc.)
3. What are the characteristics of your headache?

   How often do your headaches occur and how long do they last?

   What makes the headache better or worse?

   Do any activities, medications, or foods tend to cause or aggravate your headaches?

   Do the headaches occur under any special circumstances or at any particular time?

   Can you tell that a headache is coming? If so, what are the warning signs? (flushed face, sunken eyes, hyperactivity, feeling "not right")

   Where is the pain located? (ask patient to point)

   What is the quality of the pain? (pounding, squeezing, stabbing, other)

   Are there any other symptoms that accompany your headache: nausea, vomiting, dizziness, numbness, lightheadedness, weakness, or other?

   What do you do when you get a headache? Do you have to stop your activities when you get a headache?

Headache Characteristics and Most Likely Diagnosis

Location

Frontal, bitemporal → migraine

Occipital → posterior fossa disease, Chiari malformation

Quality

Throbbing, pounding → migraine

Pressure-like → tension-type headache

Duration

1 h and longer → migraine

Seconds to minutes → trigeminal autonomic cephalalgias (e.g., cluster headache, paroxysmal hemicrania)

Associated Symptoms

Photophobia, phonophobia, nausea, vomiting → migraine

Tearing, nasal congestion → trigeminal autonomic cephalalgias

Aggravating Factors

Activity → migraine

Valsalva maneuvers, straining, positional change → increased intracranial pressure, Chiari malformation

Alleviating Factors

Sleep, darkroom → migraine

Prodrome

Tired, irritable, hyperactive, depressed, feeling "not right" → migraine

Aura

Fully reversible visual, sensory, speech, and/or language symptoms lasting 5–60 min → migraine

(Occipital lobe epilepsy may also present with visual aura and ictal emesis)

Family History

Exploring the risk for primary headache disorders is crucial as most children with primary headache disorders such as migraine, tension-type headache, and chronic daily headache have a positive family history of headache.

Medical History

Explore the relevant medical history:

Do you have any other medical problems?

Are you taking any medications for the headache or other purposes?

Past medical history: Neurosurgical procedures—ventriculo-peritoneal shunt, endocrine disorders—hyperthyroidism, HIV, congenital heart disease-increased risk for hypertension and brain abscess, malignancy, radiation therapy, coagulopathy, pregnancy, menstrual history, SLE or other collagen vascular diseases, psychiatric disorders—depression, anxiety

Common Red Flags in Headache History for Children

Red flags for the presence of intracranial pathology in pediatric patients with headache include:

- Headache of less than 1-month duration
- Atypical onset: vertigo, intractable vomiting, thunderclap headache, or any headache that wakes the child during sleep
- Absence of family history of migraine
- Child of less than 6 years
- Occipital headache

According to American Academy of Neurology guidelines, routine laboratory testing including lumbar puncture, routine EEG, and routine neuroimaging are not recommended for the evaluation of children and adolescents with headache. Incidental abnormalities unrelated to headache symptoms have been reported in approximately 16 % of patients undergoing routine neuroimaging. Some of these abnormalities include: arachnoid cysts, Chiari malformations, paranasal sinus disease, and vascular malformations.

Migraine is the most important primary headache and diagnosed clinically. There is no test or practical way to prove that a headache is a migraine, other than by eliciting its symptoms and excluding a secondary cause. It is commonly believed that children do not get migraines. It is important to ask parents what they think might be causing their child's headache; parental insight into the situation provides parents with an opportunity to express their own concerns and also may help identify risk factors. This will allow the practitioner to specifically address these concerns once the evaluation has been completed.

Pediatric Physical and Neurological Examination

A thorough physical and neurological examination must be performed in all children with a complaint of headache. Abnormal vital signs, abnormal head circumference, fever, hypertension, nuchal rigidity, meningeal signs, signs of upper respiratory disease, visual changes, fundoscopic exam abnormalities (absent venous pulsations, papilledema, optic atrophy), neurocutaneous lesions, abnormal findings on neurological exam;

cranial nerve abnormalities (abnormal eye movements and pupils, facial movements and asymmetry), motor or sensory deficits (pronator drift, asymmetry), gait abnormalities (difficulty with tandem gait or tightrope walking), coordination abnormalities (dysmetria on finger to nose exam, intention tremor), or abnormal or asymmetric reflexes should all be further explored.

Features that raise concern for secondary causes of headache for further referral and work-up include:

- An abnormal neurological examination is the highest predictor of intracranial pathology in children and adolescents
- Physical exam features: Neurocutaneous stigmata (neurofibromatosis, tuberous sclerosis, Sturge-Weber are associated with increased risk of intracranial pathology)
- New-onset progressive and rapidly progressive headache in a patient without prior history of headache
- Headaches that awaken the child from sleep, are worse upon awakening, or are associated with early morning emesis
- Headache that worsens with straining or Valsalva maneuvers
- Toddlers (pediatric brain tumors frequently manifest in this population)
- Associated symptoms such projectile emesis, visual changes, neurological deficits, endocrine abnormalities

Clinical Vignette Revisited Case 1 was a 15-year-old overweight girl referred to the ED with double vision and worsening headaches. She described it as a constant, pounding headache all over the head. We will now utilize our previously discussed headache framework to evaluate this child.

Physical Examination

Vital signs: normal, afebrile.

Mental status: She appears to be tired and in moderate discomfort.

Cranial nerves: Visual field exam showed difficulty counting fingers on temporal fields bilaterally. Pupils are equal, reactive to light. She has difficulty abducting her right eye and diplopia on right lateral gaze; otherwise extra ocular movements are normal. Fundoscopic exam showed tortuous vessels bilaterally, absence of venous pulsation and obscuration of optic disc margins. Facial expression and sensation are intact symmetrically. Her tongue and uvula are midline. Her gag reflex is present. Motor exam: She demonstrates no nuchal rigidity or back pain. Her muscle bulk and tone are normal. Her strength is 5/5 throughout, and she has no pronator drift. Reflexes: 1+ throughout, with bilateral plantar flexor responses. Sensory exam: Intact to light touch and pinprick, Romberg's sign is negative, Coordination: She has no dysmetria on finger to nose exam. Gait: She has normal heel, toe, and tandem walks.

Discussion

The patient in this case presents signs of elevated intracranial pressure (ICP). The presence of papilledema indicates increased ICP. Isolated weakness of the lateral rectus muscle is often seen with elevated ICP and secondary to displacement of abducens nerve in subarachnoid space. There are several potential causes of her symptoms but some diagnoses can be easily ruled out. There is no fever or nuchal rigidity that would suggest an infection such as meningitis of encephalitis. Her history is not consistent with any primary headache disorder such as migraine or tension type headache. Idiopathic intracranial hypertension (IIH) is the most likely diagnosis for this case, but cerebral venous sinus thrombosis, or a slowly progressive subarachnoid bleed should be considered; evaluation should begin with a head CT. The patient would be admitted to the hospital for further evaluation and management. While an initial CT helps rule out hemorrhage, stroke, venous sinus thrombosis, masses, and infection an MRI of the brain is required better imaging for underlying structural abnormalities that may be

the cause of patient's symptoms. If the head CT is unremarkable a lumbar puncture should be done with careful measurement of the opening pressure. Patient should be lateral decubitus position with the legs extended during the procedure in order to obtain an accurate measurement. A pressure greater than 250 mm of water is diagnostic of increased intracranial pressure. An ophthalmologic evaluation and visual field testing are required to detect visual loss. Routine CSF studies, serum studies including CBC, basic chemistry panel, liver function tests, thyroid function tests, ESR, and ANA should be sent to screen for common conditions associated with IIH [5].

Evaluation and Management

The presence of visual field loss, significant diplopia, headache, and elevated ICP are signs of malignant IIH and requires hospitalization for close inpatient ophthalmologic evaluation and therapeutic lumbar punctures. Surgery is reserved for malignant IIH with rapidly deteriorating vision. Surgical options include CSF shunting and optic nerve sheath decompression.

Acetazolamide 20 mg/kg/day divided twice a day is recommended in children and should be started immediately. Furosemide has been used in combination therapies with some success. A medication history including acne medication in adolescents should be reviewed and stopped as a possible causative agent. Weight loss and exercise program should be recommended in the case of obesity.

Vignette 2 Sixteen-year-old-male presents to emergency room with a 2-week history of constant headache. A headache started after he returned from summer camp. He denies any recent fever, rash, or trauma, but reports some weight lifting during his volunteer job in the camp. His headache significantly decreases in a supine position. He describes his headache as pressure sensation on frontal area. He gets nausea and vomiting if the headache is severe. Occasionally, the headache is associated with photophobia, but he denies blurry vision, double vision, tinnitus, numbness, or weakness. He has not attended school last couple of days because of the severity of his symptoms. He has never had recurrent headaches in the past, and his family history is negative for migraine. An initial work-up included a normal head CT and routine blood work.

Physical Examination

He has a tall stature. He prefers to stay supine position.

Mental status: Awake, alert, not in distress, speech is fluent

Neurologic and physical exam: Unremarkable except positional change in his headache.

Discussion

Spontaneous low CSF pressure headache may be caused by cryptogenic, rhinogenic, or spinal leak, the latter being more common. Minor traumatic events including coughing, lifting, falls or participating sports in sports can cause CSF leak. Underlying connective tissue disorder, such as Marfan syndrome is increasingly recognized as an important cause [5]. An orthostatic headache is usually present. Characteristic MRI findings for low CSF pressure headache:

Diffuse pachymeningeal enhancement
Sagging hindbrain
Subdural collection
Pituitary enhancement

Lumbar Puncture Findings
Low CSF pressure (less than 100 mm H_2O)
Possible increased protein and pleocytosis

Evaluation and Management

This patient should be referred for a work-up for his headaches. His evaluation should begin with brain and spine MRI. A lumber puncture should be performed to evaluate opening pressure.

Identifying the specific location of the dural tear can be detected by radionuclide cisternogram or CT myelography. Conservative management with bedrest, hydration, and caffeine should be first-line treatment. Epidural blood patches, epidural injections of fibrin glue, or surgical repair are second line treatment options.

Vignette 3 A 9-year-old boy presented with a 6-month history of recurrent, severe headaches, which occur 1–2 times in a week. His headache is located in the forehead, is throbbing in character and becomes worse with physical activity. His mother reports that he would stop his activity and lie down when the headache occurred. The headache lasts 1 or 2 h and resolves after a nap. His mother decided to bring him to the doctor after he experienced vomiting with his last two episodes. He denies sensitivity to lights, sounds, or odors. He is a good student and has not reported health problems in the past, except for night terrors in early childhood. His mother says he also has motion sickness. His physical and neurologic exam are normal.

Discussion

Migraine in the pediatric population remains underdiagnosed and undertreated. In many children, not all the symptoms required by ICHD-III (Fig. 15.1) are present [1]. As in most neurologic disorders, migraine may manifest itself with different symptoms in a developing brain. The diagnosis of the childhood periodic syndromes (thought to be precursors of migraine) are often recognized due to the child focusing on their abdominal symptoms (cyclic vomiting and abdominal migraine) and/or vertigo (benign paroxysmal vertigo of childhood) rather than headaches. As the child grows older they are better able to describe the head pain, and the presence of migraine becomes more evident [1]. In this case, the history of motion sickness, and night terrors are early signs of "sensitive brain" in migraine.

In children and adolescents attacks may last 2–72 h. Migraine headache in children is more often bilateral than is the case in adults; unilateral frontotemporal pain usually emerges in late adolescence or early adult life. Occipital headaches in children are rare and suggests diagnostic caution. In young children, photophobia and phonophobia may be inferred from their behavior.

Evaluation and Management

The examination is normal in this case and frequency is stable, so this child does not meet criteria for neurologic imaging. Management should begin with a review of triggers and lifestyle practices to determine modifications. Keeping a regular sleep schedule including on the weekends, carrying a water bottle, avoiding caffeinated and sugared drinks, healthy diet, and using stress management and biofeedback techniques can control headaches. A headache calendar should be kept to describe accurate frequency, and severity. Regular exercise of 45 min at least three times in a week, will help to maintain healthy neurovascular function and should be on the to-do list. Daily preventive medications should be considered if headaches continue to occur more commonly than five times in a month, and co-exists with missing school days or social activities. Other comorbidities such as obesity, sleep difficulties, depression, or anxiety can determine the best preventive option for the patient. Acute treatment of migraine headache should include water intake (32 oz or more) and an accurate dose of NSAIDs (e.g., ibuprofen 10 mg/kg) at the onset of symptoms. The combination of an antiemetic medication with triptans and NSAIDs are effective for prolonged refractory episodes. In order to avoid medication overuse headache, NSAIDs should be limited to 3 days in a week, and triptans to 2 days in a week. School arrangements may be necessary with teachers and nurses for medications and also other accommodations as using of resource room during the episodes.

Vignette 4 A 14-year-old boy has a history of headaches since the age of 8, which began with episodic vomiting. He was seen by several neurologists and diagnosed with migraine. He had MRI of his head and neck, and EEG in the past.

*Diagnostic criteria:**

A. At least five attacks fulfilling criteria B–D

B. Headache attacks lasting 4-72 hours (untreated or unsuccessfully treated)

C. Headache has at least two of the following four characteristics:

1. unilateral location

2. pulsating quality

3. moderate or severe pain intensity

4. aggravation by or causing avoidance of routine physical activity (e.g., walking or climbing stairs)

D. During headache at least one of the following:

1. nausea and/or vomiting

2. photophobia and phonophobia

E. Not better accounted for by another ICHD-3 diagnosis

Notes:
In children and adolescents (aged under 18 years), attacks may last 2-72 hours (the evidence for untreated durations of less than 2 hours in children has not been substantiated).
Comments:
Migraine headache in children and adolescents (aged under 18 years) is more often bilateral than is the case in adults; unilateral pain usually emerges in late adolescence or early adult life. Migraine headache is usually frontotemporal. Occipital headache in children is rare and calls for diagnostic caution. In young children, photophobia and phonophobia may be inferred from their behavior.

** From Headache Classification Committee of the International Headache Society, (IHS), The International Classification of Headache Disorders, 3rd ed., Cephalalgia (vol. 33 no. 9). Reprinted by permission of SAGE.*

Fig. 15.1 Migraine without aura. From Headache Classification Committee of the International Headache Society, (IHS), The International Classification of Headache Disorders, 3rd ed., Cephalalgia (vol. 33 no. 9), copyright 2013. Reprinted by permission of SAGE

He has tried several medications including propranolol, topiramate, amitryptyline, and nortryptyline without any significant change in his headache and he is currently on valproic acid. He takes 400 mg of Advil 2 days a week, which sometimes ameliorates symptoms. He was also seen by several gastroenterologists in the past, with a normal work-up. He has been home-schooled for the past year by tutors and his father. His father reported that his son has been working at home due to headaches. The child's parent's live separately. A psychologist saw the patient 3 years ago, everything was normal as per father. Patient's mother also has migraines and is taking Valproic acid daily. Father has infrequent migraines.

Discussion

This case describes a teenager with chronic migraine. Children with chronic daily headaches represent one of the most challenging subsets of headache in children. Chronic migraine is defined as a headache occurring on 15 or more days per month for more than 3 months, which has the features of migraine headache on at least 8 days per month. The quality of life for patients with chronic migraine is often significantly influenced by the pain and associated symptoms. The patient should be allowed to speak about how the headache is affecting his life and how he thinks the headache can be treated. The initiation of multidiscipline approach and involvement of neurologists and psychiatrists is necessary. Sleep is frequently disturbed in patients with chronic migraine. Typically, the headache will not resolve until the sleep is improved. Efforts should be made to return the child to his regular schedule with help of school authorities. Although monotherapy is preferred, it is sometimes necessary to combine preventive medications. Hospital admission for pain control should be offered. A referral should be initiated to child psychiatry to address any potential comorbidities including depression and anxiety, and to learn techniques to manage pain and stressors.

The differential diagnosis of chronic daily headache includes chronic tension-type headache (CTTH), hemicrania continua (HC), and new daily persistent headache (NDPH). In the general population, CTTH is the leading cause of primary chronic daily headache. In this condition headaches are often diffuse or bilateral, and most of migraine features (throbbing, severe unilateral pain with photophobia, phonophobia, and nausea and/or vomiting) are absent. NDPH is unique; the daily headache develops abruptly, over fewer than 3 days, and the patient typically has no prior headache history. It can continue for years without alleviation despite aggressive treatment. NDPH is not a secondary headache disorder, but patients often describe a flu-like illness or stressful life event as a trigger. Epstein-Barr virus, Salmonella, Adenovirus, and Herpes Zoster have been found in patients with NDPH. HC is an indomethacin-responsive headache disorder that is characterized by a continuous, moderately severe waxing and waning unilateral headache, without disappearing completely.

Pediatrician's Perspective

Headache etiology can usually be determined by a good history and physical exam. As the pediatrician, your role will be to determine which children in your practice necessitate referral to pediatric neurology and which symptoms or portions of the history suggest a less than benign etiology. Migraine is the most important primary headache and diagnosed clinically.

The features of headaches in your patients with headaches that warrant referral to neurology or imaging include:

- Headache of less than 1-month duration
- Atypical onset: vertigo, intractable vomiting, thunderclap headache, or any headache that wakes the child during sleep
- An absence of family history of migraine
- An age of less than 6 years
- Occipital headache

The only constellation of symptoms that might suggest a referral to an emergency department or neurologic surgeon for urgent imaging or treatment include persistent morning emesis with headache (concern for raised intracranial pressure/brain tumor), positional headaches after trauma (CSF leak/fistula), or recalcitrant headaches that may require an intensive IV combinatorial therapy to break the symptoms acutely.

References

1. Hershey AD, Powers SW, Winner P, Kabbouche MA, editors. Pediatric headaches in clinical practice. Chichester: Wiley-Blackwell; 2009.
2. Young WB, Silberstein SD, Nahas SJ, Marmura MJ. Jefferson headache manual. New York, NY:

Demos Medical Publishing, LLC.; 2011. ISBN 1933864702.
3. Tepper SJ, Tepper DE, editors. The Cleveland clinic manual of headache therapy. New York, NY: Springer; 2011. ISBN 978-1-4614-0178-0.
4. Lewis DW. Clinician's manual on treatment of pediatric migraine. London: Springer Healthcare Ltd.; 2010. ISBN 978-1-907673-12-2.
5. Rosser T. Pediatric neurology. A case-based review. Philadelphia, PA: Lippincott Williams & Wilkins; 2007.

Part IV

Imaging of the Pediatric Brain and Spine

Imaging of the Fetal Brain and Spine

16

Soniya N. Pinto, Stephen T. Chasen, and Linda A. Heier

Prenatal Imaging

In most first world countries it is standard of care that pregnant women obtain a second trimester 18–20 week screening anatomic ultrasound to confirm gestational age and to identify any abnormality of the fetus including those within the central nervous system (CNS). Ultrasound is real-time imaging therefore fetal motion is not an issue as it may be during MRI. US has a well-established safety record with no evidence of any short or long term consequences to the fetus even when performed in the early stages of organogenesis [1]. The easy availability and low cost of US has guaranteed that it remains the screening study of choice for the fetus. Unfortunately, conventional 2D ultrasound has poor tissue penetration, which can result in inadequate visualization of the fetus in situations confounded by maternal obesity, oligohydramnios (decreased amniotic fluid volume), or unusual fetal presentations. It is not uncommon to be unable to visualize the more anterior cerebral hemisphere of the fetus from the overlying ossifying calvaria (skull) so only the more posterior cerebral hemisphere is clearly seen (Fig. 16.1) [2]. Likewise poor penetration often prevents multiple gestation pregnancies from having all the fetuses well visualized. Finally US is also much more operator dependent than MR as it is a manually performed scan.

Magnetic resonance (MR) imaging entered the arena of prenatal imaging in the early 1990s with the development of ultrafast sequences taking less than a second per image, which permitted the very active fetus to be caught by the MR camera (Fig. 16.2) [3]. Fetal MR imaging has several advantages over prenatal sonography but first and foremost is the improved contrast resolution. This superior contrast resolution coupled with MR's better spatial resolution, larger field of view, and multiplanar imaging capabilities, permits the morphology of the developing brain and spine to be more clearly visualized than with US. MRI allows superior delineation of the cortex, ventricles, subarachnoid spaces, and posterior fossa structures. This MR sensitivity allows assessment of the integrity of the brain parenchyma, an analysis critical in predicting neurocognitive outcome. Parenchymal US abnormalities that are better visualized with MR include malformations of cortical development, destructive lesions, sulcation

S.N. Pinto, M.B.B.S.
New York Presbyterian Hospital – Weill Cornell Medical Center, 515 E 71st St, New York, NY 10021, USA

S.T. Chasen, M.D.
Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Weill Cornell Medical College, 525 East 68th Street, New York, NY 10065, USA

L.A. Heier, M.D., F.R.C.P.(C) (✉)
Weill Cornell Medical College, 525 East 68th Street, New York, NY 10065, USA
e-mail: laheier@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_16

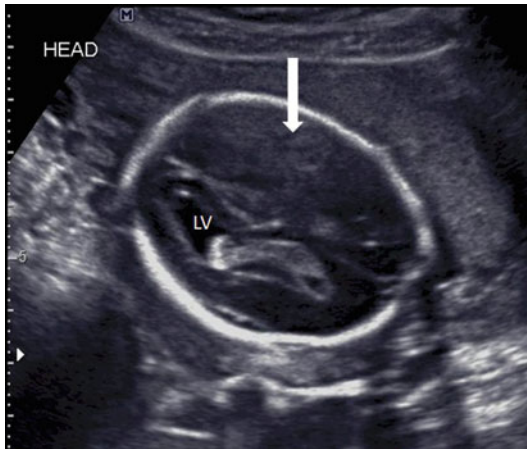


Fig. 16.1 Note the more posterior cerebral hemisphere of this normal 20 week fetus is clearly seen while the more anterior cerebral hemisphere of the fetus is obscured (*white arrow*) and the lateral ventricle (LV) is not visualized

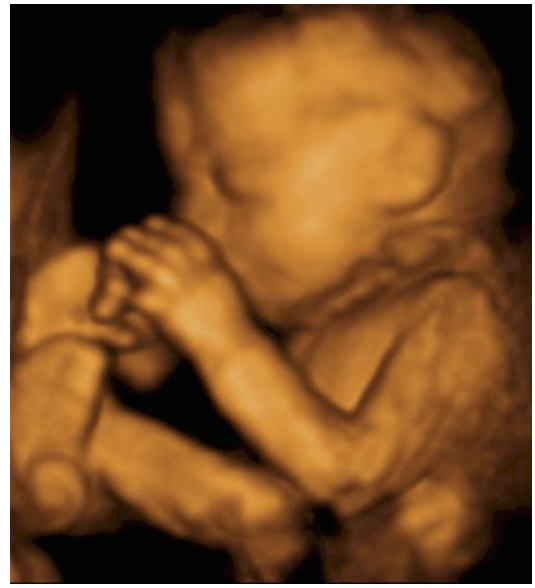


Fig. 16.3 3D US of a 23 week GA fetus

Fig. 16.2 Coronal T2 MRI of the fetal face at 23 weeks GA

anomalies, periventricular nodular heterotopia, cerebellar dysplasia, periventricular leukomalacia, germinal matrix hemorrhage, and intraventricular hemorrhage [4–8].

Abnormalities of the fetal brain typically present on the prenatal screening anatomic sonogram when fetal ventriculomegaly or an abnormal posterior fossa are most commonly identified. A subsequent MR can confirm the US abnormality but often discovers additional pathology not appreciated on US. Studies have shown that fetal MR can detect additional pathology in 36–57 % of CNS anomalies not found on conventional 2D transabdominal US [9]. Fetal MR can also prove US findings false and confirm a normal fetal brain.

The information provided by fetal MR can affect decision making for parents and physicians, altering counseling, delivery, and neonatal care. The management of the pregnancy may be changed in up to 47 % of cases [10]. Recent developments in three-dimensional (3D) sonography (Fig. 16.3) can nearly compete with the 3 plane resolution achieved by MR in some cases and there are some tissue characteristics that are still best appreciated on US such as calcification and blood flow [11]. 3D sonography is better at detecting intracranial calcification (Fig. 16.4), vascular abnormalities (Fig. 16.5), intratumoral vascularity and bone dysplasia compared to MR [12]. 3D

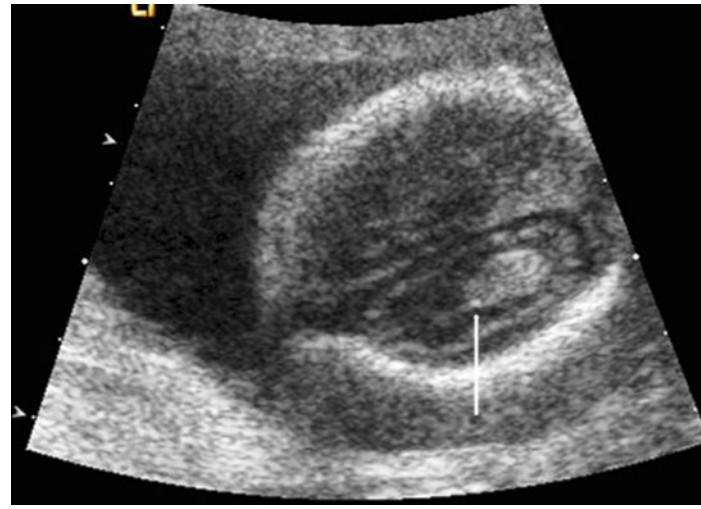


Fig. 16.4 2D US example of a periventricular calcification from congenital toxoplasmosis not seen on MR

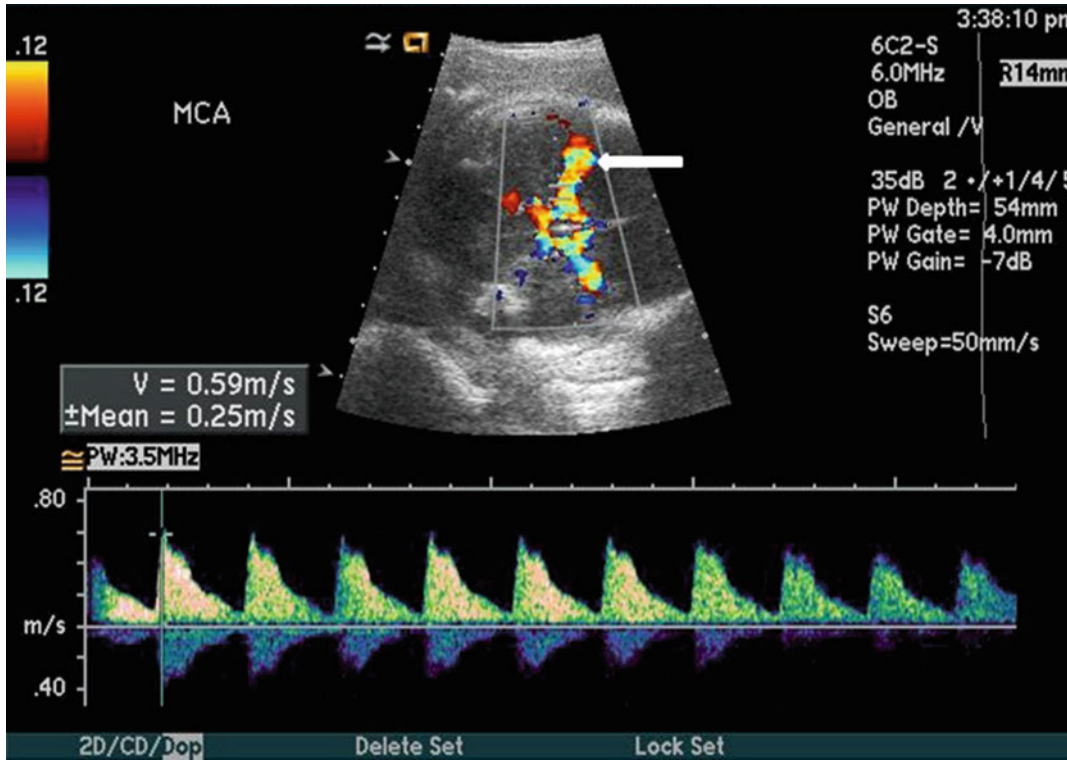


Fig. 16.5 Color Doppler of the MCA (middle cerebral artery) (*white arrow*) with increased flow in a case of anemia

ultrasound can also demonstrate the abnormalities seen outside the CNS, frequently associated with CNS abnormalities. The 3D transvaginal high-frequency approach can still be limited due to lack of penetration and skull ossification. However, 3D US especially transvaginal, can approach, if not match the detection rate of CNS abnormalities by MR according to some authors [13, 14].

The transvaginal technique however has not been successfully popularized in the United States.

The most significant limitation of fetal MR imaging remains fetal motion. Sedation of the mother and fetus is not usually done although the injection of curare into the umbilical cord to obtain fetal paralysis was used before the development of ultrafast pulse sequences [15]. Despite the continuing technical advances, which permit increasingly rapid image acquisition, fetal motion remains the greatest technical challenge to obtaining a diagnostic study.

Indications for Fetal MR

MR imaging is not a routine screening tool for the evaluation of the fetal CNS and should be reserved to better evaluate abnormal findings on the second trimester screening anatomic US or lack of cranial visualization due to the usual culprits (decreased amniotic fluid, large maternal body habitus, position of the fetal head, shadowing from the calvarium in later gestational age GA).

Common abnormalities of the brain suspected or not adequately assessed by US include vascular malformations, hydranencephaly, and infarctions. Finally the suspected congenital anomalies of the spine poorly assessed by US include neural tube defects, sacrococcygeal teratomas, caudal regression/sacral agenesis, and vertebral anomalies [16]. Destructive brain lesions related to maternal coagulation disorders, maternal hypoxia, maternal trauma, and fetal demise in multiple gestations are all indications for fetal brain MR [17].

Known central nervous system (CNS) malformations or chromosomal aberrations in siblings and a family history of genetic disorders involving the CNS also warrant MR evaluation, even with a preceding normal US examination [18].

Fetal MR imaging is now commonly used before prenatal neurosurgical intervention in confirming the diagnosis and planning potential surgical options. It is also important for screening the fetal brain both before and after other non CNS surgical interventions. The high risk to mother and fetus of potential in-utero surgery requires accurate assessment of all anomalies. This includes Chiari II/meningomyelocele, sacrococcygeal teratomas, and complications of monochorionic twins needing surgery [19–21].

Safety of Fetal MR Imaging

Fetal MR has been performed since the mid 1980s and in those 30 years no fetal injury due to MR has been documented [22, 23]. Studies performed to assess the safety of MR imaging in pregnant animals and animal embryos found no injurious results; however, there has been no official consensus that there is “no risk” of fetal MR imaging [24]. There are no published reports of adverse long-term effects of fetal MR in children who were imaged as fetuses, but these studies are limited by small sample size [25–27]. Because of the potential risk of MR imaging to the developing fetus in organogenesis and the current technical limitations of fetal MR imaging, we recommend practitioners wait until after the first trimester before performing fetal MRI.

Other fetal MRI risks include heat absorption and acoustic trauma [28, 29]. Only the 1.5T platform is used at our institution for fetal MR as at 3T the risk of heating and acoustic trauma is theoretically greater. Regarding noise, so far no studies have shown sustained increases in fetal heart rate during MRI and there is no evidence of hearing impairment in children who had undergone MRI as a fetus [27, 30].

Imaging Techniques: US

Prenatal sonography is the currently the initial modality of choice to evaluate the development of the fetal CNS. Prenatal screening for neurologic abnormalities is usually based on US performed either routinely in the second trimester or after abnormal maternal alpha-fetoprotein (AFP) screening in the second trimester. Indications of uterine infection, known teratogen exposure, abnormal fetal karyotyping, and IVF are additional reasons for a focused CNS study in the first trimester [31].

In the first trimester high-resolution transvaginal 3D ultrasound has enabled the routine

visualization of small embryos and fetuses. The anatomy of the cerebral ventricles can be seen as early as 9 weeks. US can now accurately diagnose neural tube defects such as a cranial encephalocele, acrania/anencephaly, and holoprosencephaly in the first trimester by week 12 [32]. The basic US examination in the second trimester is performed via conventional transabdominal US using 3 standard axial sections through the fetal brain.

3D/4D ultrasound allows scanning of the brain transabdominally or transvaginally generating images in all three classic scanning planes. Similar to MRI, 3D US gives the ability to view the brain from volumetric datasets. Simultaneous analysis in the three orthogonal planes facilitates both the basic and the detailed structural evaluation of the brain allowing better assessment of fetal brain from 20 weeks onward [12].

On a traditional screening to investigate the fetal brain from the second trimester onward, 2D transabdominal US, three standard axial sections through the fetal brain are generated: transventricular, transthalamic, and transcerebellar, [33]. The transthalamic (Fig. 16.6) and the more cranial and parallel transventricular plane (Fig. 16.7) display the minimal requirements for the basic mid-trimester anatomical survey of the cerebrum. The transcerebellar plane, obtained by rotating the probe posteriorly over 30°, images the posterior fossa (PF) (Fig. 16.8). Pertaining to the fetal CNS, there is a biometric component and an anatomic component. The biometric component includes the biparietal diameter (BPD) (Fig. 16.9) and head circumference (HC) (Fig. 16.6). The anatomic components include: the head, face, neck, lateral cerebral ventricles, midline falx, cavum septi pellucidi (CSP), choroid plexus, cerebellum (C), cisterna magna, and the spine (cervical, thoracic, lumbar, and sacral). The addition of color Doppler flow imaging enables the identification of arterial and venous flow.

The fetal spine typically is imaged in the three scanning planes, namely sagittal, coronal, and axial; similar to the brain scan it can be done using 2D or 3D sonography. Imaging the cervical, thoracic, lumbar, and sacral spine should display the minimal elements of an examination of the fetal spine. In addition an effort should be made to demonstrate the intact fetal skin covering the spine. When an abnormality is suspected, more extensive imaging of the spine is required. 3D views are obtained with the fetal spine in the sagittal plane. Surface and bone rendering improves visualization (Fig. 16.10).

Although the fetal face is not considered as part of the fetal CNS, its examination is an essential component of the total evaluation of the fetal CNS (Fig. 16.2).

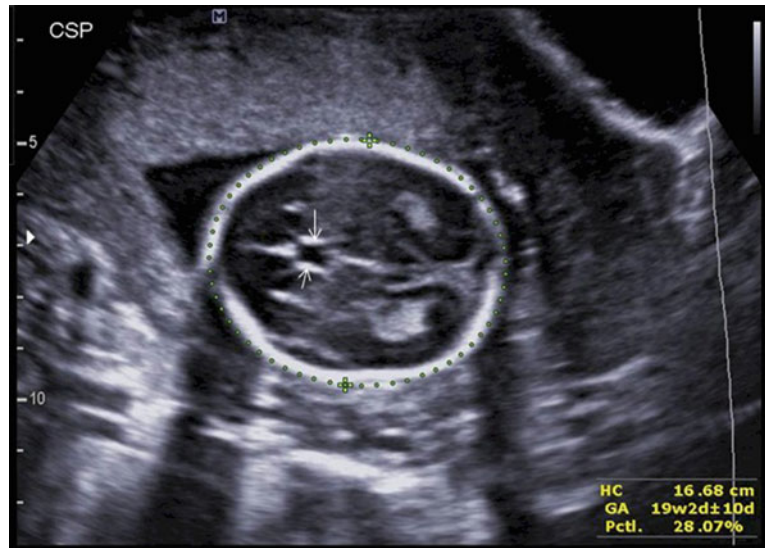


Fig. 16.6 2D US of the transthalamic plane with a head circumference measurement at 20 weeks GA. *White arrows* indicate the laminae of the normal cavum septum pellucidum

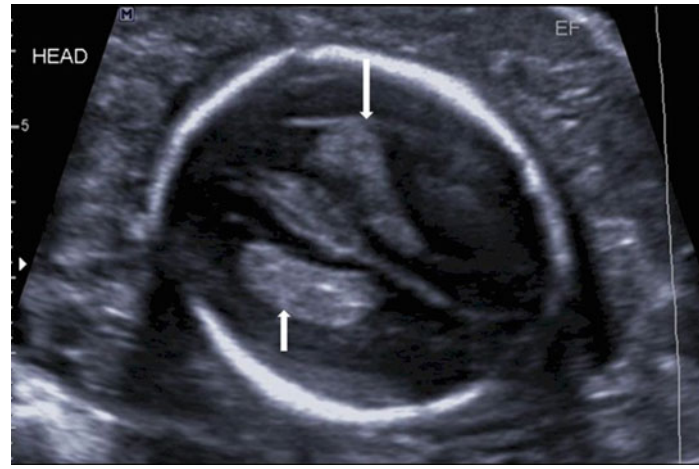


Fig. 16.7 2D US at the transventricular plane demonstrating the normal prominent choroid plexus within the ventricles (*arrows*)

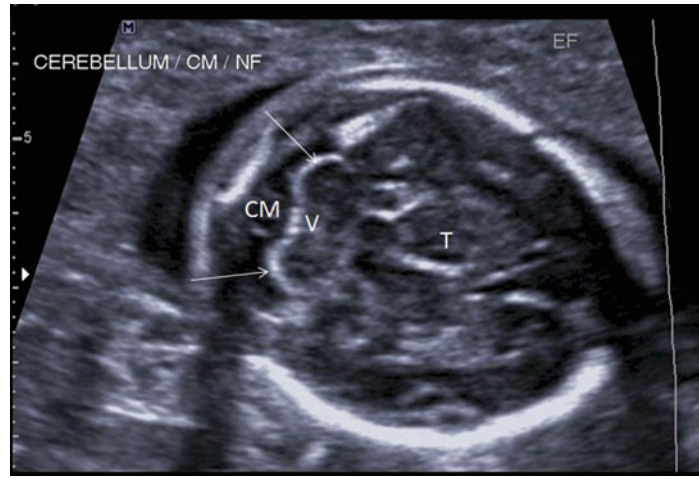


Fig. 16.8 2D US of the transcerebellar plane with both cerebellar hemispheres marked by *white arrows*. V = vermis. T = thalamus. CM = cisterna magna

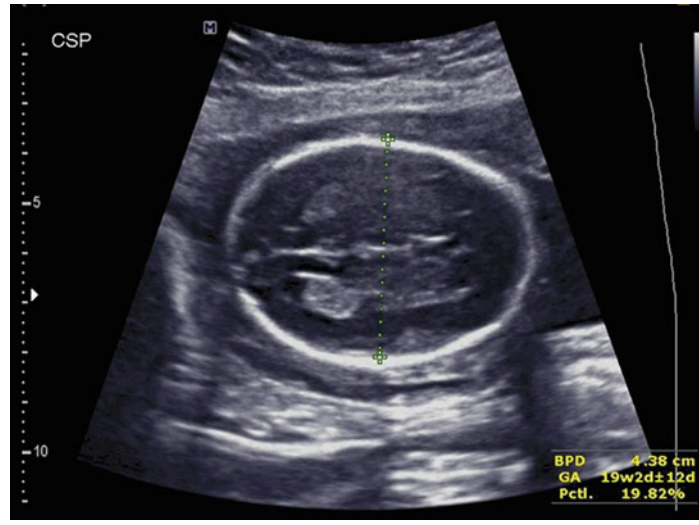


Fig. 16.9 Biparietal diameter measured at the maximum transverse width in a 20 week GA fetus

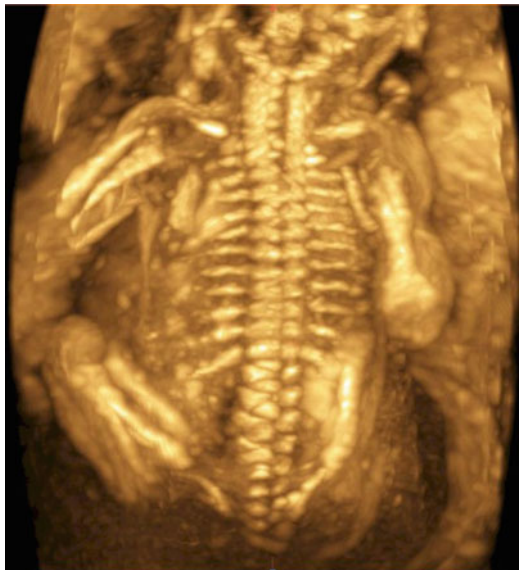


Fig. 16.10 3D US of a 20 week GA fetal thoracolumbar spine

Imaging Techniques: MR

Our routine fetal protocol attempts to reduce the potential limitations in fetal MR imaging including fetal motion, maternal discomfort, and the technical difficulties of scanning a small moving structure far from the receiver coil. To minimize the difficulties created by the small size and excessive motion of younger fetuses it is ideal to wait until at least gestational week 22 to perform the MRI. Due to parental anxiety, many studies are performed earlier but we try not to preform studies before 20 weeks especially for minor abnormalities where finding additional CNS abnormalities is the real indication for the study. Gestational age limits on termination vary state by state and must be considered in the timing of the study.

Most of the anatomic information from fetal MR is obtained from ultra fast T2 weighted sequences. Axial, sagittal, and coronal image sets of the fetal brain are obtained in a sequential manner unless the fetus moves out of the plane of acquisition, unfortunately a frequent occurrence. Images are acquired during free maternal breathing with a small field of view, adjusted for increased fetal and/or maternal size. These sequences are obtained at a slice thickness of 3 mm for the brain and at 2 mm for the spine [34].

T1 weighted imaging is less useful as the scanning times are much longer and more subject to fetal motion. FSPGR images with 5-mm slice thickness are performed during a single maternal breath hold and allow detection of hemorrhage, thrombosis, fat, or calcification (Fig. 16.11). Gradient-echo images with high sensitivity to paramagnetic susceptibility are used to identify hemorrhage and mineralization as well as osseous and vascular structures [35, 36]. Advanced MR techniques such as spectroscopy, diffusion tensor imaging (DTI), dynamic MRI, and resting state functional MRI have been successfully applied to fetal MR imaging but are not routine or diagnostic.

Normal Fetal CNS Anatomy and Development—US

The age of the pregnancy is key when imaging the fetal brain, as the CNS develops in a sequential fashion with a specific time line when each new structure should appear.

During the first trimester there is a very rapid development of the brain; however, as the second and the third trimesters approach, the CNS formation slows. By 16 weeks the ventricles, cerebral and cerebellar hemispheres are formed and much of the third trimester development is the gyration and sulcation of the hemispheres. The brain experiences a dramatic growth in utero with a near 40-fold increase in the weight of the brain by the time of birth [37].

Ventricles

Naturally the transventricular standard plane best demonstrates the size and configuration of the lateral ventricles, with the anterior landmarks of the cavum septi pellucidi seen between the frontal horns and the echogenic choroid plexus seen within the posterior ventricle. The atrial diameter is measured from inner wall to inner wall (Fig. 16.12). A measurement up to 10 mm is considered normal at any second and third trimester gestational age. The germinal matrix itself is not well-delineated with US.

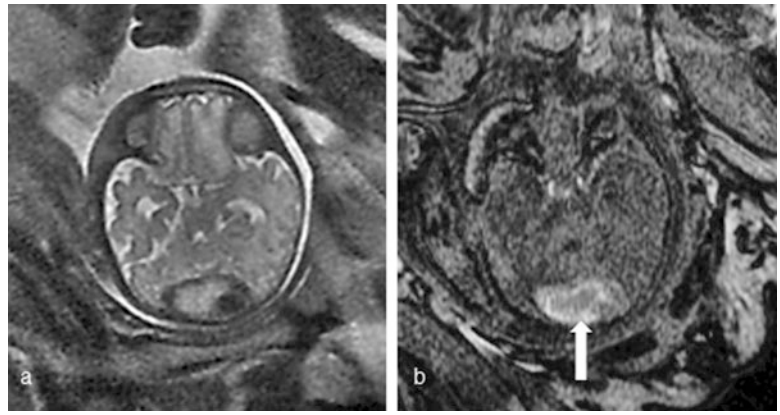


Fig. 16.11 Thrombosing dural sinus malformation with T1 hyperintense clot (*arrow*) in the enlarged torcular Herophili. (**a**) Axial T2 weighted image. (**b**) Axial T1 weighted image at same level

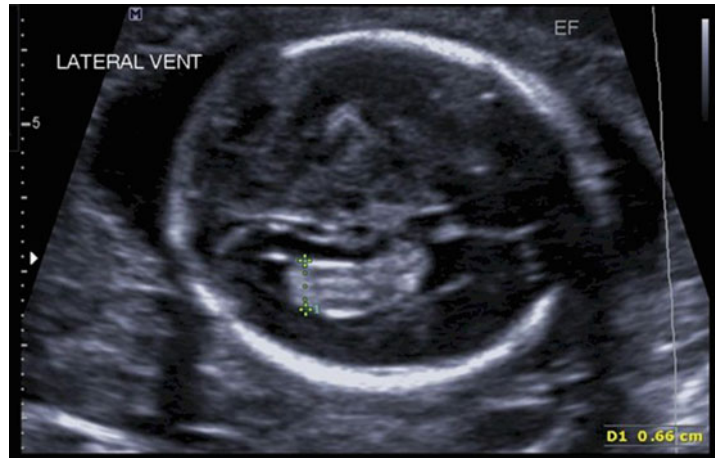


Fig. 16.12 2D US with a normal 6 mm measurement of the atrial diameter of the lateral ventricle

Midline Structures

The cavum septum pellucidi (CSP) are paired lamellae separated by CSF between the frontal horns. Under normal conditions it should be easily detected at 16–18 weeks. It is seen anterior and superior to the third ventricle during the routine measurement of the biparietal diameter (Fig. 16.6). Its identification virtually excludes complete agenesis of the corpus callosum (ACC) [33]. Lesions or non-visualization of the CSP might be associated with a variety of abnormalities, including agenesis of the corpus callosum (ACC), septo-optic dysplasia, holoprosencephaly, schizencephaly, porencephaly/hydranencephaly, basilar encephaloceles, and severe hydrocephalus [38] In the transventricular plane the CSP is seen between the frontal horns of the lateral ventricles.

Parenchyma

The fetal brain parenchyma is hypoechoic in contrast to the echogenic choroid plexus within the lateral ventricles. The supratentorium is imaged when obtaining transventricular and transthalamic views. Landmarks anterior to posterior for the transthalamic view are frontal horns of the lateral ventricles, CSP, thalami, and hippocampi.

Sulcation

The normal US appearance of the cerebral cortex in the second and third trimester is required knowledge to date the fetus as well as recognize abnormalities. A fissure or sulcus is first seen as a small dimple that deepens, forming a surface notch and an echogenic line that extends into the brain and begins to branch [39]. The interhemispheric fissure is the first to be identified at 14–15 weeks and the sylvian fissure can be recognized by 18 weeks gestation [40].

Posterior Fossa

Evaluation of the posterior fossa is achieved with the transcerebellar axial image (Fig. 16.6) obtained anterior to posterior: thalami, cerebellum, and cisterna magna (CM). The CM is a fluid collection posterior to the cerebellum with normal anterior to posterior diameter between 2 and 10 mm [41]. The vermis does not cover the fourth ventricle until 18 weeks gestation, so Dandy–Walker complex should not be diagnosed before this time [42].

Skull

The echogenicity, size, and shape of the skull must be routinely examined. The skull should have normal sutures and be scrutinized for bone defects. Bone or transparency mode and three-dimensional imaging can improve visualization of the fetal skeleton [43].

Spine

The initial 2D images should begin with the axial plane, which is best for identifying the three ossification centers of the spinal column and the integrity of the overlying skin [44]. Ossification of the vertebral bodies proceeds caudally through gestational age with the L5 arch ossified by 16 weeks, S1 by 19 weeks and S2 by 22 weeks, which also can confirm the levels [45].

Normal Fetal CNS Anatomy and Development—MR

Ventricles and Subarachnoid Spaces

In early gestation, the ventricles and subarachnoid spaces appear enlarged because of the immaturity and small size of the brain parenchyma. As the brain develops and increases in weight, the subarachnoid and ventricles appear less prominent (Fig. 16.13). The extra-axial spaces remain constant until 30 weeks, from which they decrease in size. CSF appears bright or white on T2 weighted imaging. The choroid plexus appears as a faint intraventricular T2 dark hypointensity (Fig. 16.14).

Midline Structures

The CSP is a CSF space lined by two thin leaflets, forming the medial wall of the lateral ventricles to the level of foramen of Monroe. The CSP will often enlarge in the third trimester, sometimes mimicking a cyst and disappear as a result of fusion of the leaflets at or near term (Fig. 16.15).

The corpus callosum is the largest commissure of the fetal brain. It develops anterior to posterior between 8 and 20 weeks gestation as axons from the developing cerebral hemispheres navigate across the interhemispheric fissure. The corpus callosum is seen on the coronal plane as a flat structure crossing between the hemispheres (Fig. 16.15a) and on a midline sagittal image as a dark T2 crescentic structure above the fornix (Fig. 16.15b).

Brain Parenchyma

The fetal brain on MRI demonstrates signal patterns reflecting the architecture of the parenchyma. The white matter is mainly water, lacking myelination, and is therefore hyperintense on T2 and hypointense on T1 weighted imaging.

The neurons in the germinal matrix and the cortex/cortical plate demonstrate low signal on T2 and high signal on T1 because of high neuronal cellularity (Fig. 16.16).

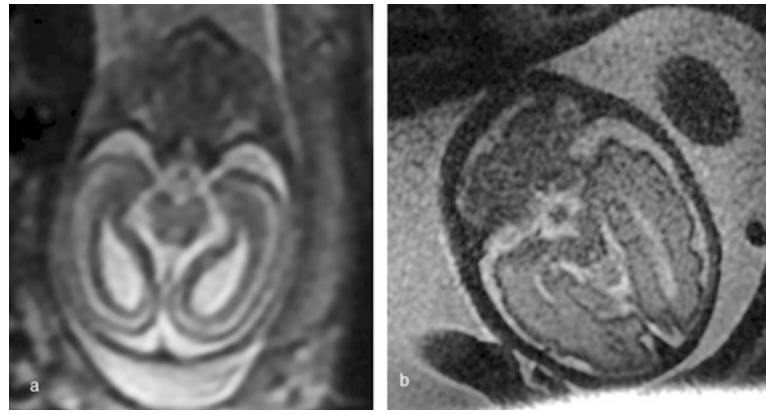


Fig. 16.13 Axial T2 weighted MRI at the level of the temporal horns. (**a**) is a 20 week GA fetus and (**b**) is a 30 week GA fetus. Note the decreasing subarachnoid space and increasing gyration of the cerebral hemispheres

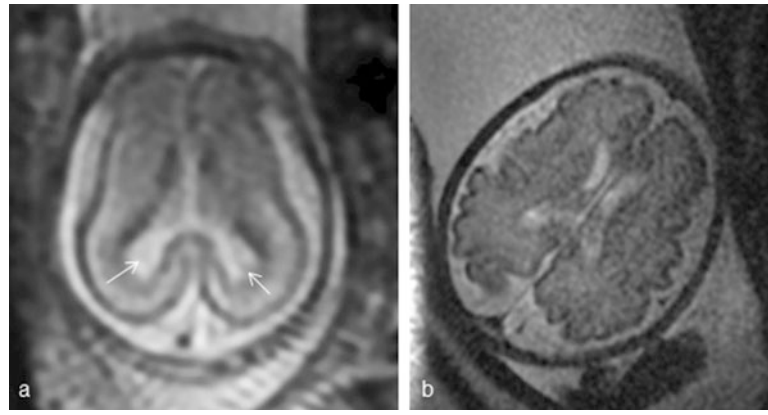


Fig. 16.14 Axial T2 weighted MRI at the level of the lateral ventricles. (**a**) is a 20 week GA fetus and (**b**) is a 30 week GA fetus. *White arrows* indicate the choroid plexus. Note the decreasing subarachnoid space and increasing gyration of the cerebral hemispheres

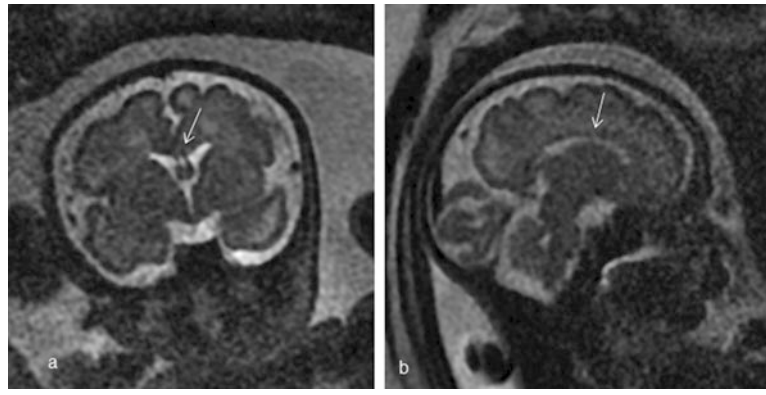


Fig. 16.15 30 week GA fetus. (**a**) Coronal T2 weighted MRI. (**b**) Sagittal T2 weighted MRI. *Arrows* indicate normal corpus callosum

The fetal neurons develop from the germinal matrix also called the ventricular zone, which is a cell dense layer lying immediately adjacent to the walls of the ventricles. Cellular proliferation takes place in the germinal matrix from 8 to 16 weeks. The germinal matrix generates the neuroectodermal elements that constitute the brain parenchyma, giving rise to both neuronal

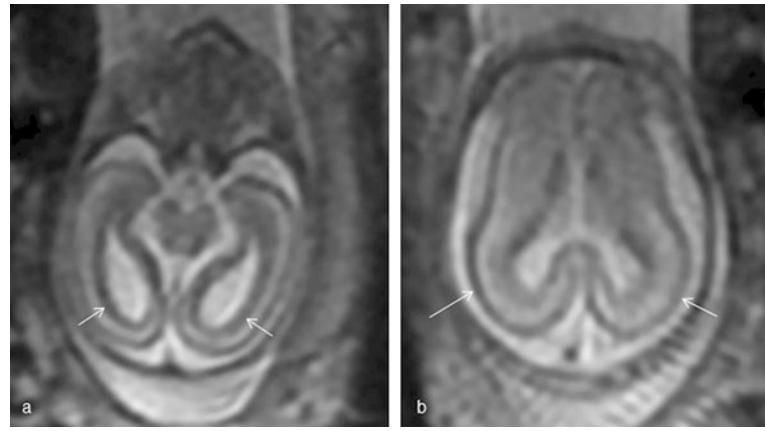


Fig. 16.16 20 week GA fetus. (**a**) Axial T2 weighted MRI. *Arrows* indicate the T2 dark germinal matrix. (**b**) Axial T2 weighted MRI. *Arrows* indicate T2 dark normal cortex/cortical plate

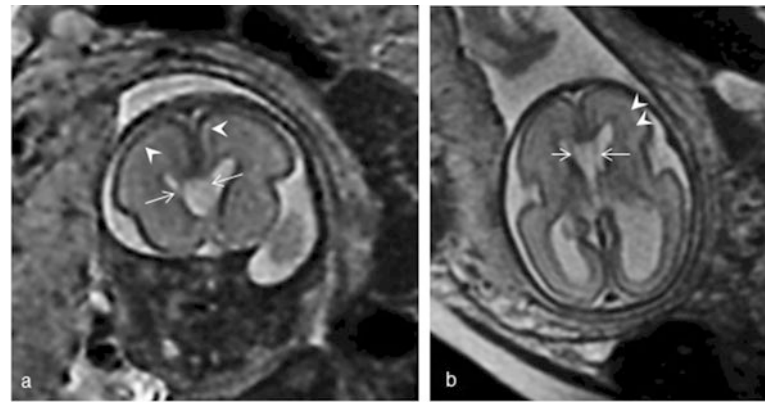


Fig. 16.17 26 week GA fetus. (**a**) Coronal T2 weighted MRI. *Arrow heads* indicate the T2 bright subplate. (**b**) Axial T2 weighted MRI demonstrating a wide cavum septum pellucidum (*arrows*) with unilateral ventriculomegaly. *Arrow heads* indicate the T2 dark subventricular and intermediate zones

and non-neuronal cells. Neuronal migration begins by gestational week 7; most migration to the cortex is complete by 24 weeks but it is not currently visualized with MR in vivo. Cells from the germinal matrix migrate radially from the ventricular wall to the surface of the brain in an inside-out fashion to form the cortical plate [46]. Once in the cortical plate, the neurons undergo cortical organization and cellular differentiation and the germinal matrix regresses but will persist in the caudothalamic groove for several months after birth [47].

The intervening parenchyma demonstrates three visible layers between the cortex and germinal matrix, which were initially described on T1-weighted images from approximately 20–28 weeks [48] (Fig. 16.17). Myelination follows an organized pattern, progressing from central to peripheral, caudal to cranial, and occipital/central to temporal/frontal [34]. Decreased T2 signal in the dorsal brainstem, consistent with early myelination, should be detected in a fetus at 20-weeks gestational age (Fig. 16.18).

Sulcation

Cortical sulcation on fetal MRI follows a predictable pattern in the fetus; it is delayed approximately 1–2 weeks behind autopsy correlation but is seen earlier than on US [49, 50]. Brain sulcation is considered the most accurate way to date a pregnancy by pathologists [51].

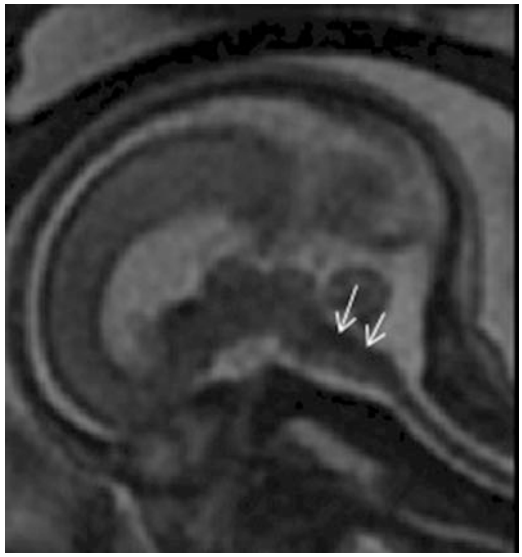


Fig. 16.18 Sagittal T2 weighted MRI of 20 week GA fetus demonstrating decreased T2 signal in the dorsal brainstem (*white arrows*) consistent with early myelination

Posterior Fossa

An ependymal lined cystic diverticulum, called Blake's pouch, develops in continuity with the fourth ventricle and then regresses with fenestration occurring in the area of the foramen of Magendie, giving rise to a normal fourth ventricle and a cisterna magna (CM) [52]. Along the walls of the fourth ventricle and rhombic lips, the germinal matrix gives rise to the neurons of the cerebellum. The cerebellar hemispheres form first, whereas the vermis forms subsequently in the midline. The vermis will cover the floor of the fourth ventricle by 18–20 weeks gestation [53, 54]. The brainstem should have a vertical configuration with rounded pons, which can also be measured to ensure adequate growth [50].

Biometrics

Evaluation of proper head size and growth can be obtained by performing biometrics just as with US. There are multiple published series of normal fetal brain measurements on MRI [55–58].

Spine

The spinal cord develops by primary and secondary neurulation at the cranial and caudal ends of the embryo respectively during organogenesis. The proximal segment, extending from the medulla to the mid-lumbar enlargement, develops by "primary neurulation" where the notochord induced neural plate rolls up and forms a hollow tube. Caudally the distal lumbar cord, conus medullaris, and filum terminale forms by secondary neurulation from a solid cell mass which undergoes "canalization and retrogressive differentiation" where the caudal cell mass develops a central cavity and remodels into a tube which aligns with the primary tube [59]. MRI at 20 weeks visualizes the spinal cord after primary and secondary neurulation are complete and an obvious spinal cord is present.

Pathology of the Fetal CNS

The US and MR appearance of CNS pathology will be described together as the studies are usually performed nearly simultaneously at approximately 20–22 weeks gestational age (GA).

Ventriculomegaly

The most common CNS abnormality found prenatally is ventriculomegaly [60] and as a result it is the most common indication for fetal MRI [61]. Ventriculomegaly is defined as an atrial width or diameter greater than 10 mm on both US and MR. Ventriculomegaly can be divided into mild (10–15 mm), moderate (>15 mm with >3 mm of adjacent cortical thickness) (Fig. 16.19), and severe ventriculomegaly (with <2 mm of adjacent cortical thickness) (Fig. 16.20) with increasing ventricular size associated with a poorer prognosis [62]. Corpus callosum anomalies such as a hypoplastic splenium will result in colpocephaly which is disproportionate dilatation of the atria and occipital horns with small frontal horns (Fig. 16.29f). Ventriculomegaly could be the result of an ex vacuo phenomenon secondary to

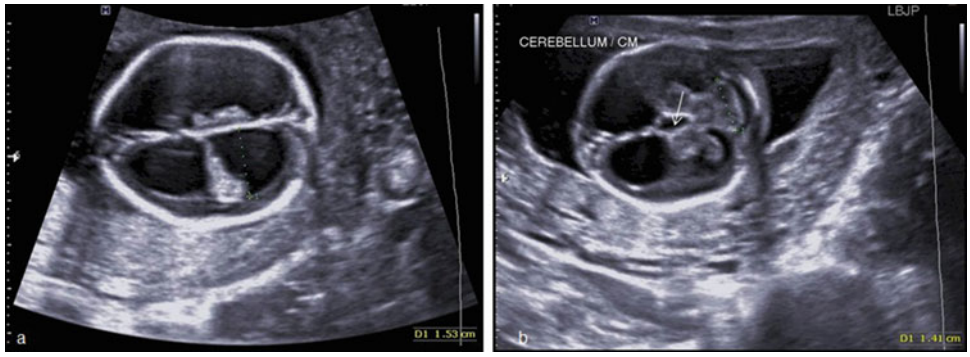


Fig. 16.19 18 week GA US with moderate hydrocephalus. (**a**) Transventricular plane demonstrating enlargement of the lateral ventricles with atrial diameters measuring 15 mm. (**b**) Transcerebellar plane showing enlargement of third ventricle (*arrow*) without enlargement of the fourth ventricle suggesting aqueduct stenosis

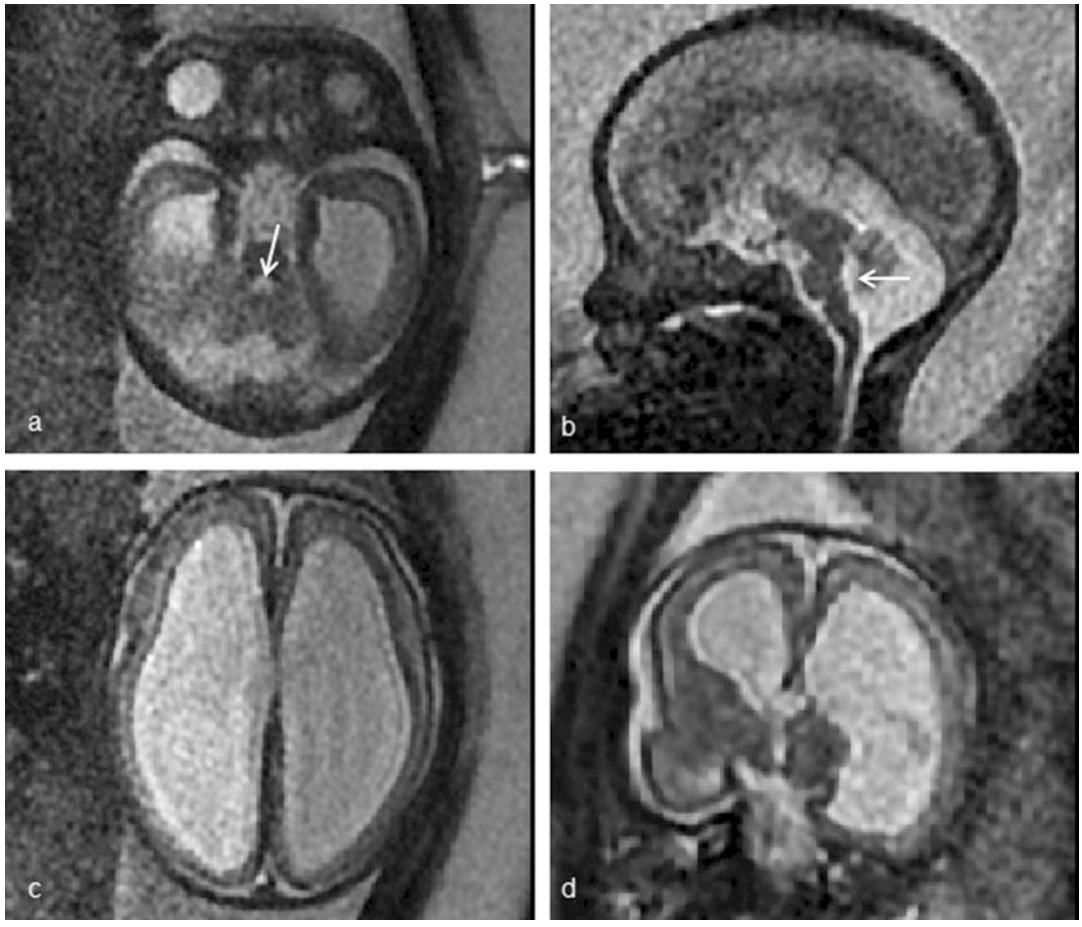


Fig. 16.20 28 week GA MRI with marked hydrocephalus. T2 weighted images in the axial (**a**, **c**), sagittal (**b**), and coronal (**d**) planes. *White arrows* indicate small fourth ventricle consistent with aqueduct stenosis

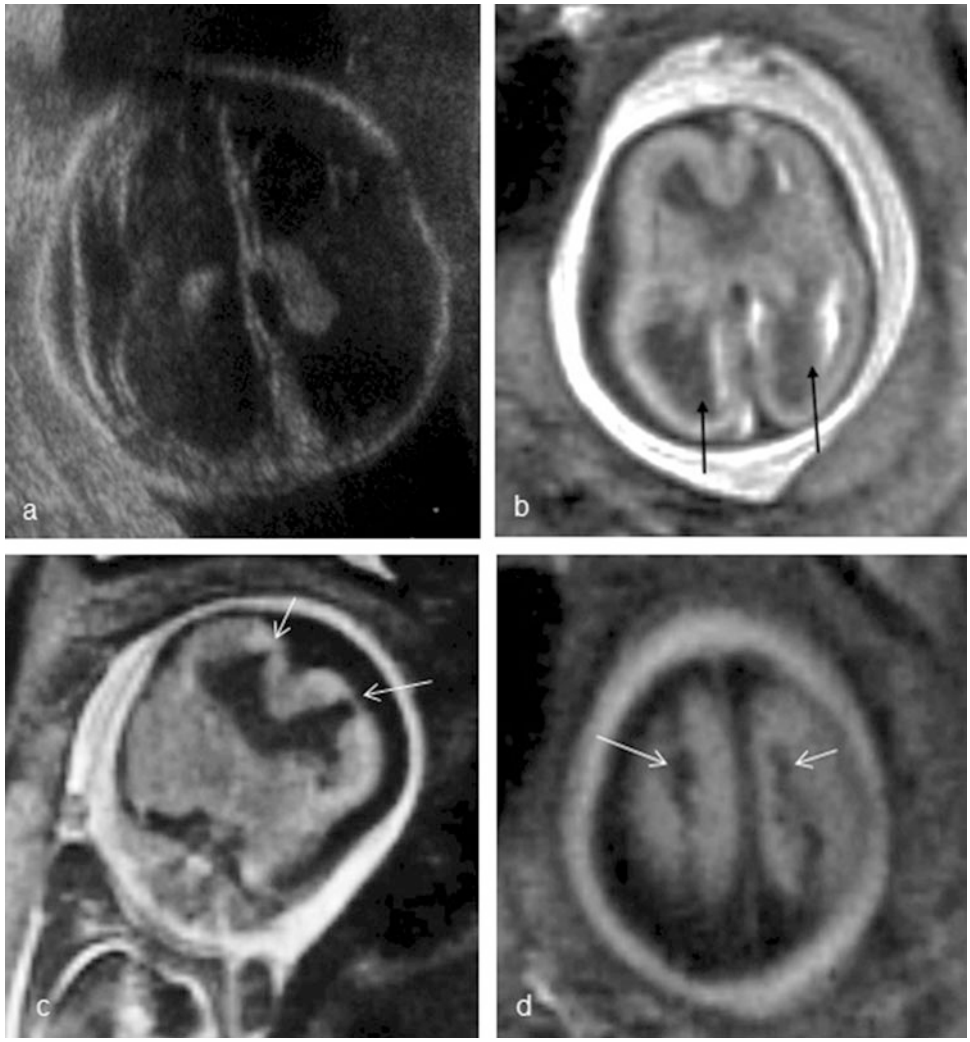


Fig. 16.21 21 week GA fetus. (**a**) US poorly visualizes the ventriculomegaly secondary to intraventricular hemorrhage. This is clearly visualized on (**b**) axial T2 MRI where *black arrows* demonstrate the layering of the hemorrhage in the ventricles. (**c**) Coronal T2 MRI and (**d**) axial T2 MRI demonstrate parasagittal encephaloclastic clefts unsuspected by US

parenchymal hemorrhage, infections, or infarction. It may also be related to hydrocephalus caused by hemorrhage (Fig. 16.21) and CSF obstruction. The prognosis of ventriculomegaly depends on the cause of the ventricular dilatation, the gestational age at which occurs, and its progression; however, neonates with developmental delay can have mild isolated ventriculomegaly in the range of 19–36 % [63].

Up to 80 % of fetuses with ventriculomegaly have additional abnormalities that are detected by prenatal sonography and/or by postnatal evaluation [61, 64, 65].

Fetal MR can detect additional CNS abnormalities not seen on US in up to 50 % of cases of fetal ventriculomegaly [66, 67]. Findings missed on US include developmental abnormalities, such as agenesis of the corpus callosum, cortical malformations, periventricular nodular heterotopia, cerebellar dysplasia, partial agenesis of the septum pellucidum, porencephaly, multicystic encephalomalacia, intraventricular hemorrhage

(Fig. 16.21), and subependymal hemorrhage [66–68]. The destructive lesions are often periventricular areas of T2 hyperintensity, focal defects in the germinal matrix, or larger areas of abnormal signal intensity with or without volume loss involving the overlying cortex (Fig. 16.21). Intraventricular hemorrhage often appears as dark layering in the dependent portion of the ventricle (Fig. 16.22).

In a large study of sonographically isolated ventriculomegaly the incidence of developmental delay was 37% in children with isolated ventriculomegaly, compared with 84% in children in whom additional abnormalities were identified at birth [69]. Variability in the reported neurodevelopmental outcome of fetal isolated mild ventriculomegaly makes counseling these parents a difficult exercise as further discussed in the next chapter.

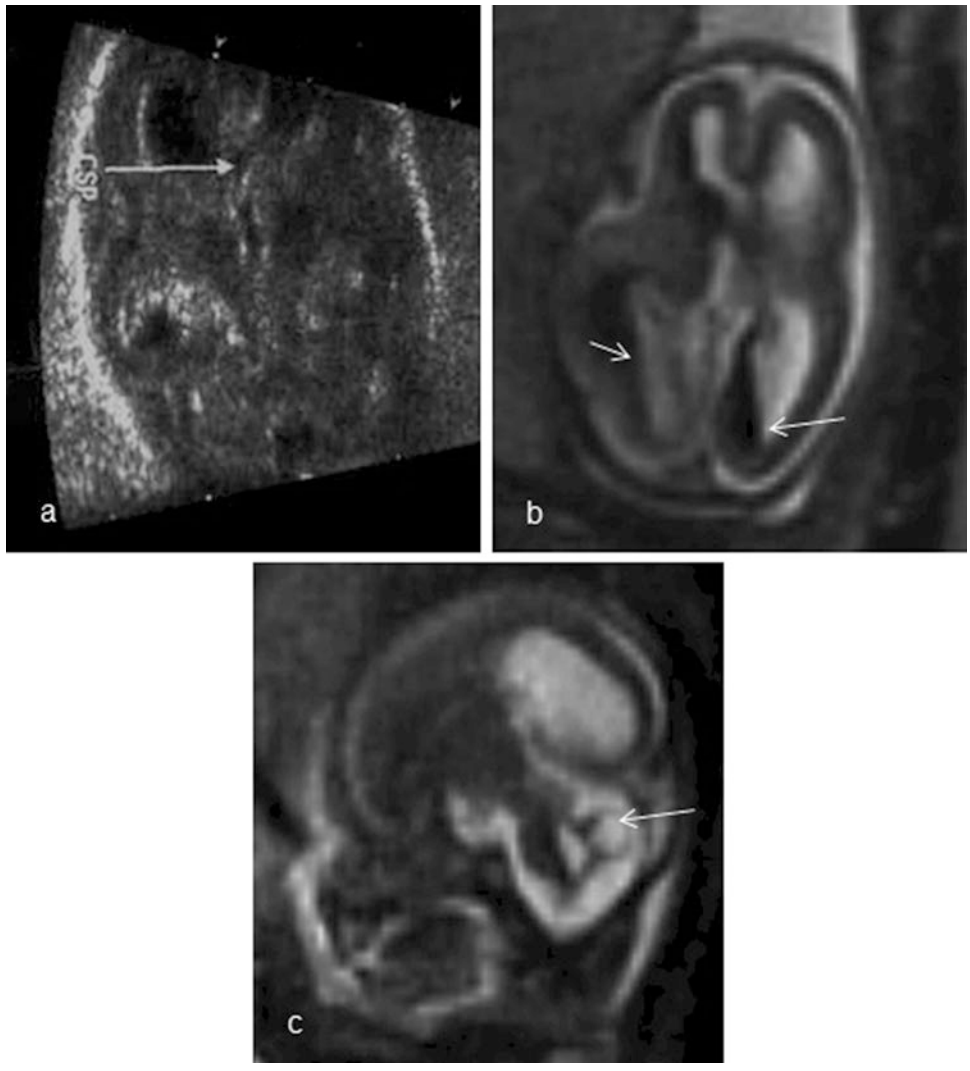


Fig. 16.22 21 week GA fetus. (**a**) US visualizes the ventriculomegaly secondary to intraventricular hemorrhage. *Arrow* indicates the CSP. (**b**) axial T2 MRI and (**d**) coronal T2 MRI show T2 dark blood fluid levels (white arrows). (**c**) sagittal T2 MRI demonstrates the vermian cyst unsuspected by US (*white arrow*)

Aqueductal Stenosis

Stenosis of the aqueduct of Sylvius is a form of obstructive hydrocephalus that can be congenital or acquired. The hallmark is a small fourth ventricle with enlarged third and lateral ventricles on both US and MR (Fig. 16.20). MRI allows direct visualization of the aqueduct and can identify areas of cortical mantle disruption, which also carry a worse prognosis.

Dorsal Induction Malformations/ Neural Tube Defects

Dorsal induction is the process by which there is closure of the neural tube in the area of the brain or spinal cord.

Anencephaly

Due to the rostral neuropore of the neural tube failing to close, no skull develops and the brain is exposed to amniotic fluid in this fatal open neural tube defect. MR is unnecessary as US is highly accurate at diagnosing anencephaly (Figs. 16.23 and 16.24) by 12 weeks [70].

Cephalocele

Encephaloceles are a milder disorder of rostral neural tube closure than anencephaly. Rather than absence of the entire calvarium, there are focal calvarial defects with extracranial herniation of various intracranial structures. The encephalocele is named by location of the skull defect; most are midline and 75 % are occipital in location. Prenatal US typically can define the

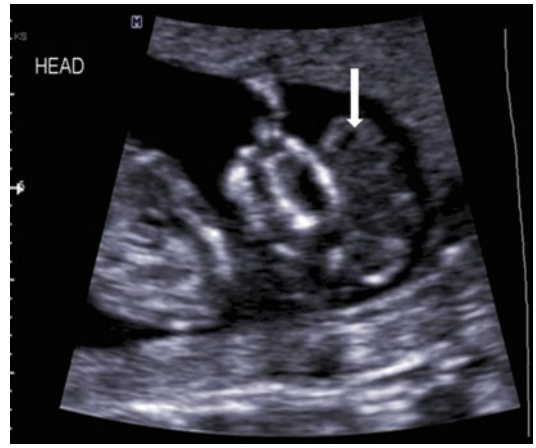


Fig. 16.23 12 week GA fetus US sagittal view. *White arrow* indicates exposed frontal lobes of the brain with no calvarium

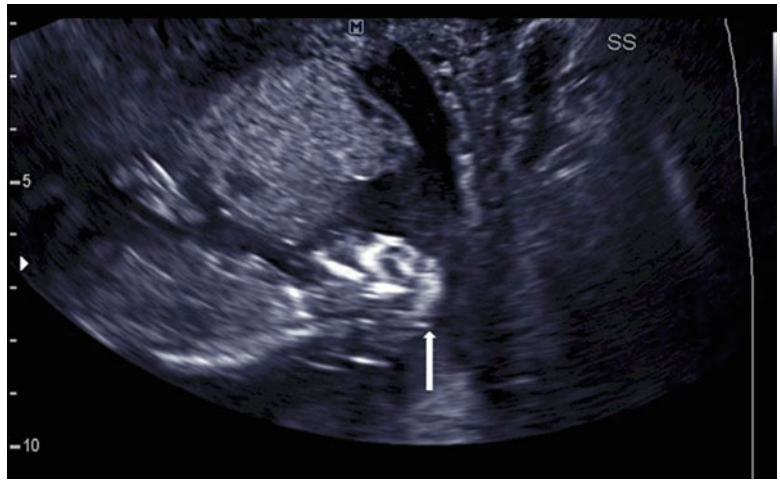


Fig. 16.24 12 week GA fetus US sagittal view. *White arrow* indicates top of the cervical spine with absent cerebral hemispheres consistent with anencephaly

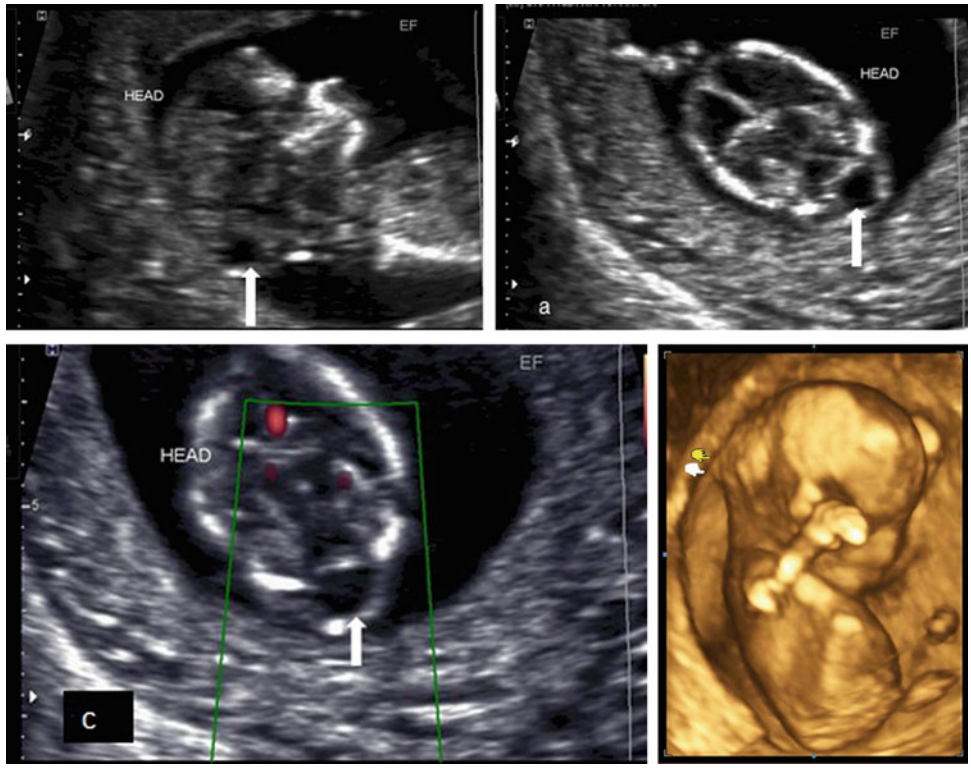


Fig. 16.25 14 week GA fetus US with midline occipital encephalocele (*white arrows*) defined on (**a**) axial US. (**b**) sagittal US and (**c**) axial US with color Doppler. No flow is noted in the encephalocele. (**d**) 3D US where the fingers point to the encephalocele

calvarial deficiency (Figs. 16.25 and 16.26), but with small defects, poor head position, or a nasal cavity herniation it will be difficult to visualize [71]. MR is much better at defining the amount brain in the defect and the associated anomalies of the supratentorial and infratentorial brain than US (Fig. 16.26). The severity of the microcephaly, the amount of herniated brain tissue, and the presence of other intracranial anomalies all negatively influence the outcome [70].

Chiari II

This neural tube defect is thought partly to be the result of a failure of caudal neuropore closure. There are abnormalities at both ends of the neural tube involving the brain and the distal lumbar spine. A small posterior fossa is associated with a myelomeningocele. A Chiari II is delineated on US utilizing the so-called "fruit signs." On US, fetal brain findings include a small biparietal diameter, colpocephaly, and the "banana" sign (Fig. 16.27a) which refers to anterior curvature of the cerebellar hemispheres with loss of the CM because of the small posterior fossa with low tonsils herniating through the enlarged foramen magnum. The second fruit sign, the "lemon sign" (Fig. 16.27b) is a bilateral groove in the frontal bones. The widening of the neural arch with a protruding CSF sac (Fig. 16.28), that identifies the associated spinal dysraphism can be difficult to see on US because of fetal position, but with assessment of the spine in all 3 planes, US detection should approach 100 % [71]. Fetal MRI is also useful at

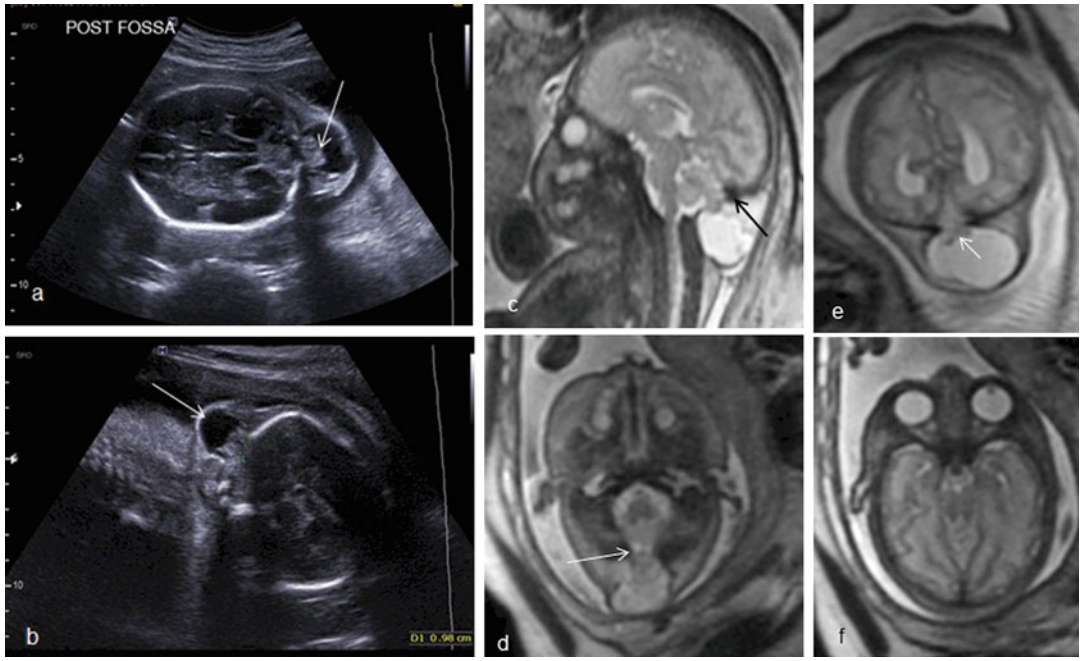


Fig. 16.26 30 week GA fetus US with midline occipital encephalocele defined on (**a**) axial US *white arrows* indicate herniated cerebellar tissue and (**b**) sagittal US where a *white arrow* marks the meningocele component. (**c**) T2 sagittal MR. *Black arrow* indicates the venous torcular with the cephalocele below. (**d**) T2 axial MR. *White arrow* indicates skull defect. (**e**) T2 axial MR. *White arrow* indicates herniated cerebellar tissue. (**f**) T2 axial MR demonstrates the loss of the normal subarachnoid space around the supratentorial brain consistent with microcephaly

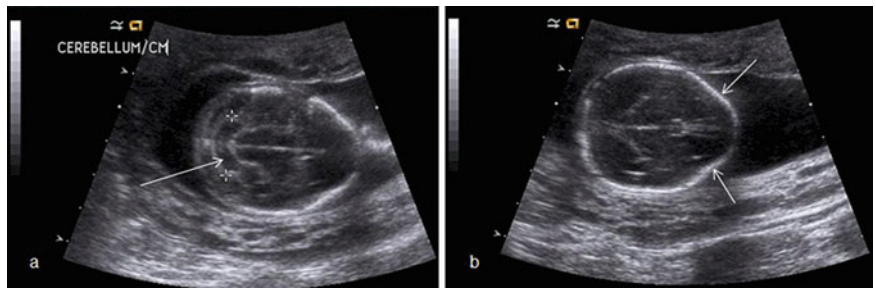


Fig. 16.27 20 weeks G.A. fetus with Chiari II Malformation illustrating the fruit signs. (**a**) Axial transcerebellar US demonstrating the banana sign where the compressed cerebellum in the tight posterior fossa looks like a banana (*white arrow*). (**b**) Axial transthalamic US with the frontal bone demonstrating the bilateral shallow grooves (*white arrows*) consistent with a lemon sign

identifying additional anomalies that can be seen in conjunction with this disorder including callosal dysgenesis, periventricular nodular heterotopia, cerebellar dysplasia, syrinx and cord anomalies such as diastematomyelia [34]. Fetal MRI provides superior assessment of ventriculomegaly and hindbrain herniation at the craniocervical junction (Fig. 16.29) [72].

Ventral (Forebrain) Induction Malformations

The cerebrum, midbrain, cerebellum, lower brainstem, and face form during ventral induction. The important division of the cerebral and cerebellar hemispheres also occurs at this time.

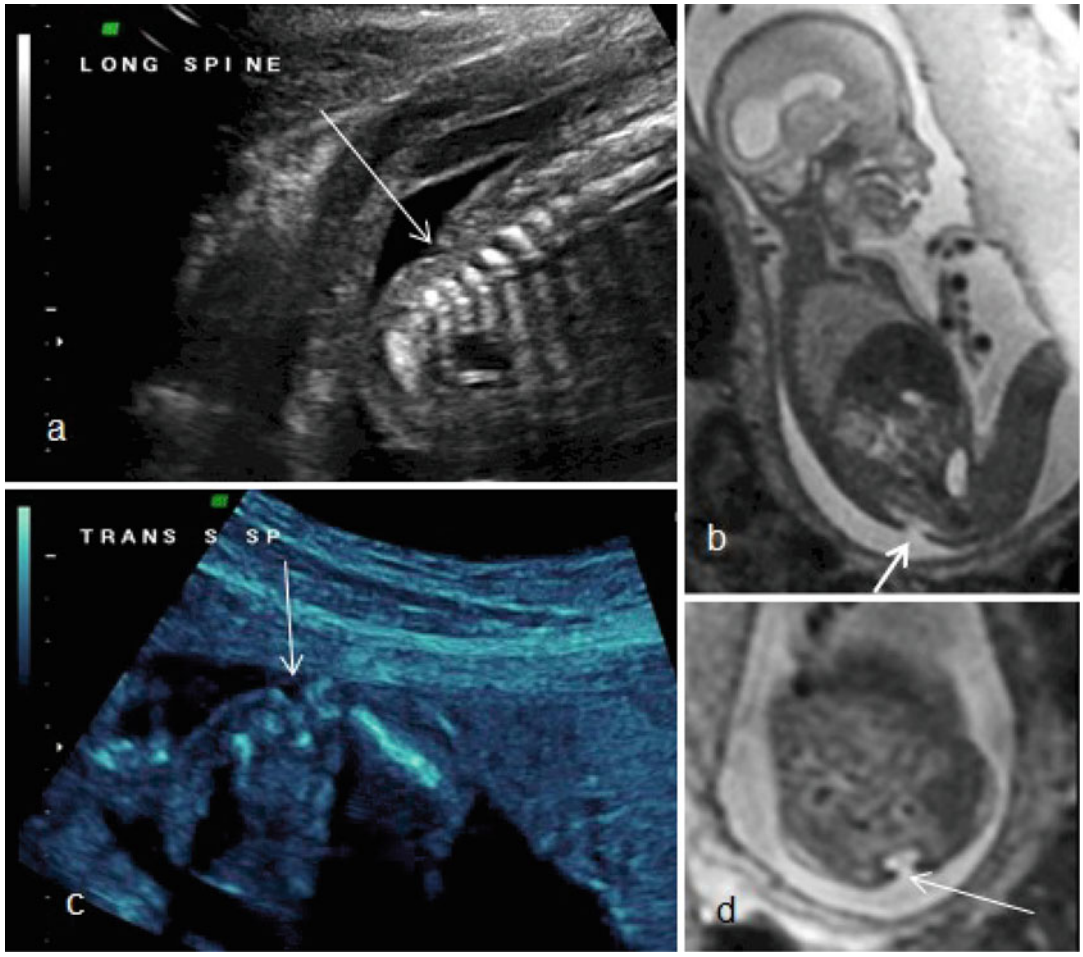


Fig. 16.28 20 weeks GA fetus with Chiari II Malformation. (**a**) sagittal US with corresponding (**b**) sagittal T2 MR. *Arrows* mark the open neural tube defect of the myelomeningocele. (**c**) Axial US with (**d**) axial T2 MR with *arrows* marking the open defect of the myelomeningocele

Holoprosencephaly

Holoprosencephaly results when the separation of the forebrain or telencephalon into the two separate cerebral hemispheres is incomplete. On US and MR, the most severe form, alobar holoprosencephaly, shows absence of the interhemispheric fissure, falx cerebri, corpus callosum, and CSP with a single ventricle and complete thalamic fusion. There is a classic monoventricle which has a boomerang shape with a posterior dorsal cyst which is recognized on US by 12 weeks (Fig. 16.30) and clearly defined by MRI at 20 weeks (Fig. 16.31). Milder forms including semilobar, lobar, and middle interhemispheric types can be difficult to detect on US [39] and MRI is more helpful as its spatial resolution and soft tissue contrast can easily allow visualization of the entire interhemispheric fissure, corpus callosum, and deep structures of the brain.

Corpus Callosum Abnormalities

The corpus callosum is the largest of the 3 commissures that connect the cerebral hemispheres and its axons cross the midline between gestational weeks 8 and 20. Developmental abnormal-

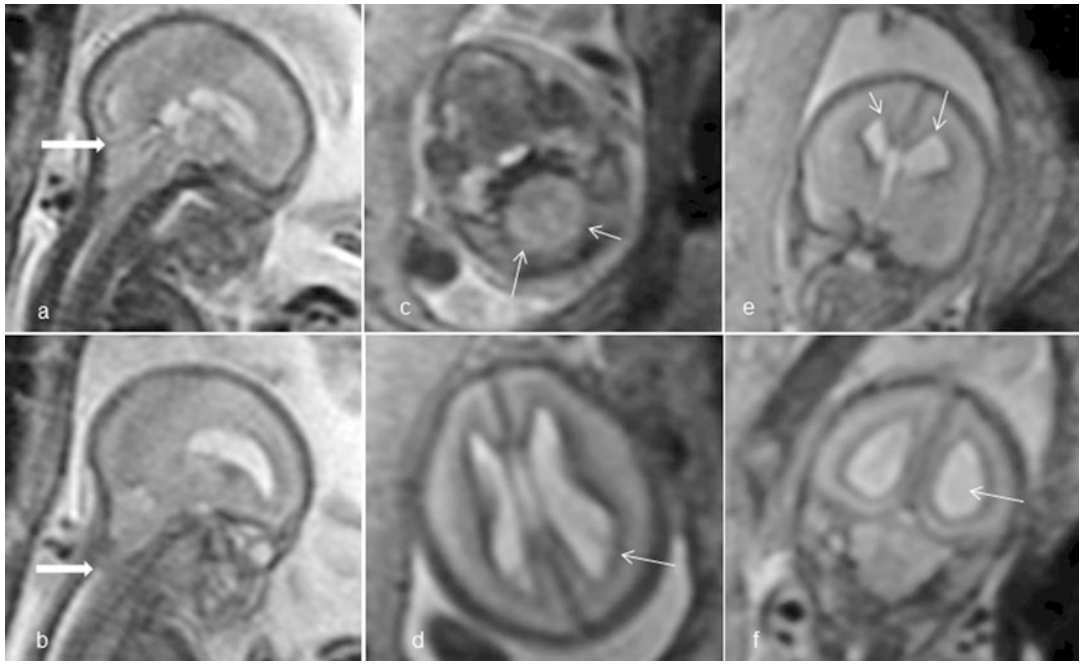


Fig. 16.29 20 weeks G.A. fetus with Chiari II Malformation. (**a**) Sagittal T2 MR with a *white arrow* marking the low insertion of the tentorium cerebelli creating a small posterior fossa. (**b**) Sagittal T2 MR with a *white arrow* showing herniation of the cerebellar tonsils through the foramen magnum. (**c**) Axial T2 MR depicting a large foramen magnum (*white arrows*) with loss of the CSF in the CM due to low cerebellar tonsils. (**d**) Axial T2 MR showing dilated lateral ventricles with colpocephaly (*arrow*) typical of a Chiari II due to hypoplasia of the splenium. (**e**) Coronal T2 MR showing blunting of the frontal horns of the lateral ventricles (*arrows*). (**f**) Coronal T2 MR with colpocephaly with enlargement of the atria of the lateral ventricles (*arrow*)

ities of the corpus callosum include complete agenesis (Fig. 16.32), hypogenesis (or partial agenesis Fig. 16.33), dysgenesis, hypoplasia, and destruction. The incidence of callosal agenesis has been estimated at 0.2–0.7 % in the general population and 3 % in mentally disabled patients [73]. Nearly 85 % are associated with other brain abnormalities producing variable neurologic symptoms, including developmental delay, cognitive impairment, and epilepsy. 62 % of callosal disorders will also have extracranial anomalies at autopsy [74]. Brain abnormalities seen in association with callosal agenesis include arachnoid cysts, Aicardi syndrome, Chiari II malformation, Dandy–Walker malformation, gray matter heterotopia, holoprosencephaly, schizencephaly, and encephaloceles [75]. The greater the number of associated CNS anomalies the poorer the neurodevelopmental outcome [74].

Fetal MRI has the ability to directly visualize the corpus callosum, primarily on the sagittal and coronal planes and is better able to depict associated malformations which are sonographically occult in up to 63 % of fetal callosal abnormalities [76]. Fetal MR imaging has both a greater sensitivity and specificity for callosal anomalies than US. MR will identify a normal corpus callosum in approximately 20 % of cases referred for an US callosal abnormality and additional findings are found on MR in 25 % of callosal agenesis cases (Fig. 16.34) [76].

Posterior Fossa Anomalies

Dandy–Walker Continuum

The Dandy–Walker continuum includes classic Dandy–Walker malformation (DWM), Dandy–Walker variant (vermian hypoplasia), mega CM, and persistent Blake pouch cyst [54].

Classic DWM on prenatal US and MRI comprises complete or partial vermian agenesis,

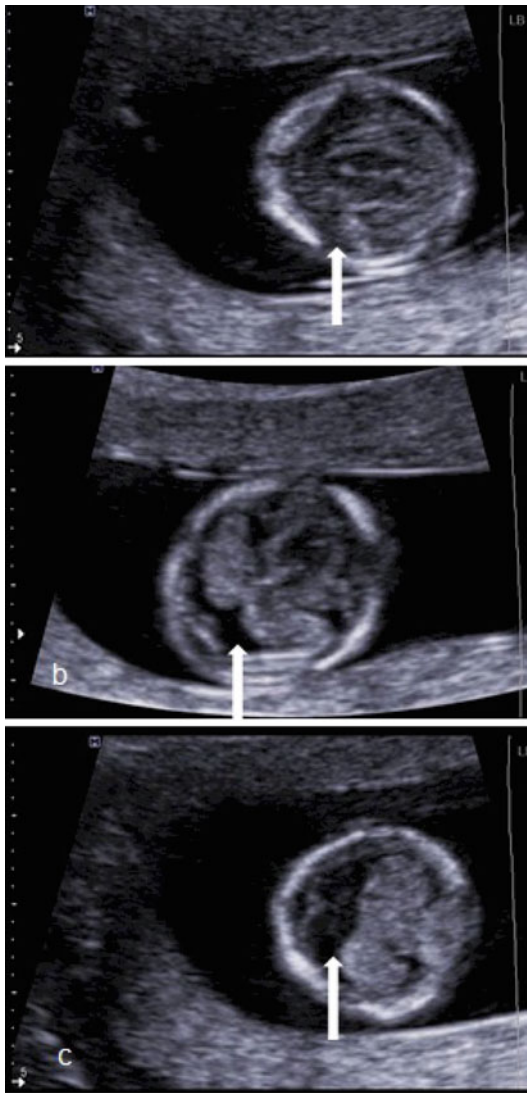


Fig. 16.30 12 weeks GA fetus with alobar holoprosencephaly on transaxial 2D US. (**a**) transventricular, (**b**) transthalamic, and (**c**) transcerebellar levels. *Arrow* marks the monoventricle

cystic dilatation of the fourth ventricle, and enlargement of the posterior fossa, with elevation of the transverse sinus, tentorium, and torcular (torcular–lambdoid inversion). On US, the diagnosis of DWM is suggested in the presence of a posterior fossa cyst, elevated tentorium, and lack of visualization of the cerebellar vermis (Fig. 16.35). However, evaluation of the posterior fossa, fourth ventricle, vermis, and cerebellum can be difficult to see with US. Fetal MRI is excellent at depicting shape and size of the vermis and brainstem and demonstrating the relationship of the cystic formation with the fourth ventricle. It also can directly identify hypoplasia of the brainstem/pons and abnormal vermian fissure anatomy indicating a poorer outcome [54]. Nearly 70 % of patients with DWM have associated supratentorial malformations, and up to 50 % have extra-cranial anomalies [77]. The additional common associated CNS anomalies include hydrocephalus, agenesis of the corpus callosum, polymicrogyria, neuronal heterotopia, and occipital encephaloceles all associated with a poorer neurologic outcome [78].

Although sonography can easily identify severe Dandy–Walker malformations, it can be more limited in distinguishing mild forms of vermian hypoplasia from a mega cisterna magna or an arachnoid cyst. The diagnosis of vermian hypoplasia on US can be identified only after 20 weeks gestation by an increase in size of the CM and abnormal communication of the fourth ventricle with the CM (Fig. 16.36). When the abnormality is seen on US, the finding should be confirmed on a midline sagittal slice, which can be difficult to obtain, especially late in pregnancy or with unfavorable fetal position. The identification of an intact vermis can help to differentiate between a Dandy–Walker variant and a mega cisterna magna.

Mega CM is a normal anatomical variant, and it is therefore important to discriminate from other posterior fossa pathologies. Fetal MRI can exclude a malformation of the posterior fossa by documenting an intact vermis in absence of other anomalies.

Mass effect on normal adjacent brain and displacement of a normal vermis might be clues to this diagnosis [52].

