PRINCIPLES OF PEDIATRIC NEUROSURGERY

Intracranial Cyst Lesions

Edited by
Anthony J. Raimondi
Maurice Choux
Concezio Di Rocco

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Principles of Pediatric Neurosurgery

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Head Injuries in the Newborn and Infant

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With 232 Figures

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Series Preface

It is estimated that the functionally significant body of knowledge for a given medical specialty changes radically every 8 years. New specialties and "sub-specialization" are occurring at approximately an equal rate. Historically, established journals have not been able either to absorb this increase in publishable material or to extend their readership to the new specialists. International and national meetings, symposia and seminars, workshops, and newsletters successfully bring to the attention of physicians within developing specialties what is occurring, but generally only in demonstration form without providing historical perspective, pathoanatomical correlates, or extensive discussion. Page and time limitations oblige the authors to present only the essence of their material.

Pediatric neurosurgery is an example of a specialty that has developed during the past 15 years. Over this period neurosurgeons have obtained special training in pediatric neurosurgery and then dedicated themselves primarily to its practice. Centers, Chairs, and educational programs have been established as groups of neurosurgeons in different countries throughout the world organized themselves respectively into national and international societies for pediatric neurosurgery. These events were both preceded and followed by specialized courses, national and international journals, and ever-increasing clinical and investigative studies into all aspects of surgically treatable diseases of the child's nervous system.

Principles of Pediatric Neurosurgery is an ongoing series of publications, each dedicated exclusively to a particular subject, a subject which is currently timely either because of an extensive amount of work occurring in it, or because it has been neglected. The two first subjects, "Head Injuries in the Newborn and Infant" and "The Pediatric Spine," are expressive of those extremes.

Volumes will be published continuously, as the subjects are dealt with, rather than on an annual basis, since our goal is to make this information available to the specialist when it is new and informative. If a volume becomes obsolete because of newer methods of treatment and concepts, we shall publish a new edition.

The chapters are selected and arranged to provide the reader, in each instance, with embryological, developmental, epidemiological,

clinical, therapeutic, and psychosocial aspects of each subject, thus permitting each specialist to learn what is most current in his field and to familiarize himself with sister fields of the same subject. Each chapter is organized along classical lines, progressing from Introduction through Symptoms and Treatment, to Prognosis for clinical material; and Introduction through History and Data, to Results and Discussion for experimental material.

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CHAPTER 1

Cytogenesis and Developmental and Functional Anatomy of the Glia and Ependyma

Eiichi Tani

Early Development of the Neural Tube

The central nervous system (CNS) of mammalian embryos is first shown as the neural plate. The lateral edges of the neural plate soon become elevated to form the neural folds, and the depressed region between the folds becomes the neural groove. Further development results in the formation of the neural tube, with a long caudal part (spinal cord) and a broader cephalic portion (brain vesicles). The neural tube is composed of three different zones:[1,2] ependymal, mantle, and marginal zones. The ependymal zone borders the lumen of the neural tube and consists of high columnar epithelial cells and large round cells. The round cells are referred to as the germinal cells and develop into neuroblasts, whereas the columnar epithelial cells give rise to spongioblasts. Both the neuroblasts and the spongioblasts migrate to a densely packed nuclear zone, the mantle zone. The marginal zone is the outermost layer of the neural tube and consists of the peripheral processes and axons of the neuroblasts.

However, serious criticism of the germinal cell theory has been raised repeatedly,[3–5] suggesting that the large round cells adjacent to the lumen are simply dividing epithelial cells and that both cell types are in fact the same. Figure 1.1 summarizes schematically the observations obtained with the following techniques: colchicine,[6–8] autoradiography,[8–14] and electron microscopy.[15,16] The cells in the wall of the neural groove or of the early neural tube are considered to form a homogeneous population that consists of only one cell type, the neuroepithelial cells, because no differentiation into neuroblasts and spongioblasts can be observed. The neuroepithelial cells form a pseudostratified epithelium and extend over the entire thickness of the wall. They are connected to each other by terminal bars in the juxtaluminal zone. During DNA synthesis the cells are wedge-shaped, with the broader part containing the nucleus in the outer zone and a slender cytoplasmic part extending toward the inner surface. Soon after DNA synthesis, the nucleus begins to move toward the lumen, while the cells contract toward the terminal bars. During metaphase the cells are round and in broad contact with the lumen, thereby often squeezing the slender cytoplasmic processes of the neighboring nondividing cells. The terminal bars do not break down during division. Soon after mitosis, the daughter nuclei return toward the outer zone and the cells assume their original wedge shape.

Gliogenesis

Astrocytes and Oligodendrocytes

Using silver techniques, Ramón y Cajal[17] noted two different cellular elements derived from the neuroepithelial cells in the spinal cord of the chick embryo. First to appear are the apolar neuroblasts. The second type, defined as the neuroglial cells, becomes visible some time later, and is considered to be dislo-

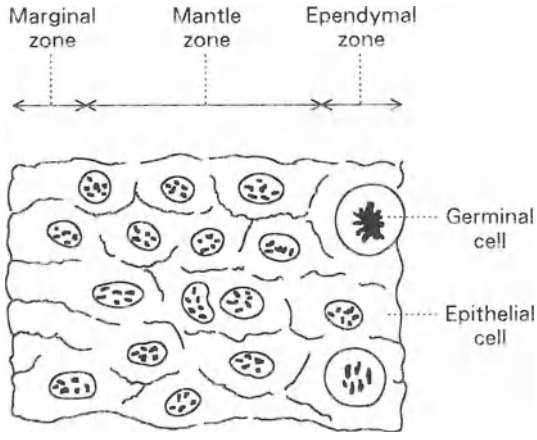

Figure 1.1. Schema of transverse section through the wall of the neural tube just after closure of the tube. According to Hardesty[2] the cell membranes are disappearing and the cells form a syncytium.

cated and greatly transformed neuroepithelial cells and classified as embryonal or modified astrocytes. Consistent with Ramón y Cajal's interpretations are the recent electron-microscopic observations of monkey fetuses, that these cells show relatively electron-lucent cytoplasm, shafts filled with microtubules, lamellate expansions at a right angle to the main radial process, and glycogen granules in the expanded end-feet.[18] The third type defined with silver carbonate technique by del Rio-Hortega[19] consists of two different types of well-branched cells, which he named oligodendroglial and microglial cells.

Recently, the immunocytochemical method has been used as a valuable adjunct to the traditional morphological techniques for the identification of cell types in the developing CNS. Golgi, immunohistochemical, and electron-microscopic studies of gliogenesis in the developing CNS reveal an orderly sequence of events characterized by the formation of radial glial cells and astrocytes and subsequently by the appearance of oligodendrocytes in the cerebrum, cerebellum, and spinal cord of humans.[20–24] It thus appears that the earliest glial cells that form within the developing CNS are radially organized and show the ultrastructural and immunocytochemical features of astrocyte differentiation in human fetal cerebrum at 12 weeks of gestation (Figure 1.2) and in human fetal spinal cord at 10 weeks of gestation. In addition, radial glia and radial glia-derived cells also give rise to differentiated astrocytes, indicating that cells of astrocyte lineage are being generated while active neurogenesis is still taking place.[22]

Although the formation of compact myelin sheaths is accomplished by more differentiated oligodendrocytes, the presence during development of cell forms intermediate electron microscopically and immunocytochemically between those of oligodendrocyte and astrocyte suggests not only a close and dynamic ontogenetic relationship between, but also a common cell lineage for, the two cell types.[25,26] Others have also described the presence of 0–

Figure 1.2. Glycogen granules (gly), glial filaments (gf), and a few microtubules are shown in the large electron-lucent glial process (GP). A 17-week-old human fetal cerebrum. (×31,000.) [Reprinted with permission from Choi and Lapham.[24]]

2A progenitor cells that differentiate into both astrocyte and oligodendrocyte in cultures of immature glial cells,[27–32] as described later. It is suggested, therefore, that these early radially organized glial cells may be the ultimate source of all macroglial cell types, including astrocytes, oligodendrocytes, and ependymal cells.

Ependymal Cells

The innermost cells of the matrix in the neural tube are bordering the cerebrospinal fluid and can be regarded as a primitive ependyma. In some cells of the ependymal zone the basal process continues to grow while the nucleus remains in the ventricular region. These cells become the so-called ependymal tanycytes.[33] In higher vertebrates, the ependymal processes are disconnected and replaced by free astrocytes with increasing thickness of the brain.

Microglial Cells

During development, the microglial cells appear first below the pia and only later in the vicinity of the ventricles.[19,34] The two main sources of origin are found at the attachment of the tela chorioidea and at the pia covering the cerebral peduncle. Small numbers also arise from the pia throughout the brain and spinal cord and from the adventitial cells of the large- and medium-sized blood vessels, suggesting that the microglial cells originate from mesenchymal elements. During their migration the microglial cells have a somewhat rounded appearance with pseudopodia.

General Histology

Astrocytes

Ramón y Cajal's work on the neuroglia is one of the most thorough studies ever made on the form and structure of astrocytes, and together with del Rio-Hortega's work, has become the standard reference for the appearance of astrocytes.

Fibrous and Protoplasmic Astrocytes

Several types of astrocytes exist, of which the most common are the fibrous and the protoplasmic (Figure 1.3). The cytoplasmic processes 20 to 50 altogether, issue directly from the cell body, in most instances in radial array, giving the cells a star-like shape. The fibrous astrocytes differ from the protoplasmic astrocytes in that their processes are fewer and longer and branch less frequently and at a more acute angle.

Fibrous astrocytes are widely distributed in the CNS, predominantly in the white matter. The inferior olivary nucleus is exceptional in that it contains a particularly heavy complement of fibrous astrocytes.[35,36] Protoplasmic astrocytes are located solely in the gray matter, and imposed by adjustments to the surface of neuronal elements. Three main classes of protoplasmic astrocytes in the gray matter may be distinguished on the basis of location: (a) neuronal (perisomatic) satellites, which are in close contact with neuronal cell bodies and with the proximal part of the axon and the dendrites; (b) interneuronal astrocytes, which are at some distance from cell bodies; and (c) vascular satellites, which lie next to vessels.[37]

Astrocyte density differs in different regions of the CNS.[38,39] For instance, the ratio of glial cells to nerve cells in the human striatum is 4:1; glial cells take up 20% of the volume of the striatum, and three-fourths of this volume is occupied by glial processes. Corresponding values for the pallidum are 100:1, 40%, and 95%.[40] The cytoplasmic processes of cerebellar Bergman and Fañanas glia occupy nearly 20% of the total space in the neuropil of the molecular layer.[41]

Fibrous astrocytes form a reticular layer over most of the surface of the cerebrum, and are called marginal astrocytes. They are closely applied to the undersurface of the pia and send out fibrous expansions parallel to the pia (Figure 1.4) and down into the cerebral tissue. These astrocytes may have perivascular end-feet, but many possess a short robust pial end-foot.[42] The end-feet participate in the formation of the external glial-limiting mem-

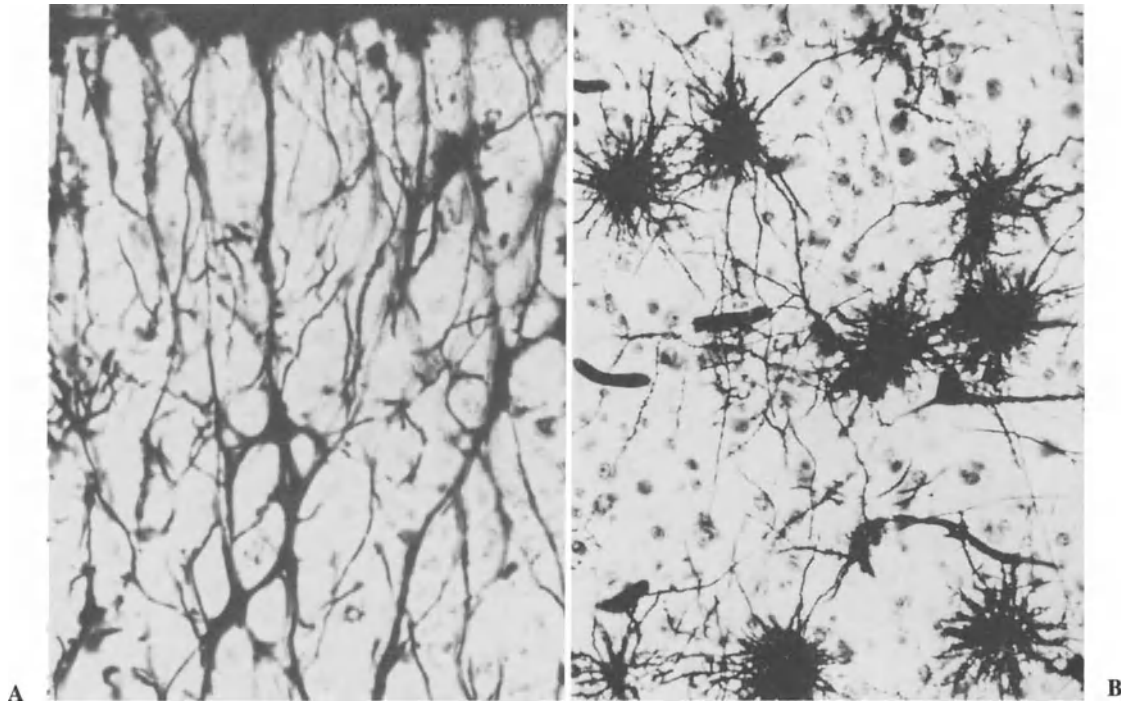

Figure 1.3. Fibrous astrocytes of the spinal cord of the monkey (A). Long astrocytic processes are located between groups of nerve fibers and directed to the pia. Protoplasmic astrocytes of the human cerebral cortex (B). A few astrocytic end-feet are to be seen. Some of the nerve cells appear to be impregnated. (Golgi-Hortega-Lavilla method.) [Reprinted with permission from Polak, Haymaker, Johnson, and D'Amelio.[90]]

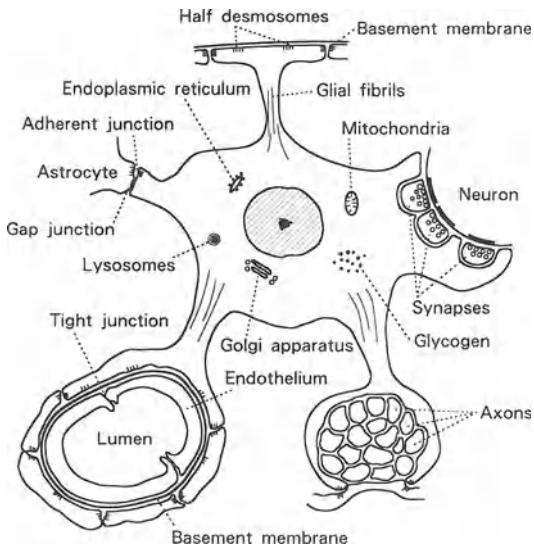

Figure 1.4. Schema of astrocyte.

brane, and a thin basement membrane adheres closely to the pial surface of these end-feet. The cytoplasmic processes of astrocytes in the cerebral parenchyma have end-feet that form a glial-limiting membrane around the adventitia of large vessels. This membrane has a basement membrane such as is present at the pia. Other astroglial cells have processes, which are implanted on the capillary wall by means of a conical sucker-foot (Figure 1.4). The astroglial end-foot is not directly applied to the capillary wall, for a space 40 to 100nm in width lies between it and the basement membrane of the capillary. Sometimes more than one process of a given astrocyte is so implanted. In addition, the neural processes are shown to be insulated from each other by the astrocytic processes (Figure 1.4).

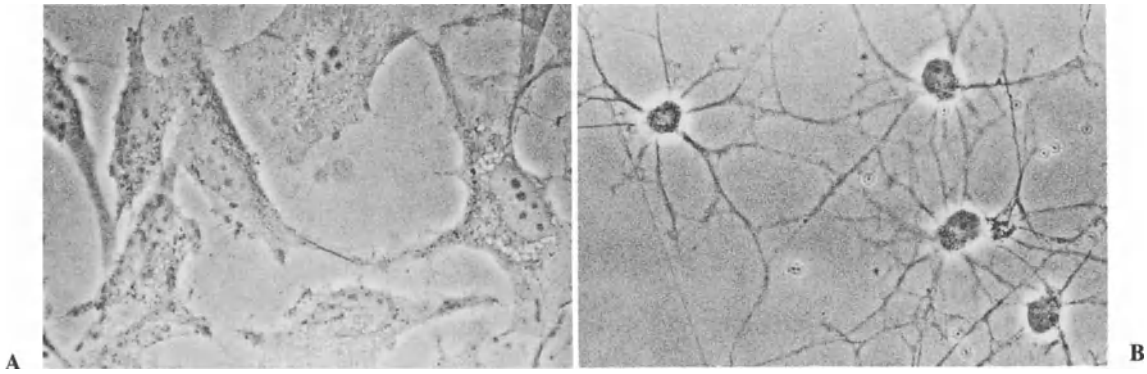

Figure 1.5. Type 1 (A) and type 2 (B) astrocytes in culture of newborn rat optic nerve.

Type 1 and Type 2 Astrocytes

Recently, it has become more and more clear that astrocytes can no longer be considered as a homogeneous cell population. Two distinct types of glial fibrillary acidic protein-positive astrocytes (type 1 and type 2) can be distinguished in cultures of developing rat optic nerve by a combination of morphological and antigenic criteria (Figure 1.5).[27,43,44] Type 1 astrocytes have a fibroblast-like morphology, proliferation in culture [especially in response to epidermal growth factor (EGF) or bovine pituitary extract], and do not bind detectable amounts of tetanus toxin or A2B5 antibody, which recognizes complex gangliosides.[45] Type 2 astrocytes have a process-bearing morphology, resembling neurons or oligodendrocytes, divide infrequently in culture (even in the presence of EGF or bovine pituitary extract), and bind tetanus toxin and A2B5 antibody.

In culture, the two types of astrocytes derive from different cell lineages: type 1 astrocytes develop from their own precursor cells, whereas type 2 astrocytes develop from a bipotential precursor cell, which also gives rise to oligodendrocytes and has therefore been called an 0–2A progenitor cell.[27,44] In vivo, cells with the antigenic phenotype of type 1 astrocytes first appear at embryonic day 16, whereas cells with the antigenic phenotype of type 2 astrocytes do not appear until the beginning of the second postnatal week.[46] However, there are still no antibodies that unambiguously distinguished type 1 and type 2 astrocytes.

There is increasing, indirect evidence that the two types of astrocytes in perinatal optic nerve cultures correspond to distinct types of astrocytes in the adult optic nerve. Type 1 astrocytes in vitro apparently correspond to astrocytes in vivo that have most of their processes oriented radially in the nerve, ending mainly on blood vessels or the pial surface (Figure 1.6).[47] Type 2 astrocytes in vitro, by contrast, apparently correspond to astrocytes in vivo that have most of their processes oriented longitudinally, associated mainly with nodes of Ranvier, suggesting that they may collaborate with oligodendrocytes to ensheathe axons and construct nodes of Ranvier

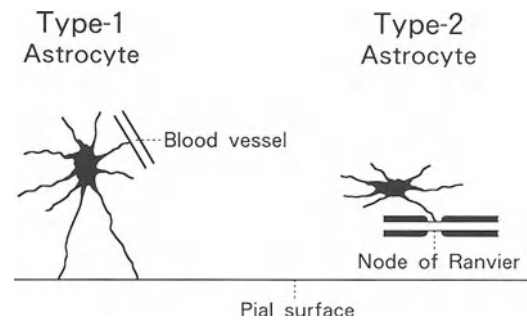

Figure 1.6. Schema of type 1 and type 2 astrocytes in adult rat optic nerve.