Malformations of Cortical Development (MCD)

MCD affect neuronal development during proliferation, migration and cellular organization. These include classic malformations like lissencephaly where the cortex is thickened and smooth

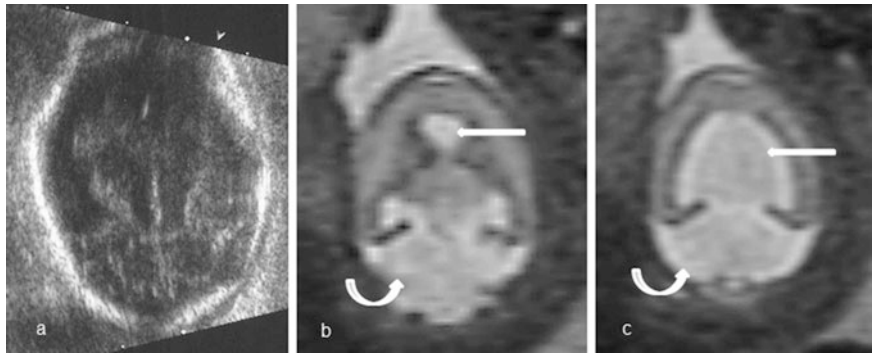


Fig. 16.31 20 weeks GA fetus with alobar holoprosencephaly (**a**) transaxial US. (**b**) T2 axial MR at level of temporal horns. (**c**) T2 axial MR at level of lateral ventricles. *Curved arrow* indicates dorsal cyst and straight arrow indicates monoventricle

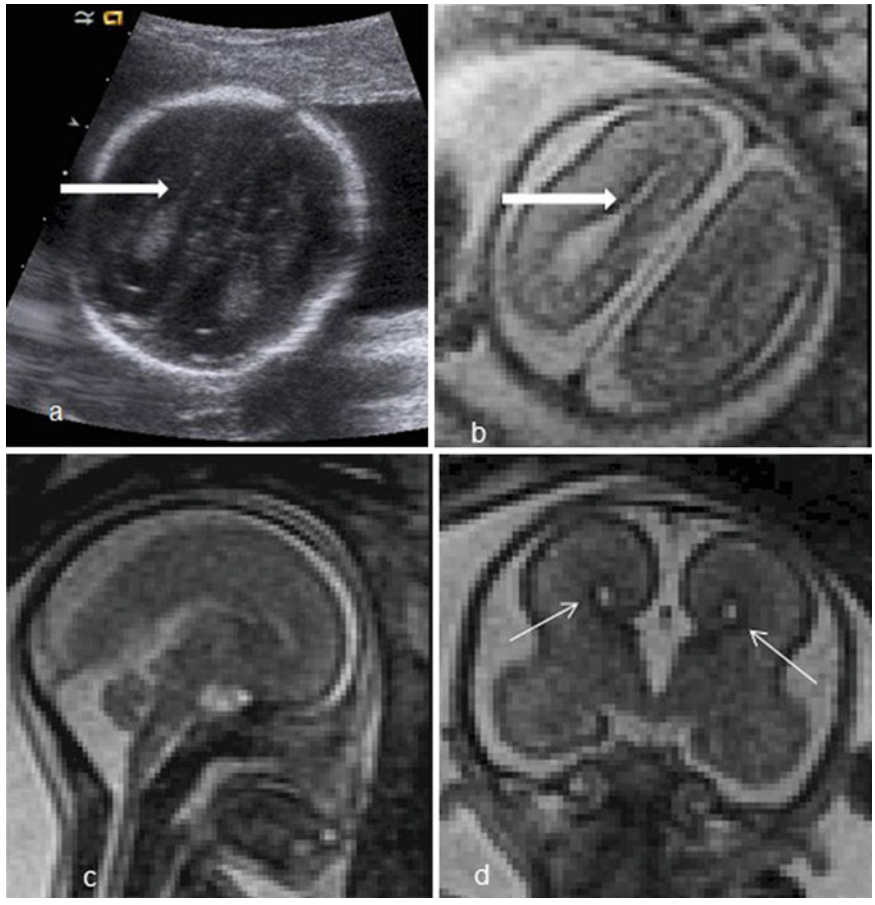


Fig. 16.32 23 week GA fetus with complete agenesis of the corpus callosum. (**a**) axial US and (**b**) T2 axial MR demonstrating the tear shaped lateral ventricles (*arrows*). (**c**) T2 sagittal MR and (**d**) T2 coronal MR demonstrating the steer horn appearance of the frontal horns (*arrows*)

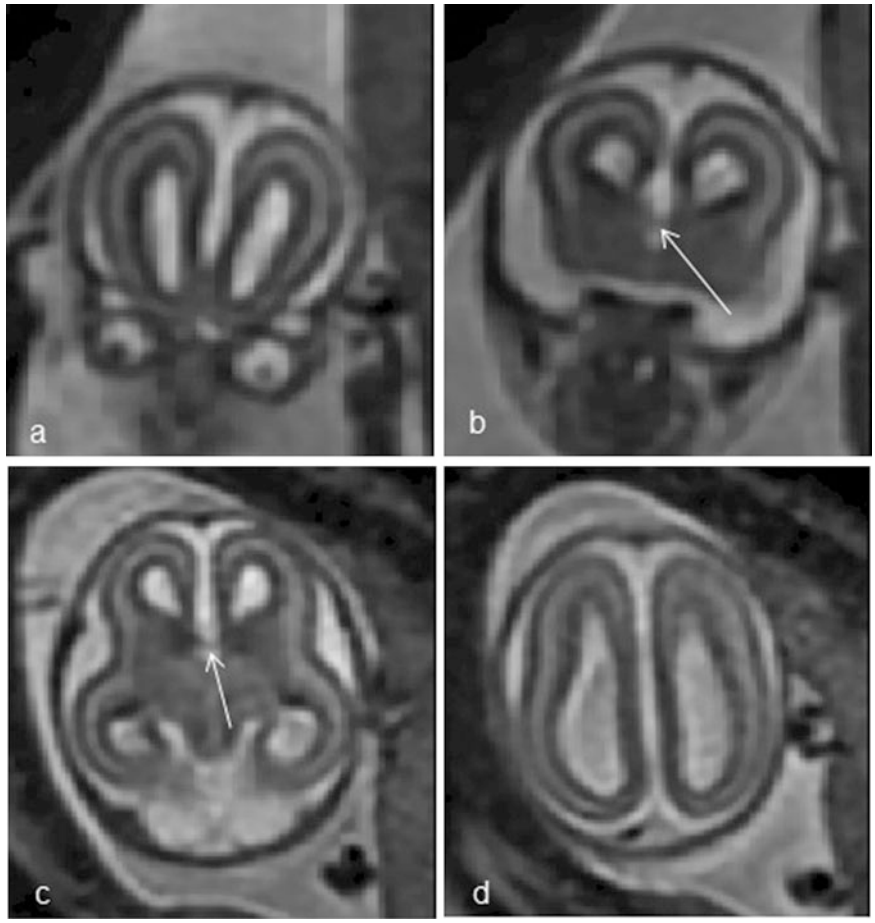


Fig. 16.33 19 weeks GA fetus with partial agenesis of the corpus callosum and absent cavum septum pellucidum. (**a**, **b**) coronal T2 MR. Note the lack of a steer horn appearance of the frontal horns. *Arrow* indicates the hypogenetic crossing fibers of the corpus callosum in (**b**) and (**c**). (**c**, **d**) coronal T2 MR with absent cavum septum pellucidum

and hemimegalencephaly where the entire cerebral hemisphere is enlarged. US can sometimes detect one of the following patterns: delayed appearance of sulcation, a thin and irregular cortical mantle (Fig. 16.37), abnormal overdeveloped sulci and gyri, or wide opening of isolated sulci [79]. However, CMDs are a very difficult prenatal US diagnosis and this is where MR shines with its sensitivity to the brain parenchyma and sulcation. Studies have shown that fetal MR imaging can detect cortical malformations that are not identified on sonography [80].

A simplified gyral pattern or microlissencephaly results in marked neurologic impairment and might result from disturbance in proliferation of the neuroblasts in the germinal zone or excess cellular death [50]. On US, microcephaly will be diagnosed with a cranial diameter 3 standard deviations below the mean [70]. The diagnosis can be confirmed later in pregnancy by MRI (Fig. 16.38). Fetal MRI also identifies encephaloclastic or destructive/ischemic events that could result in microcephaly which has a very poor outcome no matter what the etiology (Fig. 16.39).

Disorders of under migration include type 1 lissencephaly, pachygyria, and heterotopias [81]. Pachygyria has some sulcation and a thinner cortex likely a continuum. On US,

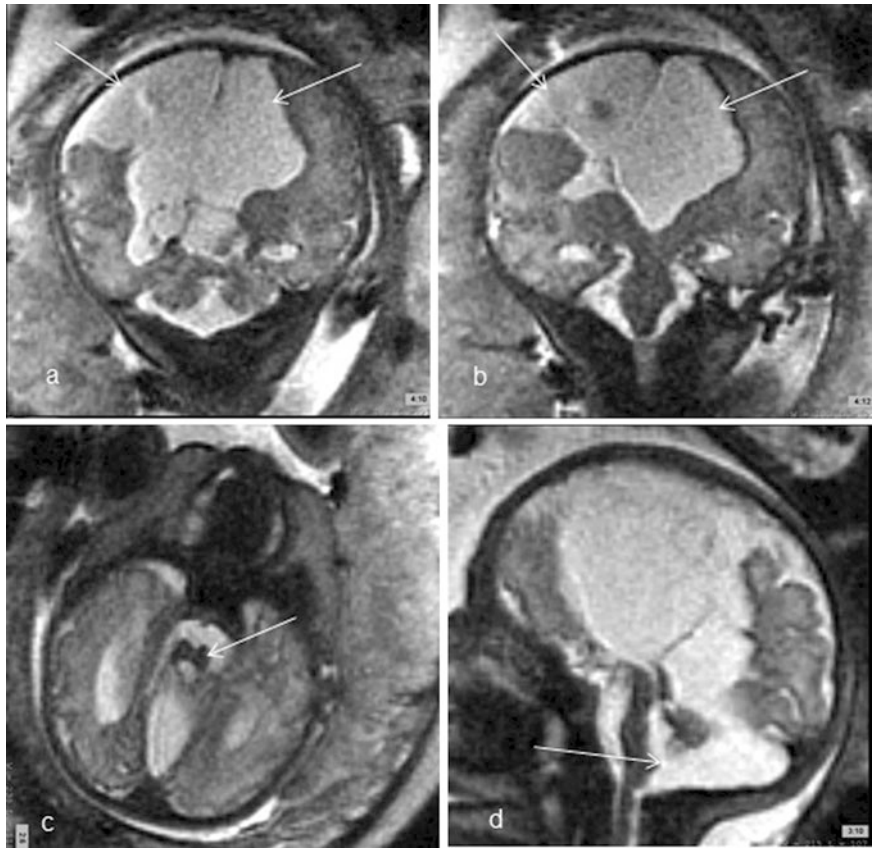


Fig. 16.34 28 weeks GA fetus with agenesis of the corpus callosum (ACC) with an interhemispheric arachnoid cyst, hypoplastic pons and inferior vermian hypoplasia. (**a**, **b**) coronal T2 MR with *arrows* marking the interhemispheric arachnoid cyst. (**c**) axial T2 MR with an *arrow* marking the hypoplastic pons. (**d**) sagittal T2 M with an *arrow* marking the inferior vermian hypoplasia

mild ventriculomegaly, reduction or absence of sulci, and incomplete opercularization of the sylvian fissures can be noted, causing a figure-8 appearance of the brain [40]. Fetal MRI has trouble excluding lissencephaly in early gestation because the brain normally demonstrates a smooth configuration [46] but the non-appearance of the parieto-occipital sulcus by 22–23 weeks will be suggestive.

Subependymal heterotopias appear as nodules that are isointense to the germinal matrix and are located along the ventricular walls (Fig. 16.40) and cannot be distinguished from subependymal nodules seen in tuberous sclerosis. Small nodular areas might be seen along the ventricular wall on US [46]; however, MRI can distinguish the abnormally migrated neuronal cells that demonstrate decreased T2 and increased T1 signal, similar to cortex.

Polymicrogyria is a derangement of the lamination of the deep layers of the cerebral cortex, resulting in numerous small gyri with intervening sulci. Various causes include infections, genetic, hypoxia, and trauma, and the most common location is perisylvian [50]. Fetal MRI will show absence of normal cortical ribbon with abnormal irregular cortex and shallow sulci (Fig. 16.41).

Schizencephaly appears as a gray matter-lined cleft extending from the ventricle to the subarachnoid space. The cleft can be open or closed and is usually lined by gray matter heterotopia and/or polymicrogyria. Prenatal US can identify

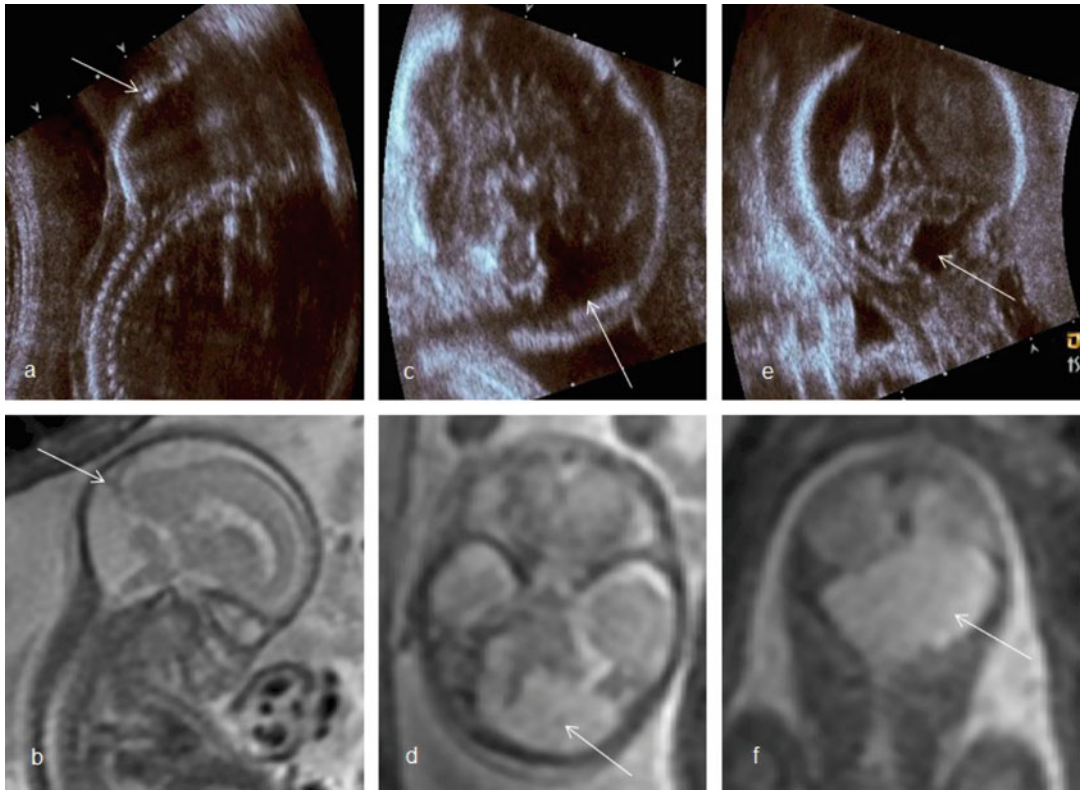


Fig. 16.35 20 weeks GA fetus with Dandy–Walker Malformation with an elevated torcular (*arrows*) on (**a**) sagittal US and (**b**) corresponding sagittal T2 MR. (**c**) axial US with corresponding (**d**) axial T2 MR with *arrows* marking the cystic dilatation of the fourth ventricle. (**e**) Coronal US with corresponding (**f**) coronal T2 MR with *arrows* marking the cystic dilatation of the fourth ventricle

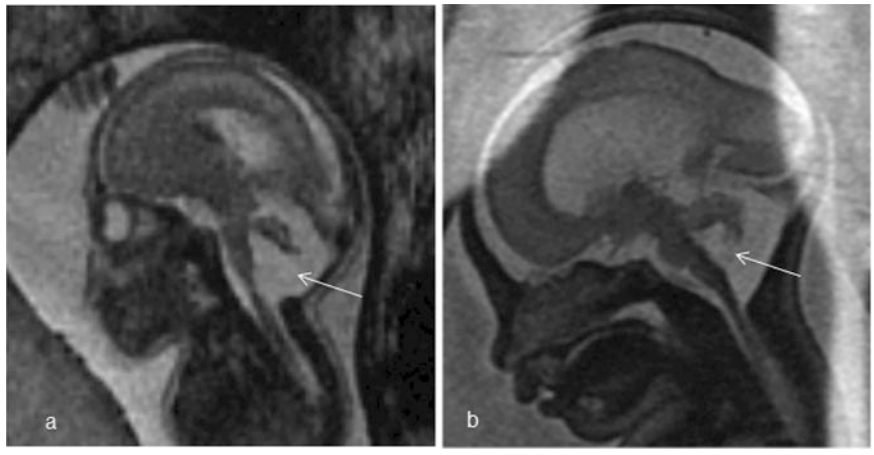


Fig. 16.36 (**a**) Sagittal T2 MR with a hypoplastic brainstem with an *arrow* marking inferior vermian agenesis in a 20 weeks GA fetus. (**b**) Sagittal T2 MR with an *arrow* marking inferior vermian hypoplasia in a 26 weeks GA fetus

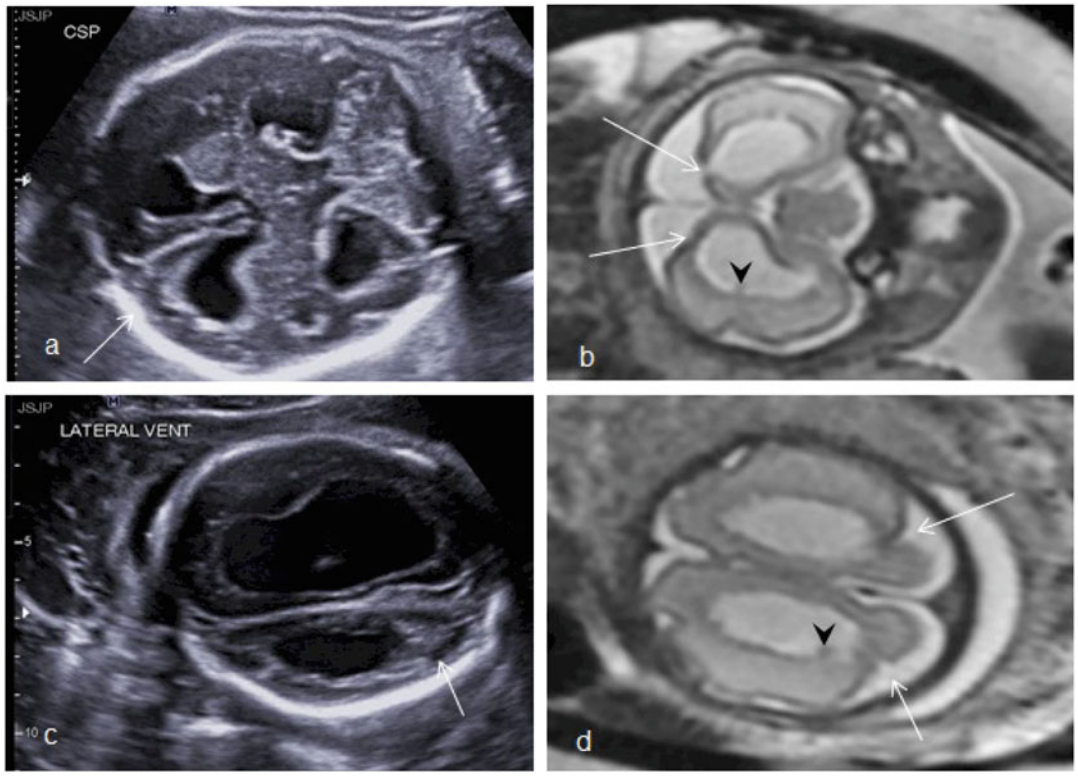


Fig. 16.37 28 weeks GA fetus with ventriculomegaly and bilateral parasagittal cortical irregularities (*arrows*) and subependymal nodules (*arrowheads*) not appreciated on US. (**a**) coronal US and (**b**) coronal T2 MRI. (**c**) axial US and (**d**) axial T2 MRI

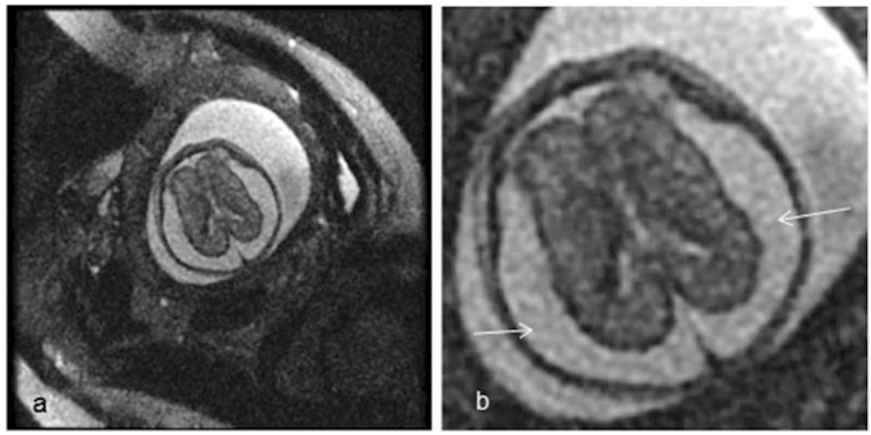


Fig. 16.38 19 weeks GA fetus with microcephaly with a simplified gyral pattern or microlissencephaly. Note the hemispheres do not fill the subarachnoid space (*arrows*) within the calvarium. (**a**) Axial T2 MR. (**b**) Axial T2 MR with magnification

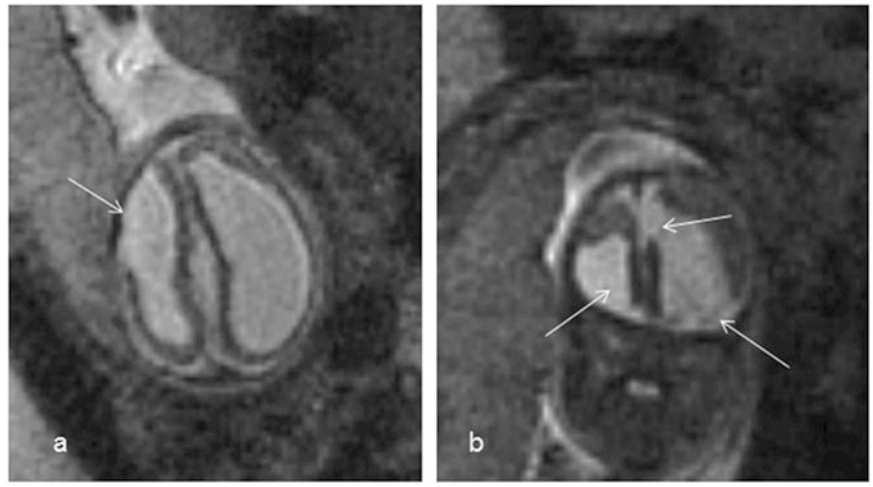


Fig. 16.39 18 weeks GA fetus with encephaloclastic cortical defects (*arrows*) in the cerebral hemispheres and microcephaly. (**a**) axial T2 MR. (**b**) coronal T2 MR

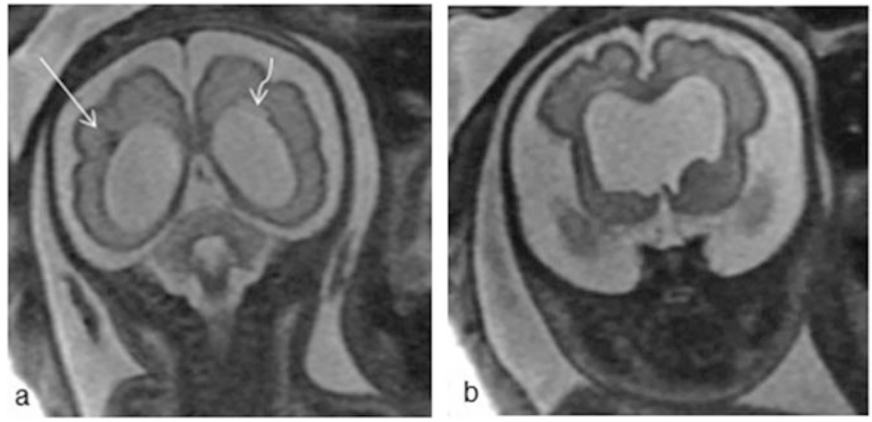


Fig. 16.40 24 weeks GA fetus with a subependymal heterotopia along the ventricular wall (*arrow*), subependymal cyst (*curved arrow*), and an absent cavum septum. (**a**) posterior coronal T2 MR at level of occipital horns. (**b**) anterior coronal T2 MR at level of frontal horns

the cystic space with open lip schizencephaly but other cystic lesions such as porencephaly or an arachnoid cyst may be difficult to differentiate. Fetal MRI demonstrates the abnormal cortex lining the cystic defect or lack of it [82]. In the presence of an absent CSP, septo-optic dysplasia, with hypoplasia of the optic nerves and hypothalamic-pituitary axis should be evaluated via MRI [76].

Monochorionic Twin Pregnancies

Fetal MR imaging is often used to identify parenchymal injury in monochorionic twin pregnancies, which are at increased risk for brain injury [83]. Twin–twin transfusion syndrome (TTTS) is characterized by abnormal blood flow from the smaller donor twin to the

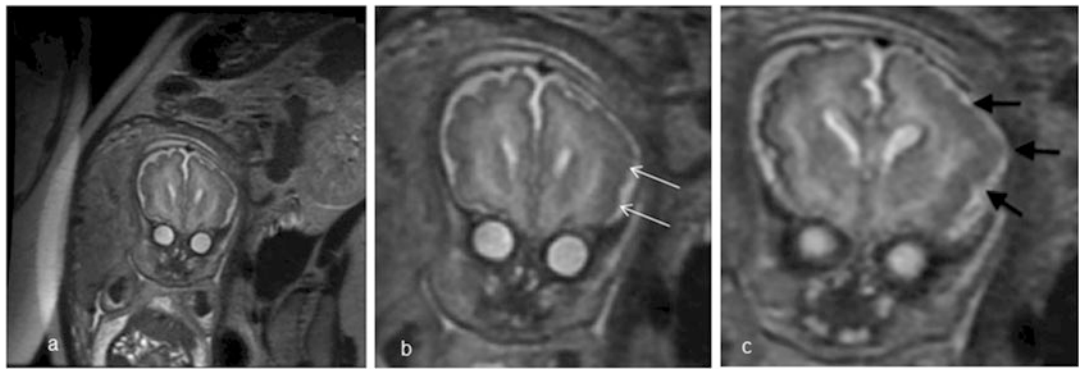


Fig. 16.41 22 weeks GA fetus with polymicrogyria (*arrows*). (**a**) coronal T2 MR. (**b**) coronal T2 MR magnification views. (**c**) coronal T2 MR magnification views

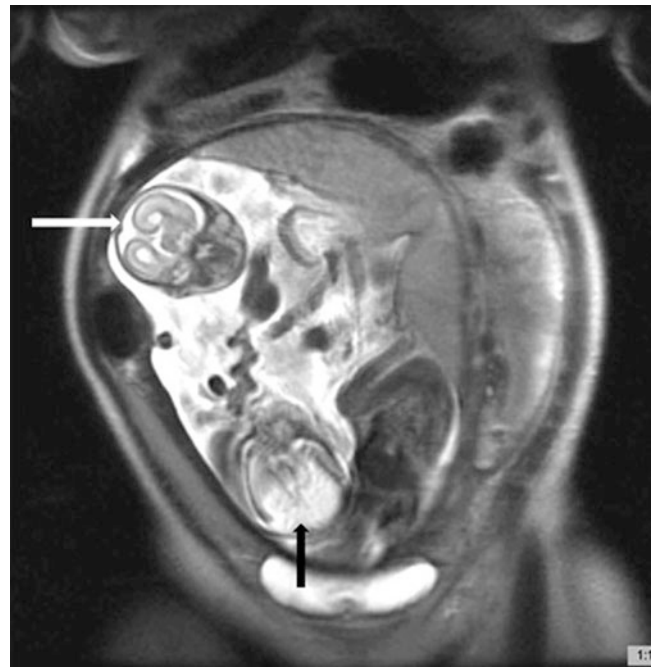


Fig. 16.42 Coronal T2 MRI of 22 weeks GA twin pregnancy. *Black arrow* indicates bilateral occipital lobe loss in cerebral hemispheres of Twin A consistent with ischemia in TTTS with Twin B appearing to have a normal brain (*white arrow*)

larger recipient twin via placental vascular connections. The recipient twin develops polyhydramnios because of volume overload, whereas the donor twin develops oligohydramnios, resulting in a "stuck twin." Approximately half of surviving twins experience neurodevelopmental abnormalities. Due to the high morbidity and mortality of TTTS, fetuses are often imaged to look for any areas of brain injury. Ischemic parenchymal injuries (Fig. 16.42) are seen on fetal MR imaging as focal or diffuse areas of increased T2 signal intensity in the germinal matrix, developing white matter, and/or cerebral cortex. Moreover, ischemic injury can lead to malformations of cortical development, such as polymicrogyria [76].

Conclusion

Understanding the normal development of the brain and spine is essential to diagnosis of prenatal pathology. Prenatal US and fetal MRI are complementary tools with MR the more definitive modality. With an organized approach and knowledge of the normal imaging patterns at each gestational age, the normal and abnormal fetal CNS can be accurately defined.

MR has a great potential for improvement, particularly in acquisition speed. Higher field strengths, stronger gradients, motion compensation techniques, and faster methods of image reconstruction will permit more diagnostic studies on younger fetuses as well as the addition of routine spectroscopy and DTI to the armamentarium. The diagnosis of CNS abnormalities should occur earlier and more accurately in the future.

References

1. Abramowicz JS, Kossoff G, Marsal K, Ter Haar G. Safety statement, 2000 (reconfirmed 2003). International Society of Ultrasound in Obstetrics and Gynecology (ISUOG). Ultrasound Obstet Gynecol. 2003;21:100.
2. Barnewolt CE, Estroff JA. Sonography of the fetal central nervous system. Neuroimaging Clin N Am. 2004;14:255–71.
3. Levine D, Hatabu H, Gaa J, Atkinson MW, Edelman RR. Fetal anatomy revealed with fast MR sequences. AJR Am J Roentgenol. 1996;167:905–8.
4. Breysem L, Bosmans H, Dymarkowski S, et al. The value of fast MR imaging as an adjunct to ultrasound in prenatal diagnosis. Eur Radiol. 2003;13:1538–48.
5. Frates MC, Kumar AJ, Benson CB, Ward VL, Tempany CM. Fetal anomalies: comparison of MR imaging and US for diagnosis. Radiology. 2004;232:398–404.
6. Levine D, Barnes PD, Madsen JR, Abbott J, Mehta T, Edelman RR. Central nervous system abnormalities assessed with prenatal magnetic resonance imaging. Obstet Gynecol. 1999;94:1011–9.
7. Quinn TM, Hubbard AM, Adzick NS. Prenatal magnetic resonance imaging enhances fetal diagnosis. J Pediatr Surg. 1998;33:553–8.
8. Twickler DM, Magee KP, Caire J, Zaretsky M, Fleckenstein JL, Ramus RM. Second-opinion magnetic resonance imaging for suspected fetal central nervous system abnormalities. Am J Obstet Gynecol. 2003;188:492–6.
9. Dietrich RB, Cohen I. Fetal MR imaging. Magn Reson Imaging Clin N Am. 2006;14(4):503–22.
10. Simon EM, Goldstein RB, Coakley FV, et al. Imaging of fetal CNS anomalies in utero. AJNR Am J Neuroradiol. 2000;21:1688–98.
11. Pooh RK, Kurjak A. 3D and 4D sonography and magnetic resonance in the assessment of normal and abnormal CNS development: alternative or complementary. J Perinat Med. 2011;39:3–13.
12. Goncalves LF, Lee W, Espinoza J, et al. Three- and 4-dimensional ultrasound in obstetric practice: does it help? J Ultrasound Med. 2005;24:1599–624.
13. Malinger G, Ben-Sira L, Lev D, Ben-Aroya Z, Kidron D, Lerman-Sagie T. Fetal brain imaging: a comparison between magnetic resonance imaging and dedicated neurosonography. Ultrasound Obstet Gynecol. 2004;23:333–40.
14. Behairy NH, Talaat S, Saleem SN, El-Raouf MA. Magnetic resonance imaging in fetal anomalies: what does it add to 3D and 4D US? Eur J Radiol. 2010;74(1):250–5.
15. Revel MP, Pons JC, Lelaidier C, et al. Magnetic resonance imaging of the fetus: a study of 20 cases performed without curarization. Prenat Diagn. 1993;13:775–99.
16. Fitzmorris-Glass R, Mattrey RF, Cantrell CJ. Magnetic resonance imaging as an adjunct to ultrasound in oligohydramnios. Detection of sirenomelia. J Ultrasound Med. 1989;8:159–62.
17. Brunel H, Girard N, Confort-Gouny S, et al. Fetal brain injury. J Neuroradiol. 2004;31:123–37.
18. Girard N, Raybaud C, Gambarelli D, et al. Fetal brain MR imaging. Magn Reson Imaging Clin N Am. 2001;9(1):19–56.
19. Beuls EA, Vanormelingen L, van Aalst J, et al. In vitro high-field magnetic resonance imaging-documented anatomy of a fetal myelomeningocele at 20 weeks' gestation. A contribution to the rationale of intrauterine surgical repair of spina bifida. J Neurosurg. 2003;98:210–4.
20. Hedrick HL, Flake AW, Crombleholme TM, et al. Sacrococcygeal teratoma: prenatal assessment, fetal intervention, and outcome. J Pediatr Surg. 2004;39:430–8. discussion 430-438.
21. Coakley FV. Role of magnetic resonance imaging in fetal surgery. Top Magn Reson Imaging. 2001;12:39–51.
22. Shellock FG, Crues JV. MR procedures: biologic effects, safety, and patient care. Radiology. 2004; 232:635–52.
23. Kanal E, Gillen J, Evans JA, Savitz DA, Shellock FG. Survey of reproductive health among female MR workers. Radiology. 1993;187:395–9.
24. Chew S, Ahmadi A, Goh PS, Foong LC. The effects of 1.5T magnetic resonance imaging on early murine in-vitro embryo development. J Magn Reson Imaging. 2001;13:417–20.

25. Baker PN, Johnson IR, Harvey PR, Gowland PA, Mansfield P. A three-year follow-up of children imaged in utero with echo-planar magnetic resonance. Am J Obstet Gynecol. 1994;170:32–3.
26. Clements H, Duncan KR, Fielding K, Gowland PA, Johnson IR, Baker PN. Infants exposed to MRI in utero have a normal paediatric assessment at 9 months of age. Br J Radiol. 2000;73:190–4.
27. Kok RD, de Vries MM, Heerschap A, van den Berg PP. Absence of harmful effects of magnetic resonance exposure at 1.5 T in utero during the third trimester of pregnancy: a follow-up study. Magn Reson Imaging. 2004;22:851–4.
28. Levine D, Zuo C, Faro CB, Chen Q. Potential heating effect in the gravid uterus during MR HASTE imaging. J Magn Reson Imaging. 2001;13:856–61.
29. Glover P, Hykin J, Gowland P, Wright J, Johnson I, Mansfield P. An assessment of the intrauterine sound intensity level during obstetric echo-planar magnetic resonance imaging. Br J Radiol. 1995;68:1090–4.
30. Vadeyar SH, Moore RJ, Strachan BK, Gowland PA, Shakespeare SA, James DK, Johnson IR, Baker PN. Effect of fetal magnetic resonance imaging on fetal heart rate patterns. Am J Obstet Gynecol. 2000;182(3):666–9.
31. Wald NJ. Prenatal screening for open neural tube effects and Down syndrome: three decades of progress. Prenatal Diagn. 2010;30(7):619–21.
32. Pooh RK, Kurjak A. 3D/4D sonography moved prenatal diagnosis of fetal anomalies from the second to the first trimester of pregnancy. J Matern Fetal Neonatal Med. 2012;25:433–55.
33. Angtuaco TL. Ultrasound imaging of fetal brain abnormalities: three essential anatomical levels. Ultrasound Q. 2005;21:287–94.
34. Glenn OA, Barkovich AJ. Magnetic resonance imaging of the fetal brain and spine: an increasingly important tool in prenatal diagnosis—Part 1. AJNR Am J Neuroradiol. 2006;27:1604–11.
35. Baldoli C, Righini A, Parazzini C, Scotti G, Triulzi F. Demonstration of acute ischemic lesions in the fetal brain by diffusion magnetic resonance imaging. Ann Neurol. 2002;52:243–6.
36. Brugger PC, Stuhr F, Lindner C, Prayer D. Methods of fetal MR: beyond T2-weighted imaging. Eur J Radiol. 2006;57:172–81.
37. Volpe JJ. Overview: normal and abnormal human brain development. Ment Retard Dev Disabil Res Rev. 2000;6(1):1–5.
38. Winter TC, Kennedy AM, Byrne J, et al. The cavum septi pellucidi: why is it important? J Ultrasound Med. 2010;29:427–44.
39. Monteagudo A, Timor-Tritsch IE. Development of fetal gyri, sulci and fissures: a transvaginal sonography study. Ultrasound Obstet Gynecol. 1997;9:222–8.
40. Ghai S, Fong KW, Toi A, et al. Prenatal US and MR imaging findings of lissencephaly: review of fetal cerebral sulcal development. Radiographics. 2006;26:389–405.
41. Serhatlioglu S, Kocakoc E, Kiris A, et al. Sonographic measurement of the fetal cerebellum, cisterna magna, and cavum septum pellucidum in normal fetuses in the second and third trimesters of pregnancy. J Clin Ultrasound. 2003;31:194–200.
42. Babcook CJ, Chong BW, Salamat MS, et al. Sonographic anatomy of the developing cerebellum: normal embryology can resemble pathology. AJR Am J Roentgenol. 1996;166:427–33.
43. Monteaguodo A, Timor-Tritsch IE. Ultrasound of the fetal brain. Ultrasound Clin. 2007;2:1–34.
44. Benacerraf B, Shipp T, Bromley B. Three dimensional US of the fetus; volume imaging. Radiology. 2006;238:988–96.
45. Budorick NE, Pretorius DH, Grafe MR, et al. Ossification of the fetal spine. Radiology. 1991;181:561–5.
46. Fogliarini C, Chaumoitre K, Chapon F, et al. Assessment of cortical maturation with prenatal MRI: Part 1—normal cortical maturation. Eur Radiol. 2005;15:1671–85.
47. Kostovic I, Judas M, Rados M, et al. Laminar organization of the human fetal cerebrum revealed by histochemical markers and magnetic resonance imaging. Cereb Cortex. 2002;12:536–44.
48. Girard N, Raybaud C, Poncet M. In vivo MR study of brain maturation in normal fetuses. AJNR Am J Neuroradiol. 1995;16:407–13.
49. Levine D, Barnes PD. Cortical maturation in normal and abnormal fetuses as assessed with prenatal MR imaging. Radiology. 1999;210:751–8.
50. Garel C. The role of MRI in the evaluation of the fetal brain with an emphasis on biometry, gyration and parenchyma. Pediatr Radiol. 2004;34:694–9.
51. Huisman TAG. Fetal magnetic resonance imaging. Semin Roentgenol. 2008;43:314–36.
52. Robinson AJ, Goldstein R. The cisterna magna septa vestigial remnants of Blake's pouch and a potential new marker for normal development of the rhombencephalon. Am Inst Ultrasound Med. 2007;26:83–95.
53. Adamsbaum C, Moutard ML, Andre C, et al. MRI of the fetal posterior fossa. Pediatr Radiol. 2005;35: 124–40.
54. Robinson AJ, Blaser S, Toi A, et al. The fetal cerebellar vermis assessment for abnormal development by ultrasonography and magnetic resonance imaging. Ultrasound Q. 2007;23:211–23.
55. Reichel TF, Ramus RM, Caire JT, et al. Fetal central nervous system biometry on MR imaging. AJR Am J Roentgenol. 2003;180:1155–8.
56. Garel C. Fetal cerebral biometry: normal parenchymal findings and ventricular size. Eur Radiol. 2005;15(4):809–13.
57. Parazzini C, et al. Prenatal magnetic resonance imaging: brain normal linear biometric values below 24 gestational weeks. Neuroradiology. 2008;50(10): 877–83.
58. Moreira NC, et al. Measurements of the normal fetal brain at gestation weeks 17 to 23: a MRI study. Neuroradiology. 2011;53(1):43–8.

59. Tortori-Donati P, Rossi A, Cama A. Spinal dysraphism: a review of neuroradiological features with embryological correlations and proposal for a new classification. Neuroradiology. 2000;42:471–91.
60. Achiron R, Schimmel M, Achiron A, et al. Fetal mild idiopathic lateral ventriculomegaly: is there a correlation with fetal trisomy? Ultrasound Obstet Gynecol. 1993;3(2):89–92.
61. Goldstein RB, La Pidus AS, Filly RA, et al. Mild lateral cerebral ventricular dilatation in utero: clinical significance and prognosis. Radiology. 1990;176: 237–42.
62. Weichert J, Hartge D, Krapp M, Germer U, Gembruch U, Axt-Fliedner R. Prevalence, characteristics and perinatal outcome of fetal ventriculomegaly in 29,000 pregnancies followed at a single institution. Fetal Diagn Ther. 2010;27(3):142–8.
63. Bloom SL, Bloom DD, DellaNebbia C, et al. The developmental outcome of children with antenatal mild isolated ventriculomegaly. Obstet Gynecol. 1997;90(1):93–7.
64. Cochrane DD, Myles ST, Nimrod C, et al. Intrauterine hydrocephalus and ventriculomegaly: associated abnormalities and fetal outcome. Can J Neurol Sci. 1985;12:51–9.
65. Gaglioti P, Oberto M, Todros T. The significance of fetal ventriculomegaly: etiology, short- and long-term outcomes. Prenat Diagn. 2009;29(4):381–8.
66. Benacerraf BR, Shipp TD, Bromley B, Levine D. What does magnetic resonance imaging add to the prenatal sonographic diagnosis of ventriculomegaly? J Ultrasound Med. 2007;26:1513–22.
67. Wagenvoort AM, Bekker MN, Go AT, et al. Ultrafast scan magnetic resonance in prenatal diagnosis. Fetal Diagn Ther. 2000;15:364–72.
68. Levine D, Barnes PD, Edelman RR. Obstetric MR imaging. Radiology. 1999;211:609–17.
69. Gupta JK, Bryce FC, Lilford RJ. Management of apparently isolated fetal ventriculomegaly. Obstet Gynecol Surv. 1994;49:716–21.
70. Nyberg DA, McGahan JP, Pretorius DH, et al. Diagnostic imaging of fetal anomalies. Philadelphia, PA: Lippincott Williams & Wilkins; 2003. p. 293–4.
71. Aubry MC, Aubry JP, Dommergues M. Sonographic prenatal diagnosis of central nervous system abnormalities. Childs Nerv Syst. 2003;19:391–402.
72. Ando K, Ishikura R, Ogawa M, Shakudo M, Tanaka H, Minagawa K, et al. MRI tight posterior fossa sign for prenatal diagnosis of Chiari type II malformation. Neuroradiology. 2007;49(12):1033–9.
73. Aicardi J, Chevrie JJ, Baraton J. Agenesis of the corpus callosum. In: Vinken PJ, Bruyn GW, Klawans HL, editors. Handbook of clinical neurology, revised series, vol. 6. New York, NY: Elsevier Science; 1987. p. 149–73.
74. Gupta JK, Lilford RJ. Assessment and management of fetal agenesis of the corpus callosum. Prenat Diagn. 1995;15:310–2.
75. Barkovich AJ, Norman D. Anomalies of the corpus callosum: correlation with further anomalies of the brain. AJNR Am J Neuroradiol. 1988;9:493–501.
76. Glenn OA, Norton ME, Goldstein RB, Barkovich AJ. Prenatal diagnosis of polymicrogyria by fetal magnetic resonance imaging in monochorionic co twin death. J Ultrasound Med. 2005;24:711–6.
77. Sonigo PA, Rypens FF, Carteret M, et al. MR imaging of fetal cerebral anomalies. Pediatr Radiol. 1998;28: 212–22.
78. Klein O, Pierre-Kahn A, Broddaret N, et al. Dandy-Walker malformation: prenatal diagnosis and prognosis. Childs Nerv Syst. 2003;19:484–9.
79. Malinger G, Lev D, Lerman-Sagie T. Normal and abnormal fetal brain development during the third trimester as demonstrated by neurosonography. Eur J Radiol. 2006;57:226–32.
80. Pistorius LR, Hellman PM, Visser GH, et al. Fetal neuroimaging: ultrasound, MRI or both? Obstet Gynecol Surv. 2008;63:733–45.
81. Okamura K, Murotsuki J, Sakai T, Matsumoto K, Shirane R, Yajima A. Prenatal diagnosis of lissencephaly by magnetic resonance image. Fetal Diagn Ther. 1993;8:56–9.
82. Tao G, Yew DT. Magnetic resonance imaging of fetal brain abnormalities. Neuroembryol Aging. 2008; 5:49–55.
83. Hu LS, Caire J, Twickler DM. MR findings of complicated multifetal gestations. Pediatr Radiol. 2006;36: 76–81.

Prenatal Counseling for Fetal Diagnoses

17

Stephen T. Chasen

The first reported case of a prenatally diagnosed fetal structural anomaly was in 1970 when anencephaly in a fetus was detected utilizing ultrasound [1]. Since that time, prenatal diagnosis of many other congenital brain anomalies has been described, with high detection rates reported at experienced centers. The diagnosis and prognosis for the most severe brain anomalies, including anencephaly, acrania, holoprosencephaly, and hydanencephaly, are usually unambiguous. For other conditions, however, the prognosis may be less straightforward, and depends on factors such as the characteristics of the specific lesion, and the presence or absence of associated anomalies. In this chapter we outline advances in the detection of fetal abnormalities and the prenatal counseling process that such findings initiate.

The following factors are important considerations for all fetal anomalies discussed in this chapter:

Ascertainment Bias

For some conditions, such as agenesis of the corpus callosum or inferior vermin agenesis, counseling following prenatal diagnosis of a brain abnormality is complicated by the lack of large studies with long term follow-up of affected fetuses. Counseling parents based on outcomes in children imaged due to developmental delay may not be appropriate, as this cohort would not include children in whom the structural abnormality represented normal variation. If possible, such ascertainment bias can be avoided by providing counseling based on studies describing outcomes of fetuses diagnosed during routine obstetric imaging.

Fetal Behavior

By the second-trimester, evaluation of fetal behavior can provide information about possible neurological dysfunction associated with structural brain abnormalities [2]. Gross body movements should be visible, and normal tone, with flexion–extension movements in the extremities and opening and closing of the hands, can be documented. Fluid should be visible in the fetal stomach ("stomach bubble"), reflecting normal swallowing of amniotic fluid. Absence of movement, joint

S.T. Chasen, M.D. (✉)
Obstetrics and Gynecology, Division of Maternal-Fetal Medicine, Weill Cornell Medical College, 525 East 68th Street, New York, NY 10065, USA
e-mail: stchasen@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_17

contractures, or polyhydramnios with a small or absent stomach bubble can reflect early evidence of neurological dysfunction, and can indicate a poor prognosis.

MRI

Ultrasound is the primary imaging modality in assessment fetal anatomy, and MRI is rarely indicated if ultrasound identifies no abnormalities. When an abnormality of the cranium or brain is suspected, however, MRI can provide crucial diagnostic information [3]. MRI may be particularly valuable in evaluating the cerebral cortex, and can identify abnormalities in neuronal migration earlier and with more precision than ultrasound. Because expertise in fetal MRI is not widespread, referral should be directed towards experienced centers and practitioners.

Genetics

Midline brain abnormalities, such as agenesis of the corpus callosum and abnormalities of the posterior fossa, are often identified as a component of a larger genetic syndrome, including single gene disorders, chromosomal abnormalities, and microdeletions or duplications. For most structural abnormalities, workup should include consultation with a genetic counselor to determine if a fetal genetic evaluation is indicated.

Timing of Prenatal Diagnosis

Diagnosis early in pregnancy is preferable to later diagnosis. Earlier diagnosis provides more time for appropriate workup and transfer of care to an appropriate facility if necessary. For patients who choose to terminate their pregnancy, earlier abortion is generally safer and more readily available [4].

Prior to the second trimester, however, only anencephaly/acrania, alobar or semilobar holoprosencephaly, and large cephaloceles can be reliably diagnosed or excluded with confidence. Ventriculomegaly is unlikely to be apparent prior to the second-trimester, and evaluation of the posterior fossa should generally be deferred until at least 16 weeks of gestation. Microcephaly and cortical dysplasias may not be apparent until late in pregnancy.

Patient Counseling

The objective of counseling after diagnosis of a fetal abnormality is to provide pregnant women with the best information about the prognosis associated with the suspected fetal diagnosis, as well as options for obstetric management. For conditions associated with a significant likelihood of a poor outcome, many reasonable patients will choose abortion. While Maternal-Fetal Medicine specialists may be capable of providing basic information about the management and range of potential outcomes, counseling should be provided by experienced pediatric neurologists and neurosurgeons.

Ventriculomegaly

Ventriculomegaly describes enlarged cerebral ventricles, and includes conditions associated with increased ventricular pressures (hydrocephalus), as well as conditions associated with abnormal cortical development. From early in the second trimester until term, the median atrial diameter is approximately 0.7 cm, with a second standard deviation above the mean of approximately 1.0 cm [5]. Thus, the diagnosis of "ventriculomegaly" can be made if the diameter of one or both atria exceeds 1.0 cm. Rarely, the third ventricle will be dilated but the lateral ventricular dimensions will be normal. Subjectively, the choroid plexus, which typically appears to "fill" the atrium, can appear to be "dangling" [6].

Mild or borderline cerebral ventriculomegaly, with atrial diameters of 1.0–1.2 cm, may represent normal variation. Borderline ventriculomegaly has been associated with higher rates of neurological morbidity, though follow-up studies suggest that most individuals with this isolated

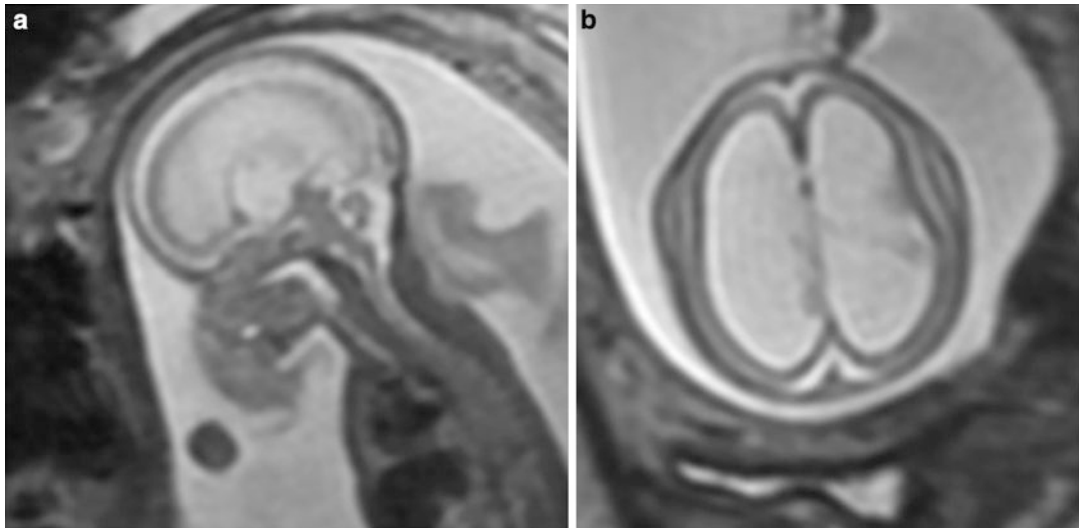


Fig. 17.1 Ventriculomegaly secondary to aqueductal obstruction is manifest in this fetus as triventricular hydrocephalus. (**a**) Sagittal and axial (**b**) views

finding are apparently normal [7, 8]. In general, the rate of poor outcomes increases with increasing degrees of ventriculomegaly, though no degree of ventriculomegaly in itself can exclude the possibility of a good outcome.

Typically, ventriculomegaly due to obstruction is bilateral, with most isolated cases representing aqueductal stenosis (Fig. 17.1). Unilateral ventriculomegaly can represent obstruction of the foramen of Munro. Just as with bilateral borderline ventriculomegaly, borderline unilateral ventriculomegaly as an isolated finding has also been associated with normal outcomes in most cases [9]. A dilated third ventricle without dilation of the lateral ventricles should raise suspicion for partial or complete agenesis of the corpus callosum.

Workup

When fetal ventriculomegaly is diagnosed or suspected, detailed ultrasound to look for associated brain abnormalities as well as extracranial abnormalities is warranted. When severe ventriculomegaly is present (atrial diameter ≥15 mm), the rate of associated abnormalities may be 50 % or greater [10]. Fetal MRI may assist in differentiating ventriculomegaly due to obstruction from cases occurring due to abnormal cortical development, hemorrhage, or abnormal vascular supply. Fetal MRI should be considered in all cases of ventriculomegaly, including those with borderline measurements [11].

Ventriculomegaly, including borderline cases, has been associated with genetic abnormalities, and workup should include karyotype as well as microarray to look for microdeletions and duplications not detectable on karyotype. In a male fetus, findings consistent with aqueductal stenosis may represent X-linked hydrocephalus, and testing for mutations of the L1CAM gene should be included. Toxoplasmosis and cytomegalovirus (CMV) infection are also associated with aqueductal stenosis. While classic features include periventricular calcifications, maternal serology and/or PCR of amniotic fluid for DNA of these agents should be considered for any unexplained cases.

If fetal intracranial hemorrhage is suspected to be the cause of ventriculomegaly, workup should include testing for alloimmune thrombocytopenia, as this condition is known to recur in future pregnancies and maternal medical therapy can prevent catastrophic outcomes [12].

Counseling

In general, the most important factor predicting outcome is whether ventriculomegaly represents obstruction of cerebrospinal fluid, such as aqueductal stenosis, or whether dilation of the ventricles is due to abnormal cortical development or cortical damage from hemorrhage or vascular insufficiency. Lesions occurring due to obstruction are amenable to treatment, and outcomes are variable. If aqueductal stenosis is due to toxoplasmosis or CMV, poor outcomes, including mental retardation and deafness, are more common. X-linked hydrocephalus is also associated with poorer outcomes compared to sporadically occurring aqueductal stenosis.

Ventriculomegaly due to fetal intracranial hemorrhage is associated with high rates of poor prognosis, though this will depend on the size and location of the lesion(s). When ventriculomegaly is due to conditions characterized by abnormal cortical development, the prognosis will be determined by the specific condition, though poor outcomes are very likely.

When borderline ventriculomegaly is isolated and stable, normal outcomes are likely. Studies assessing long term outcome of prenatally diagnosed mild or borderline ventriculomegaly (unilateral or bilateral) suggest low rates of abnormal neurological development [7–9].

If macrocephaly is present, cesarean delivery is usually recommended [13]. Delivery should occur at a facility with an experienced pediatric neurosurgeon, as neonatal transport can delay proper evaluation and management. When ventriculomegaly is severe and/or progressive, delivery as soon as fetal lung maturity can be confirmed may be considered to facilitate earlier postnatal treatment.

Posterior Fossa Abnormalities

Diagnosis

Ultrasound findings associated with abnormalities of the posterior fossa have been described late in the first-trimester or early in the second-trimester [14]. Because of wide variation in the appearance of the developing cerebellum, however, evaluation of the posterior fossa prior to 16 weeks of gestation is not recommended [15, 16].

Dandy–Walker Malformation and Inferior Vermian Agenesis

Dandy–Walker Malformation is characterized by complete or partial absence of the cerebellar vermis, widely splayed cerebellar hemispheres, and an enlarged cisterna magna that is seen communicating with the fourth ventricle (Fig. 17.2). Ventriculomegaly is typically present.

Inferior vermian agenesis, also referred to as a Dandy–Walker Variant, is less likely to be identified than the Dandy–Walker Malformation. The posterior fossa will appear normal in transverse views through the superior portion of the vermis, and the ventricles typically appear normal. Real-time scanning through the entire cerebellum can identify absence of the inferior portion of the vermis, and coronal views can confirm the diagnosis [17].

Workup

Both Dandy–Walker Malformation and inferior vermian agenesis are associated with high rates of associated anatomic and genetic abnormalities. Fetal MRI is recommended to further characterize brain anatomy, including cortical development. Data suggest that the rate of genetic abnormalities may be approximately 50 % or higher, and genetic counseling and amniocentesis are recommended [17, 18].

Prognosis

The prognosis for Dandy–Walker Malformation and inferior vermian agenesis is variable. Because inferior vermian agenesis is less likely to be identified, the true incidence of this condition is unclear, and it is possible that this could represent normal variation in some cases.

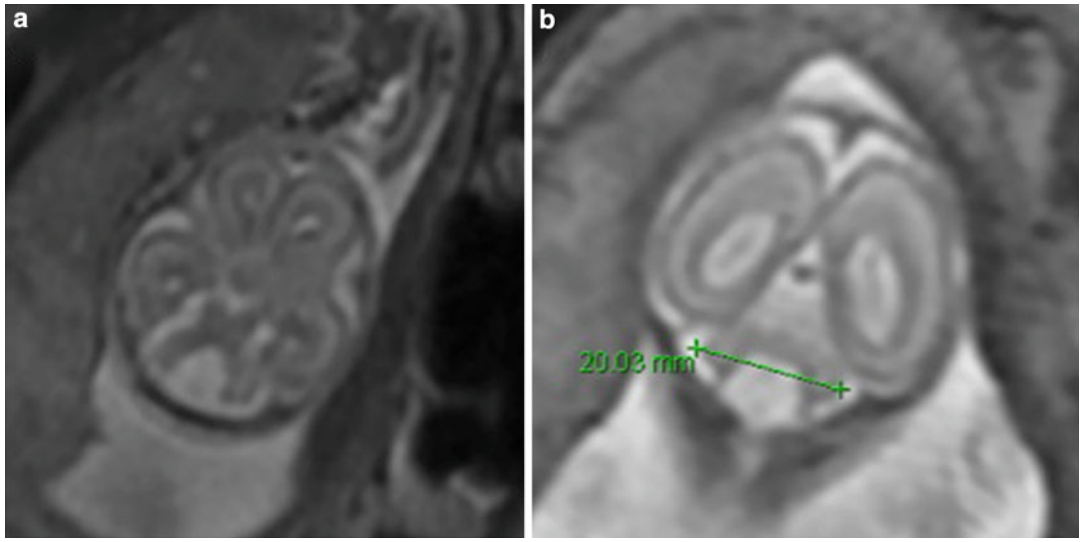


Fig. 17.2 Dandy–Walker Variant (inferior vermian agenesis). Axial (**a**) and coronal (**b**) views demonstrate malformation of the midline posterior fossa structures

Cerebellar Hypoplasia

In the second-trimester, the transverse cerebellar diameter measures approximately 1.0 mm for each week of gestation as measured from the first-day of the last menstrual period [19]. Though this is actually overstates by 2 weeks the time from conception, this method of describing gestational age is standard in the United States. Cerebellar growth is typically maintained in the growth-restricted fetus, and trans-cerebellar diameter has been proposed as an accurate method of estimating gestational age in the second or third trimesters when dating is unclear and growth restriction may be present [20].

Cerebellar hypoplasia as an isolated finding appears to be uncommon, and the prognosis is unclear. As with microcephaly, larger differences between expected and actual measurements are more concerning [18]. A lack of data correlating prenatal findings with long term outcomes precludes providing precise prognostic information.

Obstetric management is usually routine. When hydrocephalus associated with the Dandy–Walker Malformation is present, cesarean delivery may be advised [13].

Cephaloceles

Cephaloceles are defects in the skull through which intracranial tissue can herniate. If only meningeal tissue has herniated, it is referred to as a cranial meningocele. If brain tissue is present within the meningeal sac, it is referred to as an "Encephalocele".

A midline cephalocele in most cases is likely to represent an open neural tube defect affecting the cranium, though this is considerably less common than meningomyelocele or anencephaly. While maternal serum alpha-fetoprotein (MSAFP) may be elevated, lesions are often skin covered and MSAFP screening is less sensitive in detecting cephaloceles compared to spina bifida or anencephaly. Most midline encephaloceles occur in the occipital region (Fig. 17.3). A midline encephalocele in a fetus with polydactyly and cystic kidneys is likely to represent Meckel-Gruber syndrome, a lethal autosomal recessive condition [21].

Non-midline cephaloceles occur sporadically, and are associated with the amniotic band syndrome. Anterior cephaloceles, in which intracranial structures herniate into facial structures, have also been described, though prenatal diagnosis is uncommon [22].

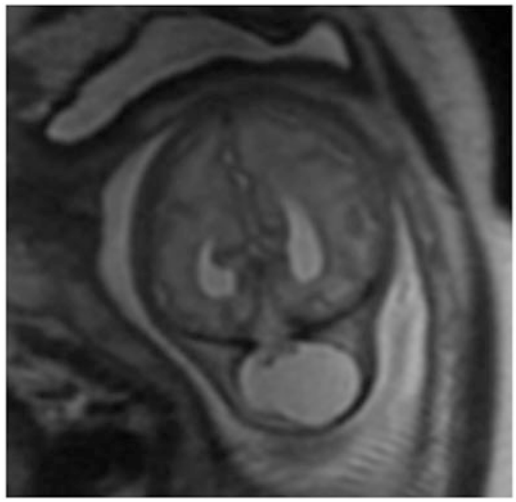


Fig. 17.3 An occipital encephalocoele is demonstrated with herniation of brain and cerebrospinal fluid in communication with the intracranial compartment through a midline defect

Cephaloceles can appear similar to other masses, such as lipomas, teratomas, and hemangiomas. To distinguish a cephalocele from a mass overlying an intact skull, a skull defect must be identified. It is important to not confuse sutures and fontanelles with a pathologic skull defect. Large encephaloceles typically are associated with ventriculomegaly or distortion of brain anatomy. Fetal MRI is very helpful in verifying or ruling out a skull defect when cephalocele is suspected, as well as evaluating associated changes in brain anatomy.

Workup

Detailed anatomic evaluation and fetal MRI are the most important components of evaluation. Isolated midline lesions representing open neural tube defects are rarely associated with abnormal karyotype, though amniocentesis should be considered. Non-midline lesions may be caused by amniotic bands, and ultrasound evaluation should look for evidence of other manifestations, including limb reduction and facial cleft [22].

Counseling

The prognosis will be related to the size, location, and degree of herniation of brain tissue. Cesarean delivery is usually performed to avoid trauma to exposed brain tissue [23].

Chiari II Malformation

The Chiari II Malformation is present in most cases of meningomyelocele. Hindbrain herniation typically causes collapse of the frontal bones and a "lemon-shaped" calvarium in the second-trimester, as well as a "banana-shaped" cerebellum in the second and third trimesters. The cisterna magna will be absent, and ventriculomegaly typically is present [24]. Early in the second-trimester, head measurements will often be small for gestational age, though macrocephaly often occurs later in pregnancy due to progressive ventriculomegaly.

When spina bifida is present, the cranial findings may be more apparent than the spinal defect, and the description of these findings led to a significant increase in the sensitivity of ultrasound in detecting spina bifida. When these findings are present, a thorough evaluation of the fetal spine is obviously important, as spina bifida cannot be diagnosed based on cranial findings alone.

Workup

While most cases of spina bifida occur with a multifactorial etiology, amniocentesis to document a normal karyotype is reasonable. MRI is not necessary to make or confirm the diagnosis, though it may be useful in establishing the level of the spinal lesion with more precision.

Counseling

The prognosis depends on the level of the lesion, and the presence or absence of associated anomalies. Based on the results of a randomized controlled

trial in those with lesions from L1-S1, in utero repair may lead to lower rates of ventriculoperitoneal shunt requirement, and improved motor function early in life [25]. Patients can be made aware of the option of fetal surgery, though any potential fetal benefit must be weighed against the increased risk of maternal morbidity. Cesarean delivery at term is generally recommended, and delivery should occur at a facility in which pediatric neurosurgery is available for early neonatal repair.

Agenesis of the Corpus Callosum

Agenesis of the corpus callosum occurs as a normal variant, and when isolated it can represent an incidental finding. Though the fetal corpus callosum is not routinely imaged sonographically, it can be directly imaged through coronal and sagittal planes. Absence should be suspected in the second or third trimesters when (1) the cavum septum pellucidum is absent; (2) the third ventricle is dilated and appears displaced superiorly; and (3) the anterior horns of the lateral ventricles are narrow and the posterior horns are dilated (colopocephaly), giving the ventricles a "teardrop" shaped configuration [26]. Partial agenesis of the corpus callosum may lack some of these features [27].

Workup

Fetal MRI is important to confirm the diagnosis, and to evaluate cortical development [28]. Since agenesis of the corpus callosum can be a feature of lissencephaly and other syndromes, fetal karyotype and testing for associated mutations is recommended.

Counseling

Based on studies assessing outcomes following prenatal diagnosis of isolated agenesis of the corpus callosum, the majority of affected individuals will have normal development [28]. The prognosis associated with partial agenesis is unclear, though high rates of associated anomalies have been described [27]. Because very poor outcomes have been described in a minority of cases of apparently isolated cases, however, many well informed patients may choose to terminate the pregnancy. In cases with abnormal cortical development, the outcome is likely to be poor.

Microcephaly

Microcephaly means "small head". Clinically, this condition is generally associated with microencephaly (small brain) and abnormal development. While certain structural brain abnormalities, such as holoprosencephaly, are associated with a small head, the diagnosis should be restricted to cases in which the head measurements are the only obvious finding. Prenatal onset can occur as a primary defect, as part of a malformation syndrome, or due to an early insult from infection or teratogenic exposure.

There is no specific cutoff to distinguish a small head due to normal variation and microcephaly. While two-standard deviations (SD) below the mean for gestational age identifies statistical outliers, most fetuses with a head circumference two SDs below the mean are normal. Using a cutoff of three or more SDs below the mean is more specific [29, 30]. If body and limb measurements are in proportion to head measurements, intrauterine growth restriction, rather than microcephaly, is likely.

Subjective findings can include an abnormally shaped calvarium with an abnormal profile in which the forehead appears recessed. In the third-trimester, an abnormal gyral pattern can reflect abnormal cortical development.

Workup

Workup should include genetic testing to determine fetal karyotype as well as microarray. Maternal serology for toxoplasmosis and cytomegalovirus are indicated, and testing for fetal infection can be performed on amniotic fluid if

maternal serology is consistent with recent exposure. Fetal MRI should be performed to evaluate cortical development, as ultrasound often fails to detect cortical abnormalities [30–32].

Counseling

The prognosis will depend on the degree of microcephaly, as well as any associated findings. If microcephaly is associated with genetic abnormalities, in utero infection, or cortical abnormality, the prognosis is likely to be poor. If infectious and genetic workups are negative and MRI identifies no additional abnormalities, the prognosis is likely to correlate with the degree of microcephaly.

Pediatrician's Perspective

As the primary physician for their children, you will often be treated as someone families can rely on for counsel during an ongoing pregnancy. Your advice regarding their unborn child may be sought for this difficult situation.

Finding a fetal central nervous system anomaly raises a wide range of ethical, moral, and very personal decision about how the mother and family would proceed. The ability to better define the anatomy and offer a meaningful prognosis of a fetus through the MRI techniques outlined above may provide a sense of control that otherwise would be absent and help the family through a difficult period.

Referring a family to a center that provides this level of both diagnostic expertise and counseling assistance is crucial, as the window between diagnosis and the ability to electively terminate a pregnancy is very small. Pediatric neurosurgeons may offer counseling as to a typical course of surgical intervention following delivery and suggest a range of neurologic outcomes, though these are often very difficult to predict from radiographic images alone.

References

1. Campbell S, Johnstone FD, Holt EM, May P. Anencephaly: early ultrasonic diagnosis and active management. Lancet. 1972;2(7789):1226–7.
2. Horimoto N, Koyanagi T, Maeda H, Satoh S, Takashima T, Minami T, Nakano H. Can brain impairment be detected by in utero behavioural patterns? Arch Dis Child. 1993;69:3–8.
3. Simon EM, Goldstein RB, Coakley FV, Filly RA, Broderick KC, Musci TJ, Barkovich AJ. Fast MR imaging of fetal CNS anomalies in utero. AJNR Am J Neuroradiol. 2000;21:1688–98.
4. Pazol K, Creanga AA, Zane SB, Burley KD, Jamieson DJ, Centers for Disease Control and Prevention (CDC). Abortion surveillance--United States, 2009. MMWR Surveill Summ. 2012;61:1–44.
5. Vintzileos AM, Campbell WA, Weinbaum PJ, Nochimson DJ. Congenital hydrocephalus: a review and protocol for perinatal management. Obstet Gynecol. 1987;69:5–11.
6. Cardoza JD, Filly RA, Podrasky AE. The dangling choroid plexus: a sonographic observation of value in excluding ventriculomegaly. AJR Am J Roentgenol. 1988;151:767–70.
7. Kutuk MS, Ozgun MT, Uludag S, Dolanbay M, Poyrazoglu HG, Tas M. Postnatal outcome of isolated, nonprogressive, mild borderline fetal ventriculomegaly. Childs Nerv Syst. 2013;29:803–8.
8. Gaglioti P, Oberto M, Todros T. The significance of fetal ventriculomegaly: etiology, short- and long-term outcomes. Prenat Diagn. 2009;29:381–8.
9. Lipitz S, Yagel S, Malinger G, Meizner I, Zalel Y, Achiron R. Outcome of fetuses with isolated borderline unilateral ventriculomegaly diagnosed at midgestation. Ultrasound Obstet Gynecol. 1998;12:23–6.
10. Hannon T, Tennant PW, Rankin J, Robson SC. Epidemiology, natural history, progression, and postnatal outcome of severe fetal ventriculomegaly. Obstet Gynecol. 2012;120:1345–53.
11. Parazzini C, Righini A, Doneda C, Arrigoni F, Rustico M, Lanna M, Triulzi F. Is fetal magnetic resonance imaging indicated when ultrasound isolated mild ventriculomegaly is present in pregnancies with no risk factors? Prenat Diagn. 2012;32:752–7.
12. Bussel JB, Zabusky MR, Berkowitz RL, McFarland JG. Fetal alloimmune thrombocytopenia. N Engl J Med. 1988;319:1374–8.
13. Kuller JA, Katz VL, Wells SR, Wright LN, McMahon MJ. Cesarean delivery for fetal malformations. Obstet Gynecol Surv. 1996;51:371–5.
14. Bornstein E, Rodríguez JL, Pavón EC, Quiroga H, Or D, Divon MY. First-trimester sonographic findings associated with a Dandy-Walker malformation and inferior vermian hypoplasia. J Ultrasound Med. 2013;32:1863–8.

15. Babcook CJ, Chong BW, Salamat MS, Ellis WG, Goldstein RB. Sonographic anatomy of the developing cerebellum: normal embryology can resemble pathology. AJR Am J Roentgenol. 1996;166:427–33.
16. Bronshtein M, Zimmer EZ, Blazer S. Isolated large fourth ventricle in early pregnancy--a possible benign transient phenomenon. Prenat Diagn. 1998;18: 997–1000.
17. Ecker JL, Shipp TD, Bromley B, Benacerraf B. The sonographic diagnosis of Dandy-Walker and Dandy-Walker variant: associated findings and outcomes. Prenat Diagn. 2000;20:328–32.
18. Gandolfi Colleoni G, Contro E, Carletti A, Ghi T, Campobasso G, Rembouskos G, Volpe G, Pilu G, Volpe P. Prenatal diagnosis and outcome of fetal posterior fossa fluid collections. Ultrasound Obstet Gynecol. 2012;39:625–31.
19. Serhatlioglu S, Kocakoc E, Kiris A, Sapmaz E, Boztosun Y, Bozgeyik Z. Sonographic measurement of the fetal cerebellum, cisterna magna, and cavum septum pellucidum in normal fetuses in the second and third trimesters of pregnancy. J Clin Ultrasound. 2003;31:194–200.
20. Lee W, Barton S, Comstock CH, Bajorek S, Batton D, Kirk JS. Transverse cerebellar diameter: a useful predictor of gestational age for fetuses with asymmetric growth retardation. Am J Obstet Gynecol. 1991; 165:1044–50.
21. Ickowicz V, Eurin D, Maugey-Laulom B, Didier F, Garel C, Gubler MC, Laquerrière A, Avni EF. Meckel-Grüber syndrome: sonography and pathology. Ultrasound Obstet Gynecol. 2006;27:296–300.
22. Budorick NE, Pretorius DH, McGahan JP, Grafe MR, James HE, Slivka J. Cephalocele detection in utero: sonographic and clinical features. Ultrasound Obstet Gynecol. 1995;5:77–85.
23. Thompson DN. Postnatal management and outcome for neural tube defects including spina bifida and encephalocoeles. Prenat Diagn. 2009;29:412–9.
24. Nicolaides KH, Campbell S, Gabbe SG, Guidetti R. Ultrasound screening for spina bifida: cranial and cerebellar signs. Lancet. 1986;2(8498):72–4.
25. Adzick NS, Thom EA, Spong CY, Brock 3rd JW, Burrows PK, Johnson MP, Howell LJ, Farrell JA, Dabrowiak ME, Sutton LN, Gupta N, Tulipan NB, D'Alton ME, Farmer DL, MOMS Investigators. A randomized trial of prenatal versus postnatal repair of myelomeningocele. N Engl J Med. 2011;364:993–1004.
26. Pilu G, Sandri F, Perolo A, Pittalis MC, Grisolia G, Cocchi G, Foschini MP, Salvioli GP, Bovicelli L. Sonography of fetal agenesis of the corpus callosum: a survey of 35 cases. Ultrasound Obstet Gynecol. 1993;3:318–29.
27. Volpe P, Paladini D, Resta M, Stanziano A, Salvatore M, Quarantelli M, De Robertis V, Buonadonna AL, Caruso G, Gentile M. Characteristics, associations and outcome of partial agenesis of the corpus callosum in the fetus. Ultrasound Obstet Gynecol. 2006;27:509–16.
28. Santo S, D'Antonio F, Homfray T, Rich P, Pilu G, Bhide A, Thilaganathan B, Papageorghiou AT. Counseling in fetal medicine: agenesis of the corpus callosum. Ultrasound Obstet Gynecol. 2012;40:513–21.
29. Chervenak FA, Jeanty P, Cantraine F, Chitkara U, Venus I, Berkowitz RL, Hobbins JC. The diagnosis of fetal microcephaly. Am J Obstet Gynecol. 1984;149:512–7.
30. Stoler-Poria S, Lev D, Schweiger A, Lerman-Sagie T, Malinger G. Developmental outcome of isolated fetal microcephaly. Ultrasound Obstet Gynecol. 2010; 36:154–8.
31. den Hollander NS, Wessels MW, Los FJ, Ursem NT, Niermeijer MF, Wladimiroff JW. Congenital microcephaly detected by prenatal ultrasound: genetic aspects and clinical significance. Ultrasound Obstet Gynecol. 2000;15:282–7.
32. Dahlgren L, Wilson RD. Prenatally diagnosed microcephaly: a review of etiologies. Fetal Diagn Ther. 2001;16:323–6.

Imaging of the Pediatric Brain

18

Hediyeh Baradaran and Apostolos John Tsiouris

Introduction

Neurologic imaging is central in clinical practice for evaluating neurologic symptoms, assisting in making accurate diagnoses, and developing appropriate clinical plans. To get the most out of imaging, understanding its strengths and limitations is critical. In addition, being able to understand the radiologic interpretations is essential for taking the next step in caring for each patient. After giving an overview of the mainstays of imaging, their indications and contraindications, and other helpful tips, we briefly outline some neurological disorders described in imaging reports, key facts about them, and classic imaging features.

Neuroimaging Techniques

While ultrasound is often used in the newborn and neonate during the period of time that the fontanelles are open, there are two main types of neurological imaging: computed tomography (CT) and magnetic resonance imaging (MRI). We focus on these two types of advanced imaging in this chapter and refer to primary uses and indications for each modality (Table 18.1). For complete evidenced-based recommendations for the appropriate imaging of children, please refer to the American College of Radiology (ACR) Appropriateness Criteria, outlined on their website (www.acr.org).

CT uses an axially rotating X-ray tube to create cross-sectional images of the head and spine. It is typically used to evaluate bony abnormalities, trauma, acute neurologic symptoms in an urgent setting, hydrocephalus, and ventriculoperitoneal shunt malfunction as well as paranasal sinus disease. Because of its very fast acquisition time limiting motion artifact, it is often preferred in the acute setting. When evaluating for trauma, acute neurologic symptoms, hydrocephalus or bony abnormalities, intravenous contrast is not necessary for CT. IV contrast is reserved for the evaluation of suspected mass lesion or infections; however, when these disease entities are suspected, an MRI is usually the preferred examination as it allows for improved characterization and localization of neurological lesions. There are no absolute contraindications to obtaining a CT of the head without contrast; however, since there is ionizing radiation, obtaining a CT in the pediatric population should be reserved for specific settings. While the dose of ionizing radiation from a single CT is very low, radiation from

H. Baradaran, M.D.
Department of Radiology, New York Presbyterian Hospital – Weill Cornell Medical Center, 525 East 68th Street, New York, NY 10021, USA

A.J. Tsiouris, M.D. (✉)
Neuroradiology Section, New York Presbyterian Hospital – Weill Cornell Medical Center, 525 East 68th Street, Starr 630C, New York, NY 10065, USA
e-mail: apt9001@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_18

Table 18.1 Best imaging recommendations for selected clinical scenarios

Clinical presentation	NCCT	CECT	MRI w/o contrast	MRI w/o and w/contrast
Trauma	X		X	
Seizure				X
Infection		X		X
Infarction	X		X	
Cancer/mass				X
Acute headache	X		X	
Chronic headache			X	
Focal neurologic deficit				X

Non-contrast head CT (NCCT), Contrast enhanced CT (CECT), MRI without contrast (MRI w/o Contrast), MRI w/o and w/contrast (MRI w/o and w/contrast)

repeated CT examinations has been linked to an increased risk of developing cancer in children in one study [1]. Since children are more sensitive to radiation and have a lifetime to manifest the potentially hazardous effects of ionizing radiation, CT scans should be reserved for specific clinical settings. Chapter 20 deals with an extensive discussion regarding these risks and efforts to reduce exposure in children.

MRI provides a more detailed anatomic evaluation of the brain, spine, meninges, and intracranial vessels. Unlike CT, which uses ionizing radiation to obtain images, MRI uses differences in chemical makeup and proton shifts in a magnetic field to create images. Intravenous contrast (gadolinium-based compounds in MRI) is recommended when there is clinical concern for a specific lesion such as mass, seizure focus, or infectious process. Because differences in *magnetic* field are the basis of MRI, there are some contraindications to MRI, including implanted or attached ferromagnetic or electronic devices such as pacemakers, ferrous aneurysm clips, and certain nerve stimulators. Gadolinium is contraindicated in patients with poor renal function as it has been rarely reported to cause nephrogenic systemic fibrosis (NSF) [2]. Metallic orthodontic devices (braces) are generally safe to use in an MRI, but since metallic materials interfere with the magnetic signal from the MR machine, these cause metallic artifacts, which affects image quality and can limit evaluation of the surrounding anatomy.

MRI is the workhorse of neurologic imaging due its precise anatomic differentiation and sequences that accurately characterize tissue properties. There are a few core sequences performed on almost all neurologic MRI examinations. The T1-weighted (T1W) sequence is one of the first sequences to be acquired when performing neurologic imaging and is the best sequence for evaluating anatomy and bony structures. It provides excellent gray–white matter differentiation. When IV contrast is administered, a T1W sequence is obtained before and after contrast administration. The T2-weighted (T2W) sequence is considered a fluid-sensitive sequence in which fluid contents are T2 bright. Fluid-attenuated inversion recovery (FLAIR) is routinely applied to the T2W sequence to suppress the normally bright signal from CSF, improving the conspicuity of periventricular and cortical lesions. Both T2W and T2W FLAIR sequences are used to evaluate the brain parenchyma and characterize tissue lesions. Another important type of MRI sequence is diffusion-weighted imaging (DWI). Bright lesions on DWI are those that restrict the normal diffusion of water in the brain; some key lesions that restrict water diffusion include purulent material, acute infarctions, and hypercellular lesions. Lastly, the gradient recall echo (GRE) or susceptibility weighted imaging (SWI) sequences use the same principle of signal changes from field inhomogeneities to create an image. Lesions that cause inhomogeneities, such as metallic substances, calcifications, or blood products appear hypointense on both GRE and SWI sequences.

Neuroimaging Indications

One of the most common reasons to image in the acute setting is trauma. If significant trauma has occurred or is suspected, a non-contrast CT (NCCT) can quickly identify intracranial hemor-

rhage, fractures, or other serious complications such as midline-shift or herniation. MRI is equally, if not more, sensitive for detecting acute hemorrhage, however, it is not always available in the emergent setting and requires more time to obtain than a CT, making it susceptible to patient motion. If the trauma history is subacute to chronic and there are persistent symptoms not explained by the initial CT scan, MRI is markedly more sensitive for detecting cerebral contusions, diffuse axonal injury, and other posttraumatic sequelae.

Emergent imaging is also indicated for suspicion of acute infarction. Cerebral and cerebellar infarctions are uncommon in pediatric patients, but can occur in children with predisposing conditions such as sickle cell-disease, moyamoya disease, fibromuscular dysplasia, vasculitis and trauma. These patients have a higher risk of ischemic stroke than the general population and imaging is usually indicated for stroke-like symptoms.

Outside of the acute setting, there are many signs and symptoms that should prompt an imaging workup. For example, a focal neurological deficit in a child is a concerning sign and warrants brain or spine imaging following appropriate clinical localization (i.e., upper versus lower motor neuron). Additionally, skin findings such as café-au-lait spots, neurofibromas, lisch nodules, facial angiofibromas, port-wine stains may suggest a neurocutaneous syndrome and neurologic imaging may be performed for further evaluation and diagnosis of possible underlying phakomatosis. In both cases, a contrast enhanced MRI is the examination of choice. Headaches with concerning features or characteristics may also prompt imaging evaluation. Concerning associated symptoms include headaches that wake a child or occur upon waking; sudden, severe headache ("worst headache of my life"); a change in quality, severity, or pattern of a headache; headache worsened by cough, micturition, or defecation; headache associated with persistent nausea or vomiting; altered mental status; or recurrent localized headache. A headache associated with ataxia, focal weakness, diplopia, or abnormal eye movements on clinical exam is also concerning and imaging may be indicated.

In pediatric patients, changes in mental status often manifest differently than in adults. Excessive somnolence can be a very concerning sign. While non-neurologic infectious or metabolic sources could be the cause of excessive somnolence, meningitis, hydrocephalus, or other serious neurologic issues could also lead to somnolence or altered mental status.

New onset seizures, especially if focal in nature can be imaged to exclude mass lesion or to evaluate for other anatomic foci for seizures, such as mesial temporal sclerosis or a neuronal migration anomaly. Contrast enhanced MRI is often performed in patients with intractable seizures or for the preoperative evaluation in epilepsy surgery. When looking for anatomic foci of seizures, fine slices through the brain are necessary to ensure subtle findings are not overlooked.

Practical Neuroimaging

A unique aspect of imaging pediatric patients is the frequent need for patient sedation to obtain interpretable images without any motion degradation. CT examinations are quick, with acquisition times ranging from 10 s to 1 min so sedation is rarely necessary. MRI may take anywhere from 20 min to 1 h depending on the number of sequences required for the exam. In order to prevent motion artifact in the images, sedation is frequently necessary. Newborns and young infants often do not need sedation, as they will remain still if they are bundled and fed or imaged while sleeping. However, pediatric patients from the age of a few months of age to around the age of 6–8 years or those with cognitive impairments typically need sedation to prevent motion artifacts and non-diagnostic exams.

Pediatric patient sedation generally requires an inpatient setting and coordination with anesthesia care. Most outpatient imaging centers do not have sedation capabilities and as such have

age cut-offs around 8-years-old. Since using anesthesia is not without inherent risk, the decision to image must be made thoughtfully.

Imaging Findings

Once the images are acquired, the neuroradiologist generates a report detailing the findings, followed by their overall impression. A second clinical "interpretation" is often necessary by the ordering physician that puts these imaging findings in the correct clinical context of the patient's case. Reported findings can vary from benign incidental findings requiring no further clinical or imaging follow-up to life-threatening findings requiring immediate hospital admission and neurosurgical consultation. The remainder of this chapter will describe various findings that may be detailed on an imaging report in pediatric patients. We have categorized the radiologic findings into those that are entirely benign and do not require follow-up, those necessitating follow-up with a neurologist, and lastly, findings for which a neurosurgical consultation is advised. While certainly not an exhaustive discussion of all possible imaging findings in pediatric patients, we hope to touch on some of the more common and interesting disease entities and outline their specific imaging characteristics.

Benign Incidental Findings on Imaging

There are a number of findings that may be incidentally noted on pediatric brain imaging that require no follow-up. These findings are considered benign incidental findings and require neither imaging follow-up nor further neurologic workup. Most of these findings are discovered in patients incidentally when imaging is done for another reason.

Developmental Venous Anomalies

Benign vascular lesions such as developmental venous anomalies (DVAs) or capillary telangiectasias, are commonly encountered incidental findings on neuroimaging. DVAs (Fig. 18.1) are one of the most commonly encountered vascular lesions with an overall prevalence of 2–9% [3, 4]. They are thought to be anatomic variants of normal venous drainage and are not considered pathologic. They are believed to form during embryogenesis as a result of adaptations to accidents during development. They form as compensatory pathways and are almost always asymptomatic, incidentally noted lesions with no clinical significance. There are only very rare reports of thrombosis and/or ischemia from these lesions. If they

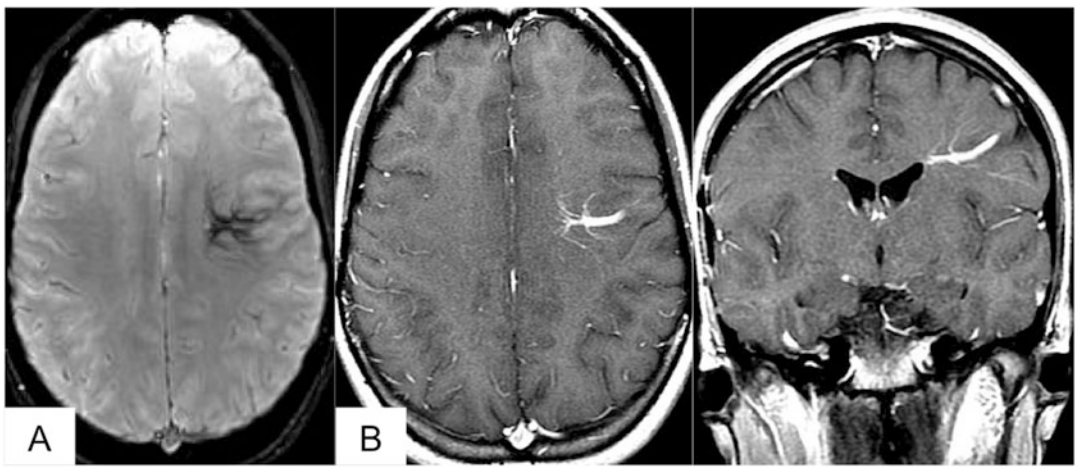


Fig. 18.1 Developmental venous anomaly (DVA). SWI (**a**) shows linear hypointensity compatible with deoxyhemoglobin within an enhancing branching vascular structure in the mid left centrum semiovale (**b**, **c**). These findings are compatible with aberrant venous drainage of the brain parenchyma into a benign DVA

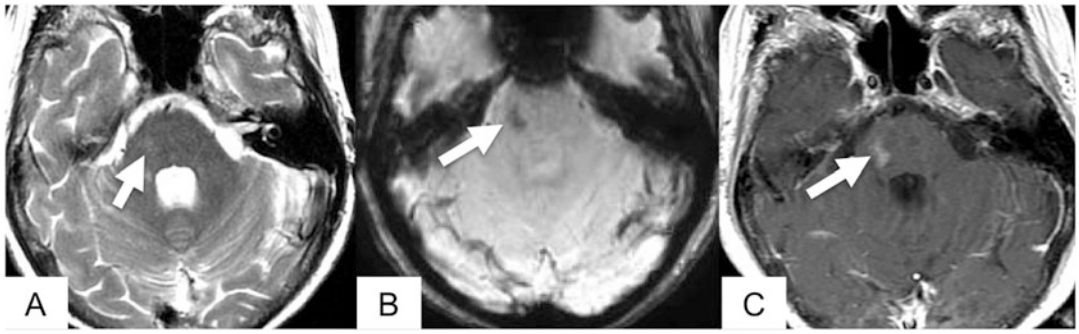


Fig. 18.2 Capillary telangiectasia. Axial T2W sequence (**a**) demonstrates faint hyperintensity associated with SWI hypointensity (**b**) secondary to deoxyhemoglobin within this vascular structure. Axial T1W post contrast (**c**) demonstrates associated ill-defined internal enhancement, also consistent with a vascular structure. These findings are pathognomonic for a benign capillary telangiectasia

are associated with hemorrhage, it is usually because there is an associated cavernous malformation, which is another type of benign congenital vascular lesion with a significantly higher risk for hemorrhage.

Capillary Telangiectasias

Capillary telangiectasias (Fig. 18.2) account for 16–20 % of intracranial vascular malformations [5] and are similarly asymptomatic. These appear as vascular channels interspersed in normal brain parenchyma on imaging. They occur most often in the brainstem or spinal cord. Multiple capillary telangiectasias are associated with syndromes such as Osler–Weber–Rendu, ataxia telangiectasia, or Sturge–Weber syndrome.

Pineal Cysts

Pineal cysts are incidentally found on a large number of MR studies in pediatric patients with reported prevalence ranging from 1.9 to 57 % [6]. The primary function of the pineal gland is to produce melatonin for circadian rhythm regulation. Pineal cysts are benign nonneoplastic glial-lined cysts within the pineal gland. They are asymptomatic and require no imaging follow-up because they have no potential for malignant transformation. There are certain imaging features that may indicate malignancy, but if a cyst has these features, they will not be described as simple pineal cyst by the radiologist interpreting the examination. Rarely, if the cysts are large enough (>1 cm) they can cause headaches or other neurologic issues such as compression of the cerebral aqueduct with secondary hydrocephalus. Some recommend following cysts if they are greater than 1 cm, although there is no reported increased incidence of malignant transformation in larger cysts [6].

Arachnoid Cysts

Another common incidental finding seen on pediatric neuroimaging is an arachnoid cyst. Arachnoid cysts are CSF-filled sacs within the arachnoid space that do not communicate with the ventricular system. They are generally well demarcated and are characteristically CSF-density on all MR pulse sequences (Fig. 18.3). They are most commonly seen in the middle cranial fossa, but can also be seen in the posterior fossa or in other intracranial locations. Patients with large arachnoid cysts are slightly more likely to develop subdural hematomas, with a cited 5 % risk in patients with middle cranial fossa arachnoid cysts [7, 8] (Fig. 18.4). Most commonly, they are incidental findings requiring no further treatment. Very large arachnoid cysts or those causing hydrocephalus can be intervened

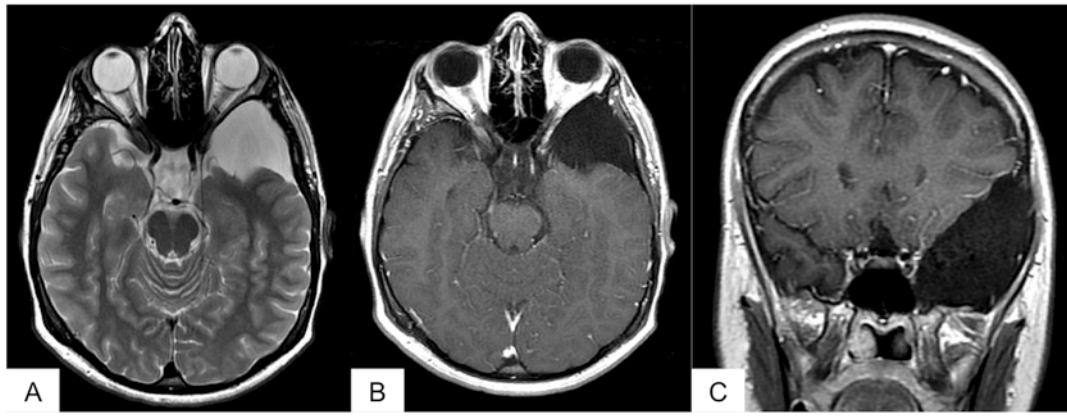


Fig. 18.3 Arachnoid cyst. A 16-year-old with a CSF-density cystic structure (**a**) in the left middle cranial fossa with no enhancement (**b**, **c**). There is subtle bony remodeling and expansion of the left middle cranial fossa and the left orbital wall; these findings are consistent with an arachnoid cyst. The middle cranial fossa is the most common location for arachnoid cysts.

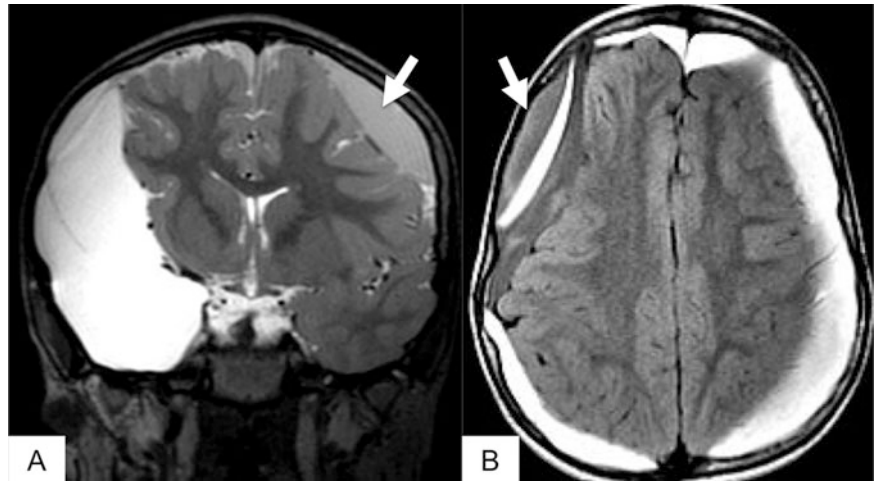


Fig. 18.4 Complicated arachnoid cyst. Children with large arachnoid cysts are more likely to get posttraumatic subdural hematomas. This 8-year-old boy had a known large right frontotemporal arachnoid cyst (**a**) and developed bilateral, left greater than right, subdural hematomas that demonstrate internal T2 hypointensity compatible with recent hemorrhage (**a**, **b**)

upon, either with resection or fenestration. Usually children with large arachnoid cysts are evaluated by a pediatric neurosurgeon.

Sinusitis

Sinus disease is also a fairly commonly encountered incidental finding on neurologic imaging. While sinusitis is a clinical diagnosis, certain imaging findings suggest more acute sinus disease while others suggest chronicity. Bony remodeling and expansion of the sinus cavities as well as mucous retention cysts are seen in chronic sinus disease. Air-fluid levels or aerosolized secretions suggest acute infection, but are nonspecific findings so clinical judgment is required to make the diagnosis. Since sinusitis is a clinical diagnosis, imaging is not usually necessary, but when surgical intervention is indicated or extra-sinus

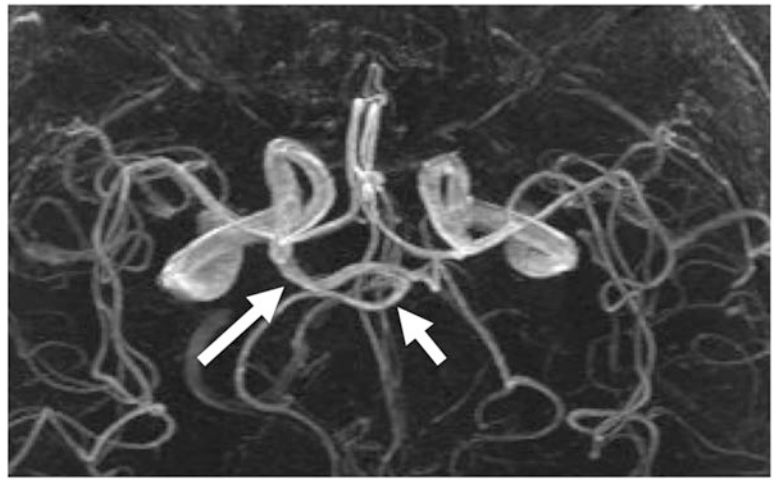


Fig. 18.5 Persistent trigeminal artery. Collapsed MIP of the circle of Willis in demonstrates a large right persistent trigeminal artery (*long arrow*) extending from the right internal carotid artery to a hypoplastic basilar artery (*short arrow*)

extension of infection is suspected (e.g., into the anterior cranial fossa or orbit), a maxillofacial CT is the preferred diagnostic study.

Persistent Congenital Vascular Anastomoses

Other incidental findings are fetal arterial anastomoses, such as a persistent trigeminal artery. Other less common fetal arterial anastomoses include persistent hypoglossal artery, persistent otic artery, persistent stapedial artery, fenestration of the basilar or other arteries, and fetal origin of the posterior cerebral artery. The persistent trigeminal artery is the most common persistent carotid–vertebrobasilar anastomosis with prevalence reported to be 0.1–0.6% [9]. A persistent trigeminal artery originates from the internal carotid artery and anastomoses with the basilar artery (Fig. 18.5). This incidental finding is important in patients from a neurosurgical perspective because in transsphenoidal surgery, accidental transection may lead to significant hemorrhage. There is an estimated 25% association between persistent trigeminal arteries and other vascular anomalies [9].

Arachnoid Granulations

Arachnoid granulations, also known as Pacchonian granulations, are arachnoid villi that project into the lumen of dural venous sinuses and can be mistaken for dural venous thrombosis (Fig. 18.6). Arachnoid granulations are asymptomatic with rare exception; it is theoretically possible, although very unlikely, to develop a headache secondary to a pressure gradient leading to venous hypertension. If a patient has an aberrant arachnoid granulation, they can be followed and surgical dural repair may be necessary if there is a persistent CSF leak. However, for the majority of patients, arachnoid granulations are incidental findings requiring no further imaging follow-up. They are commonly only described on imaging examinations simply so the finding is not confused with a dural sinus thrombosis.

Benign Enlargement of the Subarachnoid Spaces of Infancy

Benign enlargement of the subarachnoid space in infancy (BESSI) is often discovered incidentally or in the workup of infants with macrocephaly. It is considered to be a variant of normal development of the brain in which transient accumulation of CSF is seen around the frontal lobes, probably secondary to immature CSF drainage pathways leading to a buildup of CSF (Fig. 18.7). It is most commonly seen in children ages 3–8 months and resolves without therapy between 12 and 24 months [10]. Children with BESSI

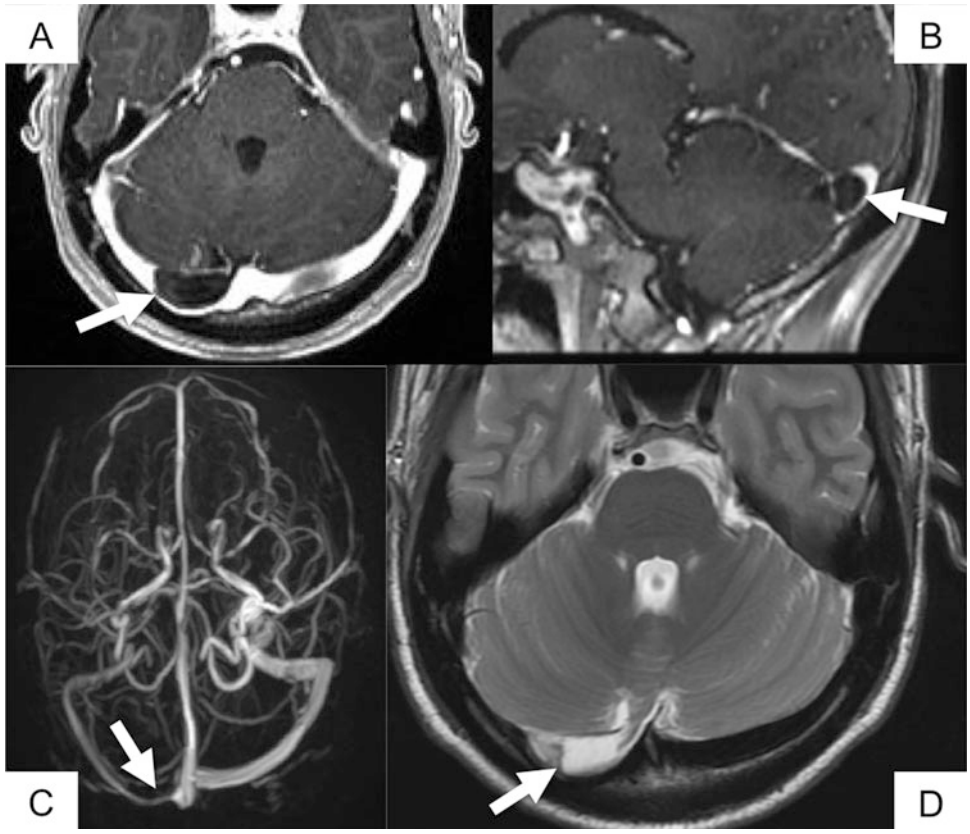


Fig. 18.6 Right transverse sinus arachnoid granulation. In this 20-year-old female, there is a filling defect within the right transverse sinus seen on contrast-enhanced axial and sagittal T1W sequences (**a**, **b**) and on the flow sensitive MRV study (**c**). This structure is CSF density (**d**), most consistent with a benign arachnoid granulation and not thrombosis

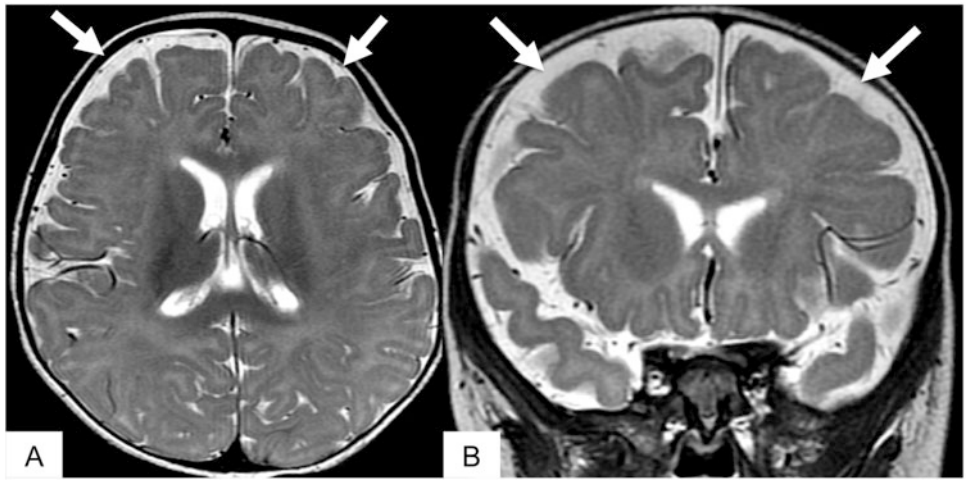


Fig. 18.7 Benign enlargement of the subarachnoid space in infancy (BESSI). Axial (**a**) and coronal (**b**) T2W images on this newborn's MRI demonstrate enlarged bifrontal extra-axial CSF spaces. These are differentiated from subdural hematomas because small vessels are present coursing through these extra-axial spaces. Mild dilatation of the frontal horns is also noted, without evidence of hydrocephalus

have a slightly increased chance of developing subdural hemorrhage either spontaneously or after minor trauma [11].

Imaging Findings Necessitating Neurological Workup

Arterial Dissections

Arterial dissections in the head and neck are not uncommon in the pediatric population. They most commonly occur secondary to trauma but can also be seen in the setting of craniocervical fusion abnormalities or connective tissue diseases. Symptoms for arterial dissection resemble stroke and vary depending on where in the cerebral circulation the dissection occurs. A dissection in the anterior circulation, may present with hemiparesis or aphasia. A dissection in the posterior circulation (i.e., vertebral artery) may cause vague symptoms including dizziness or vertigo. If a dissection is suspected in a pediatric patient, MR angiography (MRA) and MR imaging, preferably with intravenous contrast, are considered first line imaging to avoid excessive radiation while identifying the arterial dissection, subintimal thrombus, and possible brain infarction with very high accuracy (Fig. 18.8). However, CTA may be performed when MR is unavailable, when the patient is too unstable for MR imaging, or as a problem-solving tool when MR is not definitive. CTA provides excellent anatomic imaging of arterial stenoses and dissection flaps but is less sensitive than MRI to acute brain infarctions. Interventional neuroradiology (INR) may also perform a catheter digital subtraction angiogram (DSA) to further evaluate the area of dissection. Catheter-directed DSA is still considered the gold standard for diagnosis of dissection, but is not always necessary prior to

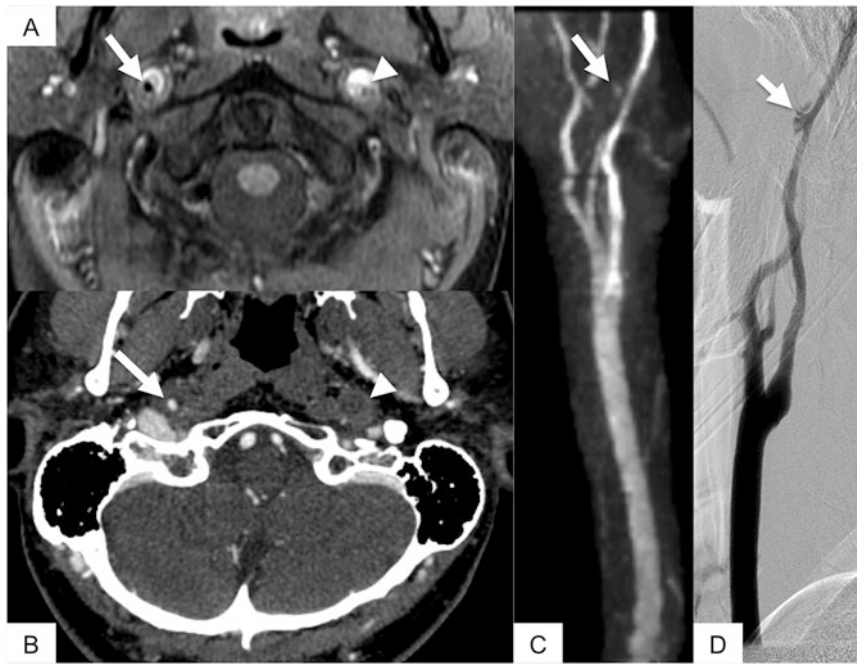


Fig. 18.8 Bilateral carotid artery dissections. An 18-year-old presents with bilateral carotid artery dissections. MRI (**a**) and CTA (**b**) demonstrate occlusion of the left internal carotid artery (ICA) demonstrated by lack of the normal intraluminal flow void on the MRI and lack of intraluminal contrast on the CTA (*arrowheads*). The right ICA demonstrates narrowing with mural thrombus with a small central flow void on MRI (*arrow*, **a**), corresponding to small area of intraluminal contrast opacification on the CTA (*arrow*; **b**). MRA (**c**) and catheter digital subtraction angiogram (DSA) (**d**) of the right ICA demonstrates an extraluminal vascular protrusion along the distal right ICA compatible with a pseudoaneurysm (*arrows*). Collagen vascular diseases should be considered in young patients with bilateral dissections

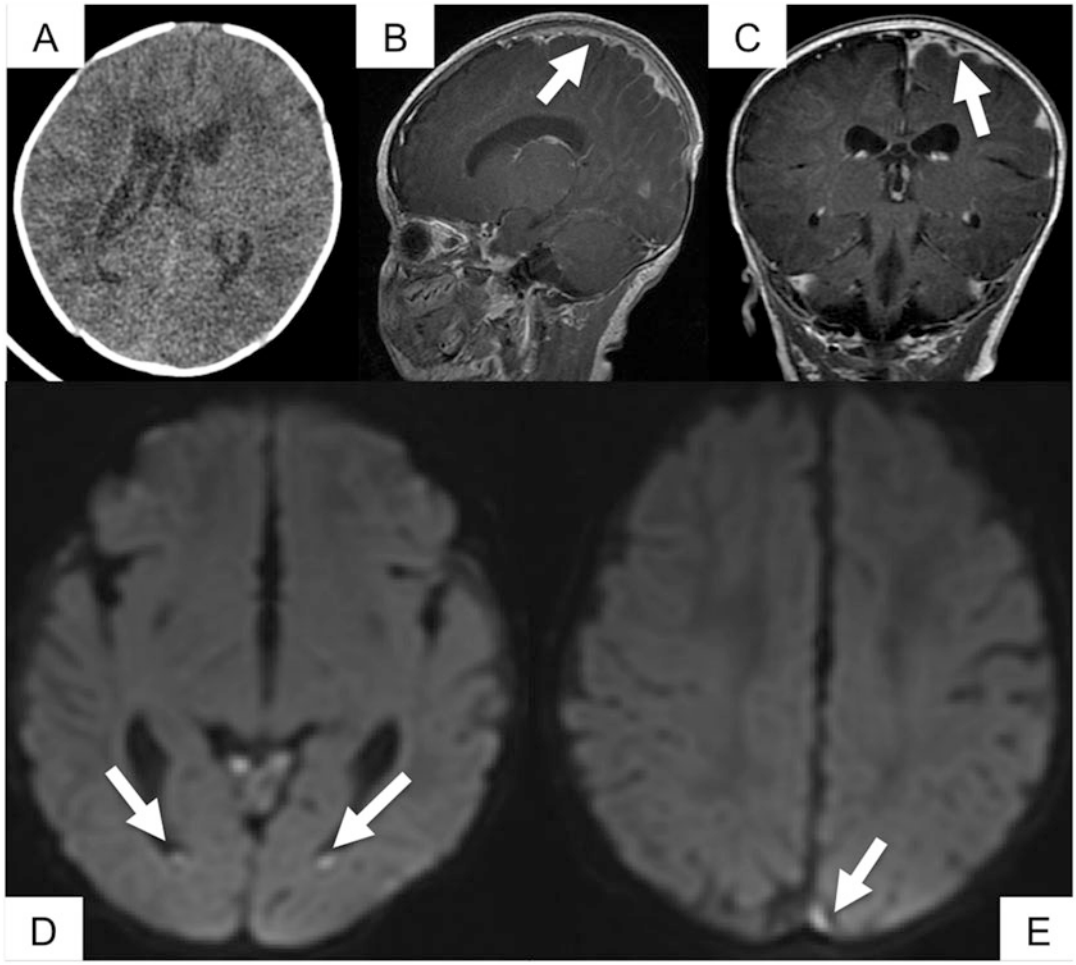


Fig. 18.9 Bacterial meningitis. In this somnolent and febrile newborn, initial NCCT (**a**) only showed hydrocephalus. A contrast-enhanced MRI of the brain demonstrated abnormal leptomeningeal enhancement along the left frontoparietal convexity (*arrows*; **b**, **c**), consistent with meningitis. In addition, there is debris layering posteriorly within the ventricles that restricts diffusion of water (*arrows*, **d**) and within the subarachnoid space (*arrow*, **e**) consistent with purulent material

initiating treatment. Patients with dissection are generally treated with anticoagulation alone. While more invasive treatment is possible, it is not often utilized in pediatric patients.

Meningitis and Brain Abscess

Bacterial meningitis and its associated complications is a relatively common and potentially devastating pediatric neurologic issue. Although CSF sampling via lumbar puncture is the mainstay for diagnosis of meningitis, imaging can be used to supplement the diagnosis, determine the extent of disease, and to evaluate for other complications such as empyema, ventriculitis, abscess, or hydrocephalus (Fig. 18.9). When meningitis is a diagnostic possibility, a contrast-enhanced MRI is the exam of choice. NCCT of the head is less helpful but in some cases, hydrocephalus, subdural effusions, or increased attenuation in the basilar cisterns or Sylvian fissures may be seen. Contrast-enhanced MRI is far more sensitive, with findings of failure of intra-sulcal and intracisternal fluid suppression on T2W FLAIR and/or diffusion restriction on DWI representing exudative

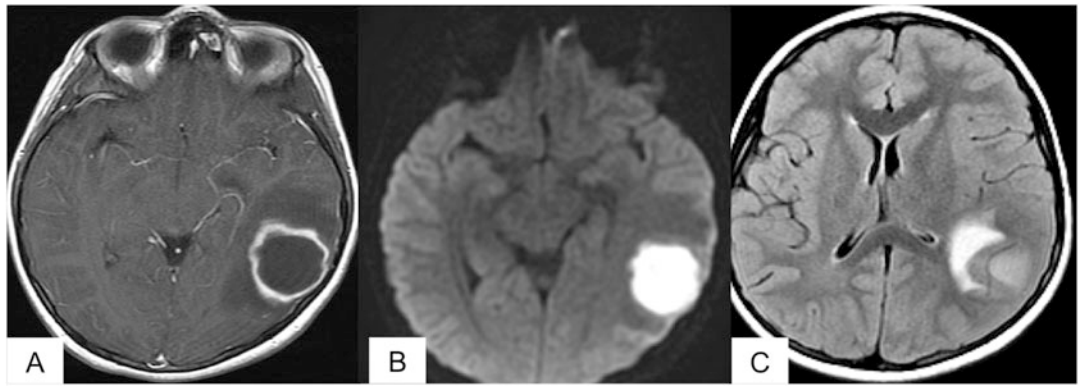


Fig. 18.10 Cerebral abscess. An ovoid ring-enhancing (**a**) left parietal lesion demonstrating internal restricted diffusion on DWI (**b**) with surrounding vasogenic edema on T2W FLAIR (**c**) was identified in this 6-year-old boy who presented with a fever and first time seizure. These imaging characteristics are typical of a bacterial cerebral abscess

material within the subarachnoid spaces. Enhancement of the leptomeninges and subarachnoid spaces can also be seen, suggesting meningitis. Importantly, it is possible for neuroimaging to be negative in a patient with meningitis so lumbar puncture and CSF sampling is crucial to making the diagnosis and imaging should be used as a supplement to evaluate for secondary complications. Complications such as subdural empyema or abscess (Fig. 18.10) generally require neurosurgical intervention. In the setting of an aseptic viral meningitis, imaging is usually normal and not routinely indicated, although diffuse brain edema, sulcal effacement and/or mild communicating hydrocephalus may be clues as to an underlying viral infection.

Congenital Neuronal Migration Anomalies

Congenital anomalies related to neuronal migration may also be seen in pediatric patients, presenting at varying stages of life. All neuronal migration anomalies are best characterized with MRI.

Lissencephaly, or "smooth brain," is the most severe neuronal migration anomaly characterized by complete or near-complete absence of sulci and gyri. Patients with lissencephaly present with severe mental retardation and refractory seizures.

Polymicrogyria is one of the most common migration anomalies and has a better prognosis than lissencephaly. It is characterized by excessive gyration of the cerebral cortex with shallow or fused microsulci. These patients present with developmental delay, seizures, and pareses. Treatment involves medical management of seizures. In some cases, surgical resection of an epileptogenic focus can be performed.

Schizencephaly is characterized by gray matter-lined clefts extending throughout the entire hemisphere. As with other neuronal migrational anomalies, the severity of clinical presentation correlates with the amount of brain involved. Clinical findings include developmental delay, epilepsy, and motor or sensory impairments.

Along with the more severe, widespread neuronal migrational anomalies, smaller, more focal malformations of cortical development, such as cortical dysplasia, can also present as foci for epileptic activity (Fig. 18.11). These foci are often very small and can sometimes be difficult to recognize and often require additional EEG-localization before they can be detected.

One of the most common causes of epilepsy in the adolescent and young adult population is mesial temporal sclerosis (MTS), characterized by hippocampal gliosis, neuronal loss, and sclerosis. Patients with MTS often have a history of infection, head trauma, or complicated febrile

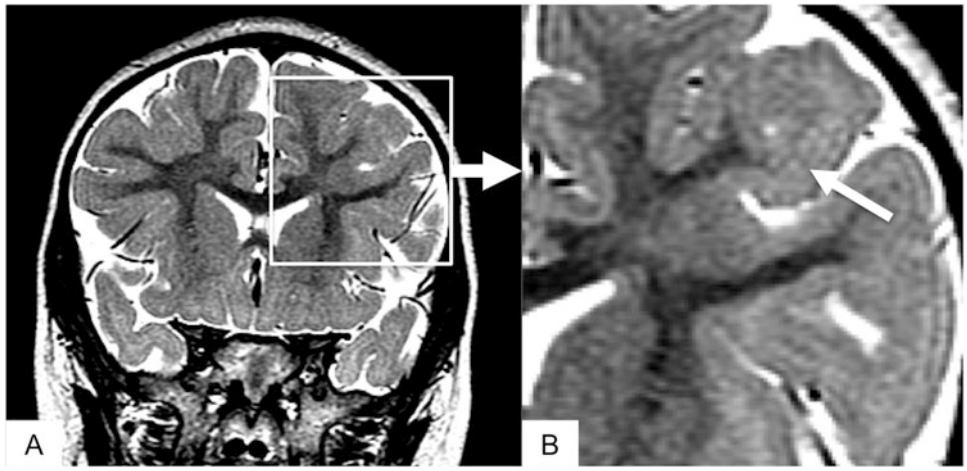


Fig. 18.11 Cortical dysplasia. Thickening and blurring of the gray matter in the left frontal lobe is seen in this child with epilepsy. This lesion correlated to abnormal EEG findings and was resected. Because of the sometimes subtle MRI appearance of cortical dysplasias, dedicated high resolution imaging must be obtained for evaluation

seizures. Imaging findings include decreased hippocampal volume, atrophy, and T2W hyperintensity within the hippocampus [12].

Pediatric White Matter Disease

Pediatric white matter diseases are categorized into two groups—demyelinating and dysmyelinating. Demyelinating diseases are acquired and involve the destruction of normal myelin. Dysmyelinating diseases are characterized by the abnormal formation and function of myelin resulting from an inherited enzyme deficiency. The destruction of normal myelin can occur as an autoimmune process, such as in pediatric multiple sclerosis or from autoimmune disease after a viral illness, such as in acute disseminated encephalomyelitis (ADEM) (Fig. 18.12).

Pediatric dysmyelinating diseases, also known as leukodystrophies, are inherited neurodegenerative diseases that affect myelin in the central and peripheral nervous system. This category is divided further into peroxisomal, lysosomal and mitochondrial diseases. Metachromatic leukodystrophy is an autosomal recessive lysosomal storage disease caused by the deficiency of arylsulfatase-A, a lysosomal enzyme necessary for metabolism of factors in the myelin sheath (Fig. 18.13).

Vasculopathies

Pediatric patients with underlying vasculopathies can also have white matter lesions due to ischemia. Some causes of vasculopathy in pediatric patients include sickle cell disease, HIV vasculopathy, or sympathomimetic vasculopathy from cocaine or methamphetamine abuse. All of these small vessel vasculopathies lead to areas of ischemia in the white matter (Fig. 18.14).

Phakomatoses

Neurofibromatosis type I (NF I), also known as von Recklinghausen disease, is the most common phakomatosis. It is an autosomal dominant neurocutaneous disorder characterized by café-au-lait spots, neurofibromas (Fig. 18.15), white matter lesions (myelin vacuolization; Fig. 18.16), optic gliomas, and skeletal dysplasias. There is variable expression of the disease and in order to make the diagnosis, two or more of the following must be present: at least six café-au-lait spots greater than 5 mm, at least two neurofibromas or one plexiform neurofibroma, axillary or inguinal freckling, an optic nerve glioma, a distinctive bony lesion such as sphenoid wing dysplasia, or a primary relative with NF I. Most NF I patients live normal lives.

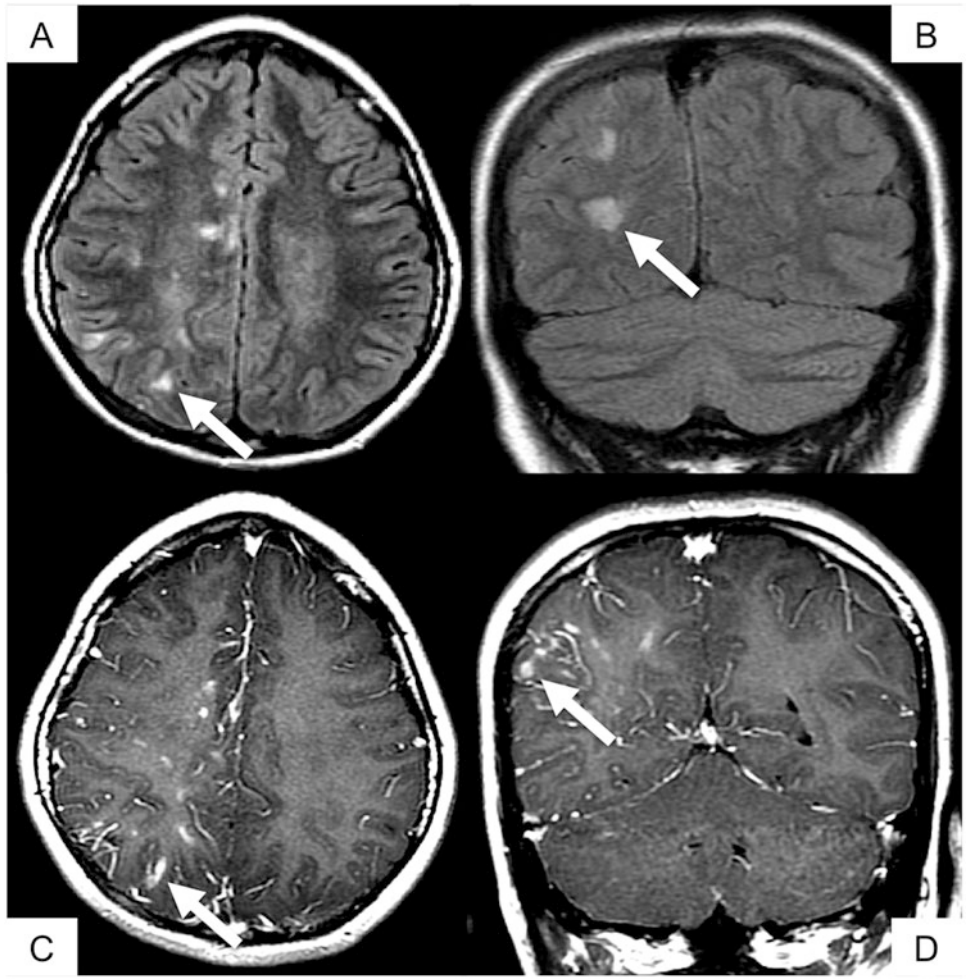


Fig. 18.12 Acute disseminated encephalomyelitis (ADEM). A 13-year-old presented with multifocal T2 hyperintense (**a**, **b**), enhancing (**c**, **d**), right hemispheric white matter lesions typical of an active demyelinating process. ADEM often affects the bilateral cerebral hemispheres, but this patient's lesions were predominantly right-sided

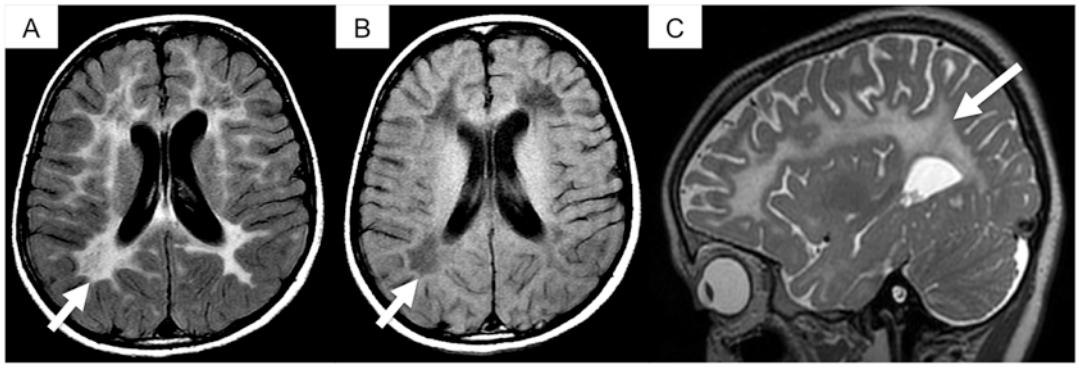


Fig. 18.13 Metachromatic leukodystrophy. A 6-year-old boy with muscle weakness and developmental delay; confluent abnormal periventricular white matter T2 hyperintensity (**a**, **c**) and T1 hypointensity (**b**) was present on his MRI. These findings are consistent with a leukodystrophy

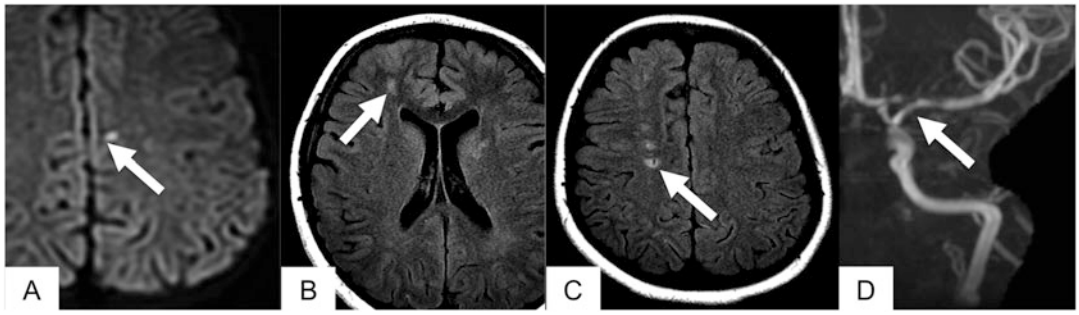


Fig. 18.14 Sickle cell vasculopathy. A 13-year-old female with history of sickle cell disease presented with an acute infarction in the left parietal lobe, seen best on DWI (**a**). Multiple chronic infarctions were also demonstrated on T2W FLAIR in the right frontal lobe (**b**, **c**). 3D MRA MIP (**d**) of the left anterior circulation shows multifocal irregularity and stenoses of the supraclinoid left ICA and the proximal M1 and A1 segments of the left MCA and ACA respectively

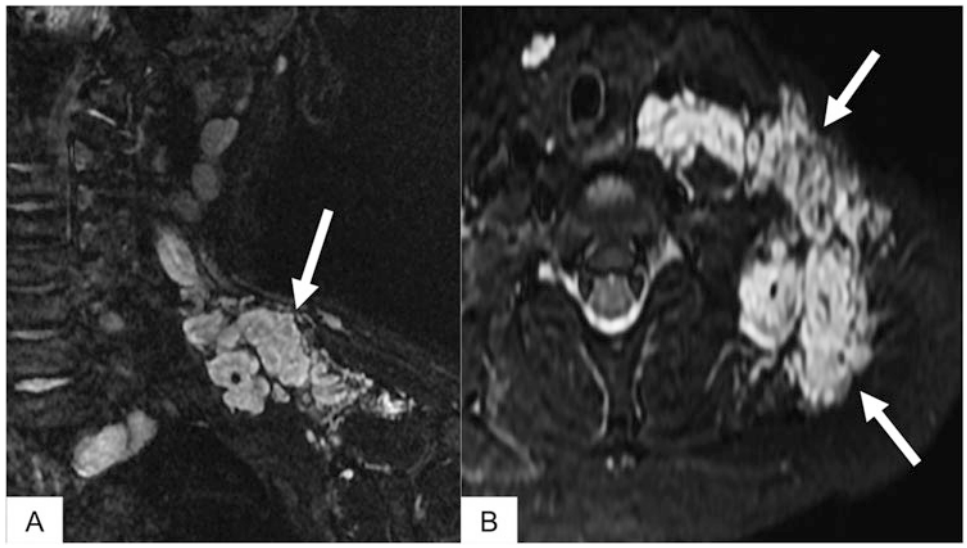


Fig. 18.15 Plexiform neurofibroma. Coronal (**a**) and axial (**b**) T2W STIR images of the lower neck in a 3-year-old female with NF I demonstrate a complex multilobulated T2 hyperintense mass along the course of the left brachial plexus, consistent with a plexiform neurofibroma

Some patients, however, can have significant issues including psychological issues from disfiguring features, morbidity, or early death.

Neurofibromatosis type II (NF II) is an autosomal dominant disease characterized by multiple schwannomas, meningiomas, and ependymomas, most classically bilateral vestibular schwannomas. Patients most commonly present with hearing loss, vertigo, or other cranial nerve symptoms. The estimated prevalence is 1 in every 25,000–30,000 people. These patients need frequent imaging surveillance to follow their masses [13].

Sturge–Weber is a rare neuro-cutaneous disorder whereby cortical veins do not develop normally characterized by epilepsy, progressive mental retardation, and facial telangiectatic nevi or "port-wine stain." Imaging features are characterized by leptomeningeal angiomatosis ipsilateral to facial angioma and intracranial calcifications.

Tuberous sclerosis (TS) is another rare autosomal dominant neurocutaneous disorder characterized by multiorgan hamartomas and multiple intracranial anomalies including cortical/subcortical tubers, subependymal nodules, subepndymal giant cell astrocytomas, and white matter lesions

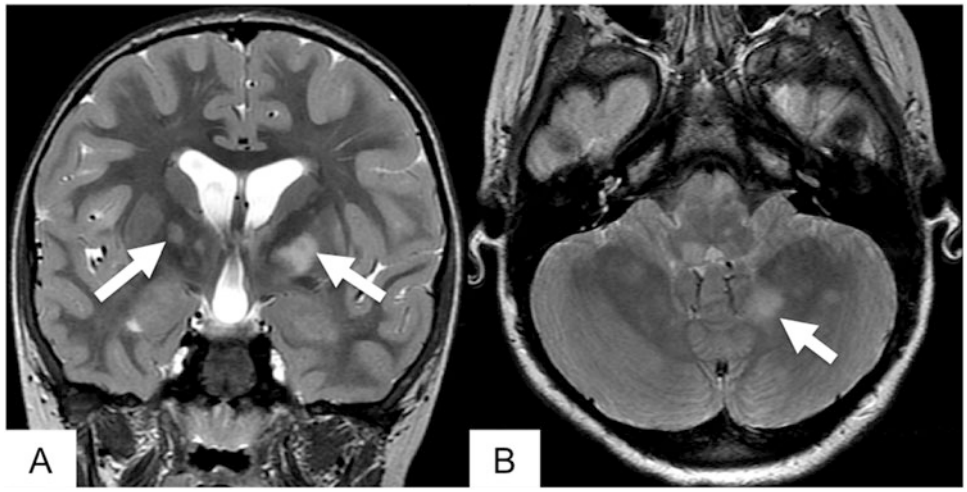


Fig. 18.16 Neurofibromatosis I (myelin vacuolization). Multifocal T2 hyperintense lesions are present in the bilateral basal ganglia (*arrows*; **a**) and dentate nuclei of the cerebellum (*arrow*; **b**) without mass effect; these findings are compatible with myelin vacuolization in a patient with NF I

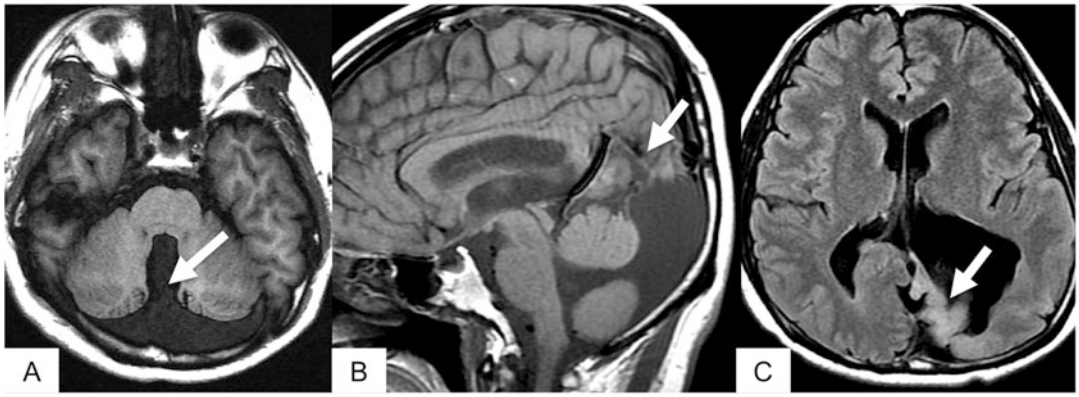


Fig. 18.17 Dandy–Walker malformation. A large retrocerebellar CSF space communicates with the fourth ventricle (*arrow*, **a**), associated with cerebellar vermian aplasia. There is associated elevation of the straight sinus and torcula (*arrow*, **b**). The medial left occipital lobe (*arrow*, **c**) is abnormally gyrated with poor gray–white matter differentiation and increased T2 signal, most consistent with cortical dysplasia, frequently associated with Dandy–Walker malformations

along neuronal migration lines. The classic clinical triad consists of adenoma sebaceum, seizures, and mental retardation although this is only seen in about half of patients with TS [14].

Dandy–Walker Spectrum

The Dandy–Walker spectrum represents a continuum of malformations of the posterior fossa with varying degrees of severity. The prevalence is 1 in every 25,000–100,000 births and accounts for 1–4 % of all hydrocephalus cases. 80 % of these cases are diagnosed by the age of 1 year [15, 16]. The clinical presentation and natural history depends on the severity of the abnormality but ranges from being an incidental finding to premature death, most commonly presenting as hydrocephalus at birth or in infancy. The "classic" Dandy–Walker malformation is characterized by cystic dilatation of the posterior fossa communicating with the fourth ventricle, hypoplasia or agenesis of the cerebellar vermis, and elevation of the tentorium and torcula (Fig. 18.17). In 70 % of

patients with a Dandy–Walker malformation, other CNS abnormalities are present including cortical dysplasia, dysgenesis of the corpus callosum, or holoprosencephaly [15, 16].

Idiopathic Intracranial Hypertension

Idiopathic intracranial hypertension (IIH), previously known as "pseudotumor cerebri," is increased intracranial pressure of unknown etiology. It most commonly presents with headaches and patients almost always have papilledema on clinical examination. IIH is more commonly seen in females and obese patients. Imaging findings for IIH are often nonspecific and include a partially empty sella and enlarged/tortuous optic nerve sheaths with increased fluid around the optic nerves.

Dural Venous Sinus Thrombosis

Dural sinus thrombosis (Fig. 18.18) can affect patients of any age and can initially present with vague symptoms such as headache or other symptoms of elevated intracranial pressure. The risk factors for dural sinus thrombosis include those that predispose patients to hypercoagulability such as pregnancy, inheritable coagulopathies, disseminated intravascular coagulation, prolonged bed rest, sepsis, trauma, and other inflammatory conditions. Children are especially susceptible to dehydration when ill and can develop venous thrombosis with little warning [17].

Non-accidental Trauma

Non-accidental trauma (NAT) is the most common cause of traumatic brain death in infancy and injuries are generally the result of direct head trauma. Intracranial injury in children is usually caused by sudden acceleration–deceleration forces from violent shaking (see Chap. 27 for complete discussion of NAT). Having multiple brain injuries involving different compartments at different stages is very suspicious for NAT. Subdural hematomas are the most common manifestation of NAT (Fig. 18.19). In addition, multiple depressed skull fractures and fractures that cross sutures or the midline are also suspicious for NAT. Lastly, hypoxic ischemic encephalopathy (HIE) may be seen in children with NAT. NCCT is often considered first line imaging for NAT, but MRI is far more sensitive for determining the extent of the traumatic brain injury and may be useful in approximating ages of intracranial hemorrhage, brain contusions and HIE, therefore helping to determine the full extent of injuries at the time of presentation [18].

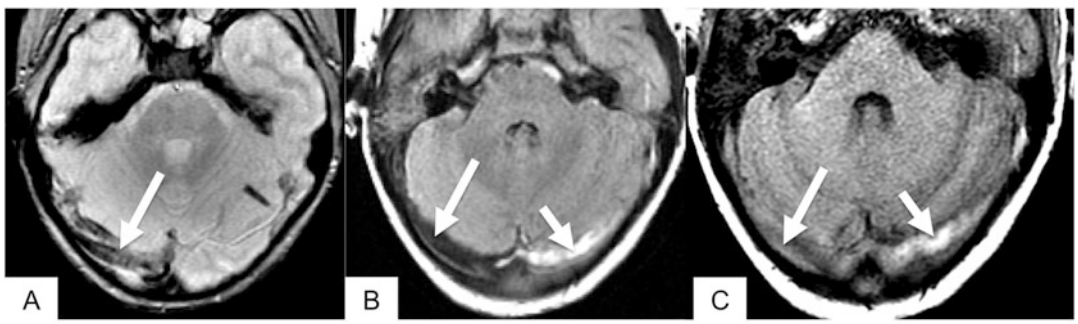


Fig. 18.18 Venous sinus thrombosis. A 13-year-old girl with ulcerative colitis presented with a severe headache. Acute thrombosis is present within the right transverse sinus (*long arrows*), demonstrating susceptibility on GRE (**a**), T2 hypointensity (**b**) and T1 isointensity (**c**). Subacute thrombus (*short arrows*) is present in the left transverse sinus, demonstrating T2 and T1 hyperintensity (**b**, **c**)

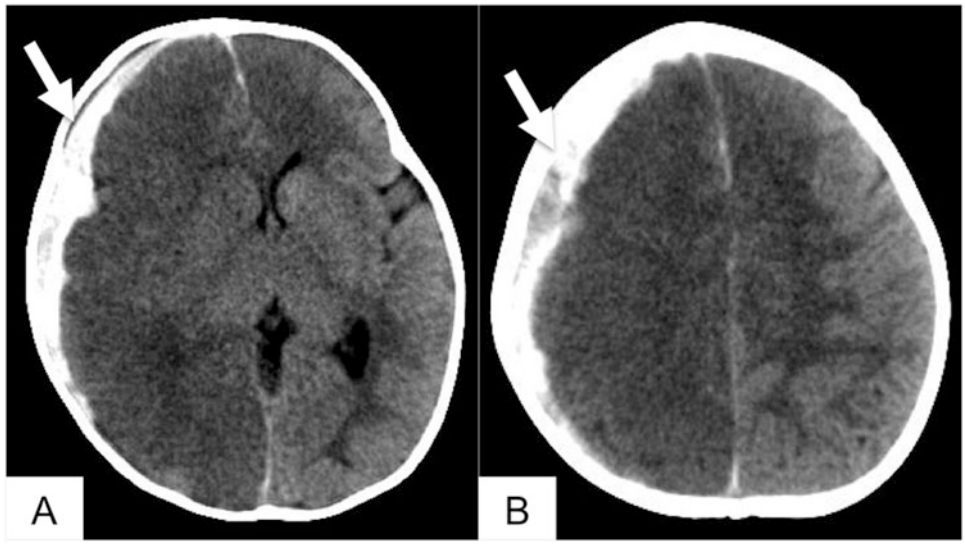


Fig. 18.19 Non-accidental trauma. An 11-month-old presents with a large right hemispheric subdural hematoma (*arrows*; **a**, **b**) with extensive hypodensity and loss of the gray–white differentiation throughout the right cerebral hemisphere and left anterior cerebral artery territory, compatible with subacute infarctions. Subdural hematomas that contain blood products of varying ages should raise suspicion for non-accidental trauma

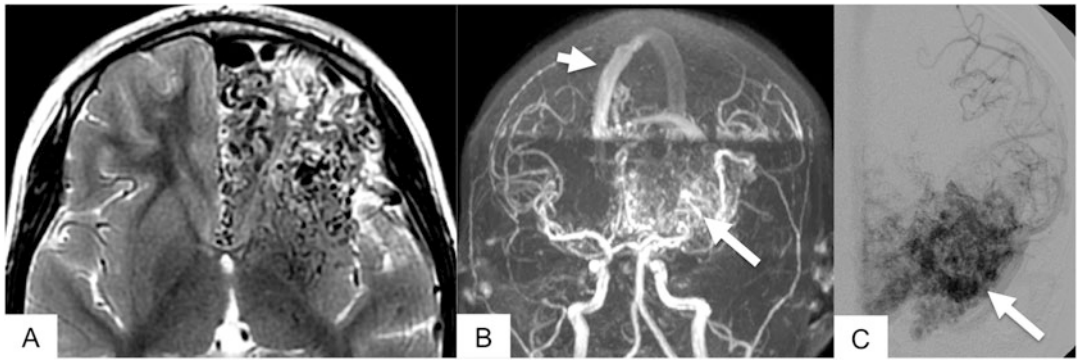


Fig. 18.20 Diffuse arteriovenous malformation (AVM). 7-year-old female with a diffuse AVM as demonstrated by multiple abnormal vessels replacing the normal left frontal lobe (**a**). MRA (**b**) and catheter DSA (**c**) of the left anterior circulation demonstrate a very large AVM nidus receiving arterial perfusion from the left middle cerebral artery (*long arrows*; **b**, **c**). On the MRA, there is early arterial filling of the superior sagittal sinus (*short arrow*; **b**)

Imaging Finding Necessitating Neurosurgical Workup

Congenital Vascular Malformations

While some vascular malformations are benign and require no follow-up, a few do necessitate neurosurgical consultation to determine if they need further intervention. Often these vascular malformations are discovered when they hemorrhage and cause acute neurologic symptoms. One such vascular lesion is an arteriovenous malformation (AVM), which accounts for 25% of intracranial vascular malformations. AVMs are abnormal connections between the arteries supplying blood to brain parenchyma and the veins that drain the parenchyma (Fig. 18.20). This abnormal connection results in arteriovenous shunting without the presence of a true capillary bed [18]. For a full

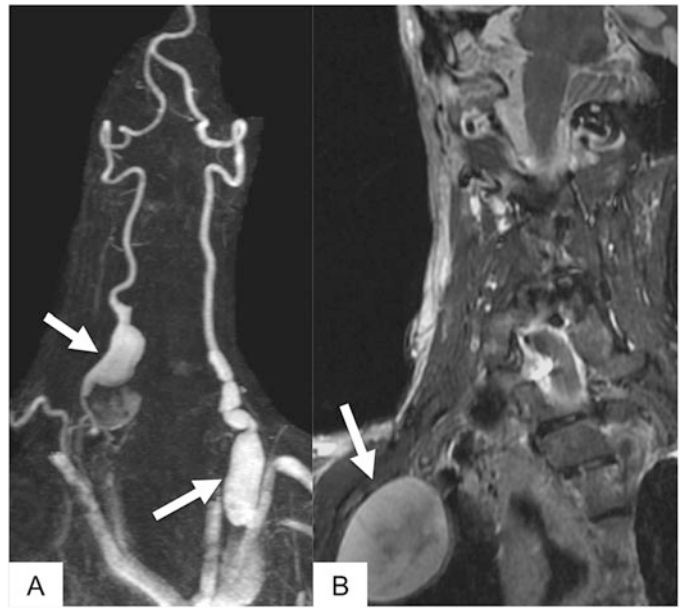


Fig. 18.21 Vertebral artery aneurysms. MR angiogram (**a**) shows multiple areas of fusiform dilatation of the bilateral vertebral arteries (*arrows*) in a patient with NF 1. Also noted on the MRI is a large right brachial plexus neurofibroma (*arrow*, **b**)

discussion of pediatric vascular malformations, please refer to Chap. 23

Cavernous malformations are vascular lesions requiring follow-up that are less common in pediatric patients. Pathologically, cavernous malformations are vascular hamartomas with immature blood vessels and no normal intervening brain tissue and are usually located within the brain parenchyma but are also rarely found along the pial surface of the brain and within the ventricles. Cavernous malformations can occur alone or in multiples in a syndrome called multiple familial cavernomas [19].

Aneurysms in children represent only 1 % of all intracranial aneurysms. Intracranial aneurysms in pediatric patients are commonly seen in the terminal ICA bifurcation and often present with subarachnoid hemorrhage (Fig. 18.21). Risk factors for aneurysm include trauma, vasculopathy, congenital HIV infection, NFI and other connective tissue diseases [20, 21].

Moyamoya Disease

Moyamoya disease is a chronic progressive occlusive disease of the distal internal carotid arteries and/or proximal anterior or middle cerebral arteries leading to extensive collateral vessel formation (Fig. 18.22). The primary inherited form is more commonly seen in pediatric patients. Most children with this rare disease present with intracranial hemorrhage, transient ischemic attacks or cerebral infarctions. First line treatment is medical, including antiplatelet therapy and calcium channel blockers. Bypass surgeries can also be performed to revascularize affected territories [22].

Chiari Malformations

Chiari I malformations are common, with an incidence thought to be around 1 % of the population. Half of patients with a Chiari I malformation are asymptomatic making this a common "incidental" finding. The most common presenting symptom is headache, often associated with the Valsalva maneuver. Additionally, children can present with neck pain or atypical scoliosis that may be progressive, painful and have an atypical curve. Children less than 2 years of age can also present with oropharyngeal dysfunction [23]. Children aged 3–5 years old are more likely to present with scoliosis, syringomyelia, and/or headache. A Chiari I malformation (Fig. 18.23) is

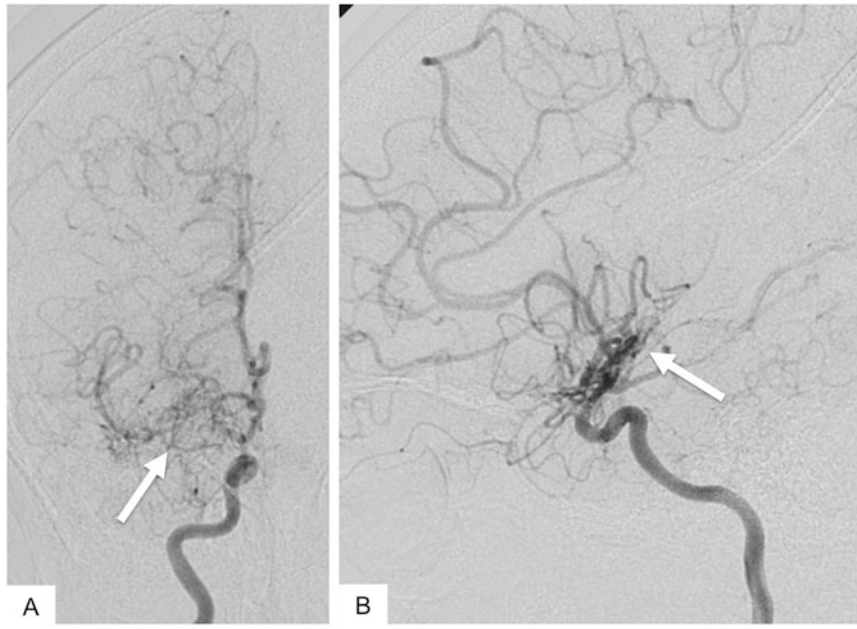


Fig. 18.22 Moyamoya disease. AP (**a**) and lateral (**b**) projections from a catheter DSA on a 10-year-old female demonstrate narrowed distal internal carotid artery with multiple small collateral moyamoya arteries (*arrows*)

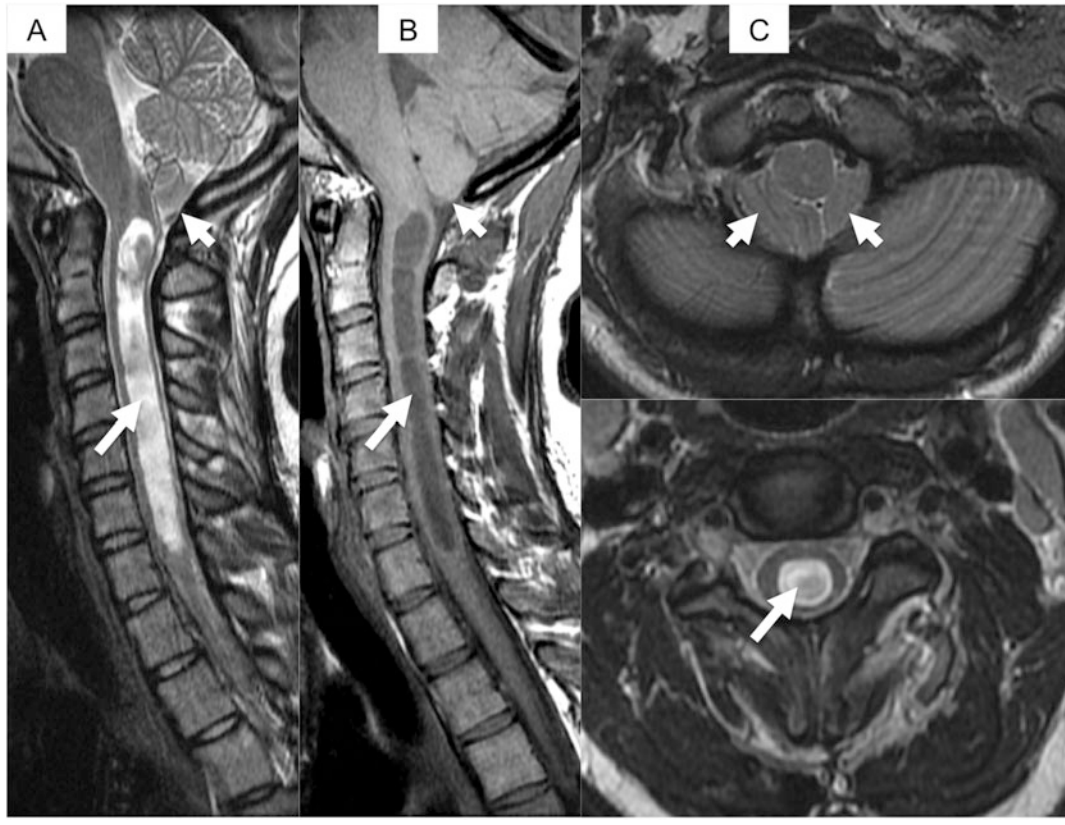


Fig. 18.23 Syringohydromyelia in Chiari I malformation. Extending from C1 to C7 is a T2 hyperintense (*long arrows*; **a**, **d**) and T1 hypointense (*long arrow*; **b**) CSF density intramedullary cavity consistent with syringohydromyelia; this finding is related to Chiari I malformations (*short arrows*; **a**, **b**, **c**) due to altered CSF flow dynamics

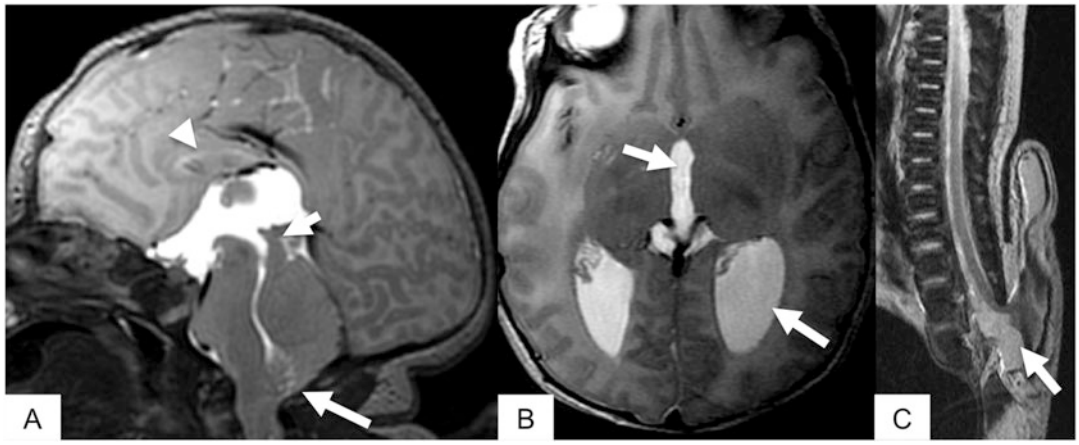


Fig. 18.24 Chiari II malformation. On the sagittal T2W image (**a**), a small posterior fossa with tonsillar herniation and cervicomedullary compression (*long arrow*), agenesis of the corpus callosum (*arrowhead*) and a beaked tectum (*short arrow*) are all noted. On the axial T2W image (**b**), there is evidence of hydrocephalus (*arrows*). Additionally, the spinal cord is tethered dorsally into large open osseous dorsal spinal defect filled with CSF compatible with a meningomyelocele (*arrow*; **c**). These are all classic findings in a neonate with a Chiari II malformation

defined by having peg-like cerebellar tonsils that extend inferiorly below the foramen magnum by greater than 5 mm (measured on a midline sagittal T1W image). These low-lying tonsils may obstruct CSF flow at the craniocervical junction leading to altered CSF flow dynamics and causing syringohydromyelia, which is accumulation of CSF within the central canal of the spinal cord [24, 25]. See Chap. 21 for a full discussion of Chiari Malformation.

Chiari II malformations are less common (seen in 0.02 % of births) and more complex than Chiari I malformations. They are characterized by a small posterior fossa leading to herniation of the cerebellum, brainstem, and/or fourth ventricle through the foramen magnum (Fig. 18.24). Myelomeningoceles, defined as a wide osseous dysraphism with extension of the spinal cord into a dorsal defect, are seen in virtually all patients with Chiari II malformations. Additionally, it is commonly associated with syringohydromyelia (in about 50 %), polygyria, or heterotopias [26].

Intracranial Mass Lesions

Intracranial tumors are the second most common type of childhood cancer (after leukemia) accounting for 20 % of all childhood tumors [27]. They are generally divided into supratentorial and infratentorial tumors. Chapter 22 contains an extensive discussion of pediatric brain tumors for additional reference.

Infratentorial Neoplasms

Outside of infancy, an infratentorial location for pediatric brain tumors are more common. The most common infratentorial or posterior fossa tumors are medulloblastoma, juvenile pilocytic astrocytoma, ependymoma, and brainstem glioma.

Medulloblastoma, a malignant embryonal cerebellar tumor, is the most common posterior fossa tumor accounting for up to 40 % of cases [27]. They commonly arise from the midline cerebellar vermis, dorsal to the fourth ventricle (Fig. 18.25). Tumoral seeding with leptomeningeal dissemination occurs in about one-third of cases at the time of diagnosis so when medulloblastoma is thought to be present, contrast-enhanced MR imaging of the entire neuroaxis is advised to evaluate for leptomeningeal disease prior to therapy.

Cerebellar juvenile pilocytic astrocytomas (JPA) generally occur in children or young adults, most commonly in the posterior fossa (Fig. 18.26). They are low-grade (WHO grade I)

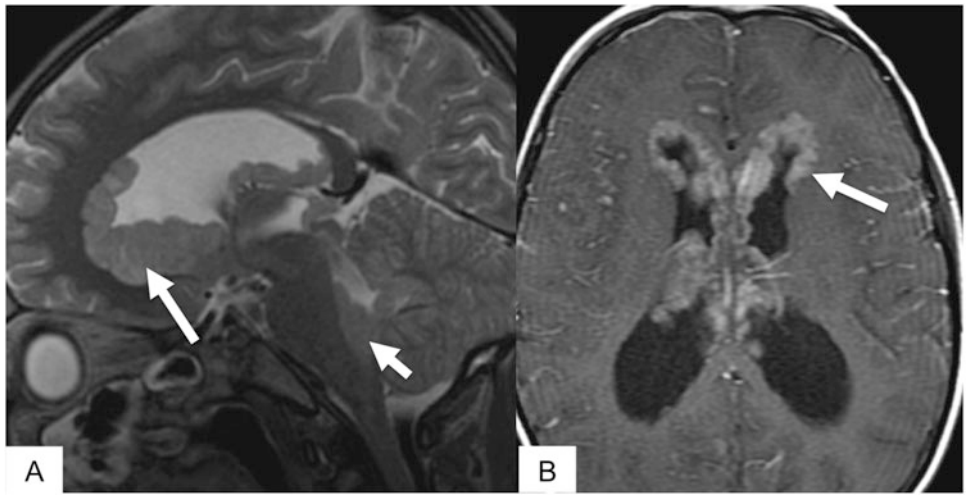


Fig. 18.25 Metastatic medulloblastoma. An 8-year-old boy with circumferential nodular enhancing lesions along the ependymal surfaces of the ventricles (*long arrows*, **a**, **b**); these findings are consistent with metastatic medulloblastoma. Nodular enhancement is also seen within the fourth ventricle (*short arrow*; **a**) causing noncommunicating hydrocephalus

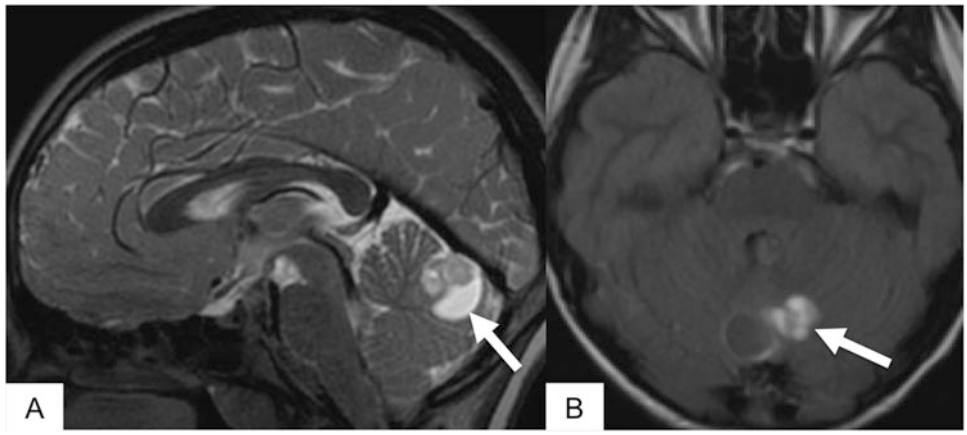


Fig. 18.26 Juvenile pilocytic astrocytoma (JPA). A mixed solid and cystic (*arrow*, **a**) lesion is present within the cerebellum of this 9-year-old child. The mass contains a solid enhancing nodule on post-gadolinium T1W imaging (*arrow*; **b**)

neoplasms with a greater than 90 % survival at 10 years [28, 29]. Surgical resection of the mass is considered curative and repeat surgical resection is performed for recurrences or growth after subtotal resection.

Ependymomas are the third most common posterior fossa tumor in children and arise from the ependymal cells that line the ventricles and the central cord canal. Although they do occur throughout the neuroaxis, 70 % of intracranial ependymomas are infratentorial. Ependymomas are soft or "plastic" tumors and are known to "squeeze" out through the fourth ventricle foramina into the cisterns. These masses are difficult to distinguish from medulloblastomas with imaging alone, but they are more likely to have calcifications, cysts and/or hemorrhage than medulloblastomas. While not as common as with medulloblastomas, ependymomas may also disseminate through the CSF; therefore, MR imaging of the entire neuroaxis is recommended at the time of diagnosis.

The fourth most common posterior fossa tumor in children is the brainstem glioma accounting for 15 % of cases. Brainstem gliomas are divided into two groups: diffuse intrinsic pontine gliomas (DIPG), which are infiltrative and have a poor prognosis, and focal gliomas, which are mostly pilocytic and have a good prognosis. Children with DIPG tumors have a relatively rapid onset of symptoms including cranial nerve deficits and ataxia. Focal gliomas often have a more gradual onset of symptoms.

Tectal gliomas are a small subset of brainstem gliomas confined to the tectal plate (Fig. 18.27) and may actually represent hamartomas. They have a very good long-term prognosis and are usually followed with serial MR imaging to document stability. They are only surgically treated in rare cases of progressive disease. Patients with tectal gliomas usually present between the ages of 6 and 10 with signs of hydrocephalus and elevated intracranial pressure secondary to aqueductal stenosis or obstruction.

Supratentorial Neoplasms

Supratentorial neoplasms in pediatric patients include but are not limited to astrocytomas, oligodendrogliomas, ependymal tumors, gangliogliomas, gangliocytomas, atypical teratoid/rhabdoid tumor, and primitive neuroectodermal tumors.

The most common suprasellar mass in pediatric patients is the craniopharyngioma (Fig. 18.28). Clinical symptoms are related to the suprasellar

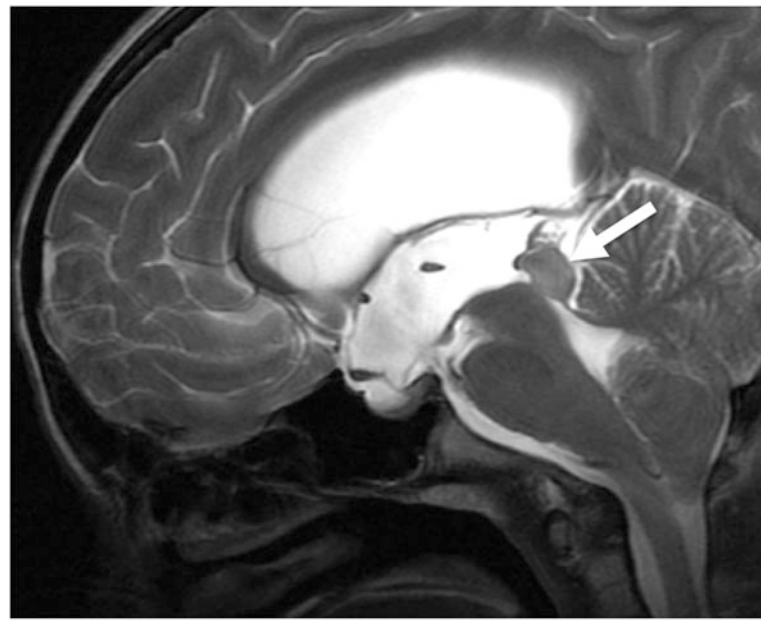


Fig. 18.27 Tectal glioma. The tectum is enlarged and T2 hyperintense consistent with a tectal glioma. There is secondary narrowing of the cerebral aqueduct resulting in noncommunicating hydrocephalus

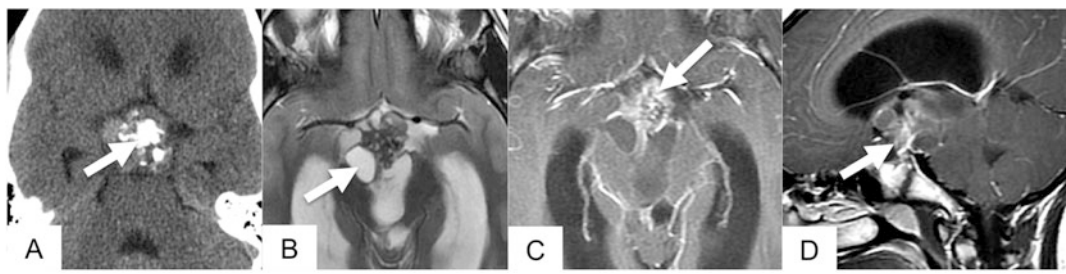


Fig. 18.28 Craniopharyngioma. 7-year-old boy with a complex cystic suprasellar mass containing calcifications on CT (*arrow*; **a**), cysts (*arrow*, **b**), and irregular mural enhancement (*arrows*; **c**, **d**). Due to its suprasellar location, this mass causes noncommunicating hydrocephalus

location and include visual disturbances (mass effect on optic chiasm), cognitive changes (mass effect on frontal lobes), hydrocephalus, and endocrine dysfunction. On imaging, they appear as lobulated, cystic and enhancing solid masses, with calcifications. They can be surgically resected, but resection is often subtotal given their proximity to vital structures. Treatment for residual or recurrent disease includes radiation or instillation of sclerosing agents into the cystic portion of the mass [30].

Supratentorial masses in children can also occur in the pineal region. The most common neoplasm of the pineal region is the germ cell tumor accounting for 3–8 % of pediatric germ cell tumors. Pineal gland teratomas are a subtype of nongerminomatous germ cell tumors (Fig. 18.29).

Supratentorial primitive neuroectodermal tumors (PNET) are cerebral embryonal tumor composed of undifferentiated neuroepithelial cells. PNETs are more common in younger children and the median age of diagnosis is 35 months. They account for 3 % of all brain tumors in children. Presenting signs and symptoms vary with size and location of tumor. They tend to have a poor outcome with 5-year survival rates around 30–35 % [31].

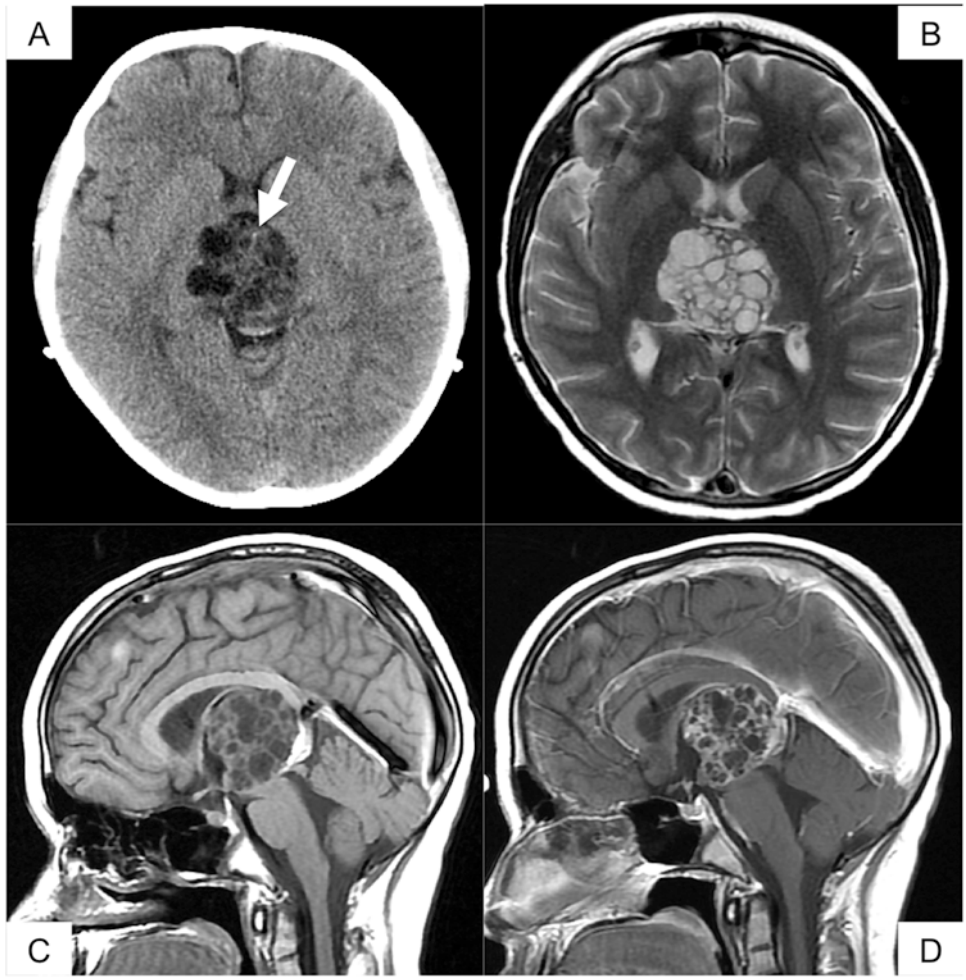


Fig. 18.29 Pineal region immature teratoma. Initial NCCT on this 10-year-old boy demonstrates a multiloculated cystic mass with few internal calcifications (*arrow*; **a**) in the pineal region. The T2W image (**b**) shows multiple fluid filled cystic structures throughout this mass. Pre and post gadolinium MRI (**c**, **d**) shows enhancement of the solid portions of this mass, typical for a teratoma

Choroid plexus papillomas are relatively uncommon low-grade intraventricular, papillary neoplasms derived from choroid plexus epithelium. They usually occur in the atria of the lateral ventricles and can spread through the subarachnoid space. These tumors usually occur in very young patients, often less than 2 years of age with 86 % presenting by the age of 5 [32]. In contrast, choroid plexus carcinomas are more aggressive and tend to be irregular, have mixed density and intensity and may even invade brain parenchyma leading to extensive vasogenic edema. They also usually demonstrate areas of necrosis and hypercellularity and have a less favorable prognosis [33].

Conclusion

Pediatric neurologic imaging has a broad scope with findings ranging from incidental to life-threatening. While the incidental findings can often be discussed and managed conservatively, certain findings necessitate further evaluation by a pediatric neurologist or neurosurgeon. Given recent evidence that ionizing radiation from CT scans are associated with increased likelihood of developing cancer in pediatric patients and that MRI is preferred for better anatomic delineation and tissue characterization, MRI is the mainstay for pediatric neuroimaging.

References

1. Pearce MS, Salotti JA, Little MP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet. 2012;380(9840):499–505. doi:10.1016/S0140-6736(12)60815-0.
2. Kuo PH, Kanal E, Abu-Alfa AK, Cowper SE. Gadolinium-based MR contrast agents and nephrogenic systemic fibrosis. Radiology. 2007;242(3):647–9. doi:10.1148/radiol.2423061640.
3. Abla A, Wait SD, Uschold T, Lekovic GP, Spetzler RF. Developmental venous anomaly, cavernous malformation, and capillary telangiectasia: spectrum of a single disease. Acta Neurochir. 2008;150(5):487–9. doi:10.1007/s00701-008-1570-5.
4. Santucci GM, Leach JL, Ying J, Leach SD, Tomsick TA. Brain parenchymal signal abnormalities associated with developmental venous anomalies: detailed MR imaging assessment. AJNR Am J Neuroradiol. 2008;29(7):1317–23. doi:10.3174/ajnr.A1090.
5. Castillo M, Morrison T, Shaw JA, Bouldin TW. MR imaging and histologic features of capillary telangiectasia of the basal ganglia. AJNR Am J Neuroradiol. 2001;22(8):1553–5. Available at: http://www.ajnr.org/content/22/8/1553.abstract.
6. Whitehead MT, Oh CC, Choudhri AF. Incidental pineal cysts in children who undergo 3-T MRI. Pediatr Radiol. 2013;43:1577. doi:10.1007/s00247-013-2742-x.
7. Gosalakkal JA. Intracranial arachnoid cysts in children: a review of pathogenesis, clinical features, and management. Pediatr Neurol. 2002;26(2):93–8. Available at: http://linkinghub.elsevier.com/retrieve/pii/S0887899401003290?showall=true.
8. Al-Holou WN, Yew AY, Boomsaad ZE, Garton HJL, Muraszko KM, Maher CO. Prevalence and natural history of arachnoid cysts in children. J Neurosurg Pediatr. 2010;5(6):578–85. doi:10.3171/2010.2.PEDS09464.
9. Dimmick SJ, Faulder KC. Normal variants of the cerebral circulation at multidetector CT angiography. Radiographics. 2009;29(4):1027–43. doi:10.1148/rg.294085730.
10. Zahl S, Egge A, Helseth E, Wester K. Benign external hydrocephalus: a review, with emphasis on management. Neurosurg Rev. 2011;34(4):417–32. doi:10.1007/s10143-011-0327-4.
11. McNeely PD, Atkinson JD, Saigal G, O'Gorman AM, Farmer JP. Subdural hematomas in infants with benign enlargement of the subarachnoid spaces are not pathognomonic for child abuse. AJNR Am J Neuroradiol. 2006;27(8):1725–8. Available at: http://www.ajnr.org/content/27/8/1725.abstract.
12. Rastogi S, Lee C, Salamon N. Neuroimaging in pediatric epilepsy: a multimodality approach. Radiographics. 2008;28(4):1079–95. doi:10.1148/rg.284075114.
13. Neff BA, Welling DB. Current concepts in the evaluation and treatment of neurofibromatosis type II. Otolaryngol Clin North Am. 2005;38(4):671–84. doi:10.1016/j.otc.2005.01.002.
14. Kalantari BN, Salamon N. Neuroimaging of tuberous sclerosis: spectrum of pathologic findings and frontiers in imaging. Am J Roentgenol. 2008;190(5):W304–9. doi:10.2214/AJR.07.2928.
15. Bolduc ME, Limperopoulos C. Neurodevelopmental outcomes in children with cerebellar malformations: a systematic review. Dev Med Child Neurol. 2009;51(4):256–67. doi:10.1111/j.1469-8749.2008.03224.x.
16. Patel S, Barkovich AJ. Analysis and classification of cerebellar malformations. AJNR Am J Neuroradiol. 2002;23(7):1074–87. Available at: http://www.ajnr.org/content/23/7/1074.abstract.
17. Provenzale JM, Kranz PG. Dural sinus thrombosis: sources of error in image interpretation. Am J Roentgenol. 2011;196(1):23–31. doi:10.2214/AJR.10.5323.
18. Osborn AG, Salzman KL, Barkovich J. Diagnostic imaging: brain. 2nd ed. Philadelphia, PA: Elsevier; 2009.

19. Rigamonti D, Hadley MN, Drayer BP, et al. Cerebral cavernous malformations. N Engl J Med. 1988;319(6):343–7. doi:10.1056/NEJM198808113190605.
20. Huang J, McGirt MJ, Gailloud P, Tamargo RJ. Intracranial aneurysms in the pediatric population: case series and literature review. Surg Neurol. 2005; 63(5):424–32. doi:10.1016/j.surneu.2004.11.023.
21. Jian BJ, Hetts SW, Lawton MT, Gupta N. Pediatric intracranial aneurysms. Neurosurg Clin N Am. 2010;21(3):491–501. doi:10.1016/j.nec.2010.03.005.
22. Burke GM, Burke AM, Sherma AK, Hurley MC, Batjer HH, Bendok BR. Moyamoya disease: a summary. Neurosurg Focus. 2009;26(4):E11. doi:10.3171/2009.1.FOCUS08310.
23. Greenlee JDW, Donovan KA, Hasan DM, Menezes AH. Chiari I malformation in the very young child: the spectrum of presentations and experience in 31 children under age 6 years. Pediatrics. 2002;110(6):1212–9. Available at: http://pediatrics.aappublications.org/content/110/6/1212.abstract.
24. Meadows J, Kraut M, Guarnieri M, Haroun RI, Carson BS. Asymptomatic Chiari type I malformations identified on magnetic resonance imaging. J Neurosurg. 2000;92(6):920–6. doi:10.3171/jns.2000.92.6.0920.
25. Krueger KD, Haughton VM, Hetzel S. Peak CSF velocities in patients with symptomatic and asymptomatic Chiari I malformation. AJNR Am J Neuroradiol. 2010;31(10):1837–41. doi:10.3174/ajnr.A2268.
26. McLone D, Dias M. The Chiari II malformation: cause and impact. Childs Nerv Syst. 2003;19(7-8):540–50. doi:10.1007/s00381-003-0792-3.
27. Brien WTO. Imaging of primary posterior fossa brain tumors in children. J Am Osteopath Coll Radiol. 2013;2(3):2–12.
28. Qaddoumi I, Sultan I, Broniscer A. Pediatric low-grade gliomas and the need for new options for therapy: why and how? Cancer Biol Ther. 2009;8(1):4–10. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=2810626&tool=pmcentrez&rendertype=abstract.
29. Fernandez C, Figarella-Branger D, Girard N, et al. Pilocytic astrocytomas in children: prognostic factors—a retrospective study of 80 cases. Neurosurgery. 2003;53(3):544. Available at: http://journals.lww.com/neurosurgery/Fulltext/2003/09000/Pilocytic_Astrocytomas_in_Children__Prognostic.3.aspx.
30. Eldevik OP, Blaivas M, Gabrielsen TO, Hald JK, Chandler WF. Craniopharyngioma: radiologic and histologic findings and recurrence. AJNR Am J Neuroradiol. 1996;17(8):1427–39. Available at: http://www.ajnr.org/content/17/8/1427.abstract.
31. Dai AI, Backstrom JW, Burger PC, Duffner PK. Supratentorial primitive neuroectodermal tumors of infancy: clinical and radiologic findings. Pediatr Neurol. 2003;29(5):430–4. Available at: http://linkinghub.elsevier.com/retrieve/pii/S0887899403003138?showall=true.
32. Naeini RM, Yoo JH, Hunter JV. Spectrum of choroid plexus lesions in children. Am J Roentgenol. 2009;192(1):32–40. doi:10.2214/AJR.08.1128.
33. Gopal P, Parker JR, Debski R, Parker JC. Choroid plexus carcinoma. Arch Pathol Lab Med. 2008;132(8):1350–4. doi:10.1043/1543-2165(2008)132[1350:CPC]2.0.CO;2.

Radiographic Evaluation of Suspected Scoliosis

19

Cathleen L. Raggio

Vignette A 10-year-old girl, an excellent athlete without any past medical history, comes to your office after a teammate on her soccer team noticed one of her shoulder blades was more prominent than the other. Her father noticed the whole spine was rotated and had a significant curve. On your examination she had no neurologic symptoms except a mild degree of hyperreflexia. You obtained scoliosis films which indicated a levoscoliotic curve with a Cobb angle of 38°.

A referral to pediatric orthopedics resulted in an MRI of her full spine due to her age, the direction of the curve, and the rapid onset of the scoliosis. The MRI demonstrated a large expansile thoracic spinal cord syrinx from T2–T9, corresponding to the apex of her thoracic scoliosis, and a referral was initiated to pediatric neurosurgery for joint management of the scoliosis and syrinx between orthopedics and neurosurgery.

Introduction

Scoliosis is typically the domain of pediatric or adult orthopedic surgeons. A short introduction and guide to scoliosis was included in this textbook because of some crucial connections that exist between specific central nervous pathologies and scoliosis. We will briefly define scoliosis to the degree that will be useful in a general pediatric practice and discuss those findings and definitions that may lead one to suspect that the cause is non-idiopathic or secondary to a true underlying neuromuscular etiology.

Definition

True scoliosis is defined as a curvature on an X-ray measuring 10° or more, associated with spinal rotation known as the ATR (angle of trunk rotation) on physical examination. The ATR is measured using a scoliometer. Alternatively, children can be visually checked by the Adam's forward bend test so asymmetry can be noted (Fig. 19.1).

Curves may be present secondary to a leg length discrepancy which "disappear" when the inequality is corrected by standing on a full shoe lift. Therefore, in evaluating a curve on X-ray, attention must be paid to the pelvis to check for any discrepancy in height.

Scoliosis may be idiopathic, i.e., the exact cause is unknown, which is the form with which most physicians are familiar. It occurs in 2–3 % of the adolescent population and its etiology is generally considered to be multifactoral with a genetic predisposition. It occurs in females four times as frequently as in males. Treatment is required in approximately 1 out of 10 patients, and general recommendations include being fit for and wearing a full-time TLSO (thoracolumbosacral orthosis).

C.L. Raggio, M.D. (✉)
Orthopedic Surgery, Hospital for Special Surgery,
535 E. 70th St., New York, NY 10021, USA
e-mail: raggioc@hss.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_19

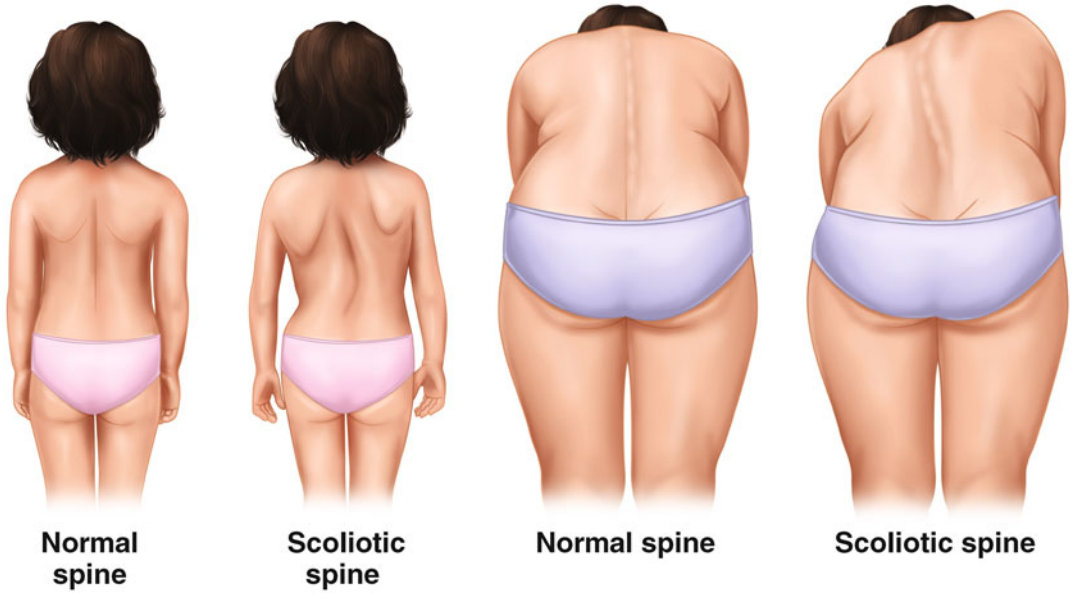


Fig. 19.1 Adam's forward bend test is a simple way to evaluate visually for asymmetry prior to obtaining radiographs

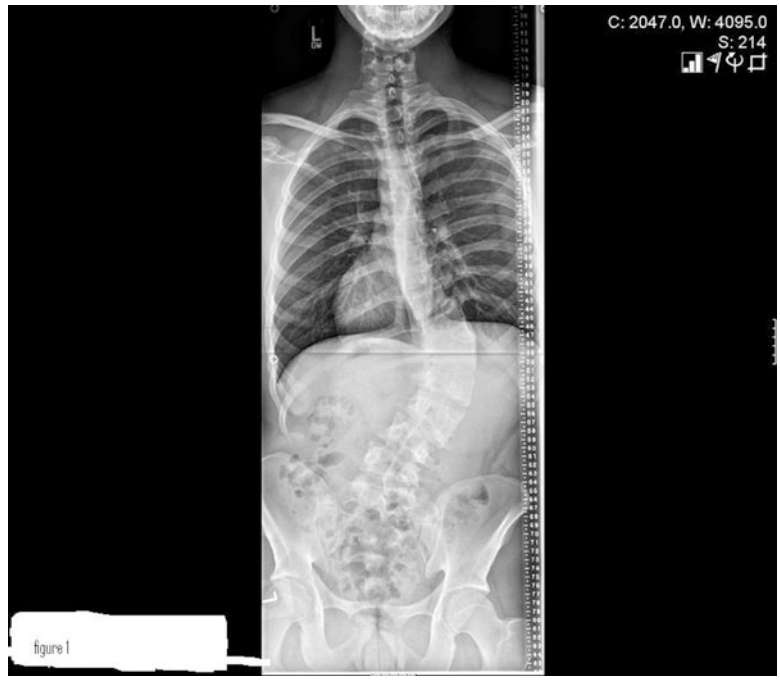


Fig. 19.2 Scoliosis as a result of a hemi-vertebra

Non-idiopathic Scoliosis

Other types of scoliosis include congenital, neuromuscular, and infantile. **Congenital scoliosis** is where the curve is secondary to an embryologic defect in formation, segmentation, or both in the vertebral somites. Scoliosis occurs secondary to an asymmetry of growth of the vertebral bodies. This can be the result of a hemi-vertebra (Fig. 19.2) and butterfly vertebra (Fig. 19.3) or due to bars or block vertebrae. **Neuromuscular**

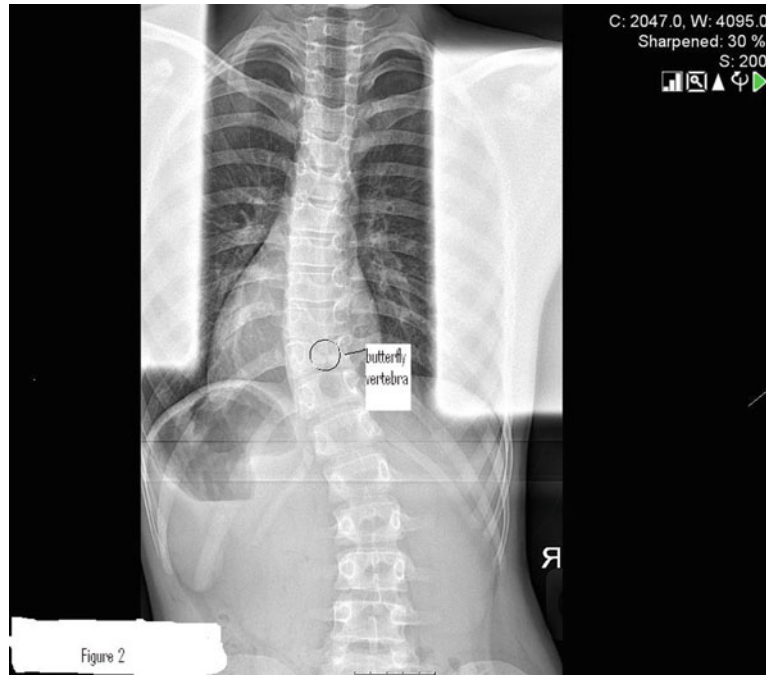


Fig. 19.3 Scoliosis as a result of a butterfly vertebra

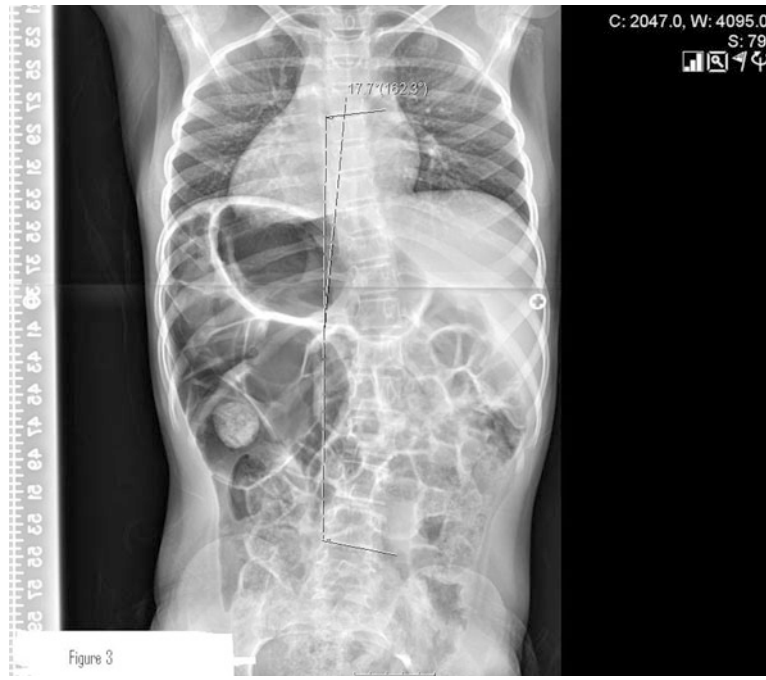


Fig. 19.4 A long sweeping scoliosis is suggestive of an underlying neuromuscular disorder

scoliosis is secondary to an underlying neurologic/muscle disorder (Fig. 19.4). These curves are generally "C" shaped, i.e., long and sweeping. The curves may occur early in life and progress into adulthood. Muscle imbalance/weakness of varying causes is thought to be the etiology. **Infantile scoliosis** occurs from birth to age 4. Many of these curves will improve with time; however, some require treatment with serial casting or bracing.

Radiographic Evaluation

X-rays are the imaging modality of choice and should be obtained when scoliosis is clinically suspected. The central series to order would be a standing AP/lateral *entire spine* on a 14 × 36 film. If your patient is unable to stand or too young to stand, a sitting film will mimic the gravity picture of the spine, though its relationship to the pelvis will not be equally appreciated. The X-ray is systematically evaluated for overall alignment, vertebral anomalies, and bone quality. Each vertebra should have two pedicles and a spinous process similar to an owl's face (Fig. 19.5). Once the general evaluation is complete, if a curvature is noted, it is precisely measured using the Cobb technique (Fig. 19.6a, b). True scoliosis is a curve greater than or equal to 10°.

The curve is defined by its position in the spine and is labeled right or left based on the direction of the convexity (Fig. 19.7).

The lateral X-ray is used to evaluate for kyphosis and lordosis. Normal values are 20–45° for kyphosis and 40–65° for lordosis (Fig. 19.8). Scoliosis is associated with increasing lordotic forces; hence, in the thoracic curves there is a decrease in kyphosis, and in the lumbar curves, there is an increase in lordosis.

Specific Orthopedic Manifestations of Pediatric Neurologic Disease

Knowing the basics of scoliosis and its "typical" X-ray appearance allows us to identify atypical or "red flag" curves or patterns. These are important to know since many can be associated with intraspinal anomalies and or Chiari I malformations. Work-up of all these curves includes a full spine MRI.

The left thoracic curve. These curves are commonly associated with a neurologic disorder or an intraspinal anomaly. A neurologic examination and a referral to a pediatric neurologist will likely be followed by an MRI and a pediatric neurosurgical evaluation (Fig. 19.9). This is referred to as levoscoliosis.

The short, sharp curve. These curves are typical in neurofibromatosis, tumors, and congenital malformations (Fig. 19.10).

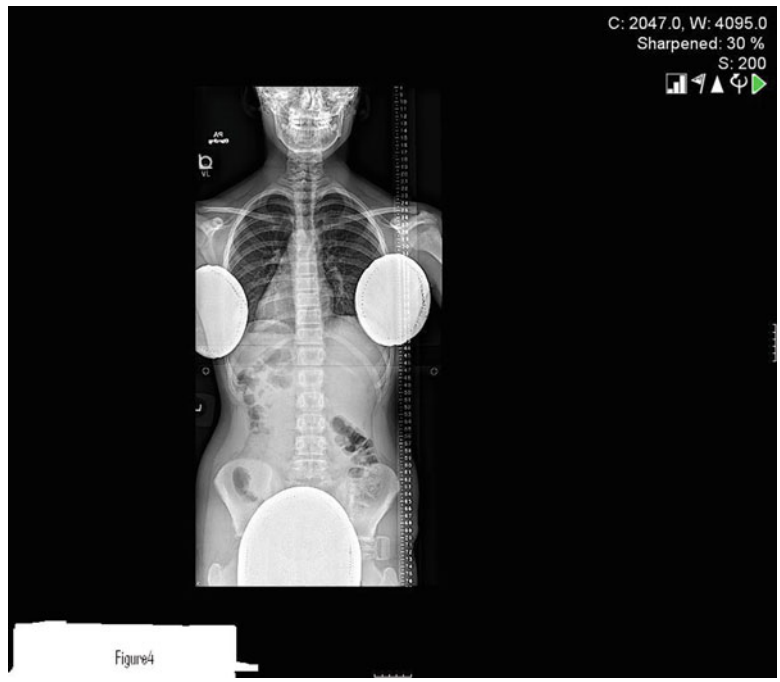


Fig. 19.5 Normal anatomic features of the vertebral body help define curve measurements

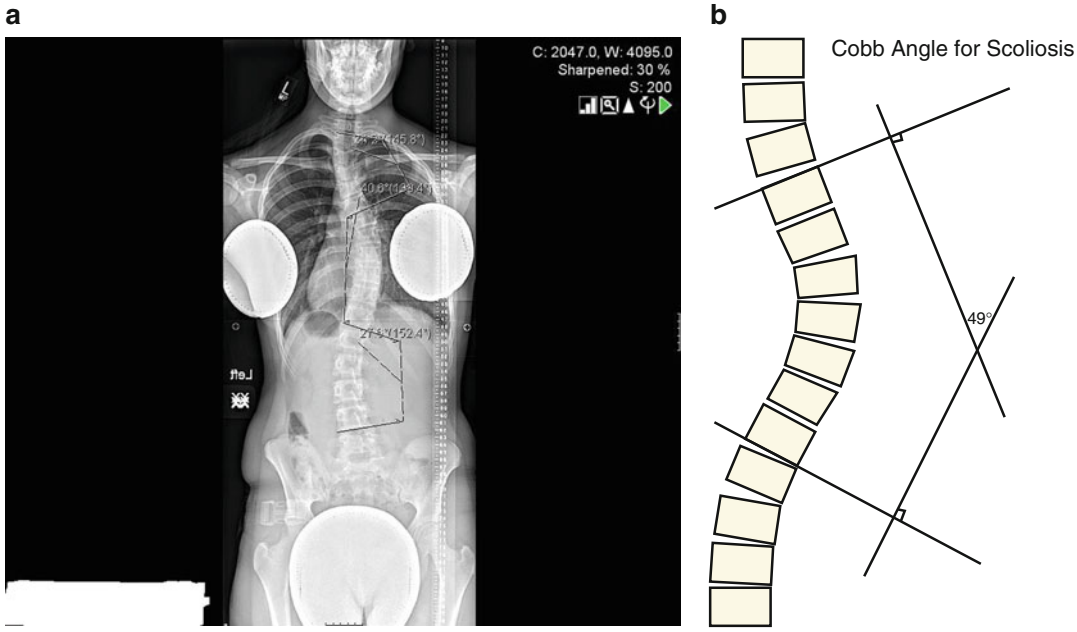


Fig. 19.6 The Cobb technique is the standard for defining scoliotic curves. Demonstrated on a radiograph (**a**) and schematically (**b**)

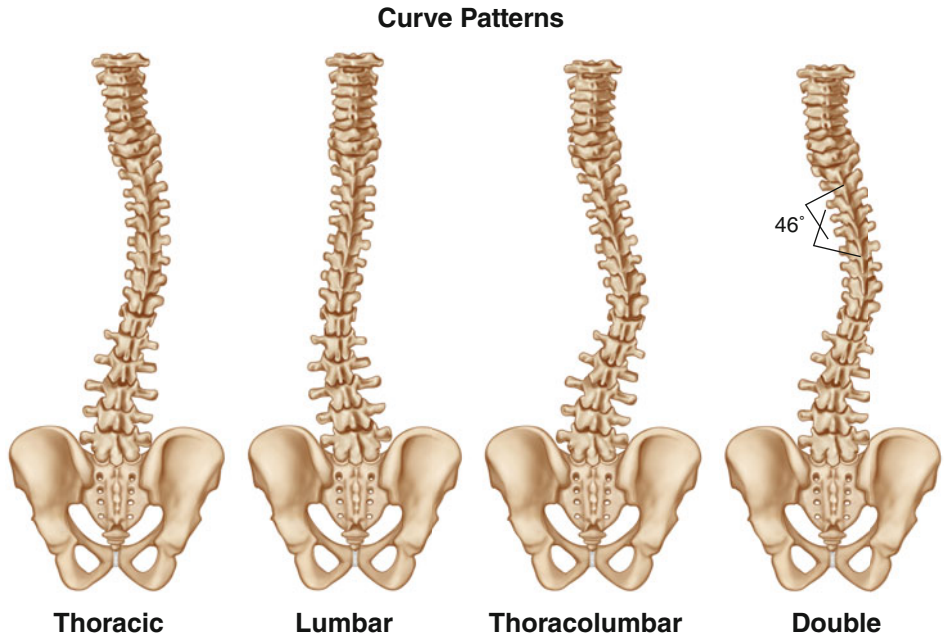


Fig. 19.7 Curves with an apex at T7, T8, and T9 are thoracic; curves with an apex at T11, T12, L1 are thoracolumbar; curves with an apex at L2, L3, and L4 are lumbar

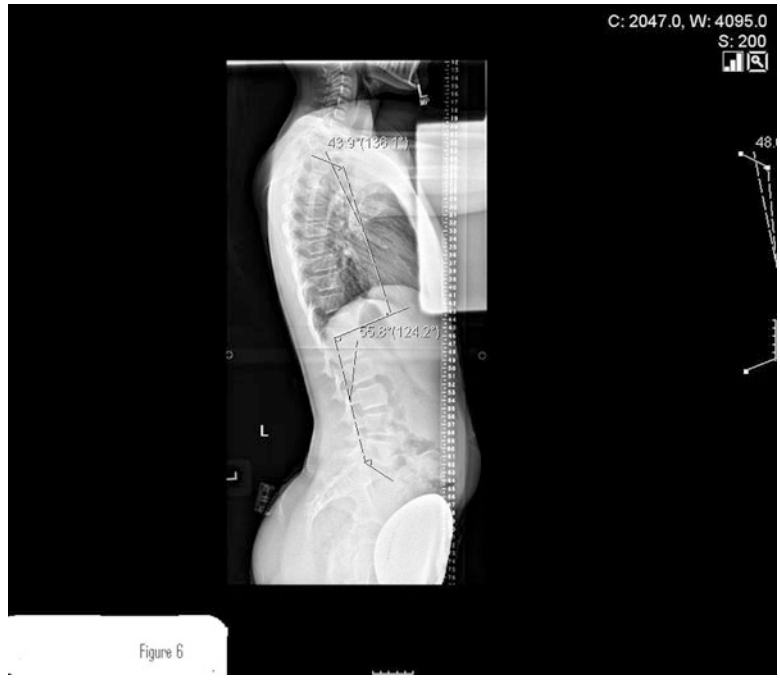


Fig. 19.8 Demonstration of kyphotic and lordotic curves on a lateral standing radiographic

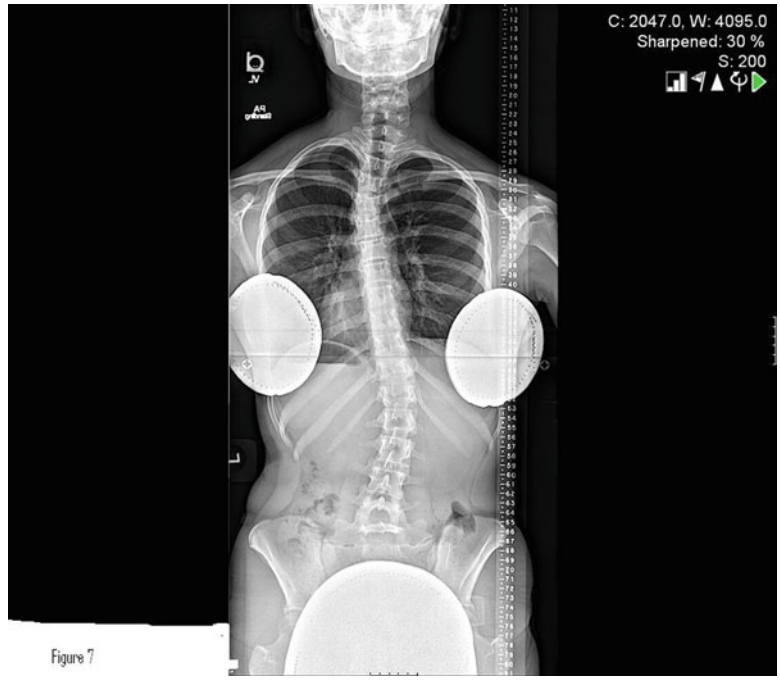


Fig. 19.9 Levoscoliosis often suggests an underlying intraspinal anomaly and mandates an MRI of the spine

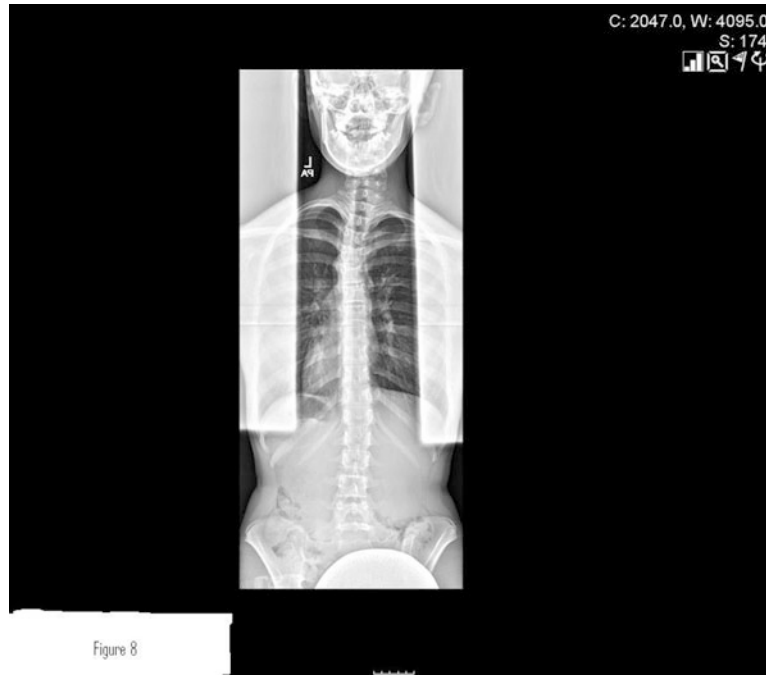


Fig. 19.10 Neurofibromatosis can be associated with a short sharp curve

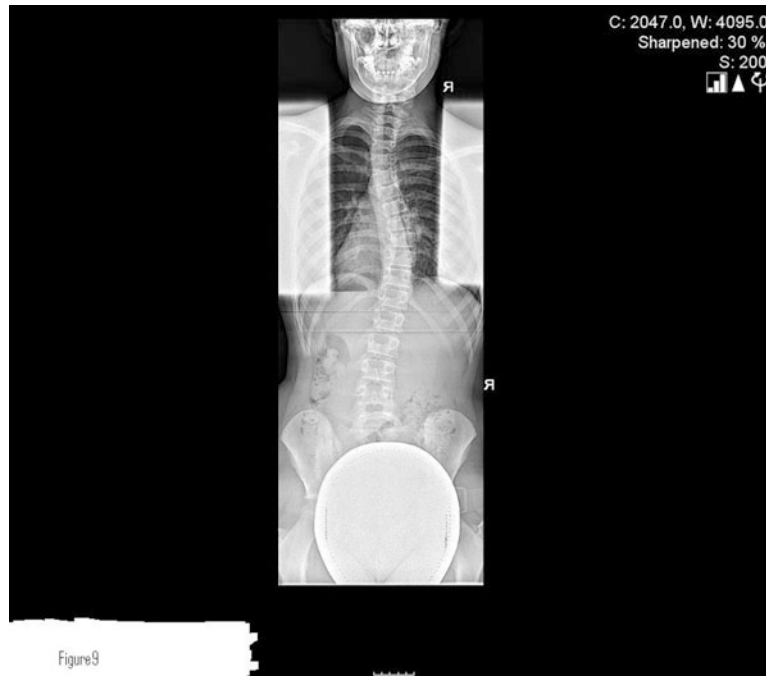


Fig. 19.11 A juvenile curve in young children also mandates an MRI like the left thoracic curve

The juvenile curve. In patients with scoliosis who are under 11 years of age, there is a ~20 % incidence of intraspinal anomalies, most commonly a syrinx noted on MRI. The anomaly does not have to be in the same location as the curve. This underlies the importance of obtaining a full spine MRI (Fig. 19.11).