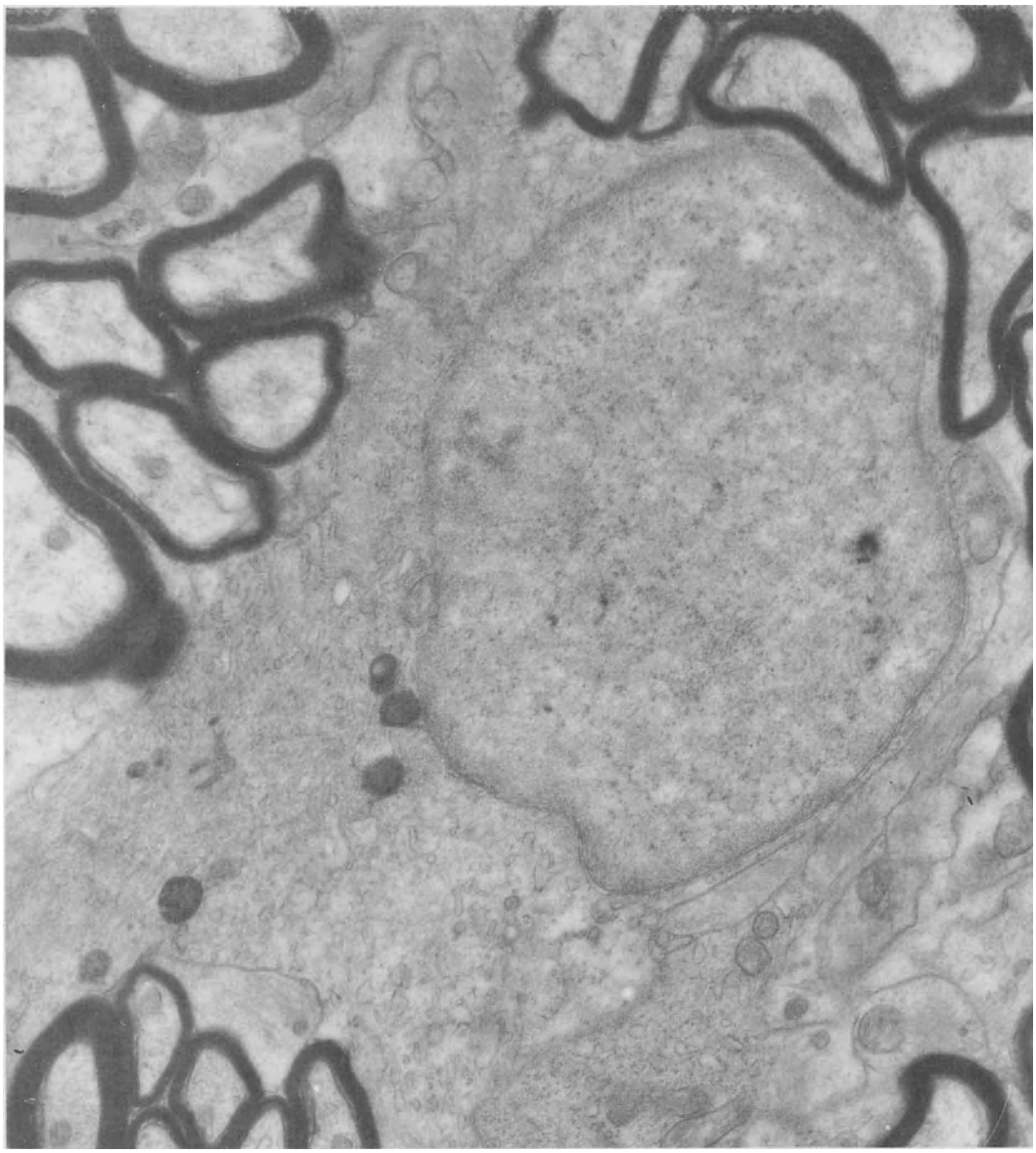

Figure 1.7. Fibrous astrocyte in rat corpus callosum. A large number of small vesicles are scattered throughout the cytoplasm. Seven lysosomes are found with polymorphic appearance. Glial filaments are visible in the perinuclear region and the cell processes. (×16,000.)

in the white matter tracts (Figure 1.6).[47] In view of the close developmental[27] and functional[47] relationship between oligodendrocytes and type 2 astrocytes, it is intriguing that these two types of glial cells seem to be connected by gap junctions at nodes of Ranvier.[48,49] Thus, type 2 astrocytes seem to be a novel type of glial cell not previously recognized as a distinct cell type.

Ultrastructure of Astrocytes

The nuclei of astrocytes have a thin rim of fairly dense chromatin along their mem-

branes, and the chromatin is rather evenly distributed throughout the remainder of the nuclei. A nucleolus is usually well developed. There are differences as well as similarities in the perikaryon of fibrous (Figure 1.7) and protoplasmic astrocytes. In both types the perikaryon is electron-lucent, though owing to the sparsity of ribosomes, it is lighter in protoplasmic than in fibrous astrocytes. They also differ with respect to their cytoplasmic filament content, fibrous astrocytes having by far the greater number.

In fibrous astrocytes the filaments are present throughout the perikaryon and extend as parallel arrays into the processes. Usually, they are assembled in bundles, and each filament measures about 6 to 9 nm in diameter. At high magnification, they are found to be round with a clear center and have a beaded wall. As viewed in longitudinal sections, the filament is seen as two parallel dense lines separated by a light core. In fetal stages of development, microtubules in fibrous astrocytes are quite numerous, but they decline in number after birth.[50]

Mitochondria are usually abundant in both the fibrous and protoplasmic astrocytes and are seen in the perikaryon and in the larger cytoplasmic processes. The cristae of mitochondria in astrocytes are often of the prismatic type.[51] Endoplasmic reticulum (ER) is sparse. In fibrous astrocytes the cisternae of ER are unevenly but prominently studded with ribosomes. In protoplasmic astrocytes the ribosomes are fewer.[50] Small aggregates of glycogen granules are distributed in the cytoplasm of both astroglial types. Lysosomes are found in both fibrous and protoplasmic astrocytes.[51,52] A further point of interest is the frequent presence of centrioles in the cytoplasm of fibrous astrocytes. Cilia may also be found, one per cell, and they contain nine peripheral pairs of microtubules but no central pair.[53]

In addition to adherent junctions (Figure 1.4 and 1.8), interastroglial gap junctions are

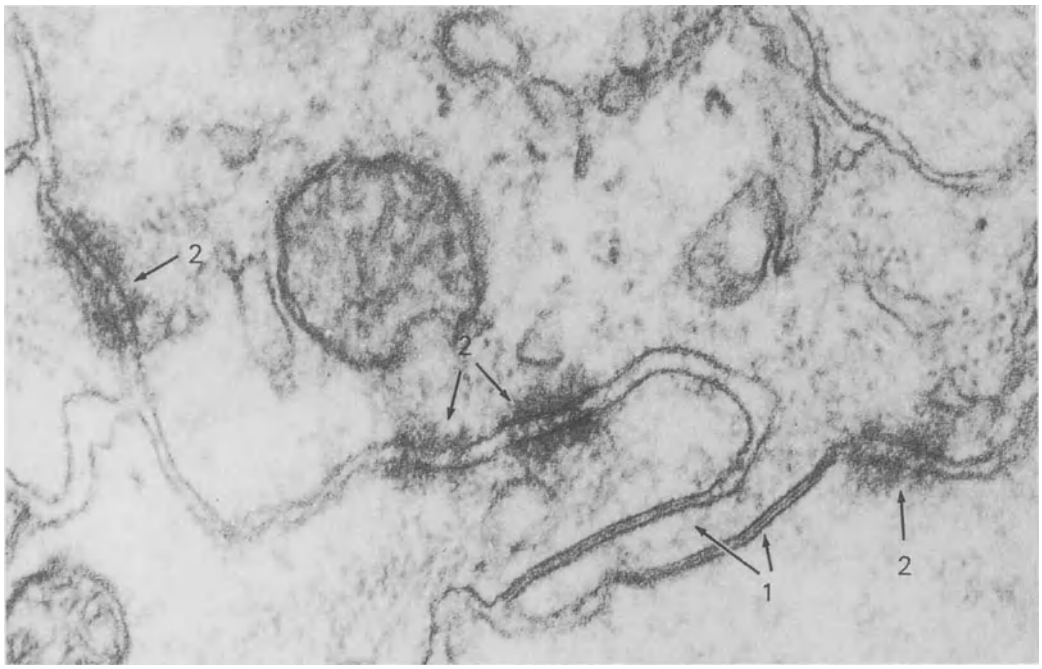

Figure 1.8. Two gap (arrows 1) and four adherent junctions (arrows 2) are found between adjacent astrocytes. (×9,000.) [Reprinted with permission from Tani and Ametani.[91]]

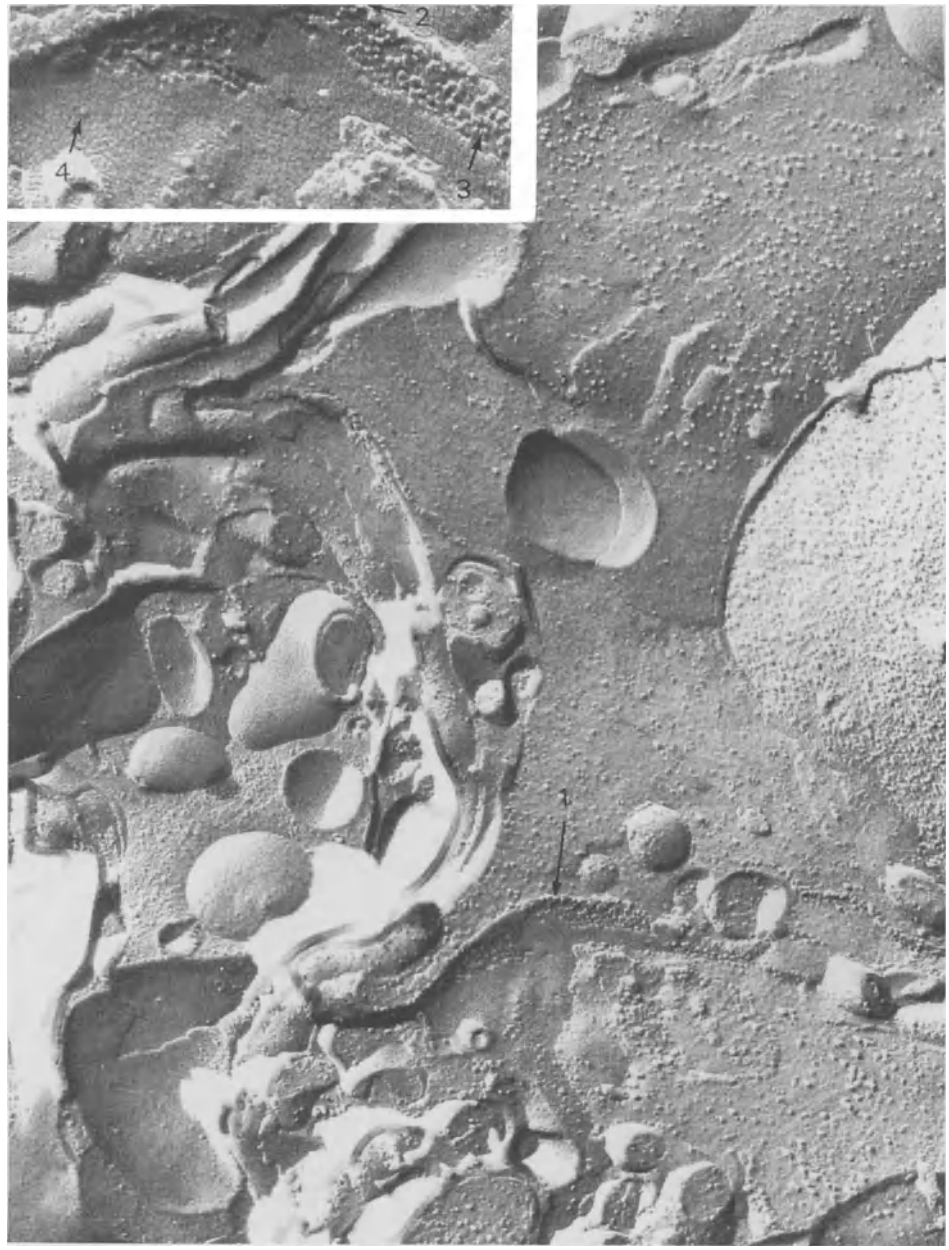

Figure 1.9. An astrocyte in freeze-fracture replica is characterized by irregular shape of cell body, scanty cytoplasmic organelles, and presence of glial filaments. A gap junction (arrow 1) is found between adjacent astrocytes, and reveals an aggregation of particles and pits in faces P and E, respectively (inset). The top surface of the particles occasionally displays a central electron-opaque (arrow 2) or white dot (arrow 3). A pit is replaced by a particle (arrow 4), which shows a central electron-opaque region in its top. (×53,000; inset ×117,000.) [Reprinted with permission from Tani, Ikeda, Nishiura, and Higashi.[71]]

often noted between two cell bodies, between two processes, and between a cell body and a cell process (Figures 1.8 and 1.9). The interspace of 10 to 20 nm in that region is narrowed to a constant width of 2 to 3nm, the gap continuous with the wider interspace.[54–56] The gap junctions are usually hexagonally packed in a crystalline array with a center-to-center distance of 85 nm.[48,57]

Numerous astrocyte-to-oligodendrocyte gap junctions are also identified.[48] These gap junctions occur between cell bodies, between processes, and between cell bodies and processes, as do the interastrocytic gap junctions. In addition, astrocytic cell processes form gap junctions with the outer turn of the myelin sheath at the level of cytoplasmic pockets, the outer loops, and the paranodal loops. In the astrocyte-oligodendrocyte gap junctions, with few exceptions, the connections are closely packed but not crystalline. The center-to-center spacing is 11 nm.

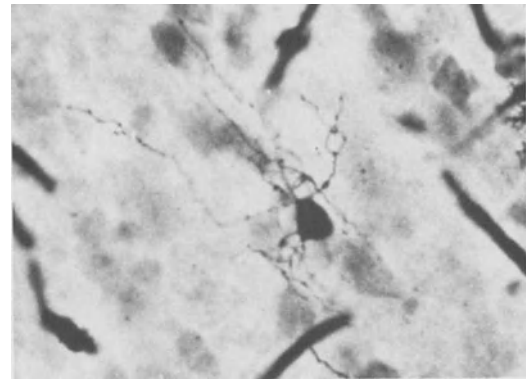

Figure 1.10. Oligodendrocyte in human corpus callosum. Oligodendrocyte has slender processes originating from spheroidal body. (Golgi-Hortega-Lavilla method.) [Reprinted with permission from Polak, Haymaker, Johnson, and D'Amelio.[90]]

Oligodendrocytes

Light Microscopy of Oligodendrocytes

Oligodendrocytes are small cells whose soma averages 6 to 8 μm in diameter. The nuclei are round or oval and relatively dense, and the cytoplasms form a narrow rim. In sections stained by silver techniques, oligodendrocytes appear as spheroidal, polygonal, or piriform cells having several slender processes that occasionally appear thorny (Figure 1.10). Oligodendrocytes are distributed in both gray and white matter, and in the gray matter they appear as neuroal (perisomatic) satellites or are found next to nerve fibers or blood vessels. In the human precentral cortex, oligodendrocytes make up 51% of the perineuronal glial population.[58,59] Interfascicular oligodendrocytes are by far the most common cell type in the white matter. Their processes tend to run parallel to nerve fibers, and give off branches that partly or completely encircle nerve fibers. In the rat corpus callosum 69.8% of the glial cells are oligodendrocytes.[60] In the rat spinal cord (anterior horn and midzone), 60% of the glia have been found to be oligodendrocytes.[61]

Ultrastructure of Oligodendrocytes

Oligodendrocytes have many ultrastructural features in common regardless of their location (Figure 1.11). The nucleoplasm has an electron density greater than that of astrocytes. The cytoplasm is electron dense.[50] Free ribosomes also abound, and the cytoplasm is rich in granular ER. The cisternae of ER are generally arranged in a circumferential manner around the nucleus but predominate on one side of the nucleus. The Golgi apparatus is usually well developed, and its cisternae and vesicles are present throughtout the perikaryal cytoplasm. Mitochondria are rather inconspicuous. Microtubules are numerous and are concentrated at the sites of origin of the cytoplasmic processes and in the cytoplasmic processes themselves. Filaments are rarely seen, and the cytoplasm contains no glycogen granules. Lysosomes sometimes encountered in the perikaryal cytoplasm have either a homogeneous appearance or contain granules, membranous components, filaments, and droplets, or even exhibit one or two clear rectangular areas.[50,62]

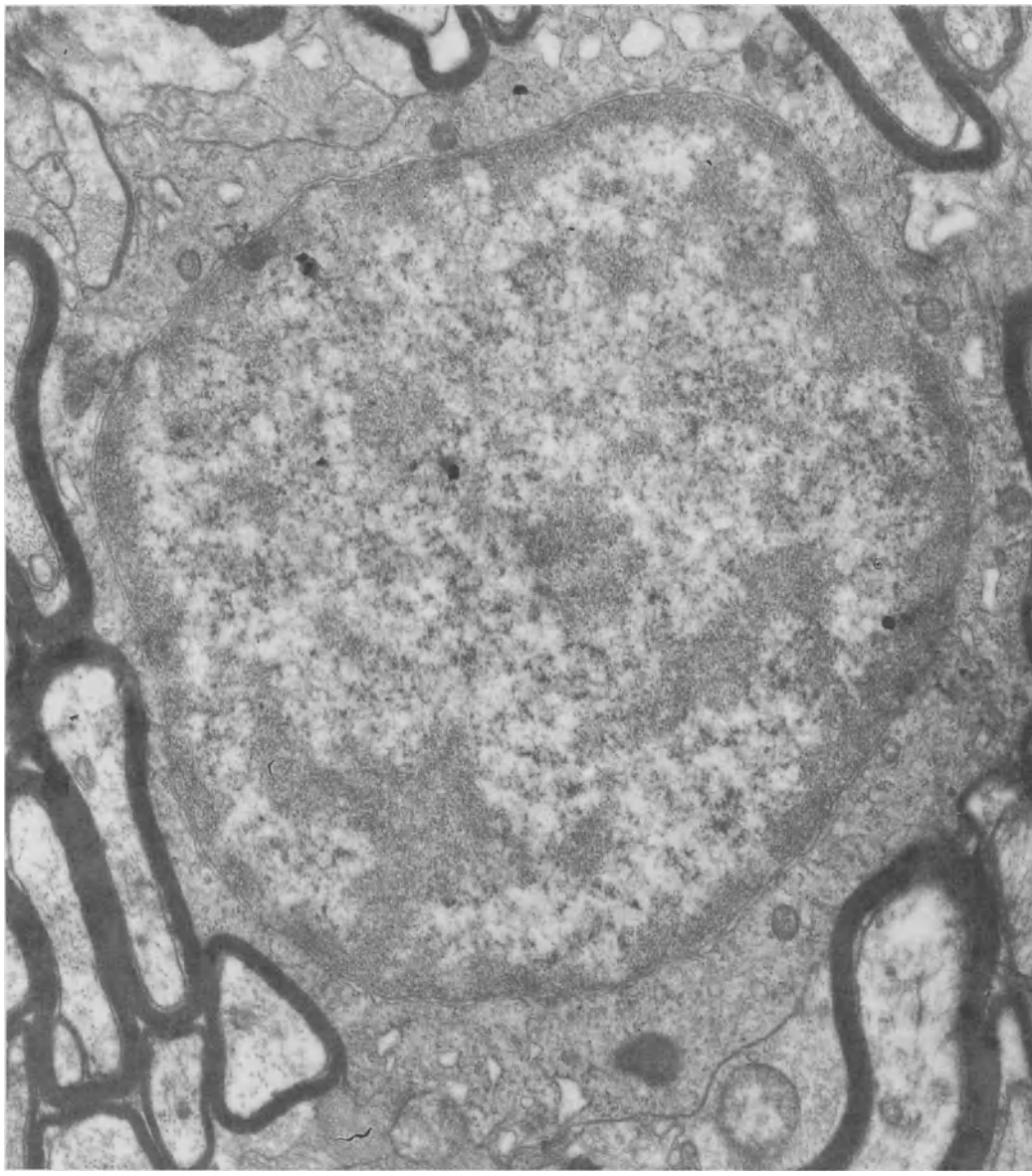

Figure 1.11. An oligodendrocyte in rat corpus callosum. The cytoplasm is dense in appearance. No glial filaments are visualized throughout the cytoplasm. (×22,000.)