The thoracic curve with kyphosis retention. This curve may indicate an underlying intraspinal or neurogenic cause for the scoliosis (Fig. 19.12).

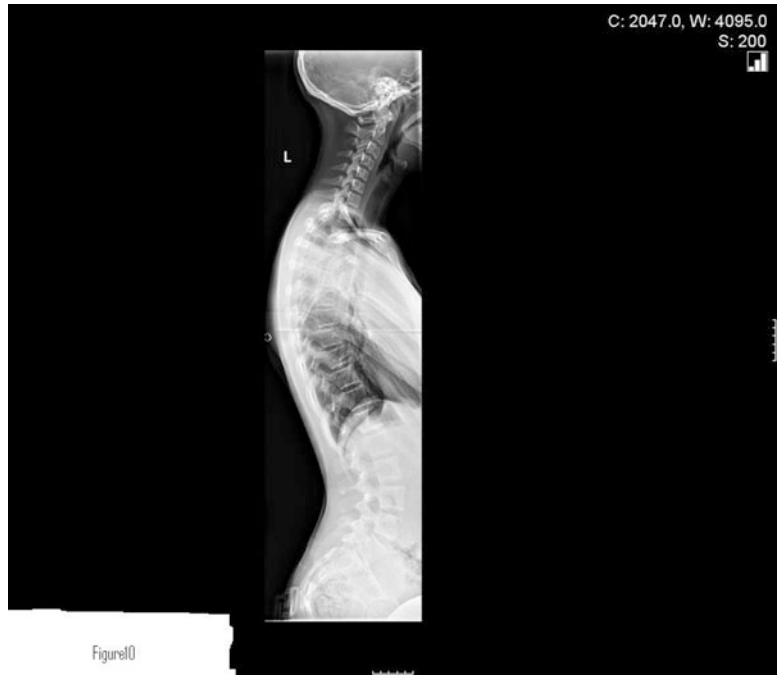


Fig. 19.12 Retention of kyphosis demonstrated despite a thoracic curve suggesting neurologic involvement

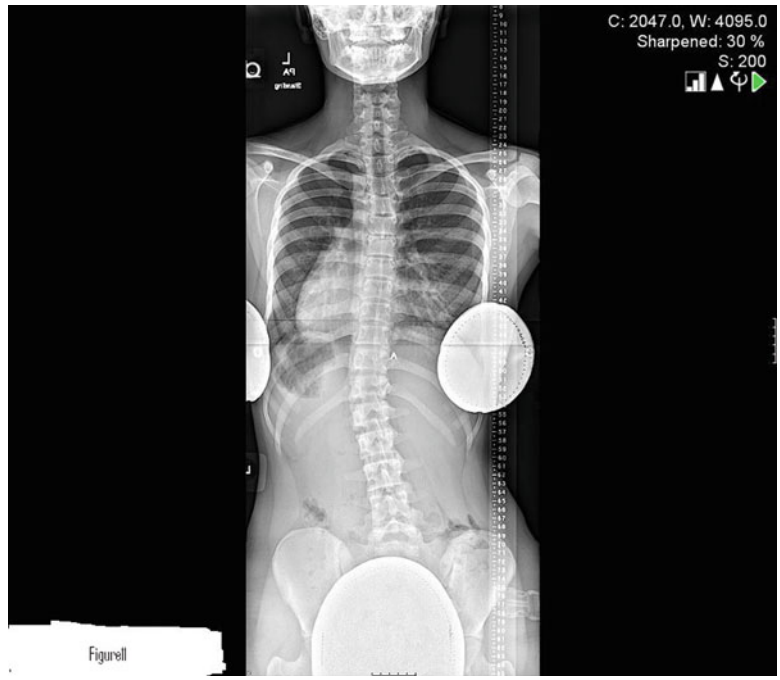


Fig. 19.13 Without rotation, this curve may be associated with a leg length asymmetry or other neurologic etiologies

The rapidly progressive curve. Idiopathic scoliosis generally progresses 1°–2° a month. If a curve progresses more rapidly, it may be associated with syrinxes, tethered cords; this is often seen in myelomeningocele.

The curve without rotation. This may be associated with leg length discrepancy, spondylolisthesis, intraspinal tumors, psychogenic curves, or pain and spasm (Fig. 19.13).

Pediatrician's Perspective

Scoliosis remains a diagnosis that pediatricians must remain vigilant about throughout a patient's entire life cycle with your practice from adolescence through puberty. Thinking of a way to incorporate a simple yearly evaluation of your patient's coronal spinal axis by having them touch their toes or bend over the exam table seems like a prudent way to avoid missing a new curve.

It is certainly within the expected initial work-up from any pediatric primary care practitioner to consider ordering a full spine X-ray as detailed above to make the first determination of a curve if there is clinical suspicion from the family, nurse, coach, or patient.

This chapter can be used as a reference tool to guide preliminary conversations with your patients regarding the likely causes of the curvature and whether further imaging may be necessary. Common sense will dictate at what point a pediatric orthopedic specialist should become involved in the evaluation, but findings on the initial X-rays of levoscoliosis, a rapidly progressive curve, and certainly any neurologic finding on exam should raise the suspicion of an intraspinal anomaly.

Bibliography for Pediatric Scoliosis

Akbarnia BA, Yazici M, Thompson GH, editors. The growing spine – management of spinal disorders in young children. New York, NY: Springer; 2010.

O'Newton P, O'Brien MF, Shufflebarger HL, Betz RR, Dickson RA, Harms J. Idiopathic scoliosis the harms study group treatment guide. New York, NY: Thieme Medical; 2010.

Slotkin J, Klimo P, Brockmeyer D. Pediatric spine surgery: normal and abnormal development of the spine. Philadelphia, PA: Elsevier; 2007.

Image Gently: Minimizing Radiation Exposure in Children

20

Linda A. Heier and Soniya N. Pinto

History of Radiation

Most lay people have the understanding that radiation is "not good for you" but have no real idea why this may be particularly true for children. To have a deeper understanding why it causes damage and how it is measured, it helps to precisely define *radiation*. Welcome to radiation for dummies. Let us start with a short history of the discovery.

William Conrad Roentgen's original paper "On A New Kind Of Rays" was published on December 28, 1895. Just weeks before on November 8, 1985, he had heated a cathode ray tube and although it was covered in black paper, he incidentally noticed a chemically coated screen glowing several feet from the tube [1].

It turned out that heating the cathode ray tube had caused electrons to come from the negatively charged filament (cathode) and cross the vacuum to the positively charged target (anode) creating a beam of invisible energy (Fig. 20.1) which passed through both the surrounding glass and paper.

L.A. Heier, M.D., F.R.C.P.(C) (✉)
Department of Radiology, Division of Neuroradiology, Weill Cornell Medical College, 525 East 68th Street, New York, NY 10065, USA
e-mail: laheier@med.cornell.edu

S.N. Pinto, M.B.B.S.
New York Presbyterian Hospital – Weill Cornell Medical Center, New York, NY 10021, USA

Roentgen called the ray of invisible energy an "X"-ray after the mathematical convention of x referring to an unknown quantity. This ray had the amazing ability to pass through solid structures making an imprint on the film or detector positioned on the other side. Bone and objects with higher electron density like metals absorb more X-rays and do not permit the same amount of X-rays to reach the detector/film as soft tissue does. This explains the darker bone and the whiter areas of soft tissue that are respectively underexposed and overexposed on this first X-ray of Roentgens' wife's hand (Fig. 20.2).

The discovery produced an immediate scientific and public sensation with Roentgen receiving the first Nobel Prize for physics. The medical potential for X-rays was swiftly realized, and 6 months after the discovery, X-rays were being used by battlefield physicians to locate bullets in wounded soldiers.

X-rays are radiant energy like light but are in the high energy part of the electromagnetic spectrum with a much shorter wavelength and higher frequency. As they pass through tissue, these beams of photons have sufficient power to knock electrons out of their orbit around an atom's nucleus. This ability to "ionize" atoms and disrupt molecular bonds is the cause of all forms of radiation damage. The fact that ionizing radiation produced tissue injury was not immediately appreciated after the discovery of X-rays.

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_20

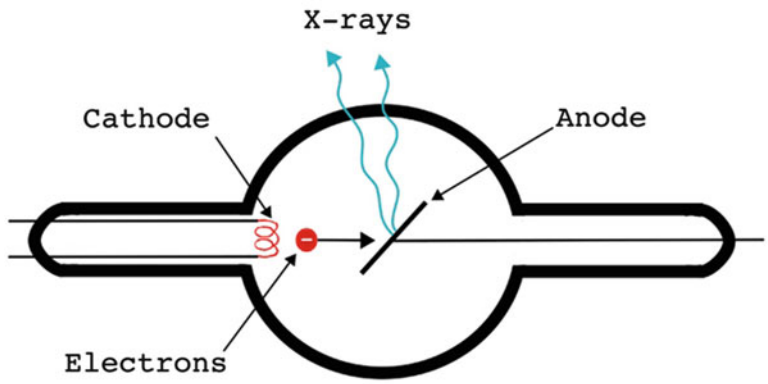


Fig. 20.1 Diagram of a cathode ray tube illustrating the production of X-rays by electrons being accelerated from the cathode to the anode

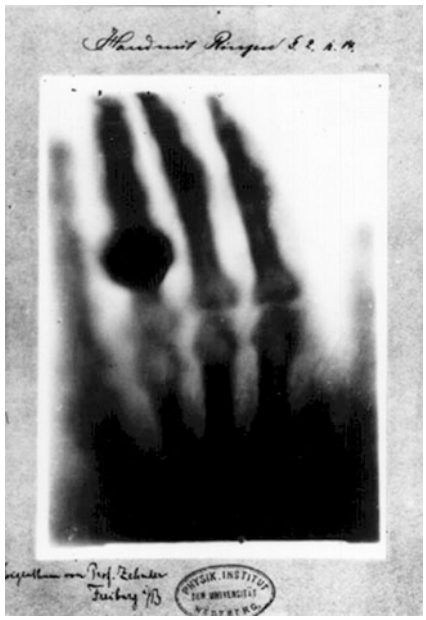


Fig. 20.2 The first X-ray was of Roentgen's wife's hand demonstrating that bone and metal (a wedding ring) appeared *dark* as they decreased the amount of X-rays from reaching the film compared to the surrounding soft tissues which were *white*. She commented that "I have seen my death" when she saw her hand as a skeleton

Within a year, Elihu Thomson of the General Electric Company performed an experiment in which he developed a severe burn after exposing the little finger of his left hand for half an hour to an X-ray tube thus proving that radiation had deleterious acute (deterministic) effects [2]. Nikola Tesla had also developed dermal burns after radiation exposure the same year but did not realize they were from the X-rays. He thought they were secondary to ozone [3].

In 1901 William Herbert Rollins, a Boston physician and dentist, demonstrated that a guinea pig in a closed, electrically insulated box could be killed by X-rays. The guinea pig died with no visible burns which indicated that lack of skin damage did not mean that a given level of X-ray exposure was safe [4]. By 1904 a glass worker by the name of Clarence Madison Dally who worked for Thomas Edison had succumbed to cancer. This was a delayed effect of testing the X-ray tubes he was making by placing his hand in the beam; Clarence died of metastatic squamous cell carcinoma after 144 failed skin grafts and bilateral arm amputations [5]. An Italian doctor who practiced radiology for 14 years without protection died of aplastic anemia, his autopsy documented in a highly publicized 1916 paper. Many early radiographers died with radiation-induced cancers [6].

It took another 20 years to realize the even more delayed genetic effects of radiation when Hermann Joseph Muller discovered the direct connection between lethal DNA mutations and increasing the radiation dose on *Drosophila* fruit flies in 1926 [7].

The subsequent detection of natural radiation emitted by elements found in nature such as uranium, polonium, and radium without an external source of energy did not produce the public media sensation that the discovery of X-rays did. The "radioactivity" discovered by Henri Becquerel and further investigated by Marie Curie and her husband Pierre was at first found to be beneficial. The Curies' recognized that radiation can kill cancer cells, creating a new oncologic therapy. The dangers were appreciated

too late. Marie died of aplastic anemia induced by radiation and to this day her papers from the 1890s are too radioactive to handle without protection [8].

Radium dial painters in America from 1917 to 1926 painted clock faces with radioactive radium paint that glowed in the dark. They were encouraged to shape their fine bristle brushes with their mouths. As a result these women developed radio-necrosis of the jaw and aggressive mouth cancers. Originally informed by the company that the paint was harmless, five female workers sued for damages and won in one of the first workman's compensation cases. Settled in 1928, each received $10,000 the equivalent of $137,345 in today's dollars [9, 10]. Perhaps radiation is responsible for the beginning of the American preoccupation with litigation.

Radiobiology

The biologic effects of ionizing radiation are of two types: dose dependent (deterministic) or non-dose dependent (stochastic).

Deterministic "effects" are dose dependent and begin when a certain threshold dose is reached and increases with increasing dose. These effects are caused by cell death and include burns, hair loss, cataracts, radiation sickness, sterility, and fetal damage [11].

Stochastic "effects" are non-dose dependent and can occur with any dose (i.e., not threshold dependent), and the severity of the "effect" (i.e., DNA mutation) is independent of dose. The "risk" of these events occurring is however dependent on dose. These effects result in permanent DNA damage, and this includes cancer induction and genetic mutations. In all cases the radiation causes damage to DNA either directly by breaking DNA links with ionization or indirectly by ionizing a water molecule into a free hydroxyl radical which then damages DNA. DNA is double stranded, thus breaks can be single or double with single being more easily repaired, but double breaks open the potential for lethal DNA connections and cell death. Alternatively DNA breaks may rejoin as a "symmetrical translocation." In this situation two different chromosomes suffer a double-strand breakage, and the broken fragments are exchanged, and the sticky ends rejoin. This may result in an oncogene fusion protein which allows potential expression of an oncogene during cell division and the development of a subsequent malignancy. It can also cause abnormal division in the reproductive cells in the ovaries and testicles, giving rise to hereditary disorders (also a stochastic effect).

As radiation damage occurs through DNA breakage, any actively dividing cell with more mitosis or a less differentiated cell is more radiosensitive. Thus tissues more sensitive to radiation include the gonads, basal epidermis, mucosa, bone marrow, and thymus and lens cells. The muscle, bones, and nervous system tissues are relatively radio resistant [11, 17].

It is this predilection for damaging DNA that accounts for the increased radiation risk in children. Children are growing with more mitotic figures in their rapidly dividing cells in general, thus their tissues are more radiosensitive. There is also a longer lifetime to manifest the late effects of radiation-induced injury such as cancer and cataracts. Each radiation exposure is cumulative over the life of the child [12].

Now that we know what radiation is and how it causes injury, we must be able to measure the dose or amount of exposure.

Radiation Dose Simplified

Before we learn to measure dose, where does most radiation exposure come from? Since 2006 the greatest radiation exposure of an individual in the United States no longer is derived from background radiation but is received directly from medical imaging at 49 %. 24 % is from computed tomography, 12 % nuclear medicine, 7 % interventional fluoroscopy, 5 % conventional radiography, and 2 % fluoroscopy (Fig. 20.3). The next greatest exposure is the natural radon and thoron background radiation at 37 %. Note the largest contribution from medical imaging is computed tomography or CT [13]. The modern X-ray tube (Fig. 20.4), where electrons produced at the

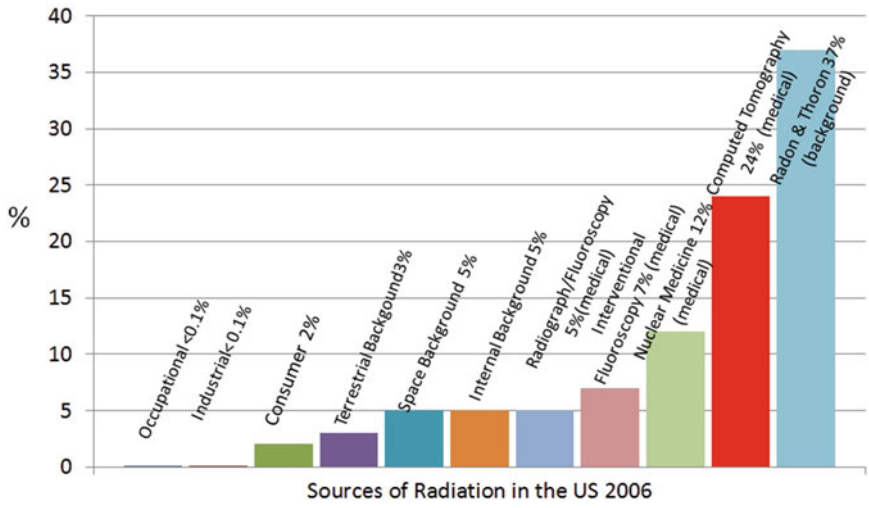


Fig. 20.3 Bar graph illustrating radiation exposure from all categories in the United States in 2006. Adapted from National Council on Radiation Protection and Measurements. Ionizing radiation exposure of the population of the United States. NCRP Report No. 160. Bethesda, Md: National Council on Radiation Protection and Measurements, 2009

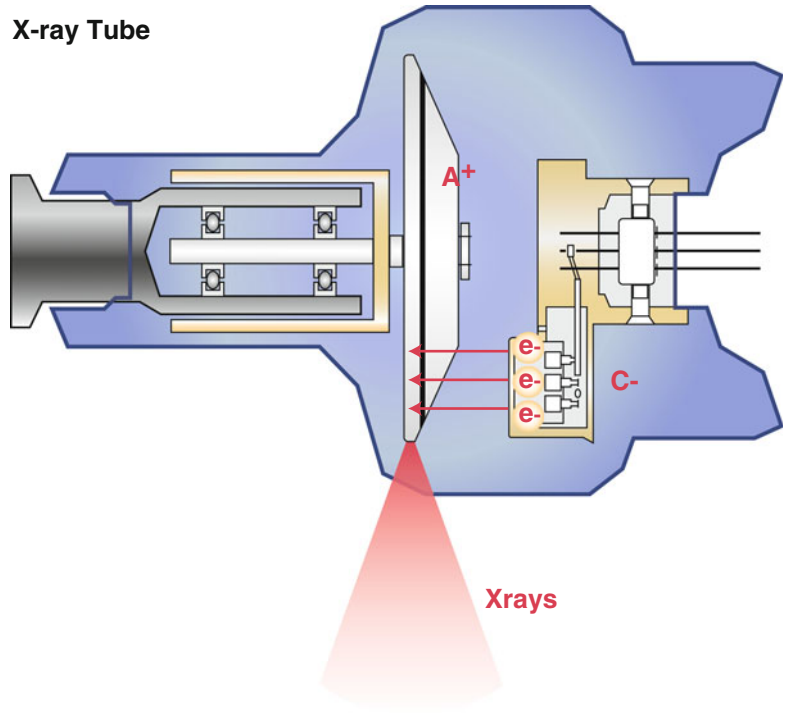


Fig. 20.4 This is a modern X-ray tube where the rotating anode (A+) is a tungsten-rhenium target on a molybdenum core backed with graphite designed to dissipate the heat produced during the exposures required for CT. C+ = cathode e = electrons

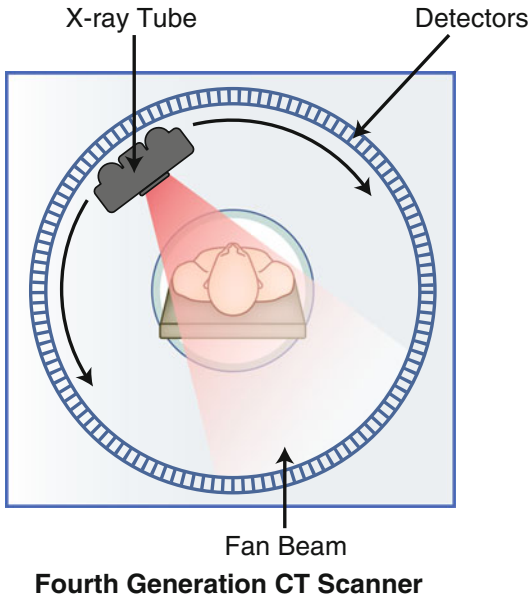


Fig. 20.5 This demonstrates a fourth-generation CT scanner which evolved from a single detector and a single X-ray tube rotating around the patient into a complete ring of stationary detectors with only the X-ray beam rotating around the patient. The scanner looks like a giant donut to children, and this appearance persists today in the latest seventh-generation scanners with cone beams and multiple detector arrays

heated negative cathode filament are accelerated across the vacuum striking the positive tungsten anode to produce X-rays, is still the principle component of CT scanners. CT began as a single X-ray tube with an opposing single detector translating around the head and evolved into a complete ring of stationary detectors (Fig. 20.5) [14]. The latest generation of CT scanners has solid rings of X-ray tubes and detectors, which rotate in opposite directions at the same time [15]. These configurations can now permit scanning of the heart in a second without a breath hold. Another development has been dual energy system where two X-ray tubes and two sets of detectors are set at 90° to one another (Fig. 20.6). Each new generation of CT has produced faster images with less radiation than previous generations [16].

The dose of all X-ray beams is related to the energy and number of the electrons within it and the time over which it is applied. The first factor affecting radiation dose is the kilovolt peak (kVp) which is the kinetic energy in kV (1 V × 1000) of the most energetic electrons arriving at the anode. If you recall your high school physics, a volt is a measure of electric potential. The kVp is the maximum voltage applied across the X-ray tube. This determines the kinetic energy of the electrons accelerated in the X-ray tube and the peak energy of the X-ray emission spectrum. This is essentially the energy of the electrons in the beam and would be analogous to the water pressure in your garden hose.

The contrast of an X-ray image which is the amount of difference between the black and whites is primarily controlled by the kVp. Each body part contains a certain type of cellular composition which requires an X-ray beam with a certain energy or kVp to penetrate it. Increasing the kVp increases the energy of the electrons producing a better quality of X-ray beam and greater penetrability which also increases the quantity of X-rays reaching the detector. Thus kVp affects both the quality and quantity of the X-ray beam [17].

The next factor controlling radiation dose is the milliampere/second (mAs) or one thousandth of an ampere per second. The ampere is a measure of the amount of electric charge passing a point per unit time, 6.241 × 1018 electrons passing a given point each second constitutes 1 A, which means this is the number of electrons per X-rays. This could be considered analogous to the size of the garden hose. Radiographic density, i.e., how many photons get through to produce the image, is primarily controlled by the mAs. Increasing mAs causes more photons (radiation) of the particular kVp energy to be produced. The tube current (mAs) affects the number of electrons and the quantity of X-rays produced. The quality of the X-ray beam produced is not affected by the mAs, only the quantity [17].

Now that we know the electrical power factors that produce the emitted radiation, how do we measure it?

The first measurement of radiation exposure was called the Roentgen. It measured ionization in air independent of area and has been redefined multiple times over the years. Currently the Roentgen is defined as 2.58×10^{-4} C of charge

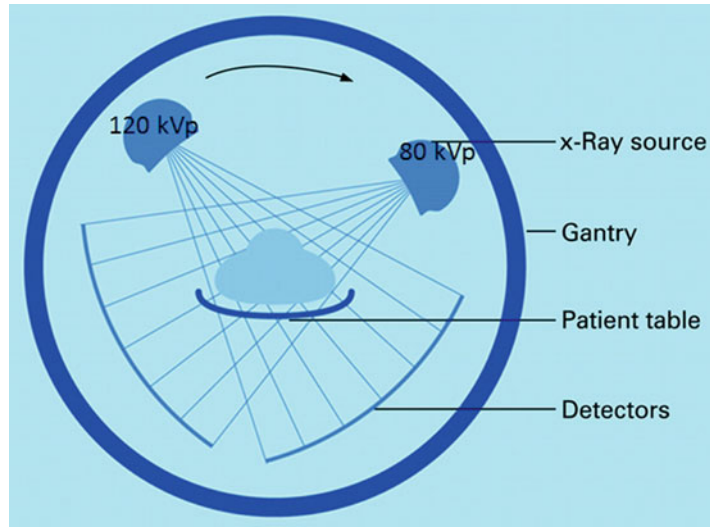


Fig. 20.6 A modern CT configuration with two X-ray tubes of different voltages oriented at 90° to each other. Dual voltage systems require more complicated calculations for dose estimates

Table 20.1 Radiation dose

Old units	System international
Roentgen (R):	Coulombs/Kg
– Unit measuring amount of radiation in air	
Rad (Roentgen absorbed dose):	Gray (Gy) [1 J/kg]
– Unit measuring absorbed energy from radiation	– 1 Gy = 100 Rads
– Absorbed dose	– 1 cGy = 1 Rad
	– 10 mGy = 1 Rad
Rem (Roentgen equivalent man):	Sievert (Sv)
– Unit measuring biological damage from radiation	– 1 Sv = 100 Rems
– Effective dose	
– Rad × QF (quality factor)	
– Biological effectiveness	

produced by X or gamma rays per kilogram of air. This does not indicate what dose actually penetrated the tissue concerned so is not very practical for medical imaging. An absorbed dose would be more useful as different tissues are more radiosensitive. The absorbed dose in *R*oentgen *a*bsorbed *d*ose or Rad = 100 ergs of energy per gram (erg = 10^{-7} J) and measures the energy absorbed in a unit mass of tissue. The old units of Rad were replaced in 1985 by the new System International (SI) by Gray (Gy) which measures Joules absorbed per kilogram [J/kg] (see Table 20.1). Measurements of "absorbed dose" are used for deterministic (dose dependent) effects of radiation, but an "effective dose" accounting for biological damage per unit dose is required to measure stochastic (dose independent) effects. The old units of effective dose were Rem (*R*oentgen *e*ffective *m*an) and were replaced in the new SI system by the Sievert where 1 Sv = 100 Rems. Effective dose must take into account a quality factor (QF) for the type of radiation but fortunately for us mathematical cripples, the QF for diagnostic X-rays is 1. The QF is different for other forms of more powerful radiation like gamma rays (Table 20.2) [17].

Table 20.3 illustrates the comparative effective dose of various imaging procedures as compared to the number of equivalent chest X-rays or days of background radiation. These metrics are very

helpful in explaining dose to patients and/or parents. For example, a head CT of an adult produces an effective radiation dose equivalent to 100 chest X-rays or 8 months' worth of background radiation. Table 20.4 demonstrates the comparative effective radiation dose for imaging procedures in a 5-year-old child. Note how the effective dose for a head CT of a 5-year-old child is 150 chest X-rays.

The younger the child, the more radiosensitive the tissues, the larger the conversion factors, and the larger the effective dose.

As we previously mentioned, the largest effective dose of radiation that people receive in this country is from diagnostic CT. CT utilization continues to increase: 85 million CT scans were performed in the United States in 2011 compared to 62 million in 2006. Over four million of these scans were performed on children. Fortunately, pediatric CT utilization began to decrease in 2003, and recent studies note the decreasing trend has persisted [18, 19], led by academic institutions [19]. This likely is due to the professional and public alarm raised by Brenner's 2001 paper "Estimated risks of radiation-induced fatal cancer from pediatric CT" [20] and the subsequent *implementation of the Image Gently* campaign. It also helped that the FDA issued an alert on October 8, 2009 informing the public that patients had received extremely high radiation doses during perfusion CT imaging due to operator error. Patients were expected to receive a dose of 0.5 Gy (max) to their head but instead received 3–4 Gy which resulted in hair loss and skin erythema with the possibility of long-term effects. The FDA began an investigation which resulted

Table 20.2 Dose equivalence

Radiation type	QF
X-ray	1
α	20
Proton	20
Thermal neutron	5
Other neutron	20

Dose equivalence = Dose × QF
Unit = Rem or Sv
Accounts for biological damage per unit dose
QF = 1 for X-rays
So, in soft tissue, 1 R ≅ 1 rad ≅ 1 rem, 1 R ≅ 10 mGy ≅ 10 mSv

Table 20.4 Imaging radiation doses: 5 years old

	mSv	CXR equivalents
3-view ankle	0.0015	1/14
2-view chest	0.02	1
Tc-99m gastric emptying	0.06	3
Tc-99m cystogram	0.18	9
Tc-99m bone scan	up to 6.2	310
FDG PET	15.3	765
Fluoroscopic cystogram	<0.33	16
Chest CT	up to 3.0	150
Abdomen CT	up to 5.0	250
Head CT	1.4 (0.6–3.2)	150

Table 20.3 Radiation dose comparison

Diagnostic procedure	Typical effective dose (mSv)	Number of chest X-rays (PA film) for equivalent effective dose[a]	Time period for equivalent effective dose from natural background radiation[b]
Chest X-ray (PA film)	0.02	1	2.4 days
Skull X-ray	0.07	4	8.5 days
Lumbar spine	1.3	65	158 days
I.V. urogram	2.5	125	304 days
Upper GI exam	3.0	150	1.0 year
Barium enema	7.0	350	2.3 years
CT head	2.0	100	243 days
CT abdomen	10.0	500	3.3 years

[a]Based on the assumption of an average "effective dose" from chest X-ray (PA film) of 0.02 mSv
[b]Based on the assumption of an average "effective dose" from natural background radiation of 3 mSv per year in the US

Patient Name:
Accession Number:
Patient ID: LightSpeed Pro 16
Exam Description: CT NECK W IV CONTRAST

Dose Report

Series	Type	Scan Range (mm)	CTDIvol (mGy)	DLP (mGy-cm)	Phantom cm
1	Scout	-	-	-	-
2	Helical	S4.500-159.250	16.61	148.89	Body 32
2	Helical	I51.500-I241.500	48.95	1027.15	Body 32
			Total Exam DLP:	1176.04	

Fig. 20.7 An example of a patient dose report from a CT scanner which is automatically produced and sent to the picture archival and communicating system (PACS) with the patients images

in their working with manufacturers of CT scanners to improve their instructions and training programs for this complex equipment and to provide software safety checks that would prevent unreasonably high radiation doses from being delivered unintentionally [21].

There are many different dose measures in medical imaging, but due to the prevalence of CT, the Computed Tomography Dose Index (CTDI) is something we see every day on the scanner console under the Dose Report header (Fig. 20.7). CTDI is the usual metric to estimate dose generated by a CT scanner. The CTDI volume is a standardized measure of the radiation output of a CT system, measured in a cylindrical acrylic phantom that enables users to gauge the amount of emitted radiation and compare the radiation output between different scan protocols or scanners. To measure the CTDI, the total radiation dose in mGy from a single CT scan is collected by a 100 mm long ionization chamber for a single axial slice divided by the nominal slice thickness. Thus CTDI is an average dose over a volume. Although CTDI is measured by using a single scan, it can be used to estimate the average dose from multiple scans where the table is incremented between successive scans [22]. It is an estimate of effective dose to either a 16 or 32 cm diameter phantom (depending on the patient's size) based on the CT parameters (kVp, mAs, length scanned) selected. It does not indicate dose to the child in the CT scanner [23]! It is just the radiation dose this scanner will emit with the particular scanning protocol programmed. The actual dose to any given patient is directly dependent on the size and shape of the patient and calculations with conversion factors (*k* factors) which are required to convert the CTDI to that particular patient's effective dose. Factors must include the patient's size, the body part, organs irradiated, age, and scan length [23].

To calculate an estimate of the effective radiation dose ("cancer risk") [23, 24] from the child's CT scan the dose length product (DLP) incorporating the length of the area scanned must be known. It also is found on the scanner console on the Dose Report header. DLP=CTDI x total length in millimeters (mm) scanned. The published "*k* factors" used to convert the DLP to effective dose previously assumed a standard patient model with organs of both sexes which of course does not exist. No adult is a perfectly cylindrical 70 kg hermaphrodite which was the "standard" patient used for adult *k* factors. For children the standard *k* factors are at 5 age intervals: newborns, 1, 5, 10, and 15 years of age

Table 20.5 Normalized values of effective dose per dose length product (DLP) over various body regions and standard patient ages [25]

Region of body	Effective dose per DLP (mSv (mGy cm)$^{-1}$) by age				
	0-year-old[a]	1-year-old[a]	5-year-old[a]	10-year-old[a]	Adult[b]
Head and neck	0.013	0.0085	0.0057	0.0042	0.0031
Head	0.011	0.0067	0.0040	0.0032	0.0021
Neck	0.017	0.012	0.011	0.0079	0.0059
Chest	0.039	0.026	0.018	0.013	0.014
Abdomen and pelvis	0.049	0.030	0.020	0.015	0.015
Trunk	0.044	0.028	0.019	0.014	0.015

[a]All data normalized to $CTDI_w$ measured in the 16-cm diameter CT dosimetry phantom
[b]Data for the head and neck regions normalized to $CTDI_w$ in the 16-cm diameter dosimetry phantom; data for the other regions normalized to $CTDI_w$ in the 32-cm diameter CT dosimetry phantom

(Table 20.5) [25, 26]. This also refers to a generic hermaphrodite child of each age. It is well known that the size assignments for age do not correlate well with the actual size of the individual patient [27]. Conversions of CTDI to effective dose are thus only rough estimates for children. As these conversion factors are not ideal, the International Commission on Radiological Protection (ICRP) publication 103 in 2007 [28] produced new recommendations for conversion factors. They were implemented by Deake et al. who concluded that separate conversion factors that take the tube voltage into account should now be used to determine the effective dose from DLP in pediatrics and the conversion factors should be specific for sex and age [29]. Lately more specific estimates of organ doses and effective whole body doses from CT are being published by age and sex [30, 31].

Acknowledging our limitations to calculate the effective dose to the 3-year-old girl who had a CT scan of her cervical spine from Fig. 20.7, we would take the total exam DLP of 102.71 mGy/cm and multiply this by the conversion factor for a 1-year-old neck looked up on Table 20.5, which was 0.012 {mSv (mGy/cm)}. This will give us 1.23 mSv as an effective dose for the study which is approximately 4 months of background radiation which was a low-dose protocol by weight. *You now know how to estimate the effective radiation dose to your patient from the dose report on the scanner and published conversion tables.* There is also a published updated radiation dose estimator with cancer risk estimates created by pediatric radiologists Adam M. Alessio and Grace S. Phillips on the website http://faculty.washington.edu/aalessio/doserisk2 using the latest more complex organ dose estimates [32].

Radiation Risk in Children

There is no doubt that in children increased radiation exposure increases the subsequent cancer risk. The unanswered question which requires further investigation is the threshold at which pediatric CT produces fatalities [20]. Whether low-dose radiation less than 100 mSieverts from diagnostic radiation can induce cancer and whether this is a linear no threshold model that can be extrapolated from higher doses has been questioned [33].

The best low-dose data available is from the Japanese survivors of the atomic bomb [34], although extrapolating low-dose radiation data from an atomic bomb blast (with whole body and gamma exposure) to a diagnostic CT scan is a stretch even if the doses are similar (Fig. 20.8) [33]. The stochastic risk of low-dose radiation in children exposed to the atom bombs has been definitely established [34]. The authors concluded "there is substantially more direct information about low dose cancer risks in the atomic bomb survivor data than is commonly believed, since the vast majority of the cohort members are

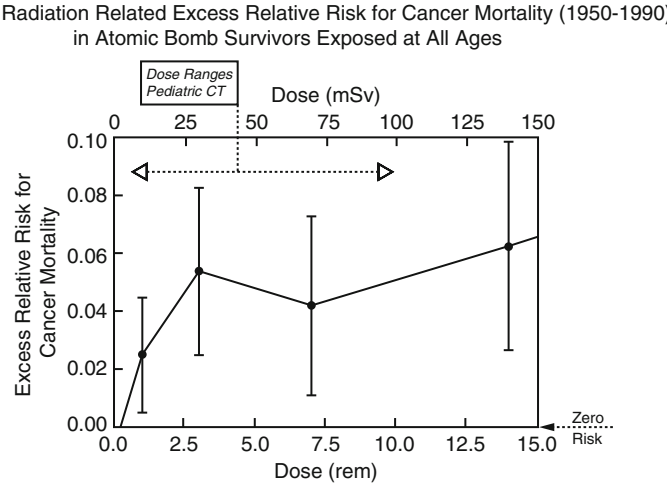


Fig. 20.8 This graph illustrates the increased cancer mortality seen with low-dose radiation equivalent to pediatric CT in atom bomb survivors of all ages [34]

Table 20.6 Excess relative risk of thyroid cancer after childhood radiation

Study	Mean thyroid dose (Gy)	ERR/Gy (CI)
Tinea capitis	0.09	32.5 (14.0–57.1)
Cervical cancer[a]	0.11	34.9 (−2.2–∞)
Atomic bomb	0.27	4.7 (1.7–10.9)
Tonsils	0.59	2.5 (0.6–26.0)
Thymus	1.36	9.1 (3.6–28.8)
Childhood cancer[b]	12.50	1.1 (0.4–29.4)

[a]ERR/Gy estimates based on regression of category-specific mean doses. The point estimate is not significant and the confidence interval is extremely large.
[b]ERR/Gy estimates based on setting dose under 2 Gy to the mean dose of 0.74 Gy.
Adapted from Thyroid Cancer after Exposure to External Radiation: A Pooled Analysis of Seven Studies. Ron E et al. Radiation Research, Vol. 141, No. 3 Mar., 1995, pp. 259–277

in the low-dose range. There is no evidence in these data that linear risk estimates from a wider dose range overestimate low-dose risks, and considerable evidence that the linear risk estimates are appropriate" [35]. Likewise therapeutic radiation in childhood from multiple sources is also an established cause of increased thyroid cancer in children (Table 20.6) [36]. These included five cohort studies (atomic bomb survivors, children treated for tinea capitis, two studies of children irradiated for enlarged tonsils, and infants irradiated for an enlarged thymus gland) and two case-control studies in patients with cervical cancer and childhood cancer. They determined that the thyroid gland in children has one of the highest risk coefficients of any organ and is the only tissue with convincing evidence for stochastic risk at about 0.10 Gy [36].

The increased relative risk of cancer in childhood associated with irradiation in utero has been documented in many case-control studies in different countries. The excess relative risk obtained from combining the results of these studies has a high statistical significance concluding that radiation doses of the order of 10 mGy received by the fetus in utero produce a consequent increase in the risk of childhood cancer [37].

However, the role of "diagnostic" radiation was less clear. One of the first studies to expose the risk of diagnostic X-rays was the incidence of breast cancer after X-rays for childhood scoliosis where twice the expected cancers were found. These results are similar to the A bomb survivors (Table 20.7) [38].

Since Brenner's paper in 2001, the most compelling studies to confirm a cancer risk at low doses of diagnostic radiation were published, respectively, in the Lancet in 2012 and in the British Medical Journal in 2013. Radiation exposure from CT scans in childhood and subsequent risk of leukemia and brain tumors: a retrospective

Table 20.7 Breast cancer incidence after diagnostic X-rays in childhood for scoliosis

Study	Values
Exposed	4822
Not exposed	644
Mean age exposure	10.6 years
Mean dose	0.11 Gy
Observed cancers	70
Expected cancers	35.7
ERR (excess relative risk) at 1 Sv	5.4
95 % CI (confidence interval)	1.2–14

Adapted from Hoffman DA et al. Breast cancer in women with scoliosis exposed to multiple diagnostic X rays. Journal of the National Cancer Institute. 1989; 81(17):1307–1312

cohort study by Pearce MS et al. investigated 178,604 children without cancer who underwent X-ray CT between 1985 and 2002 across the United Kingdom [39]. State-of-the-art dosimetric methodology was used to estimate radiation doses to individual organs of these children and identified subsequent cancers via linkage to the National Health Service Central Registry. To avoid confounding the data with CT scans performed for cancer diagnosis, they excluded leukemias occurring within 2 years of the scan and brain tumors occurring within 5 years, lag periods during which it is not thought that radiation-related cancers occur. Over follow-up of about 10 years after exposure and maximum follow-up of 23 years, statistically significant increases in leukemia incidence were found in the children with cumulative bone marrow doses from CT of at least 30 mSieverts equivalent, while significant increases in brain tumor incidence were found in children with brain doses of at least 50 mSieverts equivalent. Using current typical doses, the authors found that 2–3 head CTs could triple children's risk of brain cancer and that 5–10 head CTs could triple the risk of leukemia. To keep things in perspective, applying the dose estimates for one head CT scan before the age of 10 years would translate into approximately one excess case of leukemia and one excess brain tumor per 10,000 patients. The findings of Pearce et al. suggest a higher brain cancer risk per unit than does the atomic bomb survivor data and a similar leukemia risk [39].

Another large childhood cohort study identified 10.9 million people from Australian Medicare Records aged 0–19 years on January 1, 1985, or born between January 1, 1985, and December 31, 2005; all exposures to CT scans funded by Medicare during 1985–2005 were identified for this cohort. Cancers diagnosed in cohort members up to December 31, 2007, were obtained through linkage to national cancer records. Overall cancer incidence was 24 % greater for exposed than for unexposed people, after accounting for age, sex, and year of birth (incidence rate ratio (IRR) 1.24 (95 % confidence interval 1.20–1.29); $P < 0.001$). They concluded that "the increased incidence of cancer after CT scan exposure in this cohort was mostly due to irradiation" and recommended that "future CT scans should be limited to situations where there is a definite clinical indication, with every scan optimized to provide a diagnostic CT image at the lowest possible radiation dose" [40].

Since the suggestion that pediatric CT scans might produce a small cancer risk in 2001 by Brenner, almost 12 years later these two papers indicate it is likely true. Fortunately the risk is small as indicated by the size of the cohorts required. The www.imagegently.org website run by the Alliance for Radiation Safety in Pediatric Imaging has posted letters to parents for each of these studies where they try to put the risk into a lay person's perspective which is useful for parental reassurance. At the time of writing over ten large cohort studies of CT exposure in children from Europe, Canada, and Israel will be reporting by 2016 [41], and we may have a more definitive answer on the amount of radiation required to induce cancer in an individual in the next decade.

Radiation Dose Reduction and Alternative CNS Imaging

Pediatricians' Responsibility

As a clinician/pediatrician, the first question to ask is whether a CT study indicated? Will the result change your management? *If not, don't do it.*

Table 20.8 American College of Radiology ACR Appropriateness Criteria

Date of origin: 1999
Last review date: 2012

American College of Radiology
ACR Appropriateness Criteria®

Clinical Condition: **Headache — Child**

Variant 1: **Primary headache (chronic or recurrent headache including migraine without permanent neurologic signs or signs of increased intracranial pressure).**

Radiologic Procedure	Rating	Comments	RRL*
MRI head without contrast	3		O
MRI head without and with contrast	3		O
CT head without contrast	2		☢☢☢
CT head with contrast	1		☢☢☢
CT head without and with contrast	1		☢☢☢☢
CTA head with contrast	1		☢☢☢☢
MRA head without contrast	1		O
MRA head without and with contrast	1		O
Arteriography cerebral	1		☢☢☢☢
Rating Scale: 1,2,3 Usually not appropriate; 4,5,6 May be appropriate; 7,8,9 Usually appropriate			*Relative Radiation Level

Try and optimize the risk/benefit ratio by examining whether it is appropriate to do the exam, whether the timing is appropriate, and whether it is the appropriate modality. This leads us to the second question. *Can the CT be replaced with a plain film, MR, or US?* The American College of Radiology publishes practice guidelines for many common Pediatric CNS indications easily accessed online (acr.org) which can help inform your choice of study. The ACR Appropriateness Criteria® are found on their website under the tab *Quality and Safety*. These are evidence-based guidelines to assist referring physicians in making the most appropriate imaging or treatment decision for a specific clinical condition. By employing these guidelines, providers enhance quality of care and contribute to the most efficacious use of radiology. These guidelines have been developed by expert panels in diagnostic imaging, interventional radiology, and radiation oncology and other specialties. As of November 2013, the ACR Appropriateness Criteria covered 197 topics with over 900 variants, and we will review some of the covered pediatric CNS topics (Table 20.8). Their rating scale is from 1 to 10 where studies 1, 2, and 3 are usually not appropriate; 4, 5, and 6 may be appropriate and 7, 8, and 9 are usually appropriate. They include the radiation dose of each study with an easy to follow legend converting mSv into a symbol (Table 20.9) [42]. *When you are unsure of what is the best option, discuss what is available with the radiologist directly*. Try to order the study based on medical indications following best practices or defined protocols and *not on parental or legal pressure*. Be aware of the basic dose equivalents of the studies you most frequently order so you can speak to parents with confidence. Be aware of the Image Gently Campaign which provides web-based resources for clinicians, radiologists, technologists, and parents in an attempt to keep radiation doses as low as reasonably achievable

Table 20.9 ACR relative radiation level designations in mSv

Relative radiation level[a]	Adult effective dose estimate range	Pediatric effective dose estimate range
0	0	0
☢	<0.1	<0.03
☢ ☢	0.1–1	0.03–0.3
☢ ☢ ☢	1–10.0	0.3–3
☢ ☢ ☢ ☢	10–30.0	3–10.0
☢ ☢ ☢ ☢ ☢	30–100.0	10–30.0

[a]RRL assignments for some of the examinations cannot be made, because the actual patient doses in these procedures vary as a function of a number of factors (e.g., region of the body exposed to ionizing radiation, the imaging guidance that is used). The RRLs for these examinations are designated as NS (not specified)

in the pediatric population (www.imagegently.org) (Fig. 20.9). Since most acute CNS problems usually begin with CT imaging, we stress this modality, but there are other forms of imaging that give greater doses of radiation such as PET (positron emission tomography) and cerebral angiography. By the time these studies are ordered, however, there is a clear indication for them, and the added radiation is clearly worth the benefit. The dosing of these studies is also available on the *Image Gently* website.

Radiologists' Responsibility

Radiologists keep in mind the *As Low As Reasonably Achievable* (ALARA) principle to keep radiation doses as low as possible as long as the study is still diagnostic and able to answer the question asked. They must understand radiation doses and routinely review requests for CT studies in advance and discuss the indications with the clinicians as necessary. The CT protocol must be tailored for the indication and the need if any for sedation or general anesthesia. Talking to the parents or the referring pediatrician may help identify the children likely to stay still, thus reducing sedation and decreasing the need for repeat studies due to motion.

The technologists should limit the scan area in children and do the area requested and not include nearly the entire cervical spine on a head CT as often happens. The technologists must be responsible for shielding such as placing lead/bismuth thyroid collars or eye shields routinely on children for head CTs or shielding the gonads in cervical/thoracic/lumbar spine studies. Shielding can inadvertently increase radiation doses with the modern CT automatic exposure controls (AEC), and each CT model may be different. A medical physicist should determine how shielding is used in each scanner and inform the technical staff [43]. Since technologists often interact more with parents, they should have information made available to them for the parents. The technologist and radiologists both should be aware of prior studies as many follow-up exams can be performed at a lower dose. Strauss et al. (Table 20.10) summarizes ten effective strategies for lowering dose in the pediatric population in your radiology department [44]. Remember the three As of awareness, appropriateness, and audit when ordering CT in any population, especially in pediatrics.

Indications for Pediatric Head CT

The most common appropriate indications for a head CT include trauma (accidental and non-accidental), headache with altered behavior or neurological deficit, altered metal status after acute collapse, seizures or status epilepticus, craniofacial anomalies, bone lesions, postoperative

What Parents Should Know About CT Scans for Children:

Medical Radiation Safety

What is an X-ray?

X-rays are invisible beams of ionizing radiation that pass through the body and are altered by different tissues to create 2-dimensional images of many organs.

What is a CT scan?

CT scans use x-rays generated from a source that is rotated around the body to create 3-dimensional pictures of the body. CT studies can provide critical information for the care of your child, but obtaining the images results in more radiation exposure for the study than a single X-ray.

How much radiation is used in these exams?

We all are exposed to small amounts of radiation daily from soil, rocks, building materials, air, water, and cosmic radiation. This is called naturally occurring background radiation. The radiation used in X-rays and CT scans has been compared to background radiation we are exposed to daily. This comparison may be helpful in understanding relative radiation doses to the patient.

Radiation source	Days background radiation
Background	1 day
Chest X-ray (single)	1 day
Head CT	up to 8 months
Abdominal CT	up to 20 months

image gently℠

www.imagegently.org

Fig. 20.9 The cover of a brochure for parents provided by the Image Gently website (used with permission) explaining CT and its relative radiation dose

Table 20.10 Steps to lower CT radiation dose while maintaining image quality

1. Educate the radiologic technologists to be aware of radiation exposure
2 Utilize a medical physicist
3. Obtain an American College of Radiology Accreditation
4. Utilize alternative imaging modalities
5. Is the CT clinically indicated?
6. Establish radiation doses for adult-sized patients
7. Establish radiation doses for pediatric patients by "child sizing" CT scanning parameters
8. Optimize pediatric dose parameters
9. Scan only the indicated area: scan once
10. Prepare a child-friendly and expeditious CT environment

Adapted from Strauss KJ, Goske MJ, Kaste SC, Bulas D, Frush DP, Butler P, et al. Image gently: ten steps you can take to optimize image quality and lower CT dose for pediatric patients. American Journal of Roentgenology. 2010; 194(4):868–873

neurosurgical complications, and possible ventriculoperitoneal (VP) shunt malfunction [45]. Most of these are emergent indications to rule out space-occupying lesions and should be done without hesitation. Possible VP shunt malfunction requires head imaging to assess for ventricular size and surrounding edema which can be evaluated with ultrasound (US) under 6 months but can be an indication for CT thereafter. It should be done with a low-dose CT protocol with the kVp reduced [46]. Recently plain film shunt series have been found not to be cost-effective in diagnosing shunt malfunction [47], while *CT was overutilized in the emergency department* [48]. *When available MR of the brain with ultrafast scanning pulse is the best choice and should supplant CT in the evaluation of shunt malfunction* [49].

The use of head CT in trauma has been erratic in the past but more and more ERs use defined algorithms which help reduce unnecessary CT. Three recently published rules, the Pediatric Emergency Care Applied Research Network (PECARN) rule [50], Children's Head Injury Algorithm for the Prediction of Important Clinical Events (CHALICE) [51], and the Canadian Assessment of Tomography for Childhood Head Injury (CATCH) [52], show promise for improving clinical decision-making after minor head injury by potentially increasing recognition of injuries and reducing the frequency of CT. For each of the rules, the absence of any features of the rule obviates the need for CT by categorizing a patient as low risk for clinically important traumatic brain injury. The PECARN rules have been found to be the most accurate in predicting significant head injury along with physician practice [53]. Thankfully the role of the physician has not been entirely usurped by machines!

Imaging Algorithms for Common Neurologic Pediatric Conditions

Head Trauma

As discussed in indications for pediatric head CT, an acute head injury is unequivocally an indication for CT. If there is a suspicion of abuse or non-accidental trauma, a subsequent MR is appropriate to diagnose the usually associated cytotoxic edema on diffusion weighted imaging (DWI) [54]. It also can often diagnose retinal hemorrhages before the ophthalmologists can get a dilated exam with the newer susceptibility weighted sequences (SWI) which are exquisitely sensitive for hemorrhage [55]. In acute accidental trauma, MR is always indicated when the CT findings do not account for the child's neurological exam. In the chronic phase of trauma, MR is also the indicated study for long-term prognosis.

Cervical Spine Trauma

Whether the imaging algorithm starts with plain films (CR) or CT in children has been debated. Silva et al. showed that lateral radiographs alone

had borderline sensitivity for detecting injuries compared with CT, and additional views did not improve the diagnostic performance of radiography [56]. Nevertheless we start out with a lateral film of the cervical spine if indicated clinically by the National Emergency X-Radiography Utilization Study (NEXUS) or the Canadian Cervical Spine Rule (CCR). According to the ACR Appropriateness Criteria, these decision rules apply in children [57]. Clinical NEXUS and CCR rules symptoms without a neurologic deficit are an indication for CT of the C spine, but make sure the protocol is tailored to the size of the child by weight as the thyroid is highly radiosensitive. With a neurologic deficit, both CT and MR of the cervical spine should be performed. If a vascular injury is suspected, MRA or CTA can be performed, although we prefer to start with an MRA and if it is non-diagnostic we do a CTA. If the patient is in a collar and persistently clinically unevaluable for >48 hours, an MRI is indicated. When in doubt do the MRI which must be a trauma protocol with fat-suppressed T2 images or STIR (inversion recovery) sequences to reveal ligamentous and soft tissue injury particularly of the craniocervical junction so predominant in children under 3. The cervical spine clearance algorithm I prefer for under the age of 3 is by Anderson et al. [58].

Headache

Chronic or recurrent headache including migraine without permanent neurologic signs and no signs of increased intracranial pressure (ICP) is not an indication for CT with an ACR Appropriateness Criteria rating of 2 [59]. An MR in this case is preferable but still probably unnecessary with a rating of 3. Try ultrafast sequences to avoid sedation and lower the risk. Headache with signs of raised ICP is a sound reason for MR (ACR 8), and if MR is unavailable or there are sedation issues, utilize CT (ACR 7) [60].

Seizures

Neonatal seizures are first imaged with US (ACR rating 9), but we nearly always do an MRI of the head without contrast as well (only ACR 5), particularly for hypoxic-ischemic encephalopathy (HIE) and to exclude tuberous sclerosis and congenital malformations. Simple febrile seizures are not an indication for imaging (ACR 2). Complex febrile seizures may be imaged [61] preferably with MR (ACR 4) and indicated less with CT (ACR 3). Posttraumatic seizures are an indication for CT (ACR 9) and less so for MR (ACR 4). Partial seizures are an unequivocal indication for MR (ACR 9) as are generalized seizures in a child neurologically abnormal. A first generalized seizure in a neurologically normal child may be an indication for MR (ACR 5) and less for CT (ACR 4) [62], but this is where theory and practice differ as nearly all first time seizures are studied in our institution.

Developmental Delay

Under the age of 6 months, an US can be the initial study but MR is always next and often first. CT is only useful to confirm calcifications if TORCH is suspected or in venous hypertension seen with high flow dural malformations. Shortly SWI sequences with QSM maps may confirm calcification on MR [63].

Head Enlargement

Under 6 months of age, US is the exam of choice followed by MR. CT is to be avoided if possible. 3D T2 imaging reconstructed in 3 planes is the go to sequence for CSF obstruction whether communicating or noncommunicating.

Head Lumps and Bumps

In young infants before the anterior skull base has ossified, intracranial extension of skull lesions (e.g., nasal dermoid) may be difficult to exclude on CT. MRI has replaced CT as the primary imaging modality for early lumps and bumps [44]. We use a combination of plain films and MRI which usually provides the diagnosis and answers the question of intracranial extension of the lesion. CT is used only to answer questions MRI does not answer.

Possible Spinal Dysraphism

Under the age of 6 months, US is attempted first followed by MRI. If complex vertebral anomalies are associated, plain films are performed first and

if they do not answer the surgeons' questions, a CT is done with 3D reconstructions for preoperative evaluation.

Take-Home Messages

1. Diagnostic CT in pediatrics appears to have an extremely small but likely real risk of causing cancer in children.
2. Keep in mind the principles of ALARA, awareness, appropriateness, and audit when ordering studies utilizing radiation to ensure that the patient receives the best immediate care with the least possible consequences to their future.
3. CT provides an overwhelming benefit in the setting of acute neurologic events at any age and should not be withheld when the results can effect management.
4. Alternatives such as ultrafast MR can now replace CT for VP shunt malfunction.
5. Children are **not** little adults so radiation dosage **must** be child sized.

References

1. Roentgen WC. Eine Neue Art von Strahlen. Sitzungsberichte der Wurzburger Physik-medico Gegellschraft, 1895.
2. Thomson E. Roentgen rays act strongly on the tissues. Elect Eng. 1896;22:534.
3. Brecher R, Brecher E. The rays. A history of radiology in the United States and Canada. Baltimore, MD: Williams & Wilkins; 1969.
4. Rollins W. X-light kills. Boston Med Surg J. 1901; 44:173.
5. Brown P. American martyrs to science through the Roentgen rays. Springfield, IL: Thomas; 1936.
6. Bruwer AJ. Classic descriptions in diagnostic roentgenology, vol. 1. Springfield, IL: Thomas; 1964.
7. Muller HJ. The production of mutations by X-rays. Proc Natl Acad Sci U S A. 1928;14(9):714.
8. Lederman M. The early history of radiotherapy: 1895–1939. Int J Radiat Oncol Biol Phys. 1981;7: 639–48.
9. Kovarik Bill (Revised 2002). "The Radium Girls." originally published as chapter eight of Mass Media and Environmental Conflict. RUNet.edu.
10. http://data.bls.gov/cgi-bin/cpicalc.pl.
11. Goodman TR. Ionizing radiation effects and their risk to humans. November 2010 Available from: http://www.imagewisely.org.
12. Brenner DJ, Hall EJ. Computed tomography: an increasing source of radiation exposure. N Engl J Med. 2007;357:2277–84.
13. National Council on Radiation Protection and Measurements. Ionizing radiation exposure of the population of the United States. NCRP Report No. 160. Bethesda, MD: National Council on Radiation Protection and Measurements; 2009.
14. Hendee WR. Cross sectional medical imaging: a history. Radiographics. 1989;9(6):1155–80.
15. Euclid S. Computed tomography: Physical principles, clinical applications, and quality control. St. Louis, MO: Saunders/Elsevier; 2009.
16. Fritz JV. Neuroimaging trends and future outlook. Neurol Clin. 2014;32(1):1–29.
17. Attix FH. Introduction to radiological physics and radiation dosimetry. Hoboken, NJ: John Wiley & Sons; 2008.
18. Miglioretti DL, Johnson E, Williams A. The use of computed tomography in pediatrics and the associated radiation exposure and estimated cancer risk. JAMA Pediatr. 2013;10:1–8.
19. Hoshiko S, et al. Trends in CT scan rates in children and pregnant women: teaching, private, public and nonprofit facilities. Pediatr Radiol. 2014;44:522.
20. Brenner DJ, Elliston CD, Hall EJ, Berdon WE. Estimated risks of radiation-induced fatal cancer from pediatric CT. Am J Roentgenol. 2001;176(2): 289–96.
21. http://www.fda.gov/MedicalDevices/Safety/AlertsandNotices/ucm185898.htm.
22. Bauhs JA, Vrieze TJ, Primak AN, Bruesewitz MR, McCollough CH. CT dosimetry: comparison of measurement techniques and devices. Radiographics. 2008;28:245–53.
23. McCollough CH, Leng S, Yu L, Cody DD, Boone JM, McNitt-Gray MF. CT dose index and patient dose: they are not the same thing. Radiol Radiol Soc N Am. 2011;259(2):311.
24. Thomas KE, Wang B. Age-specific effective doses for pediatric MSCT examinations at a large children's hospital using DLP conversion coefficients: a simple estimation method. Pediatr Radiol. 2008;38(6): 645–56.
25. Shrimpton PC, Hillier M, Lewis M, Dunn M. Doses from computed tomography (CT) examinations in the UK-2003 (NRPB-W67). Chilton: National Radiological Protection Board; 2005. Available from: http://www.hpa.org.uk/radiation/publications/w_series_reports/2005/nrpb_w67.htm.
26. Shrimpton PC, Hillier MC, Lewis MA, Dunn M. National survey of doses from CT in the UK: 2003. Br J Radiol. 2006;79:968–80.
27. Kleinman PL, Strauss KJ, Zurakowski D, Buckley KS, Taylor GA. Patient size measured on CT images as a function of age at a tertiary care children's hospital. AJR Am J Roentgenol. 2010;194(6):1611–9.

28. The 2007 recommendations of the International Commission on Radiological Protection. ICRP publication 103. Ann ICRP. 2007; 37(2-4):1–332.
29. Deak PD, Smal Y, Kalender WA. Multisection CT protocols: sex-and age-specific conversion factors used to determine effective dose from dose-length product. Radiology. 2010;257(1):158.
30. Kim KP, Berrington de Gonzalez A, Pearce MS, Salotti JA, Parker L, McHugh K, et al. Development of a database of organ doses for pediatric and young adult CT scans in the United Kingdom. Radiat Prot Dosim. 2012;150(4):415–26. doi:10.1093/rpd/ncr429. PubMed PMID: 22228685, PMCID: PMC3400529.
31. American Association of Physicists in Medicine [Internet]. College Park (MD): 2011 AAPM report no. 204: size-specific dose estimates (SSDE) in pediatric and adult body CT examinations; [pdf]. Available from: www.aapm.org/pubs/reports/rpt_204.pdf.
32. Alessio AM, Phillips GS. A pediatric CT dose and risk estimator. Pediatr Radiol. 2010;40:1816–22.
33. Hendee WR, OConnor MK. Radiation risks of medical imaging: separating fact from fantasy. Radiol Radiol Soc N Am. 2012;264(2):312.
34. Radiation Effects Research Foundation [Internet]. Hiroshima, Japan. Available from: http://www.rerf.or.jp/library/dl_e/index.html.
35. Pierce DA, Preston DL. Radiation-related cancer risks at low doses among atomic bomb survivors. Radiat Res. 2000;154(2):178–86.
36. Ron E, Lubin JH, Shore RE, Mabuchi K, Modan B, Pottern LM, et al. Thyroid cancer after exposure to external radiation: a pooled analysis of seven studies. J Radiat Res. 1995;141(3):259–77.
37. Doll R, Wakeford R. Risk of childhood cancer from fetal irradiation. Br J Radiol. 1997;70:130–9.
38. Hoffman DA, Lonstein JE, Morin MM, Visscher W, Harris BS, Boice JD. Breast cancer in women with scoliosis exposed to multiple diagnostic x rays. J Natl Cancer Inst. 1989;81(17):1307–12.
39. Pearce MS, Salotti JA, Little MP, McHugh K, Lee C, Kim KP, et al. Radiation exposure from CT scans in childhood and subsequent risk of leukaemia and brain tumours: a retrospective cohort study. Lancet. 2012;380(9840):499–505.
40. Matthews JD, Forsythe AV, Brady Z, Butler MW, Georgen SK, Byrnes GB, et al. Cancer risk in 680,000 people exposed to computed tomography scans in childhood or adolescent: data linkage study of 11 million Australians. BMJ. 2013;346:1–18.
41. Einstein AJ. Beyond the bombs: cancer risks from low-dose medical radiation. Lancet. 2012;380(9840):455.
42. American College of Radiology. ACR Appropriateness Criteria®. Available from: www.acr.org/ac. Accessed March 5, 2014.
43. Raissaki M, Perisinakis K, Damilakis J, Gourtsoyiannis N. Eye-lens bismuth shielding in paediatric head CT: artefact evaluation and reduction. Pediatr Radiol. 2010;40(11):1748–54.
44. Strauss KJ, Goske MJ, Kaste SC, Bulas D, Frush DP, Butler P, et al. Image gently: ten steps you can take to optimize image quality and lower CT dose for pediatric patients. Am J Roentgenol. 2010;194(4):868–73.
45. Rao P, Bekhit E, Ramanauskas F, Kumbla S. CT head in children. Eur J Radiol. 2013;82(7):1050–8.
46. Udayasankar UK, Braithwaite K, Arvaniti M, Tudorascu D, Small WC, Little S, et al. Low-dose nonenhanced head CT protocol for follow-up evaluation of children with ventriculoperitoneal shunt: reduction of radiation and effect on image quality. AJNR Am J Neuroradiol. 2008;29(4):802–6.
47. Shuaib W, Johnson JO, Pande V, Salastekar N, Kang J, He Q, et al. Ventriculoperitoneal shunt malfunction: cumulative effect of cost, radiation, and turnaround time on the patient and the health care system. Am J Roentgenol. 2014;202(1):13–7.
48. Cohen JS, Jamal N, Dawes C, Chamberlain JM, Atabaki SM. Cranial computed tomography utilization for suspected ventriculoperitoneal shunt malfunction in a Pediatric Emergency Department. J Emerg Med. 2014;46(4):449–55.
49. Patel DM, Tubbs RS, Pate G, Johnston Jr JM, Blount JP. Fast-sequence MRI studies for surveillance imaging in pediatric hydrocephalus. J Neurosurg Pediatr. 2014;13:440.
50. Kuppermann N, Holmes JF, Dayan PS, Hoyle Jr JD, Atabaki SM, Holubkov R. Pediatric Emergency Care Applied Research Network (PECARN). Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. Lancet. 2009;374:1160–70.
51. Mannix R, Meehan WP, Monuteaux MC, Bachur RG. Computed tomography for minor head injury: variation and trends in major United States pediatric emergency departments. J Pediatr. 2012;160:136–9.
52. Osmond MH, Klassen TP, Wells GA, Correll R, Jarvis A, Joubert G, et al. CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury. Can Med Assoc J. 2010;182(4):341–8.
53. Easter JS, Bakes K, Dhaliwal J, Miller M, Caruso E, Haukoos JS. Comparison of PECARN, CATCH, and CHALICE rules for children with minor head injury: a prospective cohort study. Ann Emerg Med. 2014; 64:145.
54. Kadom N, Khademian Z, Vezina G, Shalaby-Rana E, Rice A, Hinds T. Usefulness of MRI detection of cervical spine and brain injuries in the evaluation of abusive head trauma. Pediatr Radiol. 2014;44:839.
55. Zuccoli G, Panigrahy A, Haldipur A, Willaman D, Squires J, Wolford J, et al. Susceptibility weighted imaging depicts retinal hemorrhages in abusive head trauma. Neuroradiology. 2013;55(7):889–93.
56. Silva CT, Doria AS, Traubici J, Moineddin R, Davila J, Shroff M. Do additional views improve the diagnostic performance of cervical spine radiography in pediatric trauma? AJR Am J Roentgenol. 2010; 194(2):500–8.

57. Daffner RH, Weissman BN, Wippold II FJ, Angtuaco EJ, Appel M, Berger KL et al. ACR Appropriateness Criteria® Suspected Spine Trauma. Available from: http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/SuspectedSpineTrauma.pdf. American College of Radiology. Accessed March 5, 2014.
58. Richard CE, Anderson MD, Peter K, Vanaman M, Rubsam J, Hansen KW, et al. Utility of a cervical spine clearance protocol after trauma in children between 0 and 3 years of age. J Neurosurg Pediatr. 2010;5:292–6.
59. Sempere AP, Porta-Etessam J, Medrano V, Garcia-Morales I, Concepcion L, Ramos A, et al. Neuroimaging in the evaluation of patients with non-acute headache. Cephalalgia. 2005;25(1):30–5.
60. Hayes LL, Coley BD, Karmazyn B, Dempsey-Robertson ME, Dillman JR, Dory CE, et al. ACR Appropriateness Criteria® Headache-Child. Available from: http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/Headache Child.pdf. American College of Radiology. Accessed March 5, 2014.
61. DiMario Jr FJ. Children presenting with complex febrile seizures do not routinely need computed tomography scanning in the emergency department. Pediatrics. 2006;117(2):528–30.
62. Dory CE, Coley BD, Karmazyn B, Charron M, Dempsey ME, Dillman JR, et al. ACR Appropriateness Criteria® Seizures-Child. Available from: http://www.acr.org/~/media/ACR/Documents/AppCriteria/Diagnostic/ Seizures-Child.pdf. American College of Radiology. Accessed March 5, 2014.
63. Deistung A, Schweser F, Wiestler B, Abello M, Roethke M, Sahm F, et al. Quantitative susceptibility mapping differentiates between blood depositions and calcifications in patients with glioblastoma. PLoS One. 2013;8(3):e57924.

Part V

Beyond Hydrocephalus: What Pediatric Neurosurgeons Treat Most

Chiari Malformation

21

Konstantinos Margetis and Jeffrey P. Greenfield

Clinical Vignettes

A Nonoperative Case

A 10-year-old boy with a noncontributory medical history presents with a 2-year history of intermittent headaches. The headaches occur for a few days each month; they are tension-like in character, mild in intensity, and located to temporal region bilaterally. They are usually preceded by physical activities, last approximately 1 h, resolve with rest, and rarely require acetaminophen. He denies any other symptoms including the following, which were explicitly inquired: numbness/tingling, snoring at night, and swallowing difficulties. He has a normal neurological exam, full painless range of motion of cervical spine, and no signs of scoliosis. The family of the child insisted on obtaining a brain MRI to further investigate. The MRI shows a tonsillar herniation through the foramen magnum measuring 7 mm (Fig. 21.1a), which meets the criteria for Chiari 1 malformation. There is also mild crowding at the foramen magnum, but phase-contrast imaging demonstrates CSF flow at the level of the foramen magnum (Fig. 21.1b). An MRI of the C-spine was then performed to search for asymptomatic syrinx, which was ruled out following the exam. The mild intensity and the atypical, temporal location of the headaches, the demonstration of flow at the foramen magnum, and the absence of syringomyelia all contributed to the decision for a conservative treatment of the headaches.

An Operative Case

A 16-year-old girl with a noncontributory medical history presented with a 10-month history of unremitting headaches, which interfered with her ability to attend school. She describes them as constant throughout the day; sleep was the only time she had relief. They are located at the left temporal and occipital area; they are moderate to severe in intensity and tension type in character. She denies any numbness/tingling, snoring, and swallowing difficulties. Her neurological examination is normal. A pediatric neurologist recommended a brain MRI for the workup of the headaches. The MRI (Fig. 21.2) showed that the cerebellar tonsils extend below the foramen magnum by approximately 9 mm. There was narrowing of the subarachnoid space at the craniovertebral

K. Margetis, M.D. (✉)
Icahn School of Medicine at Mount Sinai, One Gustave L., Levy Place, Box 1136, New York, NY 10029
e-mail: konstantinmarg@yahoo.com

J.P. Greenfield, M.D., Ph.D.
Associate Professor of Neurological Surgery, Weill Cornell Medical College, 525 East 68th Street, Box 99, New York, NY 10065, USA

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_21

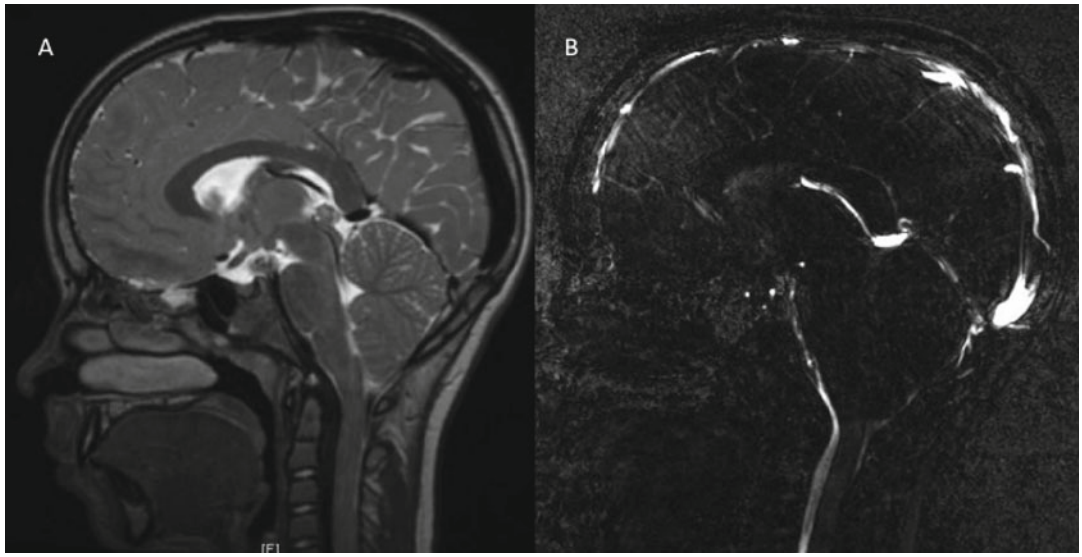


Fig. 21.1 Nonoperative Chiari 1 case (**a**). Sagittal T2W MRI image shows a Chiari 1 malformation. CSF flow artifact is evident dorsally to the spinal cord. Note that the spinal cord appears normal without a syrinx. (**b**) Phase-contrast sagittal MRI image shows CSF flow both ventrally and dorsally to the spinal cord. Note the flow signal on the superior sagittal sinus, the internal cerebral veins, and the vein of Galen

junction. On phase-contrast flow studies, there is minimal flow in the dorsal subarachnoid space at the craniovertebral junction.

A dural sparing suboccipital decompression was performed with an uncomplicated postoperative course. At the 3-month follow-up visit, the headaches had almost completely resolved, and the patient was excited with the result. A post-op MRI (Fig. 21.2) was obtained at that time that showed resolution of the tonsillar compression with reconstitution of the subarachnoid space at this region. Phase-contrast studies showed an improved CSF flow at the dorsal subarachnoid space of the craniovertebral junction.

The definition of Chiari malformation encompasses a series of posterior fossa malformations that were first described by the Austrian Professor Hans Chiari. Recently, some new variants have been added, and the increased availability of the MRI has increased the rate of diagnosis of these malformations. The pathophysiology of the symptom production is complex and probably multifactorial. Headache and neck pain are not uncommon symptoms in a general medical pediatric practice. Therefore, as Chiari malformations are not rare, it is likely that symptomatic cases might be underdiagnosed, while at the same time many children may be receiving treatment for what may be presumed incorrectly to be a symptomatic radiographic finding. The prevalence of headache and Chiari and the unknown natural history of the asymptomatic malformation highlight the significance of the primary care physician's role. The role of the primary care physician is important in identifying cases that might be symptomatic and refer for a neurosurgical evaluation prior to initiating medical treatment. The following chapter aims to present in a comprehensive yet concise manner the disorder and to acquaint the pediatrician with the diagnosis of Chiari and its surgical management.

Classification

Hans Chiari provided us with a comprehensive description of hindbrain malformations in 1891. Cruveilhier, Arnold, and Cleland should also be credited for the recognition of the hindbrain anomalies [1]. The original description by Hans Chiari [2] included the following four types of malformations:

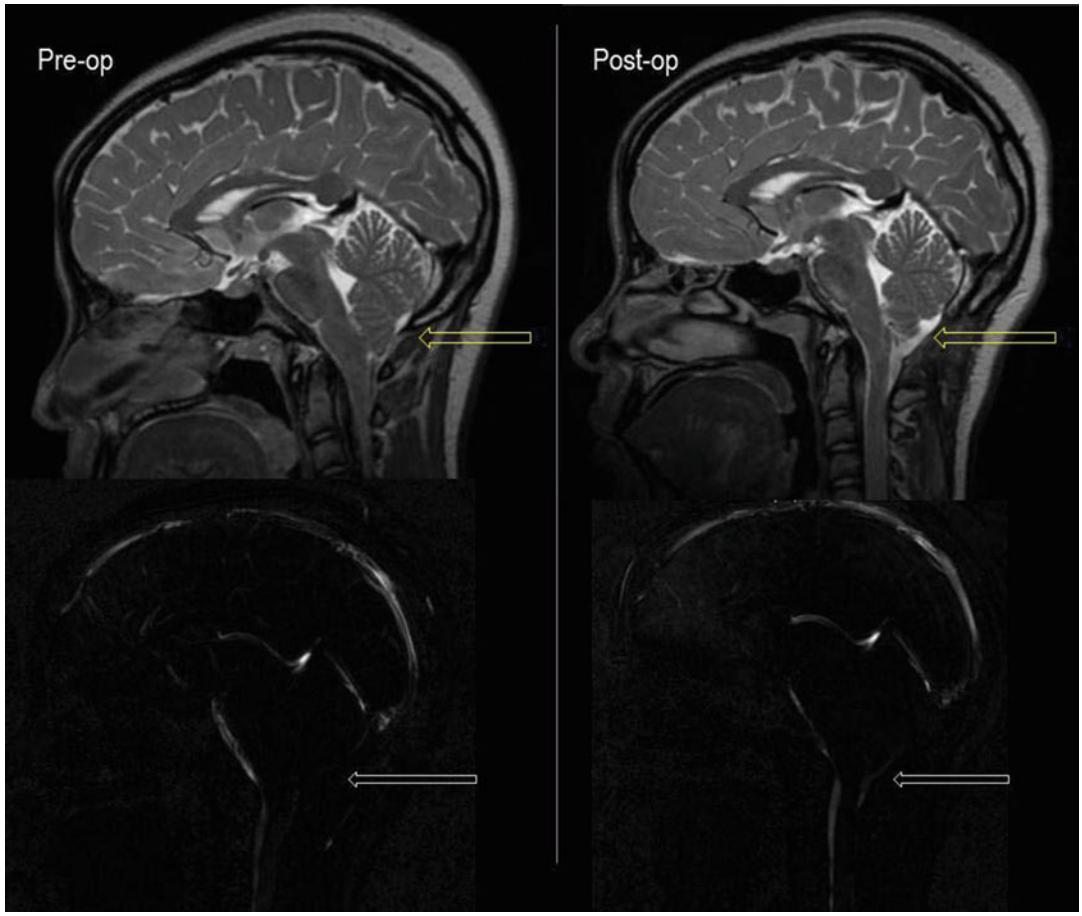


Fig. 21.2 Sagittal T2W (*upper row*) and phase-contrast (*lower row*) MRI images of a Chiari 1 patient preoperatively (**a**) and post-suboccipital decompression without duraplasty. There is significant reconstitution of the subarachnoid space dorsally to the tonsils (*yellow arrow*) and reconstitution of the CSF flow in the same region (*white arrow*)

Chiari 1 (Fig. 21.3): The cerebellar tonsils herniate below the level of the foramen magnum. An arbitrary limit of 5 mm has been set in order to differentiate between Chiari malformation and tonsillar ectopia (<5 mm). Emphasis has traditionally been placed on the degree of tonsillar herniation; however, in clinical practice, the actual caudal displacement of the tonsils often does not correlate with the presence of symptoms. Hydrocephalus is rare, but syringomyelia is often present. Syringomyelia is the presence of a fluid-filled cavity inside the spinal cord.

Chiari II (Fig. 21.4): This type is characterized by protrusion of the cerebellar vermis, medulla, and fourth ventricle through the foramen magnum into the cervical spinal canal and is associated with supratentorial anomalies [3] and almost always a myelomeningocele. It is usually diagnosed in the prenatal investigation of a fetus with a neural tube defect. In this type, it is not unusual for the cerebellar tonsils to reach the level of fifth cervical vertebra. Some rare cases of Chiari II without spinal dysraphism have been reported [4]. Although the Chiari II malformation is associated with other pathologies such as the spina bifida and hydrocephalus, the leading cause of mortality in young patients with this malformation constellation is the Chiari II malformation [5].

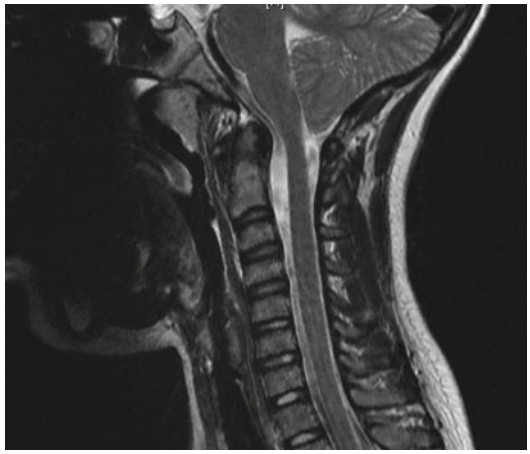


Fig. 21.3 Sagittal T2W MRI image showing a typical Chiari 1 malformation. Cerebellar tonsils herniate below the level of the foramen magnum by more than 5 mm. CSF appears hyperintense; some isointense to brain parenchyma areas inside the subarachnoid space is CSF flow artifact. The presence of the CSF-filled subarachnoid space both ventrally and dorsally to the neural structures at the foramen magnum as well as the presence of CSF flow artifact suggest that this particular Chiari case is less likely to be symptomatic

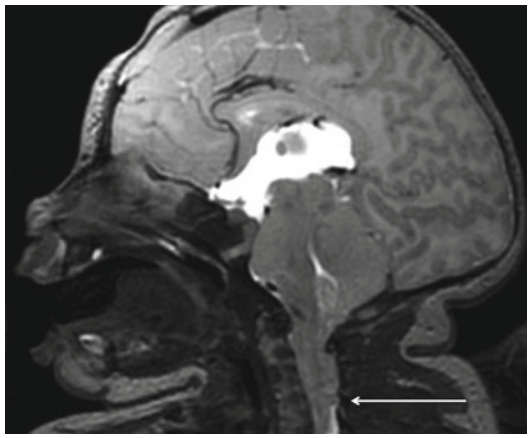


Fig. 21.4 Sagittal T2W MRI image of a neonate with Chiari 2 malformation. The tip of the tonsils (*arrow*) reaches the level of C5 vertebra. Of note the small volume of posterior cranial fossa and the low-lying torcular herophili

Chiari 3: This is a very rare form that can be considered as an encephalocele with associated cervical spina bifida and prolapse of the cerebellum into the spinal canal.

Chiari 4: This malformation is essentially a cerebellar hypoplasia/aplasia, and apart from being a hindbrain malformation, it doesn't appear to share any other characteristics with the other types of Chiari malformation.

Chiari types 3 and 4 are very rare disorders, which are diagnosed usually in the prenatal period or in neonates and are treated in specialized centers. These disorders are outside the scope of this manuscript and will not be analyzed. More recently, some new types of Chiari malformations have been introduced in the literature.

Chiari 0: This type of malformation involves minimal or null tonsillar herniation, but it is characterized by a crowding of the neural structures at the foramen magnum. This crowding obliterates the normal subarachnoid spaces in the region and effectively blocks CSF flow. This type is uncommon, accounting for 3.7 % of pediatric Chiari patients, and is often associated with intraoperative findings of arachnoid veils and adhesions at the foramen magnum [6]. Consequently, the symptomatology of blocked CSF pulsation might develop as well as syringomyelia.

Chiari 1.5 (Fig. 21.5): This is a recently introduced type of Chiari and is essentially a Chiari 1 with an added caudal displacement of the obex, below the level of the foramen magnum. The obex is the caudalmost point of the fourth ventricle that can be recognized in the MRI. This caudal displacement of the obex denotes a caudal displacement of the brainstem. It is not clear whether this patient population has any differences compared with the typical Chiari 1 cases. There is ongoing research trying to delineate whether these patients present with a different constellation of symptoms or need an alternative management plan.

Chiari 5: This is the most recently proposed type of hindbrain malformation with absence of the cerebellum and herniation of the occipital lobes through the foramen magnum [7].

The blockage of CSF flow is considered an important pathophysiological mechanism in the Chiari malformations. In our experience, the blockage of CSF flow can be caused by arachnoid septations in the subarachnoid space, perpendicular to the long axis of the neuraxis and

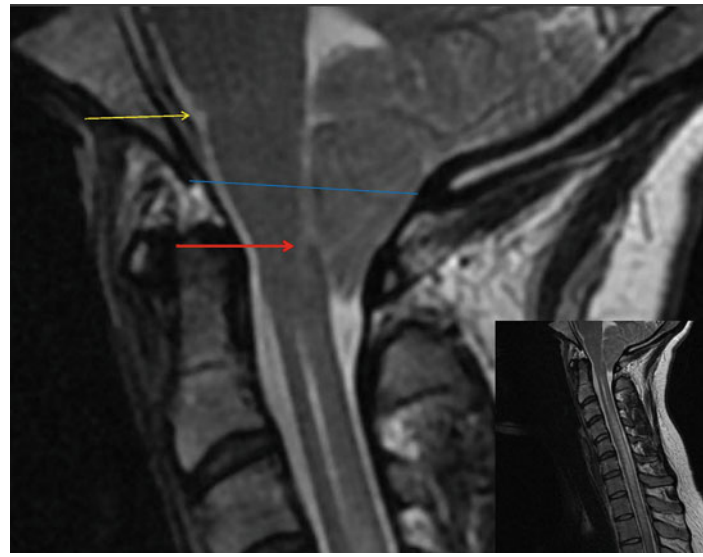


Fig. 21.5 Sagittal T2W MRI image of a Chiari 1.5 malformation. The obex (*red arrow*) lies below the foramen magnum (*blue line*). The anteriormost point of the foramen magnum is called basion (*left end* of *blue line*), while the posteriormost point is called opisthion (*right end* of the *blue line*). Note that the pontomedullary sulcus (*yellow arrow*) that is the border between pons and medulla is also low lying. The tonsils are pointed and there is also syringomyelia

the CSF flow direction. These septations can block the CSF flow and cause Chiari-like symptoms. These septations can also be seen along with typical for Chiari tonsillar herniations and might be the cause for symptom recurrence following certain decompressive surgeries in which only the bone is removed. We feel that special attention should be placed in this condition, given that it can be diagnosed by newer neuroimaging techniques. Treating this completely requires a more extensive surgery that includes intra-arachnoidal exploration.

Pathophysiology

It is important to note that the various Chiari types are essentially a classification scheme of hindbrain malformations with the most common (but not always present) feature being the hindbrain herniation. *It is not a grading scheme* of a common disorder with different degrees of severity, and as Tubbs et al. stated "no single theory could explain all forms of the Chiari malformation, and that this malformation might be a heterogeneous entity" [8].

The pathogenesis of Chiari 1 is probably multifactorial. The causative factor might be a small posterior fossa, a pressure gradient at the foramen magnum due to spinal hypotension or intracranial hypertension, the traction of spinal cord by tethering [9], cerebellar dysgenesis [10], secondary to space-occupying intracranial lesion, or occipitoatlantoaxial joint instability and cranial settling [11]. While the variety of pathology is extensive, for the purposes of this review chapter, we will focus on the most common types of presentations without delving into the minutiae of subtle variants.

Regardless of the causative mechanism of tonsillar herniation, the main theories of symptom production focus on the traction/compression of neural structures/blood vessels/pain-sensitive structures and on the obstruction of normal CSF pulsation through the foramen of Monro. The cranial cavity is nonelastic. During the systolic phase of heart cycle, the inflow of blood causes an increase of the intracranial blood volume because the venous outflow cannot match the rapid arterial inflow. The contents of the cranial cavity are the brain, the blood, and the CSF (Monro-Kellie doctrine). Since the brain cannot move out of the cranial cavity, it is the CSF that exits the cranial cavity through the foramen magnum to counteract the increase of blood volume. In the diastolic phase, the whole process is reversed. In the Chiari malformation, the flow of the CSF is blocked at the foramen magnum due to the blockage of the subarachnoid space by the herniating cerebellar tonsils. This blockage probably creates an

instantaneous cranial hypertension during the systolic phase that is at least partially responsible for the symptoms. Exertion and other conditions that cause an increase in the heart rate may reproduce and worsen symptoms [12]. Valsalva maneuvers worsen symptoms because the spinal subarachnoid pressure is increased, causing further reduction of an already diminished CSF flow through the foramen magnum.

Chiari is probably caused by a hypoplastic occipital bone that leads to posterior fossa crowding of neural structures and subsequent herniation of the relatively mobile cerebellar tonsils through the opening of the foramen magnum [13]. The blockage of CSF flow might also be involved in the pathophysiology of syringomyelia formation, as it leads to a pressure gradient between the spinal cord and the subarachnoid space [14].

Controversy exists on the contribution of congenital and acquired factors for Chiari 1 development. The normalization of hindbrain anatomic anomalies of Chiari 1 malformation following decompressive surgery suggest that even if there is a congenital predisposition, symptoms may be reversible, but there is also likely an acquired pathophysiological component [15]. On the other hand, an underlying genetic basis is suggested by the familial cases [16–18]. Recently, susceptibility to Chiari 1 malformation was attributed to specific genes involved in somitogenesis and fetal vascular development [19].

Epidemiology

The prevalence of asymptomatic Chiari I in the general pediatric population is unknown. A study in a general pediatric population who had MR imaging for symptoms related either to the Chiari I or to other diagnoses revealed a 1 % prevalence of Chiari malformation with tonsillar ectopia of 5 or more mm [20]. A borderline tonsillar ectopia was revealed in further 0.4 % of the patients, 74 % of whom were symptomatic. In a mixed pediatric and adult patient population, tonsillar herniation greater than 5 mm was identified in 0.77 % of patients [21]. Familial cases of pediatric Chiari 1 can account for 3 % of cases [22].

Presentation

Chiari 0, 1, and 1.5

To the present knowledge, the presentation of Chiari 0, 1, and 1.5 is almost identical when they are symptomatic; however, this is an area of investigation that is being prospectively studied. We usually group the presenting signs and symptoms into the following categories:

General symptoms: headache and neck pain, dizziness. The pain is typically located in the occipital and cervical region; sometimes it radiates and it becomes holocephalic. *Exertion*, *Valsalva maneuvers*, *coughing*, *and sneezing are usually identified as precipitating factors. However, it has been proposed that in the pediatric population the occipital location of the pain and association with cough or Valsalva maneuver might not be so common* [20]. The character of the pain is usually tension type, and sometimes it can also become pulsating. The onset of pain is usually gradual and the duration protracted [23]. The frequency of the headaches is highly variable as is the intensity of the pain. Often times, *nonspecific dizziness can also be elicited from the history.*

Neurological findings. The neurological signs and symptoms can be summarized for descriptive purposes in the following three categories, although significant overlap exists:

Cerebellar signs: Dysmetria on the finger-to-nose and heel-to-shin tests can be revealed by the neurological examination. Dysdiadochokinesia on rapid alternating movements is also a cerebellar sign that can be found in Chiari patients. Nystagmus and diplopia are possible findings that are caused by cerebellar and/or brainstem dysfunction. Balance and gait abnormalities are findings that can be attributed to cerebellar and/or long tract dysfunction. Another finding which can be present in up to 28 % of Chiari I children is the “cerebellar fit” and is characterized by “drop attacks with or without deterioration of consciousness, opisthotonic posturing, and varying degrees of respiratory compromise” [24].

Brainstem dysfunction: Cranial nerve dysfunction can be seen, and symptoms may include nystagmus, dysphagia, or snoring. More rarely, uvula deviation, diminished gag reflex [25], tongue atrophy and/or deviation, drop attacks, or bulbar weakness can be identified [26]. Sixth cranial nerve dysfunction can present as esotropia, and Chiari should enter the differential diagnosis of any acquired esotropia. Other ocular findings include nystagmus (mainly downbeat [27] on vertical gaze and rotary in the horizontal plane [28]), ocular dysmetria, and oscillopsia [29]. Trigeminal neuralgia can also be a presenting symptom due to either traction of the trigeminal nerve or compression of the spinal trigeminal nucleus [30] and can be bilateral [31]. Glossopharyngeal neuralgia has also been reported [32].

Long tract dysfunction: Distal extremity (hands/feet) paresthesias are a very common symptom in Chiari. Upper motor neuron dysfunction presenting as hyperreflexia, pathological reflexes (Babinski, Hoffman, and clonus), spasticity, motor weakness (usually asymmetrical [26] or even focal [33]), and muscle wasting can also be present. In cases presenting with syringomyelia, the dissociated sensory loss in cap-like distribution might be present.

Other findings: Pain limited range of motion of cervical spine is a very common finding in Chiari patients. The cervical spine movement probably causes compression or traction of pain-sensitive structures in the foramen magnum area. Scoliosis might be developing in association with syringomyelia. The pathophysiology is not well understood; however, a theoretical explanation might be that an eccentric syrinx that causes an asymmetry in the muscle tone of the paraspinal muscles [34]. Scoliosis is present in up to 30 % of Chiari patients and in up to 60 % of patients with syringomyelia associated with Chiari malformation [35].

Chiari malformation can present with sleep abnormalities. Polysomnography is very helpful in situations where sleep abnormalities are suspected because it can differentiate between obstructive and central apneas, assess the severity of the disorder, and help identify the cause of the problem. Polysomnography usually includes EEG, EMG, electrooculography, oxygen saturation, airflow, respiratory excursions, and ECG. The obstructive apnea is defined as 90 % or more reduction in airflow with persistent effort to breathe over two or more breaths; the central apnea is defined as absent effort to breathe followed by arousal or desaturation during two or more breaths [36]. The main causes of obstructive apnea in pediatric population are adenotonsillar hypertrophy, obesity, and craniofacial abnormalities, while the main causes of central apneas are epilepsy, congenital central hypoventilation syndrome, and brainstem compression [37]. Chiari can present with both central and obstructive apneas due to dysfunction of brainstem respiratory centers or of the lower cranial nerves, respectively. In the symptomatic Chiari patient population, the sleep apnea is present in up to 68–73 % of the adult and 60 % of the pediatric patients with the presence of both central and obstructive sleep events [38, 39].

Epilepsy is a rare symptom in Chiari [40]. Acute neurologic deterioration of asymptomatic Chiari is exceedingly rare [41], but it should lead to urgent posterior fossa decompression [42].

Specific Patient Populations

Chiari 1 may be associated with a multitude of pathologies that include craniosynostosis syndromes, endocrinopathies, hyperostosis, rickets, cutaneous and spinal disorders [43], and familial vitamin B12 deficit [44]. Neurofibromatosis type 1 is also present in small percentages of operated Chiari 1 patients [22]. Rhombencephalosynapsis is a rare congenital disorder characterized by fusion of the cerebellar hemispheres and can be associated with Chiari malformation [45].

Patients Younger Than 6 Years

Albert et al. studied the presentation of Chiari I in patients younger than age 6 [46]. Syringomyelia is present in 59 % and scoliosis in 28 %, almost always in the setting of syringomyelia and almost

always dextroscoliosis; 46.1 % had headaches; and oropharyngeal symptoms were present in 51.3 %. Patients younger than 2 years old were most likely to present with oropharyngeal dysfunction in the form of gastroesophageal reflex, sleep apnea, and choking, while patients aged 3–5 more commonly presented with scoliosis, syringomyelia, and headaches. Of note is that less than half of the patients had headaches, which makes the headache a less sensitive symptom in this age group especially in children younger than age 3. Another study in children below age 6 showed that from all causes of chronic headaches, Chiari accounted for 1.9 %; thus, headache is far from being a specific symptom for Chiari malformation [47] in this age group.

Craniosynostosis

Syndromic craniosynostosis is very often associated with Chiari 1 malformation; in Crouzon and Pfeiffer syndromes, the incidence of Chiari malformation reaches 70 and 50 %, respectively [48, 49]. In these cases, the premature fusion of cranial sutures leads to a small posterior fossa and to craniocerebral disproportion. The increased intracranial pressure by venous hypertension due to jugular foramen stenosis and to hydrocephalus further aggravates the tonsillar herniation. The patients with syndromic craniosynostosis and Chiari malformation may have a high incidence of central sleep apneas, which may go undiagnosed if a formal sleep study is deferred; hopefully, this disorder is curable by foramen magnum decompression [49]. Therefore, in syndromic craniosynostosis, a brain MRI is needed to assess for Chiari malformation, and if this is present, then a sleep study is imperative to early diagnose a sleep disorder that can be treated by surgery and prevent any long term of an undiagnosed sleep disorder such as respiratory failure and developmental delay [50]. An increased surgical risk for venous bleeding should be anticipated in this patient population.

Chiari malformation might be present in 5.6 % of nonsyndromic, single-suture craniosynostosis patients [51], and in this setting, a cranial vault remodeling operation might lead to an improvement of the tonsillar herniation [51].

Idiopathic Intracranial Hypertension

A very challenging presentation is the Chiari malformation associated with radiological signs of idiopathic intracranial hypertension (IIH). In these situations, differentiating what is the cause and what is the effect may be difficult, since Chiari can lead to intracranial hypertension and vice versa. The radiologic signs of idiopathic intracranial hypertension are flattening of the posterior sclera, distension of the perioptic subarachnoid space, vertical tortuosity of the orbital optic nerve, and a partially empty sella [52]. If the above signs are present along with Chiari malformation, then sound clinical judgment is needed in order to prioritize between the treatment of idiopathic intracranial hypertension by ventriculoperitoneal shunt and of the Chiari by suboccipital decompression. The incidence of Chiari malformation in patients with idiopathic intracranial hypertension can be as high as 28 % [53].

Postradiation Therapy Chiari

Radiation therapy (RT) to the skull base can affect the normal growth of the posterior fossa and especially the development of the clivus. This can lead to a small posterior fossa and tonsillar herniation. A study showed that the maximal tonsillar herniation is at around 20 months post-RT [54]. The same study showed that these patients were asymptomatic and that clival growth will eventually normalize and the Chiari will resolve. Therefore, conservative management should be emphasized in this patient population.

Acquired Chiari

Signs and symptoms of Chiari-like syndrome can develop secondary to lumboperitoneal shunting (either for communicating hydrocephalus or for relieving benign intracranial hypertension) [55], in cases with a chronic spinal leakage or as a late complication of ventriculoperitoneal shunt [56]. It is important to note that in the presence of a ventriculoperitoneal shunt, the Chiari malformation might be due to small cranial volume from skull thickening or arrested posterior cranial fossa growth and that the first surgical option should be the supratentorial skull enlargement

rather than the suboccipital decompression, which can lead to further deterioration [56].

Tethered Cord Syndrome

Tethered cord syndrome is believed to be present in 14% of Chiari patients. Clinical findings in this setting include: sphincter dysfunction, foot deformities, low back pain especially with trunk flexion, relief of symptoms by toe walking, and exacerbation by heel walking [57]. The clinical suspicion of tethered cord should lead to MRI imaging of the whole neuraxis.

Chiari Associated with Hydrocephalus

Hydrocephalus is present in 9.8% of Chiari 1 patients [43]. The pathophysiology is variable and should be explained in each case as it would guide the treatment. The Chiari can be caused by the hydrocephalus, due to an increased intracranial pressure; both pathologies can be caused by stenosis of the jugular foramina. Posterior fossa crowding might cause obstruction of the CSF flow through the foramina of Magendie and Luschka and the subarachnoid space. Treating the hydrocephalus is the preferred option for the first two cases, while in the third case, if it is associated with craniosynostosis, then cranial vault expansion should be the first choice [58].

Chiari Associated with Growth Hormone Disorders

Growth hormone (GH) deficiency has been associated with Chiari malformation. Treatment with growth hormone replacement therapy in this setting had controversial results as both neurological deterioration and Chiari resolution have been reported [59]. Close observation is recommended for these patients [60]. Chiari malformation is also present in 4.7% of acromegaly patients [61].

Chiari 2

Approximately one third of patients are symptomatic from Chiari II malformation. The common presenting signs and symptoms are due to lower cranial nerve dysfunction (apnea, dysphagia, aspiration, sleep disorders) and/or due to spinal cord compression (spasticity, paresis) and/or due to syringomyelia (upper and lower motor neuron paresis, sensory deficits) and/or scoliosis. Sleep apnea is mainly of the central type rather than obstructive in this patient population [62]. Patients younger than age 2 with respiratory issues must be evaluated emergently because Chiari II might produce acute symptoms. The traction of cranial nerve X or the compression of the brainstem might cause vocal cord paresis and stridor; in addition, the prolonged expiratory apnea with cyanosis is another potentially fatal respiratory sign in young patients with Chiari II [63].

Imaging

The gold standard examination is the MRI, due to the ability to obtain sagittal and coronal views and higher resolution of neural structures. The hallmark of the Chiari malformation (types 1, 1.5, and 2) is the caudal displacement of the cerebellar tonsils in relation to the foramen magnum. A line is drawn from the anteriormost point of foramen magnum (basion) to the posteriormost point (opisthion), and the maximum herniation of the cerebellar tonsils is measured from this line. The basion-opisthion (or McRae) line and the line that measures the maximum tonsillar herniation should be perpendicular. MRI does not depict bony anatomy as clearly as CT, and the accurate identification of the cortical bone margins is sometimes challenging. Tonsillar herniation greater than 5 mm has historically been used as the cutoff point for Chiari malformation from a neuroradiologic perspective. It is important to note that tonsils ascend with age, so in the first decade of life, over 6 mm (rather than 5 mm) of displacement is usually considered pathologic [64]. Pediatric Chiari 1 can be associated with hydrocephalus, focal cerebral heterotopia with epilepsy, or partial agenesis of the corpus callosum [65]. Less obvious herniation may be exceedingly symptomatic whereas more profound herniation may present asymptomatically; thus, strict adherence to these measurements alone as surgical criteria is not advocated.

Chiari malformations are often associated with presyrinx or syringomyelia (Fig. 21.6)—with the distinction between the two entities

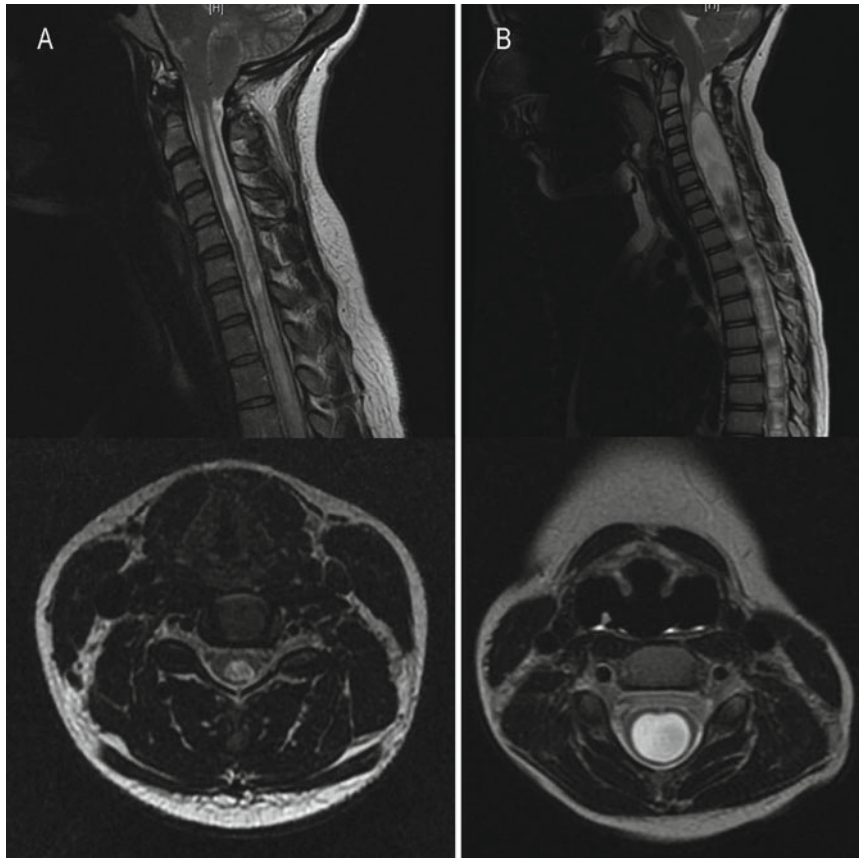


Fig. 21.6 Sagittal (*upper row*) and axial (*lower row*) T2W images of severe (**a**) and dramatic (**b**) syringomyelia

being the presence of frank spinal cord cavitation in the latter [66] or hydromyelia (distention of the central canal). If a syrinx or typical Chiari symptoms are present in the absence of tonsillar herniation, then consideration should be given to obtaining CINE MRI or MRI in the upright position. The former might reveal arachnoid velum that blocks CSF flow, while the latter might reveal tonsillar herniation that occurs only in the upright position [67]. In the case of an asymmetric tonsillar herniation, an eccentric syrinx is likely to be deviated to the side of the greater tonsillar herniation and is common to have scoliosis with the convex side similar to the side of the syrinx and the greater tonsillar herniation [68].

Chiari malformation might be associated with hereditary or spontaneous connective tissue disorders most commonly seen in association with Ehlers-Danlos syndrome. Retro-odontoid pannus can suggest ligamentous laxity and craniocervical hypermobility [69]. Basilar invagination (BI) can be associated with Chiari (Fig. 21.7), and the combination of instability and BI leads to a diagnosis of complex Chiari syndrome requiring even more specialized evaluation and management, usually surgical.

The most common neuroimaging study in the neonates is the sonogram through the acoustic window of the anterior fontanel, a technique that is not optimal for depicting anatomic relationships in the posterior fossa and craniocervical junction. Chiari II malformation can be revealed or compared with the prenatal neuroimaging studies either with brain MRI or a sonogram through the acoustic window of the foramen magnum [70].

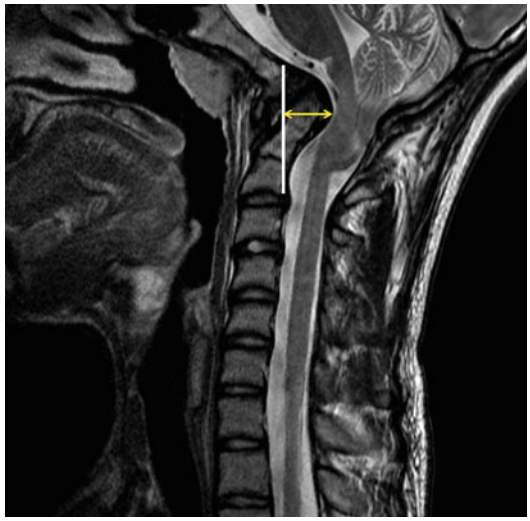


Fig. 21.7 Basilar invagination in a Chiari 1.5 patient. Ventral compression by the tip of the dens is usually quantified by the distance (*yellow line*) of the point of the greatest brainstem/spinal cord compression to a line drawn from the basion to posterior lower angle of the C2 vertebral body (*white line*). Ventral compression might be caused by the osseous tip of the dens and pannus tissue. Evaluation with dynamic flexion-extension films is highly recommended in these cases to assess for cervical spine instability or hypermobility

Natural History

A recent study followed 124 pediatric patients (mean age 7 years) with Chiari I who did not have surgery for a mean follow-up period of 2.8 years [71]. Forty-three of the patients were asymptomatic, and all but one remained asymptomatic. Sixty-seven had symptoms not attributable to Chiari, and 12 of them further deteriorated. Fourteen had symptoms typical for Chiari and five of them deteriorated. None of the 124 patients developed any neurologic deficits during the follow-up. The authors concluded "that in the majority of patients with CM-I who are not overtly symptomatic and do not have a sizeable syrinx, conservative management is a reasonable initial treatment option." Observation for asymptomatic cases is also supported by reports of spontaneous resolution [72, 73].

Treatment

Management-Indications for surgery

Although there are no guidelines, there is a consensus that symptomatic Chiari 1 patients should be treated surgically. Asymptomatic cases with syringomyelia should also be offered surgical treatment. A detailed and focused history taking from patients who are initially considered to be asymptomatic might reveal a possible sleep disorder by the presence of snoring, daytime tiredness, and frequent nighttime awakenings. Polysomnography should be recommended in these cases to establish the diagnosis of sleep disorder [74]. If a sleep disorder is confirmed by polysomnography, then surgery may be offered to these patients as well. In equivocal cases where symptoms are atypical and the diagnosis of symptomatic Chiari cannot be made with confidence, a high degree of functional impairment might justify the Chiari surgery, in an attempt to help the patient.

The full spectrum of surgical techniques for Chiari malformation includes: foramen magnum decompression, odontoidectomy, ventriculoperitoneal shunting, endoscopic third ventriculostomy, syrinx shunting, and section of the filum terminale if the cord is low lying, addressing spinal CSF leakage, if present, or cranial vault expansion. In more complex cases, ventral decompression [75] and occipital cervical spine fusion might be necessary [76]. Foramen magnum decompression is the most commonly employed procedure.

In the presence of hydrocephalus, the common practice is to treat the hydrocephalus first, ideally by ETV [10, 77]. In the rare case of a low-lying conus medullaris, then consideration should be given to the detethering of the spinal cord. In the case of significant ventral compression, an anterior odontoidectomy followed by posterior decompression and occipito-cervical fusion should be considered. In the presence of scoliosis, the suboccipital decompression is the best option, as bracing will fail most of the times to halt scoliosis evolution [78].

If the indication for surgery is clear, then surgery should not be delayed because each year is

associated with "15 % increase in likelihood of symptom persistence" following surgery [79].

Conservative

Nonoperative treatment includes various pain medications and physical activity modifications. The risk of acute neurologic deterioration in Chiari patients (even for those who were previously asymptomatic) is rare but documented [80]. A recommendation to avoid contact sports should be strongly considered in Chiari patients who are treated conservatively. Head or neck trauma can convert an asymptomatic Chiari 1 to a symptomatic one [81–83], and they have even been associated with fatalities in Chiari 1 patients [84–86].

Surgical

Suboccipital (or foramen magnum) decompression is performed in the vast majority of Chiari patients. There are several surgical variations of this type of surgery, which can be placed in a continuum in terms of invasiveness. First is the bony decompression without dural opening. Although the dura is not completely opened, some ligamentous remnants over the dura are always removed. Some variations of this technique include partial thickness dural relaxation incisions (dural scoring) or removal of the outer dural layer (dural splitting) [87]. The bony decompression is usually performed at the occipital bone and C1 lamina. Rarely, it is performed only on C1 (or to the cervical laminae as in the case of Chiari II) or to the occipital bone. The complete removal of the C2 lamina is not commonly performed although the upper edge of the lamina is sometimes resected. These dural preserving techniques are very useful in the very young patients because they minimize bleeding complications from the dural venous sinuses, which are prominent in the young patients and also reduce the risk of CSF leak. The bony decompression is performed almost always by resection of the bone (craniectomy) although some surgeons have proposed craniotomies (replacing the bone) in conjunction with cranial expansion techniques, such as placing a titanium plate that is connected on the inner surface of the bone plate and on the outer surface of the skull, thus achieving a cranial volume expansion [88].

The next option is a bony decompression with duraplasty (Fig. 21.8), which has a lower reoperation rate (2.1 vs. 12.6 %) but a higher rate of cerebrospinal fluid-related complications in certain publications (18.5 vs. 1.8 %) compared to bony decompression-only procedures [89]. Current evidence cannot suggest the superiority of one technique over the other [90], and in our opinion both techniques are invaluable for different patient populations.

The technique that we most commonly perform in our practice is the bony and dural decompression with preservation of an intact arachnoid membrane. We have a highly favorable outcome and risk profile [91]. We believe that the compression is mainly caused by the osseous structure and the dura and not the thin, elastic arachnoid membrane. The main criticism against a uniform application of this technique in every case of Chiari 1 is that this technique cannot treat any arachnoid veils that block the CSF flow at the subarachnoid space and especially the fourth ventricle outlets. Tubbs et al. [22] reported that arachnoid veils blocking the fourth ventricular outlets were found in 12 % of patients with syringomyelia, but they were very rare in patients without syringomyelia. Interestingly none of the patients with arachnoid obstruction of fourth ventricle outlets had hydrocephalus. CINE flow MRI and high-resolution T2 sequences that show flow artifacts ("flow voids"), intraoperative observation of the neural structures through the transparent arachnoid membrane, and possibly intraoperative ultrasound can guide the surgeon toward the option of performing an intra-arachnoid exploration. Intra-arachnoid exploration is always considered in reoperations for residual symptoms or syringomyelia (Fig. 21.9).

The options on what type of graft to use for duraplasty can be summarized as autologous versus nonautologous. The autologous graft is harvested by undermining the scalp at the subgaleal plane, over the occipital bone, and dissecting the pericranium. Although no option appears superior

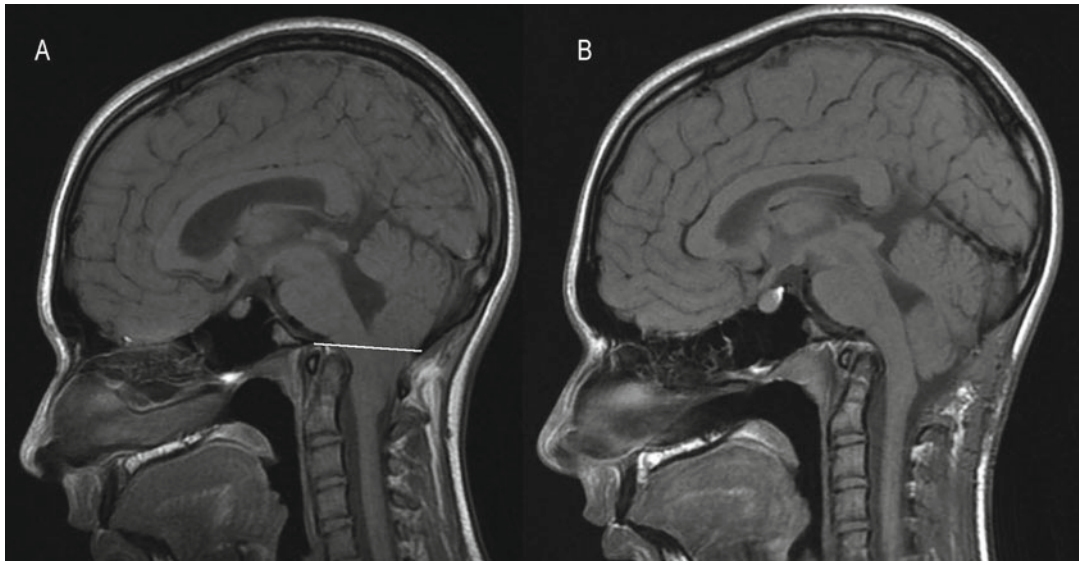


Fig. 21.8 Sagittal T1W MRI images of a Chiari 1.5 patient. Image **a** (preoperatively) shows significant crowding at the level of foramen magnum (*white line*). Image **b** is from the same patient following suboccipital bony decompression and duraplasty with autologous pericranium. The postoperative image shows reconstitution of the subarachnoid space dorsally, ascent of the cerebellar tonsils, and a more rounded appearance (compared with the pointed preoperative appearance) of the tip of the tonsils. The radiological findings were correlated with the resolution of symptoms in this patient

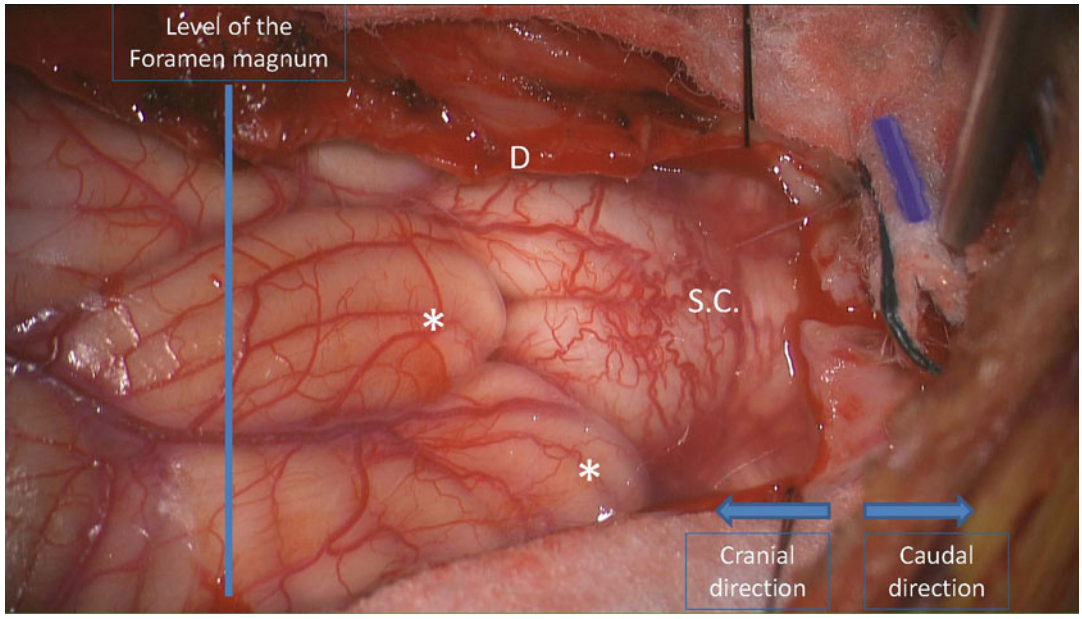


Fig. 21.9 Intraoperative photograph through the operating microscope. The dura (D) has been incised, and the dural leaflets were tacked open with sutures. The thin, transparent arachnoid membrane is left intact because it does not have any constricting effect. Preserving the integrity of the arachnoid results in the retention of the CSF inside the subarachnoid space, minimizing by this way the risk of a postoperative CSF leak. The cerebellar tonsils (*asterisks*) herniate below the level of foramen magnum, the left more than the right. The upper cervical spinal cord (S.C.) is also depicted

to any other [92], the use of autologous is generally encouraged due to the reduced cost and reduced potential for immunologic consequences. Autologous graft comes however at the cost of a slightly increased operative time, an increased theoretical risk of hematoma complications and the creation of potential space for pseudomeningocele development. It is common practice and usually the preference of patients to opt for autologous graft, with the nonautologous being an option in cases where a pericranium graft of adequate surface area or thickness could not be obtained.

Treatment of Chiari 2

Symptomatic Chiari II should be treated to address specific symptoms or prevent further deterioration. An early surgical intervention has been proposed to optimize the potential for recovery [93]. The treatment of choice is the cervical laminectomy to decompress the spinal cord. The foramen magnum is usually capacious making the suboccipital craniectomy redundant. A duraplasty in this setting is very risky as it can lead to life-threatening bleeding from a low-lying torcular herophili. The outcomes from the bony decompression procedures do not differ from the more extensive procedures that include duraplasty, and there is a 60 % rate of lasting improvement and the rest of the patients become stable [94]. A reoperation rate of up to 20 % should be expected with bone regrowth being the main cause [94]. In children with Chiari 2, treatment of the associated hydrocephalus should be the first priority, given the life-threatening potential of hydrocephalus and the possibility of Chiari symptom reversal following the shunting [95]. It is important to note that there is no lower age limit for this operation, provided that symptoms attributable to Chiari II are clearly present. For a Chiari II patient who presents later in life with symptoms, the differential diagnosis should include a shunt malfunction or a decompensated hydrocephalus in a non-shunted patient or symptomatic Chiari II and a tethered spinal cord at the area of the myelomeningocele repair. The management of such a patient should start by ruling out a shunt malfunction as this could be life threatening. Normal-sized ventricles do not reliably rule out shunt malfunction; the presence of papilledema should always lead to shunt exploration. If a shunt malfunction is ruled out, then sound clinical judgment and MRI of the spine would help with the differential diagnosis and the decision-making.

Complications

The full spectrum of reported surgical complications throughout the literature is quite extensive [96] despite the high safety profile of the procedure in our experience. It includes death [97], stroke (mainly PICA infarction), CSF leakage, meningitis (bacterial or aseptic), subdural hematomas or hygromas [98], new neurological deficits, pseudomeningocele, cerebellar hemorrhage, cerebellar ptosis, neck pain, low-pressure headaches, fibromyalgia, chronic fatigue, persistent or recurrent symptoms, scar formation, intraoperative significant bleeding, immunologic complications from nonautologous dural grafts, and acute pseudotumor cerebri [99]. Operations that include arachnoid dissection might have a higher complications rate (permanent morbidity of 3.2 % and mortality of 1.3 % [97]). This is not a surgery to be undertaken lightly or with less experienced surgeons.

Persistent or recurrent symptoms might be caused by inadequate decompression, usually at the lateral margins of foramen magnum. Residual symptoms in the case of arachnoid sparing procedures might be due to the presence of arachnoid septum or veils that block CSF flow. Additional causes that need to be considered are hydrocephalus, craniocervical instability, ventral compression by the dens (basilar invagination) or pannus, new spine pathology, or arachnoid scarring. Highly refractory cases might be suitable for occipital peripheral nerve stimulation [100, 101]. Cerebellar ptosis was first described in 1978 [102]. The cerebellar ptosis syndrome can be treated with partial cranioplasty of the posterior

fossa bone defect with split-thickness calvarial bone or titanium plate [96, 103, 104]. Prevention is achieved by minimizing the craniectomy height (craniocaudal length).

Follow-Up

Patients have a regular post-op office visit on the tenth postoperative day for suture removal and wound check. By this point there is usually minimal requirement for pain medication. Return to school or work is usually at a minimum of 2 weeks after the surgery, but strenuous physical activities are avoided until approximately 6-week post-op. A follow-up MRI and office visit is usually performed at 3–6-month post-op at which point the MRI should demonstrate a reduction in the tonsillar herniation, widening of the subarachnoid spaces at the foramen magnum region and increased CSF flow at this area along with stabilization or improvement of any associated syringomyelia.

Outcome

A favorable clinical response of up to 91.8 % can be observed following surgical decompression with duraplasty, with a complete resolution of symptoms in 70.2 % of patients [91]. In the adult patient population, decompressive surgery leads to a significant improvement in the obstructive sleep events and an even more pronounced effect in the central sleep apnea events [38]. Esotropia, if present, can be improved with suboccipital decompression in conjunction with compensatory prisms and vision therapy [29].

Scoliosis in Chiari patients might progress in up to 48 % of patients following suboccipital decompression, with the main risk factors for a poor outcome being the thoracolumbar junction scoliosis, severe scoliosis (high Cobb angle), and the persistence of the syrinx postoperatively [35]. Syrinx (if present) decompression should be the next treatment goal and should be discussed with the orthopedic surgeon before spinal deformity correction (spine fusion or growing rod technique in the younger patients) [78]. Decompressive surgery alone is usually adequate for the treatment of scoliosis with an angle of less than 20° [105].

Conclusion

Chiari malformation is characterized by an unpredictable natural history, a lack of specific signs and symptoms and its potential to be palliated by surgical intervention. There is significant ongoing clinical research on this subject that hopefully might clarify in the future many of the current gray areas. An astute pediatrician might well identify potentially symptomatic cases and be able to provide the patient with long-term follow-up in conjunction with a pediatric neurosurgeon.

Key Points

- Chiari malformation is heterogeneous group of hindbrain malformations. Chiari 1 is defined as tonsillar herniation below the level of foramen magnum greater than 5 mm.
- Chiari 2 is always associated with myelomeningocele and hydrocephalus.
- Common presentations for Chiari 1 include suboccipital headaches that worsen with cough/exertion/Valsalva maneuver and tingling of hands; neurological exam findings are variable and may be absent.
- Chiari 1 often presents with oropharyngeal dysfunction in very young patients.
- The evaluation of a Chiari 1 patient should include history taking with emphasis on headache (location, precipitating factors, cough/exertion, character), sleep disorders (snoring, frequent awakenings, daytime sleepiness), swallowing difficulties, and functional impairment. A neurological exam should be performed with emphasis on cranial nerves, cerebellar signs, and long tract signs. A pain limited range of motion of the cervical spine and signs of scoliosis should also be looked for.

- Polysomnography is indicated if there are symptoms of sleep disorder. MRI is the imaging study of choice, ideally with CSF flow sequences. Referral to a pediatric neurosurgeon is indicated if Chiari is diagnosed.
- Chiari 2 can cause life-threatening respiratory problems. In addition, any new symptoms in these patients might be due to a malfunction of the CSF shunting system. Therefore, any new neurological or respiratory symptom in a Chiari 2 patient should prompt an evaluation by an experienced health provider.
- Outcome is very favorable if there was a clear indication for surgery. Serious complications such as CSF leak/meningitis are rare.
- Contact sports are not encouraged in Chiari 1 patients who are being managed nonoperatively.

Pediatrician's Perspective

Chiari malformation is an entity, which has gained a wider understanding and appreciation over the past decade as a possible significant and reversible cause of headaches and other neurologic signs and symptoms in children.

The key role for a pediatrician when this diagnosis is obtained is to facilitate an open and honest dialogue between the pediatric neurologist and neurosurgeon. Headaches, as a rule, are more likely to be caused by non-Chiari-related diagnoses, but the radiographic demonstration of a malformation creates a unique scenario in which multiple etiologies may be suspected.

Experienced pediatric neurosurgeons who evaluate Chiari malformation can help with the initial workup, but these evaluations should involve you and a pediatric neurologist, ideally. Full spine axis imaging, sleep and swallow evaluations, ophthalmologic exams, and several other related subspecialist tests may need to be coordinated to help discern if surgery may be an option for your patient.

In the end, if nonsurgical management has not addressed the symptoms discussed in this chapter, then Chiari surgery has an extremely high success rate in the properly evaluated and diagnosed population.

References

1. Tubbs RS, Cohen-Gadol AA. Hans Chiari (1851–1916). J Neurol. 2010;257(7):1218–20.
2. Hans C. Über Veränderungen des Kleinhirns infolge von Hydrocephalie des Grosshirns. Dtsch Med Wsch. 1891;17:1172–5.
3. Miller E, Widjaja E, Blaser S, Dennis M, Raybaud C. The old and the new: supratentorial MR findings in Chiari II malformation. Childs Nerv Syst. 2008;24(5):563–75.
4. Citton V, Toldo I, Balao L, Pettenazzo A, Emanuelli E, Sartori S, et al. Chiari 2 without spinal dysraphism: does it blow a hole in the pathogenesis? J Child Neurol. 2012;27(4):536–9.
5. Juranek J, Salman MS. Anomalous development of brain structure and function in spina bifida myelomeningocele. Dev Disabil Res Rev. 2010; 16(1):23–30.
6. Chern JJ, Gordon AJ, Mortazavi MM, Tubbs RS, Oakes WJ. Pediatric Chiari malformation Type 0: a 12-year institutional experience. J Neurosurg Pediatr. 2011;8(1):1–5.
7. Tubbs RS, Muhleman M, Loukas M, Oakes WJ. A new form of herniation: the Chiari V malformation. Childs Nerv Syst. 2012;28(2):305–7.
8. Tubbs RS, Shoja MM, Ardalan MR, Shokouhi G, Loukas M. Hindbrain herniation: a review of embryological theories. Ital J Anat Embryol. 2008;113(1):37–46.
9. Waldau B, Grant G, Fuchs H. Development of an acquired Chiari malformation Type I in the setting of an untreated lipomyelomeningocele. Case report. J Neurosurg Pediatr. 2008;1(2):164–6.
10. Massimi L, Novegno F, di Rocco C. Chiari type I malformation in children. Adv Tech Stand Neurosurg. 2011;37:143–211.
11. Milhorat TH, Nishikawa M, Kula RW, Dlugacz YD. Mechanisms of cerebellar tonsil herniation in patients with Chiari malformations as guide to clinical management. Acta Neurochir (Wien). 2010;152(7):1117–27.
12. Linge SO, Mardal KA, Haughton V, Helgeland A. Simulating CSF flow dynamics in the normal and the Chiari I subarachnoid space during rest and exertion. AJNR Am J Neuroradiol. 2013;34(1):41–5.
13. Dagtekin A, Avci E, Kara E, Uzmansel D, Dagtekin O, Koseoglu A, et al. Posterior cranial fossa morphometry in symptomatic adult Chiari I malformation patients: comparative clinical and anatomical study. Clin Neurol Neurosurg. 2011;113(5):399–403.
14. Chang HS, Tsuchiya T, Fujisawa N, Oya S, Matsui T. Syringomyelia associated with arachnoid septum at the craniovertebral junction, contradicting the currently prevailing theory of syringomyelia formation. Acta Neurochir (Wien). 2012;154(1):141–5. discussion 5.
15. Heiss JD, Suffredini G, Bakhtian KD, Sarntinoranont M, Oldfield EH. Normalization of hindbrain morphology after decompression of Chiari malformation Type I. J Neurosurg. 2012;117(5):942–6.

16. Markunas CA, Tubbs RS, Moftakhar R, Ashley-Koch AE, Gregory SG, Oakes WJ, et al. Clinical, radiological, and genetic similarities between patients with Chiari Type I and Type 0 malformations. J Neurosurg Pediatr. 2012;9(4):372–8.
17. Milhorat TH, Chou MW, Trinidad EM, Kula RW, Mandell M, Wolpert C, et al. Chiari I malformation redefined: clinical and radiographic findings for 364 symptomatic patients. Neurosurgery. 1999; 44(5):1005–17.
18. Schanker BD, Walcott BP, Nahed BV, Kahle KT, Li YM, Coumans JV. Familial Chiari malformation: case series. Neurosurg Focus. 2011;31(3):E1.
19. Urbizu A, Toma C, Poca MA, Sahuquillo J, Cuenca-Leon E, Cormand B, et al. Chiari malformation type I: a case-control association study of 58 developmental genes. PLoS One. 2013;8(2): e57241.
20. Aitken LA, Lindan CE, Sidney S, Gupta N, Barkovich AJ, Sorel M, et al. Chiari type I malformation in a pediatric population. Pediatr Neurol. 2009;40(6):449–54.
21. Meadows J, Kraut M, Guarnieri M, Haroun RI, Carson BS. Asymptomatic Chiari Type I malformations identified on magnetic resonance imaging. J Neurosurg. 2000;92(6):920–6.
22. Tubbs RS, Beckman J, Naftel RP, Chern JJ, Wellons III JC, Rozzelle CJ, et al. Institutional experience with 500 cases of surgically treated pediatric Chiari malformation Type I. J Neurosurg Pediatr. 2011;7(3):248–56.
23. Headache Classification Subcommittee of the International Headache Society. The International classification of headache disorders: 2nd edition. Cephalalgia. 2004;24 Suppl 1:9–160.
24. Pandey A, Robinson S, Cohen AR. Cerebellar fits in children with Chiari I malformation. Neurosurg Focus. 2001;11(1):E4.
25. Greenlee JD, Donovan KA, Hasan DM, Menezes AH. Chiari I malformation in the very young child: the spectrum of presentations and experience in 31 children under age 6 years. Pediatrics. 2002; 110(6):1212–9.
26. Carew CL, Prasad A, Tay KY, de Ribaupierre S. Unusual presentation of Chiari I in toddlers: case reports and review of the literature. Childs Nerv Syst. 2012;28(11):1965–70.
27. Goodwin D, Halvorson AR. Chiari I malformation presenting as downbeat nystagmus: clinical presentation, diagnosis, and management. Optometry. 2012;83(2):80–6.
28. Benglis D, Levi AD. Neurologic findings of craniovertebral junction disease. Neurosurgery. 2010;66(3 Suppl):13–21.
29. Baxstrom CR. Nonsurgical treatment for esotropia secondary to Arnold-Chiari I malformation: a case report. Optometry. 2009;80(9):472–8.
30. Gonzalez-Bonet LG, Piquer J. Trigeminal neuralgia: a symptom of Chiari I malformation. Neurosurgery. 2012;71(4):E911–2.
31. Than KD, Sharifpour M, Wang AC, Thompson BG, Pandey AS. Chiari I malformation manifesting as bilateral trigeminal neuralgia: case report and review of the literature. J Neurol Neurosurg Psychiatry. 2011;82(9):1058–9.
32. Li F, Yang Y, Liu Y, Li Q, Zhu S. Glossopharyngeal neuralgia as onset of Chiari Type I malformation. Headache. 2012;52(10):1576–8.
33. Laufer I, Engel M, Feldstein N, Souweidane MM. Chiari malformation presenting as a focal motor deficit. Report of two cases. J Neurosurg Pediatr. 2008;1(5):392–5.
34. Brockmeyer DL. Editorial. Chiari malformation Type I and scoliosis: the complexity of curves. J Neurosurg Pediatr. 2011;7(1):22–3. discussion 3–4.
35. Attenello FJ, McGirt MJ, Atiba A, Gathinji M, Datoo G, Weingart J, et al. Suboccipital decompression for Chiari malformation-associated scoliosis: risk factors and time course of deformity progression. J Neurosurg Pediatr. 2008;1(6):456–60.
36. Iber C, American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Westchester, IL: American Academy of Sleep Medicine; 2007.
37. Aarts LA, Willemsen MA, Vandenbussche NL, van Gent R. Nocturnal apnea in Chiari type I malformation. Eur J Pediatr. 2011;170(10):1349–52.
38. Botelho RV, Bittencourt LR, Rotta JM, Tufik S. The effects of posterior fossa decompressive surgery in adult patients with Chiari malformation and sleep apnea. J Neurosurg. 2010;112(4):800–7.
39. Dauvilliers Y, Stal V, Abril B, Coubes P, Bobin S, Touchon J, et al. Chiari malformation and sleep related breathing disorders. J Neurol Neurosurg Psychiatry. 2007;78(12):1344–8.
40. Granata T, Valentini LG. Epilepsy in type 1 Chiari malformation. Neurol Sci. 2011;32 Suppl 3:S303–6.
41. Pettorini BL, Gao A, Rodrigues D. Acute deterioration of a Chiari I malformation: an uncommon neurosurgical emergency. Childs Nerv Syst. 2011; 27(6):857–60.
42. Wellons III JC, Tubbs RS, Bui CJ, Grabb PA, Oakes WJ. Urgent surgical intervention in pediatric patients with Chiari malformation type I. Report of two cases. J Neurosurg. 2007;107(1 Suppl):49–52.
43. Loukas M, Shayota BJ, Oelhafen K, Miller JH, Chern JJ, Tubbs RS, et al. Associated disorders of Chiari Type I malformations: a review. Neurosurg Focus. 2011;31(3):E3.
44. Welsch M, Antes S, Kiefer M, Meyer S, Eymann R. Association of Chiari malformation and vitamin B12 deficit in a family. Childs Nerv Syst. 2013.
45. Weaver J, Manjila S, Bahuleyan B, Bangert BA, Cohen AR. Rhombencephalosynapsis: embryopathology and management strategies of associated neurosurgical conditions with a review of the literature. J Neurosurg Pediatr. 2013;11(3):320–6.
46. Albert GW, Menezes AH, Hansen DR, Greenlee JD, Weinstein SL. Chiari malformation Type I in

children younger than age 6 years: presentation and surgical outcome. J Neurosurg Pediatr. 2010;5(6): 554–61.
47. Raieli V, Eliseo M, Pandolfi E, La Vecchia M, La Franca G, Puma D, et al. Recurrent and chronic headaches in children below 6 years of age. J Headache Pain. 2005;6(3):135–42.
48. Cinalli G, Chumas P, Arnaud E, Sainte-Rose C, Renier D. Occipital remodeling and suboccipital decompression in severe craniosynostosis associated with tonsillar herniation. Neurosurgery. 1998; 42(1):66–71. discussion 71–3.
49. Addo NK, Javadpour S, Kandasamy J, Sillifant P, May P, Sinha A. Central sleep apnea and associated Chiari malformation in children with syndromic craniosynostosis: treatment and outcome data from a supraregional national craniofacial center. J Neurosurg Pediatr. 2013;11(3):296–301.
50. Spence J, Pasterkamp H, McDonald PJ. Isolated central sleep apnea in type I Chiari malformation: improvement after surgery. Pediatr Pulmonol. 2010;45(11):1141–4.
51. Leikola J, Koljonen V, Valanne L, Hukki J. The incidence of Chiari malformation in nonsyndromic, single suture craniosynostosis. Childs Nerv Syst. 2010;26(6):771–4.
52. Suzuki H, Takanashi J, Kobayashi K, Nagasawa K, Tashima K, Kohno Y. MR imaging of idiopathic intracranial hypertension. AJNR Am J Neuroradiol. 2001;22(1):196–9.
53. Aiken AH, Hoots JA, Saindane AM, Hudgins PA. Incidence of cerebellar tonsillar ectopia in idiopathic intracranial hypertension: a mimic of the Chiari I malformation. AJNR Am J Neuroradiol. 2012;33(10):1901–6.
54. Aquilina K, Merchant TE, Boop FA, Sanford RA. Chiari I malformation after cranial radiation therapy in childhood: a dynamic process associated with changes in clival growth. Childs Nerv Syst. 2009;25(11):1429–36.
55. Peleggi AF, Lovely TJ. Treatment of delayed Chiari malformation and syringomyelia after lumboperitoneal shunt placement: case report and treatment recommendations. Surg Neurol Int. 2012;3:101.
56. Caldarelli M, Novegno F, Di Rocco C. A late complication of CSF shunting: acquired Chiari I malformation. Childs Nerv Syst. 2009;25(4):443–52.
57. Milhorat TH, Bolognese PA, Nishikawa M, Francomano CA, McDonnell NB, Roonprapunt C, et al. Association of Chiari malformation type I and tethered cord syndrome: preliminary results of sectioning filum terminale. Surg Neurol. 2009;72(1):20–35.
58. Di Rocco C, Frassanito P, Massimi L, Peraio S. Hydrocephalus and Chiari type I malformation. Childs Nerv Syst. 2011;27(10):1653–64.
59. Gupta A, Vitali AM, Rothstein R, Cochrane DD. Resolution of syringomyelia and Chiari malformation after growth hormone therapy. Childs Nerv Syst. 2008;24(11):1345–8.
60. Naftel RP, Tubbs RS, Menendez JY, Oakes WJ. Progression of Chiari I malformations while on growth hormone replacement: a report of two cases. Childs Nerv Syst. 2013;29(12):2291–4.
61. Manara R, Bommarito G, Rizzati S, Briani C, Della Puppa A, Citton V, et al. Herniation of cerebellar tonsils in acromegaly: prevalence, pathogenesis and clinical impact. Pituitary. 2013;16(1):122–30.
62. Alsaadi MM, Iqbal SM, Elgamal EA, Gozal D. Sleep-disordered breathing in children with Chiari malformation type II and myelomeningocele. Pediatr Int. 2012;54(5):623–6.
63. Stevenson KL. Chiari Type II malformation: past, present, and future. Neurosurg Focus. 2004;16(2):E5.
64. Chiapparini L, Saletti V, Solero CL, Bruzzone MG, Valentini LG. Neuroradiological diagnosis of Chiari malformations. Neurol Sci. 2011;32 Suppl 3:S283–6.
65. Galarza M, Martinez-Lage JF, Ham S, Sood S. Cerebral anomalies and Chiari type 1 malformation. Pediatr Neurosurg. 2010;46(6):442–9.
66. Goh S, Bottrell CL, Aiken AH, Dillon WP, Wu YW. Presyrinx in children with Chiari malformations. Neurology. 2008;71(5):351–6.
67. Silva JA, Melo LR, Araujo AF, Santos Jr AA. Resolution of syringomyelia in ten cases of "up-and-down Chiari malformation" after posterior fossa decompression. Arq Neuropsiquiatr. 2010;68(5):694–9.
68. Zhu Z, Wu T, Sha S, Sun X, Zhu F, Qian B, et al. Is curve direction correlated with the dominant side of tonsillar ectopia and side of syrinx deviation in patients with single thoracic scoliosis secondary to Chiari malformation and syringomyelia? Spine (Phila Pa 1976). 2013;38(8):671–7.
69. Milhorat TH, Bolognese PA, Nishikawa M, McDonnell NB, Francomano CA. Syndrome of occipitoatlantoaxial hypermobility, cranial settling, and Chiari malformation type I in patients with hereditary disorders of connective tissue. J Neurosurg Spine. 2007;7(6):601–9.
70. Brennan CM, Taylor GA. Sonographic imaging of the posterior fossa utilizing the foramen magnum. Pediatr Radiol. 2010;40(8):1411–6.
71. Benglis Jr D, Covington D, Bhatia R, Bhatia S, Elhammady MS, Ragheb J, et al. Outcomes in pediatric patients with Chiari malformation Type I followed up without surgery. J Neurosurg Pediatr. 2011;7(4):375–9.
72. Miller JH, Limbrick DD, Callen M, Smyth MD. Spontaneous resolution of Chiari malformation Type I in monozygotic twins. J Neurosurg Pediatr. 2008;2(5):317–9.
73. Waldau B, Domeshek LF, Leigh FA, Lum KC, Fuchs HE, Marcus JR, et al. Spontaneous resolution of a 13-mm Chiari malformation Type I in relation to differential growth of the posterior fossa volume. J Neurosurg Pediatr. 2009;3(2):110–4.
74. Khatwa U, Ramgopal S, Mylavarapu A, Prabhu SP, Smith E, Proctor M, et al. MRI findings and sleep

apnea in children with Chiari I malformation. Pediatr Neurol. 2013;48(4):299–307.
75. Grammatica A, Bonali M, Ruscitti F, Marchioni D, Pinna G, Cunsolo EM, et al. Transnasal endoscopic removal of malformation of the odontoid process in a patient with type I Arnold-Chiari malformation: a case report. Acta Otorhinolaryngol Ital. 2011;31(4): 248–52.
76. Fenoy AJ, Menezes AH, Fenoy KA. Craniocervical junction fusions in patients with hindbrain herniation and syringohydromyelia. J Neurosurg Spine. 2008;9(1):1–9.
77. Massimi L, Pravata E, Tamburrini G, Gaudino S, Pettorini B, Novegno F, et al. Endoscopic third ventriculostomy for the management of Chiari I and related hydrocephalus: outcome and pathogenetic implications. Neurosurgery. 2011;68(4):950–6.
78. Colombo LF, Motta F. Consensus conference on Chiari: a malformation or an anomaly? Scoliosis and others orthopaedic deformities related to Chiari 1 malformation. Neurol Sci. 2011;32 Suppl 3:S341–3.
79. McGirt MJ, Attenello FJ, Atiba A, Garces-Ambrossi G, Datoo G, Weingart JD, et al. Symptom recurrence after suboccipital decompression for pediatric Chiari I malformation: analysis of 256 consecutive cases. Childs Nerv Syst. 2008;24(11):1333–9.
80. Massimi L, Della Pepa GM, Tamburrini G, Di Rocco C. Sudden onset of Chiari malformation Type I in previously asymptomatic patients. J Neurosurg Pediatr. 2011;8(5):438–42.
81. Wan MJ, Nomura H, Tator CH. Conversion to symptomatic Chiari I malformation after minor head or neck trauma. Neurosurgery. 2008;63(4):748–53. discussion 53.
82. Yarbrough CK, Powers AK, Park TS, Leonard JR, Limbrick DD, Smyth MD. Patients with Chiari malformation Type I presenting with acute neurological deficits: case series. J Neurosurg Pediatr. 2011; 7(3):244–7.
83. Callaway GH, O'Brien SJ, Tehrany AM. Chiari I malformation and spinal cord injury: cause for concern in contact athletes? Med Sci Sports Exerc. 1996;28(10):1218–20.
84. Wolf DA, Veasey III SP, Wilson SK, Adame J, Korndorffer WE. Death following minor head trauma in two adult individuals with the Chiari I deformity. J Forensic Sci. 1998;43(6):1241–3.
85. Zhang J, Shao Y, Qin Z, Liu N, Zou D, Huang P, et al. Sudden unexpected death due to Chiari Type I malformation in a road accident case. J Forensic Sci. 2013;58(2):540–3.
86. James DS. Significance of chronic tonsillar herniation in sudden death. Forensic Sci Int. 1995; 75(2–3):217–23.
87. Chauvet D, Carpentier A, George B. Dura splitting decompression in Chiari type 1 malformation: clinical experience and radiological findings. Neurosurg Rev. 2009;32(4):465–70.
88. Chou YC, Sarkar R, Osuagwu FC, Lazareff JA. Suboccipital craniotomy in the surgical treatment of Chiari I malformation. Childs Nerv Syst. 2009;25(9):1111–4.
89. Durham SR, Fjeld-Olenec K. Comparison of posterior fossa decompression with and without duraplasty for the surgical treatment of Chiari malformation Type I in pediatric patients: a meta-analysis. J Neurosurg Pediatr. 2008;2(1):42–9.
90. Hankinson T, Tubbs RS, Wellons JC. Duraplasty or not? An evidence-based review of the pediatric Chiari I malformation. Childs Nerv Syst. 2011;27(1):35–40.
91. Hoffman CE, Souweidane MM. Cerebrospinal fluid-related complications with autologous duraplasty and arachnoid sparing in type I Chiari malformation. Neurosurgery. 2008;62(3 Suppl 1):156–60. discussion 60–1.
92. Abla AA, Link T, Fusco D, Wilson DA, Sonntag VK. Comparison of dural grafts in Chiari decompression surgery: review of the literature. J Craniovertebr Junction Spine. 2010;1(1):29–37.
93. Pollack IF, Pang D, Albright AL, Krieger D. Outcome following hindbrain decompression of symptomatic Chiari malformations in children previously treated with myelomeningocele closure and shunts. J Neurosurg. 1992;77(6):881–8.
94. Akbari SH, Limbrick Jr DD, Kim DH, Narayan P, Leonard JR, Smyth MD, et al. Surgical management of symptomatic Chiari II malformation in infants and children. Childs Nerv Syst. 2013;29(7): 1143–54.
95. Talamonti G, Zella S. Surgical treatment of CM2 and syringomyelia in a series of 231 myelomeningocele patients. Neurol Sci. 2011;32 Suppl 3:S331–3.
96. Choi D. Failed foramen magnum decompression for Chiari malformation: the challenge of post-operative brainstem shift and cerebellar ptosis. World Neurosurg. 2013;81(5–6):702–5.
97. Klekamp J. Surgical treatment of Chiari I malformation—analysis of intraoperative findings, complications, and outcome for 371 foramen magnum decompressions. Neurosurgery. 2012;71(2):365–80. discussion 80.
98. Filis AK, Moon K, Cohen AR. Symptomatic subdural hygroma and hydrocephalus following Chiari I decompression. Pediatr Neurosurg. 2009;45(6):425–8.
99. Furtado SV, Visvanathan K, Reddy K, Hegde AS. Pseudotumor cerebri: as a cause for early deterioration after Chiari I malformation surgery. Childs Nerv Syst. 2009;25(8):1007–12.
100. Vadivelu S, Bolognese P, Milhorat TH, Mogilner AY. Occipital neuromodulation for refractory headache in the Chiari malformation population. Prog Neurol Surg. 2011;24:118–25.
101. Vadivelu S, Bolognese P, Milhorat TH, Mogilner AY. Occipital nerve stimulation for refractory headache in the Chiari malformation population. Neurosurgery. 2012;70(6):1430–6. discussion 6–7.

102. Williams B. A critical appraisal of posterior fossa surgery for communicating syringomyelia. Brain. 1978;101(2):223–50.
103. Udani V, Holly LT, Chow D, Batzdorf U. Posterior fossa reconstruction using titanium plate for the treatment of cerebellar ptosis after decompression for Chiari malformation. World Neurosurg. 2014;81(5–6):836–41.
104. Di X, Luciano MG, Benzel EC. Acute respiratory arrest following partial suboccipital cranioplasty for cerebellar ptosis from Chiari malformation decompression. Neurosurg Focus. 2008;25(6):E12.
105. Krieger MD, Falkinstein Y, Bowen IE, Tolo VT, McComb JG. Scoliosis and Chiari malformation Type I in children. J Neurosurg Pediatr. 2011;7(1):25–9.

Pediatric Brain Tumors

22

Vita Stagno and Assem M. Abdel-Latif

Introduction

One of the greatest fears many pediatric primary care providers express is missing a clinically significant diagnosis such as a new brain tumor in a child. Unfortunately, the incidence of brain tumors has increased within the past few decades, and today brain tumors represent a major cause of cancer death in pediatric population. Thus there is a fairly good likelihood that patients within any individual provider's practice, during a career, will develop a brain tumor and present with nonspecific symptoms. In fact, brain tumors are, only next to hematologic malignancies, the second most common malignancy observed in children. Being aware of the symptoms and presentation commonalities in children with brain tumors will alert the practitioner to consider referral for imaging or neurologic consultation in those situations where the index of suspicion has been raised.

Pediatric brain tumors occur more frequently in the posterior fossa (Fig. 22.1) but generally may arise in any location inside the intracranial compartment (Fig. 22.2). Depending upon tumor location and behavior, intracranial masses may present with wide neurological signs and symptoms, leading to different clinical patterns; however there are signs that are more frequently encountered and should be recognized. Many pediatric brain tumors are responsive to surgery and/or adjunctive treatments, and early recognition can often affect the natural history of the disease, subsequent treatment, and the clinical outcome. This chapter points out the warning signs that your patient may have a brain tumor through an overview of their clinical presentation, signs, and symptoms. It is intended especially for pediatricians and pediatric neurologists, as they undertake the task, in the daily practice, of the initial evaluation of the child's symptoms.

Epidemiology and Classification

Brain tumors are the most common form of solid cancer in the pediatric population/childhood. Their incidence has increased within the past few decades, with a current annual age-adjusted rate of 3.2 cases per 100,000 children, as reported by the Cancer Statistics Report (CSR).

Pediatric brain tumors are primary classified by their location within the intracranial compartments in infratentorial and supratentorial tumors. About 60 % of brain tumors in

V. Stagno, M.D. (✉)
Department of Neurological Surgery,
Weill Cornell Medical College, 525 East 68th Street,
Box 99, New York, NY 10065, USA
e-mail: vitastagno@gmail.com

A.M. Abdel-Latif, M.D., M.Sc.
Department of Neurological Surgery, Faculty of Medicine, Ain Shams University, Abbassia,
Cairo 11566, Egypt

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_22

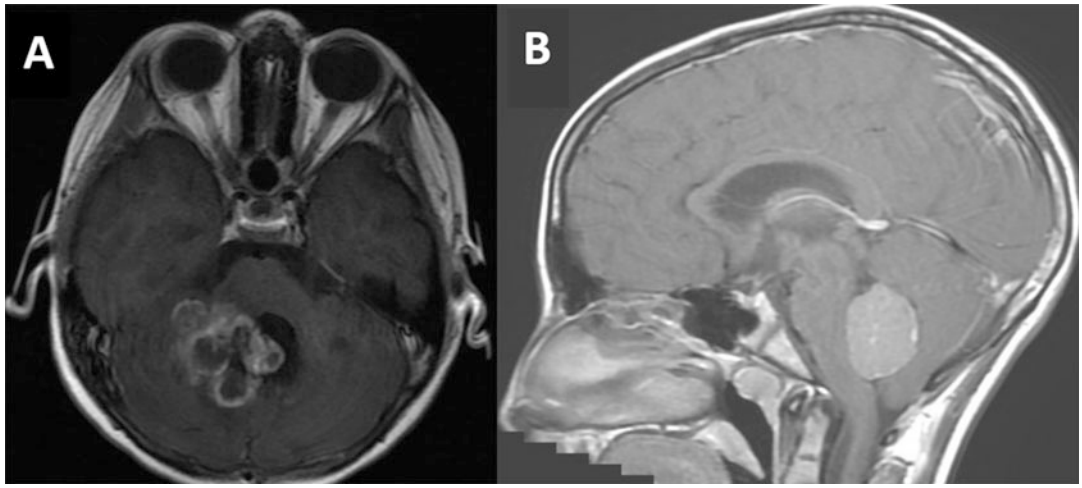


Fig. 22.1 (**a**) Axial brain MRI T1WI with contrast showing an irregularly enhancing posterior fossa fourth ventricular lesion in a child with recurrent ependymoma with spinal metastases. (**b**) Sagittal T1WI+C of a 4-year-old child with progressive headache and no neurologic deficit, showing a large 4-cm mass enhancing mass within the fourth ventricle

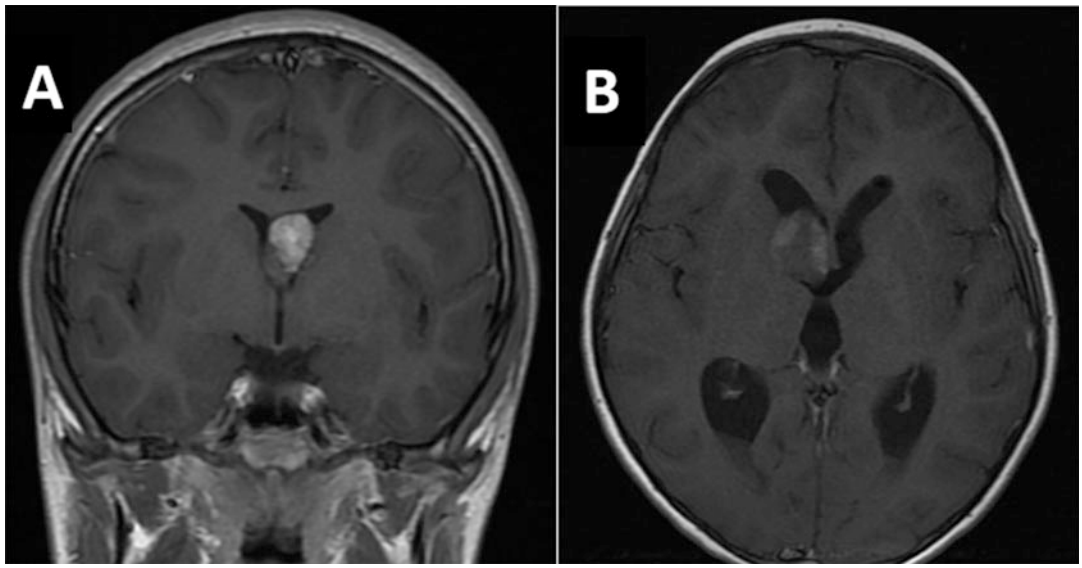


Fig. 22.2 (**a**) Brain MR and T1 contrast weighted coronal sequence showing a left lateral ventricle choroid plexus papilloma. Fifteen-year-old boy, incidentally found to have this tumor after a mild traumatic brain injury. (**b**) Axial T1WI+C of the patient in Fig. 22.1a showing metastatic ependymoma along the CSF pathways to settle in the right frontal horn

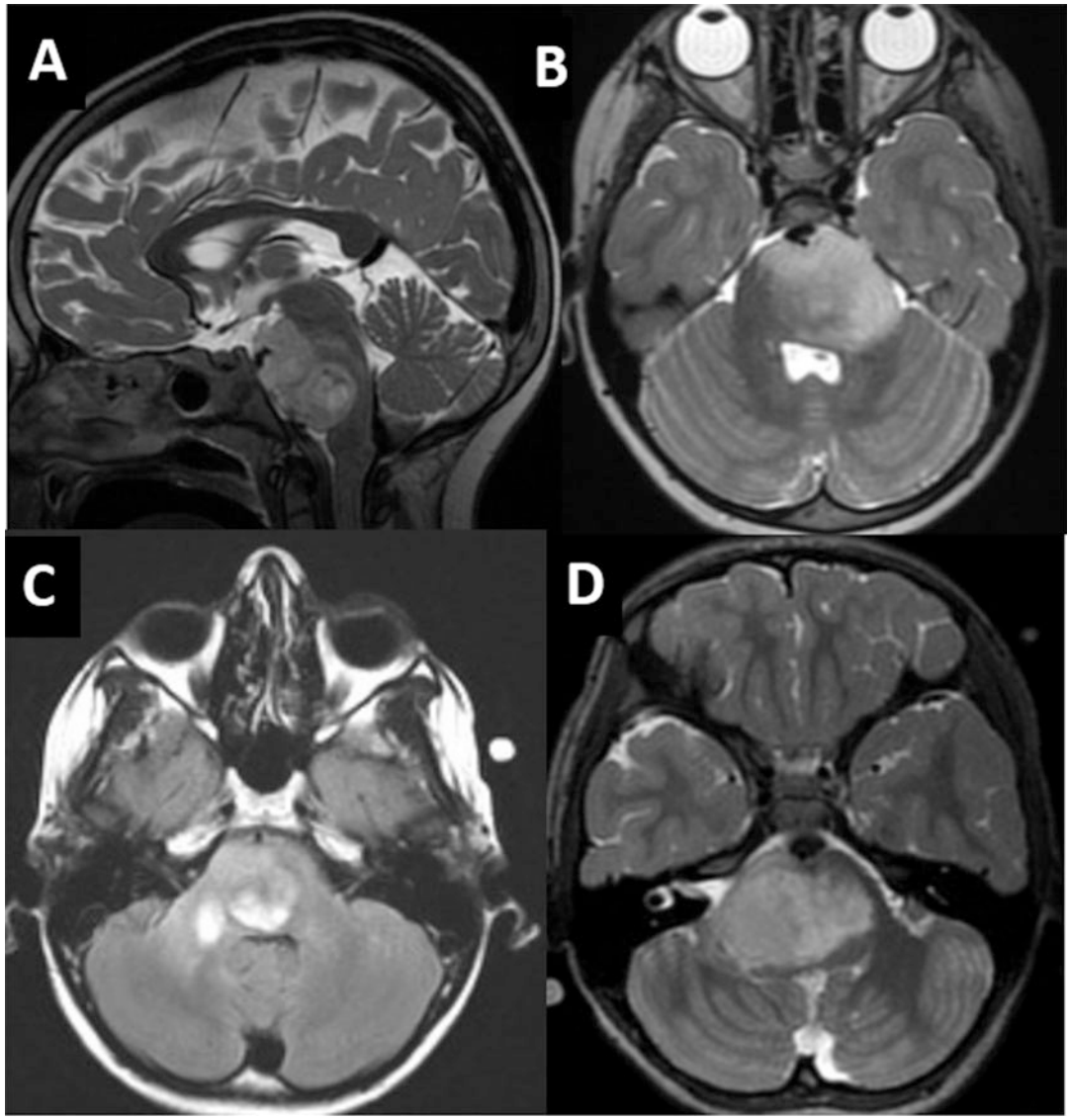


Fig. 22.3 (**a**) Brain MRI sagittal T2WI showing an expansile pontine mass that abuts the clivus in a 7-year-old girl presenting with hemiparesis; (**b**, **d**) encasing the basilar artery in axial T2WI. The actual size and extension of such lesions are more readily detected on axial FLAIR images; (**c**) in a 14-year-old child with ocular motility problems

children occur in the infratentorial compartment, and they may be intrinsic to the brain stem (Fig. 22.3) or located with the cerebellar parenchyma or cerebrospinal fluid spaces of the posterior fossa (Fig. 22.4). Supratentorial tumors are usually hemispheric (Fig. 22.5) but may also arise from the suprasellar and/or pineal region (Fig. 22.6). For the youngest children, the ratio of infratentorial versus supratentorial lesions is reversed, and in the first year of life, supratentorial tumors are actually slightly more prevalent.

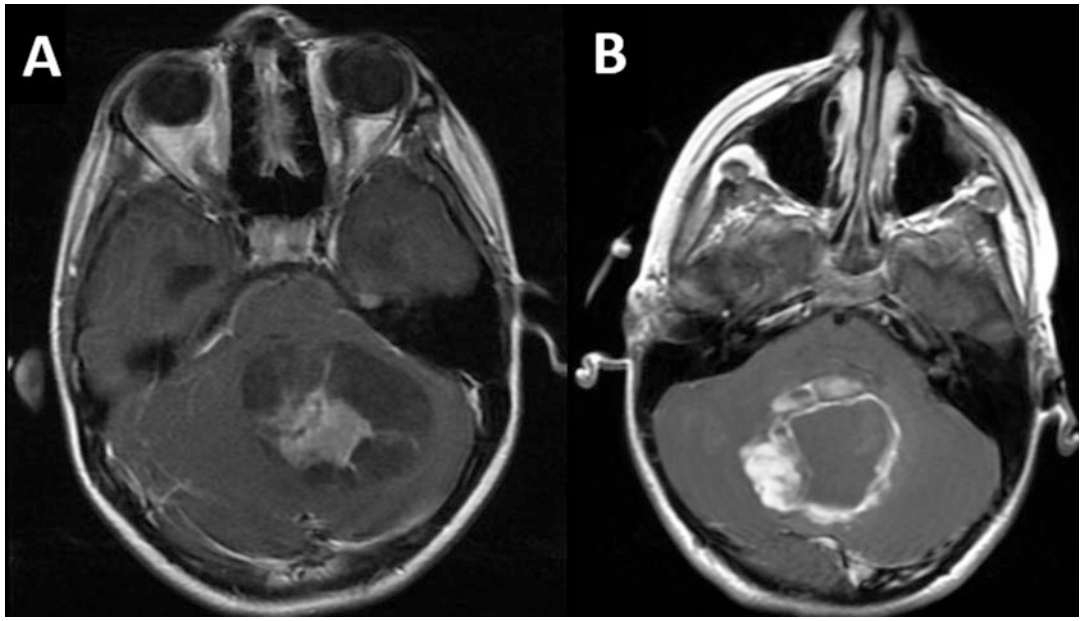


Fig. 22.4 (**a**) Axial T1WI+C in a 13-year-old child presenting with headache and progressive ataxic gait. It shows a well-defined partially cystic contrast-enhancing lesion in the left cerebellar hemisphere. Common site and configuration for JPA. (**b**) Axial T1WI+C of an 11-year-old boy with classic cerebellar manifestations of headache, nausea, and vomiting, showing an irregular ring-enhancing lesion with a more solid component to one side. Also a classic picture and presentation of juvenile pilocytic astrocytoma (JPA)

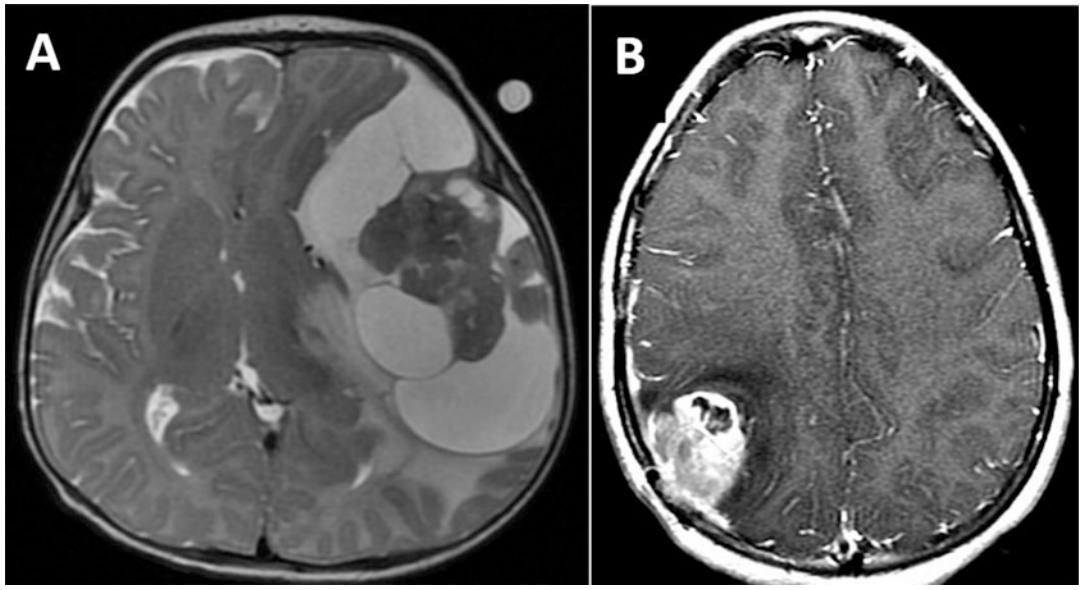


Fig. 22.5 (**a**) Brain MRI, T2WI axial sequence showing a left hemispheric desmoplastic infantile astrocytoma. Three-month-old boy that presents with a new onset seizure. (**b**) Axial T1WI+C MRI brain of a child with multiple recurrent astrocytoma GIV presenting with progressive headache, lethargy, and worsening inactivity

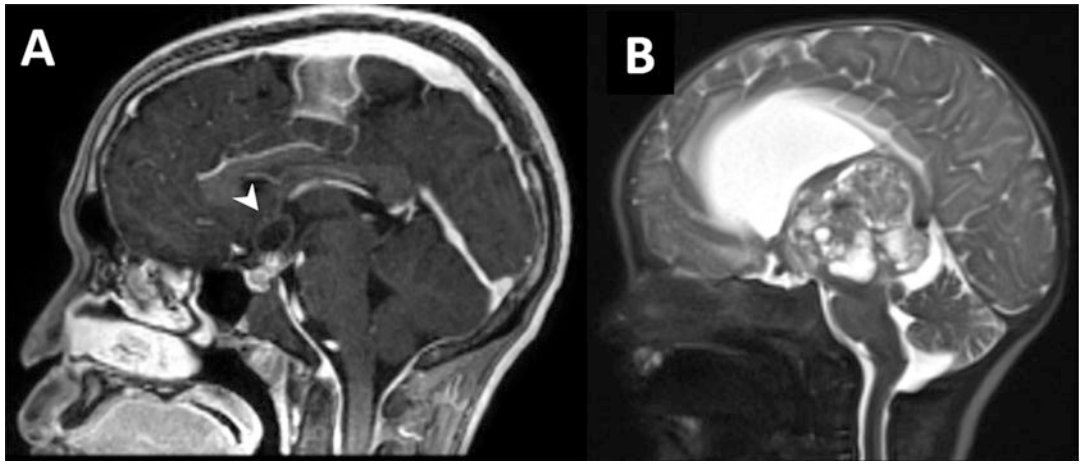


Fig. 22.6 (**a**) Sagittal T1WI+C of a 17-year-old child with incidental diagnosis of this lesion. Had no hormonal or visual problems, no clinical evidence of diabetes insipidus. He has a contrast-enhancing sellar mass with suprasellar partially cystic extension (*white arrow head*). (**b**) Brain MRI T2WI sagittal sequence showing a pineal region immature teratoma. Two-month-old girl that presented with a bulging anterior fontanel, sunset gaze, and emesis

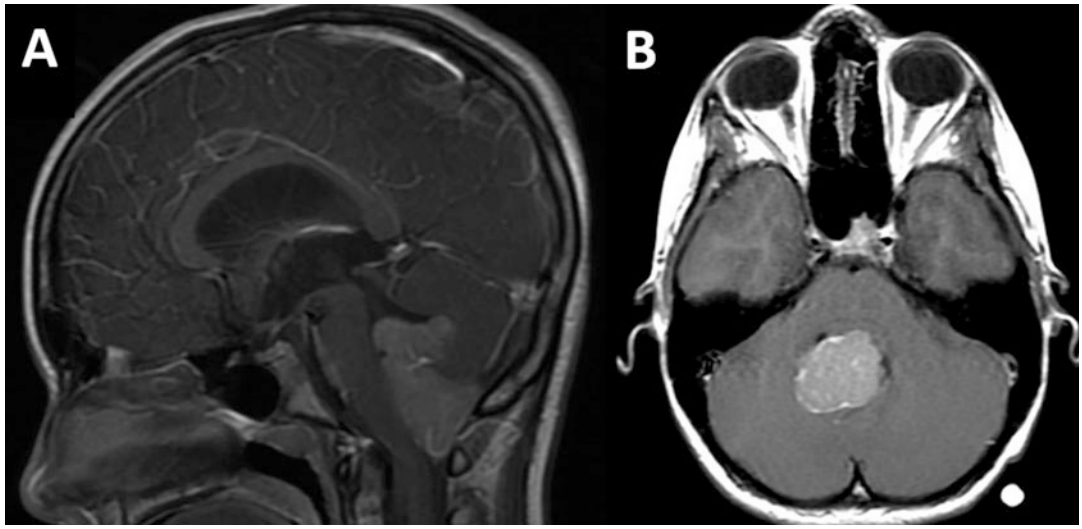


Fig. 22.7 (**a**) Brain MRI T1WI+C sagittal sequence showing a fourth ventricle medulloblastoma. Ten-year-old boy that presented with a several-month history of emesis and headaches. (**b**) Axial T1WI+C of 4-year-old child with progressive headache shown in Fig. 22.1b with posterior fossa ependymoma

The World Health Organization (WHO) outlines another important classification. This is based upon a tumor's behavior and its histopathological characteristics. Inside the infratentorial compartment, the most typical histological subtypes are cerebellar astrocytomas, medulloblastomas, ependymomas (Figs. 22.7 and 22.8), and brain stem gliomas. In the supratentorial space, gliomas and particularly low-grade astrocytomas (Fig. 22.9) remain the most common tumors of the cerebral hemispheres. Craniopharyngiomas (Fig. 22.10) and optic pathway gliomas of the suprasellar region and germ cell tumors of the pineal region are also fairly common.

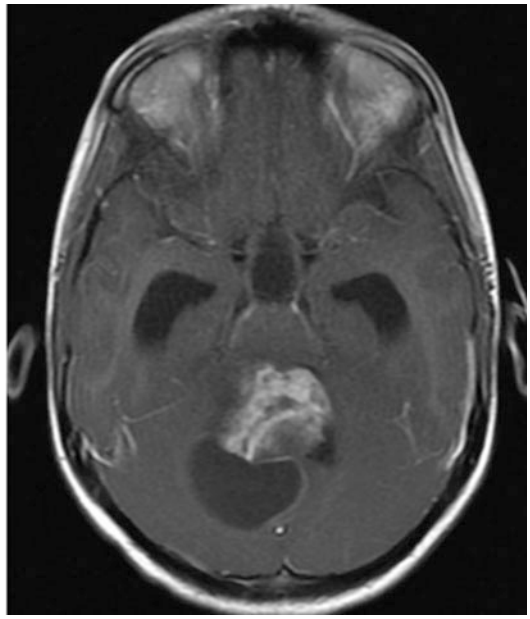


Fig. 22.8 Axial T1WI+C in an 8-year-old child with worsening headache, vomiting, and ataxia. It shows a predominantly fourth ventricular partially cystic and heterogeneously enhancing lesion. Typical site and imaging for a JPA

Clinical Presentation

Brain tumors in children are often difficult to diagnose, and it is often noted that the average time from symptom onset to diagnosis routinely exceeds several months due to many nonspecific and intermittent features of the brain tumor symptomatology. An intracranial mass can present several different ways, some slow and insidiously, some rapidly progressively, leading to disparate clinical patterns. Tumor location, rate of tumor growth, and histologic behavior are major factors in the length of time between clinical symptom onset and the diagnosis. In the reality of daily practice, pediatric primary care providers will be the first to have the opportunity to discern which symptoms could be related to the presence of an undiagnosed brain tumor. Clinical symptoms are usually relapsing, remitting, or subtle and often mimic less serious and unrelated diseases. Their misinterpretation is responsible for delay of the diagnosis. Often, at the time of the clinical onset, intracranial masses have reached fairly impressive size. This is due both to the elasticity of the infant skull and the tremendous plasticity of the developing nervous system to compensate for deficits.

Specific and Nonspecific Symptoms

Generally, the most specific clinical symptoms of brain tumors in children can be categorized into three groups: focal neurologic deficits, symptoms of raised intracranial pressure, and seizures. Any of these three should prompt a child to be forwarded to higher acuity care and subspecialty medical attention. The end result is usually an imaging study and a more detailed neurological evaluation by a pediatric neurologist or neurosurgeon.

Focal neurological deficits occur either from direct compression of a tumor mass on specific neuroanatomical structures or via invasion of the growing tumor. Focal deficits are more commonly seen with hemispheric or brain stem lesions or with tumors that involve cranial nerves. For example, a child in whom a unilateral sixth nerve palsy is detected is likely to have a lesion in the pontine region of the brain stem within which the nucleus of the sixth cranial nerve resides.

In contrast, tumors, juvenile pilocytic astrocytomas (JPAs), medulloblastomas, and ependymomas, that obstruct the ventricular system such as posterior fossa often present with signs or symptoms of increased intracranial pressure. These are subacute, nonspecific, and non-localizing. A triad of symptoms that should concern any practitioner is morning headaches, vomiting, and somnolence. Headache in this scenario is generally relieved by vomiting and is gradually lighter during the day. Vomiting is usually not coincident with meals and it becomes a concern when it persists over few weeks. Gastroenteritis, influenza, strep throat, and other common illnesses in the pediatric population are much more commonly suspected before a brain tumor is diagnosed in cases where no localized signs predominate and where headache and emesis are the only features. It is easy to understand why the diagnoses can be delayed, but the triad above should alert the primary care practitioner to the possibility of a more ominous etiology.

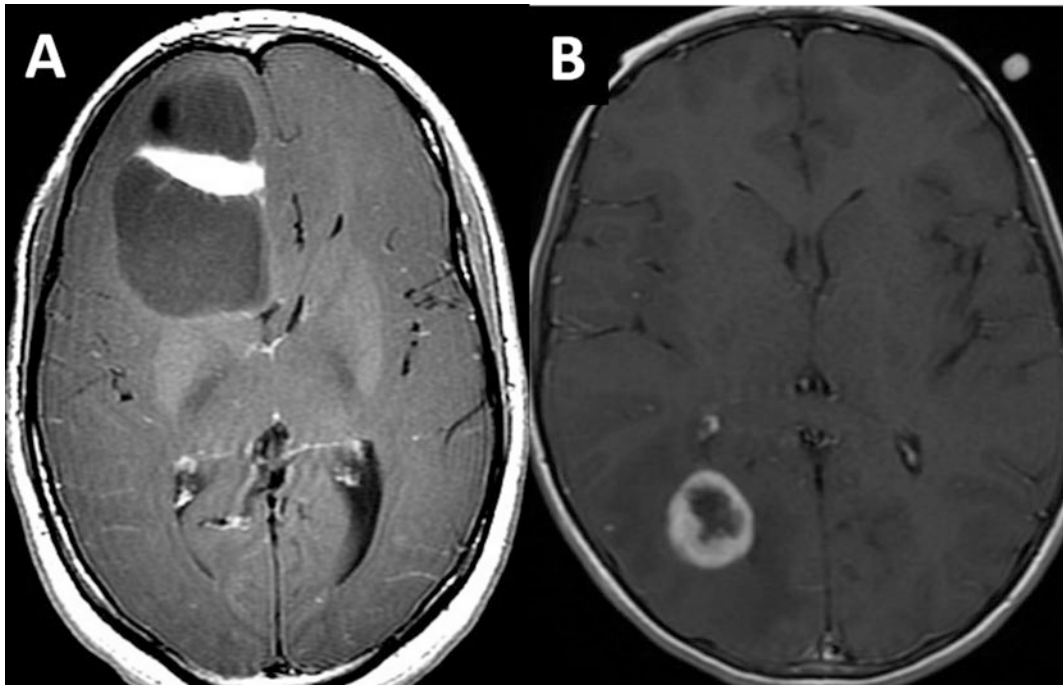


Fig. 22.9 (**a**) Brain MRI T1WI + contrast axial sequence showing a right frontal juvenile pilocytic astrocytoma (JPA). Fifteen-year-old girl with neurofibromatosis type 1 that presented with gait unsteadiness. (**b**) Same sequence shows a right parietal contrast-enhancing JPA in an 11-year-old child with headache and visual field deficits. Both are atypical locations and radiological pictures of JPA

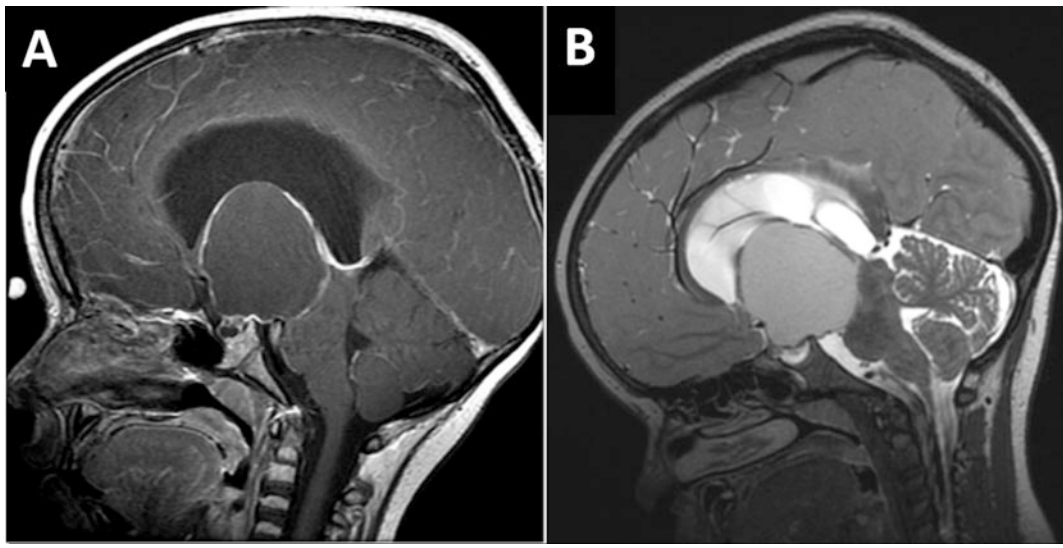


Fig. 22.10 (**a**) Sagittal brain MRI T1WI showing sellar lesion with heterogeneous contrast enhancement and large cystic suprasellar extension obliterating the third ventricle and causing obstructive hydrocephalus. This was a craniopharyngioma in child presenting with visual symptoms and progressive intellectual decline. (**b**) Sagittal T2WI sequence of the same patient

Finally, seizures almost exclusively occur due to lesions arising in the cerebral hemispheres. In an otherwise healthy child, it would be rare that a first-time seizure in a child, other than within the context of the classic infantile febrile seizure, would not prompt medical attention and result in a CT or MRI being performed. At the very least, a semi-urgent evaluation by a neurologist or ED would be expected if no obvious history or etiology could be defined to explain the seizure.

In infants under 1 year of age, often the only presenting signs bringing a child to medical attention may be an increase in head circumference with diastasis of the sutures or change of the usual interaction or level of alertness. Head circumference will increase as a means to compensate for raised intracranial pressure. Anorexia, non-resolving emesis, and milestone regression can also be seen. Older infants, who often cannot communicate their symptoms, have the ability to mask a deficit by compensating with another extremity or unconsciously changing their behavior. School-aged children may demonstrate declining academic performance and personality changes. Often they complain of vague intermittent headaches and fatigue, again fairly difficult and nonspecific symptoms.

When raised intracranial pressure occurs secondary to direct obstruction of the cerebrospinal fluid (CSF) pathways, hydrocephalus is invariably present. The severity of the hydrocephalus is responsible for the changes noted in the child's level of consciousness, resulting in lethargy and confusion, while the headache becomes persistent and restricts daily activities including school, hobbies, and sports. Once the lethargy stage is reached, a rapid deterioration of the child can occur any time, leading to Cushing triad (hypertension, bradycardia, and hypoventilation), coma, and death from brain herniation. This is a medical emergency and requires immediate referral to a medical center with pediatric neurosurgical services.

The final common tumor location, which requires attention due to a frequently overlooked set of signs and symptoms, is tumors of the anterior skull base in the region of the pituitary gland. The possibility of a suprasellar mass, such as a craniopharyngioma, optic glioma, or pituitary tumor, should be considered when there are symptoms suggesting compression or dysfunction of the pituitary gland, hypothalamus, or optic apparatus (nerves and chiasm). Ophthalmologic signs such as blurry vision, field cuts, intermittent double vision, eye deviation, or papilledema (though more often associated with raised ICP) should give pause as to a possible tumor-based etiology. Endocrinopathies classically demonstrated in specific tumors are growth arrest (GH deficiency) from craniopharyngioma and diabetes insipidus for tumors on the infundibulum (pituitary stalk) including germ cell tumors such as germinoma. *A child whose growth curve shows sudden deceleration in conjunction with blurry vision or headaches likely has a craniopharyngioma. An 8-year-old child waking up 3–4 times a night to urinate*, *who has been drinking water continuously*, *likely has a germ cell tumor.*

While specific symptoms may alert you to a diagnosis, the key here is not to expect or worry that as a primary care provider, you would be expected to localize an intracranial tumor based upon neurologic signs, but rather be aware of the common presenting features and trust your instinct when symptoms persist for too long, or the clinical scenario is atypical for what has been suspected.

Pediatrician's Perspective

Entire textbooks are dedicated to specific pathologies briefly introduced and discussed in the previous chapter. There is no way for a primary care provider to have the level of expertise to diagnose the subtypes of brain tumors seen in a pediatric hospital. For an in-depth discussion of the diagnosis and management of any particular brain tumor one of your patients may have, we recommend a primary source textbook such as *Textbook of Neuro-Oncology* edited by Michael S. Berger and Michael D. Prados (Elsevier, 2004). What a pediatrician should be able to discern are the few key features of pediatric brain tumors which are more likely to raise the suspicion of an underlying pathology rather than a nonspecific illness. There is also a propensity for guilt and second

guessing after a diagnosis of a brain tumor has been made, but be assured that the early nonspecific signs you assessed and general reassurance you provided were well within the accepted and expected practice guidelines. If you are able to keep focal neurologic deficits, morning emesis, growth arrest, or changes in arousal/mentation in your field of view, you will not miss an opportunity to refer a child for timely and appropriate care to a pediatric neurosurgeon.

Key Points

1. Brain tumors may present in one of three broad categories: focal neurological deficits, symptoms of raised intracranial pressure, or seizures.
2. Focal deficits often suggest intrinsic brain tumors of the brain stem in children.
3. The triad suggesting raised ICP in children includes morning headaches, vomiting, and somnolence. This often occurs with obstructive lesions of the fourth ventricle in children, such as medulloblastoma.
4. Growth arrest and diabetes insipidus may suggest to you pituitary-hypothalamic axis dysfunction.
5. Blurry vision, papilledema, and field cuts can represent raised ICP or mass lesions compressing the optic apparatus.

Suggested Reading[1]

Albright AL, Pollack IF, Adelson PD. Principles and practice of pediatric neurosurgery. 2nd ed. New York, NY: Thieme; 2011.

Berger MS, Prados M. Textbook of neuro-oncology. 1st ed. Philadelphia, PA: Saunders; 2004.

Yousem DM, Zimmerman RD, Grossman RI. Neuroradiology: the requisites. 3e (Requisites in radiology). 3rd ed. St. Louis, MO: Mosby; 2010.

[1] Due to the scope and breadth of pediatric neuro-oncology, we refer any interested readers to three outstanding textbooks for more information about any of the common pediatric brain tumors.

Pediatric Neurovascular Disease

23

Benjamin I. Rapoport, Scott W. Connors, and Caitlin E. Hoffman

Clinical Vignette

The mother of one of your patients calls you at home. The patient is a 28-month-old male who was delivered at full term without complications and has been developmentally appropriate. His mother reports that the patient was walking through the living room when he suddenly lost consciousness and began writhing on the floor. The episode lasted approximately 90 s, after which the patient regained consciousness, though he currently remains lethargic. His mother states that the patient has never had such an episode before. She denies any prior head trauma or family history of seizure disorders. The patient takes no medications and neither he nor any members of the family have been ill recently. You instruct the mother to bring her son immediately to the emergency department of the local hospital, which you know has a neurologist and neurosurgeon on staff at all times and is equipped with advanced neuroimaging capabilities. The child remains lethargic on arrival to the emergency department and begins complaining of headache. A low-radiation head CT is obtained immediately and demonstrates diffuse subarachnoid hemorrhage.

What are the most appropriate next steps in management and diagnosis?

B.I. Rapoport, M.D., Ph.D. • S.W. Connors, B.S.
C.E. Hoffman, M.D. (✉)
Department of Neurological Surgery, Weill Cornell Medical College, New York-Presbyterian Hospital, 525 East 68th Street, Starr Pavilion, 651, New York, NY 10065, USA
e-mail: Ceh2003@med.cornell.edu

Introduction

Neurovascular lesions can be divided broadly into several categories: vascular malformations, aneurysms, vasculopathies, and other causes of ischemic stroke.

The first category, vascular malformations of the brain and spinal cord, includes arteriovenous malformations (AVMs), cavernous malformations, capillary telangiectasias, and venous malformations. Estimating the prevalence of these conditions in pediatric patients is difficult, as most of the epidemiologic data is derived from adult autopsy studies and case series; one series of 5734 autopsies estimates the overall prevalence of vascular malformations at 4.6 %, with 0.5 % attributed to AVMs, 0.3 % to cavernous malformations, 0.8 % to capillary telangiectasias, and 3.0 % to venous malformations [1].

As for aneurysms, these lesions are rare in the pediatric population, and some series of thousands of pediatric autopsies and thousands of pediatric angiograms find no incidental intracranial aneurysms. In one autopsy series of 6101 patients, however (including 2017 children), an

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_23

intracranial aneurysm was found in 0.8 % of patients aged 10–19, and no aneurysms were found in patients aged 1–9 or less than 1 year (of 265, 287, and 1465 cases, respectively, in these age ranges) [2].

We address vasculopathy and other causes of ischemic stroke in a single section of this chapter, emphasizing moyamoya syndrome and moyamoya disease because these conditions are particularly amenable to surgical intervention. Although these conditions are rare among children in the general population, the population of patients who come to neurologic and neurosurgical attention is enriched for vascular lesions, and they are encountered and treated regularly at many large hospitals.

Aneurysms

Intracranial aneurysmal disease in children differs in many respects from that in adults. Whereas the majority of unruptured aneurysms in adults are found incidentally (during neuroimaging for atypical headache, trauma, or other neurologic complaints or conditions), diagnosis of unruptured intracranial aneurysms in children is less likely, as children rarely undergo neuroimaging outside the emergency setting. Aneurysmal disease may present with a variety of neurological symptoms, including focal deficit or cranial neuropathy due to the mass effect from an unruptured aneurysm or, in the acute setting, the hematoma from a ruptured aneurysm. Subarachnoid hemorrhage or intraparenchymal hemorrhage from a ruptured aneurysm can also cause headache, lethargy, vomiting, and a variety of other more subtle signs in pediatric patients who are variably able to articulate their symptoms.

In this section, we provide an overview of the epidemiology, pathophysiology, diagnosis, and management of aneurysms and aneurysmal subarachnoid hemorrhage (SAH) in the pediatric population. The reader is also referred to recent reviews of these subjects [3, 4].

Epidemiology

Although cerebral aneurysms are certainly rare in children, the reported incidence in the pediatric population varies. In one review of the literature, the annual incidence of pediatric aneurysmal subarachnoid hemorrhage was approximated at one per million [5]. A series of 3000 pediatric autopsies found no incidental cases of cerebral aneurysms, and two series involving a total of 15,000 pediatric angiograms similarly revealed no incidental intracranial aneurysms [6]. Major surgical series of intracranial aneurysms provide a somewhat different perspective, however, reporting that between 0.5 and 3.1 % of intracranial aneurysms are diagnosed in children [7].

Several features of pediatric aneurysmal disease are quite different from the corresponding disease in adults. Pediatric aneurysms are more common in males than in females, by a ratio of 1.3–2.8:1; the opposite gender predilection is observed in adults. Fascinatingly, giant aneurysms (greater than 25 mm in diameter) comprise a greater proportion of aneurysms seen in infants than in either adolescents or adults [8]. The presence of multiple intracranial aneurysms in a child typically suggests a syndromic etiology; aneurysm-associated syndromes will be addressed individually later in this chapter (Fig. 23.1).

Presentation and Clinical Features

The clinical presentation of ruptured intracranial aneurysms in children differs in several respects from adults. Clinical series have also shown differences in the natural history and overall outcome for pediatric intracranial aneurysms.

Unlike adults, who may come to attention electively following incidental diagnosis of an unruptured intracranial aneurysm, children almost always present emergently, symptomatic at the time of diagnosis. Warning signs heralding a major aneurysmal rupture are sometimes observed in the form of a “sentinel bleed,” which

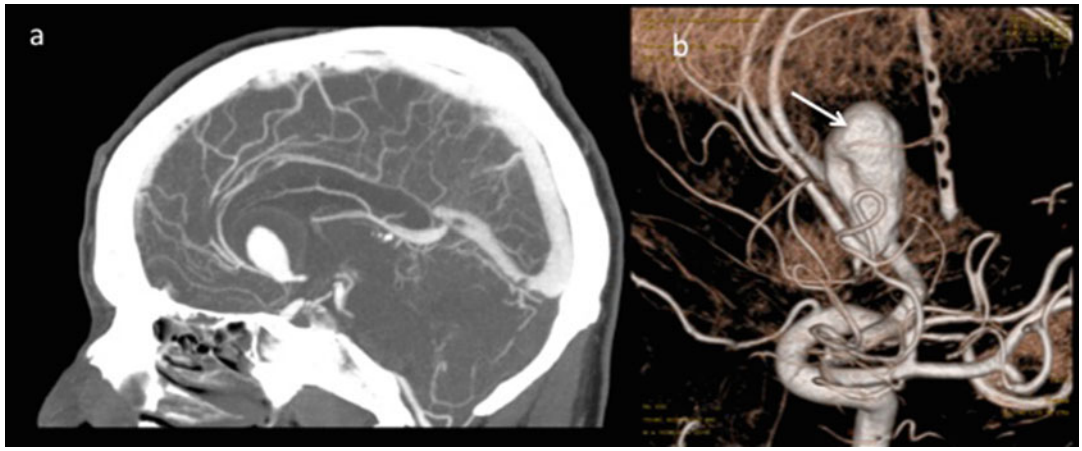


Fig. 23.1 CT angiogram (**a**) and 3-dimensional reconstruction (**b**) showing a giant (2.5 × 2.7 cm) anterior communicating artery aneurysm (*arrow*). Peripheral thrombus can be seen in the CTA. This aneurysm was treated endovascularly, and the patient made an excellent recovery from a severe subarachnoid hemorrhage

presents as headache, nuchal rigidity, emesis, or cranial nerve palsy (usually optic and oculomotor) in approximately 10–15 % of patients [5].

Subarachnoid Hemorrhage

Intracranial aneurysms in children most commonly come to clinical attention following rupture, with associated subarachnoid hemorrhage (SAH). A review of several patient series suggests that approximately 52–67 % of pediatric intracranial aneurysms are ruptured at diagnosis [5]. Ruptured aneurysm is believed to be the most common etiology of SAH among patients younger than 20 years. In a series of 167 children with proven subarachnoid hemorrhage, 52 % were found to have ruptured aneurysms, while 26 % had bleeding AVMs, and 19 % of cases were idiopathic [9]. The onset of subarachnoid hemorrhage is typically sudden, with headache, fever, vomiting, meningismus, cranial nerve palsy, seizure, paresis, deterioration in consciousness, and coma being common signs.

Focal Neurologic Findings

Enlargement of an unruptured aneurysm most commonly leads to cranial nerve findings related to the location of the aneurysm. Classically, anterior communicating artery aneurysms are associated with optic nerve findings, posterior communicating artery and basilar tip aneurysms with third nerve palsy, and posterior circulation aneurysms with lower cranial nerve palsies. Chronic nerve compression can also lead to unilateral papilledema ipsilateral to the aneurysm. Third nerve palsy manifests as ptosis and mydriasis (drooping eyelid and dry eye) and ophthalmoplegia (inability to move the eye vertically or medially). Lower cranial nerve palsies in children are most evident as difficulty swallowing and snoring or apnea at night.

Seizures

While seizures are rarely associated with unruptured aneurysms, seizures do occur in 15–25 % of children with subarachnoid hemorrhage [5]. Seizures following subarachnoid hemorrhage are particularly dangerous in the cases of ruptured aneurysms. These seizures can cause dangerous increases in blood pressure that can precipitate rebleeding from the aneurysm, a major cause of morbidity and mortality. Therefore, anticonvulsants are used acutely for seizure management and prophylaxis. Seizures following subarachnoid hemorrhage rarely progress to epilepsy.

Giant Aneurysms and Mass Effect

Intracranial aneurysms reach "giant" size (>2.5 cm) with much greater frequency in children than in adults. "Tumorlike presentation" is therefore significantly higher in early childhood (18.1 %) than in adulthood (2.5 %) [10]. Common present-

ing signs include lethargy, vomiting, and papilledema; infants may demonstrate a tense anterior fontanelle and splayed sutures. In the case of giant aneurysms, focal neurologic findings from mass effect may be due to the aneurysm itself. In approximately one-third of cases, hematoma was present at diagnosis [11].

Hydrocephalus

Hydrocephalus often develops following aneurysmal subarachnoid hemorrhage. Subarachnoid and intraventricular blood impairs resorption of cerebrospinal fluid (CSF) at the arachnoid granulations, leading to hydrocephalus. In these cases, emergent surgical intervention may be necessary to divert the cerebrospinal fluid in order to control intracranial pressure; in the acute setting, a ventriculostomy may be performed emergently for placement of an external ventricular drain, both to monitor intracranial pressure and to divert CSF. Many children will never fully recover sufficient capacity to resorb CSF and may require permanent shunting to divert cerebrospinal fluid.

Vasospasm

In the adult literature, cerebral vasospasm is well known to contribute significantly to morbidity and mortality following SAH. Case series data suggest, however, that in children vasospasm is not as significant a concern. While approximately 25 % of children develop severe angiographic vasospasm following aneurysmal subarachnoid hemorrhage and another 25 % develop mild radiographic vasospasm, no associated increase in morbidity or mortality has been shown in these children [5].

Genetics and Associated Syndromes

Up to 55 % of pediatric patients with intracranial aneurysms harbor an underlying comorbid syndrome or factor associated with aneurysm formation. These conditions may be congenital or acquired and include cranial irradiation, moyamoya, fibromuscular dysplasia, cardiac myxoma, systemic infection, or arteriovenous malformation. In addition to these conditions, congenital anatomic variants are sometimes implicated in aneurysm formation. Additionally, cerebrovascular complications of HIV are increasingly recognized, and a high incidence of multiple aneurysms has been reported in patients with HIV. Multiple aneurysms in children are also associated with a number of genetic syndromes and have also been observed in association with thalassemia minor, sickle cell disease, and glucose-6-phosphatase dehydrogenase deficiency.

Polycystic Kidney Disease

The autosomal dominant form of polycystic kidney disease (ADPKD) affects multiple organs including the heart, gastrointestinal tract, and kidneys. This form of the disease is associated with an increased risk of intracranial aneurysms, although a review of several series reveals that the observed prevalence of aneurysms in these patients varies from 0 to 41 % [5]. In 85 % of cases, adult polycystic kidney disease is attributable to a defect in the gene *PKD1* on chromosome 16; the remaining 15 % of cases are attributable to a defect in *PKD2* on chromosome 4. Both genes encode proteins with postulated roles in cell-cell matrix interactions and are thought to be relevant in vessel wall development [12].

Tuberous Sclerosis

Tuberous sclerosis (TS) is classically described as a developmental dysplasia affecting both ectodermal and mesodermal derivatives, and so the disease has manifestations in multiple organ systems, including the kidneys (renal cysts) and the brain (cortical tubers, subependymal nodules, subependymal giant cell astrocytomas, and intracranial aneurysms). Clinically, it is associated with the triad of mental retardation, epilepsy, and adenoma sebaceum (red facial angiofibromas). The syndrome is known to be associated with mutations in two genes, *TSC1* and *TSC2*, which encode the proteins hamartin and tuberin, respectively. The latter gene collocates on chromosome 16 with *PKD1*, explaining some of the associations with polycystic kidney disease. Tuberous sclerosis is thought to give rise to a congenital

defect in the arterial wall, predisposing to the formation of multiple and fusiform (as opposed to saccular) intracranial aneurysms.

Coarctation of the Aorta

Coarctation of the aorta (narrowing at the insertion of the ligamentum arteriosum) is consistently reported to be associated with single or multiple intracranial aneurysms. The true strength of this association is difficult to estimate because the majority of intracranial aneurysms do not come to clinical attention until adulthood. However, one review of 200 patients with aortic coarctation reported only five patients (2.5 %) diagnosed in life with cerebral aneurysms [13].

Ehlers–Danlos and Marfan Syndromes

Ehlers–Danlos refers to a group of disorders in collagen synthesis. The best known clinical manifestations of these syndromes are hyperelastic skin and hyperextensible joints. The classic phenotype is not present in Ehlers–Danlos type IV (defective type III collagen synthesis), which carries an association with intracranial aneurysm formation [14]. In Marfan syndrome, the genetic defect is in the *FBN1* gene on chromosome 15, encoding a connective tissue matrix glycoprotein [15].

Pathophysiology

The acquired risk factors known to predispose to intracranial aneurysm formation and subarachnoid hemorrhage in adults (hypertension, diabetes, alcohol use, hyperlipidemia, obesity, cigarette smoking, and oral contraceptive use) are virtually irrelevant in the pediatric population. With the exception of traumatic and mycotic (infectious) aneurysms, the pathogenesis of pediatric intracranial aneurysms is more commonly congenital or syndromic, associated with many of the syndromes listed in the previous section.

Idiopathic Aneurysms

Histologically, pediatric intracranial aneurysms resemble their adult counterparts. Within the aneurysm, intima and smooth muscle are absent, and the wall of the aneurysm is formed only by the external elastic membrane. Saccular aneurysms form at arterial branch points, where shear forces are high. The walls of the cerebral vasculature are considerably thinner than those of systemic arteries; types I and III collagen predominate in these vessels. Detailed work by Stehbens has suggested that even in children, aneurysm formation may reflect a process involving hypertension, birth or in utero injury, and trauma [16].

Traumatic Aneurysms

Traumatic aneurysms are false or pseudoaneurysms, meaning there is disruption of the entire vessel wall. Rather than being contained by vascular tissue, the aneurysm has no true wall and is contained by surrounding neural structures—for this reason, they are friable, highly unstable lesions, and more prone to rupture than a true aneurysm [5, 17]. Traumatic aneurysms are more common in children due to their increased brain mobility and more fragile vessels. The presentation of traumatic aneurysms includes epistaxis, otorrhagia (bleeding from the ear), and cranial nerve palsy. These patients may also present with signs of hemorrhage with a history of trauma or penetrating injuries that could result in direct vessel injury. Cases presenting with epistaxis and otorrhagia are typically the result of carotid injuries associated with skull base fractures. To avoid operative morbidity and mortality, these lesions are commonly observed, with surgical or endovascular treatment reserved for cases demonstrating progressive enlargement. Overall morbidity and mortality from this condition is reportedly as high as 50 % [17].

Giant Aneurysms

The term "giant aneurysm" refers to a saccular aneurysm greater than 25 mm in maximal diameter. It is not known whether they expand dynamically, growing rapidly early in life from smaller initial lesions. It is known, however, that giant aneurysms make up a greater proportion of aneurysms seen in young children than they do in other age groups. While case series of intracranial aneurysms suggest that giant aneurysms represent 2–5 % of cases across all age groups, among children less than 5 years old, 30–50 % of aneurysms are giant.

Infectious Aneurysms

Though still used in reference to infectious aneurysms, the term "mycotic," introduced by Sir William Osler in 1885, is misleading as it suggests a fungal etiology. Most infectious aneurysms in children are associated with bacterial rather than fungal infections. The most common causative organisms in children are alpha *Streptococcus*, *Staphylococcus*, *Pseudomonas*, and *Haemophilus* species. Aneurysms attributable to fungal infections are rare, but when they do occur, typically in immunocompromised patients, *Aspergillus* and *Candida* are the organisms most frequently responsible.

Infectious aneurysms may be classified into three primary types [18]. The first type is most common and occurs in the setting of bacterial endocarditis with subsequent embolization to the intracranial circulation. The second type involves direct extension from an adjacent infectious source, as may occur in meningitis, osteomyelitis, or sinusitis. The third type of infectious aneurysm is isolated to the intracranial circulation, with no identifiable source elsewhere in the body.

Surgical treatment is not typically indicated for these lesions, both for technical reasons and because they commonly stabilize and regress with medical therapy alone. Antibiotic therapy for 4–6 weeks should be initiated, with serial imaging at 3, 6, and 12 months. Typically, surgical treatment is indicated only in the setting of aneurysmal rupture or progression despite appropriate antibiotic therapy.

Diagnosis

Although conventional four-vessel cerebral angiography remains the gold standard for precise characterization of cerebral aneurysms, this modality has largely been replaced by computed tomography angiography (CTA) or magnetic resonance angiography (MRA) as the primary diagnostic modalities to detect aneurysms, particularly in children. CTA and MRA have come into favor given their accuracy and the ubiquity of these scanners in modern medical practices; moreover, they do not require invasive access or risk catheter-related vascular damage. At present, standard MRA can reliably identify lesions with diameter greater than or equal to 3 mm. CTA is capable of identifying smaller lesions. Nevertheless, cerebral angiography should be used in the case of indeterminate results from MRA or CTA or when clinical suspicion is high.

In the setting of symptoms suspicious for SAH, a non-contrast CT should be obtained first, with possible lumbar puncture for indeterminate scans with a strong clinical suspicion for SAH. Transfontanelle ultrasound is a useful neuroimaging modality in infants.

When subarachnoid hemorrhage has been confirmed, a four-vessel cerebral angiogram should be performed, with vessels studied in an order based on the highest suspicion for aneurysm location so as to ensure highest diagnostic yield in the event the procedure must be aborted, which is of special concern in children. The literature suggests that a lesion is identified on angiography in 50–70 % of cases. Of the remaining cases, another 10–20 % demonstrate a lesion on 2-week follow-up angiogram [19].