The plasma membrane of oligodendrocyte forms the myelin lamellae.[63–65] Multiple mesaxonal processes extend from the perikaryon of oligodendrocyte and ensheathe the axons in broad, inwardly directed, spiral lamellae (Figure 1.12). After myelin formation is completed, the sheath components are oriented in a spiral, the major and the intermediate dense lines in the myelin lamellae formed by the fusion of the inner and the outer plasma membranes of oligodendrocyte, respectively, and only the inner- and outer-most layers

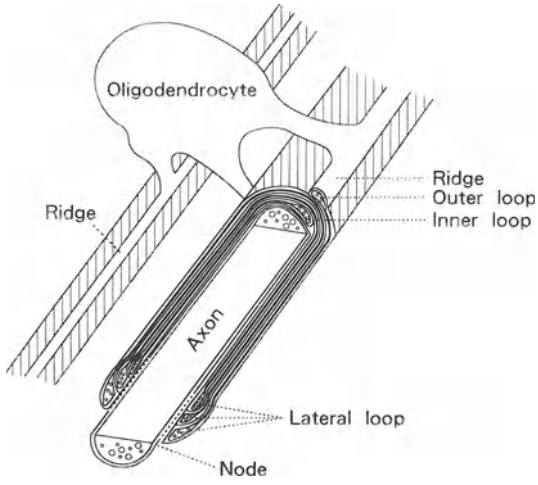

Figure 1.12. Schematic representation of relationship between an oligodendrocyte and myelin in the central nervous system.

ending in loops. The outer loop forms a ridge along the internode length and may be continuous with the cell body of oligodendrocyte. In the longitudinal plane, every myelin unit terminates in a separate loop at both ends of the internode. Within these loops, glial cytoplasm is also retained.

Tight junctions occur exclusively between oligodendrocytic plasma membranes (Figure 1.13);[48,66] between two cell bodies, between a cell body and process, or between a cell body and the outer loop of myelin sheath. Tight junctions between different turns of the myelin sheath membrane are also observed. Interoligodendrocytic gap junctions are not observed.[48]

Ependymal Cells

Structure of Ependymal Cells

In most ependymal cells the nuclei are oblong, with the long axis being parallel to the long axis of the cell (Figure 1.14). The cytoplasm contains mitochondria, predominately vesicular ER, granular ER, and Golgi apparatus, which are mostly situated above the nucleus in the apical part of the cell. In addition, the apical cytoplasm contains microtubules and rootlets of numerous cilia. Most ependymal cells show glial filaments, identical with those found in fibrous astrocytes.[67–70] The cytoplasm of ependymal cells may also contain various forms of lysosomes. At the luminal surface there is a regionally varying number of microvilli and cilia. The structure of cilia conforms to the 9 + 2 pattern and the rootlets and necklace have been described in detail in rat[69,71] and in cat.[70]

The plasma membranes of neighboring ependymal cells are folded and interdigitated, particularly near the apical end of the perikaryon. Sometimes long and flat processes are formed that overlap part of the surface of an adjacent cell. Near the ventricular surface, the intercellular clefts seem to be sealed with terminal bars. The electron-microscopic studies have revealed that the terminal bars of the ependyma are rather complicated and are composed of two types of cell junctions: adherent and gap junctions (Figures 1.14 and 1.15).[54,71] The gap junctions occasionally occur directly at the ventricular surface, but more frequently they are enclosed between two apical, adherent junctions.

At the base of many ependymal cells there is a process that may be branched or unbranched and of varying length. According to the form of the basal end, three variants are differentiated in rabbit ependymal cells,[68] namely (a) the simple columnar cell with an ovoid base; (b) the ependymal tanycyte, a columnar cell with a single unbranched process;[33] and (c) the ependymal astrocyte, which is characterized by a basal process giving off several branches. Some basal processes of rabbit ependymal cells reach subependymal capillaries where they are wrapped around the basement membrane in the form of small sheets.[72] In the wall of the rat third ventricle, the tanycytes form the ventral 40% at the level of the median eminence, and along the middle 20% of the wall of the third ventricle is a transition zone in which the ciliated ependymal cells and the tanycytes are interdigitated.[73] The presence of tanycytes in the lower region of the wall of the third ventricle is also reported in humans.[74]

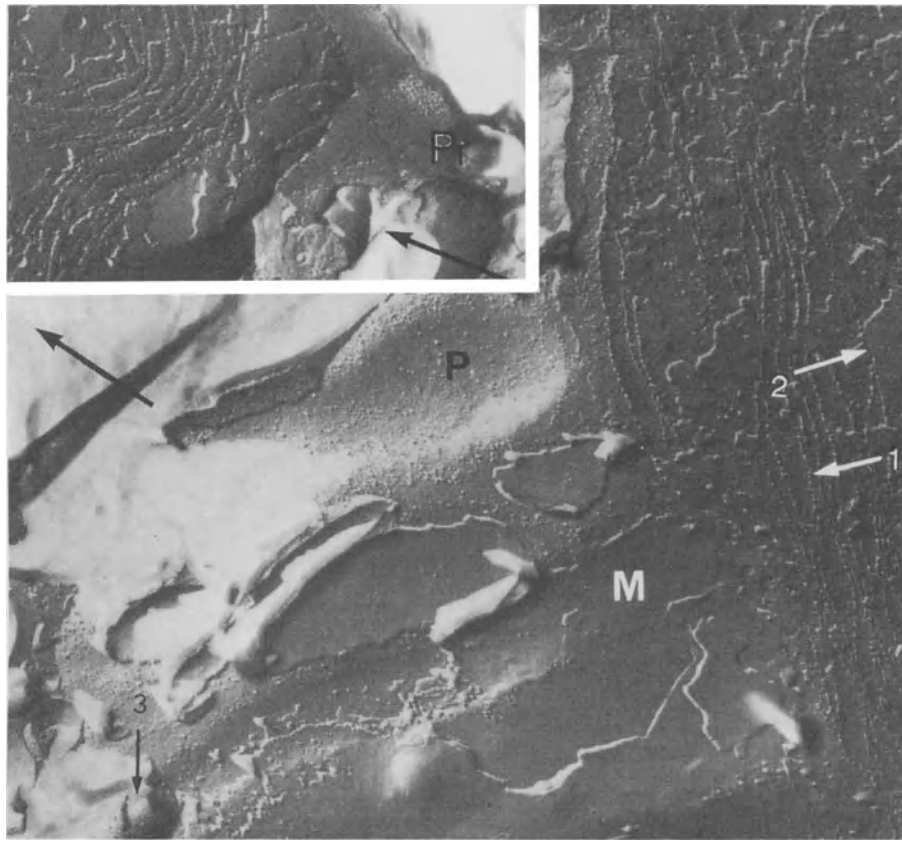

Figure 1.13. Freeze-fracture replica of rat corpus callosum. Conspicuous parallel rows of linear aggregates of particles or ridges (arrow 1) and occasional furrows (arrow 2) are shown in the P face of oligodendrocyte cell membrane. Myelin sheets (M) and myelinated nerve fibers (arrow 3) are located on the broad depressions of oligodendrocyte cell membrane (P). The P face studded with junctional strands (inset) shows a small process (Pr) of oligodendrocyte. The long arrows in the corners indicate the direction of shadow casting. (×32,000; inset ×28,000.) [Reprinted with permission from Tani, Itagaki, and Nakano.[66]]

Special Cells and Nerve Endings

In addition to the three variants of the typical ependymal cell,[68] the ventricular wall may contain elements of an entirely different nature in the rabbit third and fourth ventricles.[72,75–77] There may be sensory endings and cells with a protruding apical end, which shows neurotubuli, synaptic regions, and myelinated fibers. From the distribution of the synaptic vesicles it can be concluded that the nerve fiber is presynaptic and the ependymal cell postsynaptic. In addition, a passage of neurosecretory substances into the ventricular lumen has been described in the hypothalamus of many mammalian species by means of light and electron microscopy.[78,79]

Subependymal Layer

In adult primates, underneath the ependyma of most regions of the ventricles there is a meshwork of glial fibers followed by a row of astrocytes, forming the subependymal layer. The numerous glial fibers underneath the ependyma form a compact layer that usually contains only a few cell nuclei. Although some of the fibers seem to arise from the basal pro-

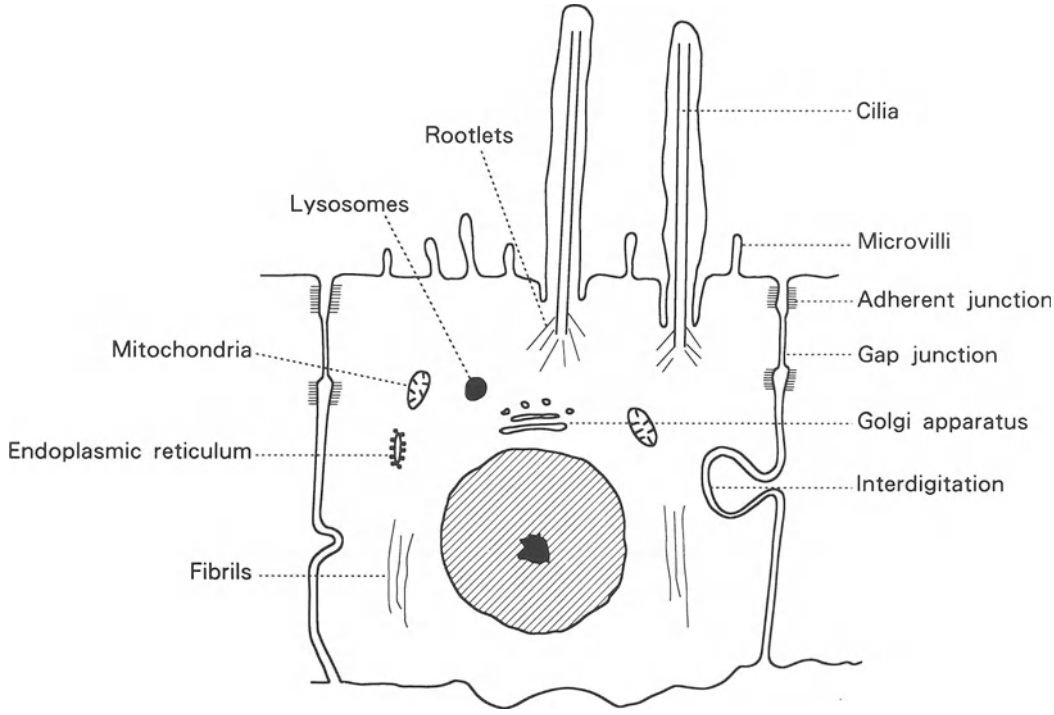

Figure 1.14. Schema of ependymal cell.

cesses of ependymal cells, the majority originates from subependymal astrocytes.[80]

In addition to the varying amount of glial fibers and astrocytes, the subependymal layer regularly contains microglial cells. As already noted in the brain of many mammalian species,[19,81] the microglial cells are situated immediately underneath or even between the basal ends of the ependymal cells. Furthermore, in some regions of the ventricular wall and particularly in the anterior horn, the subependymal layer contains accumulation of

Figure 1.15. Four gap junctions in freeze-fractured ependyma are discontinuous in distribution and composed of a hexagonal packing of particles and pits in faces P and E, respectively. (×83,000.) [Reprinted with permission from Tani, Ikeda, Nishiura, and Higashi.[71]]

small, undifferentiated cells with darkly staining nuclei, which can be differentiated from microglial cells electron microscoically, suggesting remnants of the embryonic matrix.[82] The regional differences of the ventricular wall have been reported in detail by Schwanitz,[83] Leonhardt,[72,75,76] and Schimrigk.[84]

Microglial Cells

Light Microscopy of Microglial Cells

Based on the configuration, microglial cells of humans may be classified as follows:[19] (a) monopolar cells, (b) bipolar cells, (c) multipolar cells, and (d) lamellar cells. The multipolar cells are the most numerous among the family of microglial cells.

Ultrastructure of Microglial Cells

The ultrastructural feature of microglial cells resembles that of oligodendrocytes, and considerable confusion exists regarding the cytological characteristics of the microglial cells.[52,85] The differences in ultrastructure of microglial cells from those of oligodendrocytes are (a) the irregular form of the nuclei, (b) the condensation of chromatin to the periphery of nuclei, (c) the presence of lysosomes, and (d) inconspicuous microtubules.[86–89]

Thus, the neuroepithelial cells of the neural tube are thought to give rise to the neurons, astrocytes, oligodendrocytes, and ependymal cells. However, it is unknown what determines the choice of differentiation pathway taken by individual neuroepithelial cells, nor when these choices are made. Progress in understanding neural cell lineages and the mechanisms and timing of neural cell determination has been severely impeded by the complexity and inaccessibility of the developing CNS and by the uncertainties involved in distinguishing one immature cell type from another by morphological criteria. Among the various methodological procedures, molecular biology has a great potential to understand the molecular basis of complex processes during gliogenesis.

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CHAPTER 2

Cytogenesis and Developmental Anatomy of the Pia–Arachnoid and Pacchionian Granules

Luca Rigobello

Meninges

Introduction

The membranous coverings, essentially composed of connective tissue, that surround the whole neuraxis are called meninges. The word dates back to Erasistratus,[1] whereas Galen distinguished "the pacheia and the lepte," and after translation into Arabic and at last Latin, the terms *dura mater* and *pia mater* came to the modern era.[2]

It is well known that the leptomeninx is a unique complex, even if morphologically we identify the arachnoid and the pia mater.[3–6] The internal leptomeninx or pia is comprised of a single interrupted layer of cells, with collagenous, reticulinic, and scarce elastic fibers, tightly adhering to the cerebral cortex over all the convolutions, fissures, and sulci.[4,5,7] Between the splenium of corpus callosum and the pineal gland there is a duplication of the pia, called velum interpositum, which contains the choroidal arteries, and branches of the posterior cerebral artery and of the internal cerebral veins. Collagen fibrils form connections from the internal surface of the pia to the brain.[6]

The pia is highly vascularized by a lower venous network and chiefly by an external network of small arteries that does not furnish capillaries to the leptomeninx whereas it does to the cerebral cortex.[5] Funnel-shaped elongations of the pia accompany the vessels that extend into the brain.

Over the pia mater, a loose meshwork of delicate elastic and collagenous fibrils, rare trabeculae and arachnoid cells, fibrocytes, and histiocytes constitutes the median part of the leptomeninx, in which cerebrospinal fluid (CSF) freely flows. The arachnoid tissue does not have its own vascularization. The great cerebral arteries that pass through the arachnoid spaces usually lack vasa vasorum and their adventitial wall is probably nourished by the CSF.[5,7]

An arachnoid diaphanous membrane constitutes the outer limiting layer of the arachnoid tissue and spaces. This arachnoid barrier passes as a bridge over all the fissures and sulci, so that the subarachnoid spaces are limited between the pial and the arachnoid membrane. The subarachnoid spaces have variable thickness; where they enlarge and collagenous fibrils become scarce or absent, the so-called cisterns develop, filled with CSF.

The major arachnoid cisterns are the cerebello-medullary, the pontine, the interpeduncular cistern, the cistern of the great cerebral vein (superior cistern, cisterna ambiens), the chiasmatic cisterns, and the cistern of the Sylvian fissure.[5–7] Cisternae are wider in children than in adults.[8] The arachnoid network is separated from the thick collagenous dura mater by an interfacial layer or subdural neurothelium, which has relatively more cells than all the other meningeal strata (from two to eight cell layers).[2,9]

This interfacial layer consists of the strict adherence of a dural border layer (belonging to the pachymeninx) and the arachnoid barrier layer (the above mentioned arachnoid

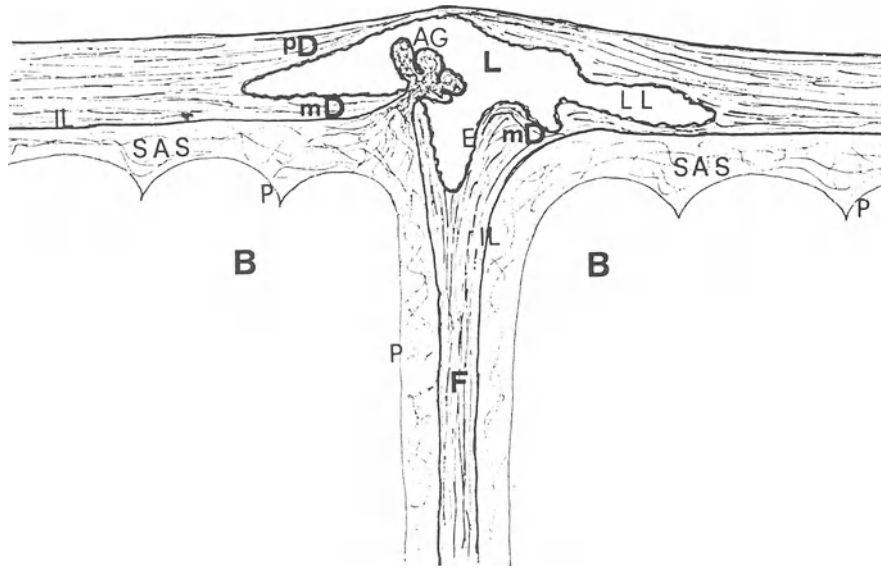

Figure 2.1. Representation of the meningeal structures in a coronal section at the level of the superior sagittal sinus. L, lumen of the venous sinus; E, endothelium; LL, lateral lacuna; AG, arachnoid granulation; pD, periosteal dura; mD, meningeal dura; SAS, subarachnoid spaces; IL, interface layer (dural border layer adherent to arachnoid barrier layer); p, pia; F, falx; B, brain tissue.

membrane), so that a subdural space does not exist under physiological conditions.[2,5,10,11] Intradural and transdural protrusions of the arachnoid membrane and spaces and tissue, usually in relation to the walls of dural veins, constitute the arachnoid villi and granulations (Fig. 2.1).