After two negative angiograms, the likelihood of finding an aneurysm is small, and the remainder of the differential diagnosis for nontraumatic subarachnoid hemorrhage should be carefully considered. In children, this includes systemic disorders such as leukemia, idiopathic thrombocytopenic purpura, and various coagulopathies. Other important diagnostic considerations include nonaneurysmal intracranial lesions such as ruptured arteriovenous malformations, vein of Galen malformations, tumoral hemorrhage, intracerebral hemorrhage with subarachnoid extension, and hemorrhage from spinal lesions.

Screening and Implications for Family

In children, the decision to screen for unruptured intracranial aneurysms must be approached in a manner different from the adult case due to the radiation exposure involved in the required diagnostic neuroimaging. Although no formal consensus guidelines have been established, there is general agreement that screening of asymptomatic children should typically be limited to children with the syndromes discussed in the preceding

sections or those with strong family history of intracranial aneurysms. In all such pediatric patients and particularly those with disorders known to affect the kidneys (such as polycystic kidney disease and tuberous sclerosis), MR angiography is a reasonable first screening test in patients without neurologic signs or symptoms. Syndromic patients with neurologic signs or symptoms should undergo urgent four-vessel cerebral angiography.

Several authors have addressed the question of when to screen children with familial history of intracranial aneurysms [20, 21]. There are quantifiable risks involved in screening, including not only cranial irradiation of young patients (not applicable to magnetic resonance angiography) but also the risks of angiography, identification, and further evaluation with possible intervention for asymptomatic, unruptured aneurysms. There is general agreement that screening is not indicated for patients with one affected family member but that patients with a history of two or more close relatives with intracranial aneurysms should be screened.

Autosomal dominant polycystic kidney disease may represent a special case, as studies suggest an incidence of intracranial aneurysms of up to 18 % in members of families carrying a *PKD1* mutation with at least one affected family member [22].

When to Refer to a Neurosurgeon

Emergent neurosurgical consultation is indicated in all cases of subarachnoid hemorrhage. Decisions related to treatment or observation of unruptured, asymptomatic, or incidentally discovered intracranial aneurysms should also involve a neurosurgeon specializing in cerebrovascular disorders.

Treatment, Outcomes, and Prognosis

Unruptured Aneurysms

The natural history of asymptomatic, unruptured intracranial aneurysms is a subject of ongoing interest to investigators and has been addressed in a number of large longitudinal studies over the past several decades [23]. There is general agreement that no intervention is indicated for such aneurysms when the diameter is <7 mm and that these lesions may be safely observed with interval MRI; intervention may be considered for symptomatic, large, or expanding lesions.

Ruptured Aneurysms

The estimated immediate mortality after aneurysmal subarachnoid hemorrhage is approximately 10–20 % in children, as compared with 20–30 % in adults. Estimates of overall mortality range from 13 to 34 % in the literature [5], as compared with approximately 45 % in adults [24].

Definitive treatment of a ruptured intracranial aneurysm is obliteration of the aneurysm through microsurgical or endovascular treatment. In children, evidence suggests that surgical or endovascular treatment should almost always be attempted, as intervention consistently yields better outcomes than medical management alone [5]. Emergent referral to a center with a neurosurgeon on staff should be a priority in cases of suspected aneurysmal rupture.

Cavernous Malformations

Definition

Cavernous malformations, also known as cavernomas, cavernous angiomas, or cavernous hemangiomas, are abnormal collections of dilated blood vessels that can be found throughout the central nervous system. These lesions do not contain normal brain parenchyma. They are low-flow, dynamic lesions and may therefore appear spontaneously and change in size over time.

There are two principal varieties of cavernous malformation: sporadic and familial. Familial lesions tend to appear at younger ages, more commonly present with multiple lesions, and carry an overall higher risk of hemorrhage [5, 7, 17]. The familial form appears to be inherited in an autosomal dominant manner with variable penetrance [5, 7, 17]. However, no clear guidelines currently exist regarding the screening of patients with strong family history of cavernous malformations, as is further discussed below.

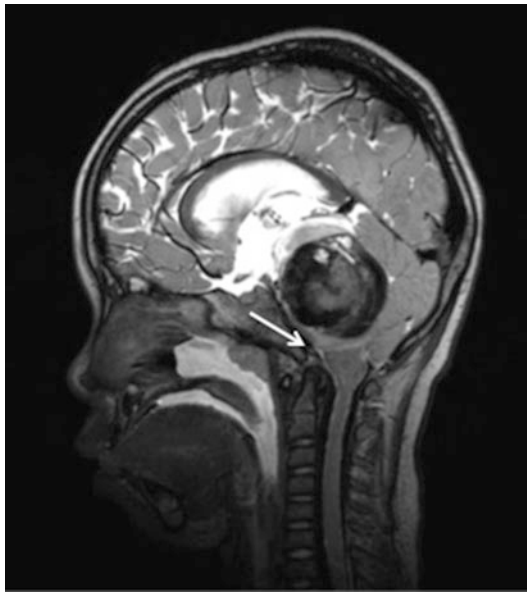


Fig. 23.2 MRI of a 5-year-old girl who presented comatose. The hypointensity is largely hemorrhagic and represents a large cavernous malformation of the pons (*arrow*). Surgery was performed to resect the lesion, and she regained near-normal neurologic status after rehabilitation

Epidemiology

Cavernous malformations have been estimated to be present in approximately 0.4–0.8 % of the population [7], and approximately 25 % of these lesions affect children [5, 7, 17]. No significant difference in prevalence between genders has been noted [7]. Several studies have commented on a bimodal distribution of ages at presentation with patients between 1–3 and 11–16 years having higher incidence of symptomatic lesions [7]. Rarely, however, are lesions clinically evident before 1 year of age [7]. Cranial irradiation has been noted in several studies to be a risk factor for development of cavernous malformations [7, 17]. The average time from radiation to detection of these lesions is approximately 9 years [14], and they appear more prone to hemorrhage than sporadic cavernous malformations (Fig. 23.2).

Clinical Presentation

Reports have indicated that up to 40 % of cavernous malformations are asymptomatic [17]. Since children are less likely to undergo neuroimaging, the reported proportions of lesions that are clinically silent may be underestimated, as many of them may go undetected. Only 14.2 % of childhood cavernous malformations are detected incidentally [7].

Seizure is the most common presenting symptom for patients with symptomatic cavernous malformations. Such seizures may be partial or generalized and are the presenting symptoms in up to 70 % of cases [5]. Other signs and symptoms of cavernous malformation are related to hemorrhage, including signs of increased intracranial pressure and acute onset neurological deficits [7, 14, 17]. Importantly, cavernous malformations in children are approximately two to three times more likely to present with hemorrhage than corresponding lesions in adults [7, 14, 21], and cavernomas found in children tend to be larger than those in adults [7].

Diagnosis

MRI is the most important diagnostic study for cavernous malformations. The sensitivity and specificity of MRI are superior to CT [7, 14, 17], and the findings of these lesions on MRI are so distinct as to be pathognomonic for cavernous malformation [7]. The classic MRI findings of cavernous malformations are a reticulated core of mixed signal intensity with a rim of decreased signal intensity on a T2-weighted series [23]. The sensitivity and specificity of CT are inferior to MRI for detecting cavernous malformations [23], but CT does readily detect acute hemorrhage and may lead to the acquisition of more correct or specific investigations [7].

Pathophysiology

Cavernous malformations are dilated vascular spaces lined by a single layer of endothelial cells [17, 23]. Typically, these spaces do not have smooth muscle or elastin [17]; histologically, cavernous malformations do not resemble capillaries, arteries, or veins [17, 23]. No normal intervening neural tissue is contained in these lesions

[7, 17, 21, 24]. Neural tissue surrounding cavernous malformations shows accumulation of hemosiderin-laden macrophages, reactive gliosis, and deposits of lead and calcium [17]. The mechanisms causing cavernous malformations are unclear, although some have suggested disrupted cerebral hemodynamics, due to the presence of developmental venous anomalies [25, 26].

When to Refer to a Neurosurgeon

The vast majority of patients with diagnosed cavernous malformations should be referred for neurosurgical evaluation. The largest question is whether these evaluations need to be made on an emergent basis. Clearly, patients with evidence of acute hemorrhage should be emergently referred to the care of a neurosurgeon. For clinically stable patients without evidence of hemorrhage, the referral is less urgent, but all symptomatic patients should have a neurosurgical consultation.

MRI Screening for Family Members in Familial Cavernous Malformations

As previously stated, there are no clear guidelines regarding whom to screen or when to screen in cases of strongly suspected or genetically confirmed familial cavernous malformations. It is well recognized that the familial form of the disease produces highly dynamic lesions, with de novo cavernoma formation a common event over the natural history of these patients [27, 28]. If a patient is screened, MRI is certainly the modality of choice; however, it is not clear that MRI screening of asymptomatic family members of those with confirmed or suspected familial cavernous malformations can improve outcomes.

Treatment

It is generally agreed that asymptomatic cavernous malformations should be treated conservatively and observed for clinical signs of hemorrhage and with serial imaging studies to assess for lesion progression [7, 14, 17]. This is particularly true for cavernomas located in eloquent cortex or in the brain stem or other locations difficult to access surgically [7].

For symptomatic cavernous malformations, the total surgical excision is the treatment of choice [7, 14, 17, 24]. Complete excision of the lesion eliminates the risk of bleeding from remnant lesion, which may occur in up to 25 % of subtotal excisions [7]. Results of surgical series have shown drastic improvement in seizure control of patients with seizures referable to the cavernous malformation [5, 7]. Early removal of cavernous malformations causing seizures can be curative [5, 7], and as a result, more patients are having early surgical excision of these cavernomas [7]. Surgery is also the recommended management strategy for cavernous malformations causing hemorrhage or worsening neurological deficits [7, 14].

Radiosurgery has been suggested as an alternative to surgery for cavernous malformations located in surgically inaccessible areas. The results obtained through radiosurgery have not consistently demonstrated a significant improvement over the natural history of these cavernous malformations [7, 14]; radiosurgery is not currently a recommended treatment strategy for pediatric cavernous malformations.

Prognosis and Outcome

The annual risk of hemorrhage from cavernous malformations inclusive of all age groups is approximately 1.6 % per year [29]. Cavernoma hemorrhage appears to produce less harm and presents more insidiously than hemorrhage from higher flow lesions such as arteriovenous malformations [17]. However, these lesions may rebleed and produce recurrent seizures or progressive neurologic deficits [7, 17]. Surgical treatment tends to produce good outcomes in children—preventing subsequent hemorrhage and curing or significantly reducing the frequency of seizures [7, 17]; the surgical treatment of brain stem lesions is less straightforward, as resection has a higher probability of temporary or permanent neurological deficits [30, 31].

Cerebral Venous Malformations (Venous Angiomas and Developmental Venous Anomalies)

Definition

Cerebral venous malformations, also referred to as venous angiomas or developmental venous anomalies, are benign congenital anomalies of the venous circulation. These lesions consist of an area of anomalous veins draining into a larger trunk. Depending on location, this trunk may drain into the superficial or deep cerebral venous system. These anomalous veins are intertwined with otherwise normal brain parenchyma, and there are no associated anomalous arterial vessels. Although they are developmental venous anomalies, these venous malformations provide venous drainage to normal brain tissue.

Epidemiology

Venous malformations constitute the most common form of intracerebral vascular lesion, with a population prevalence of approximately 3 % [25]. The risk of spontaneous intracranial hemorrhage from a venous angioma is very low, with annual hemorrhage rates of between 0.15 and 0.34 % per patient per year confirmed in several natural history studies [25].

Clinical Presentation and Diagnosis

Venous malformations are most commonly asymptomatic. They are found in association with cavernous malformations and may be discovered incidentally during the workup of symptoms related to the cavernous malformation. In rare cases, venous malformations will produce symptoms, most commonly seizures or hemorrhage. It is very important to bear in mind, however, that intracranial hemorrhage in patients with cerebral venous malformations is not typically due to the venous malformation; instead, it is more commonly due to a more pernicious, coexisting lesion, such as a cavernous malformation.

Venous malformations may be diagnosed incidentally on CT or MR imaging or on cerebral angiograms performed for other indications. They appear on contrast-enhanced CT as linear enhancing structures in the hemispheric white matter. On MRI, they are classically described as producing contrast-enhancing "stellate flow voids" that extend toward the ventricles. Angiography usually demonstrates a prominent vein passing through the white matter, ending in a "caput medusae" of draining veins.

When a patient presents with new neurologic symptoms and is found to have a venous malformation, alternate explanations for the symptoms should still be sought; venous angiomas should be regarded as incidental in patients with recurrent headache and certain other symptoms [32].

Pathophysiology

Cerebral venous malformations are thought to arise as aberrations in regional vein development, as brain parenchyma in the vicinity of these lesions tends to be poor in normal-appearing veins. The classic "caput medusae" appearance of venous angiomas on angiogram is due to the configuration of dilated medullary veins running through normal brain parenchyma and arranged around venous channels into which they drain. Again, venous angiomas function as a component of the cerebral arteriovenous network, draining the normal brain parenchyma incorporated by these lesions.

When to Refer to a Neurosurgeon

Many patients with cerebral venous malformation may already have been referred to a neurosurgeon at the time of diagnosis due to the association of these lesions with other vascular malformations, particularly cavernous malformations. Incidental discovery of an asymptomatic venous malformation does not warrant neurosurgical referral. However, decisions regarding treatment for venous malformations that are thought to be symptomatic should include a neurosurgeon.

Treatment

Given the low risk of spontaneous intracranial hemorrhage and their role in cerebral venous drainage, cerebral venous malformations are typically managed conservatively.

Radiation is not typically advised, as this modality carries a high risk of complications (in approximately 30 % of patients) and may not completely obliterate a venous malformation.

It is very important to recognize that these lesions drain normal areas of the brain. Therefore, excisional surgery eliminates venous drainage from a region of normal brain and may result in venous infarction and cerebral edema. For this reason, surgical excision is not typically pursued in asymptomatic cases.

Arteriovenous Malformations

Definition

An arteriovenous malformation (AVM) is a vascular malformation in which arterial circulation flows directly into the venous drainage system without an intervening capillary bed. The center of such a lesion, where there is a transition from the arterial to the venous system, is known as the nidus and contains no neural parenchyma. The fundamental danger of these lesions arises from the feeding of the high-flow, high-pressure arterial system into the low-pressure venous system; these configurations establish the potential for a pressure-flow mismatch that overcomes the strength of the vascular wall, resulting in vascular rupture and hemorrhage.

AVMs are the result of embryonic malformations that are not fully understood.

Epidemiology

Typically, AVMs present between the ages of 20 and 40 years; pediatric AVMs are rare. Indeed, one notable series of more than 15,000 pediatric cerebral angiograms found zero incidental aneurysms or AVMs [7]. Nevertheless, intracranial aneurysms and AVMs together represent the most common etiologies of intracranial hemorrhage in both children and adults. In adults presenting with intracranial hemorrhage, a ruptured aneurysm is approximately 6.5 times more likely than an AVM to account for the bleed. By contrast, more than 30 % of all AVMs bleed before age 20 years, whereas only approximately 1.5 % of intracranial aneurysms rupture before that age. *Consequently, overall, intracranial hemorrhage in a child is approximately four times more likely due to an AVM than a ruptured aneurysm* [7] (Fig. 23.3).

Presenting Clinical Features

Approximately 80 % of children who are symptomatic from intracranial arteriovenous malformations (AVMs) present with intraparenchymal, intraventricular, or subarachnoid hemorrhage. Hence, the classic presentation in children is a previously well child who suffers a sudden onset, severe headache. This is in contrast with the adult population, in which AVMs may have more varied presentations including symptoms suggestive of ischemia, headache, dementia, seizure, hemorrhage, or progressive neurologic deficits. Although less common, these presentations can be witnessed among children as well. AVMs are an uncommon but well-documented cause of chronic epilepsy in children [33].

Pathophysiology

AVMs are believed to form as a result of structural deficits in the embryologic arteriolar–capillary network that normally separates the intracranial arterial and venous circulations. Development of these capillary beds takes place in the period between 40 and 80 mm embryonic length. Most AVMs appear to develop prior to the end of this period, but further details as to the formation of these lesions are not well understood.

Because AVMs lack a high-resistance capillary bed separating the arterial from the venous side of the circulation, they tend to have low resistance and consequently high blood flow, with an associated tendency to undergo active

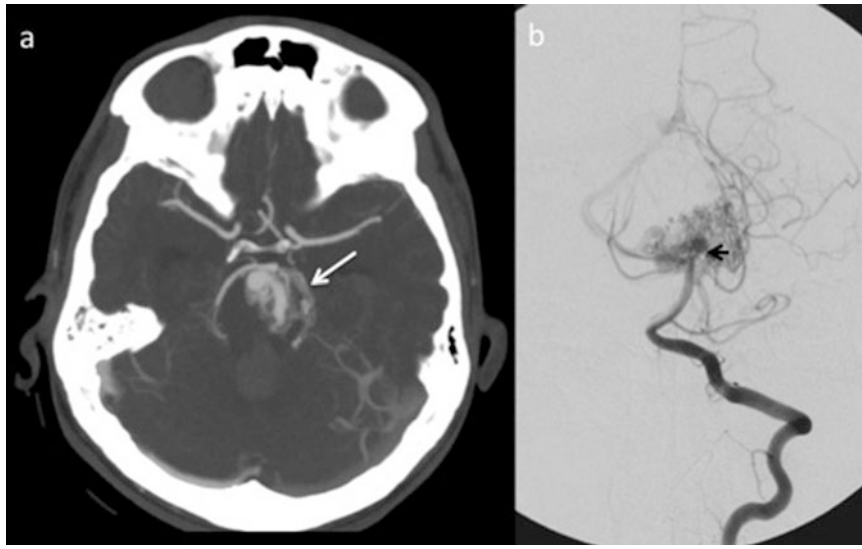


Fig. 23.3 (**a**) Sixteen-year-old male with a brain stem arteriovenous malformation (*arrow*) with multiple intranidal aneurysms (**b**, *arrowhead*). This was managed with a combination of embolization and ventriculoperitoneal shunt and will require further multimodal treatment with staged radiation and embolization treatments

remodeling (mediated, in part, by vascular endothelial growth factor, VEGF) and to increase in size and tortuosity over time.

Diagnosis and Imaging

Noncontrast head CT will reveal hematoma or calcification associated with an AVM, and contrast-enhanced CT or CT angiography can be used to study the abnormal vessels feeding and draining the lesion. MRI and MR angiography presently have a limited role in the evaluation of AVMs, particularly in the case of small lesions as the correspondingly small feeding and draining vessels associated with these lesions may be difficult or impossible to visualize using MR imaging, especially in the presence of hematoma. Conventional, selective angiography remains the definitive imaging modality for studying AVMs.

Natural History

Natural history studies report significant variability in the rupture rate of untreated AVMs [27], but this rate is typically estimated at approximately 2–4 % per year [28]; multiple studies suggest that the annual risk of hemorrhage is independent of age [27]. One well-known approach to approximating risk of AVM rupture based on natural history data maintains each year as carrying a constant and independent risk of hemorrhage, yielding the following formula for the risk of hemorrhage after *y* years:

$$\text{Risk of hemorrhage (after } y \text{ Years)} = 1 - (\text{annual probability of no hemorrhage})^{y} = 1 - (1 - \text{annual risk of hemorrhage})^{y}$$

According to this formula, for example, a 10-year-old patient with a 3 % annual AVM hemorrhage risk (hence a 97 % annual probability of no hemorrhage) and a remaining life expectancy of 62 years (based on demographic data that neglects the presence of the AVM) has a lifetime risk of hemorrhage of

$$1 - (0.97)^{62} = 85\,\%.$$

The principal factors known to increase the likelihood of future hemorrhage include prior hemorrhage, small AVM size, the presence of a single draining vein, drainage into a deep vein, and “diffuse” morphology of the AVM nidus [34].

Each AVM hemorrhage event is associated with approximately 10 % risk of death and 30–50 % risk of neurologic deficit [35].

When to Refer to a Neurosurgeon

Given the high lifetime risk of AVM rupture for children, neurosurgical referral is recommended for all children found to have arteriovenous malformations. In cases of acute hemorrhage, emergent neurosurgical referral is imperative, as AVM rupture carries significant probability of morbidity and mortality, as discussed above.

Treatment

The definitive treatment for cerebral arteriovenous malformations is complete excision.

Because of the high lifetime risk of hemorrhage and associated morbidity and mortality in children with untreated AVMs, conservative management is rarely appropriate. Approximately 80 % of patients with AVMs will be found to have hemorrhaged at the time of diagnosis; these patients will almost certainly require surgery [7]. Among patients presenting with hemorrhage, the size and location of the hematoma and the clinical status of the patient will determine whether immediate surgery is required or whether definitive intervention may be delayed. In the remaining approximately 20 % of patients who present for reasons other than hemorrhage, intervention is less urgent but will likely require eventual surgical intervention.

Preoperative catheter-directed angiography is often indicated, both for surgical planning and to facilitate partial (or occasionally complete) embolization of the lesion prior to resection.

The role of radiosurgery in the treatment of arteriovenous malformations is still being defined, but radiosurgery may be useful in the management of deep AVMs whose locations preclude surgical intervention. There is evidence to suggest that radiosurgery can completely obliterate approximately 80 % of lesions smaller than 3 cc in volume [36], but the incidence of new neurologic deficits is high [7]. Furthermore, the time to obliteration following radiosurgery is prolonged, and unfortunately, the risk of AVM rupture does not seem to change until the AVM has been completely obliterated. As a result, radiosurgery is certainly not an option in the setting of acute rupture.

Prognosis and Outcome

The overall probability of death due to rupture of an arteriovenous malformation is approximately 12 % [7, 31]. Approximately 35 % of children present after AVM rupture either with normal level of consciousness or drowsy but without significant neurologic deficit; approximately 20 % are moribund on presentation [7, 31]. In one series of 160 children with ruptured AVMs, 82 % (131) of patients underwent surgery. Of the patients who underwent surgery, complete resection was achieved in 67 % (88); 55 % returned to "normal performance," whereas 24 % retained permanent neurologic deficits postoperatively. In this series, which included data from the pre-CT era, overall mortality was 21 %; following the advent of CT, mortality after AVM rupture declined to 12 %. In the 18 % of patients in this series who did not undergo surgery, resection was deferred either due to moribund neurologic status at presentation or to good neurologic status in the setting of an AVM located in eloquent cortex [7, 31].

It has been reported that 59 % of pediatric patients with seizures referable to an AVM become seizure free and are able to discontinue antiepileptic medications following surgery [7, 31] and that up to 70 % are seizure free or "nearly" seizure free when AVM resection is extended to include surrounding epileptogenic tissue [33, 38].

Ischemic Stroke

Definition and Classification

Ischemic stroke can be classified according to the anatomic origin of the ischemia as either arterial or venous. Arterial ischemic stroke refers to the direct occlusion of a cerebral artery, as, for example, from atheroembolism resulting in one of the major classic stroke syndromes (such as middle cerebral artery occlusion). Venous infarction, for example, as a result of cerebral venous sinus thrombosis (CVST), arises when an occlusion within the venous system prevents outflow of venous blood, producing congestion and increased hydrostatic pressure within the vascular system

and the brain as a whole. In severe cases, the pathologically raised tissue hydrostatic pressure can exceed arterial pressure, preventing arterial circulation and producing an ischemic stroke.

Epidemiology

Estimates suggest that arterial ischemic stroke has an incidence of between 2 and 13 per 100,000 people per year, with males more commonly affected [5, 7]. However, the individual risk for stroke varies considerably with etiology. For example, by age 20, the estimated prevalence of ischemic stroke in children with sickle cell disease is 11 % [17].

Stroke in childhood is undoubtedly a rare phenomenon, but partly as a result of its rarity, it may also be under-recognized [7, 21]. Of note, the majority of epidemiologic studies of pediatric stroke are retrospective and will therefore overlook such unrecognized cases by design [14].

Hospitalizations for childhood arterial ischemic stroke have been rising over the past decade [17, 23] for several reasons, including increased use of MR imaging for stroke detection, increased awareness of pediatric stroke and its manifestations, and the increasing prevalence of stroke risk factors, especially traditional cardiovascular risk factors such as hypertension, obesity, diabetes, and tobacco use among children [17, 24].

For cerebral venous sinus thrombosis (CVST), approximately 40 % of pediatric cases are among neonates, with an estimated incidence of 2.6 per 100,000 [25]. The overall childhood incidence is less, between 0.4 and 0.7 cases per 100,000 person-years [25].

Similar to arterial ischemic stroke, the incidence estimates for CVST are believed to underestimate the true prevalence [25] (Fig. 23.4).

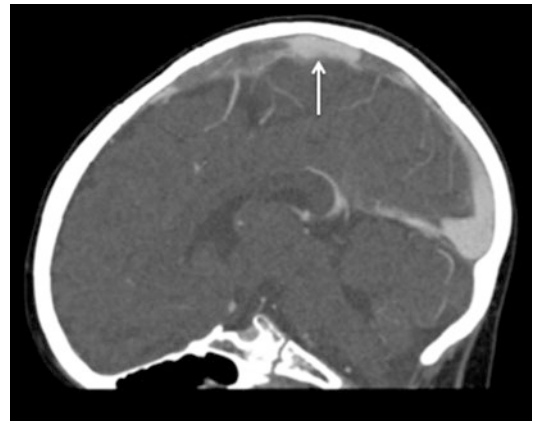


Fig. 23.4 Four-year-old male with acute lymphocytic leukemia who presented with headache, lethargy, and emesis. A large non-occlusive superior sagittal sinus thrombosis (*arrow*) related to hypercoagulability from therapy. Six months of oral anticoagulation resulted in almost complete resolution

Clinical Presentation

Diagnosing pediatric stroke remains a clinical challenge due to the manifestations that may not resemble stereotypical stroke presentations in adults. Therefore, stroke is often initially misdiagnosed or undiagnosed in children [26]. Maintaining a high index of suspicion, even in the face of nonspecific presenting signs, is crucial to making a timely diagnosis, particularly in children at risk of stroke due to coexisting, predisposing conditions.

The full range of possible presenting signs of ischemic stroke in children is diverse, and many such signs are not specific to stroke. The most common presenting signs do resemble those seen in adults: approximately 70–80 % of children present with hemiparesis, and approximately 60 % present with dysphasia [27]. Non-focal symptoms are also common in children and include headache, vomiting, and decreased level of arousal [27]. Headaches are seen in approximately one-third of cases and typically present around the time of stroke [27].

Seizures and behavioral disturbances are also potential presenting features of pediatric stroke [5, 27] and may mislead clinicians given their relatively broad differential diagnosis. Seizures are seen in over a third of cases, most commonly in patients <1 year [5, 27]. Behavioral alterations are noted in approximately 10 % of cases [27].

Cerebral venous sinus thrombosis (CVST) typically presents with subtle, nonspecific signs and symptoms, some of which may also correspond to

conditions that predispose to CVST formation, including infection and dehydration [25]. Among neonates, CVST often presents with seizures [25, 29]. In older children, the presentation may be more variable and may include focal neurologic deficits and signs of increased intracranial pressure including headache, vomiting, and decreased level of consciousness [25, 29]. Symptom onset in cases of CVST is typically more insidious, progressing over hours to days, whereas onset of arterial ischemic stroke is typically acute or hyperacute [29].

Diagnosis

Given the variable clinical presentation, neuroimaging is of special importance in the diagnosis in pediatric stroke. MRI is the most important imaging modality for rapid stroke detection. Diffusion-weighted images (DWI) and perfusion-weighted sequences are highly sensitive and specific for detecting regions of ischemia [5, 7, 28]. High-quality images require that the patient remain still for a prolonged period in the MR scanner, and it may be challenging to obtain in younger children without sedation [5, 7]. CT is far less sensitive to early ischemia but remains an appropriate first imaging modality for patients with an acute presentation [29], particularly given its sensitivity for acute hemorrhage. In general, however, CT is a poor choice to diagnose ischemic stroke, missing up to 84 % of cases in one study [31]. If there is suspicion for CVST, MR or CT venograms should also be obtained [7, 25].

Pathophysiology

A detailed discussion of the differential diagnosis and pathophysiology of pediatric stroke syndromes is beyond the scope of this chapter, and these subjects have been reviewed extensively in recent literature [39–41]. One arteriopathy does merit special attention, however, as it often requires surgical management: moyamoya.

Moyamoya syndrome is characterized by stenosis of the arteries of the circle of Willis, most commonly the distal internal carotid artery and proximal middle carotid artery. Around these stenosed arteries, extensive collaterals form that classically yield a "puff of smoke" appearance on standard digital subtraction angiography [5, 14].

A distinction is made between "moyamoya disease" and "moyamoya syndrome [42]." The former is idiopathic but influenced by genetics and is seen more frequently in Asian populations and has clear associations with certain genetic loci [5, 14, 29]; in contradistinction with "moyamoya syndrome," it is not associated with any other known risk factors for moyamoya vasculopathy. Moyamoya syndrome refers to cases in which the vasculopathy is observed in the setting of established risk factors, such as sickle cell disease, trisomy 21, neurofibromatosis type I, or cranial irradiation [5, 14].

Treatment of Pediatric Ischemic Stroke

Treatment of ischemic stroke in children is an ongoing source of clinical investigation. At the time this chapter is being written, expert guidelines have been published by the American College of Chest Physicians (ACCP), the Royal College of Physicians (RCP), and the American Heart Association (AHA) [30, 37, 40] in regard to the management of ischemic stroke in adults. However, none of these guideline documents systematically incorporates evidence from studies conducted in children; rather, each is based on expert opinion and data extrapolated from adult studies [7, 14]. Importantly, thrombolytic therapy, a pillar of contemporary management of ischemic stroke, is at present only approved for use in patients age 18 years or older [4]; at the time of this writing, a randomized clinical trial to determine the safety, efficacy, and dosing of thrombolytic therapy for acute arterial ischemic stroke in pediatric patients is ongoing [3, 4]. Additionally, consensus opinion on endovascular interventional options for the treatment of acute ischemic stroke, including clot retrieval procedures, is undergoing a paradigm shift in the wake of promising outcomes from several major, multicenter clinical trials [43].

Surgical management for pediatric stroke is typically reserved for cases of malignant edema

associated with large areas of infarction. Ischemic strokes affecting large vascular territories can lead to life-threatening cerebral edema, resulting in increased intracranial pressure; in such cases, craniectomy can be the only option available to manage the ensuing malignant intracranial hypertension, which would otherwise cause brain stem herniation [7, 39]. In adults, studies have shown hemicraniectomy to be beneficial, preventing mortality in the acute period and reducing overall morbidity [39, 41]. A randomized study in children demonstrating benefit is lacking, but several small studies have retrospectively examined surgical outcomes after hemicraniectomy in pediatric patients and have suggested that decompressive hemicraniectomy may be lifesaving procedure even for patients presenting in coma [39, 44].

Moyamoya vasculopathy represents a special case of a stroke syndrome amenable to surgical management on a nonemergent basis. This condition has been reviewed extensively in the neurologic and neurosurgical literature, and a family of operations have been developed, all designed to promote formation of robust collateral circulation around the dysfunctional moyamoya vessels to revascularize the affected cerebrovascular territories and prevent future ischemic stroke [42, 45].

When to Refer to a Neurosurgeon

Ischemic stroke, with a few exceptions, is not treated surgically. Cases of suspected pediatric stroke should immediately be referred for emergent evaluation, preferably at a designated stroke center with expertise in pediatric neurology. Surgical interventions, such as hemicraniectomy for large territorial infarction or revascularization procedures for moyamoya vasculopathy or biopsies for definitive diagnosis or diagnostic exclusion, are typically planned jointly by a vascular neurologist and a vascular neurosurgeon.

Prognosis and Outcome

Historically, it has been widely believed that ischemic strokes are tolerated better by children than by adults, ostensibly because the plasticity of the young brain allows it to compensate under circumstances that would almost certainly cause profound, long-term neurologic deficits in adults with comparable lesions; the belief has been that functional outcomes are overall better in children than in adults [28]. More recent data on outcomes of pediatric stroke have called this philosophy into question. Persistent neurological deficits are present in more than half of children following ischemic stroke [7, 46]. Younger patients may, in fact, be at greater risk for long-term sequelae of stroke, with greater cognitive and behavioral impairment noted among younger stroke patients [7]. The most common long-term deficits include weakness (particularly hemiparesis) and gait ataxia, and pediatric stroke often gives rise to seizure disorders requiring long-term medical management [7, 28].

Stroke recurrence is also common, although the risk of recurrence depends on stroke etiology. While the overall risk of recurrence ranges from 10 to 25 %, recurrence risk may be as high as 90 % in patients with sickle cell disease [7] and above average for patients with untreated moyamoya or other vasculopathies [14]. Overall mortality from stroke is 3 % in the pediatric population, which is considerably lower than overall mortality from stroke in the adult population, which rises above 50 % at 5 years in some population studies [14, 47]. Mortality increases with recurrent strokes and may be as high as 15 % following recurrent stroke [14, 48, 49].

Vein of Galen Malformations

Definition and Classification

Vein of Galen malformations, or vein of Galen aneurysmal malformations, are rare congenital arteriovenous fistulas arising during the fetal period [50]. These malformations result from abnormal communications between the primitive choroidal arteries and midline venous structures [51]. Vein of Galen malformations are dangerous lesions that carry significant morbidity and mortality despite advancements in treatment and management.

Vein of Galen malformations are commonly classified as either mural or choroidal [50, 52] based on specific patterns of feeding and draining vascular networks.

Epidemiology

Vein of Galen malformations are rare, comprising less than 1 % of all intracranial arteriovenous malformations [53, 54]; in the pediatric population, however, vein of Galen malformations are more common, constituting up to 30 % of pediatric vascular malformations [54]. Of note, vein of Galen malformations are frequently detectable on fetal ultrasound screening. As a result, they are the most common cerebral arteriovenous malformation detected in the prenatal period [53] (Fig. 23.5).

Clinical Presentation

The clinical presentation of vein of Galen malformations is somewhat variable and depends in part on the size and configuration of each particular malformation and on the age at which symptoms become evident. In the contemporary era, many of these malformations are detected prenatally on routine screening ultrasound examinations; smaller malformations may only become clinically evident later in infancy or in early childhood, however.

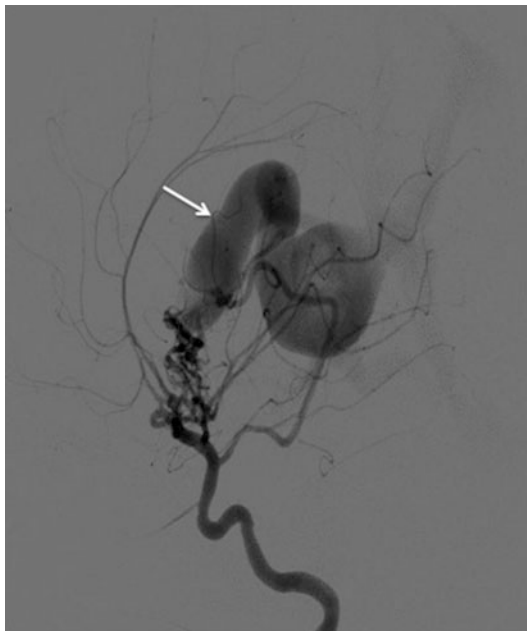


Fig. 23.5 Three-month-old female with macrocephaly. This image demonstrates a lateral view of a carotid artery injection showing massive venous filing during the arterial phase of a vein of Galen malformation (*arrow*)

The abnormal hemodynamic state established by a vein of Galen malformation profoundly affects both cardiovascular and neurologic development. The arteriovenous communication in vein of Galen malformations produces a high-flow, low-resistance system; in extreme cases, the total flow recruited (and thereby essentially stolen from the systemic circulation) can be sufficient to cause high-output congestive heart failure [50, 54]. In such severe cases, signs of cardiac damage can be seen in utero on sonographic evaluation [54]: when present, ultrasound findings of cardiomegaly, tricuspid insufficiency, pleural or pericardial effusion, and edema or ascites portend a very poor prognosis [54]. High flow into the venous system can cause venous congestion and edema, resulting in cerebral atrophy. Diversion of blood flow away from the developing venous sinuses may also impede normal flow-dependent development of the venous system of the developing brain. If not detected in utero, such cases almost always come to clinical attention within the first few days of life [50].

Cases discovered in infancy tend to present with enlarged head circumference and hydrocephalus [50, 55]. Vein of Galen malformations may cause obstructive hydrocephalus by directly occluding the cerebral aqueduct; communicating hydrocephalus appears to be more common, however, and results from diminished capacity for cerebrospinal fluid resorption due to venous hypertension [50, 55].

Diagnosis

Many cases of vein of Galen malformation are diagnosed in utero during the third trimester of pregnancy using Doppler ultrasonography [53, 54]. Doppler ultrasound classically demonstrates a mixed arteriovenous flow within a midline structure located in the posterior third ventricle, and color-enhanced visualization techniques produce

a characteristic pattern. To confirm the diagnosis, a fetal MRI should be obtained [54].

For neonates with patent fontanelles, transfontanelle ultrasound can be used to demonstrate the presence of a vascular abnormality. However, MRI should again be obtained in order to confirm the diagnosis [50] in these neonates and in all older children. Conventional digital subtraction angiography remains the gold standard for diagnosis and evaluation of vessel anatomy. However, it should be deferred until required as part of a therapeutic endovascular procedure, as MRA or CTA can noninvasively provide sufficient detail for diagnosis [50].

Pathophysiology

The embryologic dysfunction that results in anomalous fistula formation between the primitive choroidal arteries and midline venous structures is beyond the scope of this chapter; the subject has been reviewed by a number of authors, including Raybaud and colleagues [56].

When to Refer to a Neurosurgeon

Although surgery was once considered essential for definitive treatment of vein of Galen malformations, advances in endovascular techniques have essentially relegated microsurgical approaches to a second-line treatment option. In the modern era, all patients with vein of Galen malformations should be referred to a center where endovascular and microneurosurgical options can be assessed in collaborative fashion. The urgency of these referrals is determined by the clinical status of the patient. For a neonate exhibiting signs of congestive heart failure, the referral should be made emergently. In cases of older children with stable symptoms, the matter is less urgent.

Treatment

Surgery was historically the intervention of choice for vein of Galen malformations, but the prognosis for patients with these malformations was dismal, even after technically sound surgical management. The advent of endovascular techniques, which may be used to establish a more natural, physiologic separation between arterial and venous circulations, has improved outcomes and established the endovascular route as standard of care for the management of vein of Galen malformations [50, 55, 57].

The timing of endovascular intervention depends on a number of factors, including age at presentation, clinical status, and the angiographic characteristics of the malformation [50]. For neonates with very severe symptoms, such as cardiogenic shock, multisystem organ failure, or permanent brain damage, endovascular treatment may be considered futile due to the poor overall prognosis. Neonates presenting with more moderate symptoms, but still unable to tolerate temporizing medical management, should be strongly considered for urgent endovascular intervention. Finally, for neonates that can safely be managed medically, endovascular treatment should be deferred until the patient is 4 or 5 months old to allow for cerebral and arterial maturation. Older patients should receive endovascular treatment at the time of diagnosis to prevent clinical progression and deterioration.

Prognosis and Outcome

Early case series of vein of Galen malformations were based on microsurgical outcomes and reported dismal prognoses. Mortality in these cases approached 100 % for neonatal patients. In the modern era, prognosis for neonatal patients remains poor, with mortality of approximately 52 % even in neonates who undergo endovascular intervention [58]. The prognosis is worse for patients who exhibit signs of cardiac dysfunction or cerebral damage in utero, for whom mortality approaches 80 % [50, 54, 59]. In the largest reported series of patients treated endovascularly, overall mortality was 10.6 % [58]. While neonatal mortality remained high, mortality was 7.2 % in infants and 0 % in children; 74 % of surviving patients remained neurologically intact and cognitively normal, 15.6 % exhibited moderate mental retardation, and 10.4 % were severely mentally retarded [58].

Careful prenatal counseling should therefore be offered after a vein of Galen malformation is discovered on fetal ultrasound; questions regarding termination of pregnancy in such cases often arise. The associated ethical and other implications are outside of the scope of this chapter, but counseling as to treatment options and prognosis should be offered.

Spinal Vascular Malformations

Definitions and Classification

Although even less common than the corresponding vascular malformations of the brain, arteriovenous malformations, arteriovenous fistulas, cavernous malformations, and telangiectasias may also occur in the spinal cord. These lesions are pathologically similar to the corresponding brain lesions described in a prior section; their typical clinical presentations, however, differ as a function of their location in the spinal cord.

Arteriovenous malformations are differentiated from arteriovenous fistulas by the presence of a nidus, an enlarged area of connection between arterial and venous circulations. Solitary vascular malformations containing a nidus are referred to as arteriovenous malformations, whereas malformations lacking a nidus are referred to as arteriovenous fistulas. Some lesions may contain both nidal and fistulous components, making them difficult to classify.

Arteriovenous malformations can be further classified based on the location of the nidus, which may lie either within or at the surface of the spinal cord. Although less important for initial management, the nidal location has important neurosurgical treatment implications.

Fistulous lesions are classified as "single-hole" fistulas or multiple fistulas; multiple fistulas account for nearly half of pediatric spinal cord arteriovenous fistulas and are nearly twice as common in pediatric patients as they are in adults [26]. Arteriovenous fistulas may also be classified according to flow rate through the lesion, as high flow or low flow.

Epidemiology

Spinal vascular malformations are overall rare and account for approximately one tenth of central nervous system vascular malformations. Patients typically present between the ages of 10 and 30 years.

Arteriovenous fistulas account for approximately 20 % of spinal vascular malformations and are more common in children and in patients with Osler-Weber-Rendu syndrome.

Spinal cavernous malformations are especially rare and account for only 1.7 % of pediatric intramedullary spinal lesions.

Presenting Clinical Features

Spinal cord arteriovenous malformations in children tend to present more acutely than comparable lesions in adults, with acute spinal compromise due to spinal subarachnoid hemorrhage and hematomyelia. Presentation of these lesions will vary depending on the level and site of injury within the spinal cord but will likely include lower extremity motor and sensory deficits, with or without proprioceptive deficits and bowel or bladder dysfunction. Hemorrhage also typically produces a sudden onset of severe upper back or interscapular pain with no nuchal rigidity.

Genetics and Associated Clinical Syndromes

Several syndromes have known associations with spinal vascular malformations, including some with both cutaneous and vascular manifestations: Osler-Weber-Rendu, Klippel-Trénaunay-Weber, Parkes Weber, and Cobb syndromes, as well as neurofibromatosis type 1. Cobb syndrome involves the skin, vertebrae, and spinal cord of the affected metameres, and arteriovenous malformations are found in a metameric distribution.

Diagnosis and Evaluation

MRI has nearly 100 % sensitivity for detecting spinal cord arteriovenous malformations and is the imaging modality of choice for initial evaluation and follow-up of these lesions. On MRI, spinal arteriovenous malformations appear as "signal voids" within or on the surface of the spinal cord, corresponding to dilated arteries or veins. Other features of these lesions are also detected on MRI, including hematomyelia and spinal cord edema.

Decisions with regard to treatment and the feasibility of surgical or endovascular intervention are frequently based on spinal angiography, which is considered the definitive imaging modality for evaluating spinal cord vascular malformations.

When to Refer to a Neurosurgeon

Vascular malformations of the spine are concerning lesions that typically require neurosurgical care. Any patient with such a lesion should be promptly referred to a neurosurgeon for evaluation. In particular, patients with presentations suggestive of acute spinal cord compromise require an emergent neurosurgical referral.

Treatment, Prognosis, and Long-Term Outcome

Each hemorrhage from a ruptured spinal vascular malformation is associated with a 10–20 % risk of death, as well as a very high risk of severe neurologic deficit below the level of the hemorrhage. Untreated spinal arteriovenous malformations therefore carry poor prognosis, particularly in children.

Treatment of spinal arteriovenous malformations is complex and depends on the specific classification of the lesion. However, in general, endovascular embolization has become an important modality in the treatment of these lesions and is almost always indicated in children, even in those with associated neurologic deficits at the time of presentation. Complete obliteration of arteriovenous fistulas is often feasible, and embolization can significantly decrease or eliminate the risk of subsequent hemorrhage even if the vascular anatomy prohibits complete obliteration [26, 60, 61].

In the case of spinal cavernous malformations, surgical management is rarely recommended for lesions that have not bled. Similar to the corresponding intracranial lesions, spinal cavernous malformations have an unknown risk of bleeding, and given the dangers of operating around or within the spinal cord, conservative management is typically the first step. For patients with documented bleeding from a spinal cavernous malformation, however, surgical excision should be strongly considered. Surgery can eliminate the risk of rebleeding, stabilize neurologic function, and potentially reverse deficits attributable to hematoma or mass effect from the lesion itself.

Key Points

1. Pediatric vascular lesions include several dangerous conditions (notably aneurysms, arteriovenous malformations, and cavernous malformations) that may present acutely, with rupture resulting in intraparenchymal, intraventricular, or subarachnoid hemorrhage. Such conditions have the potential to cause significant morbidity and mortality.
2. Seizure, altered level of consciousness, or acute onset of a focal neurologic deficit heralding intracranial hemorrhage is frequently the initial presentation for neurovascular lesions, and patients presenting in this manner require emergent referral for neurosurgical evaluation and intensive-care-unit-level care. Ultimately, many such patients are likely to require surgical or endovascular interventions to definitively treat the symptomatic lesions.
3. Although certain lesions (such as some cavernous malformations and many venous malformations) may have more benign natural histories, we recommend that almost all patients with diagnosed vascular abnormalities be referred to a neurosurgeon who can provide input on diagnostic and therapeutic options and appropriate follow-up.

Pediatrician's Perspective

There are two scenarios in which primary care pediatricians will encounter a vascular malformation of the brain or spine in one of their patients. The first scenario is upon receiving the report of an incidental vascular malformation after an MRI scan had been obtained for headaches, or concussion, or any other unrelated indication. This chapter should be able to guide you to counsel a family when reviewing the report, as to the urgency of an evaluation and some basic appreciation of the natural history for the suspected lesion.

The second scenario is the emergent phone call during which a parent informs you of a sudden change in mental status, with headache, nausea, and subsequent unresponsiveness. These circumstances obvious dictate management and transfer to a tertiary level care hospital with pediatric neurosurgical care and intensive-care-unit capabilities. For a new hemorrhage in a child, an arteriovenous malformation must be the first thing considered and will be managed as a life-threatening situation by the emergency response, emergency room physicians, and pediatric neurosurgical consultation.

Close communication with the pediatric neurosurgeon in the acute and subacute period will be important to discuss recovery and rehabilitation of the child and the need for future surveillance, prophylaxis, or intervention for any of the wide range of vascular etiologies discussed above.

References

1. McCormick MF. Pathology of vascular malformations. In: Wilson CB, Stein BM, editors. Intracranial arteriovenous malformations. Baltimore: Williams and Wilkins; 1984. p. 44–63.
2. McCormick WF. Pathology and pathogenesis of intracranial saccular aneurysms. Semin Neurol. 1984;4:13.
3. Gemmete JJ, Toma AK, Robertson F, Brew S. Pediatric cerebral aneurysms. Neuroimaging Clin N Am. 2013;23:9.
4. Garg K, Singh PK, Sharma BS, et al. Pediatric intracranial aneurysms—our experience and review of literature. Childs Nerv Syst. 2013;30:11.
5. Ozgur BM, Khoo LT, Levy ML. Intracerebral aneurysms. In: Albright AL, Pollack IF, Adelson PD, editors. Principles and practice of pediatric neurosurgery. New York: Thieme; 2007.
6. Housepian EM, Pool JL. Systematic analysis of intracranial aneurysms from the autopsy file of the Presbyterian Hospital 1914–1956. J Neuropathol Exp Neurol. 1958;17:409–29.
7. Humphreys RP. Arteriovenous malformations. In: Albright AL, Pollack IF, Adelson PD, editors. Principles and practice of pediatric neurosurgery. New York: Thieme; 2007.
8. Choux M, Lena G, Genitori L. Intracranial aneurysms in children. In: Raimondi AJ, Choux M, Rocco CD, editors. Cerebrovascular diseases in children. New York: Springer; 1992.
9. Hourihan MD, Gates PC, McAllister VL. Subarachnoid hemorrhage in childhood and adolescence. J Neurosurg. 1984;60:1163–6.
10. Ito M, Yoshihara M, Ishii M, Wachi A, Sato K. Cerebral aneurysms in children. Brain Dev. 1992;14:263–8.
11. Ostergaard JR, Voldby B. Intracranial arterial aneurysms in children and adolescents. J Neurosurg. 1983;58:832–7.
12. Wakabayashi T, Fujita S, Ohbora Y, Suyama T, Tamaki N, Matsumoto S. Polycystic kidney disease and intracranial aneurysms. Early angiographic diagnosis and early operation for the unruptured aneurysm. J Neurosurg. 1983;58:488–91.
13. Tyler HR, Clark DB. Neurologic complications in patients with coarctation of aorta. Neurology. 1958;8:712–8.
14. Malfait F, Wenstrup R, Paepe AD. Ehlers-Danlos syndrome, classic type. In: Pagon R, Adam M, Ardinger H, editors. GeneReviews. Seattle: University of Washington; 2011.
15. Stehbens WE, Delahunt B, Hilless AD. Early berry aneurysm formation in Marfan's syndrome. Surg Neurol. 1989;31:200–2.
16. Stehbens WE. Aneurysms and anatomical variation of cerebral arteries. Arch Pathol. 1963;75:45–64.
17. Altali K, Arruza L, López-Ibor L, Aleo E. Effective coil embolization of intracavernous carotid artery pseudoaneurysm with parental artery preservation following severe head trauma in a pediatric patient. Childs Nerv Syst. 2014;30:4.
18. Karsner HT. Acute inflammations of arteries. Springfield, IL: Charles C. Thomas; 1947.
19. Sahs AL, Perret G, Locksley HB, Nishioka H, Skultety FM. Preliminary remarks on subarachnoid hemorrhage. (Intracranial aneurysms and subarachnoid hemorrhage: a cooperative study). J Neurosurg. 1966;24:782–8.
20. ter Berg HW, Dippel DW, Limburg M, Schievink WI, van Gijn J. Familial intracranial aneurysms. A review. Stroke. 1992;23:1024–30.
21. Roach ES, Riela AR. Pediatric cerebrovascular disorders. Mount Kisco, NY: Futura Publishing; 1988.
22. Lasjaunias PL, Campi A, Rodesch G, Alvarez H, Kanaan I, Taylor W. Aneurysmal disease in children.

Review of 20 cases with intracranial arterial localisations. Interv Neuroradiol. 1997;3:215–29.
23. Wiebers DO, International Study of Unruptured Intracranial Aneurysms Investigators. Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment. Lancet. 2003;362:103–10.
24. Bederson JB, Connolly ES, Batjer HH, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage (AHA/ASA guideline: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association). Stroke. 2009;40:30.
25. Scott RM, Kamaly-Asl ID. Cavernous and venous malformations. In: Albright AL, Pollack IF, Adelson PD, editors. Principles and practice of pediatric neurosurgery. New York: Thieme; 2007.
26. Niimi Y, Berenstein A, Song JK. Spinal vascular malformations. In: Albright AL, Pollack IF, Adelson PD, editors. Principles and practice of pediatric neurosurgery. New York: Thieme; 2007.
27. Kondziolka D, Lunsford LD. Management of cerebrovascular malformations: arteriovenous malformations, cavernous malformations, and venous malformations. In: Albright AL, Pollack IF, Adelson PD, editors. Principles and practice of pediatric neurosurgery. New York: Thieme; 2007.
28. Greenberg MS. Handbook of neurosurgery. 6th ed. New York: Thieme; 2006.
29. Noonan FP, Webber LJ, De Fabo EC, Hoffman HA, Bendich A, Mathews-Roth M. Dietary beta-carotene and ultraviolet-induced immunosuppression. Clin Exp Immunol. 1996;103:54–60.
30. Gross BA, Batjer HH, Awad IA, Bendok BR, Du R. Brainstem cavernous malformations: 1390 surgical cases from the literature. World Neurosurg. 2013;80:5.
31. Humphreys RP, Hoffman HJ, Drake JM, Rutka JT. Choices in the 1990s for the management of pediatric cerebral arteriovenous malformations. Pediatr Neurosurg. 1996;25:277–85.
32. Rigamonti D, Spetzler RF, Medina M, Rigamonti K, Geckle DS, Pappas C. Cerebral venous malformations. J Neurosurg. 1990;73:560–4.
33. Yeh HS, Kashiwagi S, Tew Jr JM, Berger TS. Surgical management of epilepsy associated with cerebral arteriovenous malformations. J Neurosurg. 1990;72:216–23.
34. Pollock BE, Flickinger JC, Lunsford LD, Bissonette DJ, Kondziolka D. Factors that predict the bleeding risk of cerebral arteriovenous malformations. Stroke. 1996;27:1–6.
35. Hartmann A, Mast H, Mohr JP, et al. Morbidity of intracranial hemorrhage in patients with cerebral arteriovenous malformation. Stroke. 1998;29:931–4.
36. Levy EI, Niranjan A, Thompson TP, et al. Radiosurgery for childhood intracranial arteriovenous malformations. Neurosurgery. 2000;47:834–41. discussion 41–2.
37. Spetzler RF, Martin NA. A proposed grading system for arteriovenous malformations. J Neurosurg. 1986;65:476–83.
38. Leblanc R, Feindel W, Ethier R. Epilepsy from cerebral arteriovenous malformations. Can J Neurol Sci. 1983;10:91–5.
39. Lyle CA, Bernard TJ, Goldenberg NA. Childhood arterial ischemic stroke: a review of etiologies, antithrombotic treatments, prognostic factors, and priorities for future research. Semin Thromb Hemost. 2011;37:786–93.
40. Cárdenas JF, Rho JM, Kirton A. Pediatric stroke. Childs Nerv Syst. 2011;27:16.
41. Numis AL, Fox CK. Arterial ischemic stroke in children: risk factors and etiologies. Curr Neurol Neurosci Rep. 2014;14:422.
42. Scott RM, Smith ER. Moyamoya disease and moyamoya syndrome. N Engl J Med. 2009;360:1226–37.
43. Furlan AJ. Endovascular therapy for stroke—it's about time. N Engl J Med. 2015;372:2347–9.
44. Rooney CM, Kaye EM, Scott RM, Klucznik RP, Rosman NP. Modified encephaloduroarteriosynangiosis as a surgical treatment of childhood moyamoya disease: report of five cases. J Child Neurol. 1991;6:24–31.
45. Smith ER. Ischemic stroke in the pediatric population. In: Albright AL, Pollack IF, Adelson PD, editors. Principles and practice of pediatric neurosurgery. New York: Thieme; 2007.
46. Outwater EK, Platenberg RC, Wolpert SM. Moyamoya disease in Down syndrome. AJNR Am J Neuroradiol. 1989;10:S23–4.
47. Hu P, Sun J, Jin Y, Shi X, Yang X. Conventional computed tomography and axial magnetic resonance T2-weighted imaging of horizontal segment of middle cerebral artery in moyamoya disease or syndrome in adult patients. J Stroke Cerebrovasc Dis. 2015;24:2555–60.
48. Phi JH, Wang KC, Lee JY, Kim SK. Moyamoya syndrome: a window of moyamoya disease. J Korean Neurosurg Soc. 2015;57:408–14.
49. Koton S, Schneider AL, Rosamond WD, et al. Stroke incidence and mortality trends in US communities, 1987 to 2011. JAMA. 2014;312:259–68.
50. Lo Presti A, Weil AG, Fallah A, Peterson EC, Niazi TN, Bhatia S. Treatment of a cerebral pial arteriovenous fistula in a patient with sickle cell disease-related moyamoya syndrome: case report. J Neurosurg Pediatr. 2015;16:207–11.
51. Pavanello M, Severino M, D'Antiga L, et al. Pretransplant management of basilar artery aneurysm and moyamoya disease in a child with Alagille syndrome. Liver Transpl. 2015;21:1227–30.
52. Lo FS, Wang CJ, Wong MC, Lee NC. Moyamoya disease in two patients with Noonan-like syndrome with loose anagen hair. Am J Med Genet A. 2015;167:1285–8.
53. Thines L, Petyt G, Aguettaz P, et al. Surgical management of Moyamoya disease and syndrome: current concepts and personal experience. Rev Neurol. 2015;171:31–44.
54. Griessenauer CJ, Lebensburger JD, Chua MH, et al. Encephaloduroarteriosynangiosis and encephalomyoarteriosynangiosis for treatment of moyamoya syn-

drome in pediatric patients with sickle cell disease. J Neurosurg Pediatr. 2015;16:64–73.
55. Ni J, Zhou LX, Wei YP, et al. Moyamoya syndrome associated with Graves' disease: a case series study. Ann Trans Med. 2014;2:77.
56. Raybaud CA, Strother CM, Hald JK. Aneurysms of the vein of Galen: embryonic considerations and anatomical features relating to the pathogenesis of the malformation. Neuroradiology. 1989;31:109.
57. Degirmenci E, Bir LS, Yagci B, Nazliel B, Siva A. Moyamoya syndrome or Behcet's disease? Int J Rheum Dis. 2014;17:920–2.
58. Fujimura M, Niizuma K, Endo H, et al. Quantitative analysis of early postoperative cerebral blood flow contributes to the prediction and diagnosis of cerebral hyperperfusion syndrome after revascularization surgery for moyamoya disease. Neurol Res. 2015;37:131–8.
59. Hyakuna N, Muramatsu H, Higa T, Chinen Y, Wang X, Kojima S. Germline mutation of CBL is associated with moyamoya disease in a child with juvenile myelomonocytic leukemia and Noonan syndrome-like disorder. Pediatr Blood Cancer. 2015;62:542–4.
60. Berenstein A, Lasjaunias P, Ter Brugge K. Spinal arteriovenous malformations. In: Berenstein A, Lasjaunias P, Ter Brugge K, editors. Surgical neuroangiography. New York: Springer; 2004.
61. Rodesch G, Lasjaunias P, Berenstein A. Embolization of arteriovenous malformations of the spinal cord. In: Valavanis A, editor. Interventional neuroradiology. New York: Springer; 1993.

Pediatric Seizures

24

Alison S. May and Juliann M. Paolicchi

Vignette Eleven-year-old Sarah was an active soccer player on her local travel team. She and her mother traveled to an out of town tournament where the team had an evening practice followed by a pizza night for the team. They were expected to get to bed early, since their team was scheduled to play early in the morning and the coaches wanted to hold an early morning warm up. Despite her best efforts, Sarah's mother could not get Sarah to sleep. She was too excited about the news that she would be the starting goalie in the morning—a position she had been working toward all season.

As the alarm clock rang, Sarah's mother was not surprised to find Sarah not responding and making a funny groaning sound. Moving toward her bed, though, she was surprised at what she saw. Sarah's head was turned to one side, there was drool on the pillow, and her body was rhythmically jerking. Sarah's mother tried to "shake her out of it" but quickly realized it was more serious and picked up the phone to call 911. She watched as Sarah's jerking movements eventually calmed down over minutes, and then Sarah started breathing heavily but remained unresponsive. Sarah's mother checked frequently to make sure Sarah was still breathing. When the EMTs arrived, they asked Sarah's mother a few questions, including whether epilepsy runs in the family. They gave her instructions to drive to the hospital and then transported Sarah to the hospital. Sarah's mother remembered it as the longest drive of her drive and dreaded how she would see Sarah once she got there.

When parents hear the term "epilepsy," tears and worry often follow. For most pediatricians, a call to the pediatric neurologist is the first step, and that may also be accompanied by specific concerns: how to be sure the child actually had a seizure, how to prevent another seizure from occurring, and how soon can you see my patient! This chapter is designed to guide the pediatrician through the diagnosis of a first time seizure, febrile seizure, and acute seizure. It will outline common pediatric seizure types and epilepsy conditions and give initial suggestions to management. More complicated epilepsy syndromes and their management will also be briefly described to be used as a reference.

A.S. May, M.D.
Department of Pediatrics, New York Presbyterian Hospital, New York, NY 10021, USA

J.M. Paolicchi, M.A., M.D., F.A.N.A. (✉)
Pediatric Neurology, Komansky Center for Children's Health, Weill Cornell Medical Center, Suite 605, 1320 York Ave., New York, NY 10021, USA
e-mail: jup9037@med.cornell.edu

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_24

Although the term "epilepsy" may be frightening in terms of its implications, the condition refers simply to a patient having more than one unprovoked seizure in a period greater than 24 h. There are many etiologies of epilepsy including structural intracranial abnormalities and central nervous system (CNS) infections or having a genetic predisposition toward having a seizure, but for many pediatric patients, no other condition exists. Given the wide variety of potential etiologies and seizure characteristics referred to as semiology, seizures can be an extremely challenging entity to diagnose and treat for neurologists and pediatricians alike.

To characterize a simple approach to evaluating a child presenting with seizures, we will review different seizure types to make the recognition of abnormal movements or behaviors as seizures; more obvious, we will delineate when a suspected seizure is an emergency and when the workup is less urgent and address acute seizure management and basic antiepileptic medication initiation.

Seizure Semiology

There are two basic categories within which to characterize seizures, generalized and focal. Generalized seizures initiate from both brain hemispheres simultaneously. Typically, patients with generalized seizures will lose consciousness. These seizures are common in febrile seizures, genetic epilepsy syndromes, metabolic derangements, and other systemic illnesses. Focal seizures may originate from a single area or one hemisphere of the brain. As a result, consciousness is often preserved and the seizure semiology reflects the part of the brain that is the epileptogenic focus. For example, seizures from the occipital lobe often present with visual deficits, seizures from the dominant temporal lobe with automatisms and language arrest, and seizures from the frontal lobe with motor manifestations. In contrast, focal seizures are more suggestive of an underlying structural abnormality such as a tumor, hemorrhage, vascular malformation, or a developmental anomaly such as a cortical dysplasia [1, 2]. These seizures can generalize or spread to the other cerebral hemisphere quickly. Therefore, it is the *start* of the seizure that can help identify a seizure focus.

The evaluation of both types of seizures requires an electroencephalogram or EEG. Most generalized epilepsy syndromes, such as childhood absence epilepsy (CAE), will show characteristic abnormal EEG findings, which are generalized. Patients with focal seizures may have EEGs that show the area of abnormality or may be normal. Patients with focal epilepsy will in general require a diagnostic neuroradiologic study, in most instances an MRI, to look for a possible focal lesion.

Generalized Seizures

Generalized Tonic-Clonic Seizures

Generalized tonic-clonic seizures are the "classic" seizure that most physicians associate with whole-body shaking; but the term is often misapplied to any seizure that involves some degree of involuntary body movement. Characteristically, there are several phases to the seizure. The first phase is a loss of consciousness, followed by tonic stiffening of the body. The clonic phase follows a variable period with repetitive movement due to synchronous muscle contractions. The contractions then slow in frequency until they stop. Urinary incontinence and tongue biting can be associated with GTCs, but they are not constant features. It is important to counsel parents and caregivers that patients cannot swallow their tongues and that nothing should be placed in the patient's mouth during a seizure. Unnecessary injuries may occur to the caregiver and the patient when this is attempted. The period of time directly following any seizure is referred to as the "postictal state." After a GTC, patients will often manifest a prolonged depressed level of consciousness.

Myoclonic Seizures

Myoclonus is simply a brief muscle contraction. Myoclonus can be due to many etiologies, such as medication side effects, hypoxic ischemic injury, or metabolic disturbances. Myoclonic seizures occur when muscle contractions are due to epileptic activity. During epileptic myoclonus, the EEG shows a generalized poly spike and wave discharge. Epileptic myoclonus can be seen in anoxic brain injury, in genetic epilepsy syndromes, or in other progressive myoclonic epilepsies. In the most common myoclonic epilepsy syndrome, juvenile myoclonic epilepsy, the myoclonus typically occurs in the morning and consists of a series of multiple jerks, and if the cluster is brief, the patient may not lose consciousness.

Tonic Seizures

Tonic seizures are a sustained stiffening or posturing of limbs. These are of short duration, usually 5–20 s in duration. They are accompanied by what is described as paroxysmal fast activity on an EEG during the time of muscle contraction. Tonic seizures are seen in otherwise relatively healthy young children but, in older children, are often a sign of more serious epilepsy syndromes.

Atonic Seizures

Atonic seizures are the opposite of tonic seizures and are characterized by a sudden loss of tone. They have also been described as "drop attacks." As a result, these seizures can cause serious facial, dental, and head injuries, especially if the patient is standing at the time of the seizure. Parents and caregivers of patients with this seizure type may be mistaken as causing injury to their child. If poorly controlled, some children with atonic seizures wear helmets to prevent injury due to falls. In myoclonic-astatic epilepsy or Doose syndrome, atonic seizures can abate, but for most children, atonic seizures are present in the context of serious epilepsy syndromes [3].

Absence Seizures

Absence seizures are the most common generalized seizure type in children. They consist of brief, staring episodes that are very short, typically lasting only 10–20 s in duration. They have no aura and do not manifest a postictal state. Children with absence epilepsy tend to have multiple seizures per day prior to treatment. Automatisms are common, involving the face, eyes, or mouth, such as eye blinking, mouth twitching, or brief lip smacking. A variant of absence seizures, atypical absence seizures, can be longer, up to 30 s, have less distinct on and off phases, and may be accompanied by myoclonic seizures [3]. Typical absence seizures are seen in primary genetic epilepsy syndromes, as discussed below. Atypical absence seizures are seen in more severe epilepsy syndromes. The differential diagnosis of absence seizures in children includes focal seizures with loss of consciousness and daydreaming. A detailed history with EEG confirmation can sort out the different episodes, but it is clinically important to remember that *all children who stare are not experiencing an absence seizure*.

Infantile or Epileptic Spasms

Spasms are a seizure type, which typify the entity of infantile spasms or West syndrome. They present as a cluster of brief, bilaterally symmetric contractions of the muscles of the trunk, neck, and extremities. They can be flexor or extensor or a mixed flexion/extension response. The severity varies from child to child and even a small head nod in a cluster may be the manifestation of an epileptic spasm. Many parents will report that the clusters are more common during state changes, either upon awakening or falling asleep. Associated eye changes, such as nystagmus or eye deviations, are common, and infants often cry at the end of the suspected episode. Even though there are benign imitators of spasms we will review later in the chapter, early recognition and treatment of this epilepsy syndrome are crucial to decrease the potential for poor neurologic and cognitive outcomes.

Focal Seizures

Temporal Lobe Seizures

Patients with seizures originating in the temporal lobe often experience an aura (a preceding symptom) before the full seizure. These are variably described as olfactory sensations, mood changes, and feelings of fear or epigastric discomfort. The patient may then proceed to automatisms and then a decreased level of responsiveness. Automatisms are a set of unconscious behaviors, such as lip smacking, chewing, or finger rubbing. If the seizure secondarily generalizes, a temporal lobe seizure can evolve into a full GTC.

The mesial (or medial) temporal lobe is very epileptogenic. Children who have seizures that originate in the temporal lobe are sometimes found to have an isolated lesion such as a tumor, cyst, cortical dysplasia, or hemorrhage. In young adolescents, the etiology of temporal lobe epilepsy is often scarring of the mesial temporal lobes, also known as mesial temporal lobe sclerosis (MTS). The EEG often demonstrates sharp waves in the temporal leads. Seizure control can be achieved in about 60 % of children with MTS using medication [3]. Patients who only partially respond to seizure medication do not respond at all or, in whom medication side effects are intolerable, can often be excellent candidates for resective surgical approaches with a very high cure rate.

Frontal Lobe Seizures

The frontal lobe is involved in motor planning and executive functions. As a result, frontal lobe seizures often present with motor symptoms that may be very complex or bizarre. Patients may demonstrate hemi-clonic movements or assume tonic postures, such as the fencer pose. They may also manifest sexual automatisms like pelvic thrusting. Given that the frontal lobes are in close proximity, rapid spread to the other frontal lobe is common.

Among frontal lobe epilepsies, autosomal dominant nocturnal frontal lobe epilepsy is perhaps the best understood. Mutations in the nicotinic acetylcholine receptor have been identified in this rare condition. It presents in late childhood and is characterized by stereotyped hyperkinetic seizures usually at night. Often patients have preserved consciousness during the spells. The EEG is usually normal between events and the EEG during an event shows rhythmic frontal lobe discharges. The prognosis is good, but this syndrome can be difficult to diagnose; patients are often misdiagnosed as having parasomnias, paroxysmal nonepileptic events, or sleep apnea. An overnight EEG is essential for this diagnosis.

Occipital Lobe Seizures

Because the visual cortex is located within the occipital lobe, seizures originating from this region are often associated with visual phenomena. Patients describe unformed images including flashing lights or frank visual hallucinations; there can also be visual distortions in size, shape, and color. Complete ictal (during the seizure) blindness has also been described. Seizures originating in this area exhibit variable spread or generalization to other regions of the brain.

Benign childhood occipital epilepsy, or Panayiotopoulos syndrome, is characterized by occipital lobe seizures with a peak onset at 3–6 years of age. Despite that EEG demonstrates a multifocal spike and wave pattern predominantly in the occipital regions, children with these seizures usually present with a migraine condition with associated autonomic symptoms. A headache-like syndrome with emesis and associated pallor, flushing, and mydriasis is suggestive of these seizures. The seizures can evolve into unilateral convulsions as well. These children are often misdiagnosed with migraine, cyclic vomiting, encephalitis, gastroenteritis, or syncope. Most children have a good prognosis and outgrow their seizures 2–3 years after presentation. If the seizures are very frequent, treatment with antiepileptic medication can be effective, especially those also effective for mitigating the symptoms of migraines such as valproate or topiramate.

Parietal Seizures

Parietal seizures are uncommon and poorly characterized. They can have auras of tingling and numbness and can have asymmetric tonic or clonic movements.

For a full list of generalized and focal seizures, see Table 24.1.

Vignette Continued [2]

Once Sarah's mother arrived at the emergency department, she was relieved to see Sarah tired but responsive. Sarah could remember going to bed, being excited about playing goalie, and then waking up in the ambulance. The nurse who was taking care of Sarah advised her mother that her vital signs were now stable, that she was on a monitor as a precaution, that some blood work had been taken, and that a doctor would be in to talk to her.

The pediatrician on duty in the emergency room explained, after Sarah's mother told the history, that Sarah had a generalized tonic-clonic seizure with possible focal features given the head turning. The pediatrician explained that they were going to monitor Sarah and determine what next to do. The pediatrician was relieved that Sarah did not have a fever and that Sarah had not had generalized tonic-clonic events previously. The doctor also explained that Sarah's examination was normal, including her neurologic examination. Sarah interrupted and asked if she could eat now. Her mother knew she must be feeling better.

Table 24.1 Summary of seizure types

Generalized seizure type	Characteristics
Generalized tonic-clonic seizures (GTCs)	Loss of consciousness, tonic stiffening followed by clonic phase; can have urinary incontinence, elevated HR and BP
Absence seizures	Sudden onset of behavioral arrest lasting <15 s, can have automatisms
Tonic seizure	Sudden sustained posture, <20 s
Atonic seizure	Sudden loss of tone, lasts <10 s
Myoclonic seizure	Brief muscle contraction, <0.5 s
Epileptic spasm	Brief flexor and/or extensor posture, often clusters
Focal seizure	Characteristics
Temporal lobe	Aura, impaired consciousness, oral and limb automatisms
Frontal lobe	Hyperkinetic complex movements and automatisms, nocturnal predominance, can have fencing posture, bicycling, eye deviation
Occipital lobe	Visual hallucinations, eye deviation, forced blinking
Parietal lobe	Somatosensory auras

Approach to the First Seizure

Pediatricians frequently ask about the management strategies for the first seizure in a child. The approach differs whether the initial seizure is febrile or afebrile and the child's age. Pediatricians should also be aware of the most common genetic epilepsy syndromes in children and the approach to each of these conditions.

Febrile Seizures

Febrile seizures are the most common seizures in children. They occur in 2–5 % of all children less than 5 years of age [4]. A febrile seizure is defined as a seizure in infancy or childhood, between 6 months and 6 years of age, that is associated *with* fever but *without* any evidence of intracranial infection. The peak onset is 18 months. There are two types of febrile seizures: simple and complex, and the difference is important for prognostication. Simple febrile seizures occur as isolated events, are generalized in onset, and are less than 15 min. Complex febrile seizures, in distinction, have one or more of the following features: a duration longer than 15 min, more than one episode occurring within a 24 h period, or symptoms that point to a focal part of the brain.

There is a clear genetic predisposition for febrile seizures in some families: 10–20 % of first-degree relatives of children with febrile seizures will have experienced febrile seizures. A variety of genetic loci have been identified, and serious genetic epilepsy syndromes such as severe myoclonic epilepsy of infancy, or Dravet's

syndrome, may initially present with complex febrile seizures. Febrile seizures have also been associated with several viral and bacterial antigens including influenza, human herpes virus 6, adenovirus, and Para influenza [5].

The typical presentation of a febrile seizure is a generalized tonic-clonic seizure during the early phase of a febrile illness. Postictal lethargy is common and the majority of febrile seizures last less than 15 min. If there are atypical features such as a prolonged event or other associated neurocognitive deficits, it is imperative that more concerning etiologies such as central nervous system infections are ruled out. In the older child, signs and symptoms of a CNS infection may be more easily detected by neurological exam, whereas in the younger child, this can be more of a diagnostic dilemma. Other etiologies to consider in the differential diagnosis of febrile seizures are rigors in a child with fevers or breath-holding spells within the correct clinical context.

The emergency department of intensive care unit evaluation includes a lumbar puncture for any child presenting with meningismus, bulging fontanelle, prolonged lethargy, recurrent seizures, or status epilepticus. Additionally, in children less than 1 year of age, lumbar puncture is recommended if they are considered to be deficient in *Haemophilus influenzae* type b or *Streptococcus pneumoniae* immunizations. In otherwise healthy children over 1 year of age, a simple febrile seizure alone does not require significant workup. There is limited utility for performing a head CT in a child presenting with febrile seizures, especially when considering the negative side effects of ionizing radiation. EEGs are not indicated with initial presentation of a febrile seizure, but consideration may be given to perform an EEG in children with febrile seizure if the child is known to have a neurodevelopmental abnormality and a strong family history of childhood epilepsy or if they manifest with frequently recurring febrile seizures. Brain MRI may have utility in children who present with complex febrile seizures, but are typically performed only in children with other neurologic deficits and focal seizures or in whom focal EEG findings suggest that searching for a subtle brain malformation or lesion may be higher yield [5].

When a child recovers rapidly to their neurologic baseline after a febrile seizure, an underlying CNS infection is very unlikely. Therefore, a child presenting with first time febrile seizure warrants medical observation, but their admission to the hospital is usually not indicated. Though most febrile seizures are less than 15 min, if a seizure becomes prolonged, it will require symptomatic treatment with a benzodiazepine (see acute seizure management section below.) It is important to counsel family that the risk of recurrence is high. Approximately 33 % of children with a first febrile seizure will have a recurrence at some point. Sixteen percent will occur within 24 h of their first and 10 % will have more than three febrile seizures following the first one [5]. The main risk factors for recurrence are a positive family history and an early age of presentation. Though the risk of recurrence is high, the risk of developing future epilepsy in children with simple febrile seizure is 1 %, which is the same risk as in the general population. For complex seizures, the risk is minimally higher, 2–4 % that the child will proceed to develop epilepsy.

Given that the risk of epilepsy is not significantly greater than the general population and because febrile seizures are a benign, self-limited age-dependent response to fever, long-term prophylactic *treatment with an antiepileptic medication is not indicated*. Controlling the fever with antipyretic is a logical solution; however, in studies of children with febrile seizures, treatment with an antipyretic medication does not actually decrease the risk of febrile seizure. In fact, research has shown that 50 % of children with febrile seizures had already received an antipyretic medication prior to the seizure [5]. For children with prolonged seizures, the option of administering rectal diazepam at home exists, and for children with frequent febrile seizures, rectal or oral diazepam at the onset of a febrile illness has been demonstrated to decrease the risk of having a seizure by 50 % [6].

Nonfebrile Seizures

Every year, about 25,000–40,000 children in the USA experience their first nonfebrile seizure. Nonfebrile seizures are by definition not associated with a fever and therefore should eliminate any concern over CNS infection. It is important to establish that the child experienced a true seizure because children can present with seizure-like symptoms that may not represent seizures, also known as nonepileptic events. A detailed history from a reliable observer will usually help distinguish between seizures and other nonepileptic events such as breath-holding spells, syncope, gastroesophageal reflux, migraines, and psychogenic nonepileptic seizures.

After determining the patient had an epileptic event, the next management question is whether it was provoked. Again, history and physical exam are the most important as to whether there has been an ingestion, trauma, or metabolic derangement. Based on the history, the appropriate diagnostic workup should be completed within the context of a referral to a pediatric neurologist. Studies of children older than 6 months who present with a nonfebrile seizure in the absence of suggestive history or symptoms have shown that abnormalities on standard laboratory evaluations are rare. Therefore, laboratory tests are recommended only when there is clinical concern including vomiting, diarrhea, dehydration, pregnancy, or possible drug exposure or failure to return to baseline after the event. Additionally, there is no evidence to support performing a lumbar puncture unless the child is less than 6 months, has persistent alteration in mental status, or has concerning meningeal signs. If there is any suspicion for an increase in intracranial pressure, imaging of the brain prior to the LP may be warranted [7].

Many researches have looked into the utility of ordering a routine head CTs and MRIs in identifying a brain abnormality in a child with their first nonfebrile seizure. While there is some variability in results, up to one-third of children with first seizure have been shown to have abnormalities on imaging studies; however, *only about 2% have clinically significant findings that contribute to further clinical management*. Routine neuroimaging for a child presenting with their first nonfebrile seizure is therefore *not* recommended unless warranted by the clinical scenario. Emergent neuroimaging should be performed in a child who has not returned to baseline within several hours after the seizure and in a child with a persistent focal neurological deficit. Nonurgent studies, which may be performed several days after the seizure, should be considered in a child with a focal seizure onset and a history of cognitive or motor impairment of unknown etiology [7]. In general, if a study is obtained, an MRI is the preferred study and should be scheduled in a facility with expertise in pediatric sedation, on a high-strength (3 T) magnet and with pediatric epilepsy protocols (including coronal T2 and FLAIR sequences). Head CTs are only indicated in the emergent setting if there is concern for hemorrhage, cerebral edema, mass effect, or hydrocephalus.

Multiple studies have confirmed that an EEG is not required prior to leaving the emergency department, but certainly is an important part of the evaluation of a child recovering from an initial unprovoked seizure. Routine EEGs read as normal can certainly be seen in patients with epilepsy, but an abnormal EEG can help diagnosis the type of seizure, and epileptiform discharges on the EEG may aid an epileptologist in predicting seizure recurrence. In general, the standard approach to a first time, nonfebrile seizure is an outpatient routine EEG [7]. Long-term video-EEG monitoring is indicated for patients with further seizures, patients with unclear events, and patients whose events are unresponsive to medications. Whenever children with epilepsy warrant further evaluation for changes in their conditions or for considerations of possible surgical therapies, repeat long-term video-EEG evaluation is often helpful in capturing both ictal and non-ictal electrographic events.

Epilepsy Syndromes

Once the workup of a first nonfebrile seizure is complete and underlying structural and metabolic disturbances are ruled out, the next consideration

for the pediatrician and pediatric neurologist is to consider if the child's seizures suggest an underlying epilepsy syndrome. These different syndromes are characterized by seizure type and age of onset and may also be categorized as genetic epilepsy syndromes through familial association or the presence of a mutation in known genetic loci. Identifying a patient with a specific epilepsy syndrome is helpful for parents to better understand their child's prognosis and for epileptologists to suggest most efficacious management strategies. The most common syndromes in children are described below.

Benign Childhood Epilepsy with Centrotemporal Spikes (Also Known as Rolandic Epilepsy or Benign Rolandic Epilepsy of Childhood)

This is the most common childhood focal epilepsy with a prevalence of 10–15 %. Children present with this disorder between 7 and 9 years of age. The seizures in this syndrome occur mainly at night and often begin with a pins and needles sensation of the limbs and can be associated with guttural sounds and drooling. Patients may have preserved consciousness initially but may lose consciousness if the seizure generalizes. The EEG will show either bilateral or unilateral centrotemporal spikes that activate in sleep. The prognosis is excellent in that the seizures often remit without intervention during puberty. With the high likelihood of resolution, the decision to treat depends on the frequency of the seizures. Attention to sleep hygiene is often the first management recommendation. This is a genetic epilepsy syndrome; therefore, no MRI is required to evaluate this condition.

Childhood Absence Epilepsy (CAE)

This disorder is characterized primarily by frequent absence seizures. This is also a common syndrome with a prevalence about 5–12 %. These children, between the ages of three and seven, can experience dozens of absence seizures daily. There is a juvenile variant of this disorder, which has the same phenotype, differing only in the onset after puberty. Forty percent of children with CAE also have generalized tonic-clonic seizures and some rarely have myoclonic seizures. Hyperventilation brings out the absence seizures in 90 % of patients and can be performed in the office setting. The EEG for this condition shows a classic generalized 3 Hz spike and wave pattern. Fortunately, up to 80 % of children will have a complete remission of their seizures in late adolescence. These children respond well to ethosuximide, lamotrigine, and valproate. Children should also be screened for associated neurocognitive issues, especially attentional and learning disorders.

Juvenile Myoclonic Epilepsy (JME)

This syndrome has its onset between 10 and 18 years, with the peak age of presentation between 12 and 16. The prevalence is approximately 5–10 %. Patients with JME often present with myoclonic seizures or generalized tonic-clonic seizures upon awakening. This history is often difficult to elicit and requires specific questioning about early morning clumsiness and difficulty getting dressed or eating breakfast. There is a family history in 20–50 % of patients. The EEG demonstrates generalized poly spike and wave complexes. JME generally requires lifelong treatment with antiepileptic medications; the most common treatment choices are depakote, lamotrigine, and levetiracetam.

Lennox-Gastaut Syndrome (LGS)

LGS is a serious and progressive epilepsy syndrome, also known an epileptic encephalopathy due to the severe cognitive deterioration children experience as part of the syndrome. Children with LGS have impaired development in the context of refractory seizures. LGS seems to be a common final pathway of epilepsy with several proposed etiologies, including structural, metabolic, and genetic. The prevalence is 1–5 %. Onset is usually within the first 5 years of life. It is characterized

by a triad of multiple seizure types, cognitive impairment, and classic EEG findings. The seizure types are usually atonic, tonic, and atypical absence seizures. Generalized tonic-clonic seizures do occur but with a lower frequency. The EEG shows slow (1.5–2.5 Hz) spike and wave discharges. This type of epilepsy syndrome is very difficult to treat, often requiring multiple antiepileptics to improve children's quality of life. Options include lamotrigine, topamax, depakote, zonisamide, keppra, and felbamate. Nonpharmacologic options also exist, such as vagus nerve stimulator therapy, dietary therapies such as the ketogenic and modified Atkins diet, and palliative surgeries discussed below.

West Syndrome (Also Known as Infantile Spasms or Epileptic Spasms)

West syndrome occurs in infants or young children who develop epileptic spasms (previously known as infantile spasms) and cognitive impairment. These children typically present between 3 and 12 months, with a peak age of onset of 4–9 months. The prevalence is 1–5 %. In a pattern similar to LGS, children with epileptic spasms may also have various etiologies including genetic, idiopathic, and structural/metabolic that can result in the same phenotype. The spasms, as previously described, can be of various types, but they tend to cluster and are more common during state changes. Hypsarrhythmia is a pathognomonic and characteristic EEG pattern associated with the syndrome and consists of a high-amplitude chaotic pattern followed by a decremental response. Half the children will go on to have epilepsy later in life. The first-line treatment for these patients is either ACTH or vigabatrin, but in certain cases, such as in children diagnosed with tuberous sclerosis, the evidence suggests vigabatrin as a first-line agent. Alternate treatment options include topiramate and the ketogenic diet. For certain children, particularly those with tuberous sclerosis, cortical dysplasia, or congenital structural malformations, epilepsy surgery can often be very effective at palliating or curing seizures. Prognosis is dependent upon the response to early treatment as well as the underlying etiology; therefore, early identification and aggressive treatment are crucial to neurodevelopmental outcome, a common theme in many pediatric epilepsy conditions.

Acute Seizure Management

Regardless of the etiology of the seizure, the treatment of seizures in the acute setting is similar; treating a prolonged seizure methodically and calmly is a vital skill for any physician. The following outlines the acute seizure management plan.

In the acute setting, while the patient is actively having an event, it may be a challenge to determine if they are seizing. Clues to diagnosis of an epileptic etiology include unresponsiveness to stimuli, an inability to follow commands, pupillary dilation, lack of response to noxious stimuli, an elevated heart rate, and an elevated blood pressure. When in doubt, it is safer to assume a seizure is occurring, especially if the patient has a known history of epilepsy; however, it is important to continually reassess the patient. Many patients continue to receive unnecessary acute therapy even when postictal. The rationale behind aggressive seizure management is derived from studies demonstrating that prolonged seizures can be harder to stop and may cause damage to brain parenchyma. Though previous definitions of status epilepticus include seizures lasting 30 min or longer, newer evidence recommends treating early status epilepticus or the phase when a seizure is longer than 5 minutes. Targeting seizure treatment to this phase, at the 5–10 min duration, clearly decreases the morbidity and mortality of epilepsy [8].

Management of acute seizures should be approached similar to one's mindset in a code setting. If a patient is seizing for more than 5 min, there may be associated cardiorespiratory compromise and the basics of pediatric resuscitation should be employed when necessary. In parallel, the patient should be given a benzodiazepine. Lorazepam can be given if IV access is available, and if not, both buccal midazolam and rectal

diazepam are effective options. If two doses of benzodiazepines do accomplish seizure, cessation, fosphenytoin, or phenytoin should be administered. Phenobarbital is considered a second-line agent for status epilepticus or for patients with a documented allergy to phenytoin/fosphenytoin [8]. After stopping the seizure and managing the airway, the next critical part of managing acute seizures is to evaluate for subclinical seizures. In all children with seizures, there is a high risk of subclinical seizures. Therefore, even if it appears that you have stopped the clinical convulsive activity, it is essential that these patients are monitored immediately on continuous EEG.

General Seizure Precautions

In any child with a seizure history, from an epilepsy syndrome, febrile seizures, or a CNS injury, it is a critical part of any pediatric caregiver to feel comfortable counseling parents on how to manage seizures at home. The key feature during a home seizure is to protect the child from secondary dangers. For example, in a convulsive seizure, it is important to lay the child on the floor and remove him from a high surface he/she could fall off of, like a couch or bed. The child should not be near any furniture with hard corners or sharp edges. Lay the child on his or her side to prevent aspiration from increased secretions. Never put anything in the mouth as this can damage both the patient and the parent. Finally, try to stay calm and watch the clock. If the seizure is becoming prolonged, longer than 5 min, EMS should be activated. Many parents of children with epilepsy will have emergency rectal midazolam available at home, and decisions on when to administer this should be discussed by the pediatric neurologist managing the child's medications.

Antiepileptic Choices

When to treat a child with an antiepileptic medication is very individualized and should take into account the child's safety, quality of life, and goals of the patient and family. In a neurologically normal child with no history of a prior neurologic illness who has had one unprovoked seizure, there is a 24 % risk of having another seizure in the next year. Waiting to treat until after the second seizure does not affect the long-term prognosis. Therefore, most patients, families, and physicians will not treat with an antiepileptic medication after the first seizure. However, the recurrence risk increases to almost 40 % in children who have a prior neurologic insult and increases further to 70 % in a child who has had two seizures separated by 24 h. In these scenarios, most physicians and families will opt for a medication to decrease likelihood of further seizures.

Pharmacologic management of pediatric epilepsy is an exciting and growing field. There are many available medications and many new ones being actively studied for use in pediatric epilepsy. For list of common antiepileptic medications and side effects, see Table 24.2. For certain epilepsies, there are clear indications for syndrome and medication pairing, such as ethosuximide as the initial agent for childhood absence epilepsy; however, in other clinical scenarios, there are several medications one can choose from. We use seizure type, generalized or focal, to narrow down the medication options and then utilize secondary side effects to help us tailor the mediation to each patient. See chart for a list of commonly used antiepileptic medications, the seizures and syndromes they are used for, and the main side effects.

Nonpharmacologic Seizure Management

Many children are able to achieve good seizure control with antiepileptic medications; however, approximately one-third of children will not achieve satisfactory seizure control. In these children with treatment-resistant epilepsy, there are other options that can be used to try to decrease seizure frequency and improve their quality of life. One common approach is a trial of the ketogenic diet. This is a high-fat, low-carbohydrate diet with moderate protein intake. The ratio of fat to carbohydrate is

Table 24.2 Antiepileptic medications and side effects

Medication	Indications	Common and severe side effects
ACTH	Epileptic spasms	Hypertension, immunosuppression, cardiomyopathy, irritability, GI bleed
Carbamazepine	Focal and generalized seizures	Nausea, dizziness, rash, and SJS
Clobazam	LGS	Sedation, drooling, hypotonia
Ethosuximide	Absence seizures	Nausea, vomiting, drowsiness
Felbamate	LGS, focal seizures	Aplastic anemia, hepatic failure
Gabapentin	Focal seizures	Sedation
Lamotrigine	Focal and generalized seizures	Rash, nausea, SHS
Levetiracetam	Focal and generalized seizures	Sedation, mood changes
Oxcarbazepine	Focal and generalized seizures	Sedation, headache, dizziness, rash, hyponatremia, SJS
Phenytoin	Focal and generalized seizures	Gingival hyperplasia, hirsutism, rash, osteopenia, ataxia
Phenobarbital	Focal and generalized seizures	Sedation, hypotonia
Rufinamide	LGS	Somnolence and vomiting, short QT
Topiramate	Focal seizures	Decreased appetite, paresthesias, decreased sweating, metabolic acidosis, kidney stones
Valproate	Focal and generalized seizures	Weight gain, hair loss, nausea, thrombocytopenia, hepatotoxicity, pancreatitis
Vigabatrin	Epileptic spasms	Peripheral vision loss, sedation, MRI changes
Zonisamide	Focal, generalized, myoclonic	Ataxia, somnolence, decreased sweating

increased as one initiates the diet and can be adjusted for different ages and clinical limitations. It is effective in achieving some degree of seizure control in patients with all types of epilepsy. In particular, the diet has been shown to work well in patients with Lennox-Gastaut syndrome, epileptic spasms, and other idiopathic genetic epilepsies [9, 10].

Epilepsy surgery is another option that we consider in children who have persistent, frequent seizures despite medical management. Surgery should be considered as a possibility early on in epilepsy management, as studies have showed that early epilepsy surgery can be associated not only with seizure freedom in 70 % but with also with remarkable cognitive gains.

Surgical options are generally grouped into palliative or curative approaches. Curative epilepsy surgery generally involves resecting small areas of cortex in the active epileptogenic region after a period of intense and precise mapping of the brain areas responsible for seizure onset. This is particularly effective in children with cortical dysplasias, tuberous sclerosis, or other migrational anomalies. With complete surgical resections of an epileptogenic focus, patients can achieve complete seizure freedom. Even a partial resection can offer from 60 to 80 % seizure freedom with an equally important reduction in antiepileptic medication burden and restoration of cognitive and psycho-social development [11].

Other curative surgery options exist for patients with more extension lesions. Hemispherectomies, where one damaged hemisphere is partially resected and completely disconnected from the remaining unaffected hemisphere, are indicated in treatment-resistant epilepsy in patients who have conditions that affect one cerebral hemisphere diffusely, such as Sturge-Weber, Rasmussen encephalitis, hemimegalencephaly, and some severe post-traumatic brain injuries with unilateral damage.

Palliative surgical approaches are offered as a way to reduce seizure frequency, duration, and medication burden. Corpus callosotomy is a well-studied procedure in which the anterior two-thirds of the corpus callosum is sectioned, disconnecting the two hemispheres. This is indicated in patients with frequent atonic seizures where drop attacks pose a serious risk to the child's safety. By disconnecting the hemispheres, seizure propagation is interrupted, restricting the electrical spread within the ipsilateral hemi-

sphere, preventing a loss of tone on both sides, and eliminating the drop attacks that would otherwise invariably follow. Less invasive surgical options involve implantation of neurostimulatory devices. The vagus nerve stimulator (VNS) is the best known device. VNS consists of a small battery implanted under the pectoralis muscle and attached to small corkscrew electrical leads that are wrapped around the left vagus nerve. By modulating the frequency and stimulation of the nerve utilizing a percutaneous programming wand, approximately 50 % seizure reduction in frequency and durations can be achieved in patients who otherwise are not candidates for resection as an adjunctive treatment.

Vignette Continued [3]

Since Sarah showed no further problems and had no history of neurologic problems or previous seizures, Sarah's mother agreed with the emergency room doctors to have her evaluated in her hometown. Her pediatrician referred her for an EEG and to a child neurologist. The EEG showed bilateral centrotemporal spikes during sleep in a normal background, consistent with the discharges seen in benign centrotemporal or Rolandic epilepsy. When Sarah spoke to the neurologist, she had recalled times when she may have had a "funny tingly feeling" in her face and mouth when she had gotten very tired or sick. The neurologist explained that these may have been small auras or small seizures associated with benign centrotemporal epilepsy.

Because Sarah had only one seizure and it was in the context of a sleepless night, both the neurologist and Sarah's parents agreed not to treat with antiepileptic medications. Instead, the parents and Sarah agreed to focus on lifestyle changes that could reduce the risk of seizures, especially sleep hygiene. Since the EEG showed a benign epilepsy pattern and Sarah's examination and neurocognitive history were normal, the neurologist explained that there was no need for neuroradiographic imaging at this time. Acute seizure management was reviewed with the parents. A follow-up appointment was scheduled for 6 month's time or as necessary for another event. Both the parents and Sarah were relieved to hear that she could continue to play soccer without restrictions.

Conclusion

Employing a calm, rationale strategy is the first and most important step in the approach to the pediatric patient presenting with any type of seizure. Pediatricians and other pediatric first-line providers can then proceed through a series of logical steps regarding the evaluation of the child that are based upon a careful history and physical: was it an epileptic event or a benign physiologic event in childhood such as breath holding? If epileptic, is the patient febrile? Does the patient warrant a full infectious evaluation including LP, or is cautious observation appropriate? If febrile or nonfebrile, has the patient returned to baseline or warrant transfer to the intensive care for further treatment? If nonfebrile, are there other clues to a trigger such as a toxin, a recent diarrheal illness, or a tick bite? Can the patient safely be discharged for outpatient evaluation or do they warrant further observation? Is there a history of possible events in the past that warrant an EEG, such as previous staring episodes or unexplained episodes of unresponsiveness? If the child has a history of epilepsy and is continuing to have seizures, should they be referred to an epilepsy center for exploration of alternative therapies or possibly surgery to help alleviate the burden and consequences of epilepsy? This stepwise approach will help direct the patient and caregivers to the correct diagnosis and treatment and demystify a process, which might otherwise seem foreboding.

References

1. Subcommittee on febrile seizures. Febrile seizures: guideline for the neurodiagnostic evaluation of a simple febrile seizure. Pediatrics. 2011;127:389–94.
2. Paolicchi J. Epilepsy. In: Lynn E, Newton H, Rae-Grant A, editors. The 5 minute neurology consult. Philadelphia, PA: Lippincott Williams & Wilkins; 2004. p. 186–97.

3. Hirtz D, et al. Practice parameter: evaluating a first nonfebrile seizure in children: report of the quality standards subcommittee of the American academy of neurology, the child neurology society and the American epilepsy society. Neurology. 2000;55:616–23.
4. Hausr W. The prevalence and incidence of convulsive disorders in children. Epilepsia. 1994;35(2):S1–6.
5. Riviello JJ, et al. Practice parameter: diagnostic assessment of the child with status epilepticus (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology. 2006;67:1542–50.
6. Vendrame M, et al. Localization of pediatric seizure semiology. Clin Neurophysiol. 2011;122:1924–8.
7. So E. Value and limitations in seizure semiology in localizing seizure onset. J Clin Neurophysiol. 2006;23:353–7.
8. Thammongkol S, et al. Efficacy of the ketogenic diet. Which epilepsies respond? Epilepsia. 2012;53:55–9.
9. Kossoff E, et al. Optimal clinical management of children receiving the ketogenic diet: recommendations of the international ketogenic diet study group. Epilepsia. 2009;50:304–17.
10. Lerner JT, et al. Assessment and surgical outcomes for mild type I and severe type II cortical dysplasia: a critical review and the UCLA experience. Epilepsia. 2009;50:1310–35.
11. Paolicchi JM, et al. Predictors of outcome in pediatric epilepsy surgery. Neurology. 2000;54:642–7.

Approach to Spasticity in the Pediatric Patient

25

Neil Haranhalli and Rick Abbott

Case Vignette An 11-year-old girl with cerebral palsy, known to you for the past 5 years, presents with 6 months of worsening pain and rigidity of her upper extremities. Her parents find it nearly impossible to dress her in the morning without pain medication and state that although her dose of oral baclofen was increased almost 9 months ago, they have not noticed any improvement. They are intrigued by the prospect of surgical therapies that could relieve their daughter of daily challenges.

Introduction

The successful treatment of spasticity, a diagnosis often misunderstood and oversimplified by practitioners, requires a careful, multidisciplinary, and patient-directed approach. An accurate understanding of the definition and spectrum of spastic disorders is paramount to any patient assessment. In this chapter, we will provide a systematic guide for general practitioners who may encounter patients with spasticity in an age-based manner.

Spasticity is defined as a "a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks, resulting from hyperexcitability of the stretch reflex." It is often seen in patients with cerebral palsy, a nonprogressive neurologic disorder affecting muscle tone, movement, and posture in children. Spasticity can be seen in up to 60 % of patients with cerebral palsy but is also secondary to other congenital or acquired injuries to the central nervous system such as trauma to the spinal cord or brain. Spasticity is often accompanied by other motor disorders, and these other disorders can strongly influence the options for treatment that are available as well as rational goals one might hope to achieve with these treatments. In the pediatric population, primary care physicians are the first to identify developmental problems of movement, posture, and muscle tone and therefore should be comfortable in accurately assessing these problems in the office.

Many patients may present with a mixed disorder where both spasticity and dystonia are present. Whereas spasticity is a *velocity-dependent movement disorder*, dystonia can be described as a syndrome of sustained muscle contractions resulting in *twisting*, *repetitive movements*, *and abnormal postures*. In patients with cerebral

N. Haranhalli, M.D., B.S.
Albert Einstein College of Medicine,
3316 Rochambeau Avenue, Bronx, NY 10467, USA

R. Abbott, M.D. (✉)
Montefiore Medical Center, 111 E. 210th St., Bronx, NY 10583, USA
e-mail: rickabbott@me.com

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_25

palsy, both spasticity and dystonia can be present independently or as a mixed syndrome.

The distribution of tone abnormalities will vary according to the site of injury in the CNS. It can involve both legs symmetrically referred to as spastic diplegia or asymmetrically affect one side of the body which is referred to as spastic hemiplegia. When spasticity involves all four limbs, it is termed quadriplegia unless the manifestations are markedly asymmetric in which case the condition is may be termed double hemiplegia.

Examining a Child with Spasticity

A careful history and physical exam are helpful in differentiating between these motor disorders and identifying patients with pure spasticity. First, a detailed history should be taken including birth history, pre- and postnatal complications, and developmental milestones. Children with pure spasticity often have a history of *preterm birth*, *generally around 30 weeks' gestation*, whereas children with other forms of hypertonia tend to have dystonia or a mixed hypertonia.

The physical exam of a child with a hypertonic disorder, like any other, begins with careful and meticulous observation. Spasticity is a hypertonia that worsens with movement and in its pure form is not associated with low tone in the trunk or involuntary movements. Any abnormal posturing, choreoathetoid or writhing movements often seen in the fingers, or a floppy erect torso posture should signal the examiner to consider a mixed disorder of hypertonia rather than pure spasticity.

The physical exam continues with an assessment of upper and lower extremity movements. First, slow passive movement of each extremity is attempted noting the range of motion (goniometric measurement) and any resistance. The limb is then moved rapidly and repetitively while paying careful attention to the loss in range of motion at this higher velocity. Any reduction in the range of motion in the limb's joints as compared to that seen during slow passive movement indicates that spasticity exists in that limb. In addition to velocity-dependent changes in range of motion, there may also be accompanying increases in muscle tone during rapid movement (manifest by an increase in resistance to passive movement).