Over the dural border layer, the bulk of dura mater is thick and fibrous, with a paucity of cells. Within the cranial vault, the internal periostium fuses usually with the pachymeninx, so that the cranial dura is composed of two strata, the meningeal dura and the periosteal dura. These are divided to enclose the dural venous sinuses and the intrasellar space. In the spine, the two dural layers are separated, and an extradural space is distinguishable.[5,6]

Origin of the CNS and Its Coverings

The nervous system originates from the ectodermal tissues of the embryonic disk. The first appearance of neuroectodermic tissue is visible at about the 16th to 17th postovulatory day, when the neural plate develops from the ectoderm overlying the mesodermic notochordal process.[2,4,5,12] The prechordal plate, a mass of mescenchyme located rostrally to the notochordal mesoderm, shows a great proliferative activity and induces the differentiation of the forebrain, while the spinal cord, rhomboencephalon, and mesencephalon are induced by the parachordal mesoderm.

Neurulation is the term used to describe the three successive stages of development of neuroectoderm. At first, the neural plate becomes thick, more at the cephalic end, and differentiates from the peripheral ectoderm. Then, the paraxial mesenchyme that is developing from the primitive streak causes elevation of the neural folds, while a neural sulk appears on the sagittal midline; thus a neural groove is identified.[5,12] The process concludes with the fusion of the edges of the groove to form the neural tube, with thickening of the neuroectodermal tissue that separates completely from the thin surface ectoderm, destined to give origin to the epidermal coverings. The closure of the neural

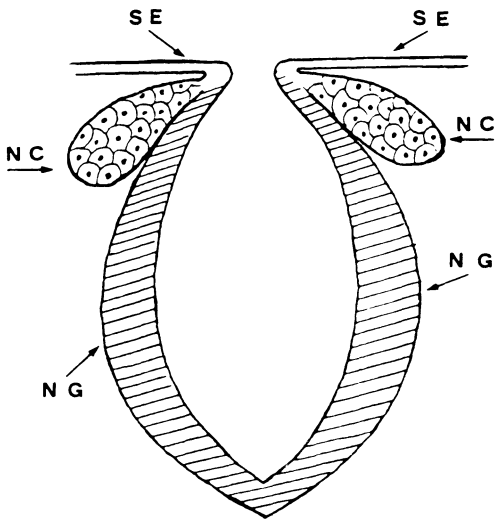

Figure 2.2. Schematic drawing of the closing neural tube in a human embryo of about 21 gestational days. NG, neural groove; NC, neural crest; SE, surface ectoderm.

tube begins at the level of the future lower romboencephalon and extends toward the two extremities of the neural groove. The three stages of neurulation coexist in different regions of the human embryo at the same time (21 to 22 postovulatory days).[2,12]

When the neural folds are fusing, groups of cells on each side become distinct both from the neural tube and from the surface ectoderm, forming the *neural crests* (Fig. 2.2). These structures extend as longitudinal tracts from the caudal neural tube to the midbrain region, increase in extent, and progressively fragment. They give origin to different tissues and are chiefly involved in the leptomeningeal differentiation.[2,12,13] Briefly, it must be pointed out that the neural crests give rise: (a) to the peripheral nervous system (the spinal and cranial sensory ganglia and roots, the sympathetic and parasympathetic ganglia, the carotid sinus and other paraganglionic structures, the adrenal medulla, the Schwann cells and peripheral nerve sheaths); (b) to the pigmented cells of the skin, meninges, and those of virtually the entire body (melanophores, xanthophores, iridophores), and also to the migrating microglial cells of the CNS; (c) to the ectomesenchyme and its derivatives[2,5,12–14] (Fig. 2.3). The term *ectomesenchyme* reflects the real difficulties encountered by embryologists in determining whether this particular tissue has an ectodermal or mesodermal origin.[13]

It is accepted that the ectomesenchyme results from mesenchymal differentiation of neuroectodermal cells of the neural crests that aquire a strict relation with the mesenchyme, mesodermal in origin, which gradually surrounds the neuroepithelial tube from the ventrolateral to the dorsal regions.[2,12] The ectomesenchyme is regarded as the source of the soft meninges, the dermis of the head, the skeleton, and perhaps the muscles of the branchial arches.[12,13]

The mesenchyme of mesodermal origin, surrounding the neural tube, was described as meninx primitiva,[15–17] but a distinction has to be made between an outer skeletogenous layer (the dense mesenchyme from which the bone tissues develop around all the neuraxis) and the true primitive ectomeninx.[2,6]

An inner delicate layer, essentially of ectomesenchyme which surrounds the neural tube growing from the dorsolateral to the ventral regions, constitutes the primitive endomeninx: this structure directly covers the developing brain and medullary tissue, giving rise later to the distinct arachnoid and pia of the leptomeninx.

Development of Meninges

The development of human meninges is controversial, as their possible sources are numerous and complicated.[2]

Bischoff in 1842 suggested that all three meninges arise from the neural tube.[18] In contrast, von Kolliker reported that the spinal meninges arise from the somites[19] and other authors maintained a mesodermal origin for all meningeal layers.[20]

Oberling in 1922 affirmed that the meninges do not have a purely mesodermal origin and that the leptomeningeal cells show ambiguous characteristics.[21] He described a "neuroectodermal supporting system" and proposed a "supporting neuroepithelial cell," maintaining

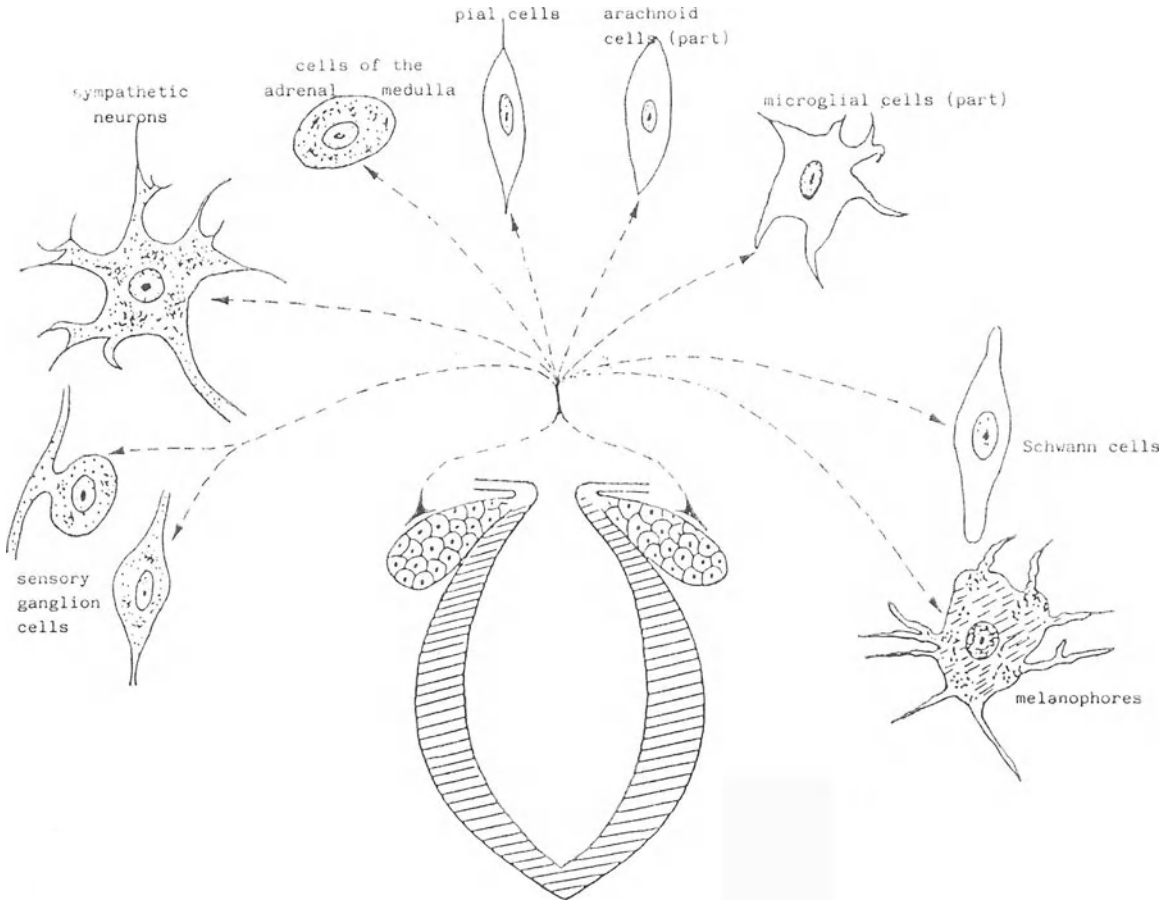

Figure 2.3. The picture represents the cells regarded as derivatives from the neural crests.

that the leptomeninx "is formed entirely by neuroglial tissue."

Experimental studies on animal embryos[22,23] have demonstrated that defects of the neural crest result in absence of the leptomeninx but not of the dura. Therefore it seems that the neural crest cells are precursors of the leptomeningeal cells.

Harvey and Burr stressed that the leptomeninx is formed by neural crest cells in the earlier embryonic period, while the dura arises from the mesenchyme later on.[24]

Sensenig, carefully describing the embryology of human spinal meninges, maintained that the mesenchyme of mesodermal origin gives rise to the dura and arachnoid, and the ectomesenchyme to the pia.[17] The first meninx to develop should be the so-called entomeninx which corresponds to the following pia and arachnoid.[3]

One of the best studies about the developmental steps of the cranial meninges in human embryos is due to O'Rahilly and Muller.[2] They describe the appearance of, at about the 18th to 24th postovulatory days, the primitive mesenchyme, part of which gives origin to the meninges: this tissue is clearly derived from different sources, like the primitive streak, the prechordal plate, the neural crest, and gradually surrounds the neural tube.[2] The lateral portions of the neural tube are ensheated by mesenchyme earlier than the basal and roof areas.[2] The outer mesenchyme will differentiate into the skeletogenous layer and the median mesenchyme into the pachymeninx. The inner mesenchyme will form the leptomeninx,

of which the pia is identified in the thin layer situated between the primitive blood vessels and the cerebral wall.[22] A primitive pia mater is observable at the 24th to 26th postovulatory day in the region of the medulla oblongata and midbrain and is derived from the neural crests.[2] In the same embryonal period, an analogous source from the neural crests is described by Sensenig for the primitive pia mater of the spine.[17]

At about 32 to 33 days, in the mesencephalic flexure, the primitive medial part of the tentorium cerebelli appears, formed by leptomeningeal layers connected with the cellular sheath of the notochord.[2] At about 35 to 38 days, a loose mescenchyme surrounds the entire neuraxis as a "meninx primitiva." Also the longitudinal fissure between the developing cerebral hemispheres is filled with mesenchyme, the precursor of the falx. Later on, the primitive endomeninx bordering the mesial surface of the hemispheres differentiates in a pial layer adherent with each cerebral wall and an arachnoid tissue in the midline.[6]

After 41 days, in the outer mesenchyme of mesodermal origin, a dural limiting layer begins to differentiate from the skeletogenous layer, and in the lateral diencephalic region it gives origin to the rostrolateral and caudolateal parts of the tentorium, which later gradually fuse causing the progressive disappearance (during the third month) of the primitive leptomeningeal medial part of the tentorium.[2,6,16]

The dural limiting layer is gradually observable over the other parts of the brain, differentiating from the external thicker skeletogenous layer (about 42 to 58 days).[2] Later on, at about the third month, a proper dural layer is identifiable in the lateral skull base regions.[25]

In the spine, at about 44 days, Sensenig observed a condensation and separation in the primitive mesenchyme surrounding the neural tube, so that in the ventral part the skeletogenous vertebral layer differentiates from the primitive pachymeninx.[17] The dural sac is complete at about 56 days in the spine, and remains separated from the periosteal endorachis.[2] In the head, the definitive dura mater originates from the peripheral mesenchyme situated between the skeletogenous layer and the dural limiting layer, under which the arachnoid differentiates gradually from the pia.[2] A distinct arachnoid membrane becomes evident only in the last fetal period.

Intradural veins are observable after the 51st day. The venous sinuses can be seen later: they originate from veins situated between the inner surface of the skeletogenous layer and the dural limiting layer, so that finally they are located between the periosteal dura and the true meningeal dura. A schematic picture of all the layers that differentiate covering the nervous tissue during the whole embryonal period is represented in Fig. 2.4.

In about the same period in which the dural limiting layer first appears, at 43 to 44 postovulatory days, the meninx primitiva shows cavitations caused by the rupture of the mesenchymal syncytium surrounding the primitive neuraxis, with infiltration of a liquid that probably is derived from the small vessels covering the cerebral wall. Dilatation of the mesenchymal intercellular spaces increases and a true leptomeningeal meshwork containing liquor is observable around the brain.[2,6,26,27] At last, in the fetal period, connective tissue cells, histiocytes, and collagenous and elastic fibers appear mixed between the leptomeningeal layers.[2,5,28] The mesenchymal layers of the roof of the fourth ventricle are thinner in comparison with basal areas, especially in the so-called "area membranacea superior" of Weed.[2,6,26] This restricted area allows the passage of fluid to the extern, so that a dehiscence enlarges the central part of the primary meninx, expanding the interstices of the meshwork, precursors of the subarachnoid spaces.[2,6,26]

From the posterior region over the rhombic roof, these spaces progressively extend forward, forming the intracranial arachnoid spaces and cisterns, and downward, forming the spinal arachnoid spaces and cisterns.[5,6,26] The enlargement of the spaces between the developing cerebellum and the oblongata, in the fourth ventricle roof area, constitutes the first cistern, the future great cerebellomedullaris cistern, that becomes covered by the

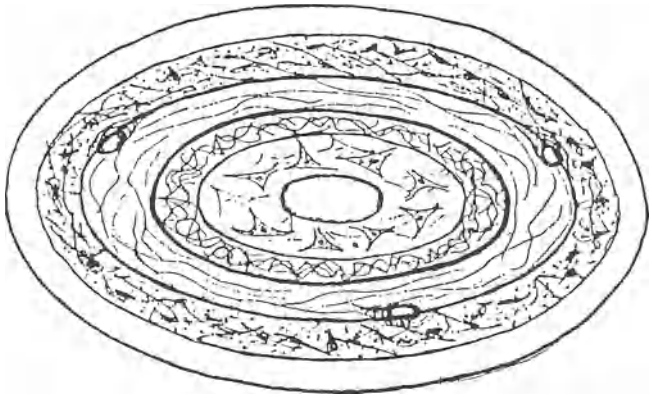

Figure 2.4. Schematic representation of the multiple layers and tissues which differentiate from the mesenchyme of mesodermal and neurectodermal origin that surrounds the developing neuraxis.

limiting layer at about 54 days.[2,5,26] In the forebrain, the first enlargement of the leptomeningeal meshwork indicative of a future cistern is visible in the prechiasmatic region, in the eighth fetal week.[2] The subarachnoid spinal spaces become cell-free at about 57 to 58 days.

A further increase of CSF in the subarachnoid spaces occurs when the apertures of the fourth ventricle open, so that a real CSF circulation is established.[6,29,30] The median aperture of Magendie opens about at the end of the embryonic period; the lateral apertures of Lusckha are patent in the second trimester.[31–33] In birds, an ependymo-pial pouch forms from the distal end of the fourth ventricle, a condition comparable with the Dandy–Walker malformation in humans.[2,34,35]

Over the cerebral hemispheres, the subarachnoid cisterns gradually extend later than in the posterior and basal regions, and are already present in the early fetal period.

At birth the development of the subarachnoid spaces and cisterns is almost complete, with further maturation in the size of structures and the amount of connective tissue.[30]

From the last fetal period, along the cranial vault, it is possible to see that the subarachnoid tissue and spaces form particular relationships with the dural veins and sinuses, forming specialized vegetations called arachnoid villi.

Arachnoid Villi and Granulations

Definition

Arachnoid villi and granulations arise on the external surface of the arachnoid membrane, like protrusions of the subarachnoid connective tissue and spaces.[2,5,36,37]

Most of them make contact with the dural venous vessels and seem the ideal structures for CSF reabsorption from the subarachnoid spaces into the bloodstream.[26,38–44]

The great Pacchionian granules may be considered as arborized vegetations of the same histological structure of arachnoid villi, consisting of a spongy tissue with collagenous fibers and arachnoid cells that delimit intercellular spaces filled with CSF and directly communicating with the arachnoid spaces. There is general agreement to name granulations those structures observable with the naked eye, while the villi are seen only under a microscope.[1,45,46]

[1]In the last decade, the author participated in a complex research program in Padua, focussing on the functional anatomy of human arachnoid villi. Great interest for this argument was promoted by Prof. S. Mingrino, M.D., Neurosurgeon in Chief in Padua. Moreover, Prof. G.C. Andrioli, M.D., Prof. A. Baroni, M.D., M. Scanarini, M.D., D. D'Avella, M.D., C. Dollo, M.D., R. De Aloe, M.D., and the technicians U. Barbolini and V.

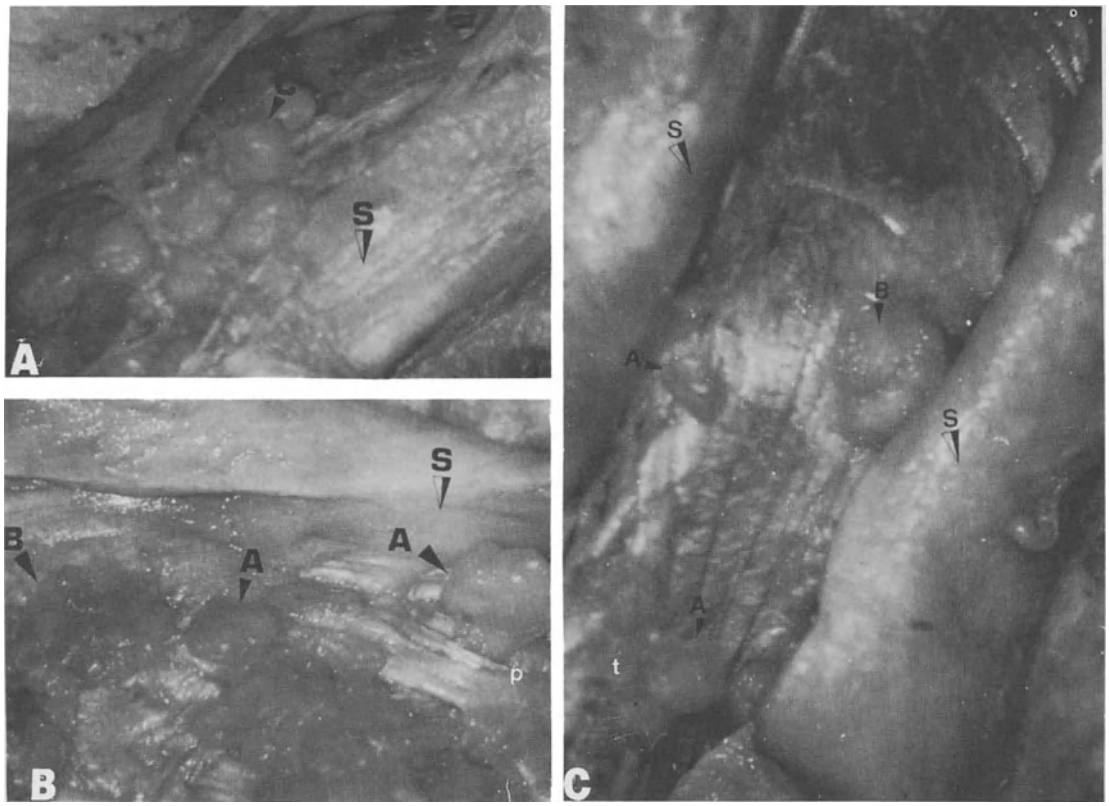

Figure 2.5. Human arachnoid granulations in the superior sagittal sinus. Autoptic dissections in three distinct cases. Different examples of (A) polypoid, (B) verrucous, (C) papillomatous granulations. S: opened layer of the dural sinus. Photomicrographs by operatory microscope, ×16.