Assessment of the pattern of active movement of the limbs during gait is the next key step in a complete physical examination for hypertonia. In younger children, this analysis may be done prior to passive movement of the limbs if the passive examination is expected to upset the child. Typical features to observe during the gait cycle include persistent flexion at the hips, hyperlordosis compensating for hip flexion, and inward rotation at the hip joints with an associated scissoring of the legs. Scissoring can be described as a hyper-adduction of the advancing hip resulting in crossing of that limb in front of the weight-bearing limb. There is often notable spasticity of the hamstring muscle presenting as a difficulty with knee extension and resulting in a crouched stance and shortened stride. Finally, there may also be an equinovalgus deformity at the ankles, where the heels are raised off the ground and oriented outwards throughout the stride. All of these findings (velocity-dependent hypertonia and the above-described gait pattern), in the absence of writhing movements and in the presence of good truncal tone, should offer any provider confidence in suggesting a diagnosis of pure spasticity.

In some patients, however, spasticity of lower limbs may actually be beneficial in regards to weight-bearing ability. For this reason, a complete hypertonia evaluation must assess whether a child is relying on their spasticity to aid in ambulation, and if so, would losing a significant amount of their hypertonicity secondary to a surgical procedure be counterproductive to functional measures. If the child can repeatedly and successfully transition between a squatting and standing position without using their arms or other supports, they are likely to possess adequate underlying muscle strength to maintain the limb's function in spite of the lost of hypertonia.

Overview of Treatment Goals

When primary care providers see children with spasticity, there are essentially two ways to think about their goals of treatment. Parents can either be guided toward the goal of trying to improve overall motor function or, as is more often the case, toward

the goal of reducing spasticity enough to ease the burden of care for daily activities. When deciding upon a successful treatment of patients with pure spasticity, a complete functional assessment should be performed by a physiatrist or physical therapist with specific expertise in these assessments. Relying solely on the physical exam to guide treatment, goals and options would be an injustice to the patient as true functional capabilities are of utmost importance in setting patient, parent, and caretaker expectations for treatment outcomes. *While the majority of treatment modalities significantly reduce muscle tone and improve ease of care*, *they do not directly improve function*. It is very important to insure that all those involved (i.e., parents, primary providers, surgeons, physiatrists, and physical therapists) are aware of this while discussing treatment goals and expectations.

The treatment of spasticity is often directed at reducing the burden of care and adequately lowering muscle tone such that daily activities and therapies are more comfortable for the patient and caretaker alike. Routine tasks such as bathing and dressing a child can be severely limited and painful for patients with spastic quadriplegia. Both nonsurgical and surgical treatments aim to decrease the hypertonicity that the caregiver must battle when bathing and dressing the child. In the more highly functioning children with spastic diplegia, the treatment goals may focus more upon obtaining improved function in the legs so as to increase the level of independence for the child within their community. Open and frank communication about the expectations of parents and caretakers and comparing them to the expected functional outcomes after the hypertonia is relieved is of utmost importance in successful treatment. Many parents may have expectations of a fully functional child posttreatment; with these families, discussing realistic outcomes can significantly improve perceptions of success postoperatively.

Overview of Treatment Options

Treatment modalities for spasticity can be roughly split into two broad categories: nonsurgical and surgical therapies. It is important to understand that for any treatment, the goal is to optimize ease of care and overall functioning. The neurosurgical mandate for managing hypertonicity in these children is to offer intervention to lessen hypertonia if it will improve the likelihood of the physiatrist and physical therapists obtaining meaningful improvement in function. Each method of managing a patient's hypertonia differs slightly in the type of hypertonia targeted and overall goals of treatment. Therefore a patient's treatment plan must be developed in a patient-centered manner.

Nonsurgical Therapies

Nonsurgical therapies of hypertonicity address easing muscle tone and increasing flexibility at the joints. Options include intensive stretching regimens, oral spasmolytics, and botulinum toxin injections. Involvement of a multidisciplinary approach will increase the probability that all nonsurgical options are considered and that a tailored nonsurgical treatment plan is developed for the child. Joint contractures are common occurrences and can be prevented by effectively stretching spastic muscles several times daily. Physiotherapists often direct this therapy, but stretching routines are often maintained by a trained caretaker. For more aggressive stretching of muscles, certain devices such as serial casting can be utilized.

Oral antispasmodics have been used for decades with varying efficacies. Medications may target reductions in muscle tone through central nervous system (i.e., baclofen and diazepam) or peripheral muscular targets (i.e., dantrolene). All oral medications are fraught with varying side effects (i.e., drowsiness, hypotension, muscle weakness) which often limits their use. Oral baclofen has low solubility through the blood–brain barrier and therefore is not optimal for treating spasticity; however, it is still utilized as a first-line oral medication.

Botulinum toxin injections have been used for decades and act peripherally but only locally at neuromuscular junctions of the muscular target within which they are introduced. This treatment may offer patients months of targeted relief and is

most often used to treat hypertonia in the legs of children, but the result is transient and repeated injections may be undesirable. A low side effect profile has made Botox increasingly popular for patients who do not perfectly fulfill or wish to pursue surgical criteria, but significant evidence is still absent regarding long-term efficacy and benefits.

Surgical Therapies

Surgical therapies are often directed at either treating complications of spasticity (muscle contractures, limb deformities, and joint dislocations) or at primarily reducing spasticity and hypertonia. Orthopedic procedures are often the treatment of choice in the former, while neurosurgical treatments target hypertonia. In young children, chronic leg muscle may result in serious complications such as muscle contractures, distortion in limb growth, and joint subluxation. Tendon lengthening procedures are often helpful in preventing and treating some of these occurrences. However, contracture of the effected limbs' muscles due to spasticity commonly recurs as the underlying spasticity has not been treated. This cycle often results in the need for further tendon lengthening procedures. In older children, who are near skeletal maturity, more intricate osteotomies and arthrodesis may be necessary to treat rotational deformities and improve joint stability.

A variety of neurosurgical procedures exist, directed at treating the underlying spasticity of a patient. The two most common procedures are selective dorsal rhizotomy (SDR) and placement of intrathecal (IT) baclofen infusion systems. Selection of either of these treatments requires a team-based approach for each individual case assessing the type of hypertonia present, the preoperative functionality, the goals of treatment, and the anticipated postoperative care/therapy needs.

SDR is an effective treatment for patients with pure spasticity. Spasticity is felt to arise as a result of a hypersensitive reflex arc at the level of the spinal cord. The premise of SDR is that by interrupting sensory inputs of a hyperactive reflex circuit, the spinal cord's hyperexcitability at the level of the anterior roots can be prevented, thereby reducing spasticity. This interruption however can result in altered control of the leg's muscle groups, effectively reducing functionality acutely. For that reason, it is very important that children undergoing an SDR received skilled postoperative therapy to reestablish normal control over movement. A skilled preoperative assessment can usually predict the postoperative functional outcome for the majority of patients. SDR in patients with dystonia and/or mixed movement disorders has been associated with treatment failure, and therefore this therapy is best considered for patients with pure spasticity disorders.

Intrathecal infusion pumps for the delivery of intrathecal baclofen can be used for both patients with pure spasticity and mixed hypertonia disorders. While oral baclofen does not effectively cross the blood–brain barrier, intrathecal baclofen pumps deliver a significantly higher dose directly to the drug's targets within the spinal cord. This treatment reduces the hyperexcitability thought to underlie spasticity by blocking the excitatory interneuron synapses with α-motor neurons. While this procedure can be tremendously successful in treating spasticity, it carries with it the potential for complications ranging from hardware malfunctions/disconnections to infections and wound breakdown. Serious, life-threatening complications can rarely occur with this treatment, so patient and family education is imperative along with integrative postoperative care and follow-through.

Age-Based Guide to Approaching Families and Patients

The treatment of a child with spasticity is best achieved on a case-by-case basis, but a generalized, overarching approach will structure the initial evaluation and treatment protocol. Here, we provide an age-guided framework that practitioners can utilize while assessing children with spasticity.

Infant

Case Presentation 1

A mother brings her 7 month-old son to clinic after noticing that while crawling he moves his right leg greater than the left. She also comments that he tends to reach at objects in front of him more with his right hand than his left, even if the object is held to his left. On exam, you notice that it is very difficult to stimulate active movement on the left and the child cannot cooperate with passive movement testing.

While assessing patients in infancy, exposing spasticity on physical exam can be difficult, and therefore attention to a detailed pregnancy and birth history is integral. At this stage, the key role of a practitioner is to prepare families for what to expect and to begin to organize a multidisciplinary team for treating the child. In the first year of life, abnormalities in development are generally the most commonly noticed symptoms of patients thought to have a cerebral palsy. Discussing with the parents and caretakers, the possible diagnosis will set the stage for the development of a treatment plan.

Two Years Old

Case Presentation

A 27-month-old girl with known cerebral palsy is brought in by her parents when they notice that she is extremely reluctant to sit on the floor in daycare and refuses to let anyone touch her right leg. On exam you notice clonus of the left foot and significantly reduced range of motion in the right knee and hip joints.

As a child with hypertonia grows past 1 year of age, the body begins to feel the pressures of increased and unbalanced muscle tone. Although a patient's function remains difficult to assess at this age, due to the limited range of activities a child participates in as well as the limited mental capacity to follow complex commands, the child may still experience secondary complications. While therapy in this age group is directed at prevention of secondary complications from the hypertonia, rarely a patient can present with dislocations of the hips. Procedures performed at this time should aim at halting any progression in a deformity or abnormality and are not intended to greatly affect the functionality of a given limb or patient. Approaching these cases from an interdisciplinary standpoint is also crucial for maintaining long-term treatment options. As with patients with spasticity of all ages, providing parents and caretakers with realistic expectations will allow for a much more refined, holistic approach.

Three–Four Years Old

Case Presentation

A 3-year-old boy with spastic hemiplegia who is followed at your clinic presents with worsening symptoms, and his caretaker remarks that she is finding it increasingly difficult to bathe and get him ready in the morning. They have come to your office to discuss possible therapies that make their day easier.

By the time a patient has grown to be a toddler, the importance of instituting a multidisciplinary team to approach his/her care is crucial. At this stage, a standard motor and muscle tone exam is not sufficient to assess a patient's functional ability or to set treatment goals. A detailed functional assessment, preferable performed by an experienced physical/occupational therapist or rehabilitation specialist, is needed before proceeding with any treatment. Understanding the abilities of a patient, the degree of hypertonia present, and how it is adversely impacting functional development can direct a team toward choosing a medical or surgical treatment for the hypertonia. At any point when a child has established a working relationship with a therapist, an orthopedic or neurosurgical surgical intervention can be considered to treat a hypertonia that is impeding the success of therapy to foster functional development. This is typically after the child has reached the age of three.

It is at this time, most often, that the critical decision of how to further define the goals of treatment is made. Children in this age group will very often require significant intervention within the next few

years and hence remain within the window to consider surgery for preservation and improvement of overall motor function. When a patient's symptoms are due to a more severe spasticity and fit a picture of quadriplegia, the prospect for function-saving surgery diminishes and goals of therapy is directed at easing the burden of care for daily activities.

Older Than Four Years

Case Presentation

An 11-year-old girl with cerebral palsy, known to you for the past 5 years, presents with 6 months of worsening pain and rigidity of her upper extremities. Her parents find it nearly impossible to dress her in the morning without pain medication and state that although her dose of oral baclofen was increased almost 9 months ago, they have not noticed any improvement. They are intrigued by the prospect of surgical therapies that could relieve their daughter of daily challenges.

Patients presenting in young childhood and beyond may exhibit any and all signs of hypertonia. The most extreme of these is quadriparesis secondary to diffuse hypertonia. By this age, it is appropriate to seriously consider, if it has not already occurred, neurosurgical procedures such as SDR or an intrathecal baclofen delivery system. As stated in the above text, patients with pure spasticity are excellent candidates for SDR as changes in function are generally predictable in these cases. Ideally, this is done when the child is a toddler before elementary school demands start and their weight increases during mid-childhood. ITB on the other hand can be used for patients with mixed hypertonicity and is not as sensitive to age restrictions. Nevertheless patients of any age group can be considered for these treatments in a setting where all options are considered and integrated through an interdisciplinary setting.

Conclusion

Childhood hypertonicity is a wide-ranging condition that results in a limiting of motor function and in limb contraction. Often a result of prenatal and perinatal events and commonly associated with cerebral palsy, childhood hypertonicity has a progressive nature and requires a guided approach while assessing pediatric patients at different stages in the disease. Treatment options are directed at very specific goals, ranging from reducing the burden of care to allow for more comfortable involvement in daily activities to an actual improvement in motor function. The most successful treatment of patients with hypertonicity arises from an interdisciplinary team including neurosurgeons, orthopedic surgeons, rehabilitation specialists, physical therapists, and, of course, the patient and caretakers. With a cohesive team and communication of appropriate and realistic expectations, a significant improvement in quality of life for these patients can result.

Bibliography

Abbott I, Johann-Murphy M, Forem S. Childhood spasticity assessment. In: Sindou M, Abbott I, Keravel Y, editors. Neurosurgery for Spasticity: a multidisciplinary approach. Wien: Springer; 1991. p. 51–8.

Abbott R, Deletis V, Spielholz N, Epstein FE, editors. Selective posterior rhizotomy, pitfalls in monitoring. Basil: Karger; 1990.

Abbott R, Johann-Murphy M, Shiminski-Maher T, Quartermain D, Forem SL, Gold JT, et al. Selective dorsal rhizotomy: outcome and complications in treating spastic cerebral palsy. Neurosurgery. 1993;33:851–7. discussion 857.

Albright AL, Turner M, Pattisapu JV. Best-practice surgical techniques for intrathecal baclofen therapy. J Neurosurg. 2006;104(4 Suppl):233–9.

Albright AL. Intrathecal baclofen in cerebral palsy movement disorders. J Child Neurol. 1996;11 Suppl 1: S29–35.

Ashworth B. Preliminary trial of carisoprodol in multiple sclerosis. Practitioner. 1964;192:540–2.

Bleck E. Orthopedic management in cerebral palsy. Philadelphia, PA: JB Lippincott; 1987.

Chung CY, Chen CL, Wong AM. Pharmacotherapy of spasticity in children with cerebral palsy. J Formos Med Assoc. 2011;110(4):215–22.

Coffey JR, Cahill D, Steers W, Park TS, Ordia J, Meythaler J, Herman R, Shetter AG, Levy R, Gill B. Intrathecal baclofen for intractable spasticity of spinal origin: results of a long-term multicenter study. J Neurosurg. 1993;78(2):226–32.

Cohen AR, Webster HC. How selective is selective posterior rhizotomy? Surg Neurol. 1991;35:267–72.

Deletis V, Vodusek D, Abbott R, Epstein F, Turndorf H. Intraoperative monitoring of the dorsal sacral roots. Minimizing the risks of iatrogenic micturition disorders. Neurosurgery. 1992;30:72–5.

Elk B. Preoperative assessment and postoperative surgical occupational therapy for children who have undergone a selective posterior rhizotomy. S African J Occup Ther. 1980;14:49–50.

Fasano VA, Broggi G, Zeme S, Lo Russo G, Sguazzi A. Long-term results of posterior functional rhizotomy. Acta Neurochir Suppl (Wien). 1980;30:435–9.

Gerszten PC, Albright AL, Barry MJ. Effect on ambulation of continuous intrathecal baclofen infusion. Pediatr Neurosurg. 1997;27(1):40–4.

Krach LE. Pharmacotherapy of spasticity: oral medications and intrathecal baclofen. J Child Neurol. 2001;16(1):31–6.

Lance JW. Symposium Synopsis. In: Feldman RG, Young RR, Koella WP, editors. Spasticity: disordered motor control. Chicago, IL: Year Book Medical Publications; 1980. p. 485–500.

Lang FF, Deletis V, Cohen HW, Velasquez L, Abbott R. Inclusion of the S2 dorsal rootlets in functional posterior rhizotomy for spasticity in children with cerebral palsy. Neurosurgery. 1994;34:847–53. discussion 853.

Langerak NG, Lamberts RP, Fieggen AG, Peter JC, Peacock WJ, Vaughan CL. Functional status of patients with cerebral palsy according to the International Classification of Functioning, Disability and Health model: a 20-year follow-up study after selective dorsal rhizotomy. Arch Phys Med Rehabil. 2009;90(6):994–1003.

Lannin N, Scheinberg A, Clark K. AACPDM systematic review of the effectiveness of therapy for children with cerebral palsy after botulinum toxin A injections. Dev Med Child Neurol. 2006;48(6):533–9.

McNeal D, Hawtrey C, Wolraich M, Mapel J. Symptomatic neurogenic bladder in a cerebral-palsy population. Dev Med Child Neurol. 1983;25:612–6.

Mittal S, Farmer JP, Al-Atassi B, Montpetit K, Gervais N, Poulin C, et al. Functional performance following selective posterior rhizotomy: long-term results determined using a validated evaluative measure. J Neurosurg. 2002;97:510–8.

Molnar G. Rehabilitation in cerebral palsy. West J Med. 1991;154:569–72.

Morota N, Abbott R, Kofler M, Epstein FJ, Cohen H. Residual spasticity after selective posterior rhizotomy. Childs Nerv Syst. 1995;11:161–5.

Park TS, Johnston JM. Surgical techniques of selective dorsal rhizotomy for spastic cerebral palsy. Technical note. Neurosurg Focus. 2006;21:e7.

Peacock WJ, Eastman RW. The neurosurgical management of spasticity. S Afr Med J. 1981;60(22):849–50.

Sanger TD, Delgado MR, Gaebler-Spira D, Hallett M, Mink JW. Task Force on Childhood Motor Disorders. Classification and definition of disorders causing hypertonia in childhood. Pediatrics. 2003;111(1):e89–97.

Steinbok P, Kestle JR. Variation between centers in electrophysiologic techniques used in lumbosacral selective dorsal rhizotomy for spastic cerebral palsy. Pediatr Neurosurg. 1996;25:233–9.

Steinbok P, Langill L, Cochrane DD, Keyes R. Observations on electrical stimulation of lumbosacral nerve roots in children with and without lower limb spasticity. Childs Nerv Syst. 1992;8:376–82.

Steinbok P, Reiner AM, Beauchamp R, Armstrong RW, Cochrane DD, Kestle J. A randomized clinical trial to compare selective posterior rhizotomy plus physiotherapy with physiotherapy alone in children with spastic diplegic cerebral palsy. Dev Med Child Neurol. 1997;39(3):178–84. PubMed PMID: 9112967.

Steinbok P. Selection of treatment modalities in children with spastic cerebral palsy. Neurosurg Focus. 2006; 21(2):e4.

Steinbok P. Selective dorsal rhizotomy for spastic cerebral palsy: a review. Childs Nerv Syst. 2007;23(9): 981–90.

Assessment and Management of Minor Head Injuries in Toddlers and Adolescents

26

David Kimball and Jeffrey P. Greenfield

Vignette

A mother presents to the emergency room with her 6-month-old male infant. The mother explains that approximately 1 h earlier, she briefly left the infant on the couch. The infant fell off the couch and hit his head on the hardwood floor. She explains that she does not think there was a loss of consciousness, but the infant did cry inconsolably for quite some time. The mother cannot localize the point of impact, but reports that the infant has been somewhat "fussy" since the fall without emesis.

Case Presentation

Within the vignette presented above, the mother was quite sure that there was *not* a loss of consciousness, but that the infant did cry inconsolably for quite some time. *This is a crucial first question to ask*. The mother cannot localize the point of impact, but reports that the infant has been somewhat "fussy" since the fall. A lack of scalp trauma is also reassuring about the force of impact on the scalp and skull. There has been no vomiting and the mother states that the child has been previously healthy. Emesis and seizure-like activity raise the suspicion of a mild TBI such as concussion or contusion and should begin directing one's attention toward higher-level assessments.

In the emergency room, on physical exam, the infant's vital signs are within normal limits. The child is upset and crying, but is somewhat consolable by the mother. There is a 3 cm swelling on the right parietal-occipital portion of the occiput that is soft and tender, making assessment of any underlying evidence of bony deformity difficult to achieve. The infant has no other external signs of trauma. The pupils are bilaterally equal and reactive to light. The child is moving all four extremities spontaneously, withdraws to touch/pain, and has bilaterally symmetric reflexes. The anterior fontanel is soft. Physical exam is negative for hemotympanum, raccoon eyes, or Battle's sign, and there are no other signs of basal skull fracture.

A head CT scan is ordered. On review, there is no evidence of any underlying traumatic brain injury despite a linear skull fracture and the palpable subgaleal hematoma. The patient is subsequently discharged home. The mother and patient follow up with their pediatrician the next day without sequelae.

D. Kimball, B.S. (✉)
St. George's University School of Medicine,
3500 Sunrise Highway, Bldg 300, Great River, NY 11739, USA
e-mail: jpgreenf@med.cornell.edu

J.P. Greenfield, M.D., Ph.D.
Associate Professor of Neurological Surgery,
Weill Cornell Medical College, 525 East 68th Street,
Box 99, New York, NY 10065, USA

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_26

Introduction to Pediatric Head Injuries

Traumatic brain injury is the leading cause of death and disability in children worldwide and accounts for approximately 650,000 emergency department (ED) visits per year in the USA [11, 15, 18]. Conventionally, traumatic brain injury (TBI) is graded on a continuum ranging from mild to severe [10]. Mild head trauma is defined as a blunt trauma to the head resulting in a child who is alert and awake (in children under 2 years of age) or has a Glasgow Coma Scale of 14 or 15 (in children 2 years of age and older) [7, 17]. Most children who present with mild head trauma have little or no neurologic sequelae; a minority, however, who present with a minor head injury may have an underlying traumatic brain injury (TBI) and are at risk of deterioration and progression toward poorer neurologic outcomes [6, 13].

While over 85 % of the TBIs occurring annually in the USA are considered mild [1, 18], more severe injuries are associated with significant morbidity and mortality [10]. As such, considerable attention has been devoted to their understanding and management [10]. It has been estimated that 3–5 % of pediatric patients who present to the emergency department (ED) with a minor head injury have a TBI, and *less than 1 % of these patients require neurosurgical intervention* [9, 18].

Assessing the Patient

When evaluating the pediatric patient with suspected mild head injury, it is important to keep in mind the overall goals of assessment: It is the responsibility of the clinician to identify those children with a mild head injury who may have an underlying traumatic brain injury and may require immediate surgical intervention or medical monitoring. Due to the high-risk nature of these injury and potential for delayed neurologic sequelae, it is important to maintain a high degree of suspicion of TBI when a possible mechanism is identified.

Although controversy exists over the use of clinical predictors of intracranial injury in pediatric mild head injuries (MHI), there are some widely accepted indicators that every clinician should recognize when taking a history and physical (H&P) exam [18]. Findings within the history that may point to a more serious underlying pathology include amnesia, abnormal drowsiness, vomiting, or episode(s) of seizure [8]. On physical exam, findings that are more likely to suggest an underlying TBI include a GCS < 14, focal neurologic signs, or signs of a basilar skull fracture (periorbital hematoma, or "raccoon eyes," hemotympanum, Battle's sign, rhinorrhea, or otorrhea) [8] (Fig. 26.1). In children ≤ 2, scalp hematoma has also been shown to be a significant predictor of underlying TBI [15]. Finally, the mechanism of injury should be considered: A motor vehicle collision, fall from a height > 3 ft, or a high-speed injury from a projectile or object should all raise the suspicion of an underlying TBI requiring neurosurgical intervention [8].

Imaging and Decision-Making

Although most pediatric patients with mild head injuries can be safely discharged after some period of observation, a minority of patients will have an underlying TBI requiring neurosurgical intervention [14]. Intracranial injuries that may be amenable to surgical intervention include, but are not limited to, epidural hematomas, subdural hematomas, intraparenchymal hemorrhage, and intraventricular hemorrhage (Fig. 26.2). These lesions may result in increased intracranial pressure, mass effect, brain herniation, and ultimately death.

The use of computed tomography (CT) is integral in the early detection and diagnosis of TBIs requiring surgical management [14]. Cranial CT is currently the reference standard investigative procedure for intracranial injury. It provides rapid identification and guides management. Early diagnostic imaging has been linked to improved outcomes and reduced admission rates [12, 13, 16].

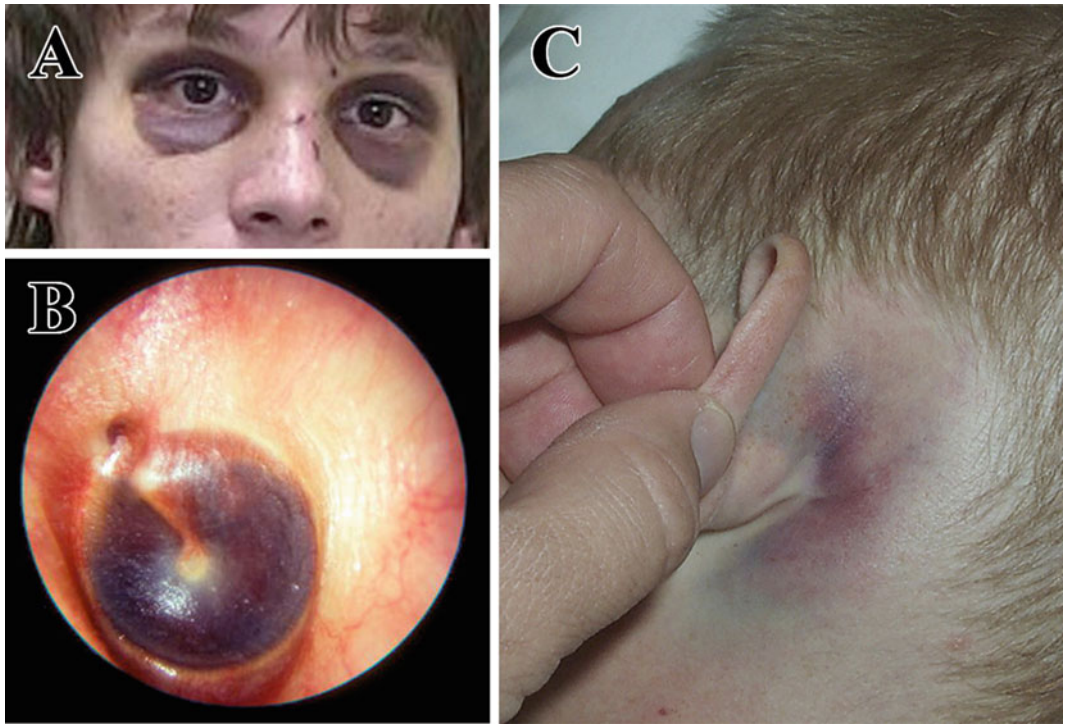


Fig. 26.1 Clinical signs of basal skull fractures. (**a**) Periorbital ecchymosis or "raccoon eyes." (**b**) Hemotympanum, or presence of blood within the middle ear, as seen through an otoscope. (**c**) Battle's sign, or mastoid ecchymosis, indicating a fracture of the middle cranial fossa

Over the past decade, the use of CT for minor head injury has become increasingly common [14]. About 50 % of children assessed in North American emergency departments for head trauma undergo CT [11].

An important question should be addressed: Due to the high-risk nature of the injury and potential for serious and life-threatening sequelae, why not image every pediatric patient with a mild head injury? The answer is twofold: The increased use of CT scans adds substantially to rising healthcare costs, and more importantly, scanning every child with a mild head injury would expose a large number of children each year to the potentially harmful effects of ionizing radiation [2–4, 13, 14]. See Chap. 20 (L. Heier) for a full review of this important topic. The estimated rate of lethal malignancies from CT is between 1 in 1000 and 1 in 5000 pediatric cranial CT scans, with risk increasing as age decreases [2, 4, 11]. The responsibility, therefore, falls on pediatricians providing primary care for the mild head injury pediatric patient to make a sound clinical decision regarding the need for further imaging. Fast, limited sequence MRI protocols for head injuries and hydrocephalus are gradually being introduced and utilized and pediatric hospitals, but routine use across the country remains more of an ideal than a reality. The vast majority of emergency departments are not equipped with 24-h MRI availability, pediatric anesthesiologists, and the expertise to institute these protocols. CT is faster and cheaper, rarely requires sedation, and is ubiquitous.

Clinical decision rules (CDRs) are algorithms, based on peer-reviewed studies, that help clinicians make well-informed, evidence-based medical decisions. They use elements of patient history, physical examination, or simple tests to provide the clinician with a decision-making tool. In an

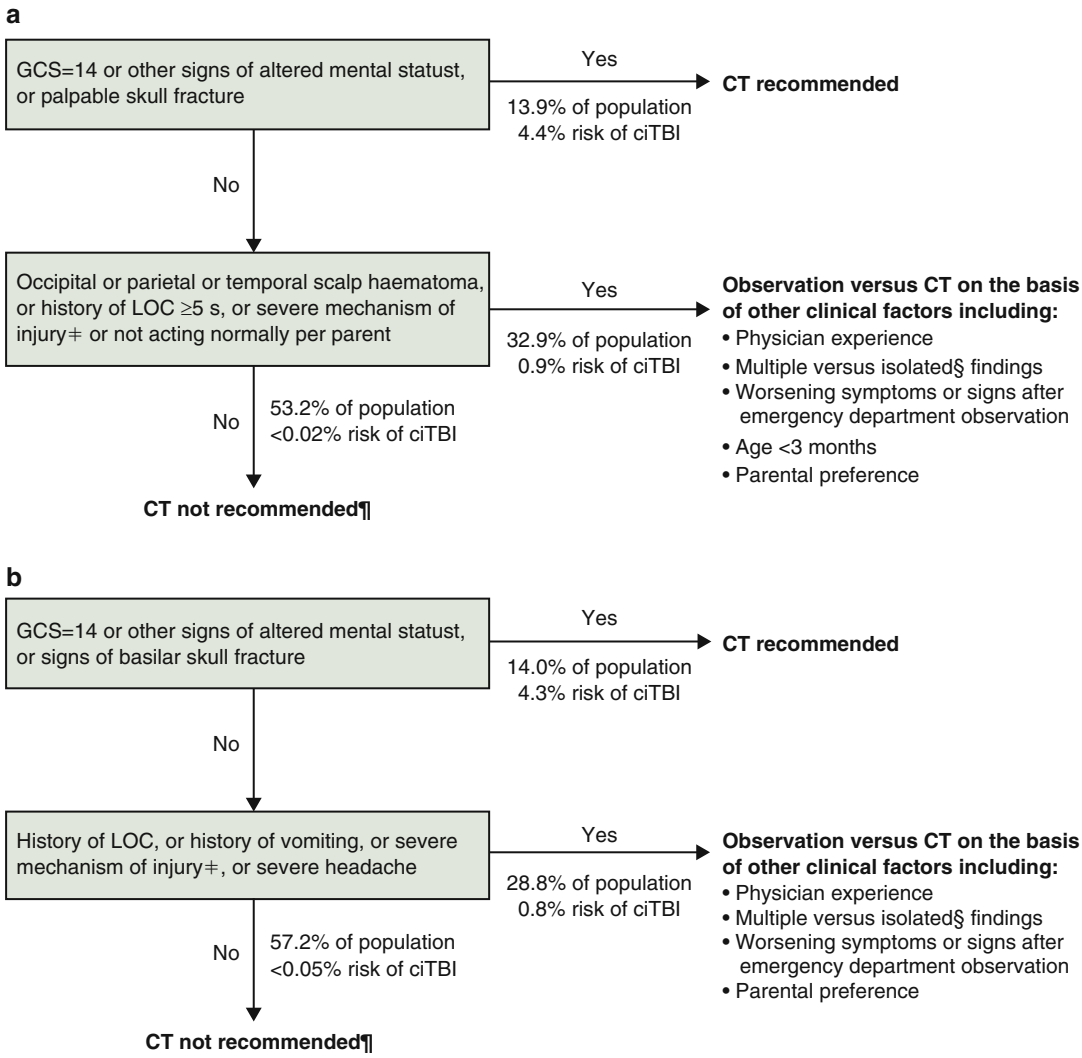


Fig. 26.2 Suggested CT algorithm for children younger than 2 years (**a**) and for those aged 2 years and older (**b**) with GCS scores of 14–15 after head trauma. GCS = Glasgow Coma Scale. ciTBI = clinically important traumatic brain injury. LOC = loss of consciousness. †Other signs of altered mental status: agitation, somnolence, repetitive questioning, or slow response to verbal communication. ‡Severe mechanism of injury: Motor vehicle crash with patient ejection, death of another passenger, or rollover; pedestrian or bicyclist without helmet struck by a motorized vehicle; falls of more than 3 ft (or more than 5 ft for panel **b**); or head struck by a high-impact object. §Patients with certain isolated findings (i.e., with no other findings suggestive of traumatic brain injury), such as isolated LOC, isolated headache, isolated vomiting, and certain types of isolated scalp hematomas in infants older than 3 months, have a risk of ciTBI substantially lower than 1%. ¶Risk of ciTBI exceedingly low, generally lower than risk of CT-induced malignancies. Therefore, CT scans are not indicated for most patients in this group

attempt to optimize the balance between identifying significant intracranial injury and minimize the risks associated with cranial CTs, several CDRs for mild pediatric head injuries have been derived [8, 11, 14]. There are three large, well-recognized, CDR studies regarding the use of CT scans in the pediatric patient with mild head injury. They include the PECARN [11], CHALICE [8], and CATCH [14] studies. All are well written and regarded highly and provide a

decision-making tool regarding CT imaging in the pediatric patient with minor head injury.

We will review the results and CDRs from the Pediatric Emergency Care Applied Research Network (PECARN) study to provide an infrastructure upon which primary care providers may make their own evidence-based decisions and to gain a more complete understanding of CT decision-making rules in the pediatric patient presenting with mild head injury. Compared to the CATCH and CHALICE studies, PECARN had the largest number of enrolled patients and has been prospectively validated.

PECARN is a large-scale, prospective study whose aim was to identify children at very low risk of clinically important traumatic brain injuries (ciTBI) for whom CT might be unnecessary. A clinically important traumatic brain injury was defined as a TBI that resulted in a hospital admission of more than one night, intubation for more than 24 h, neurosurgical intervention, or death. The authors enrolled patients younger than 18 years presenting within 24 h of head trauma with Glasgow Coma Scale scores of 14–15 in 25 North American emergency departments. Age-specific prediction rules for ciTBI were then derived.

Below, we present the recommendations from the PECARN study in order to help educate and guide the pediatrician appropriately. It is important to remember, however, that although this algorithm was developed in order to help guide the clinician, there is no replacement for sound clinical judgment and clinical experience. As such, the pediatrician should take the following recommendations in context.

Recommendations for CT in Children Under 2 Years of Age Derived from PECARN

A CT scan is recommended if the child has a GCS of less than 15 (i.e., anything less than a perfect GCS score) or has any other signs of altered mental status, including agitation, somnolence, repetitive questioning, or slow response to verbal communication. Additionally, if the child has a palpable skull fracture, it is recommended to obtain a head CT. In the PECARN study, this group included 13.9 % of enrolled children under the age of two presenting with a mild head injury. Within that population, there was a 4.4 % risk that those children would have a "clinically important" traumatic brain injury (TBI) as defined above.

If the patient (younger than 2 years of age) has none of the aforementioned signs or symptoms, the clinician must then consider the following questions: Does the patient have an occipital, parietal, or temporal scalp hematoma? Notably, there was no significant increased risk of clinically important TBI, according to the PECARN study. Did the child lose consciousness for more than 5 s? Was there a severe mechanism of injury? The PECARN study included severe mechanisms of injury as motor vehicle crash with patient ejection, death of another passenger, or rollover; pedestrian or bicyclist without helmet struck by a motorized vehicle; falls of more than 3 ft (more than 5 ft in children 2 years and older); or head struck by a high-impact object. Finally, an important question that should be directed toward the parent is as follows: Is the child acting abnormally? If the answer to all of the above questions is "no," then it is suggested to not proceed with a CT scan. In the PECARN study, a CT scan was not recommended in the majority (53.2 %) of enrolled children under the age of two that presented with a mild head injury. Within this group of children, the associated risk of ciTBI was less than 0.02 %. If "yes" was answered to any of the above questions, then the child falls into a third category.

The third category is described as "observation versus CT on the basis of other clinical factors." In the PECARN study, 32.9 % of the enrolled participants fell within the third category. The risk of a ciTBI (0.9 %) is still low in this group of patients. In this group, the physician may make a clinical decision as to whether or not the patient should be taken for a CT based on their experience. Additionally, the parents may have a preference after weighing the pros and

cons of a CT scan, as explained by the pediatrician. Although it is widely accepted that effects of harmful ionizing radiation increase with decreasing age of the patient, a CT scan should be more strongly considered in patients under 3 months of age. Notably, in patients with certain isolated findings (i.e., with no other findings suggestive of traumatic brain injury), such as isolated loss of consciousness, isolated headache, isolated vomiting, and certain types of isolated scalp hematomas in infants older than 3 months, a head CT may not be warranted. These patients have a risk of ciTBI substantially lower than 1 %. Of course, worsening signs or symptoms should prompt the clinician to obtain a head CT.

PECARN Recommendations for Obtaining a CT in Children 2 Years of Age and Older

The PECARN algorithm obtaining a head CT in children 2 years of age and older is similar to that of the algorithm for that of children less than 2 years, with slight differences. A CT scan is recommended if the child has a GCS of less than 15 or has any other signs of altered mental status, including agitation, somnolence, repetitive questioning, or slow response to verbal communication. If the child has signs of a basilar skull fracture (Fig. 26.2), it is recommended to obtain a head CT. In the PECARN study, this group included 14.0 % of enrolled children over two who presented with mild head injury. Within that population, there was a 4.3 % risk that those children would have a ciTBI.

If the child has none of the aforementioned signs or symptoms, the clinician must then consider the following questions: Does the patient have a history of loss of consciousness, vomiting, or severe headache? Was there a severe mechanism of injury? If the answer to all of the above questions is "no," then one should not recommend a CT scan. In the PECARN study, a CT scan was not recommended in the majority (57.2 %) of enrolled children two and over that presented with a mild head injury. In this group, the associated risk of ciTBI was less than 0.05 %. Similarly to the <2 years of age group, if there was a "yes" answered to any of the above questions, then the patient falls into a third category.

The third category is described as "observation versus CT on the basis of other clinical factors." In the PECARN study, 28.8 % of the enrolled participants fell within the third category. The risk of a ciTBI (0.8 %) is still low in this group of patients. Similarly to the <2 years of age group, the physician may make a clinical decision as to whether or not the patient should be taken for a CT based on their experience and after parental education by the pediatric practitioner. In patients with certain isolated findings (i.e., with no other findings suggestive of traumatic brain injury), such as isolated loss of consciousness, isolated headache, and isolated vomiting, a head CT may not be warranted. Like their <2 years of age counterparts, these patients have a risk of ciTBI substantially lower than 1 %. Of course, worsening signs or symptoms should always prompt the clinician to obtain a head CT.

What to Tell Parents

In the acute period, the immediate management goals for the child's caretakers are twofold. First, if the child is not going to be observed in a hospital or other medical setting, all healthcare personnel should ensure that the family is competent to identify and act upon medical emergencies [10]. Most life-threatening problems after mild head injuries occur within the first 24 h, but caretakers must remain vigilant for any change in the child's status for several days post-injury [10]. Second, similar to management at the individual youth level, making sure caregivers have an adequate understanding of mild TBIs and the typical clinical course is beneficial. Misconceptions about brain injury are common in lay populations [10]. It is important, therefore, for the pediatrician to

provide a satisfactory amount of educational information to the parents regarding TBIs [10]. Parents should be guided accordingly in order to obtain *credible and reliable* educational material regarding TBIs. There are commercial publications, as well as multiple handouts, available for free online (e.g., from the US Centers for Disease Control and Prevention http://www.cdc.gov/TraumaticBrainInjury/index.html). Education and reassurance of parents is an important part of the care of this population of patients, and one might take the opportunity of the post-injury office visit to readdress common causes of head injury and recommended practices to reduce the incidence.

Prevention

In the CATCH study [14], the four leading causes of head injury were falls, sports, "head struck or hit by object," and bicycle-related trauma. Combined, these four mechanisms accounted for 88 % of the mild head injuries of the children enrolled in the study. It is possible, therefore, to prevent many of these injuries by taking the necessary precautions.

There is strong evidence to support the use of bicycle helmets to prevent mild traumatic brain injury [5]. As such, the authors find it appropriate for the pediatrician to make a recommendation for the child to always wear a helmet when bicycling as part of active teaching. Additionally, bicycle helmets should be fitted and worn properly. We recommend wearing a helmet for other sport-related activities in addition to riding a bicycle. Skateboarding or in-line skating, contact sports, and skiing all warrant the use of a helmet. Parents should use sound judgment to properly protect their children among such activities, and graded supervision is recommended for all childhood participating in sporting events.

In terms of preventing mild and severe TBIs, car safety is key. Car seats and booster seats should be installed correctly, and the child should *always* remain within the confines of the seat while riding in the car. A booster seat should be utilized until the child can sit comfortably without the booster seat and the seat belt should stretch across the shoulder (not the face). Many states have specific booster seat regulations. As such, pediatricians should check with their local state department regarding additional booster seat regulations or requirements. It is important to note that local police departments are usually trained in the correct installation of car and booster seats. Parents should not hesitate to ask for help when unsure of the correct installation of a car or booster seat.

Home safety is also an important topic to discuss with parents. In general, parents should install a safety gate on the tops and bottoms of stairs until the child is able to go up and down safely. Children should not play on stairs. Finally, parents should not leave infant alone on beds, changing tables, or couches where there is potential for fall, which may lead to head injury.

Conclusion

Most children who present with mild head trauma have little or no neurologic sequelae. A very small number of children, however, who present with a minor head injury may have an underlying traumatic brain injury and are at risk of preventable poor neurologic outcomes. It is the responsibility of the clinician to identify those children with a mild head injury who may have an underlying traumatic brain injury and may require immediate surgical intervention or medical monitoring. Due to the high-risk nature of intracranial injuries and the potential for unfavorable outcomes, the clinician must maintain a high degree of suspicion of TBI. The PECARN study provides clinicians with a useful decision-making tool to determine whether or not a head CT scan is warranted. It is important to remember, however, that although this algorithm was developed in order to help guide the clinician, there is no replacement for sound clinical judgment and clinical experience.

Findings within the history that may point to a more serious underlying pathology include: amnesia, drowsiness, emesis, or episode(s) of seizure.

Signs of a basilar skull fracture indicative of serious force head strike:

Periorbital hematoma, or "raccoon eyes," hemotympanum, Battle's sign, rhinorrhea, or otorrhea

Major risks of severe TBI: a motor vehicle collision, a fall from a height>3 ft, or a high-speed injury from a projectile

Pediatrician's Perspective

Helping guide a parent on the phone or in the office, through the difficult decision-making of whether to seek medical attention for a witnessed head strike, is extremely challenging. The red flag signs listed above should help guide care toward a facility—office from home or emergency room from office—where a healthcare provider can medically assess the child and offer imaging if deemed to meet established criteria.

A CT scan is recommended in a child less than 2 if the child has a GCS of less than 15 or has any other signs of altered mental status, including agitation, somnolence, repetitive questioning, or slow response to verbal communication. The rarity of neurosurgical sequelae should be reassuring to providers, but as in this difficult primary care scenario, identifying the one child who sounds like they meet evaluation or imaging criteria could be life saving.

References

1. Bazarian JJ, Mcclung J, Shah MN, Ting Cheng Y, Flesher W, Kraus J. Mild traumatic brain injury in the United States, 1998-2000. Brain Inj. 2005;19(2): 85–91.
2. Brenner DJ. Estimating cancer risks from pediatric CT: going from the qualitative to the quantitative. Pediatr Radiol. 2002;32(4):228–31.
3. Brenner DJ, Elliston CD, Hall EJ, Berdon WE. Estimated risks of radiation-induced fatal cancer from pediatric CT. Am J Roentgenol. 2001;176(2):289–96.
4. Brenner DJ, Hall EJ. Computed tomography—an increasing source of radiation exposure. N Engl J Med. 2007;357(22):2277–84.
5. Cassidy JD, Carroll L, Peloso P, Borg J, Von Holst H, Holm L, et al. Incidence, risk factors and prevention of mild traumatic brain injury: results of the WHO Collaborating Centre Task Force on Mild Traumatic Brain Injury. J Rehabil Med. 2004;36:28–60.
6. Crowe L, Babl F, Anderson V, Catroppa C. The epidemiology of paediatric head injuries: data from a referral centre in Victoria, Australia. J Paediatr Child Health. 2009;45(6):346–50.
7. Davis RL, Mullen N, Makela M, Taylor JA, Cohen W, Rivara FP. Cranial computed tomography scans in children after minimal head injury with loss of consciousness. Ann Emerg Med. 1994;24(4):640–5.
8. Dunning J, Daly JP, Lomas JP, Lecky F, Batchelor J, Mackway-Jones K. Derivation of the children's head injury algorithm for the prediction of important clinical events decision rule for head injury in children. Arch Dis Child. 2006;91(11):885–91.
9. Haydel MJ, Shembekar AD. Prediction of intracranial injury in children aged five years and older with loss of consciousness after minor head injury due to nontrivial mechanisms. Ann Emerg Med. 2003;42(4):507–14.
10. Kirkwood MW, Yeates KO, Taylor HG, Randolph C, McCrea M, Anderson VA. Management of pediatric mild traumatic brain injury: a neuropsychological review from injury through recovery. Clin Neuropsychol. 2008;22(5):769–800.
11. Kuppermann N, Holmes JF, Dayan PS, Hoyle Jr JD, Atabaki SM, Holubkov R, et al. Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. Lancet. 2009;374(9696):1160–70.
12. Lyttle MD, Crowe L, Oakley E, Dunning J, Babl FE. Comparing CATCH, CHALICE and PECARN clinical decision rules for paediatric head injuries. Emerg Med J. 2012;29(10):785–94.
13. Lyttle MD, Cheek JA, Blackburn C, Oakley E, Ward B, Fry A, et al. Applicability of the CATCH, CHALICE and PECARN paediatric head injury clinical decision rules: pilot data from a single Australian centre. Emerg Med J. 2013;30(10):790–4.
14. Osmond MH, Klassen TP, Wells GA, Correll R, Jarvis A, Joubert G, et al. CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury. Can Med Assoc J. 2010; 182(4):341–8.
15. Palchak MJ, Holmes JF, Vance CW, Gelber RE, Schauer BA, Harrison MJ, et al. A decision rule for identifying children at low risk for brain injuries after blunt head trauma. Ann Emerg Med. 2003;42(4):492–506.
16. Pickering A, Harnan S, Fitzgerald P, Pandor A, Goodacre S. Clinical decision rules for children with minor head injury: a systematic review. Arch Dis Child. 2011;96(5):414–21.
17. Schutzman SA, Greenes DS. Pediatric minor head trauma. Ann Emerg Med. 2001;37(1):65–74.
18. Thiessen ML, Woolridge DP. Pediatric minor closed head injury. Pediatr Clin North Am. 2006;53(1):1–26.

Evidence Based Medicine Resources

PECARN: Kuppermann N, Holmes JF, Dayan PS, Hoyle Jr JD, Atabaki SM, Holubkov R, et al. Identification of children at very low risk of clinically-important brain injuries after head trauma: a prospective cohort study. Lancet 2009; 374(9696): 1160–1170. (Kuppermann et al., 2009)

CHALICE: Dunning J, Daly JP, Lomas JP, Lecky F, Batchelor J, Mackway-Jones K. Derivation of the children's head injury algorithm for the prediction of important clinical events decision rule for head injury in children. Arch Dis Child 2006; 91(11): 885–891.

CATCH: Osmond MH, Klassen TP, Wells GA, Correll R, Jarvis A, Joubert G, et al. CATCH: a clinical decision rule for the use of computed tomography in children with minor head injury. Can Med Assoc J 2010; 182(4), 341–348.

Non-accidental Head Trauma

27

Lara M. Gordon

Vignette A 7-month-old child is brought into your office after the mother noticed a swelling over the right side of the parietal skull. The child has been slightly fussy when awake for the past week and sleeping considerably longer than normal. You order a skull X-ray which demonstrates a significant skull fracture and shows a subgaleal collection. Mom vehemently denies any trauma but does admit that the child is not with her for 8 h every day while she is at work. You suggest she take the baby to the emergency department.

History

In 1946, Dr. John Caffey, a pediatric radiologist, was the first to describe an association between long-bone fractures and intracranial hemorrhages without external signs of injury in children [6]. He concluded in his report that the same traumatic mechanism caused both injuries. In 1971, A.N. Guthkelch looked at "infantile subdural hematomas and its relationship to whiplash injuries" [15]. He concluded that subdural hematomas were the result of "acceleration-deceleration" forces seen with shaking rather than "direct violence" from impact to the infant's head. Caffey later coined the term "whiplash shaken baby syndrome" to describe the combination of intracranial hemorrhage, long-bone fractures, and retinal hemorrhages with minimal or absent signs of external trauma [7]. Availability of computed tomography (CT) in the 1970s and magnetic resonance imaging (MRI) by the mid-1980s assisted exponentially with diagnoses of non-accidental head trauma which previously had been hard to radiographically define. These new technologies have helped to better understand the timing and evolution of intracranial hemorrhages after an injury. In 1987, Duhaime et al. reported that while shaking may be involved in causing an infant's injuries, in some cases, especially in those that present in the more severe form, blunt impact may also come into play. These injuries involve the impact that results in focal injury and acceleration-deceleration forces that occur as the head is moving forward and then stopped at the point of impact, causing shearing forces on the bridging blood vessels and brain parenchyma [11].

The importance of impact has been a controversial issue and efforts to better understand the precise mechanism continues. The term *shaken baby syndrome* alone does not accurately represent those infants who demonstrate not only

L.M. Gordon, M.D. (✉)
Department of Pediatrics, New York Presbyterian Hospital – Weill Cornell Medical Center,
215 East 79th Street, New York, NY 10075, USA
e-mail: larobno@yahoo.com

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_27

acceleration-deceleration injuries but also impact injuries. Because the specific mechanism of injury is rarely known with certainty, the terms *abusive head trauma* or *non-accidental head trauma* have been adopted as more broad and inclusive. These terms allow for the possibility of different mechanisms to explain a child's clinical and radiographic findings and do not narrowly define an injury as a single occurrence or event. Understanding the biomechanical and biochemical events behind each individual finding has been paramount toward improving the diagnosis and treatment of these injuries, as well as the development of prevention programs to educate the public about this devastating type of physical child abuse.

Epidemiology: Incidence and Prevalence

Head trauma is the most common cause of child abuse fatalities. Incidence and prevalence are difficult to measure due to varied definitions and criteria for diagnosing intentional head trauma, unrecognized abuse, and a degree of physician reluctance to report certain injuries as abuse. The incidence during the first 2 years of life has been estimated to be between 16 and 30 cases per 100,000 infants per year. Children under 1 year of age are at the highest risk, with lower risk between 1 and 2 years, and the rate decreases thereafter [2, 19, 29]. Mortality has been found to be higher in children with inflicted injury (16.8%) compared to those with accidental injury (10.7%) [29].

Risk Factors

Several studies have looked at the relationship between the infant and the perpetrators of abusive head trauma. Most studies show that males are identified as the perpetrator more often than females [20, 31, 32]. Debra Esernio-Jenssens et al. found when examining the effect of perpetrator gender on victim presentation and clinical outcomes that male perpetrators were younger and more likely to confess and be convicted. They also found that victims of male perpetrators had more serious acute presentations and suffered worse outcomes [13].

When looking at socioeconomic factors, households with young parents, single parents, lower socioeconomic status, presence of extended family or unrelated adults in the home, and/or previous child abuse are at higher risk for abusive head trauma [30, 31]. Infant prematurity, illness, and disability also put an infant at risk. Episodic crying in the newborn period where an infant is inconsolable may a trigger an inexperienced or frustrated caretaker to engage in a shaking event.

Due to the varied ways children can present as a result of abusive head trauma with often a lack of history given by the caretaker, intentional head trauma can be missed by physicians. When examined in isolation, each finding can result from inflicted trauma, accidental trauma, or other nontraumatic causes. This is most common in cases where a child presents with more nonspecific, less severe symptoms that are common to infancy, such as fussiness, crying, vomiting, lethargy, and loss of appetite. Abusive head trauma is also missed when there are no apparent external signs of trauma, such as scalp swelling or bruising. Carole Jenny et al. studied 173 children with abusive head injuries and found that 32.2% (54 cases) were missed [18]. When these missed cases were compared to recognized cases, several differences were found regarding age, race, family composition, and severity of symptoms at the initial visit. Infants less than 6 months of age, of minority race, and with parents living apart were found to be more likely missed at the initial visit. Children who presented with irritability or vomiting were less likely identified as opposed to children presenting with respiratory distress, seizures, or facial bruising. This study demonstrates the difficulty in making a correct diagnosis in cases of abusive head trauma, especially when the caretaker gives an inaccurate history. For this reason, *abusive head trauma should be considered in the differential diagnosis in cases of an infant with nonspecific symptoms*.

Biomechanics and Non-accidental Head Trauma

Skull fractures, intracranial bleeding, retinal hemorrhage, and skeletal findings can be found in cases of non-accidental head trauma. The biomechanical conditions that cause these injuries have been studied to help understand how these injuries occur and help in prevention, diagnosis, and treatment approaches. Shaking is a commonly reported mechanism of injury reported by perpetrators who admitted to abuse. Starling and her colleagues [32] found that, in 81 cases where the perpetrator admitted to injuring the baby, 61% reported shaking. Impact trauma, either alone or combined with shaking has also been described and can result in significant head injury. In severe cases, cervical spine injury has also been found.

The mechanism of injury that leads to injuries seen in abusive head trauma, such as subdural hematomas, retinal hemorrhage, diffuse axonal injury, and skeletal findings, has been greatly discussed in the literature. One large debate has been whether shaking alone can cause the severe injuries seen in infants. This is the reason the terminology has changed from *shaken baby syndrome* to *abusive head trauma*. This term does not limit the mechanism to shaking alone but includes other possible mechanisms that may be involved. Due to the lack of physical models, many biomechanical questions remain unanswered.

The forces acting on the head in non-accidental trauma include contact and inertial (acceleration and/or deceleration) forces. Contact forces occur when the head is struck by an object or comes in contact with a hard surface, as in a fall. Upon impact, there is deformation at the point of impact and forces are distributed. This is why visible signs of impact may not always be seen. Inertial forces occur as the brain and its structures are placed in motion. This includes the acceleration-deceleration motion that occurs when these structures are in motion and suddenly stopped. Inertial forces can be either translational, in which structures move in a straight line, or rotational, in which they move around an axis or center of rotation. The center of rotation is usually the cervical spine in the case of shaking. These forces can cause shearing of parasagittal bridging veins which leads to subdural hematomas and diffuse axonal injury. This also explains some contrecoup injury at the point opposite to impact where the brain is stopped in its motion. The acceleration-deceleration forces not only have an impact on the bridging vessels of the brain but also can cause diffuse axonal injury, injury to the vessels and nerves of the eye, and spinal cord injury.

In addition to the type of force that is involved, the amount of force is equally important in predicting and assessing intracranial injuries. Impact forces depend on the amount of force applied to the head by an object or the height of a fall. The higher the fall, the greater the impact on the head. The magnitude of rotational forces are influenced by the velocity of the acceleration and deceleration. The greater the velocity, the greater the forces of acceleration and deceleration. Generally, the greater the forces, the greater the severity of injury and the deeper it extends into the brain [28].

Medical terminology should reflect the medical diagnosis. For this reason, the term "shaken baby syndrome" should not be used in infants with impact alone or with multiple mechanisms of head and brain injury. In the 2009 policy statement by The American Academy of Pediatrics, they recommended the adoption of the term "abusive head trauma" as the diagnosis. This term more accurately describes the "constellation of cerebral, spinal, and cranial injuries that result from inflicted head injury to infants and young children" [8].

Clinical Presentation

The presentation of a child who has suffered abusive head trauma can vary greatly depending on the mechanism and severity of the injury. The presentation of accidental trauma and abusive head trauma can also overlap and look very similar, making a diagnosis of intentional trauma difficult. However, most low-impact injuries and short-distance falls are well tolerated and severe

injuries are less likely to result. Since much of the research and analysis of abusive head trauma is focusing on the mechanism of injury and acute and delayed distributed injuries, the classification had been divided into *primary* and *secondary* traumatic brain injury much the way accidental head trauma research has divided the acute and delayed effects of severe TBI.

Primary Traumatic Brain Injury

Primary brain injury is that which is the direct result of the initial traumatic force. These include neuronal and glial disruptions, vascular injuries, axonal shearing, and penetrating lacerations. Primary traumatic injury can be divided into focal and diffuse injuries [14]. The focal injuries can result from contact or translational inertia forces. Contact forces include soft tissue injuries, skull fractures, acute epidural and subdural hematomas, superficial cortical contusions, and/or lacerations. Translational inertial forces include contrecoup lesions, intracerebral bleeds, and petechial hemorrhages. The diffuse injuries occur as a result of rotational inertia and are associated with immediate alterations of consciousness. These include concussions, subdural hematomas, subarachnoid hemorrhages, and traumatic axonal injury. These alterations of consciousness may be prolonged or brief. There can certainly be some overlap between focal and diffuse primary brain injuries as seen with intracranial bleeds. The term "primary injury" does not imply that the symptoms that arise from them are necessarily immediate; they may take time to evolve. These symptoms include change in mental status, loss of consciousness, apnea, seizures, vomiting, lethargy, irritability, or cardiorespiratory distress due to brain stem dysfunction.

Secondary Traumatic Brain Injury

Secondary traumatic brain injury occurs as a result of the complications that arise from the primary brain injury. Tissue that was not initially damaged becomes affected due to sequelae of the primary injury. Usually these result from complications caused by systemic and metabolic factors, such as electrolyte abnormalities, damage from seizures, and systemic hypotension. Common secondary injuries in abusive head trauma include focal and diffuse cerebral edema, hypoxic-ischemia, mass effect, and herniation. Some clinical signs and symptoms of secondary traumatic brain injury are decreased mental status due to progressive brain swelling with or without herniation, seizures, irritability, vomiting, and focal neurologic findings.

There can often be a delay in the clinical deterioration of children with abusive head trauma. This can be due to slowly evolving mass effect from accumulating chronic hematomas, brain edema, electrolyte imbalances, and hypoventilation with hypercarbia. Children may also present with subclinical seizures that are not readily recognizable by an observing physician. This can lead to missed diagnoses in children who have been abused. Many of these symptoms are nonspecific with little to no external evidence of injury. In many cases, inaccurate or incomplete histories are given and the physician is unsuspecting.

Diagnostic Evaluation

History Taking

History of Present Illness

A large part of the diagnostic evaluation in any form of child abuse is obtaining a thorough and detailed history from the caregivers as to the events that lead to the present injury. Many times this history is inaccurate, incomplete, or fabricated. It is the job of the physician to determine if the history given is consistent with the injuries found in the child. The details that are important to obtain include: (a) The child's health prior to the injury and when the child was last known to be clinically well; (b) Any history of trauma, including any impact to the head or fall; (c) If there was a fall, the height from which the child fell and the position the child was found in; (d) Any loss of consciousness, vomiting, or seizure activity following the fall. In addition, it is important to ask who, if anyone, was present during the event and what was done from the time of the injury

leading up to the child's presentation to medical attention. It is important to note any discrepancies in the history given by more than one caretaker and/or if these histories change over time. It is also important to note any developmental inconsistencies in the history.

Past Medical History

Getting a thorough and complete past medical history is an important part of the medical work-up for abusive head trauma. It should include pregnancy history, birth history, and neonatal history, including prematurity. It should also include past hospitalizations, chronic illnesses, and previous injuries. Going through a review of symptoms can also be helpful in finding out if a child has any symptoms related to brain injury.

Social History

Obtaining a social history involves finding out who lives in the home with the child and who are the primary caretakers. It is also important to screen for any social stressors in the home like recent divorce, illness, unemployment, and death in the family. Screening for previous child protective services involvement may also be helpful.

Family History

Family history of bleeding disorders, metabolic conditions, or bone disorders should be explored. It is often necessary to rule out any genetic predisposition to bleeding or fractures before making a determination of abusive head trauma.

Physical Exam

The first step in medically examining any child is to ensure there is a competent airway, sufficient respirations, and appropriate circulation. A child with apnea or in respiratory distress should be considered for intubation because hypoventilation could worsen any existing brain injury. Next, as in most trauma cases, spine immobilization should be performed to prevent any further injury and until spinal injury is ruled out by radiologic means. Once the child is stabilized, a head to toe exam should be performed.

Head and Neck

Examination of the head begins with obtaining a head circumference. An enlarged head size can indicate a congenital disorder such a glutaric aciduria type I, which can cause enlargement of the head and unexplained subdural hematomas. In the absence of this disorder, the sudden enlargement of the head may indicate the development of subdural hematomas. Palpating the scalp may reveal bogginess or crepitus over an area of a skull fracture. Since skull fractures heal quickly and cannot be dated, their presence lends itself to a more acute injury. Blood from the ears could indicate a basilar skull fracture. The head and neck should also be examined for any lacerations, abrasions, swelling, or bruising. Lesions on the neck may suggest ligature marks or fingerprints which raise the possibility of strangulation. Inside the mouth should also be examined to look for any frenulum tears, missing teeth, or other mucosal injuries that may suggest a blow to the mouth.

Skin

While marks seen on the head and neck are very telling, the skin over the rest of the body should be closely examined to look for any other associated injuries. This means that the child should be rolled over so both the front and back of the body is examined. Both old and new cutaneous findings are significant. Some of these skin markings could represent a specific pattern, indicating the instrument used to cause the injury. These marks could represent whipping with a belt or cord, handprints, bite impressions, or fingerprints in areas where the child was forcibly grabbed.

Abdomen

It is imperative to examine for any intra-abdominal injury as abdominal trauma is the second most common cause of death from child abuse. Look for signs of abdominal tenderness, rigidity, rebound, guarding, or loss of bowel sounds. If there is any suspicion of abdominal trauma, the child should be sent immediately for computed tomography (CT) scan. It could be argued that every child with reduced consciousness should be sent for CT of the abdomen since the mechanism of injury is unknown and the consequences of missing abdominal trauma is severe.

Genitals

Sex abuse can occur in conjunction with physical abuse, and for this reason, close attention should be placed on the genital exam. Each child can be examined in the frog-legged position, even if they are immobilized, and the genitals should be checked for bruises, abrasions, or lacerations.

Neurologic Exam

A carefully performed neurologic exam should be performed initially and serially during the admission. The child's mental status, responsiveness, and Glasgow scores should be documented. Look for any signs of seizure activity which could be as subtle as a gaze preference. Document any hypo- or hypertonicity, abnormal movements, or pupillary changes. Infants who do not grimace or cry when exposed to noxious stimuli are likely to have significant cortical impairment [1].

Neuroradiologic Evaluation

After obtaining a detailed history and performing a comprehensive physical exam, the next step is to obtain the appropriate radiologic studies to determine any intracranial, intra-abdominal, or bony injuries. Neuroimaging is essential in the "timely and accurate diagnosis of traumatic head injury" [17]. Neuroimaging is used to identify an injury in an infant who is either uncooperative or unconscious, examine the severity of the injury, and assist in the timing of the injury that can be helpful in a forensic investigation. Many neuroradiologic findings are closely associated with and help define abusive head trauma. Acute subdural hematomas in the interhemispheric fissure, the coexistence of acute and chronic subdural hematomas or any coexisting subdurals of multiple ages, subdural hematomas without any associated skull fractures, and the presence of old brain injuries in conjunction with the acute injury are all more commonly seen in children who are victims of abusive head trauma than accidental trauma (Boos, S in Frasier L 2006).

Computed Tomography

A child who presents with concerning neurologic signs should receive a computed tomography (CT) of the head. Even infants who do not exhibit any specific neurologic findings, but who present with associate injuries, such as unexplained fractures, bruising, or abdominal trauma concerning for non-accidental trauma, should be evaluated with a head CT. This is the preferred modality due to its accessibility, speed, ability to accommodate resuscitative equipment, and sensitivity to acute bleeding. Noncontrast head CT can identify acute intracranial hemorrhage, skull fractures, and severe cerebral edema and delineate mass effect.

Magnetic Resonance Imaging

Magnetic resonance imaging (MRI) of the head is performed if the findings on the head CT do not sufficiently explain the neurologic signs seen in a patient or to better define what is seen or suspected on CT. It is more sensitive for small and non-hemorrhagic traumatic brain injuries [17] and is useful in demonstrating subarachnoid hemorrhage, hypoxic-ischemic injury, diffuse axonal injury, and infarction. MRI is also the best modality to detect subacute and chronic subdural blood particularly with respect to accurately aging blood products due to the predictable degradation of heme and its clear signal on MRI. The downside of MRI is that it is not readily accessible in all centers and it often requires sedation to ensure there is no motion artifact.

Ultrasound

While head ultrasound is portable and easily performed at the bedside of an unstable child, it is not particularly useful as a screening tool. It is helpful for following the resolution of known blood collections and evaluation of hydrocephalus and midline shift in infants. It can also be useful in the assessment of white matter tears.

Plain Radiographs

Skull fractures can often be appreciated on the skull films that are included in the skeletal survey that is performed as part of the non-accidental trauma work-up. In fact, fractures can often

be seen more clearly on radiographs than CT due to the orientation of axial CT slices parallel to potential fracture planes. The skull films do not assist in dating an injury since callous formation does not occur in cranial bones. However, it can be helpful in distinguishing between a depressed fracture which suggests blunt trauma onto a curved or unsmooth surface as opposed to a linear skull fracture caused by impact onto a flat surface.

X-rays are also used to rule out any associated skeletal injury, such as posterior-lateral rib fractures and classic metaphyseal lesions. Rib fractures occur when an infant is held around the chest, below the axilla, and there is a squeezing force applied while the back is unsupported [22]. This is a common hand position during the shaking of an infant. Classic metaphyseal lesions (CMLs) can occur from the shearing forces of the limbs flailing during a shaking episode which puts stress on the ends of long bones of the arms and legs. CMLs involve "a series of microfractures through the most immature portion of metaphyseal bone" which is the site where maximum bone growth and turnover is occurring [21]. Neither of these skeletal findings are necessary in order to make a diagnosis of abusive head trauma, but their presence along with intracranial injury shifts the focus more toward an intentional mechanism.

Laboratory Evaluation

In conjunction with the physical exam, a comprehensive laboratory work-up is a mandatory part of this evaluation. This is done to both reveal any complications of abusive head trauma and to rule out any hematologic or metabolic disorders that could mimic the appearance of abusive head trauma. A hematologic evaluation, including a complete blood count (CBC) assesses for anemia and a white blood cell count, can rule out infection or malignancy. Platelet count and coagulation factors are drawn to explore the possibility of a clotting disorder. These include prothrombin time (PT) which when increased can reflect vitamin K deficiency and disseminated intravascular coagulation (DIC), and liver disease; partial thromboplastin time (PTT) which when prolonged may suggest a factor deficiency; and von Willebrand factor (vWF). Coagulation studies may be difficult to interpret in the setting of acute injury because the stress of injury alone often elevates these levels. Kent Hymel performed a study comparing coagulation studies of abusive head trauma victims with and without parenchymal damage (contusions, shearing injury, diffuse axonal injury, edema, atrophy) and found that 54% with parenchymal damage versus 20% without damage had mild PT prolongation. He concluded that head trauma causes tissue factor release from damaged parenchymal cells which then activates coagulation via the extrinsic pathway leading to DIC [16]. A fibrinogen level, D-dimer, and thrombin time can also be performed in these patients. The blood tests should also include a comprehensive metabolic panel, including liver function tests and amylase which have all been found to be sensitive indicators of occult intra-abdominal trauma, like hepatic or pancreatic injury.

A spinal tap may be performed if the child presents with nonspecific symptoms similar to meningitis. The CSF in cases of abusive head may appear to be similar to a traumatic tap. However, if multiple tubes are collected and elevated levels of red blood cells are seen in every tube without clearing, this may suggest subarachnoid hemorrhage from trauma. The presence of crenated cells in the tube suggests that they were present in the CSF and not due to a traumatic tap [14].

Lastly, some metabolic disorders can cause an increased risk of subdural hemorrhage and retinal hemorrhage. Glutaric aciduria type I is the most common described disorder which may first present as macrocephaly at birth or it may develop within the first few weeks of life. There is an accumulation of glutaric acid and its metabolites in the urine and the deficiency of the enzyme glutaric acid dehydrogenase in leukocytes or fibroblasts [26]. This disorder can cause frontotemporal atrophy, diffuse cortical atrophy, internal and external hydrocephalus, and subdural effusions. In some cases, subdural hematomas and/or retinal hemorrhages can be the first presenting sign of the disease and needs to be ruled out before a diagnosis of abusive head trauma is made.

Serum Brain Biomarkers

Biochemical markers are often used to indicate injury in specific organ systems. Injury and/or cell death to a cell within an organ results in the release of specific biomarkers from the injured cell. Lack of metabolite excretion may conversely result in intracellular accumulation. In brain injury, biomarkers may be released from brain tissue and passed into the cerebrospinal fluid and serum. Just as liver function tests indicate hepatic injury due to a variety of mechanisms, serum brain biomarkers cannot identify the etiology of the injury (i.e., abusive vs. non-abusive trauma). They can, however, serve as a screening tool for brain injury. Two studied biomarkers are S100B and neuron-specific enolase (NSE) [5]. S100B is a calcium-binding protein found in astrocytes and is used as a markers of glial injury. It is non-specific for brain injury in children less than 2 years of age, so it is not useful to this age group. NSE is an enzyme found in neuronal cytoplasm and is a marker of neuronal death which is increased in different types of head trauma. There are no biomarkers sensitive or specific for abusive head trauma vs. accidental head trauma. However, they can be used to guide the clinician in their work-up of brain injury to help explain nonspecific signs and symptoms such as vomiting, respiratory distress, and lethargy. Some biomarkers can also be used to help date an injury. For example, myelin basic protein (MBP) does not begin to rise until 24–48 h after injury. The presence of MBP in the serum of a child with suspected abusive head trauma suggests that the injury is not acute. Peak NSE levels occur between 24 and 36 h, so if the levels are initially high and then begins to decrease, it is possible that the injury did not occur in the 6–12 h prior to presentation [17]. The search for specific and sensitive biomarkers for abusive head trauma is a continued source of research and has great diagnostic potential for the future.

Ophthalmologic Exam

An ophthalmologic examination of children with suspected abusive head trauma should be performed using an indirect ophthalmoscope on a dilated pupil that allows viewing of the entire retina. Examination by a pediatrician using a direct ophthalmoscope is not sufficient. The eye can be injured directly by blunt head trauma involving the orbit. In addition, papilledema resulting from increased intracranial pressure or injury to the optic chiasm or cortical visual impairment due to parenchymal brain damage should be assessed by this crucial exam. The acceleration-deceleration forces seen in the setting of shaken baby syndrome can lead to retinal hemorrhage and optic nerve injury [25]. *Retinal hemorrhage along with subdural hemorrhage has been considered a red flag for abusive head trauma in infants*. Duhaime et al. found in one of their studies that retinal hemorrhages were found more often in children with abusive head trauma than in cases of accidental head trauma [12]. Only one patient in their study sustained retinal hemorrhage from accidental injury (motor vehicle accident). Bechtel et al. performed a study to determine the incidence of retinal hemorrhages in young hospitalized patients with accidental and abusive head trauma [4]. They found that retinal hemorrhages were seen significantly more often in children with abusive head trauma than accidental trauma, but they were seen in up to 10% of those with accidental injury. However, they also found that the type and location of the hemorrhages differed between the two groups. Hemorrhages seen in children with accidental trauma were most often unilateral, involved only one layer of the retina and confined to the posterior pole, and were often single bleeds. In those with abusive head trauma, the bleeds were more likely to be multi-layered throughout the retina involving the preretinal and intraretinal layers, multiple in number, and bilateral. Additionally, the bleeds extended into the periphery of the retina. Thus, it is not the presence alone of retinal hemorrhages that are diagnostic of abusive head trauma. Their location and number are helpful indicators of abuse.

The differential diagnosis of retinal hemorrhage should be considered since it is essential to identify cases where their presence is not a result of abusive head trauma. The most common cause of retinal hemorrhage in infancy is birth. These bleeds can occur throughout the retina and resolve

without sequelae. The most superficial ones resolve within 3–5 days and the deeper ones can take up to 6 weeks to disappear [23]. Therefore, *retinal hemorrhages seen after 6 weeks of age cannot be attributed to birth*. Hydrocephalus and increased intracranial pressure can cause retinal hemorrhages, but these are usually limited to the peripapillary area of the retina. Some hematologic abnormalities, such as leukemia, von Willebrand disease, vitamin K deficiency, DIC, and protein S and C deficiency have been associated with retinal hemorrhage [24]. For this reason, a thorough hematologic work-up should be performed to rule out these etiologies. However, the isolated presence of retinal hemorrhage in the absence of involvement of other organ systems makes this etiology unlikely.

Prevention

Child abuse prevention programs can be thought of as primary, secondary, and tertiary efforts [10]. Primary prevention targets a broad segment of the population. In the case of abusive head trauma, this would be education for all new parents and caregivers of infants. Secondary prevention focuses on a specific subset of the population considered to be at high risk for child maltreatment, such as home visitation programs to those families that are felt to be high risk for abusive head trauma. Tertiary prevention programs target perpetrators of child maltreatment and hope to prevent recidivism.

Like most forms of child maltreatment, abusive head trauma is intentional, but may be preventable with education and public awareness. In many cases where perpetrators of abusive head trauma were interviewed and confessed, the majority of the incidents were triggered by inconsolable crying or unrealistic developmental expectations by a caregiver. The caregivers expressed feelings of extreme stress and helplessness and acted in a moment of anger and/or frustration. By educating caregivers early on about what to expect in the newborn and infancy period, caregiver anxiety and helplessness can be alleviated.

Crying has been found to be the most common trigger for abusive head trauma in infants. The "*Period of PURPLE Crying*" prevention materials were designed and produced by the National Center on Shaken Infant Syndrome to educate new parents and other caretakers [27]. The letters in the word "PURPLE" each stand for a property of crying that is frustrating to caregivers: P for peak pattern, where crying increases weekly, peaks during the second month, and then declines; U for unexpected onset of crying bouts; R for resistance to soothing; P for pain-like facial grimace; L for long crying bouts; and E for evening clustering. The materials reinforce the normalcy of crying while acknowledging the frustration caregivers may experience when an infant does not soothe. They suggest ways to comfort a crying infant, but also enforce the importance of placing the crying infant in a safe place and walking away in order to calm oneself before getting to the point of shaking a child in frustration.

Age-specific shaken baby syndrome incidence curves have a similar onset and peak pattern as crying curves in normal infants [3]. The "normal crying curve" and the associated behavior pattern (inconsolable crying and fussiness) starts around the second week of life, peaks around the second to third month, and decreases to lower stable levels by the fourth month of life. This time frame was found to coincide with the peak incidence of abusive head trauma. Because of this correlation, many programs have focused on targeting newborn parents to educate them on the normalcy of crying in the newborn period and the dangers of shaking. To address this issue, there have been a few educational programs implemented to catch new parents prior to their discharge from the hospital with their newborn. Evidence from these programs have been encouraging and the hope is that they can reduce the incidence of abusive head trauma in areas where these programs are used. One such program was developed by Dr. Mark Dias who introduced a hospital-based, primary prevention program targeting newborn parents in a maternity ward in upstate New York [9]. Nurses were trained to disseminate information to new parents via a one-page leaflet, a video, and posters on the ward. Each parent was also asked to sign a commitment statement prior to their discharge with their baby affirming their receipt and understanding of the materials. Dias et al. reported a positive result from their program

in that the rates of shaken baby syndrome following the introduction of their program decreased by 53%. The use of educational videos has been widespread at many hospitals because it has the potential to accurately demonstrate the circumstances leading up to a shaking event. Videos portraying true stories of infants who have suffered from abusive head trauma have a strong emotional impact. The videos and other educational materials should also advise new parents of a plan of action, such as handing a crying baby over to another person when agitated or frustrated.

Starling et al. reported that fathers, followed by boyfriends, female babysitters, and mothers, in descending order, were the most common perpetrators [31]. For this reason, prenatal classes, posters, and public service announcements targeted toward men should be implemented. These materials could address any fears and concerns new and expectant fathers may have and provide realistic expectations. In addition to teaching new parents, childcare workers also need training and education on the dangers of shaking since they are potentially faced with caring for inconsolable infants. Childcare workers often establish close relationships with families and have the unique opportunity to educate young parents.

Role of the Pediatrician

Pediatricians are considered mandated reporters of child abuse, which means that they are in a unique position to identify and report any suspected cases of non-accidental trauma to the appropriate child welfare agencies for further investigation. Mandated reporters are required to report suspected child abuse or maltreatment when, in their professional roles, they are presented with *reasonable cause* to suspect abuse or maltreatment. Reasonable cause to suspect child abuse or maltreatment means that, based on their observations, professional training, and experience, they feel the parent or person legally responsible for a child has harmed that child or placed that child in imminent danger or harm. Therefore, pediatricians have the responsibility to recognize and respond to any case of suspected abusive head trauma. The ability of pediatricians to recognize the often subtle signs and symptoms of abusive head trauma is crucial to prevent future neurologic injury and abuse. Since a diagnosis of abuse carries serious social, psychological, and legal ramifications for families, pediatricians also have the responsibility to consider alternative causes of medical findings and formulate a differential diagnoses to ensure that all other possibilities are considered. The assistance of other medical subspecialties, such as neurology, neurosurgery, ophthalmology, hematology, and orthopedics, is frequently requested to work through these differential diagnoses before any legally mandated steps are taken. Pediatricians may also seek the help of a subspecialist in child abuse pediatrics to ensure that the proper steps have been taken and a thorough medical investigation has been completed in order to come to an accurate conclusion. Another role of the pediatrician is to translate and interpret the medical findings for child protective services and law enforcement in order to help them in their investigation. Since the pediatrician has a responsibility to the family of the abused child, honest disclosure of all medical findings is encouraged without laying blame or acting in the role of law enforcement. Their role is to identify the medical problem, treat any injuries, and offer as much information to the family as they can [8].

Pediatricians are often in a great position to offer anticipatory guidance and education to families. They can work to help prevent abusive head trauma by speaking with new parents about the normalcy of infant crying, providing developmental expectations at each age, and warning about the dangers of shaking and impact. They can offer positive parenting methods and help new parents develop coping skills when caring for a fussy, crying infant.

References

1. Aborgast KB, Marguilies SS, Christian CW. Initial neurologic presentation in young children sustaining inflicted and unintentional fatal head injuries. Pediatrics. 2005;116:180–4.

2. Barlow KM, Minns RA. Annual incidence of shaken impact syndrome in young children. Lancet. 2000;356:1571–2.
3. Barr RG, Trent RB, Cross J. Age-related incidence of publicly reported shaken baby syndrome cases: convergent evidence of crying as a trigger to shaking. Child Abuse Negl. 2007;28(4):288–93.
4. Bechtel K, Stoessel K, Leventhal JM, Ogle E, Teague B, Lavietes S, et al. Characteristics the distinguish accidental from abusive injury in hospitalized young children with head trauma. Pediatrics. 2004;114:165–8.
5. Berger RP, Dulani T, Adelson PD, et al. Identification of inflicted traumatic brain injury in well- appearing infants using serum and cerebrospinal markers: a possible screening tool. Pediatrics. 2006;117:325–32.
6. Caffey J. Multiple fractures in long bones of infants suffering from chronic subdural hematoma. Am J Roentgenol. 1946;56:163–73.
7. Caffey J. The whiplash shaken infant syndrome: manual shaking by the extremities with whiplash induced intracranial and intraocular bleedings, linked with residual permanent brain damage and mental retardation. Pediatrics. 1974;54:396–403.
8. Christian CW, Block R. Abusive head trauma in infants and children. Pediatrics. 2009;123(5): 1409–11.
9. Dias MS, Smith K, DeGuehery K, Mazur P, Li V, Shaffer ML. Preventing abusive head trauma among infants and young children: a hospital-based, parent education program. Pediatrics. 2005;115:e470–7.
10. Dubowitz H. Prevention of child maltreatment: what is known. Pediatrics. 1989;83:570–7.
11. Duhaime AC, Gennerelli TA, Thibault LE, Bruce DA, Margulies SS, Wiser R. The shaken baby syndrome: a clinical, pathological, and biomedical study. J Neurosurg. 1987;66:409–15.
12. Duhaime AC, Alario AJ, Lewander WJ, et al. Head Injury in very young children: mechanisms, injury types, and ophthalmologic findings in 100 hospitalized patients younger than 2 years of age. Pediatrics. 1992;90:179–85.
13. Esernio-Jenssen D, Tai J, Kodsi S. Abusive head trauma in children: a comparison of male and female perpetrators. Pediatrics. 2011;127:649–57.
14. Fraiser L, Rauth-Farley K, Alexader R, Parrish R, editors. Abusive head trauma in infants and children: a medical legal and forensic reference. 1st ed. St. Louis, MO: G. W. Medical Publishing; 2006.
15. Guthkelch AN. Infantile subdural haematoma and its relationship to whiplash injuries. Br Med J. 1971; 2:430–1.
16. Hymel KP, Abshire TC, Luckey DW, Jenny C. Coagulopathy in pediatric abusive head trauma. Pediatrics. 1997;99:371–5.
17. Jenny C, editor. Child abuse and neglect: diagnosis, treatment and evidence. 1st ed. Philadelphia, PA: Elsevier Saunders; 2011.
18. Jenny C, Hymel KP, Ritzen A, et al. Analysis of missed cases of abusive head trauma. JAMA. 1999;281:621–6.
19. Keenan HT, Runyan DK, Marshall SW, et al. A population-based study of inflicted traumatic brain injury in young children. JAMA. 2003;290:2542–3.
20. Kessler H, Dias MS, Shaffer M, Rottmund C, Cappos K, Thomas NJ. Demographics of abusive head trauma in the Commonwealth of Pennsylvania. J Neurosurg Pediatr. 2008;1:351–6.
21. Kleinman PK. Diagnostic imaging in infant abuse. Am J Roentgenol. 1990;155:703–12.
22. Kleinman PK, Schlesinger AE. Mechanical factors associated with posterior rib fractures: laboratory and case studies. Pediatr Radiol. 1997;27:87–91.
23. Levin A. Retinal haemorrhage and child abuse. In: David T, editor. Recent advances in paediatrics, vol. 18. London: Churchill Livingstone; 2000. p. 151–219.
24. Levin A. Retinal hemorrhage in abusive head trauma. Pediatrics. 2010;126:961–70.
25. Levin A. Eye injuries in child abuse. In: Jenny C, editor. Child abuse and neglect: diagnosis, treatment and evidence. 1st ed. Philadelphia, PA: Elsevier Saunders; 2011. p. 402–12.
26. Morris AA, Hoffman GF, Naughten ER, et al. Glutaric aciduria and suspected child abuse. Arch Dis Child. 1999;80:404–5.
27. National Center on Shaken Baby Syndrome, Barr RG. Period of PURPLE crying shaken baby syndrome prevention program. Ogden, UT: National Center on Shaken Baby Syndrome; 2004.
28. Reece RM, Christian CW, editors. Child abuse: medical diagnosis and management. 3rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 2009.
29. Sills MR, Libby AM, Orton HD. Pre-hospital and in-hospital mortality: a comparison of intentional and unintentional traumatic brain injuries in Colorado children. Arch Pediatr Adolesc Med. 2005;159: 665–70.
30. Schnitzer PG, Ewigman BG. Child deaths resulting from inflicted injuries: household risk factors and perpetrator characteristics. Pediatrics. 2005;116: e87–693.
31. Starling SP, Holden JR, Jenny C. Abusive head trauma: the relationship of perpetrators to their victims. Pediatrics. 1995;95(2):259–62.
32. Starling SP, Patel S, Burke BL, Sirotnak S, Rosquist P. Analysis of perpetrator admissions to inflicted traumatic brain injury in children. Arch Pediatr Adolesc Med. 2004;158(5):454–8.

A Pediatrician's Guide to Concussion Management

28

Kenneth R. Perrine, Emilie A. George, and Katie Shayna Davis

Epidemiology

Concussion is one of the most common injuries sustained in the pediatric population and by far the largest subset of traumatic brain injury (TBI). The Centers for Disease Control and Prevention estimate that between 50,000 and 300,000 pediatric concussions are suffered each year among contact sports athletes, due to the popularity of contact sports such as football, lacrosse, soccer, and basketball in elementary, middle, and especially high school and college years. The CDC estimates that from 2001 to 2009, US emergency departments treated an estimated 173,285 sports and recreation-related TBIs, including concussions, among children from birth to 19 years [10]. A study of the emergency department (ED) pediatric visits from 2001 to 2005 found that there were 502,000 visits for concussion, with approximately half related to sports [3]. These visits included 35 % of children in the 8–13-year-old range and 65 % in the 14–19-year-old range. However, most cases of concussion are not seen in an ED and are therefore not accounted for in studies like these.

These statistics demonstrate a significant increase in the reporting of concussions over the past decade [17], both clinically and in the media. It is very likely that the average pediatrician will see children and adolescents presenting to their practice with concussions and field phone calls asking for management and referral advice. In fact, many states have passed a legislation mandating that any elementary or high school child sustaining a concussion in a school function must see a physician for clearance before returning to practice and play or even to resume regular school attendance. The majority of these children will seek out their pediatrician as the primary physician to assess the presence, severity, and treatment of concussion.

Although concussion has recently become a buzzword among parents, coaches, and athletes, it may be surprisingly difficult to clearly define and explain. The exact clinical definition of concussion has undergone a number of revisions over the last decade (for review see [5]). Multiple professional and governmental organizations have proffered definitions, including the World Health Organization, American Academy of Neurology,

K.R. Perrine, Ph.D. (✉)
Department of Neurological Surgery, Weill Cornell Medical College, 520 East 70th Street, Starr 651, New York, NY 10065, USA
e-mail: krp2003@med.cornell.edu

E.A. George, B.A.
Weill Cornell Medical College, 1300 York Avenue, New York, NY 10065, USA

K.S. Davis, M.S.
Division of Child and Adolescent Psychiatry, New York State Psychiatric Institute, 1051 Riverside Drive, New York, NY, 10032 USA

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_28

American College of Rehabilitation Medicine, the Centers for Disease Control and Prevention, and the National Institutes of Health [19]. The most thorough and scientifically based definitions, complete with consensus statements, have derived from meetings organized by the International Conference on Concussion in Sport. This definition has moved away from the older, traditional Glasgow Coma Scale-based definition that rates level of consciousness to instead include the array of signs and symptoms experienced by patients with concussion. The most recent meeting issued a thorough definition as well as comprehensive guidelines for the identification and management of sport concussions [21]:

> Concussion is a brain injury and is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces. Several common features that incorporate clinical, pathologic and biomechanical injury constructs that may be utilized in defining the nature of a concussive head injury include:
>
> 1. Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an 'impulsive' force transmitted to the head.
> 2. Concussion typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, symptoms and signs may evolve over a number of minutes to hours.
> 3. Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies.
> 4. Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course. However, it is important to note that in some cases symptoms may be prolonged.

The biological mechanism of concussion is believed to derive from several factors. One aspect to recognize is a temporary disruption of transmitters in the brain in a so-called biochemical cascade [11]. Neurometabolic changes can include changes in the neuronal cell membrane depolarization, changes in neurotransmitters and electrolytes, ATP changes, and calpain activation and apoptosis [19]. In addition to neurochemical changes, the direction of force transferred to the brain results in actual axonal damage. Rotational forces exerted on the brain produce concussion far more frequently than lateral (side to side) or anterior-posterior (front to back) forces. Numerous neurobiological effects occur in the axonal processes (white matter tracts) due to their length and susceptibility to rotational forces. These axonal tracts course from the cortical mantle that surrounds the brain down through the brain stem making them especially vulnerable. Damage to these tracts is likely to produce the disruption of arousal and consciousness seen in concussion. Rotational forces are very common as the brain moves violently within the cranial vault with the brain stem as the fulcrum. The actual damage to the axons may in the worst injuries, consist of tearing and shearing, which can produce "diffuse axonal injury." In addition to damaging long axonal tracts, more serious head injuries can produce skull fractures, focal contusions, cerebral edema, acute intracerebral hemorrhages, and subdural and epidural hematomas. Although concussions by definition exclude these more serious consequences of traumatic brain injury, they must be ruled out to diagnose a simple concussion. The rationale for keeping a patient awake or awakening them every few hours is to determine if there are any hemorrhages in which signs and symptoms can develop over hours or days. Suspicion of these more severe injuries necessitates transport to the ED and possible rapid neurosurgical intervention.

Resolution of Concussion

Once potential severe brain injury such as hemorrhage or skull fracture is ruled out, and a primary diagnosis of concussion is made, the next steps involve moving toward resolution of concussion. By definition, concussion is primarily characterized by functional disturbance, and as a result, recovery is largely measured by return to baseline functioning. After the initial injury, most concussions resolve within 7–10 days with complete clearing of symptoms [4, 21]. There is some evidence to suggest, however, that recovery time may be slightly longer in children and adolescents [8, 21].

Despite the generally rapid recovery time, a subset of patients experience prolonged symptoms weeks and even months after the initial concussion. Post-concussion syndrome (PCS), while generally characterized as lingering concussion symptoms, has yet to be well defined. Some estimates suggest that 15–20 % of concussion patients report concussion symptoms 3 months or more after their initial injury. However, the classification of PCS is vague and often consists of highly nonspecific symptoms such as headache, dizziness, and irritability that occur in a myriad of non-concussed groups [19]. Somatization is an important factor to consider when approaching PCS. Depression, anxiety, and stress have been connected to prolonged concussion symptoms suggesting a neuropsychological link to the disorder. Furthermore, patients may begin to attribute symptoms present pre-concussion, such as headache and difficulty concentrating, to the injury when in fact these problems may not have been caused by or associated with head injury [7].

Additional societal factors contribute to the incidence of PCS. Children or parents may view a concussion as an excuse to stay home from school or seek accommodations such as extra time for exams or standardized tests like the SAT. Unfortunately, given our society's litigious environment, some children may be encouraged by their parents to emphasize symptoms for litigation and financial gain.

Special Considerations in the Pediatric Population

The majority of TBI data, and therefore definitions of concussion historically, have reflected an adult-biased research population; however there are several relevant differences between adult and pediatric concussed patients. Children are more likely than adults to sustain a concussion and manifest poorer long-term outcomes than adults with similar injuries [16]; this suggests that special considerations should be made when dealing with concussion in the pediatric population.

There are a number of risk factors that put children at a higher risk for sustaining a concussion. Biologically, younger children are more likely to sustain a concussion because their white matter tracts are not yet fully myelinated, and less force is required to produce a concussion than in adults [12]. In fact, full myelination is not reached until the late teens or early twenties. Head versus torso weight ratios change rapidly through the first 10 years of life as well, making toddlers and adolescents prone to excessive rotational force concussive injuries due to a larger lever arm, weaker neck muscles, and therefore propensity for headstrike. There are also situational factors that make children more likely to suffer a concussion. Differing rates of physical development lead to a large degree of size disparity among athletes on youth sports teams. As a result, smaller children may encounter physical opponents who are much more physically developed [13]. Finally, a history of recent prior concussions is also a risk factor for future concussions [15].

Within the pediatric population, certain subgroups are at increased risk. There is some evidence that children with a history of learning disabilities or other mild developmental disorders are more likely to sustain a concussion because of clumsiness [24]. Although girls may sustain more concussions than boys and may report different types of symptoms than boys after accounting for sports-related exposures, the symptom resolution time and return-to-play duration are thought to be similar [9] though gender-specific differences are still being debated and underlying mechanical and biological differences in susceptibility and response to mild TBI are suspected.

Office Visit for Concussion

There are five essential parts to the office visit of a child with a suspected concussion: a complete history of the injury, a review of post-concussion signs and symptoms, the physical and neurologic exam, diagnosis and feedback, and finally a treatment plan with recommendations for return to school and/or sports.

History of the Injury

The most important part of the office visit is obtaining an accurate and complete history of the injury and the current symptoms. When inquiring about the injury, it is best not only to ask the child but also a collateral source (parent or coach). The most important factors are:

Actual Injury

Inquire about what happened. Factors such as the suspected energy of the impact and whether the head was struck directly or in a rotational matter can be helpful, but are often difficult to ascertain.

Retrograde Amnesia

This is amnesia for events prior to the injury. Ask the child the last thing he or she recalls before the impact. Mild concussions may not be accompanied by any retrograde amnesia, but more severe ones may have loss of memories for minutes or even hours prior to the injury.

Loss of Consciousness (LOC)

This historical factor is more difficult to define than one would think. If the child was injured and lying facedown, she/he may have been unconscious or simply trying to regain bearings and deal with pain. Ask both the child, who will probably not be able to report definitively how long any LOC was, and a collateral source, especially the coach or athletic trainer, if the injury was during an athletic event.

Posttraumatic Amnesia (PTA)

This is the most important historical factor to obtain, because it is the most predictive of the severity of the concussion as well as the prognosis for recovery. PTA is defined as the length of time between when the child regains consciousness (if there was any LOC) and when he or she resumes encoding new memories. PTA can occur with or without LOC. For example, it is common for a concussed football player to recall the impact, not actually lose consciousness, but have no recollection of coming off the field or into the locker room despite being awake, talking, and walking. PTA sometimes shrinks as days pass after the injury—the patient may initially have a period of PTA for a half hour the day of the injury, but several days later have a vague recollection of coming off the field.

Test Results

If possible, try to obtain the results of any testing done after the injury. If the concussion occurred during a sports event, the team's athletic trainers or coaches may have administered the SCAT-3 (Sport Concussion Assessment Tool) that may be available for review. The Sport Concussion Assessment Tool has a version for children over age 12 years and adults (SCAT-3, [2]) and a simpler version for children ages 5–12 years (Child-SCAT3 [1]). This multifaceted but user-friendly inventory has several sections including a guide for when to transport a patient to the hospital, a Glasgow Coma Scale, a Maddocks Score inquiring about recent events, a list of symptoms, the Standardized Assessment of Concussion (SAC) [18], an examination of the neck, the Balance Error Scoring System (BESS, [14]), and a coordination exam. Although seemingly extensive, the SCAT-3 takes only about 10–15 min to administer and is common among athletic trainers. This tool may provide more reliable and objective information that the child or parent report. Particularly important is the presence or absence of LOC and amnesia. Also review the symptom inventory, both for the number of symptoms and the ones that are especially specific to concussion such as vertigo, blurred or double vision,

nausea/vomiting, photophobia, sonophobia, and "feeling in a fog." If the full SCAT-3 was not given, parts of it such as the Standardized Assessment of Concussion (SAC) may have been administered and is useful to review. The school or team may also have administered the ImPACT computerized test battery of cognitive functions, but interpretation of the test requires some training. Ask if the trainers or coaches have been trained in interpretation, and call them if necessary to determine what the tables mean. The most important part of the printout is the second page that lists the "composite" scores. Changes that are statistically significant are printed in red or in boldface, but be cognizant of the tendency of some athletes to "sandbag" (perform poorly) the baseline ImPACT administration, making a *statistically* significant decline less likely even in the face of a *clinically* significant decline. The developers of the test can help in interpretation.

Post-Concussion Signs and Symptoms

There are many signs and symptoms that may be produced by a concussion, and these can be categorized in various ways. Post-concussion signs are obviously more reliable, given that they are observable. These include gait disturbance, often accompanied by a subjective report of feeling off-balance, ataxia or dysmetria on cerebellar testing, nausea/vomiting, nystagmus or strabismus, and impaired memory on testing.

Subjective symptoms are more difficult to assess. Start by asking an open-ended question of the child's symptoms after the concussion. However, as they may not think of all the phenomena they experience, utilization of a symptom checklist greatly facilitates surveying PCS symptoms. The checklist from the SCAT-3 or Child-SCAT3 derived from the 4th International Conference on Concussion in Sports [21] is thorough and very current. Each symptom is rated on a 0–6 Likert scale based on severity. It is also helpful to determine the progression of the symptoms by specifically inquiring about symptoms directly following the injury in contrast to symptoms present at the time of the visit. The checklist in Fig. 28.1 was developed by the senior author to track symptoms from the SCAT-3 immediately after the injury and in succeeding days. Younger children often report more mood or behavioral symptoms than cognitive or physical complaints. There are also symptom inventories specifically used for children (e.g., Post-Concussion Symptom Inventory for Children, Version 8–12).

Physical and Neurologic Exam

The physical exam of the head may show lacerations, bruises, or other signs of impact from the injury. However, it is important to note that the site of injury to the head does not reflect any damage referred to the brain. As noted previously, coup-contrecoup and rotational forces are far more important than the site of the external impact. The neurologic examination is usually normal except very early nystagmus or other extraocular movement deficits, pupillary changes, mild ataxia or dysmetria observed on cerebellar testing, and anosmia (it is helpful to include CN I given its sensitivity to TBI from orbital frontal abrasions from the cribriform plate). It is recommended to spend more time than usual on the cerebellar part of the exam, including tests of upper extremity coordination (finger-to-nose as well as finger-nose-finger), lower extremity coordination (heel-to-shin), and gait (normal, tandem, heel walking, toe walking). A useful and sensitive adjunct to the cerebellar examination is the Balance Examination Scoring System (BESS; [14]). This exam is part of the SCAT-3 [2] and many other PCS tools and is quick and easy to administer. There are three lower extremity stances utilized: feet together, tandem stance, and (for older children) standing only on the nondominant leg. Detailed instructions are given in the SCAT-3 form that is available for download from the CDC.

Concussion Symptoms

With your child's help as well as your observation, please rate the presence of the following symptoms of concussion. Rate each symptom separately for during the game, that night, the next today, other days if relevant, and today. Rank them compared to how your child usually feels.
Rate the symptoms on a scale of **0 to 6** using this scale:

None Mild Moderate Severe

0 1 2 3 4 5 6

	During game	That night	Next Day	(Date)	(Date)	TODAY
Date:						
Headache						
Feeling "pressure" in head						
Neck Pain						
Nausea or vomiting						
Dizziness						
Blurred or double vision						
Balance problems						
Sensitivity to light						
Sensitivity to sound						
Feeling slowed down						
Feeling "in a fog"						
"Don't feel right"						
Difficulty concentrating						
Difficulty remembering						
Fatigue or low energy						
Confusion						
Drowsiness						
Trouble falling asleep						
More emotional than usual						
Irritability						
Sadness						
Nervous or anxious						
Total Score:						

Fig. 28.1 Post-concussion symptom inventory

Diagnosis and Feedback

Counseling the child and parent on the natural course of concussion is obviously important. The intense media attention given to concussion has produced a near-hysteria among some parents and schools, and you may be asked if the concussion sustained will leave the child at risk for two of the buzzwords frequently occurring in the popular press: second impact syndrome and chronic traumatic encephalopathy.

Second Impact Syndrome

This is a controversial outcome of concussion. It was originally depicted as sudden death following a concussion within the context of a recent previous concussion and was attributed to rapid cerebral swelling from dysautoregulation occurring after the second concussion [6]. However, most cases of "second impact syndrome" were single-case studies and had little or nothing to do with a preceding concussion when reviewed in detail [20]. Instead, diffuse cerebral swelling is a well-recognized complication of a single TBI that is more common in children and adolescents. As such, the presence of a prior concussion can be pure coincidence, and some have proposed that the term "second impact syndrome" be abandoned and replaced by a single episode of diffuse cerebral swelling [20]. In addition, some media reports of "second impact syndrome" have simply been the result of an epidural, subdural, or subarachnoid hemorrhage, either in isolation or as a result of a ruptured aneurysm or arteriovenous malformation with a coincidental prior concussion. However, there is a recent report of a second concussion occurring before the resolution of a CT-confirmed first concussion that resulted in rapid cerebral edema with severe and permanent sequelae [23]. The presence of a profound and persistent headache could indicate the presence of cerebral swelling and should be investigated by an ED experienced in TBI.