The first author who described particular warty excrescences in the lumen of the great dural sinuses of the vault was A. Pacchioni in 1705. Luschka then recognized their arachnoidal nature, as leptomeningeal digitations bulging into the dura mater and the lumen of the great sinuses.[2,47–49]

In memorable studies Key and Retzius (1875) first correlated the morphology of subarachnoid spaces and arachnoid granulations with the possible function of CSF drainage into the bloodstream.[50]

Gross Anatomy

The variable macroscopic appearance of arachnoid granulations in different species was described in several works.[5,36,37,40,42,44,51,52]

In humans, three shapes are usually seen: (a) isolated small polypuses ranging in size from 0 to 2 mm, often with a thin peduncle; (b) verrucous plaques, with a compact and less prominent aspect; (c) complex papillomatous structures in size from 2 to 5 mm, with larger and sometimes bifid or trifid peduncles (Fig. 2.5).

Granulations may appear soft and meat, but with aging they are often sclerotic and sometimes calcified. Small granulations and villi

Rampazzo are to be mentioned among the other participants in the various experimental studies performed on biopsy and autopsy materials of human arachnoid villi and granulations, using the operatory microscope, optic microscope, transmission electron microscope, and scanning electron microscope. The author is at present responsible of the Neuropathological Laboratory of the Neurosurgical Department of Padua, where the specimens and original photomicrographs of villi are conserved and further studies on this matter are in progress.

may be isolated, while usually the larger Pacchionian bodies are grouped in irregular nests projecting on the internal surface of the dural great venous emissaries of the convexity.[5,6,36] However, not all the arachnoid protrusions in the dural layers perforate the pachymeninx; neither are all related to venous vessels.[5,53] It has been suggested that only those villi and granulations that reach the blood circulation in a venous lumen may be involved in CSF reabsorption.[54] In order of frequency they are encountered within the superior sagittal sinus (chiefly in the middle third), within the adjacent lacunae laterales and afferent dural veins, within the transverse sinus, the cavernous sinus, the great cerebral vein, and other venous dural vessels along all the neuraxis.[5,36,41,48,50,54,55] Bulging into the dura and its veins, larger granulations provoke erosion of the skull under the effects of CSF pressure and chiefly of the bloodstream pulsations. The "foveolae granulares" of the internal surface of the calvarium may end blindly or also form a relationship with diploic veins.[5,6]

Arachnoid villi were demonstrated also in the meninges of the spine[56–58] and of the optic nerve in man and monkey.[59] Although the villi are present in all mammals, true granulations of major complexity are present only in the sheep, dog, horse, monkey, and man.[6] Macroscopic granulations are not observable in humans until 18 months after birth.[36,60] During infancy and adolescence they increase in number and size. Arachnoid villi, on the contrary, are observable microscopically not only at birth but also in 8-month fetuses.[2,41,48,49] It was stressed that during the fetal and perinatal periods both the arachnoid and the dura may fulfill the reabsorptive function of the later villi and granulations.[37] On the other hand, there are in the literature case reports of congenital communicating hydrocephalus in patients whose venous sinuses completely lacked arachnoid villi and granulations.[60,61] In recent etiopathogenetic classifications of hydrocephalus, agenesis or dysplasia of arachnoid villi is also considered.[62,63]

Histology

The typical microscopic appearance of a single villus is that of a diverticulum from the subarachnoid tissue through the dura, like a digitation bulging in a vein (Fig. 2.6).

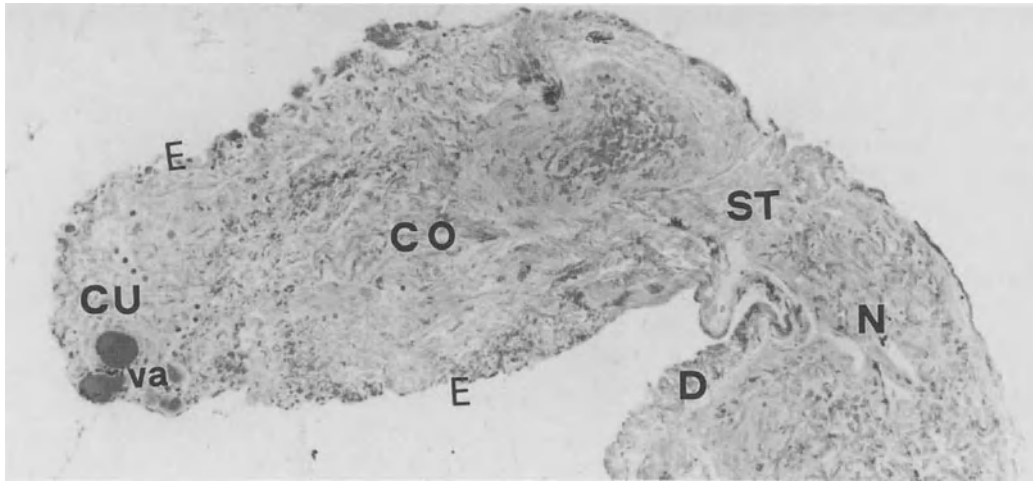

Figure 2.6. Human arachnoid villus isolated from a dural vein. Autoptic material. D, residual dural layer; N, neck of the villus; ST, stalk; CO, core; CU, cuf; E, endothelium; L, venous lumen; va, optic dense vacuoles (postmortem fixation). Toluidine blue, ×60.

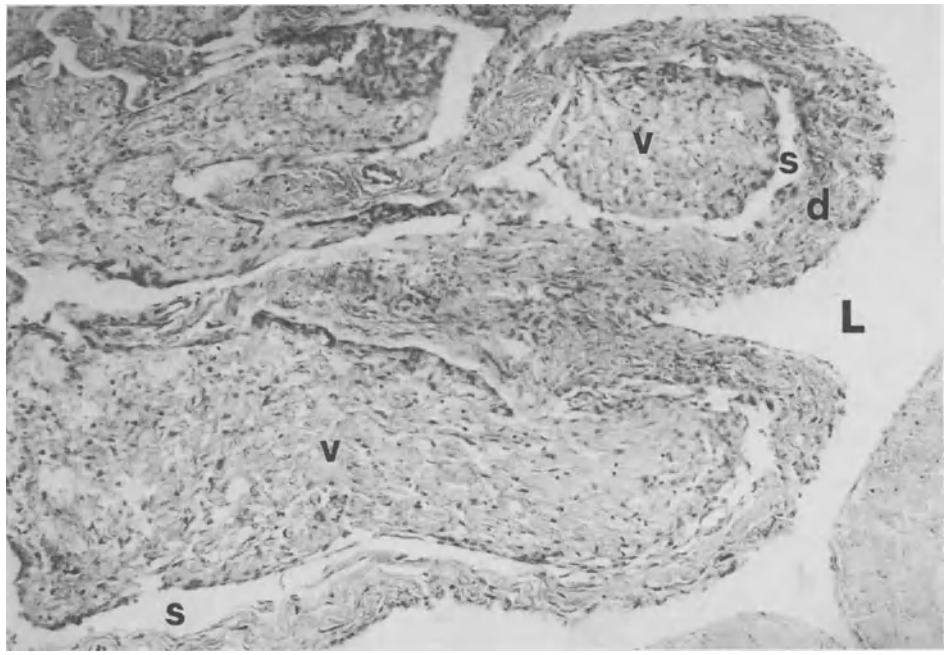

Figure 2.7. Section of a lobulated human arachnoid granulation bulging in the superior sagittal sinus. Single villi are seen, surrounded by a continuous dural sheet. Autoptic material. d, dural layer; s, subdural space; v, villus; L, venous lumen. H & E, ×100.

Andres[37] maintained that larger villi have a core of arachnoid tissue and a covering formed by: (1) a neurothelial layer (dural border layer); (2) a basement membrane; and (3) the venous endothelium. However, recent studies on biopsy specimens in humans demonstrated that the villi arising in the dural veins of the convexity have neither a dural sheath, nor a basement membrane under the venous endothelium.[43,64]

Some authors observed in human autopsy specimens a continuous dural layer covering single arachnoid villi and creating a subdural space.[49,50,53,65] On the other hand, distinct points of larger granulations took direct contact with the lumen of dural sinuses, without a dural sheet; a pachymeningeal sheath was also not found in granulations of rhesus monkey.[53]

Other studies in human autopsy gapless sectioned granulations of the major dural sinuses have demonstrated that arachnoid villi of the same subject may or may not be covered by a continuous dural sheet[54] (Fig. 2.7). Recent studies seem to confirm that only distinct apical areas of the human arachnoid villi are usually covered by a simple endothelial layer[51] or, at the extreme condition, by a thin arachnoidal layer.[52]

It seems reasonable that the villi of the dural veins, devoid of a pachymeningeal layer sheath,[43,64] are much more important for CSF reabsorption than arachnoid granulations in the great sinuses, a part of which may be conceived as non-functioning entities because of their dural covering.[51,54] Functioning villi perforate gaps in the dura and protrude naked into the venous lumen, covered only by a thin endothelium (Fig. 2.8). So, a subendothelial rather than a subdural space is identified[43,46,51,64,66–68] (Fig. 2.9). The subdural space, which is already virtual in normal conditions between the pachimeninx and arachnoid, is obliterated at the base of the peduncle called the neck of the villus[2,5,43] (Fig. 2.10).

The subarachnoid tissue expands in the

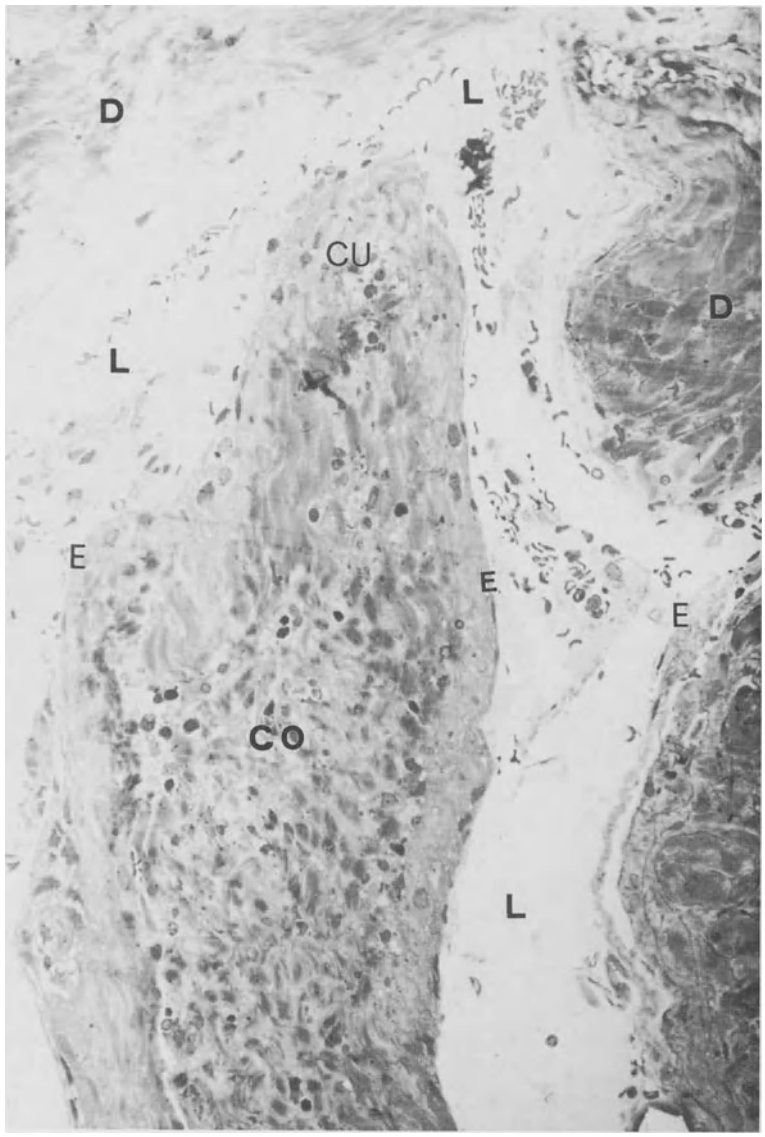

Figure 2.8. Section of a human arachnoid villus projecting into a dural vein of the vault. The arachnoid tissue in the core is well distended and intercellular spaces are visible. Only a thin endothelial layer separates the CSF-arachnoid compartment from the bloodsteam. Bioptic specimen. CO, core; CU, cuff of the villus; E, endothelium; D, dura; L, venous lumen. H & E, ×250.

stalk and in the core of the villus, with collagenous fibers and more "mesothelial" cells of the normal arachnoid membrane. The CSF passes in the intercellular spaces that freely communicate with the subendothelial space and the inner subarachnoid spaces.[43,51,68]

The cuff of the villi has many more elements (fibrocytes, histiocytes, arachnoid cells, mast-cells) than fibers and its surface is strictly correlated to the physiological and pathological processes of CSF reabsorption.[43,64,69] Controversies have existed for several years about the mechanisms of CSF drainage through the intercellular spaces, the subendothelial spaces of the villi, and the surface endothelium.[38,41,46] Based on contradictory histological descriptions of arachnoid villi studied in different experimental conditions and in different species, an "open system" versus a "closed system" for CSF reabsorption were proposed. The concept of an open system was suggested by Cushing[70] and sustained by other authors.[38,41,45,46] Studying monkeys, Welch (1963) described a labyrinth of coated tubules

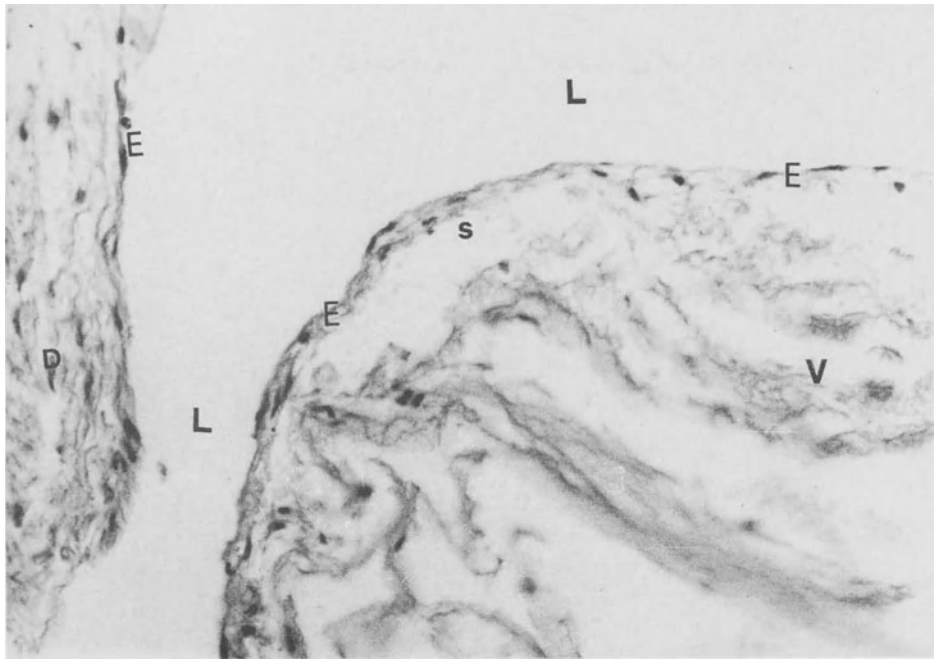

Figure 2.9. Apex of a villus bulging into the superior sagittal sinus. Autoptic material. D, dural layer of the opposite wall of the sinus; E, endothelium; s, subendothelial space; L, venous lumen; V, villus. H & E, ×200.

of 4 to 12 nm in width in the core of the villi,[38] like a valved system that under pressure changes may allow the passage of CSF to the subendothelial space. In sheep, Jayatilaka observed that this subendothelial space contains endothelium-lined channels of large diameter that seem continuous with tubule-like spaces of the core of the villi and maintain a free communication with endothelial crypts of 100 to 300 nm in size.[45] Other observations supported the existence of a pressure-dependent mechanism with "open channels" for CSF bulk flow to the venous bloodstream.[46,69,71] On the contrary, accurate studies of Weed (1914), supported by other authors,[2,26,42,49,67,68] were consistent with the concept that arachnoid villi end blindly and that CSF filtration occurs through a "closed system" essentially represented by the continuous endothelial layer.[6,27] These controversies about the functional morphology of arachnoid villi remained unresolved by traditional histological studies but received new impulse from electron microscopy.

Ultrastructure and Functional Aspects

Ultrastructural studies of arachnoid villi also appear to give contradictory descriptions because of the differences in the microanatomy of various animals (dogs, pigs, cats, sheep, and monkeys) and man. Furthermore, the experimental conditions may be extremely disparate and the human autopsy specimens seem inadequate to maintain the delicate ultrastructural and dynamic characteristics of the villi.[42,43,51,66–69] Despite the fact that human biopsy specimens are seldom available (Fig. 2.10), advances were obtained in the last years about the controversial question of the presence of "open channels" versus "closed membrane surface" in the apex of the villi.[43,64,72] Regarding the core and the cuf of a dural vein villus (Fig. 2.11), desmosomes

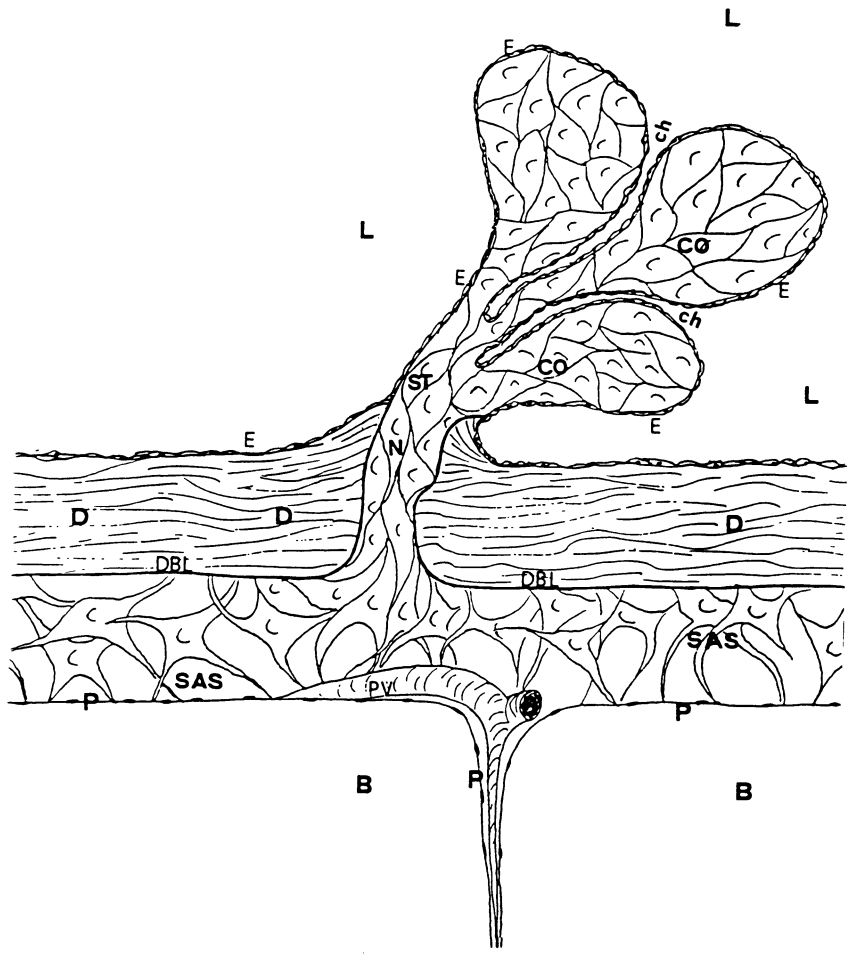

Figure 2.10. Representation of a paradigmatic arachnoid granulation in a large sinus of the dura. E, endothelium; N, neck; ST, stalk; CO, core; ch, endothelium-lined large channel which separates single villi of the same granulation and maintains a blind end (see Fig. 2.14); L, venous lumen; D, dura mater; DBL, dural border layer; SAS, subarachnoid spaces and tissue; P, pia mater; PV, pial vessel; B, brain cortex.

and zonulae occludentes were found between the elongated and interdigitated arachnoid cells that delimit CSF-filled intercellular spaces without the appearance of coapted tubuli.[43,64] Micropinocytotic vesicles are present in the arachnoid cells.

Much more interest was focused on the endothelial layer of human arachnoid villi, the critical structure for CSF outflow. Here, a basement membrane is absent[43,64] and the typical junctions between neighboring endothelial cells consist of rare zonulae adherentes, while free intercellular spaces are visible between overlapping endothelial cells.[43,64,72] Moreover, true endothelium-lined channels of relatively large diameter are seen from the subendothelial spaces to the venous lumen.[43,72] Micropinocytotic phenomena in the endothelial cells are usually seen, together with large intracellular electronmicroscopically empty vaculoes that may open into the venous lumen.[43,52,64,72] (Fig. 2.12). These pictures are consistent with active processes of CSF transport through the cytoplasm of endothelial cells, a mechanism that seems regulated by a low pressure system.[43,64]

In arachnoid villi removed in pathological conditions, significant changes were observed in the openings between the endothelial cells, in the type and adhesiveness of endothelial

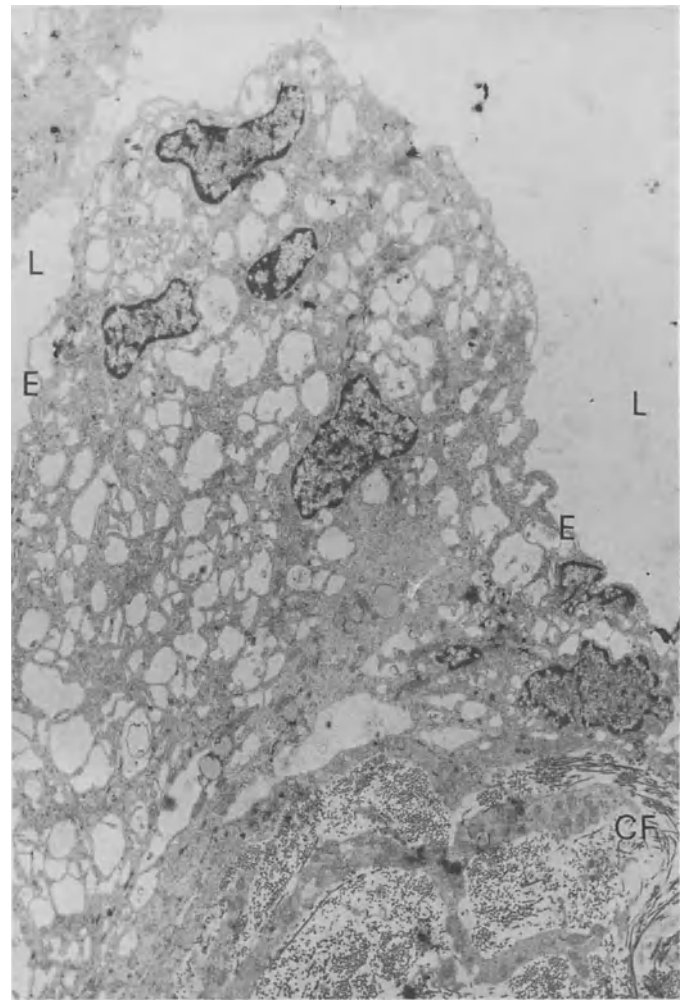

Figure 2.11. Human arachnoid villus. Bioptic specimen from a dural vein of the vault. Transmission electron microscopy: a loose meshwork of arachnoid cells and large empty spaces is observable in the cuf of the villus. L, lumen; E, endothelium; CF, collagenous fibers. ×2000.

cell junctions, and in the number and size of intracellular vesicles.[64]

Structures interpreted as endothelial-lined channels are actually seen by transmission electron microscopy and scanning electron microscopy as running from the subendothelial space to the venous lumen (Fig. 2.13). These open channels have a great functional significance, giving ultrastructural evidence of a mechanism of bulk flow of CSF in the bloodstream.[43,52,64,72] They are large enough to allow the passage of erythrocytes that may used as natural tracers, but their wideness and form are quite different from the "endothelial tubules" reported in previous work on histological preparations. It would seem that the "endothelial tubules" observed through the optic microscope are invaginations of the venous endothelium between different villi of the same granulation (Fig. 2.14). These "canyons" appear to maintain a blind cul de sac and are much more enlarged than the open channels demonstrated by electron microscopy in the region of the cuf of a single villus.

In conclusion, ultrastructural studies furnish evidence for both closed and open systems for CSF reabsorption at the level of arachnoid villi and granulations, but the functional phenomena appear more complicated depending on different pathways, regulated by low and high pressure systems and subject to variations in pathological conditions.[43,51,52,64,72]

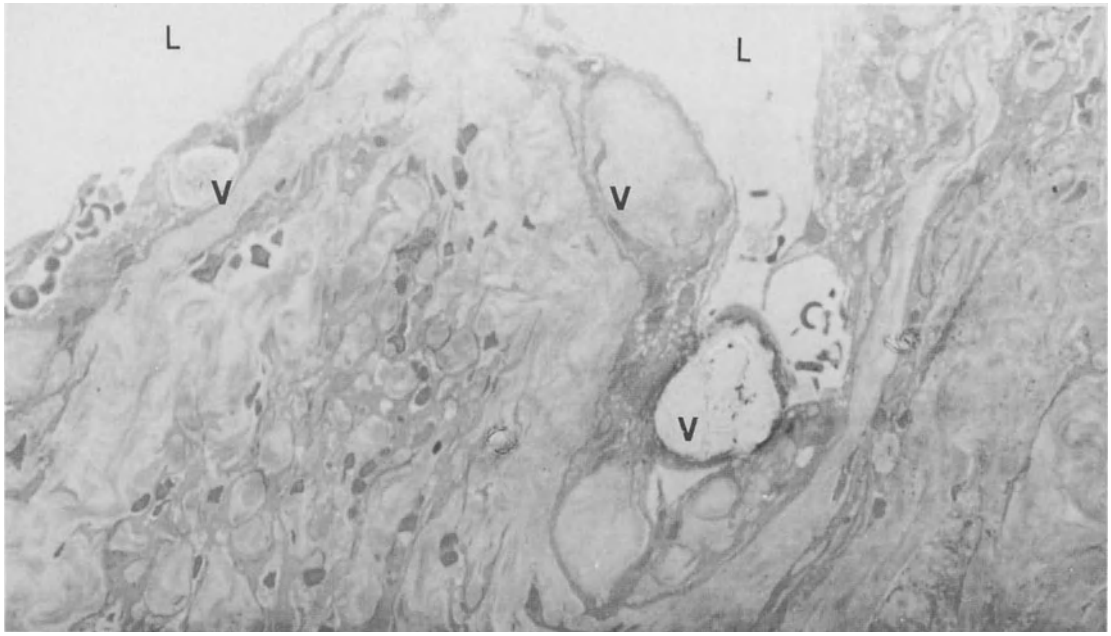

Figure 2.12. Human arachnoid villus. Bioptic specimen. Semifine section for electron microscopy. Large vacuoles are prominent at the level of the surface endothelium and tend to open into the venous lumen. V, vacuoles; L, venous lumen. Toluidine blue, ×400.

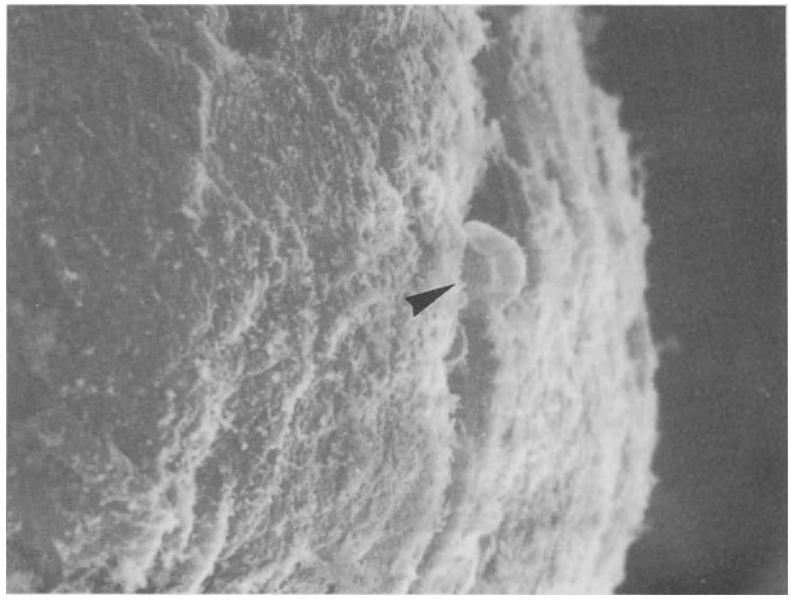

Figure 2.13. Human arachnoid villus. Bioptic specimen from a dural vein of the vault. Scanning electron microscopy. See the surface endothelial cells provided of numerous microvilli. An erythrocyte is emerging from an open channel between two adjacent endothelial cells (arrow). ×10,000.

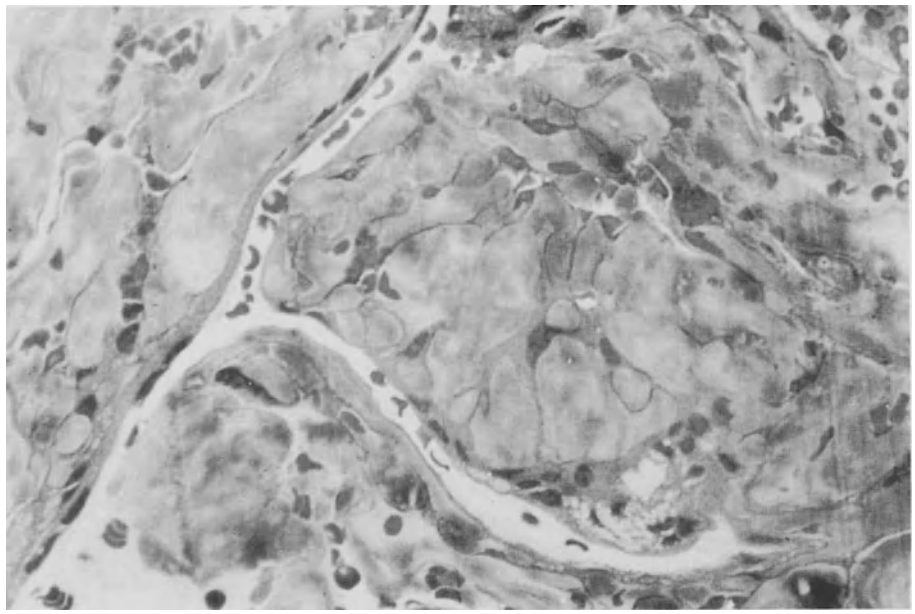

Figure 2.14. Human arachnoid granulation. Bioptic specimen from a dural vein. Semifine section for electron microscopy. Large endothelium-lined channels separate single villi or lobules of the same granulation, maintaining a blind termination without a distinct communication with the subendothelial space. Toluidine blue, ×400.

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CHAPTER 3

Morphological Basis for Fluid Transport Through and Around Ependymal, Arachnoidal, and Glial Cells

Shinya Kida and Roy O. Weller

Introduction

Cerebrospinal fluid in man is produced by the choroid plexus in the ventricular system at the rate of 500 ml a day; the total cerebrospinal fluid (CSF) is some 150 ml.[1] Approximately 20% of the CSF is in the ventricles, but the majority is in the subarachnoid space over the surface of the brain and the spinal cord. There is also interstitial fluid within the extracellular spaces of the gray and white matter of the brain and spinal cord. Such extracellular fluid may be greatly increased in amount when there is cytotoxic and vasogenic cerebral edema associated with trauma, infection, or infarction of the brain or around a tumor.[1–3] Extracellular fluid may also be increased in the periventricular white matter in acute hydrocephalus due to the insudation of CSF from the ventricles.[4]

In considering the morphology of fluid drainage pathways from the human brain, a number of routes will be considered. Some of these routes appear to be important in experimental animals but their true significance in man cannot be judged because of the lack of suitable tracer experiments. Much of the data regarding drainage pathways has come from the study of normal brain and of pathological states in which there is cerebral edema or hydrocephalus. Initially, extracellular fluid from the brain may drain into the CSF either directly from the white matter or along perivascular spaces from the gray matter. Resorption of interstitial fluid into blood vessels of the brain may occur, particularly in hydrocephalus.[2]

Major drainage pathways of CSF back into the blood in man involve the arachnoid villi and granulations in the superior sagittal sinus and associated with spinal nerve roots. However, in experimental animals, tracers injected into the CSF have identified drainage pathways for CSF into the lymphatic system[5] and drainage of tracers along sheaths of optic nerves.[6] The connection of CSF drainage pathways with the lymphatic system has important implications for relationships between the central nervous system and the lymphoid and immune systems. However, there is, as yet, little direct evidence that drainage of CSF into nasal lymphatics is as important in man as it appears to be in the rat and rabbit.[7,8]

Drainage of Extracellular Fluid from the Central Nervous System

The preferential accumulation of edema fluid in the cerebral white matter of the human brain can be appreciated not only at postmortem but also in computed tomography (CT) scans and by magnetic resonance imaging (MRI). Tracer studies in experimental animals suggest that such edema fluid from the white matter drains toward the ventricular system[9] and enters the CSF. Similarly when particulate tracers such as India ink are injected into the white matter, the particles spread dif-

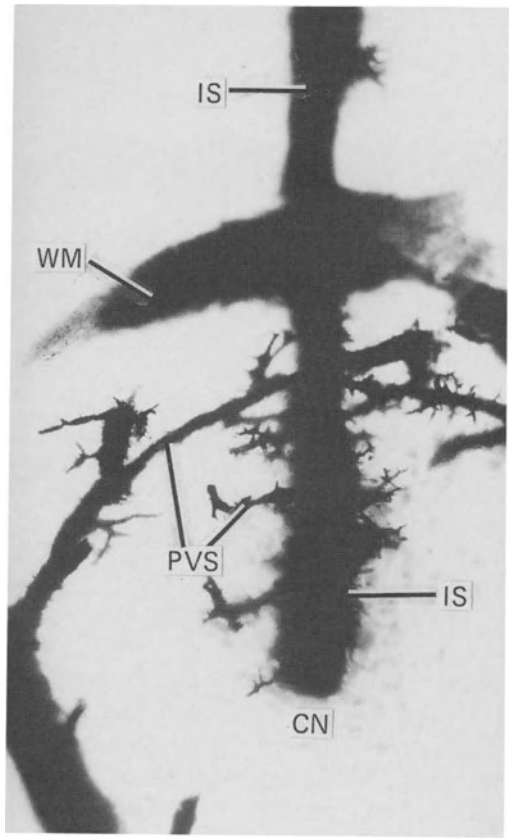


Figure 3.1. Spread of Indian ink tracer following injection into the rat brain. The injection site (IS) runs vertically into the caudate nucleus (CN). Ink has spread diffusely through the white matter (WM), but in the gray matter ink spreads along the perivascular spaces (PVS) outlining the major blood vessels. (Transilluminated Indian ink injected rat brain, ×10.) (Figure kindly supplied by Dr. E. T. Zhang.)

fusely between nerve fibers in the white matter.[10]

In contrast to the diffuse spread of extracellular fluid in the white matter, injections of tracers into the gray matter of rabbit and rat brains show that fluid spreads preferentially along perivascular spaces within the brain (Figure 3.1) and then into perivascular spaces of the meningeal vessels before entering the CSF.[10,11] Such tracers, including proteins, eventually enter the lymphatic system.