Second impact syndrome has mistakenly also come to mean a concussion sustained before a first concussion has fully resolved. This phenomenon is quite real [22]. It is very important to make sure that the child has recovered fully from reliable signs and symptoms of a concussion before resuming activities (especially contact sports) in which there is a possibility of a subsequent concussion. Factors such as balance problems, visual difficulties, and slowed responses may make the child more prone to sustain an injury resulting in a concussion. The brain itself is more vulnerable to an impact resulting in concussion if there is a prior concussion, such that a "hit" that would previously have not resulted in any meaningful injury can result in a second concussion. How long to avoid activities that could produce a concussion is somewhat controversial and will be discussed below under return to play with respect to contact sports.

Chronic Traumatic Encephalopathy

The term does not refer to a newly discovered disorder, but instead is simply a renaming of an older term called "dementia pugilistica" that referred to dementia with a unique histological pattern confirmed at autopsy resulting from multiple sub-concussive blows and concussions sustained by professional boxers. Although there are some anatomical differences between what is now called CTE arising from non-boxing contact sports and dementia pugilistica, both are an autopsy-proven deposition of the tau protein predominantly in the frontal and temporal lobes and localized to perivascular areas deep in the sulci. It is very important to stress to the parents that CTE can only be diagnosed at autopsy, that is, it occurs only in contact sports with frequent blows to the head over a long period of time. Even if a child has sustained previous concussions, reassure the parents and child that there is no scientific evidence that another concussion will produce CTE, especially in a child.

Although the terms *mild traumatic brain injury* and *concussion* are sometimes used interchangeably, in providing feedback it would probably be best to emphasize the term *concussion* so as not to alarm the child or parents. Explain that the latter term by definition necessitates evidence of actual structural damage to the brain, whereas concussion produces transient changes in neurochemical functioning that completely remit and do not leave any permanent damage to the brain. Under ICD-10, concussion is diagnosed S06.0X0 (without LOC) or S06.0X1 (LOC <=30 min) and in ICD-9 as 850.0 (no LOC) or 850.1 (LOC <30 min). In ICD-9, although the term "concussion" is used for longer durations of LOC, these should more correctly be termed mild traumatic brain injury.

The diagnosis of post-concussion syndrome should be made only if signs or symptoms linger beyond a 2–6-week period of recovery (or longer

in younger children). Care should be given on how feedback is provided regarding the likelihood of psychological or complex biopsychosocial factors that could be maintaining symptomatology. Some patients, including children, may have a somatization disorder that contributes to the maintenance of these symptoms. Feedback that is too abrupt or direct about the absence of a medical explanation for the symptoms could "pull the rug out" from a patient who is relying on the diagnosis for psychological reasons.

Treatment Plan and Recommendations

When to Refer for an Emergent Neurosurgical Consultation

Immediate transfer to a hospital should be arranged if a child shows any of the following, either at your examination or from parent report after the visit:

- Glasgow Coma Scale less than 15
- Deteriorating mental status
- Behaves unusually, seems confused, or is overly irritable
- Cannot recognize people or places
- Potential spinal injury
- Progressive, worsening symptoms or new neurologic signs
  - Weakness, numbness, unsteady walking or standing, slurred speech
- Difficulty understanding speech or directions
- Worsening headache
- Persistent, severe vomiting
- Evidence of skull fracture (otorrhea, rhinorrhea, meningeal signs)
- Posttraumatic seizures
- Coagulopathy
- History of neurosurgery (e.g., shunt)
- Multiple injuries

The CDC has a useful handout available to parents for what to look out for in the first 24–48 h after a concussion (http://www.cdc.gov/concussion).

Recommendations for Return to School and to Sports

This is a difficult decision for a pediatrician to make. Most importantly, the child must never return to any sport or active play on the same day as a suspected concussion. The first few days after a concussion, the child may have a wide range of symptoms of varying severity. There is no hard and fast rule about when to recommend that a child stay out from school. Instead, these recommendations should be individualized to the specific child's symptoms, severity, and school circumstances. It was once thought that children (and adults) should avoid all activities involving sustained concentration, such as schoolwork, for a period of time after the injury. However, more recently experts have suggested that a child who is mildly to moderately symptomatic return to school, but with instructions to report to the school nurse and/or return home if class work exacerbates any symptoms. Prolonged absences from school should be avoided unless the signs and symptoms of the concussion are especially severe, given that the child can be stressed by later having to catch up with missed exams or projects. Additionally, some concentration in school (or at home) can be beneficial, much like patients who have back pain benefit more from mild exercise or activity than from going on bed rest. The schools may be overly conservative and want the child held out, but they should be informed in writing of what your opinions are and what you recommend. Accommodations may be offered to assist the child in returning to school, such as shortened school days, fewer classes, rest breaks, reduced workload, and extended time for tests.

Determining when the child may return to sports is also difficult; most guidelines were researched and developed for professional athletes first and then adapted for children. Professional sports such as football (NFL) and hockey (NHL) have very well-researched and reasonable guidelines for return to practice and play, generally following the recommendations of the 4th International Conference on Concussion in Sport and those listed on the CDC's website.

These organizations recommend that the athlete begin an escalating program of exercise *after* the patient is symptom-free or has symptoms equivalent to baseline and has neuropsychological testing that is normal or equivalent to baseline. ImPACT testing, the BESS, and re-administration of the Child-SCAT3 can be helpful in tracking recovery of cognitive and motor functioning. However, be aware that an athlete may have intentionally produced poor ImPACT scores at baseline in anticipation of retesting after a concussion to be able to return to play faster or hurried through the battery without sufficient effort at baseline.

A typical exercise program would include riding a stationery bicycle up to a heart rate of 120 and then 160 bpm on 1 day, weight or strengthening exercise on a second day, noncontact practice on a third day, and finally practice with contact or equivalent intensity on subsequent days. If at any time the exercise produces any symptoms, the program should back down to the previous step (as long as that does not cause symptoms). Take steps to ensure that coaches, PE teachers, and athletic trainers are informed of this graduated approach.

Recommendations for activities at home or away from school should be similar. Video games, TV, and computers do not necessarily have to be avoided and, like classroom work, may be of some benefit as long as the concussion signs and symptoms are not severe. Again, titrating the activities to the child's reaction is the best plan of action. For both home and school, gradually increasing the amount of time spent in activities requiring sustained concentration helps speed recovery and curtails the tendency of some children to become chronic patients. Also be cognizant of secondary gain. Some children may enjoy the attention they receive while at home, and prolong their symptoms (consciously or subconsciously) to avoid school, chores at home, etc. and enjoy being told to rest while at home.

Medication

There is no medication that will facilitate the recovery from a concussion. Instead, the signs and symptoms that occur following a concussion can be treated individually. Headache is the most common complaint that is amenable to medication. However, any medication should be avoided or minimized in the first 24–48 h to assure that a possible hemorrhage is not developing that could be masked by analgesics. It is common to have headaches persist throughout the recovery period. Clinicians differ in their views on treating continuing headaches, with some encouraging their patients to avoid analgesics. However, a number of neurologists have been prescribing amitriptyline, an older tricyclic antidepressant, for posttraumatic headaches with reported success. Although there have been no controlled studies on this drug, anecdotal reports suggest that it can be beneficial. If the child has a history of migraines or if the posttraumatic headaches resemble idiopathic migraines, medication used in treating classic migraine could be considered until the headaches subside.

When to Refer for a Neuropsychological Consultation

Patients may be referred for consultation by a neuropsychologist if assistance is needed in determining an appropriate return to play and especially return to school timeline. Evaluation should be performed by a neuropsychologist familiar with sports-related concussion. The American Academy of Clinical Neuropsychologists (AACN) provides a directory of board-certified clinicians which may be helpful in identifying a qualified consulting neuropsychologist (http://www.theaacn.org).

The Pediatric Concussion Patient: Case Reports

In practice, there is a broad spectrum over which patients may present under the umbrella of concussion. On one end, there is an incidence of patients with apparently mild injury who report extreme post-concussion symptoms. On the other extreme are patients with relatively severe injury

who endorse few symptoms. Here, four cases are reviewed to sample the diversity of clinical presentation of the pediatric concussion patient.

Case Report 1: Sailing Injury

History of the Injury: A 13-year-old female presented for neuropsychological evaluation approximately 7 weeks post concussion. She was struck in the head by a sailboat boom while sailing on two separate occasions in the span of 3 days. There was no LOC and no retrograde or posttraumatic amnesia for either of the injuries.

Post-Concussion Signs and Symptoms: Following the second incident, the patient reported a headache to her mother, describing pressure along her brow line and at the back of her head. These symptoms persisted and the patient was subsequently taken to the ED a few days after the injuries where she was diagnosed with a concussion. The patient was then seen at a concussion center and placed on propranolol without any relief. Upon advice from the concussion center, the patient began attending school for half days. She reported experiencing sensitivity to light and sound, nausea, difficulty following instructions, and persistent pressure headaches days after the concussion. At the time of neuropsychological evaluation, she had not yet returned to school full time. Attempts at low-impact exercise resulted in reports of dizziness. The patient completed the ImPACT test at the concussion center. When symptoms persisted, the test was readministered and her performance declined. Her mother reported some degree of abnormal behavior after the concussion, including a decreased desire to socialize, some sadness and agitation, and diminished use of the computer and television. On a self-report inventory of post-concussion symptoms, she scored 74, a markedly high endorsement of a broad range of symptoms including headache, pressure in the head, sensitivity to light and sound, not feeling "right," low energy, irritability, anxiety, sadness, drowsiness, and difficulty concentrating. This score would ordinarily be associated with a much more severe concussion. Additionally, her pattern of responses suggested that her symptoms were mildest when she was in the ED, then became worse the following week, and had persisted and even worsened without relief.

Physical and Neurologic Exam: The neurological exam was grossly within normal limits including speech, memory, naming, repetition, comprehension, ability to follow commands, affect, cranial nerves, motor exam, reflexes, coordination, and gait. Additionally an MRI of the brain was normal.

Neuropsychological Evaluation: The patient was seen for neuropsychological evaluation 6 weeks after her concussion. At this time, she scored in the average range on a wide variety of tasks including assessments of concentration, processing speed, verbal fluency, and verbal learning. However, complex scanning, sequencing, and alternation of cognitive set were impaired. The patient's mother reported that after her concussion, the patient began displaying difficulty with executive functions such as planning, organizing, initiating, and working memory. The result of neuropsychological testing suggested that the patient was somewhat overstating her problems and recommended a gradual return to normal activity starting with school and a referral for psychotherapy.

Diagnosis and Feedback: The patient was advised by the neurologist to taper off and stop propranolol. She was prescribed Elavil to start for headache prophylaxis. She was advised to return to school for at least 1–3 h per day and return to a more normal routine with moderation and to consider seeking psychological or psychiatric support. She was also counseled to ensure proper diet, because under-eating may have been exacerbating her headaches.

Discussion: This patient falls at one extreme of concussion patients as she described a relatively mild injury while endorsing extreme symptoms. A key finding in the examination of this patient is the deterioration between the first and second ImPACT batteries with worsening of performance as well as self-reported symptoms over time instead of the expected improvement over time. It

was important here to be especially sensitive about discussing the possibility of somatization.

Case Report 2: Schoolyard Concussion

History of the Injury: An 11-year-old male presented for neuropsychological evaluation approximately 6 weeks post concussion. He sustained the concussion by colliding with a stationary object while playing in the schoolyard. There was no LOC and no retrograde or posttraumatic amnesia.

Post-Concussion Signs and Symptoms: The patient reported feeling dizzy, hazy, and off-balance immediately after the injury. His mother stated that when she arrived at the school, he showed balance problems, and complained of fogginess, and a severe headache. Upon consultation over phone with his pediatrician, he was kept awake at home with head injury precautions. Over the next few days, he continued to feel groggy and reported a persistent headache. As a result his mother arranged an extremely reduced school schedule. The patient reported continued symptoms and later developed vertigo, sonophobia, and photophobia for which he took Imitrex. The development of these symptoms at a later date was anomalous. On a self-report inventory of post-concussion symptoms, he scored 53, endorsing a wide variety of symptoms at the time of neuropsychological evaluation.

Neuropsychological Evaluation: The patient was seen for neuropsychological evaluation 5 weeks after the initial injury. Assessment found impairments in verbal learning, recall, and recognition; however the patient demonstrated significant test anxiety surrounding this task. The patient showed an anomalous pattern of scores, performing worse on a simple sequencing tasks and better on a more complex sequencing task; similarly, he showed worse recognition memory than free recall, a more difficult task. These irregular patterns suggested a non-physiologic basis for the large number of symptoms the patient reported.

Physical and Neurologic Exam: The patient was eventually referred to a neurologist who reported a normal neurologic exam. He showed low average visual memory on the ImPACT test, but no other abnormalities.

Diagnosis and Feedback: The patient was advised to gradually reverse school accommodations and incrementally return to full school participation. His anomalous complaints of moderately severe symptoms suggested that psychosocial factors may have been contributing to an exaggeration of symptoms.

Discussion: While the initial symptomatology was consistent with classic concussion presentation, follow-up neuropsychological testing strongly suggested a non-physiologic etiology for many of his performance issues; the ability of parental and patient anxiety to confound concussion recovery may be a powerful phenomenon.

Case Report 3: Head-to-Head Collision

History of the Injury: A 14-year-old female presented for neuropsychological testing approximately 2 days post concussion. She was injured during a basketball game as she went up for a rebound and banged heads with another player. There was no LOC and no retrograde or posttraumatic amnesia. She recalls the injury and continued playing immediately afterwards.

Post-Concussion Signs and Symptoms: The patient reported experiencing dizziness for approximately 15 minutes post collision along with a headache that continued into the night. On ImPACT testing performed the day after the concussion, she endorsed a mild headache and very mild dizziness, sensitivity to noise, and difficulty concentrating. At the time of neuropsychological assessment, she reported improvement in photosensitivity and irritability from the day before. On a self-report inventory of post-concussion symptoms, she scored 19.

Neuropsychological evaluation: The patient was seen for neuropsychological evaluation 2 days after the injury. The primary finding was difficulty in visuo-motor tasks. She scored in the low average range on tasks of visuo-motor speed, fine motor dexterity, and in the impaired range in non-verbal learning and recall of symbols. The patient showed average processing speed, attention, and concentration. A report of concussion symptoms revealed that the patient continued to endorse mild symptoms including headache and dizziness with some symptoms already beginning to resolve as compared to the day before.

Physical and Neurologic Exam: The patient was examined by the athletic trainer at her school the day after she sustained the injury. The ImPACT was administered 1 day post concussion and a baseline test was available. She demonstrated a significant decline in the visual memory composite, no change for verbal memory, and no significant change in reaction time or visual motor speed.

Diagnosis and Feedback: The results of neuropsychological testing suggested a mild, uncomplicated concussion from which the patient was rapidly recovering. She was advised to withhold strenuous exercise until her symptoms completely cleared and to avoid concentrating or reading for extended periods of time but only if it induced post-concussion symptoms. She was advised to consult the athletic trainer and abide by CDC guidelines for gradually escalating exercise.

Discussion: This patient displayed a more typical presentation of concussion symptoms and a classic rapid resolution of signs and symptoms.

Case Report 4: Motor Vehicle Accident

History of the Injury: A 13-year-old female presented for neuropsychological testing approximately 4 weeks post concussion. She was struck by a vehicle at a pedestrian resulting in approximately 30 min of LOC. She recalls walking toward the median, but not seeing the vehicle that hit her or the impact. Her next recollection was an unclear memory of seeing her father in the ED. A CT scan showed a linear skull fracture, and an MRI of the brain was normal except for an enlarged pituitary. She was discharged 2 days later and returned to school 1 week later.

Post-Concussion Signs and Symptoms: The patient reported residual headache and head pain upon returning to school 10 days post injury. She was very fatigued and had some difficulty in class. She denied any problems with taking notes, listening to her teachers, or taking quizzes. At the time of neuropsychological evaluation, she completed a self-report inventory of post-concussion symptoms. Her total score was 10 with only moderate drowsiness and mild memory problems reported.

Physical and Neurologic Exam: The patient was alert and oriented. The patient was seen by a neurologist who reported no focal neurologic deficits and referred her for neuropsychological testing.

Neuropsychological Evaluation: The patient was seen for neuropsychological evaluation 4 weeks after her initial injury. The results of testing revealed mild deficits for cognitive processing speed and sustained concentration. The majority of her scores, however, were in the average or above average range including assessments of cognitive flexibility, word fluency, visual scanning, verbal learning, recall and recognition, and fine motor dexterity. The patient's mother reported no significant changes in frontal executive behavior since the time of the concussion.

Diagnosis and Feedback: The patient was diagnosed with mild residual effects of a concussion and no specific intervention was recommended. She was encouraged to take breaks and see the school nurse if she became overly fatigued and was advised to refrain from contact sports. She was instructed to gradually resume some exercise when she no longer showed post-concussion symptoms with incremental escalation in intensity. Additionally, her parents were advised to notify her school of her injury should she need accommodations for timed tests.

Discussion: This patient demonstrates an opposite extreme from the first case report. Here the patient presents with loss of consciousness and skull fracture, yet endorsed relatively few post-concussion symptoms.

Summary

Pediatric concussion is seen in pediatrician's offices and pediatric emergency departments with growing frequency as a result of increased participation in sports, improved concussion awareness, rising media attention, and changes in legislation regulating the course of concussion in schools. Many parents will seek out a pediatrician to advise and treat concussions sustained by children. Understanding the definition of concussion as outlined by the International Conference on Concussion in Sport represents an important first step in identification and diagnosis. Special considerations within the pediatric population must also be addressed including the increased propensity for concussion as compared to adults, as well as social factors that may influence the reporting of symptomatology. The pediatric patient's desire to return, or not to return, to school or sports may have a profound influence on symptom endorsement. The office visit will require an in-depth history and may require the involvement of patients, parents, and coaching staff.

Making a determination as to return to school and play may necessitate involvement of neuropsychological evaluation and should strike a careful balance between returning too soon which may exacerbate symptoms and not returning soon enough which can cause children to fall behind or lose motivation. Consideration of post-concussion syndrome characterized by lingering symptoms may also affect the physician's plan. Treatment of concussion should involve careful counseling and education of not only the patient but also the caregivers. The case reports presented in this chapter demonstrate the heterogeneity of concussion patients that may seek medical care under the umbrella of "concussion." Although increasingly common, concussion is often a complex and nuanced diagnosis requiring a holistic approach to patient care.

References

1. Child SCAT3. Br J Sports Med 2013; 47(5): 263.
2. SCAT3. Br J Sports Med 2013; 47(5): 259.
3. Bakhos LL, Lockhart GR, Myers R, Linakis JG. Emergency department visits for concussion in young child athletes. Pediatrics. 2010;126(3): e550–6.
4. Bleiberg J, Cernich AN, Cameron K, Sun W, Peck K, Ecklund PJ, Reeves D, Uhorchak J, Sparling MB, Warden DL. Duration of cognitive impairment after sports concussion. Neurosurgery. 2004;54(5):1073–8. discussion 1078-1080.
5. Bodin DY, Yeates KO, Klamar K. Definition and classification of concussion. In: Handbook of pediatric concussion. New York, NY: Guilford Press; 2011.
6. Cantu RC. Second-impact syndrome. Clin Sports Med. 1998;17(1):37–44.
7. Ferguson RJ, Mittenberg W, Barone DF, Schneider B. Postconcussion syndrome following sports-related head injury: expectation as etiology. Neuropsychology. 1999;13(4):582–9.
8. Field M, Collins MW, Lovell MR, Maroon J. Does age play a role in recovery from sports-related concussion? A comparison of high school and collegiate athletes. J Pediatr. 2003;142(5):546–53.
9. Frommer LJ, Gurka KK, Cross KM, Ingersoll CD, Comstock RD, Saliba SA. Sex differences in concussion symptoms of high school athletes. J Athl Train. 2011;46(1):76.
10. Gilchrist J, Thomas K, Xu L, McGuire L, Coronado V. Nonfatal sports and recreation related traumatic brain injuries among children and adolescents treated in emergency departments in the United States, 2001-2009. MMWR Morb Mortal Wkly Rep. 2011;60(39): 1337–42.
11. Giza CC, Hovda DA. The neurometabolic cascade of concussion. J Athl Train. 2001;36(3):228.
12. Gomez JE, Hergenroeder AC. New guidelines for management of concussion in sport: special concern for youth. J Adolesc Health. 2013;53(3):311–3.
13. Grace MT. Concussion in the Pediatric Patient. J Pediatr Health Care. 2013;27(5):377–84.
14. Guskiewicz KM. Assessment of postural stability following sport-related concussion. Curr Sports Med Rep. 2003;2(1):24–30.
15. Guskiewicz KM, McCrea M, Marshall SW, Cantu RC, Randolph C, Barr W, Onate JA, Kelly JP. Cumulative effects associated with recurrent concussion in collegiate football players. JAMA. 2003;290(19):2549–55.
16. Hessen E, Nestvold K, Anderson V. Neuropsychological function 23 years after mild traumatic brain injury: a comparison of outcome after paediatric and adult head injuries. Brain Inj. 2007;21(9):963–79.
17. Kelly JP. Traumatic brain injury and concussion in sports. JAMA. 1999;282(10):989–91.
18. McCrea M. Standardized mental status assessment of sports concussion. Clin J Sport Med. 2001;11(3): 176–81.

19. McCrea M, American Academy of Clinical Neuropsychology. Mild traumatic brain injury and postconcussion syndrome: the new evidence base for diagnosis and treatment. Oxford, NY: Oxford University Press; 2008.
20. McCrory P. Does second impact syndrome exist? Clin J Sport Med. 2001;11(3):144–9.
21. McCrory P, Meeuwisse WH, Aubry M, Cantu RC, Dvorak J, Echemendia RJ, Engebretsen L, Johnston K, Kutcher JS, Raftery M, Sills A, Benson BW, Davis GA, Ellenbogen R, Guskiewicz KM, Herring SA, Iverson GL, Jordan BD, Kissick J, McCrea M, McIntosh AS, Maddocks D, Makdissi M, Purcell L, Putukian M, Schneider K, Tator CH, Turner M. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport, Zurich, November 2012. J Athl Train. 2013;48(4):554–75.
22. Silverberg ND, Lange RT, Millis SR, Rose A, Hopp G, Leach S, Iverson GL. Post-concussion symptom reporting after multiple mild traumatic brain injuries. J Neurotrauma. 2013;30(16):1398–404.
23. Weinstein E, Turner M, Kuzma BB, Feuer H. Second impact syndrome in football: new imaging and insights into a rare and devastating condition: case report. J Neurosurg Pediatr. 2013;11(3):331–4.
24. Yeates KO. Mild traumatic brain injury and postconcussive symptoms in children and adolescents. J Int Neuropsychol Soc. 2010;16(6):953.

Pathophysiology and Diagnosis of Concussion

29

Baxter B. Allen

Abbreviations

CDC	Centers for Disease Control and Prevention
CT	Computed tomography
DTI	Diffusion tensor imaging
ER	Emergency room
GCS	Glasgow Coma Scale
LTP	Long-term potentiation
MRI	Magnetic resonance imaging
PET	Positron emission tomography
SPECT	Single-photon emission computed tomography
TBI	Traumatic brain injury

Traumatic brain injuries are the leading cause of death and disability in children ages 1–19 years old. They have a large economic impact on the US health system and significant consequences for the individuals and families who suffer from them. According to the CDC, there are at least 1.7 million TBIs every year, about 75 % of which are concussions or other forms of mild TBI. While concussions have frequently gone unreported and untreated, new laws in multiple states require that a medical professional evaluate all head injuries. From 1997 to 2007, emergency department visits for sports concussions alone doubled in the 8–13-year-old group and increased by more than 200 % in 14–19-year-olds [3]. As these trends are likely to continue, the time healthcare providers commit to caring for these patients is likely to increase as well. An initial assessment for a concussion patient can take upward of 90 min if computer testing is performed, and frequent follow-up may be required. To maximize patient care and to provide the best treatment possible, it is important to know what to look for and how to manage the common sequelae of concussion.

B.B. Allen, M.D. (✉)
New York Presbyterian Hospital – Weill Cornell Medical Center, 525 East 68th Street, New York, NY 10065, USA
e-mail: bba2003@nyp.org

Definition

Over the past two decades, "concussion" has been defined and redefined by multiple scientific committees, frequently leading to confusion among patients, families, and even healthcare providers. It has also been used reciprocally with other terms: minor traumatic brain injury, mild traumatic brain injury, minor closed head injury, mild closed head injury, minimal head injury, mild head injury, and mTBI [8]. In 1993, the American Congress of Rehabilitation Medicine defined concussion as an "alteration of consciousness (amnesia or confusion), less than

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0_29

30 min LOC, or less that 24 h of posttraumatic amnesia, with focal neurological deficits that 'may or may not be transient'" [39]. In 2001, the 1st International Conference on Concussion in Sport defined concussion in greater detail; the definition has been revised three times since, most recently in 2013:

> Concussion is a brain injury and is defined as a complex pathophysiological process affecting the brain, induced by biomechanical forces. Several common features that incorporate clinical, pathologic and biomechanical injury constructs that may be utilised in defining the nature of a concussive head injury include:
>
> 1. Concussion may be caused either by a direct blow to the head, face, neck or elsewhere on the body with an "impulsive" force transmitted to the head.
> 2. Concussion typically results in the rapid onset of short-lived impairment of neurological function that resolves spontaneously. However, in some cases, symptoms and signs may evolve over a number of minutes to hours.
> 3. Concussion may result in neuropathological changes, but the acute clinical symptoms largely reflect a functional disturbance rather than a structural injury and, as such, no abnormality is seen on standard structural neuroimaging studies.
> 4. Concussion results in a graded set of clinical symptoms that may or may not involve loss of consciousness. Resolution of the clinical and cognitive symptoms typically follows a sequential course. However, it is important to note that in some cases symptoms may be prolonged. [2, 53]

Concussion has been defined by several other professional societies, including the American Association of Neurological Surgeons, which defines concussion on their website as "a clinical syndrome characterized by immediate and transient alteration in brain function, including alteration of mental status and level of consciousness, resulting from mechanical force or trauma." Further grades of concussion, based primarily on loss of consciousness, have also been defined. These grading systems have fallen out of favor in research and clinical settings, as they appear to have little predictive value in determining if a patient will have a prolonged recovery [9, 15, 20, 72].

Epidemiology

According to data from the CDC, the average annual number of emergency room (ER) visits for traumatic brain injury was 473,947 between the years of 2002–2006, with roughly 75 % of these occurring because of concussion. The incidence was highest in 0–4-year-olds, with 1256 ER visits per 100,000 children; there was a second peak in older children aged 15–19, with 757 per 100,000. Patients 5–9 and 10–14 were roughly equal at 600 per 100,000, still higher than all other age groups except the elderly. In children 0–14 years old, most injuries (~50 %) occurred after falls, with significant portions being caused by collisions with moving or stationary objects (~25 %) and motor vehicle accidents (~7 %). Older children, aged 15–19, were most likely to have an injury due to motor vehicle accident (~26 %), followed by collision (~23 %), fall (~20 %), or assault (~14 %) [23]. Overall, males sustain concussions at roughly double the rate of females [12].

Concussion in Sports

In concussion specifically, roughly half of the ER visits for children ages 8–19 were sports related [3]. From 2001 to 2004, roughly 4 in 1000 children aged 8–13 and 6 in 1000 children aged 14–19 had ER visits for a sports-related concussion; about one third of these visits occurred secondary to leisure activities (e.g., cycling, skiing, playground activities, skateboarding, etc.) and half occurred secondary to organized team sports. The sports most frequently associated with concussion were ice hockey (10 concussions per 10,000 participants for 7–11-year-olds and 29 per 10,000 for 12–17-year-olds), American football (8 per 10,000 for 7–11-year-olds and 27 per 10,000 for 12–17-year-olds), soccer (1 per 10,000 for 7–11-year-olds and 8 per 10,000 for 12–17-year-olds), basketball (1 per 10,000 for 7–11-year-olds and 4 per 10,000 for 12–17-year-olds), and baseball (1 per 10,000 for 7–11-year-olds and 3 per 10,000 for 12–17-year-olds). The

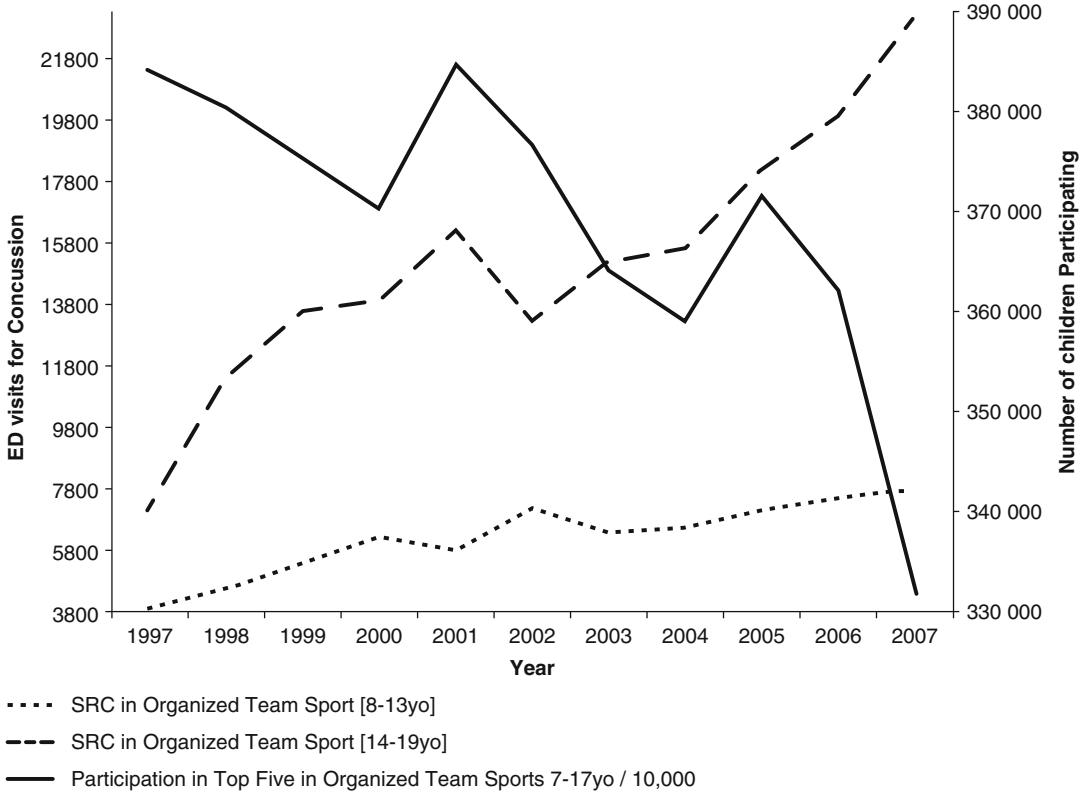


Fig. 29.1 Estimated ED visits for sports-related concussions for ages 8–13 (*dotted line*) and ages 14–19 (*dashed line*) and participation for ages 7–17 (*solid line*) in the top five organized team sports (football, basketball, baseball, soccer, and hockey) from 1997 to 2007 (participation data restricted to 7–17 because of NSGA constraints). Reproduced with permission from *Pediatrics*, Vol. 126, Page(s) e550–e556, Copyright 2010 by the AAP

total number of ER visits doubled between 1997 and 2007 for patients 8–13 years old and more than tripled in patients 14–18 years old (Fig. 29.1).

In 2010, over 7.6 million students participated in high school sports. While concussion risk is obvious in some sports, like football and ice hockey, the risk may be less clear in "noncontact" sports, like baseball. Concussion rates in all sports appear to be higher during competitions than during practices. Multiple studies have found the majority of concussions to occur during games, despite spending much more time in practice. Additionally, the majority of sports concussions occur in children who have not had prior concussion, with only 10–15 % of reported concussions occurring in children who have already had at least one [13]. Having one concussion approximately doubles the risk of having a second concussion [82]. In gender comparable sports (i.e., soccer, basketball, baseball/softball), girls had roughly double the risk of concussion, both new and recurrent [13, 46].

Concussions are much more likely to result from player-player contact (~70 %) than player-playing surface contact (i.e., collision rather than falls). In sports with extra equipment (e.g., baseball bats/balls, lacrosse sticks/balls, hockey sticks/pucks), player-equipment contact is a frequent cause of concussion as well. Rates are highest in full-contact sports (American football, ice hockey, lacrosse), but still occur at significant rates in minimal contact when compared to noncontact sports [46, 82].

Given the popularity of the sport and the frequency of concussions within it, special attention

has been paid to the epidemiology of concussion in American football [27]. Multiple studies have attempted to determine the incidence of concussion in this group, with estimates ranging from 5 to 20 % annually in high school football and 4–5 % annually in college football, accounting for anywhere between 90,000 and 290,000 concussions every year. Given the frequency of high impacts, one study found that nearly 15 % of those athletes who suffered from one concussion sustained a second injury during the same season. The athletes who played defensive back, offensive line, running back, or linebacker positions were the most frequently injured [27, 46]. In football more than any other sports, prior concussion is a risk for recurrent concussion, leading to a two to fourfold increase in risk.

Pathophysiology of Concussion

Biomechanics of Injury

Acceleration/deceleration injuries, rather than direct blows to the head, are the most frequently cause of concussions [64]. When a force is applied to the body or to the head itself, the brain experiences these forces as angular rotation rather than translational (Figs. 29.2 and 29.3). The spinal cord and the brain stem are generally fixed in space by the confines of the spinal column and attachments at the base of the skull (e.g., vessels, cranial nerves). The upper midbrain, thalamus, and cerebral hemispheres are suspended on the brain stem within the skull, surrounded by fluid and connective tissue. These structures are not fixed within this space and are free to move within the skull to varying degrees. The cerebrospinal fluid around the brain acts as somewhat of an inertial damper, redirecting forces that are transmitted to the skull around the brain rather than through it. But it can only dampen so much force, and what force is applied causes the brain to rotate around its more fixed and deep structures. The brief loss or alteration of consciousness associated with concussion is likely an effect of these forces acting on the junction of the upper midbrain and thalamus, leading to a transient disruption in the functioning of the reticular neurons that maintain alertness [76].

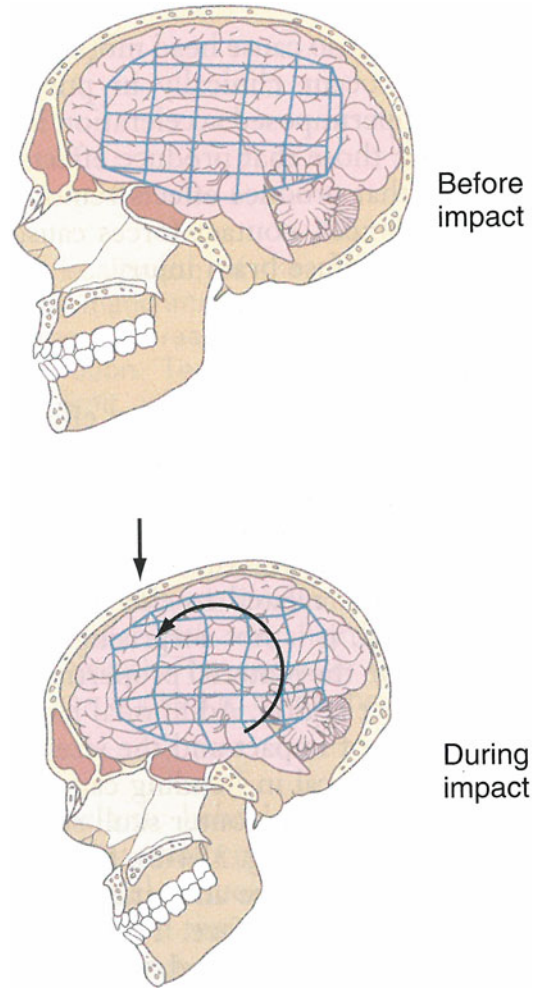


Fig. 29.2 Head motion injuries. Impact can cause local contact effects, but two additional effects contribute to the lesions observed clinically. Because of its inertial properties, the brain slides relative to the inner skull surface, and cortical vessels connecting the brain to the dural membrane may tear. Additionally, the inertial loading delivered to the brain, coupled with its soft material properties, leads to deformation of the brain contents. This deformation is visualized with a superimposed grid pattern that deforms from the acceleration imparted during impact (shown as an *arrow*). This figure was published in Youmans Neurological Surgery, Vol. 4, David F. Meaney, Stephen E. Olvey, and Thomas A. Gennarelli, Chapter 324 Biomechanical Basis of Traumatic Brain Injury, p. 3280, Copyright Elsevier, 2011

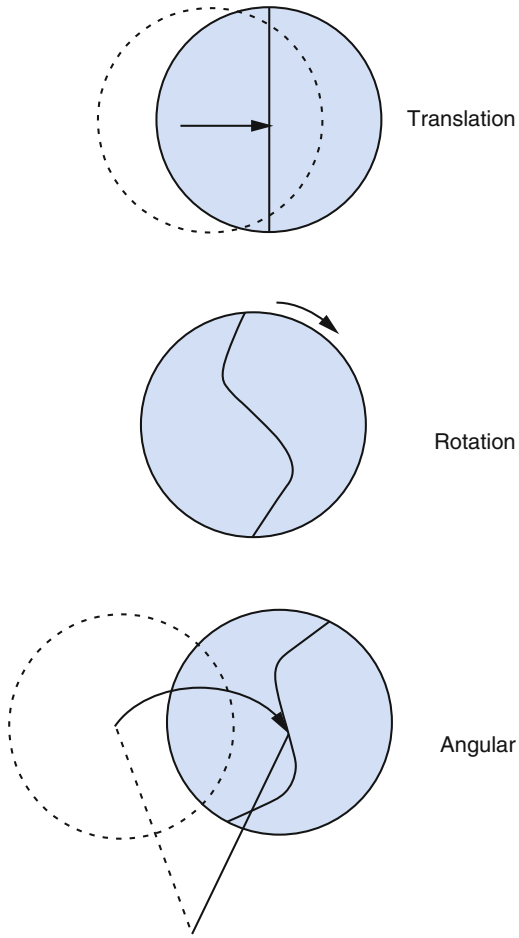


Fig. 29.3 Types of head acceleration. Translational acceleration will move the head in a linear path. Alternatively, rotational acceleration will induce rotation about the head's center of mass, which is located approximately in the pineal region. It is rare to find instances of pure translational or rotational acceleration in "real-world" injury situations. Rather, angular motion is more common. The angular motion leads to combined translational and rotational acceleration, thereby creating injury patterns that arise from both accelerations types. This figure was published in Youmans Neurological Surgery, Vol. 4, David F. Meaney, Stephen E. Olvey, and Thomas A. Gennarelli, Chapter 324 Biomechanical Basis of Traumatic Brain Injury, p. 3281, Copyright Elsevier, 2011

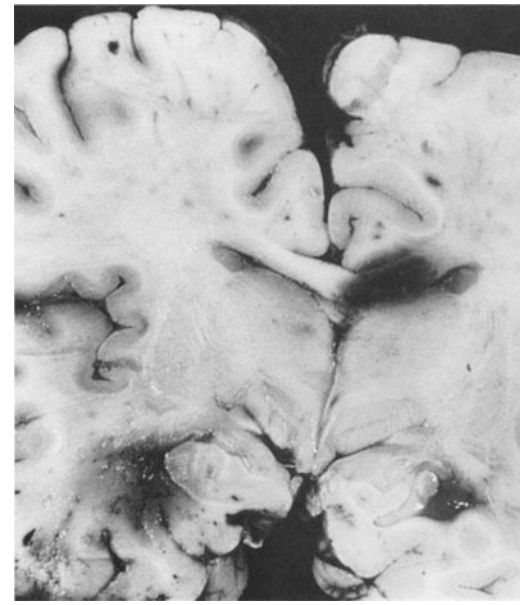


Fig. 29.4 Characteristic hemorrhagic lesion in the corpus callosum in a patient with a fatal head injury from a motor vehicle accident. Note the paramedial distribution of the lesion affecting the full thickness of the corpus callosum. Adapted from Sahuquillo-Barris et al. Acute subdural hematoma and diffuse axonal injury after severe head trauma. *J Neurosurg* 68: 894–900, 1988

Forces applied to the brain become angular rotational forces due to the structures that constrain the base of the brain [5, 6]. White matter, likely due to the myelin sheaths around axons, is stiffer than gray matter, so the strain generally concentrates at the intersections of these two areas. In concussion, these strains are not associated with visible structural abnormalities on conventional neuroimaging. In a more severe traumatic brain injury, however, large magnitudes of force applied in the same fashion will frequently cause disruptions at the gray-white junction (i.e., diffuse axonal injury) (Fig. 29.4) [58].

While human pathophysiology studies have tried to describe the motion of the brain in concussive injuries, the chemical and neuronal response to concussion has mostly been described in animal models [4, 14]. After the initial mechanical trauma to the brain, there is a complex neurochemical and neurometabolic response. Neuronal axons are stretched, leading to membrane deformation and a release of neurotransmitters and ions. This shift leads to an alteration in glucose metabolism and mitochondrial functioning. Cells respond by downregulating excitatory neurotransmitter receptors and eventually reset themselves to their normal state over several days. Depending on the severity of

the injury, the mechanical stretching on axonal cell membranes can cause disruption of the cytoskeleton and likely reversible axonal injury.

Glutamate Release and Ionic Flux (Fig. 29.5)

With the initial trauma, axonal stretching leads to membrane deformation and an indiscriminate flux of ions through previously regulated ion channels [22]. There is a large efflux of potassium and a release of excitatory amino acids, especially glutamate [37]. This release of glutamate leads to indiscriminate activation of neuronal cells through binding to NMDA and AMPA ionic channels [21]. At the same time, cells work to restore the normal ionic balance through the ATP-dependent Na+/K+ pumps. Due to the shift in ions beyond a normal physiologic level, cellular metabolism is strained and lactate production increases, leading to local acidosis, increased membrane permeability, and cerebral edema [36, 38, 104].

Alterations to Brain Metabolism and Activation

After an initial period of hyperglycolysis, lasting approximately 6 h, a prolonged period of glucose hypometabolism can occur [105]. Activation of NMDA channels leads to an influx of calcium ions, which accumulate in mitochondria and lead to dysfunction in glucose oxidation [43, 75, 100, 104]. In studies of humans with moderate to severe TBI, PET imaging has shown glucose hypometabolism to last for months [7]. While no short-duration, longitudinal, within-subject studies have confirmed it, it is believed that a similar disruption in mild TBI and concussion recovers much more rapidly.

Likely in response to over-activation by glutamate, NMDA receptors are downregulated by post-injury day 2–4 and appear to return to normal by day 7 [25]. NMDA channels are associated with learning and long-term potentiation (LTP), and post-injury animal models have shown a decrease in LTP induction after post-injury day 2 [73, 84]. While this generally recovers after 1–2 weeks, it has been seen to take up to 8 weeks to fully return to normal [79]. Human fMRI studies have shown abnormal activation of neural circuits in patients with cognitive deficits at 1 week after injury [32]. When these changes have been observed, the affected individuals seem to have a prolonged clinical recovery [45, 50].

Axonal Injury

In addition to the neurometabolic effects that occur after axonal stretching, disruptions of the cytoskeleton can occur as well. Acutely, neurofilament compaction can occur due to phosphorylation or sidearm proteolysis [34, 92]. As calcium accumulates, microtubules can become destabilized [49]. Axonal transport can be interrupted, and eventually blebbing and disconnection can occur [68, 78].

This process has been observed in animal dissection studies and more recently in human studies using advanced MRI and DTI techniques (Fig. 29.6) [61, 88]. Using DTI, it has been observed that fractional anisotropy, a measure of linear water diffusion, is decreased in several white matter regions after mild TBI. These decreases have been correlated to decreased attention control and memory in adults, as well as to changes in motor speed, executive function, and behavior in children (Fig. 29.7) [62, 101].

Acute Response to Repeat Concussion and the "Second Impact Syndrome"

The most dreaded consequence of concussion is the reported "second impact syndrome." When a second concussion occurs in close temporal proximity to an initial concussion, a catastrophic syndrome of cerebral edema can result in coma, severe neurologic deficit, and death [10, 11, 80]. It is unclear how long concussion patients are at risk for second impact syndrome, leading to the

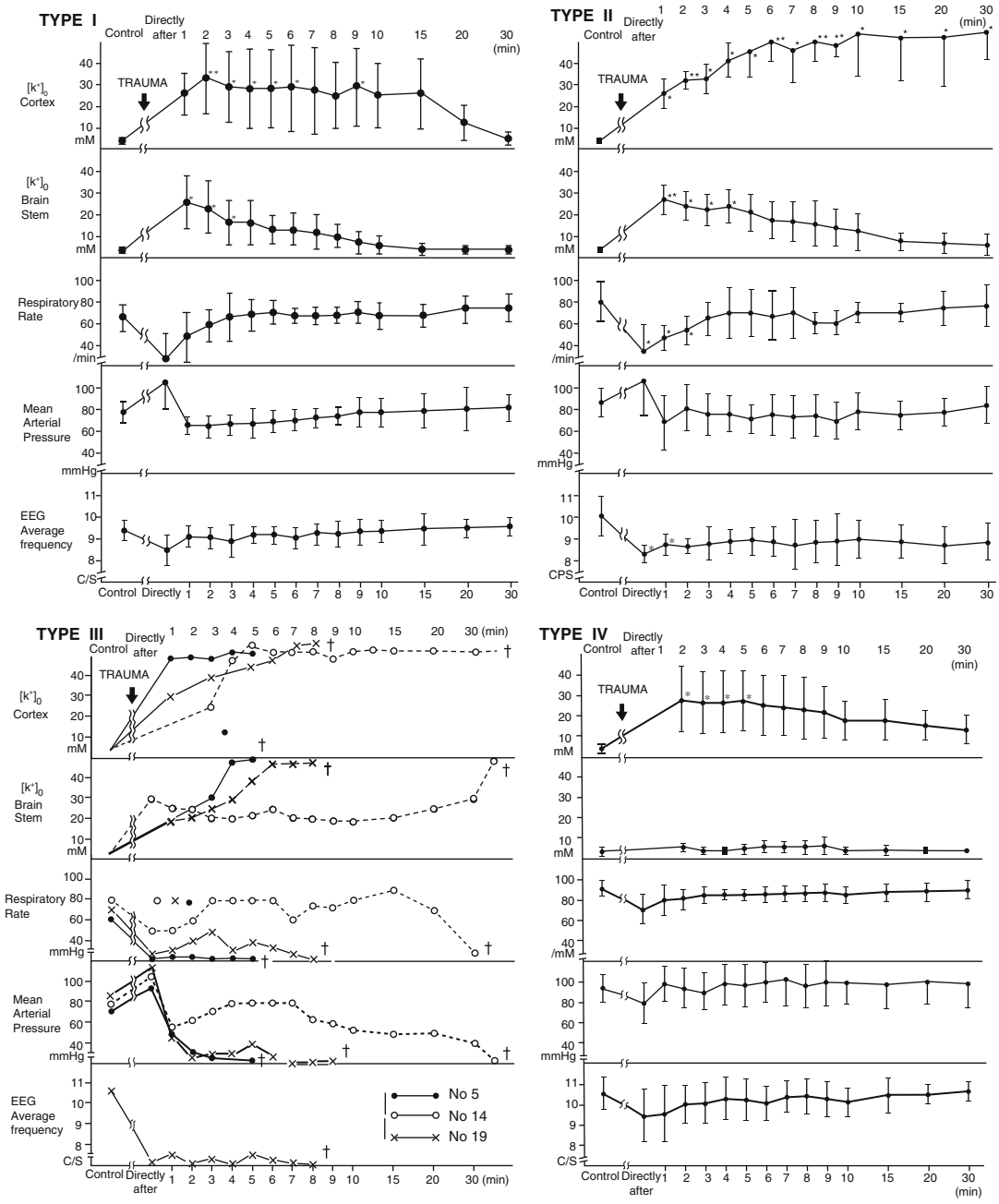


Fig. 29.5 Summary of changes of all parameters in rats who recovered from trauma (Type I), suffered brain contusions (Type II), died (Type III), or who had only mild changes (Type IV), in which changes are demonstrated with mean value and standard deviation. Type I animals are believed to represent severe concussions, while Type IV represent more mild concussions. Adapted from Takahashi et al. Changes in extracellular plasma concentration in the cortex and brain stem during the acute phase of experimental closed head injury. *J Neurosurg* 55: 708–717, 1981

extensive debate over return to play timelines [41, 71]. Several animal studies have demonstrated a period of transient metabolic and physiologic vulnerability that may exacerbate the cellular injury caused by repeated mild injury [44, 95, 97].

After the initial injury, the previously described alterations in metabolism and brain

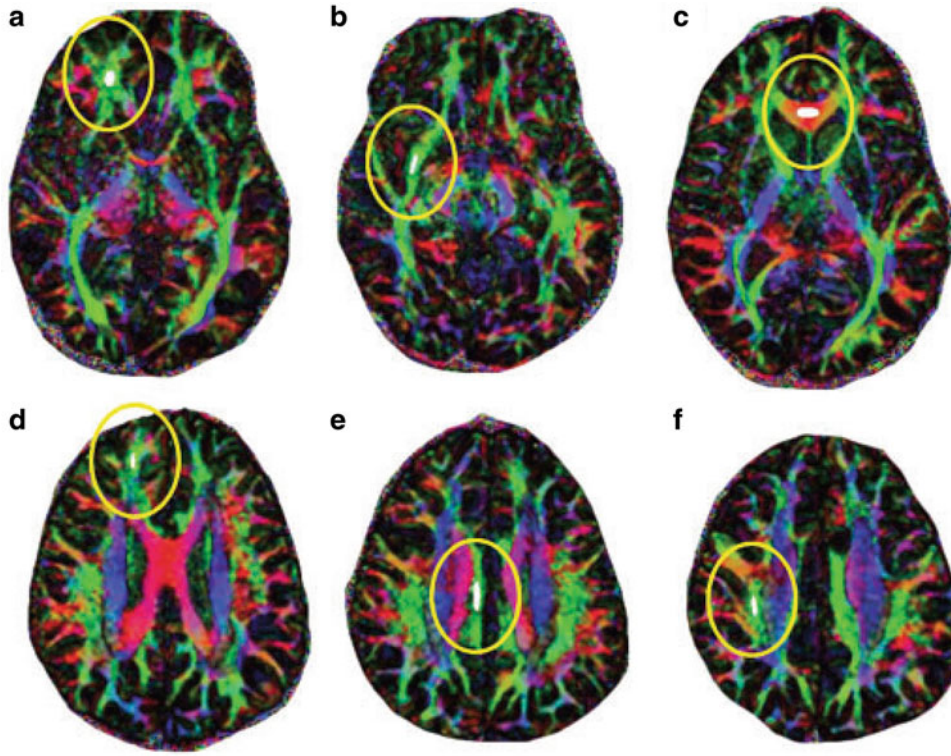


Fig. 29.6 Region of interest (ROI) placement for DTI analysis. Shown are corresponding ROIs for the right hemisphere. The *solid ellipse within yellow outline* indicates the location and size of the ROI. (**a**) uncinate fasciculus, (**b**) inferior longitudinal fasciculus, (**c**) genu of the corpus callosum, (**d**) anterior corona radiata, (**e**) cingulum bundle, (**f**) superior longitudinal fasciculus. Adapted from Niogi SN et al., Structural dissociation of attentional control and memory in adults with and without mild traumatic brain injury, *Brain*, 2008, vol 131, issue 12, pp 3209–3221, by permission of Oxford University Press

activity occur. In a rat model, repeated mild injuries occurring 3 days after an initial mild injury cause damage similar to that which occurs after a single severe TBI [97, 99]. When the second injury occurred after 5 days, the resulting perturbations were similar to the initial injury itself. Given that translating such a time window to humans is difficult, it is reasonable that individuals who have suffered from a concussion do not put themselves in harms way while they are still symptomatic from the initial injury.

Special Considerations in the Pediatric Population

While the majority of the biomechanical experiments on mild TBI have occurred in adult populations, there are a few special items to consider in the pediatric population. Given the relative size of the head to the rest of the body in children, angular motion of the head is likely intensified. In helmeted sports in particular, the added weight of the helmet itself compared to the weight of the head and body leads to an increase in angular motion and likely a proportional increase in the forces transferred to the brain [17]. While the overall smaller size of the brain in children may be somewhat protective (i.e., more force is required to cause injury), the increases in force described in helmeted sports likely negate this protection [65].

Evaluation of Concussion Patients

The most important part of the initial evaluation of a patient after a head impact is ruling out injury requiring surgical intervention. In the early

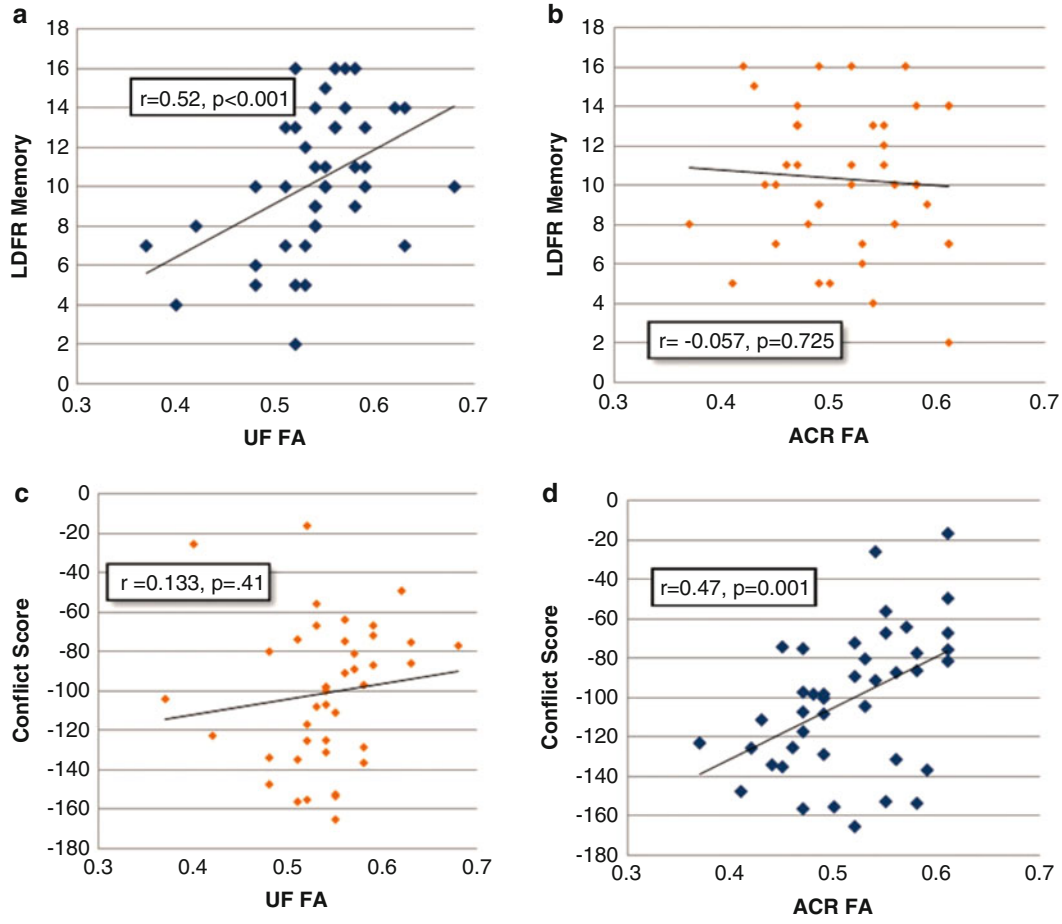


Fig. 29.7 Two cognitive functions are specifically associated with white matter microstructure in two distinct regions in adults with mild TBI. (**a**) Correlation of memory performance and average bilateral uncinate fasciculus (UF) fractional anisotropy (FA) in both hemispheres ($r=0.52$, $P<0.001$). (**b**) The anterior corona radiata (ACR) FA does not correlate significantly with long delay free recall memory ($r=-0.057$, $P=0.725$). (**c**) The UF FA does not correlate significantly with attentional control ($r=0.133$, $P=0.41$). (**d**) Correlation of attentional control measured by conflict score and the left ACR FA ($r=0.47$, P - 0.001). Adapted from Niogi SN et al., Structural dissociation of attentional control and memory in adults with and without mild traumatic brain injury, *Brain*, 2008, vol 131, issue 12, pp 3209–3221, by permission of Oxford University Press

1990s, several studies reported that a substantial portion (up to 20 %) of patients with minor head injuries had intracranial lesions on CT based on retrospective data [28, 90, 91]. It was suggested based on this data that every patient with a minor head injury should have a CT scan. However, further prospective studies on patients with a GCS score of 15 showed an intracranial lesion rate of only 6–9 % on CT [33, 56, 57]. Studies have demonstrated the utility of clinical findings as predictors of intracranial lesions, with sensitivities of 96 and 98 % for intracranial lesions and 100 % sensitivity for patients requiring neurosurgical intervention [56, 106]. Two more recent studies have demonstrated even greater sensitivity (100 % experimental sensitivity), based on a number of clinical findings [29, 93]. The New Orleans Criteria for CT scan in patients with minor head injury as described by Haydel et al. were as follows:

1. GCS score < 15
2. Short-term memory deficit
3. Intoxication

4. Age >60 years
5. Seizure
6. Headache
7. Vomiting
8. Evidence of trauma above the clavicle

The second study by Stiell et al. led to the publication of the Canadian CT Head Rules:

High risk for neurological intervention

1. GCS score < 15 at 2 h after injury
2. Suspected open or depressed skull fracture
3. Any sign of basal skull fracture (hemotympanum, "raccoon" eyes, cerebrospinal fluid otorrhea/rhinorrhea, Battle's sign)
4. Vomiting, two or more episodes
5. Age 65 years or older

Medium risk for brain injury on CT

1. Amnesia for events more than 30 min prior to impact
2. Dangerous mechanism (pedestrian struck by motor vehicle, occupant ejected from motor vehicle, fall from height > 3 ft or five stairs)

Both of these criteria have been validated by multiple studies in their sensitivity for intracranial lesions and prediction of lesions likely to require surgical intervention [60, 77, 87, 89, 94]. These same validation studies have consistently found the Canadian CT Head Rule to be more specific and believe its implementation would lead to a decrease in the frequency of CT head scans for mild traumatic brain injury. Given the delicate balance between detecting lesions and avoiding unnecessary radiation of pediatric patients, these are important rules to consider during an initial evaluation.

Clinical History and Exam

When a patient is brought to you for an evaluation after concussion, it is important to perform a detailed history and physical. A history of headaches (especially migraines), prior concussion, depression, anxiety, post-traumatic stress disorder, and attention deficit hyperactivity disorder all increase the risk that a patient will endure prolonged symptoms. Female sex and a higher intelligence quotient are also associated with prolonged symptoms [55]. The patient's pre-injury functioning should be assessed: How have they done in school? Do they have difficulties in any particular subject area? When did they meet important developmental milestones?

Regarding the concussion itself, it is important to note the patient's initial response: Was there loss of consciousness? Does the patient remember the events leading up to the injury? Does the patient remember the events after the injury? Was there a convulsive event before or after? If the answer is "yes" to any of these questions, documenting the length of time (e.g., length of loss of consciousness, how many minutes were forgotten before or after) should also be done.

The next step generally involves a concussion symptom scale, such as the Pittsburgh Post-Concussion Scale (Fig. 29.8) [107]. In adults and older adolescents, you can ask the patient to fill out the scale before hand, rating each of 21 symptoms on a scale of 0–6, where 0 is no symptom and 6 is severe. In younger children, you may need to go through the symptoms individually to get a response. While younger children may have difficulty differentiating between a 3 and a 6 in terms of symptom severity, they generally understand if something is better or worse than previously (e.g., "is your headache worse today or was it worse yesterday?"). In our practice, we ask that patients fill out the scale for the evening of the injury, the day after the injury, and the day of the evaluation, which allows us to track symptom progress over time.

Finally, a detailed neurological exam should be performed. In concussion, there should be no focal neurological deficits. However, it is not uncommon to see a decrease in short-term memory (e.g., recalling two of three objects 5 min after registration), coarse eye movements on visual pursuit, mild dysmetria, or gait/balance disturbances. Focal neurological deficits should be evaluated as neurological emergencies and triaged to the ER accordingly. If symptoms per-

Players Name: _____ Team: _____ Positions: _____

SYMPTOMS	RATING None Mod Severe	BASELINE Date:	TESTING 2 Date:	TESTING 3 Date:	TESTING 4 Date:	TESTING 5 Date:
Headache	0 1 2 3 4 5 6					
Nausea	0 1 2 3 4 5 6					
Vomiting	0 1 2 3 4 5 6					
Balance Problems	0 1 2 3 4 5 6					
Dizziness	0 1 2 3 4 5 6					
Fatigue	0 1 2 3 4 5 6					
Trouble falling asleep	0 1 2 3 4 5 6					
Sleeping more than usual	0 1 2 3 4 5 6					
Sleeping less than usual	0 1 2 3 4 5 6					
Drowsiness	0 1 2 3 4 5 6					
Sensitivity to light	0 1 2 3 4 5 6					
Sensitivity to noise	0 1 2 3 4 5 6					
Irritability	0 1 2 3 4 5 6					
Sadness	0 1 2 3 4 5 6					
Nervousness	0 1 2 3 4 5 6					
Feeling more emotional	0 1 2 3 4 5 6					
Numbness or tingling	0 1 2 3 4 5 6					
Feeling slowed down	0 1 2 3 4 5 6					
Feeling mentally "foggy"	0 1 2 3 4 5 6					
Difficulty concentrating	0 1 2 3 4 5 6					
Difficulty remembering	0 1 2 3 4 5 6					
TOTAL SCORE						

Fig. 29.8 The Pittsburgh Post-Concussion Symptom Scale. Adapted from MR Lovell and MW Collins, Neuropsychological assessment of the college football player, J Head Trauma Rehabil, Vol 13, issue 2, pp 9–26

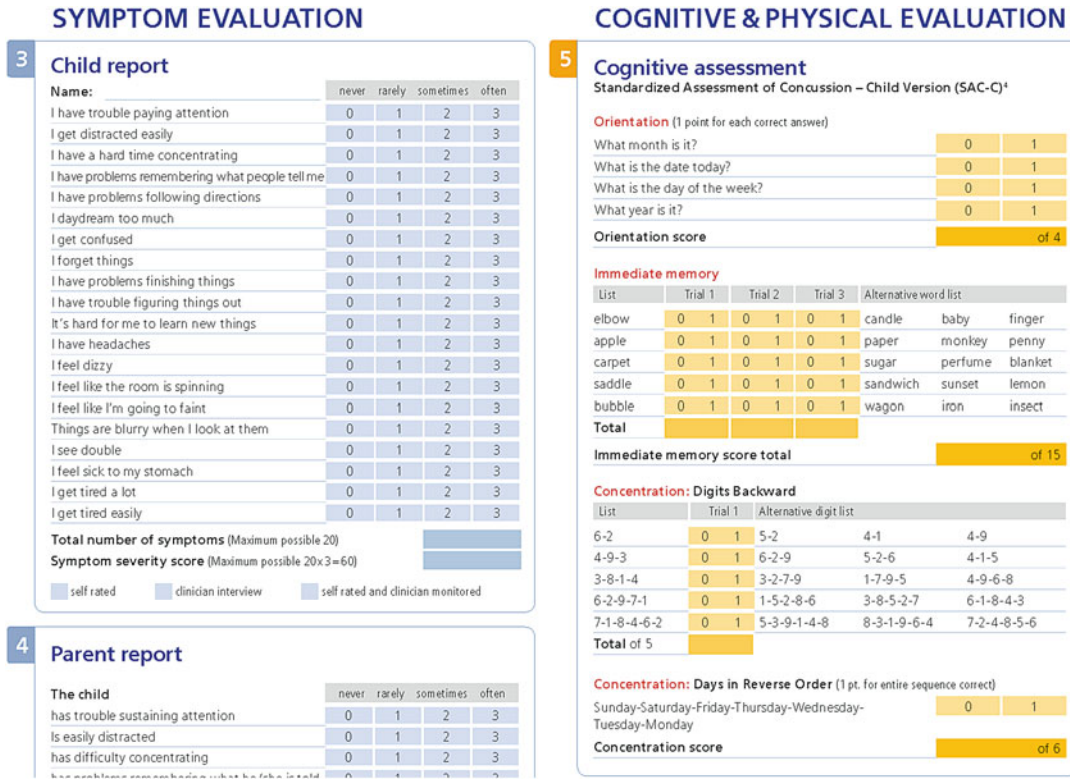
sist beyond 2–3 days, patients should be evaluated by a neurologist or another medical professional that specializes in concussions. Cognitive complaints (e.g., decreased attention, decreased memory) may require detailed testing by a neuropsychologist.

Sideline Testing

Several sideline assessment tools have been designed to aid in the evaluation of a concussion patient [51, 52]. While these tools have been widely studied, it is not recommended that these tools be used to decide if a patient can return to play after sustaining a head injury. If a concussion may have occurred and these tests are to be performed, then it is the current recommendation of multiple medical associations that the individual be withheld from same-day return to play and receive a complete evaluation from a fully licensed and trained medical professional. Several of the sideline assessment tools may be used as part of a clinical decision to allow someone to return to play, but their use as a standalone tool should be limited. When these tools are used, serial documentation of a subject's performance should be documented, including baseline testing prior to participation in a sport. These tools allow for initial documentation of symptoms (e.g., headache), physical signs (e.g., LOC, amnesia), behavioral changes (e.g., irritability), and cognitive impairment (e.g., memory deficits) (Fig. 29.9) [53].

Neurocognitive Testing

Several neurocognitive testing paradigms have been developed for the evaluation of patients with concussion. The most widely used, the Immediate Post-Concussion Assessment and Cognitive Testing (ImPACT), scores patients with six modules and a symptom scale. It derives composite scores on verbal memory, visual memory, reaction time, visual motor processing speed, and impulse control to identify specific cognitive domains that a concussed patient may have difficulty with. In a recent study on high school athletes, researchers were able to correctly classify patients as control or post-concussion utilizing



SYMPTOM EVALUATION

3 Child report

Name:

	never	rarely	sometimes	often
I have trouble paying attention	0	1	2	3
I get distracted easily	0	1	2	3
I have a hard time concentrating	0	1	2	3
I have problems remembering what people tell me	0	1	2	3
I have problems following directions	0	1	2	3
I daydream too much	0	1	2	3
I get confused	0	1	2	3
I forget things	0	1	2	3
I have problems finishing things	0	1	2	3
I have trouble figuring things out	0	1	2	3
It's hard for me to learn new things	0	1	2	3
I have headaches	0	1	2	3
I feel dizzy	0	1	2	3
I feel like the room is spinning	0	1	2	3
I feel like I'm going to faint	0	1	2	3
Things are blurry when I look at them	0	1	2	3
I see double	0	1	2	3
I feel sick to my stomach	0	1	2	3
I get tired a lot	0	1	2	3
I get tired easily	0	1	2	3

Total number of symptoms (Maximum possible 20)

Symptom severity score (Maximum possible 20x3=60)

self rated clinician interview self rated and clinician monitored

4 Parent report

The child	never	rarely	sometimes	often
has trouble sustaining attention	0	1	2	3
Is easily distracted	0	1	2	3
has difficulty concentrating	0	1	2	3

COGNITIVE & PHYSICAL EVALUATION

5 Cognitive assessment

Standardized Assessment of Concussion – Child Version (SAC-C)[4]

Orientation (1 point for each correct answer)

What month is it?	0	1
What is the date today?	0	1
What is the day of the week?	0	1
What year is it?	0	1
Orientation score		of 4

Immediate memory

List	Trial 1	Trial 2	Trial 3	Alternative word list		
elbow	0 1	0 1	0 1	candle	baby	finger
apple	0 1	0 1	0 1	paper	monkey	penny
carpet	0 1	0 1	0 1	sugar	perfume	blanket
saddle	0 1	0 1	0 1	sandwich	sunset	lemon
bubble	0 1	0 1	0 1	wagon	iron	insect
Total						

Immediate memory score total of 15

Concentration: Digits Backward

List	Trial 1	Alternative digit list		
6-2	0 1	5-2	4-1	4-9
4-9-3	0 1	6-2-9	5-2-6	4-1-5
3-8-1-4	0 1	3-2-7-9	1-7-9-5	4-9-6-8
6-2-9-7-1	0 1	1-5-2-8-6	3-8-5-2-7	6-1-8-4-3
7-1-8-4-6-2	0 1	5-3-9-1-4-8	8-3-1-9-6-4	7-2-4-8-5-6
Total of 5				

Concentration: Days in Reverse Order (1 pt. for entire sequence correct)

Sunday-Saturday-Friday-Thursday-Wednesday-Tuesday-Monday	0	1
Concentration score		of 6

Fig. 29.9 Portion of the Child Sideline Assessment Tool 3 (Child SCAT3). The full Child SCAT3 can be obtained free of charge from the website of the British Journal of Sports Medicine at bjsm.bmj.com/content/47/5/263.full.pdf. Reproduced from *Br J Sports Med*, McCrory et al., Vol 47, page 263, 2013 with permission from the BMJ Publishing Group Ltd

composite scores from the ImPACT test battery in approximately 85 % of cases [81].

Given the competitive nature of many athletes, relying on self-reported symptoms can lead to the underdiagnosis of concussion and premature return to play decisions. In one recent study, the sensitivity of concussion diagnosis increased by 19 % when self-reported symptom scores were combined with computerized neurocognitive testing, compared to symptom scores alone [98]. Further, neurocognitive testing can help determine if patients have fully returned to baseline after a concussion, even after previously reported symptoms have resolved [19, 24]. However, the limitations of neurocognitive testing alone have been demonstrated in a large study on professional football players, where evaluations by clinical staff kept athletes out of participation despite resolution of neurocognitive test scores due to other clinical variables [66].

As with sideline assessments, neurocognitive testing should not be interpreted in a vacuum. Testing can provide a window into specific areas that a subject may be deficient in and can help guide further diagnostic testing by neuropsychologists. It is most useful when patients have preparticipation testing performed to act as a baseline. However, in children, these tools are generally more limited given the varied pace at which individuals progress. Even baseline testing can be unreliable in children, as their scores on neurocognitive tests can improve dramatically over time, and peer-to-peer comparisons are frequently just as fraught with variation.

More formalized neuropsychological testing, performed by a psychologist specially trained in

cognitive testing, may be indicated if patients exhibit chronic deficits in any cognitive domains, even if their overall functioning has appeared to return to baseline. It is important that children especially get these evaluations to insure their return to school occurs in an organized and productive manner.

Neuroimaging

As described at the beginning of this section, the vast majority of patients who suffer concussions do not require neuroimaging. Standard CT and MRI imaging will be negative in a concussion, but can be used to evaluate for more serious brain injuries. CT is useful for the evaluation of bone fractures, intracranial bleeding, cerebral contusions, and general mass effects; it should only be used in the acute setting if clinically indicated and is generally not useful in patients with persistent symptoms. MRI, on the other hand, is more sensitive for evaluating symptoms that worsen or persist beyond a reasonable period of time. For example, if a patient has headaches that start to worsen or become positional, if they develop seizures after the injury, or if they have persistent balance or neurocognitive deficits, MRI can be used to evaluate brain architecture very finely.

New MRI techniques, including DTI and functional MRI, can detect minor abnormalities that do not show up on traditional imaging. These may have some utility in predicting long-term recovery, but their clinical relevance is unclear. Functional MRI demonstrates neuronal dysfunction by examining regional differences and changes in blood oxygenation patterns while an individual performs functional tasks (e.g., memory tasks, tapping tasks). Several studies have shown changes in functional imaging after concussion, including apparent utilization of greater brain area while performing similar tasks, and a decrease in the activation of prefrontal regions when performing working memory tasks [70, 86].

DTI provides detailed structural imaging of the white matter tracts that connect one part of the brain to another by measuring the direction of water diffusion within the brain. After concussion, these white matter tracts can be disrupted, and specific disruptions have been correlated to deficits in attentional control and memory [62, 63].

Other imaging techniques, including PET and SPECT, may also detect abnormalities, but are of little clinical utility due to their cost, the potential exposure to radioisotopes, and the time the studies themselves take to complete.

Eye Tracking

Recently, predictive visual tracking was examined as a screening measure for mild traumatic brain injury [47]. Using cameras to follow pupillary movement as a target moves on a predetermined path, researchers were able to determine that gaze error variability correlated significantly with performance on attention and working memory measures, as well as with DTI imaging results that show the same. While the study sample compared uninjured controls with patients with chronic post-concussive syndrome, the quick test could provide another tool in the clinician's arsenal for concussion evaluation.

Treatment of Concussion and Management of Symptoms

There is no proven therapy to shorten the duration of symptoms or reverse the effects of concussion [67, 83]. Currently, cognitive and physical rest are the only commonly prescribed treatments, although the evidence of their effectiveness is limited. One recent study showed improved performance on ImPACT and decreased symptom reporting after a period of prescribed rest [59]. The study was limited by a lack of a control group (all patients were prescribed rest), an inability to control the rest environment, small sample size, and the fact that over half of the subjects were prescribed an extra week of rest based on no set criteria. Another review on phsyician practices showed that the majority believed cognitive rest was an important part of concussion

management, but only a small minority actually prescribed it. [1].

True cognitive rest is extremely difficult to follow: it requires no reading, no television viewing, minimal conversation, no texting, no attending school, no exercise, and increased rest and sleep. The prescription itself can cause psychological symptoms, as well as have deleterious effects on grades and social lives. In our practice, we recommend symptom avoidance: if a patient experiences symptoms while watching television, they're advised not to watch television; if they feel worse after reading, they're advised to break reading up or to use an alternative method (e.g., audiobooks); if they experience headaches after sitting in a loud lunchroom, they are told to eat in a quiet place and avoid unnecessary auditory stimuli.

Additionally, it is important that brief psychological counseling be provided to the patient and their family. This should consist of reassurance that symptoms should eventually dissipate, education on the need for rest and the risks of repeated injury, support from the healthcare provider team and educational assistance as needed, and regular monitoring of patient progress through recovery [108].

Pharmacologic Management of Symptoms

While no specific pharmacologic treatment is validated for concussion, there are several studies on the use of specific medications to manage individual symptoms [67]. This again points to the importance of individualized management of patients, rather than grouping everyone into categories of "acute concussion" or "chronic post-concussion syndrome" [40]. 80–90 % of concussions resolve without any intervention within a period of 7–10 days [53]. Concussion symptoms have been suggested to take longer to resolve in pediatric patients, although a large study of high school athletes showed that symptoms recover within 1 week in about 85 % of patients diagnosed with a first concussion and about 80 % in recurrent concussion [13].

When symptoms last beyond this 10-day period, they are generally described as persistent post-concussion symptoms; if they last longer than 3 months, a post-concussion syndrome is diagnosed. If symptoms are not seriously impacting the lives of a patient, then there is little indication that pharmacologic intervention should be instigated [67]. However, in patients where symptoms have a significant impact (e.g., severe headache, attention disorders effecting school performance, post-injury anxiety, or mood disorders), pharmacologic treatment is clearly indicated. When choosing an agent, those with the least side effects and least probability of harm should be used first: low-dose acetaminophen or ibuprofen as needed for headache as a first-line agent, rather than immediately using migraine prophylaxes or abortives; melatonin supplementation for sleep aide instead of zolpidem or Benadryl; and caffeine for excessive fatigue, rather than neurostimulants.

Additionally, well-tolerated and low-risk nutritional supplements like fish oils (docosahexaenoic acid or eicosapentaenoic acid), vitamin complexes, or coenzyme Q-10 are being used with increasing frequency. There have been multiple animal studies showing decreased symptom duration and higher injury thresholds when high-dose docosahexaenoic acid is given (40 mg/kg/day or roughly 2 g for a 50 kg adolescent), with a long track record of safety from heart health studies [18, 26, 42, 85, 103]. Non-pharmacologic interventions (e.g., biofeedback, low-impact exercise, massage) may be helpful on a case-by-case basis, but there are no clear indications or clinical trials. Small trials are currently evaluating the use of computer training programs to aid in recovery of short-term memory and attention, but no data are available for analysis.

Post-Concussion Syndrome

When symptoms persist for longer periods of time, patients are generally diagnosed with post-concussion syndrome (or post-concussive syndrome). Roughly 15 % of patients experience persistent symptoms, and they are more likely to

have had prior concussion, premorbid psychiatric diagnoses, and higher intelligence quotient and to be female [55]. Additionally, longer duration of posttraumatic amnesia, younger age, and headache and migrainous symptoms 7-day post-injury have been associated with poorer outcome and longer recovery times [9, 15, 20, 72]. The syndrome can last for weeks, months, or even years, and there is not currently a good explanation as to why this occurs or how to treat it [102]. There is also some evidence that a subset of patients with prolonged symptoms have no true cognitive deficits, but rather post-concussive psychopathology that causes the rest of their symptoms [69].

Cumulative Effects of Concussion

There have been multiple retrospective studies on the effects of repeated concussion and subconcussive events on functioning. Particularly prevalent in boxing and professional football, the cumulative effects of multiple concussions have been linked to early dementia and death [35, 74]. However, the threshold needed to have such an impact is not known. In high school collegiate, and professional sports, the effects of one or two concussions on long-term cognitive functioning appear to be minimal [31]. In soccer, there appears to be an effect on cognition whether or not concussions have occurred, although the number of concussions further impacts cognitive testing [48]. In young men with prior head injury, single concussions were not associated with cognitive deficits, but single moderate-severe traumatic brain injuries and multiple concussions were associated [96]. Additionally, amateur athletes with multiple prior concussions were more likely to have a new, symptomatic concussion and to have memory deficits on neurocognitive testing [16, 30].

Return to Play

Guidelines provided by multiple medical associations, including the American Academy of Neurology, the American Medical Society for Sports Medicine, and the 4th International Conference on Concussion in Sport, advocate for a graduate return to play based on individual assessments [53, 109, 110]. When concussion is suspected, there should be no return to play on the same day of injury.

The injury should be followed by an initial period of limited activity while the patient recovers. After symptoms have resolved, the patient should participate in light aerobic exercise (e.g., walking, swimming, or light stationary bike). If this is tolerated, the patient can progress to sports-specific exercises (e.g., skating drills in hockey, running drills in soccer, shooting drills in basketball), followed by noncontact training drills (e.g., passing drills in hockey or football) with progressive resistance training. If a patient experiences symptoms during any of these activities, then they should rest again and take a step back on the progression (e.g., from sports-specific exercise to light aerobic exercise). Once they are able to successfully participate in noncontact training drills without symptoms, they can progress to full-contact practices after clearance from a licensed healthcare provider trained in the evaluation and management of concussion. Finally, patients can return to normal game play once their functional skills have recovered as assessed by coaches and athletic trainers (Table 29.1).

There are no clear-cut guidelines for disqualification or retirement from a sport or sports. Cases should be handled on an individual basis, taking into account the number of prior injuries, the severity of injury, persistent cognitive deficits or diminished academic performance, and the level of competition. It should be a deliberation between the care provider, family members, the patient, and other involved parties with an emphasis on the risks and unknowns [109, 110].

Return to School

While returning to sports may be the most important thing to a young athlete, return to school should be the first priority in all children. There

Table 29.1 Graduated return to play protocol

Rehabilitation stage	Functional exercise at each stage of rehabilitation	Objective of each stage
1. No activity	Symptom limited physical and cognitive rest	Recovery
2. Light aerobic exercise	Walking, swimming, or stationary cycling keeping intensity <70 % maximum permitted heart rate. No resistance training	Increase HR
3. Sports-specific exercise	Skating drills in ice hockey, running drills in soccer. No head impact activities	Add movement
4. Noncontact training drills	Progression to more complex training drills, e.g., passing drills in football and ice hockey. May start progressive resistance training	Exercise, coordination, and cognitive load
5. Full-contact practice	Following medical clearance participate in normal training activities	Restore confidence and assess functional skills by coaching staff
6. Return to play	Normal game play	

Reproduced from *Br J Sports Med*, McCrory et al., Vol 47, pages 250–258, 2013 with permission from the BMJ Publishing Group Ltd

are no standardized guidelines published on how to effectively get students back in class after a concussion, especially when symptoms worsen with cognitive stress and increasing workloads [54]. Academic support and accommodations, including reduced workload, extended test-taking time, modified school days, and even alternative assessments should be utilized on a case-by-case basis. Unfortunately, many of these accommodations are unavailable in most schools due to limited resources, and there have yet to be widespread laws passed to provide funding and adequate academic support services for these children.

References

1. Arbogast K, McGinley A, Master C, et al. Cognitive rest and school-based recommendations following pediatric concussion: the need for primary care support tools. Clin Pediatr. 2013;52:397–402.
2. Aubry M, Cantu R, Dvorak J, et al. Summary and agreement statement of the First International Conference on Concussion in Sport, Vienna 2001. Phys Sportsmed. 2002;30(3):57.
3. Bakhos L, Lockhart G, Myers R, Linakis J. Emergency department visits for concussion in young child athletes. Pediatrics. 2010;126:e550–6.
4. Barkhoudarian G, Hovda D, Giza C. The molecular pathophysiology of concussive brain injury. Clin Sports Med. 2011;30:33–48.
5. Bayly PV, Cohen TS, Leister EP, et al. Deformation of the human brain induced by mild acceleration. J Neurotrauma. 2005;22:845–56.
6. Bayly PV, Black EE, Pedersen RC, et al. In vivo imaging of rapid deformation and strain in an animal model of traumatic brain injury. J Biomech. 2006;39:1086–95.
7. Bergsneider M, Hovda DA, Shalmon E, et al. Cerebral hyperglycolysis following severe traumatic brain injury in humans: a positron emission tomography study. J Neurosurg. 1997;86(2):241–51.
8. Bodin D, Yeates K, Klamar K. Definition and classification of concussion. In: Apps J, Walter K, editors. Pediatric and adolescent concussion: diagnosis, management and outcomes (9-19). New York, NY: Springer Science + Business Media, LLC.; 2012.
9. Cantu RC. Posttraumatic retrograde and anterograde amnesia: pathophysiology and implications in grading and safe return to play. J Athl Train. 2001;36:244–8.
10. Cantu RC. Second-impact syndrome. Clin Sports Med. 1998;17:37–44.
11. Cantu R, Voy R. Second impact syndrome: a risk in any sport. Phys Sportsmed. 1995;23:27–36.
12. Cassidy JD, Carroll LJ, Peloso PM, et al. Incidence, risk factors, and prevention of mild traumatic brain injury: results of the WHO collaborating centre task force on mild traumatic brain injury. J Rehabil Med. 2004;43:28–60.
13. Castile L, Collins C, McIlvain N, Comstock R. The epidemiology of new versus recurrent sports concussions among high school athletes, 2005-2010. Br J Sports Med. 2012;46:603–10.
14. Choe M, Babikian T, DiFiori J, et al. A pediatric perspective on concussion pathophysiology. Curr Opin Pediatr. 2012;24:689–95.
15. Collins MW, Iverson GL, Lovell MR, et al. On-field predictors of neuropsychological and symptom deficit following sports-related concussion. Clin J Sport Med. 2003;13:222–9.
16. Collins M, Loevell M, Iverson G, et al. Cumulative effects of concussion in high school athletes. Neurosurgery. 2002;51(5):1175–9.
17. Corner JP, Whitney CW, O'Rourke NO, et al. Motorcycle and bicycle protective helmets:

requirement resulting from a post crash study and experimental research, Vol 3, 1979-1987. Canberra ACT: Australian Transport Safety Bureau; 1987.
18. Dyall S, Michael-Titus A. Neurological benefits of omega-3 fatty acids. Neuromolecular Med. 2008;10:219–35.
19. Echemendia RJ, Putukian M, Makin RS, et al. Neuropsychological test performance prior to and following sports-related mild traumatic brain injury. Clin J Sport Med. 2001;11:23–31.
20. Erlanger D, Kaushik T, Cantu R, et al. Symptom-based assessment of the severity of a concussion. J Neurosurg. 2003;98:477–84.
21. Faden AI, Demediuk P, Panter SS, et al. The role of excitatory amino acids and NMDA receptors in traumatic brain injury. Science. 1989;244(4906): 798–800.
22. Farkas O, Lifshitz J, Povlishock JT. Mechanoporation induced by diffuse traumatic brain injury: an irreversible or reversible response to injury? J Neurosci. 2006;26(12):3130–40.
23. Faul M, Xu L, Wald MM, Coronado VG. Traumatic brain injury in the united states: emergency department visits, hospitalizations and deaths 2002–2006. Atlanta, GA: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2010.
24. Fazio VC, Lovell MR, Pardini JE, et al. The relation between post concussion symptoms and neurocognitive performance in concussed athletes. NeuroRehabilitation. 2007;22:207–16.
25. Giza CC, Maria NS, Hovda DA. N-methyl-D-aspartate receptor subunit changes after traumatic injury to the developing brain. J Neurotrauma. 2006;23(6):950–61.
26. Gomez-Pinilla F. The combined effects of exercise and foods in preventing neurological and cognitive disorders. Prev Med. 2011;52:S75–80.
27. Guskiewicz KM, Weaver NL, Padua DA, et al. Epidemiology of concussion in collegiate and high school football players. Am J Sports Med. 2000;28:643–50.
28. Harad FT, Kerstein MD. Inadequacy of bedside clinical indicators in identifying significant intracranial injury in trauma patients. J Trauma. 1992;32: 359–61.
29. Haydel MJ, Preston CA, Mills TJ, et al. Indications for computed tomography in patients with minor head injury. N Engl J Med. 2000;343:100–5.
30. Iverson GL, Gaetz M, Lovell MR, et al. Cumulative effects of concussion in amateur athletes. Brain Inj. 2004;18:433–43.
31. Iverson GL, Brooks BL, Lovell MR, et al. No cumulative effects of one or two prior concussions. Br J Sports Med. 2006;40:72–5.
32. Jantzen KJ, Anderson B, Steinberg FL, et al. A prospective functional MR imaging study of mild traumatic brain injury in college football players. AJNR Am J Neuroradiol. 2004;25(5):738–45.
33. Jeret JS, Mandell M, Anziska B, et al. Clinical predictors of abnormality disclosed by computed tomography after mild head trauma. Neurosurgery. 1993;32:9–15.
34. Johnson GV, Greenwood JA, Costello AC, et al. The regulatory role of calmodulin in the proteolysis of individual neurofilament proteins by calpain. Neurochem Res. 1991;16(8):869–73.
35. Jordan BD, Relkin NR, Ravdin LD. Apolipoprotein E4 associated with chronic traumatic brain injury in boxing. JAMA. 1997;278:136–40.
36. Kalimo H, Rehncrona S, Soderfeldt B. The role of lactic acidosis in the ischemic nerve cell injury. Acta Neuropathol Suppl. 1981;7:20–2.
37. Katayama Y, Becker DP, Tamura T, et al. Massive increases in extracellular potassium and the indiscriminate release of glutamate following concussive brain injury. J Neurosurg. 1990;73(6):889–900.
38. Kawamata T, Katayama Y, Hovda DA, et al. Lactate accumulation following concussive brain injury: the role of ionic fluxes induced by excitatory amino acids. Brain Res. 1995;674(2):196–204.
39. Kay T, Harrington DE, Adams R, et al. Definition of mild traumatic brain injury. J Head Trauma Rehabil. 1993;8:86–7.
40. Kirkwood M, Yeates K, Wilson P. Pediatric sports-related concussion: a review of the clinical management of an Oft-neglected population. Pediatrics. 2006;117:1359–71.
41. Kissick J, Johnston KM. Return to play after concussion: principles and practice. Clin J Sport Med. 2005;15(6):426–31.
42. Lewis M, Bailes J. Neuroprotection for the warrior: dietary supplementation with omega-3 fatty acids. Mil Med. 2011;176(10):1120–7.
43. Lifshitz J, Sullivan PG, Hovda DA, et al. Mitochondrial damage and dysfunction in traumatic brain injury. Mitochondrion. 2004;4(5–6):705–13.
44. Longhi L, Saatman KE, Fujimoto S, et al. Temporal window of vulnerability to repetitive experimental concussive brain injury. Neurosurgery. 2005;56(2):364–74. discussion: 364-74.
45. Lovell MR, Pardini JE, Welling J, et al. Functional brain abnormalities are related to clinical recovery and time to return-to-play in athletes. Neurosurgery. 2007;61(2):352–9. discussion: 359–60.
46. Marar M, McIlvain N, Fields S, Comstock R. Epidemiology of concussion among united states high school athletes in 20 sports. Am J Sports Med. 2012;40:747–55.
47. Maruta J, Suh M, Niogi S, et al. Visual tracking synchronization as a metric for concussion screening. J Head Trauma Rehabil. 2010;25(4):293–305.
48. Matser EJT, Kessels AG, Lezak MD, et al. Neuropsychological impairment in amateur soccer players. JAMA. 1999;282:971–3.
49. Maxwell WL, Povlishock JT, Graham DL. A mechanistic analysis of nondisruptive axonal injury: a review. J Neurotrauma. 1997;14(7):419–40.

50. McAllister TW, Sparling MB, Flashman LA, et al. Neuroimaging findings in mild traumatic brain injury. J Clin Exp Neuropsychol. 2001;23(6): 775–91.
51. McCrea M, Kelly JP, Kluge J, et al. Standardized assessment of concussion in football players. Neurology. 1997;48:586–8.
52. McCrory P, Johnston K, Meeuwisse W, et al. Summary and agreement statement of the 2nd international conference on concussion in sport, Prague, 2004. Clin J Sport Med. 2005;15:48–57.
53. McCrory P, Meeuwisse W, Aubry M, et al. Consensus statement on concussion in sport: the 4th International Conference on Concussion in Sport held in Zurich, November 2012. Br J Sports Med. 2013;47:250–8.
54. McGrath N. Supporting the student-athlete's return to the classroom after a sport-related concussion. J Athl Train. 2010;45:492–8.
55. Meares S, Shores EA, Taylor AJ, et al. Mild traumatic brain injury does not predict acute postconcussion syndrome. J Neurol Neurosurg Psychiatry. 2008;79:300–6.
56. Miller EC, Holmes JF, Derlet RW. Utilizing clinical factors to reduce head CT scan ordering for minor head trauma patients. J Emerg Med. 1997;15: 453–7.
57. Miller EC, Derlet RW, Kinser D. Minor head trauma: is computed tomography always necessary? Ann Emerg Med. 1996;27:290–4.
58. Moen K, Skandsen T, Folvik M, et al. A longitudinal MRI study of traumatic axonal injury in patients with moderate and severe traumatic brain injury. J Neurol Neurosurg Psychiatry. 2012;83:1193–200.
59. Moser R, Glatts C, Schatz P. Efficacy of immediate and delayed cognitive and physical rest for treatment of sports-related concussion. J Pediatr. 2012;161: 922–6.
60. Mower WR, Hoffman JR, Herbert M, Wolfson AB, Pollack Jr CV, Zucker MI. Developing a decision instrument to guide computed tomographic imaging of blunt head injury patients. J Trauma. 2005;59: 954–9.
61. Niogi SN, Mukherjee P, Ghajar J, et al. Extent of microstructural white matter injury in postconcussive syndrome correlates with impaired cognitive reaction time: a 3T diffusion tensor imaging study of mild traumatic brain injury. AJNR Am J Neuroradiol. 2008;29(5):967–73.
62. Niogi SN, Mukherjee P, Ghajar J, et al. Structural dissociation of attentional control and memory in adults with and without mild traumatic brain injury. Brain. 2008;131(Pt 12):3209–21.
63. Niogi S, Mukherjee P. Diffusion tensor imaging of mild traumatic brain injury. J Head Trauma Rehabil. 2010;25(4):241–55.
64. Ommaya AK, Gennarelli TA. Cerebral concussion and traumatic unconsciousness: correlation of experimental and clinical observations on blunt head injuries. Brain. 1974;97:633–54.
65. Ommaya AK, Goldsmith W, Thibault L. Biomechanics and neuropathology of adult and pediatric head injury. Br J Neurosurg. 2002;16:220–42.
66. Pellman EJ, Lovell MR, Viano DC, et al. Concussion in professional football: neuropsychological testing—part 6. Neurosurgery. 2004;55:1290–305.
67. Petraglia A, Maroon J, Bailes J. From the field of play to the field of combat: a review of the pharmacological management of concussion. Neurosurgery. 2012;70:1520–33.
68. Pettus EH, Povlishock JT. Characterization of a distinct set of intra-axonal ultrastructural changes associated with traumatically induced alteration in axolemmal permeability. Brain Res. 1996;722(1–2):1–11.
69. Ponsford J, Willmott C, Rothwell A, et al. Factors influencing outcome following mild traumatic brain injury in adults. J Int Neuropsychol Soc. 2000;6: 568–79.
70. Ptito A, Chen JK, Johnston KM. Contributions of functional magnetic resonance imaging (fmri) to sport concussion evaluation. NeuroRehabilitation. 2007;22:217–27.
71. Putukian M. Repeat mild traumatic brain injury: how to adjust return to play guidelines. Curr Sports Med Rep. 2006;5(1):15–22.
72. Reddy CC, Collins MW. Sports concussion: management and predictors of outcome. Curr Sports Med Rep. 2009;8(1):10–5.
73. Reeves TM, Lyeth BG, Povlishock JT. Long-term potentiation deficits and excitability changes following traumatic brain injury. Exp Brain Res. 1995; 106(2):248–56.
74. Roberts GW, Allsop B, Bruton C. The occult aftermath of boxing. J Neurol Neurosurg Psychiatry. 1990;53:373–8.
75. Robertson CL, Saraswati M, Fiskum G. Mitochondrial dysfunction early after traumatic brain injury in immature rats. J Neurochem. 2007;101(5):1248–57.
76. Ropper A, Gorson K. Concussion. N Engl J Med. 2007;356:166–72.
77. Rosengren D, Rothwell S, Brown AF, Chu K. The application of North American CT scan criteria to an Australian population with minor head injury. Emerg Med Australas. 2004;16:195–200.
78. Saatman KE, Abai B, Grosvenor A, et al. Traumatic axonal injury results in biphasic calpain activation and retrograde transport impairment in mice. J Cereb Blood Flow Metab. 2003;23(1):34–42.
79. Sanders MJ, Sick TJ, Perez-Pinzon MA, et al. Chronic failure in the maintenance of long-term potentiation following fluid percussion injury in the rat. Brain Res. 2000;861(1):69–76.
80. Saunders RL, Harbaugh RE. The second impact in catastrophic contact-sports head trauma. JAMA. 1984;252:538–9.
81. Schatz P, Pardini JE, Lovell MR, et al. Sensitivity and specificity of the ImPACT test battery for concussion in athletes. Arch Clin Neuropsychol. 2006;21:91–9.

82. Schulz MR, Marshall SW, Mueller FO, et al. Incidence and risk factors for concussion in high school athletes, North Carolina, 1996-1999. Am J Epidemiol. 2004;160:937–44.
83. Scorza K, Raleigh M, O'Connor F. Current concepts in concussion: evaluation and management. Am Fam Physician. 2012;85(2):123–32.
84. Sick TJ, Perez-Pinzon MA, Feng ZZ. Impaired expression of long-term potentiation in hippocampal slices 4 and 48 h following mild fluid-percussion brain injury in vivo. Brain Res. 1998;785(2): 287–92.
85. Shin S, Dixon C. Oral fish oil restores striatal dopamine release after traumatic brain injury. Neurosci Lett. 2011;496:168–71.
86. Slobounov SM, Zhang K, Pennell D, et al. Functional abnormalities in normally appearing athletes following mild traumatic brain injury: a functional MRI study. Exp Brain Res. 2010;202:341–54.
87. Smits M, Dippel DW, de Haan GG, et al. External validation of the Canadian CT Head Rule and the New Orleans Criteria for CT scanning in patients with minor head injury. JAMA. 2005;294:1519–25.
88. Spain A, Daumas S, Lifshitz J, et al. Mild fluid percussion injury in mice produces evolving selective axonal pathology and cognitive deficits relevant to human brain injury. J Neurotrauma. 2010;27(8): 1429–38.
89. Stein SC, Fabbri A, Servadei F, Glick HA. A critical comparison of clinical decision instruments for computed tomographic scanning in mild closed traumatic brain injury in adolescents and adults. Ann Emerg Med. 2009;53:180–8.
90. Stein SC, Ross SE. The value of computed tomographic scans in patients with low-risk head injuries. Neurosurgery. 1990;26:638–40.
91. Stein SC, Ross SE. Mild head injury: a plea for routine early CT scanning. J Trauma. 1992;33:11–3.
92. Sternberger NH, Sternberger LA. Neurotypy: the heterogeneity of brain proteins. Ann N Y Acad Sci. 1983;420:90–9.
93. Stiell IG, Wells GA, Vandenheem K, et al. The Canadian CT Head Rule for patients with minor head injury. Lancet. 2001;357:1391–6.
94. Stiell IG, Clement CM, Rowe BH, et al. Comparison of the Canadian CT head rule and the New Orleans Criteria in patients with minor head injury. JAMA. 2005;294:1511–8.
95. Tavazzi B, Vagnozzi R, Signoretti S, et al. Temporal window and metabolic brain vulnerability to concussions: oxidative and nitrosative stresses—part II. Neurosurgery. 2007;61:390–6.
96. Teasdale TW, Engberg AW. Cognitive dysfunction in young men following head injury in childhood and adolescence: a population study. J Neurol Neurosurg Psychiatry. 2003;74:933–6.
97. Vagnozzi R, Tavazzi B, Signoretti S, et al. Temporal window of metabolic brain vulnerability to concussions: mitochondrial-related impairment–part I. Neurosurgery. 2007;61(2):379–88. discussion: 88–9.
98. van Kampen DA, Lovell MR, Pardini JE, et al. The value added of neurocognitive testing following sports-related concussion. Am J Sports Med. 2006;34:1630–5.
99. Vagnozzi R, Signoretti S, Tavazzi B, et al. Hypothesis of the postconcussive vulnerable brain: experimental evidence of its metabolic occurrence. Neurosurgery. 2005;57(1):164–71. discussion: 164-71.
100. Verweij BH, Muizelaar JP, Vinas FC, et al. Mitochondrial dysfunction after experimental and human brain injury and its possible reversal with a selective N-type calcium channel antagonist (SNX-111). Neurol Res. 1997;19(3):334–9.
101. Wilde EA, McCauley SR, Hunter JV, et al. Diffusion tensor imaging of acute mild traumatic brain injury in adolescents. Neurology. 2008;70(12):948–55.
102. Williams W, Potter S, Ryland H. Mild traumatic brain injury and Postconcussion Syndrome: a neuropsychological perspective. J Neurol Neurosurg Psychiatry. 2010;81:1116–22.
103. Wu A, Ying Z, Gomez-Pinilla F. The salutary effects of DHA dietary supplementation on cognition, neuroplasticity, and membrane homeostasis after brain trauma. J Neurotrauma. 2011;28:2113–22.
104. Xiong Y, Gu Q, Peterson PL, et al. Mitochondrial dysfunction and calcium perturbation induced by traumatic brain injury. J Neurotrauma. 1997;14(1): 23–34.
105. Yoshino A, Hovda DA, Kawamata T, et al. Dynamic changes in local cerebral glucose utilization following cerebral conclusion in rats: evidence of a hyper and subsequent hypometabolic state. Brain Res. 1991;561(1):106–19.
106. Nagy KK, Joseph KT, Krosner SM, et al. The utility of head computed tomography after minimal head injury. J Trauma. 1999;46:268–73.
107. Lovell M, Collins MW. Neuropsychological assessment of the college football player. J Head Trauma Rehabil. 1998;13(2):9–26.
108. Gronwall D. Rehabilitation programs for patients with mild head injury: components, problems, and evaluation. J Head Trauma Rehab. 1986;1:53–62.
109. Harmon KG, et al. American Medical Society for Sports Medicine position statement: concussion in sport. Br J Sports Med. 2013;47:15–26.
110. Giza CC, Kutcher JS, Ashwal S, et al. Summary of evidence-based guideline update: evaluation and management of concussion in sports: Report of the Guideline Development Subcommittee of the American Academy of Neurology. Neurology. 2013;80:2250–7.

Index

J.P. Greenfield, C.B. Long (eds.), *Common Neurosurgical Conditions in the Pediatric Practice*,
DOI 10.1007/978-1-4939-3807-0