Tracer studies are not possible in man but the anatomical pathways by which similar drainage could occur have been described in the human brain.[12–14] Despite the long-held view that the subarachnoid space over the surface of the human brain is in direct continuity with the perivascular spaces within the brain, recent anatomical studies[12] have shown that the pia mater is reflected from the surface of the brain onto blood vessels in the subarachnoid space, thus separating the perivascular spaces from the subarachnoid space. Such an anatomical arrangement is depicted in Figure 3.2. which also shows how the perivascular coating of leptomeningeal cells, derived from the pia mater, extends down into the brain and surrounds arteries and arterioles almost to the level of capillaries.[14] No similar coating is seen around veins. The sheath of leptomeningeal cells could have two major functional consequences. First, the leptomeningeal cells may act as a barrier between the autonomic nerves supplying the walls of the blood vessels and the surrounding brain. Leptomeningeal cells contain catechol-O-methyltransferase[15] and glutamine synthetase;[16] both these enzymes might prevent catecholamines and other neurotransmitters released from nerve endings around the vessels from reaching surrounding brain tissue. Second, the ensheathement of arteries by leptomeningeal cells forms an anatomical pathway by which fluid could drain along arteries and into the perivascular spaces of arteries within the subarachnoid space,[14] as suggested by experimental studies.[11] Cells of the pia mater and leptomeningeal cells surrounding arteries in the brain are joined by gap junctions and desmosomes,[13] but, as yet, no firm evidence for tight junctions between these cells is forthcoming. This suggests that the leptomeningeal sheaths of vessels in the subarachnoid space may allow interstitial fluid draining along perivascular spaces to pass freely into the subarachnoid CSF.[14]

Circulation of Cerebrospinal Fluid

It is estimated that 80% of the CSF is produced by the choroid plexuses at the rate of 0.3 ml per minute in man.[1] Functionally, the CSF fills the ventricular system and the sub-

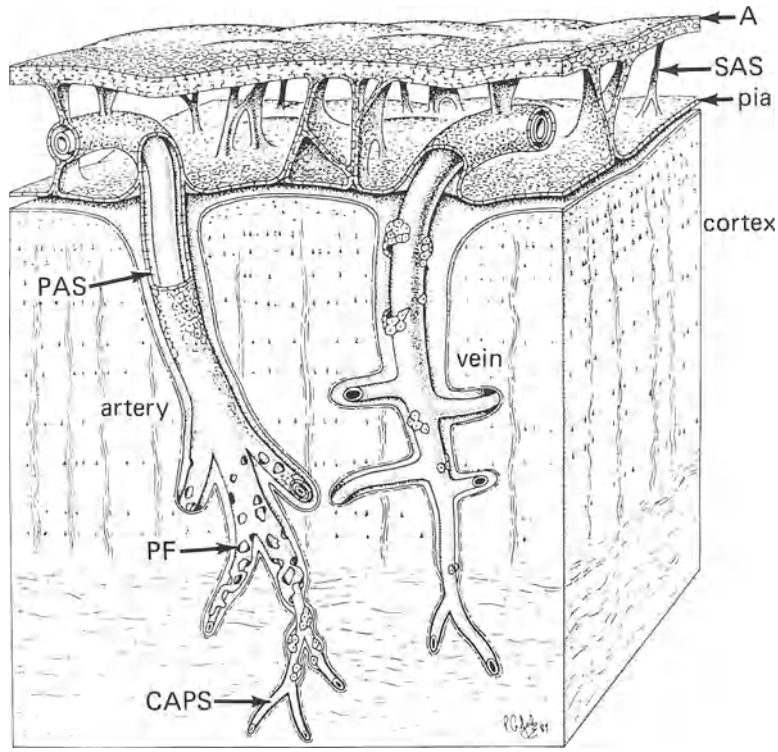


Figure 3.2. Diagram demonstrating the relationships of the pia mater and intracerebral blood vessels. Subarachnoid space (SAS) separates the arachnoid (A) from the pia mater overlying the cerebral cortex. An artery on the left of the picture is coated by a sheath of cells derived from the pia mater; the sheath has been cut away to show that the periarterial spaces (PAS) of the intracerebral and extracerebral arteries are in continuity. The layer of pial cells becomes perforated (PF) and incomplete as smooth muscle cells are lost from the smaller branches of the artery. The pial sheath finally disappears as the perivascular spaces are obliterated around capillaries (CAPS). Perivascular spaces around the vein (right) are confluent with the subpial space and only small numbers of pial cells are associated with the vessel wall. (Reproduced with permission from Zhang et al.[14])

arachnoid space and provides mechanical support for the brain. In addition, it is thought that the CSF acts as a sink into which many of the waste products and metabolites of the brain drain and are thus transported away from brain tissue.[1,9] CSF from the ventricles drains through the foramina of Luschka and Magendie into the subarachnoid space and ultimately it passes over the surface of the cerebral hemispheres to drain back into the blood via the arachnoid granulations and villi. Over much of the surface of the brain, the subarachnoid space is traversed by sheet-like and filiform trabeculae (Figure 3.2) that join arachnoid to pia and are attached to blood vessels within the subarachnoid space.[13] Such trabeculae are formed from collagenous cores surrounded by leptomeningeal cells that are joined by gap junctions and desmosomes. A number of large cisterns are present, particularly at the base of the brain in which the arachnoid and pia are widely separated and the cisterns are traversed by few trabeculae.

There is free communication of CSF in the subarachnoid spaces of the cerebral and spinal compartments through the foramen magnum. A complex array of ligaments traverses the spinal subarachnoid space.[17] The dentate ligaments form focal attachments between the subpial connective tissue surrounding the cord and the dural ensheathement, and delicate fenestrated ligaments are formed on the dor-

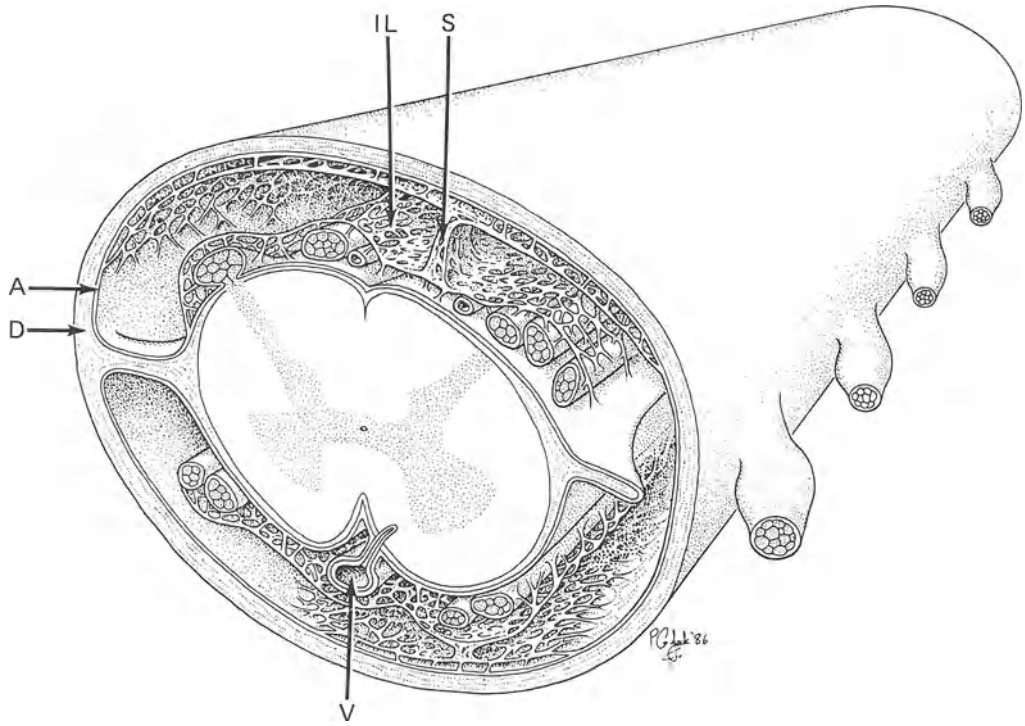


Figure 3.3. Diagrammatic representation of the human spinal cord with surrounding meninges. The arachnoid mater (A) is closely applied to the thick outer dura (D). An intermediate leptomeningeal layer (IL) lies between the arachnoid mater and the pia mater. This layer is fenestrated and is attached to the inner aspect of the arachnoid mater. It is reflected to form the dorsal septum (S). The intermediate layer spreads over the surface of the cord and is connected to blood vessels, nerve roots, and pia mater by fine trabeculae. Dentate ligaments are present on either side of the cord and are covered by a layer of pia arachnoid. The collagenous core of the dentate ligaments fuses with subpial collagen medially and at intervals laterally with dural collagen, as shown on the left side of the diagram. Blood vessels (V) within the subarachnoid space are coated by a leptomeningeal sheath continuous with the pia mater. (Reproduced with permission from Nicholas & Weller.[17])

sal and lateral aspects of the spinal cord from an intermediate layer of arachnoid that spreads out over nerve roots and vessels[17] (Figure 3.3). Morphologically, the trabeculae that form the fenestrated sheets over the surface of the cord are similar to those that traverse the cerebral subarachnoid space.[13,17] They are composed of cores of collagen surrounded by leptomeningeal cells. As over the brain, the pia mater separates the subarachnoid space from the subpial spaces and perivascular spaces of the spinal cord.[17]

Free communication also exists between CSF in the ventricles and extracellular fluid in the periventricular white matter of the brain.[18] The directions of bulk flow of fluid between these two compartments depends upon pressure gradients.[19] Thus, in the normal brain, there is a flow of extracellular fluid from the white matter into the ventricular CSF, whereas in hydrocephalus, when the intraventricular pressure is raised, CSF is forced into the periventricular white matter. This may be accompanied by disruption of the ependyma and wide expansion of the extracellular fluid spaces resulting in edema of the periventricular white matter.[4,20] Such edema is recognizable histologically and by

imaging techniques such as CT scanning and MRI. There is good evidence both in experimental animals[4,21] and in man[20] that such periventricular edema is accompanied by damage to axons within the edematous white matter and subsequently by gliosis of subependymal tissue.

Tracer studies using radiolabeled human iodinated serum albumin (RHISA) suggest that the bulk of the CSF passes over the surface of the cerebral hemispheres toward the sagittal sinus for drainage through arachnoid granulations in man.[1]

Pathways of Cerebrospinal Fluid Drainage and Absorption

It was shown more than 100 years ago[22] that tracers injected into the CSF of experimental animals drain into cervical lymph nodes. This can be dramatically confirmed by the injection of India ink which drains into cervical lymph nodes within a few seconds.[23] The immunological importance of this pathway has been recently emphasized by Harling–Berg et al.,[24] who have shown that infusion of human serum albumin (HSA) into the CSF of rats results in a rise in serum anti-HSA antibody levels with the cervical lymph nodes as the site of maximum antibody production. One major route by which CSF drains into cervical lymph nodes is through the cribriform plate and into nasal lymphatics.[5] Other routes include the sheaths of cranial nerves and spinal nerve roots.[6] The proportion of CSF that drains by such routes varies among different species with 5% to 15% in the cat and 30% in the rabbit[7]—an amount that is increased by elevation of CSF pressure.

The free communication of CSF and extracellular fluid in the periventricular white matter of the brain suggests that this may also be a route by which CSF could drain back into the blood. However, this pathway appears to be significant only in hydrocephalus when the normal drainage pathways are blocked and the intraventricular pressure is elevated.[25] Similarly, absorption of CSF by the choroid plexus has been suggested but, again, this only appears to be important under conditions of raised intraventricular pressure.

Morphology of Arachnoid Villi and Granulations in Man

It is now well established from experimental studies in various species and from the classical work of Key and Retzius,[26] and of Weed,[27] that the arachnoid villi and granulations provide a major route for drainage of CSF.

Arachnoid villi and granulations are present in the walls of the intracranial venous sinuses[28–30] and within the walls of veins associated with spinal nerve roots. The distinction between arachnoid villi and granulations in man is based mainly upon size. Microscopic arachnoid villi are present in the superior sagittal sinus of the fetus and newborn infant;[31] each villus consists of a protrusion of arachnoid through the dural wall of the sinus and is covered by sinus endothelium. Arachnoid granulations are larger than villi and they protrude through the dural wall of the sinus and are visible to the unaided eye. Such granulations become obvious in the parieto-occipital region of the superior sagittal sinus by the age of 18 months and are visible in the transverse sinuses in the posterior fossa by the age of 3 years.[30]

There is considerable species variation in the shape, size, and morphology of arachnoid villi and granulations. In animals such as sheep and monkeys that are commonly studied, arachnoid villi are much smaller and simpler in their organization than human villi. In the rat, arachnoid villi exist as protrusions of arachnoid elements into the wall of the superior sagittal sinus and do not extend into the lumen of the sinus except under conditions of raised CSF pressure. Arachnoid villi in the monkey are similar to those in the human fetus and are seen as delicate protrusions of arachnoid projecting into the venous sinus and covered by sinus endothelium.[32] Although arachnoid granulations in sheep are visible to the unaided eye, they are similar in their construction to arachnoid villi in human infants.

Arachnoid granulations in man are distrib-

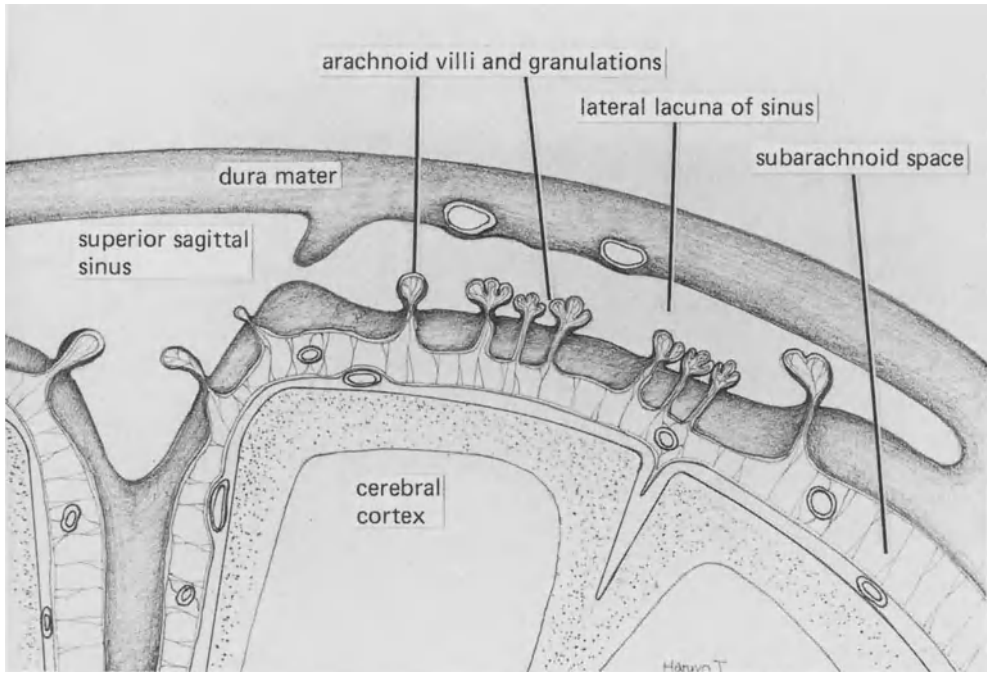


Figure 3.4. Schematic diagram showing a coronal section of meninges, superior sagittal sinus, and cerebral cortex to show relation of arachnoid villi and granulations to the dural venous sinus.

uted in both the venous sinuses and latera lacunae that form the intradural portions o veins and sinuses draining blood from the brain (Figure 3.4). The granulations protrude into the sinus (Figure 3.5) as bulbous structures covered by endothelium (Figure 3.6). By scanning electron microscopy, the microvilli marking the borders of each endothelial cell are clearly seen (Figure 3.6B). Small veins pass through the granulations and open into the sinus (Figure 3.6). No gaps are seen between the endothelial cells. Arachnoid villi are also visible in the superior sagittal sinus by scanning electron microscopy (Figure 3.5) and they appear as smaller frond-like structures projecting into the sinus.

Figure 3.5. Scanning electron microscopy of the surface of arachnoid granulations (G) and villi (V) as they project into the superior sagittal sinus. (×35.) (Reproduced with permission from Upton and Weller.[28])

Internal Structure of Arachnoid Granulations

The internal structure of arachnoid granulations and their relationships with the subarachnoid space, dura mater, and lining of the venous sinus can be appreciated by examining

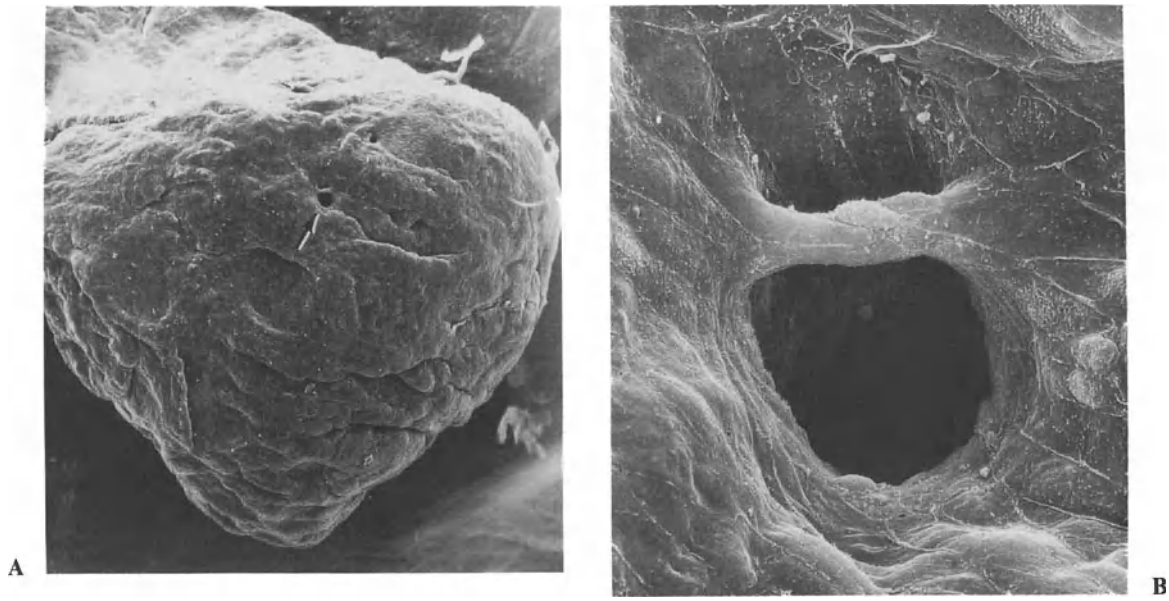


Figure 3.6. Scanning electron micrographs. A: View of the sinus endothelial surface of an arachnoid granulation with endothelium-lined vein opening into the sinus (arrow). (×77.) B: Higher-power view of the endothelium-lined venous opening shown in A. (×950.) (Reproduced with permission from Upton and Weller.[22])

sections of the granulations in various planes and by light and electron microscopy. In adults, lobulated granulations, partially coated by a dural cupola, can be seen protruding through the dura (Figure 3.7). At the apex of each granulation, there is a cap of arachnoid cells and over this cap the dural cupola disappears and arachnoid cells come into direct contact with the sinus endothelium[29,30] (Figure 3.8). The dome-shaped cap of arachnoid cells is approximately 150 μm thick and it surmounts a collagenous core in the center of the granulation. Cerebrospinal fluid drains from the subarachnoid space into the central collagenous core of the granulation and through a network of channels 7 to 40 μm wide (Figure 3.9). Although in man the trabeculae separating the channels appear to be hypocellular, they have the same basic construction as the trabeculae in the subarachnoid space,[13] i.e., central cores of collagen surrounded by leptomeningeal cells[28] (Figures 3.9 and 3.10). A similar arrangement has been described in other primates.[32] Channels extend into the arachnoid cap region of the granulation (Figure 3.11), although these channels, up to 100 μm in diameter, are more widely spaced than in the central collagenous core of the granulation. Such channels extend right up to the subendothelial regions (Figure 3.11)

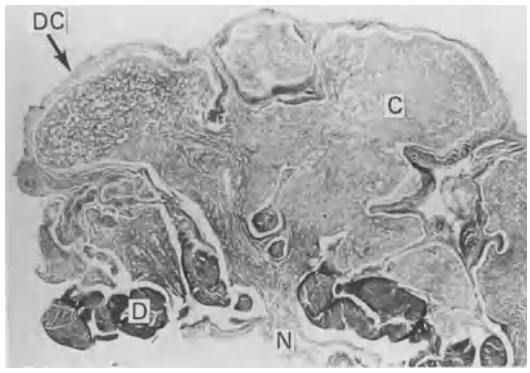


Figure 3.7. Photomicrograph of a vertical section through an arachnoid granulation. DC, dural cupola; C, core; N, neck of the granulation; D, dura of the sinus wall. (Hematoxylin van Gieson, 20.) (Reproduced with permission from Upton and Weller.[28])

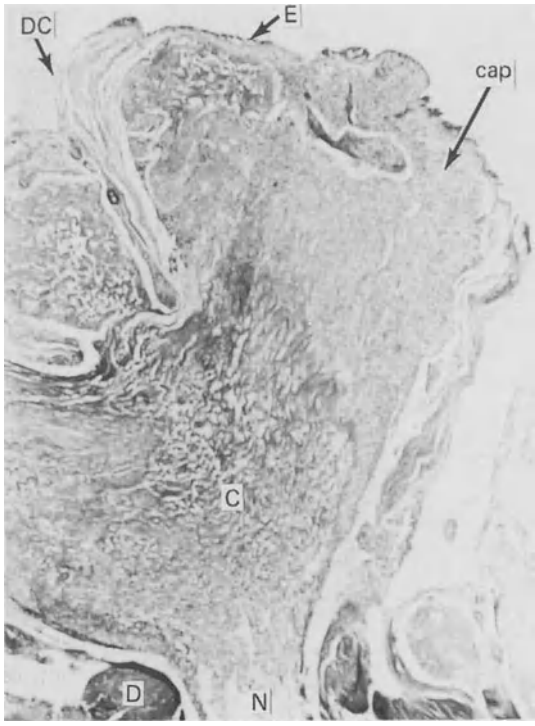


Figure 3.8. Photomicrograph of a vertical section through an arachnoid granulation. DC, dural cupola; E, sinus endothelium; C, core; N, neck; D, dura of the sinus wall. (Hematoxylin van Gieson, ×40.) (Reproduced with permission from Upton and Weller.[28])

and most probably represent the anatomical pathways by which CSF drains from the subarachnoid space to reach the endothelium lining the superior sagittal sinus.

A three-dimensional view of arachnoid granulations can be appreciated by scanning electron microscopy. Figure 3.12 shows a complex arachnoid granulation that has been split longitudinally. It consists of three granulations similar to that seen in Figure 3.7. The granulation on the left is 0.5 mm wide and 1.6 mm long. An elongated core of tissue extends down into the subarachnoid space. There is an artifactual space between the dural cupola and the central core of the granulation that is, itself, coated by arachnoid cells. Although the dura is easily separated from the underlying arachnoid, it is thought that under normal circumstances the outer layer of the arachnoid is firmly apposed to the inner layer of the dura.[28,33] The cap region of the left-hand granulation in Figure 3.12 is roughened where it has been pulled away from its endothelial attachment.

In the center of Figure 3.12, the granulation has been avulsed, leaving its point of attachment with the endothelium exposed. It can be seen that the point of attachment of the granulation is relatively restricted to an area

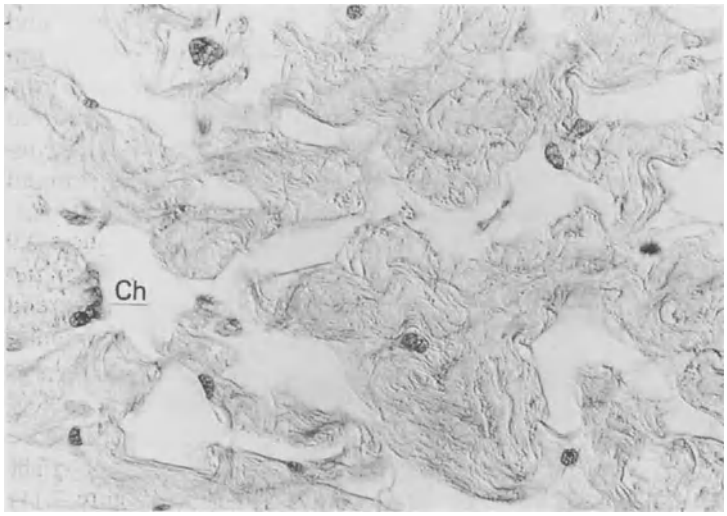


Figure 3.9. Photomicrograph of the collagenous core of a granulation showing channels (Ch) between the collagenous trabeculae. (Hematoxylin van Gieson and Normarski optics, ×270.) (Reproduced with permission from Upton and Weller.[28])

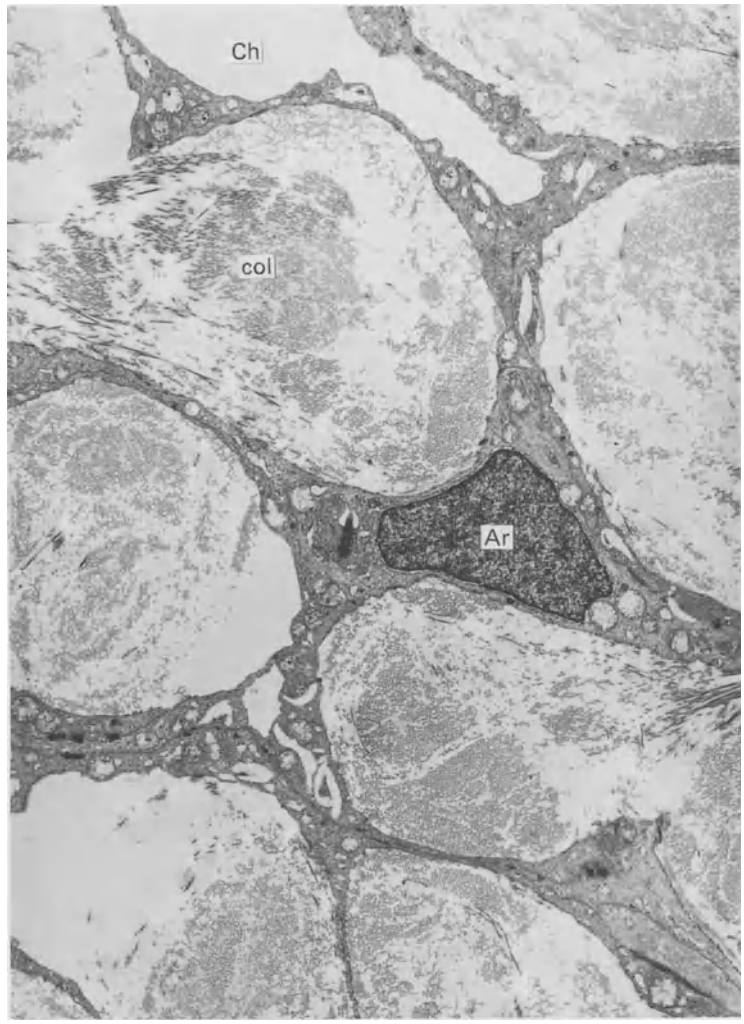


Figure 3.10. Transmission electron microscopy of the central collagenous core of an arachnoid granulation showing bundles of collagen fibers (col) surrounded by arachnoid cells (Ar) with elongated processes. CSF channel (Ch) is lined by arachnoid cells. (×5,200.) (Reproduced with permission from Kida et al.[27])

some 150 μm in diameter. This region corresponds to the endothelium-coated cap region depicted in Figure 3.8. A granulation split longitudinally is seen on the right-hand side of Figure 3.12 and the central collagenous core is exposed to reveal a complex network of channels. At higher power (Figure 3.13) the collagenous trabeculae coated by arachnoid cells form a honeycombed mass of channels similar to those seen by light and transmission electron microscopy (Figures 3.9 and 3.10). Immunocytochemistry reveals the presence of macrophages within this core region but no endothelial cells.[29] When the arachnoid cap region at the apex of the granulation is fractured horizontally and internal structure exposed, a network of wide channels is seen (Figure 3.14) and these correspond to the channels seen by light microscopy in Figure 3.11.

To summarize the structure of the arachnoid granulations in man, the diagram in Figure 3.15 has been constructed. It depicts the subarachnoid space traversed by trabeculae and the continuity of this space with the cen-

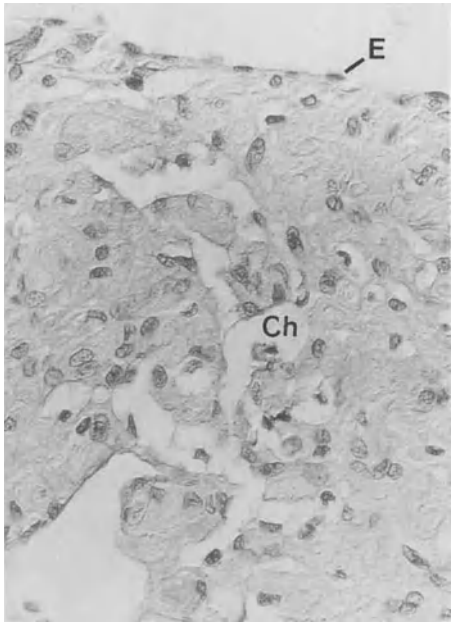
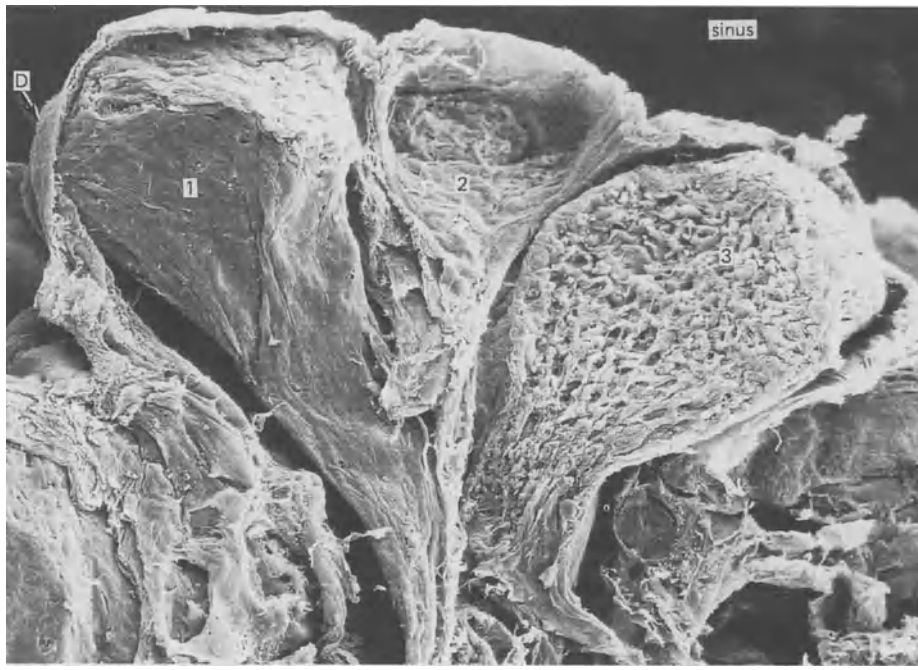


Figure 3.11. Photomicrograph of a horizontal section of an arachnoid granulation taken through the apical cap of arachnoid cells. E, sinus endothelium; Ch, channels. (Hematoxylin van Gieson and Normarski optics, ×270.)

tral core of the arachnoid granulation. It emphasizes the close relationship of the dura to the outer layers of the arachnoid and the core of the granulation.[28] The dural cupola only partly covers the granulation as, at the apex, the arachnoid cap region is in direct contact with the endothelium of the venous sinus.

Arachnoid Granulations and Subarachnoid Hemorrhage

Following subarachnoid hemorrhage, red blood cells and other blood components are distributed through the subarachnoid space. In this way, red blood cells can act as a natural tracer in man to outline the main drainage pathways of CSF. For example, the lack of direct communication between the subarachnoid space and the perivascular spaces within the human brain is emphasized by the almost complete lack of penetration of red blood cells from the subarachnoid space into the perivascular spaces following subarachnoid



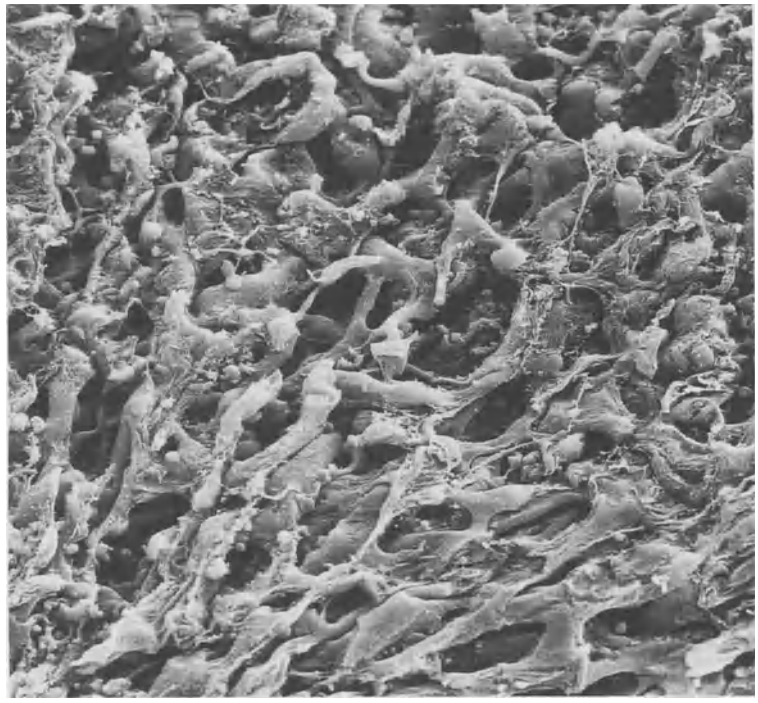
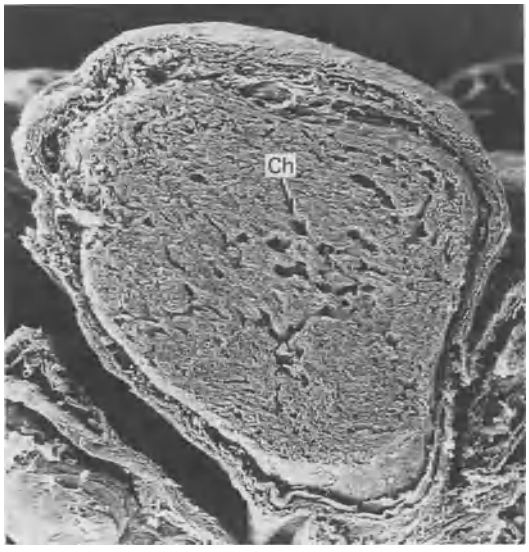


Figure 3.13. Scanning electron micrograph showing collagenous trabeculae and channels in the core of granulation (3) in Figure 3.12. (×380.) (Reproduced with permission from Upton and Weller.[28])



hemorrhage.[12] Arachnoid granulations examined soon after subarachnoid hemorrhage, however, do reveal the presence of red blood-cells in channels both within the collagenous core and within the arachnoid cap,[28,29,34] the red cells are even seen within the subendothelial channels (Figures 3.11 and 3.16). Such channels (Figure 3.16) are mostly lined by arachnoid cells, although in some instances bundles of collagen fibers are abutting the

Figure 3.14. Scanning electron micrograph of a horizontal section through an arachnoid cap showing channels (Ch) approximately 10 μm in diameter. (×95.) (Reproduced with permission from Upton and Weller.[28])

Figure 3.12. Scanning electron micrograph of a vertical section through three arachnoid granulations. The granulation on the left (1) is intact, that in the middle (2) has been avulsed, and that on the right (3) has been split longitudinally. (For further explanation, see text). D, dural cupola. (×194.) (Reproduced with permission from Upton and Weller.[28])

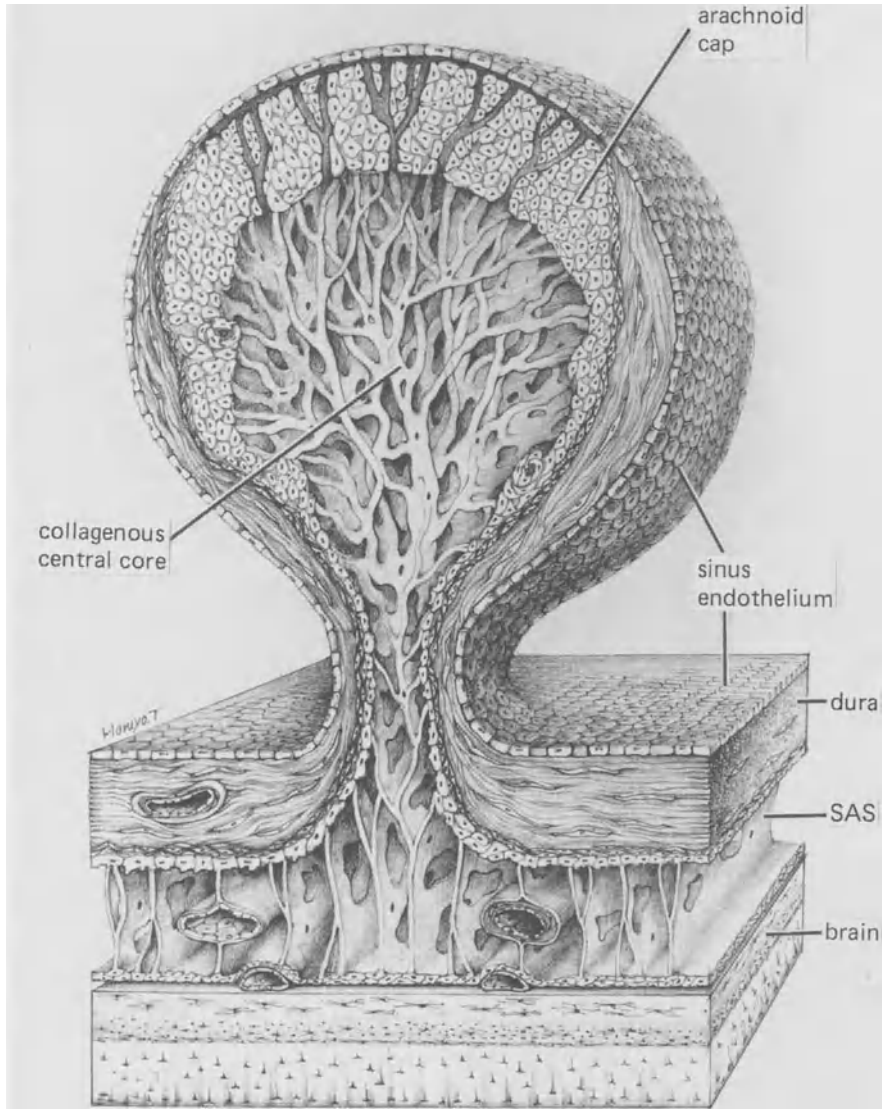


Figure 3.15. Schematic diagram of a human arachnoid granulation, projecting into the venous sinus. SAS, subarachnoid space.

walls of the channels. These channels correspond to the fluid drainage channels seen in Figures 3.11 and 3.14 and illustrated in Figure 3.15.

Weed's[27] original concept was that the arachnoid granulations acted as filters for the CSF, and experimental studies[35] have suggested that blood and tissue debris is phagocytosed by arachnoid cells within the meshwork of channels in arachnoid villi. In human arachnoid granulations, immunocytochemical preparations suggest that macrophages lie within the channels of the collagenous core and cellular caps, and may therefore be responsible for phagocytosis and the elimination of particulate matter such as erythrocytes.[27]

Hydrocephalus may develop either acutely or after some weeks or months following subarachnoid hemorrhage. Attention has therefore been focused upon the arachnoid

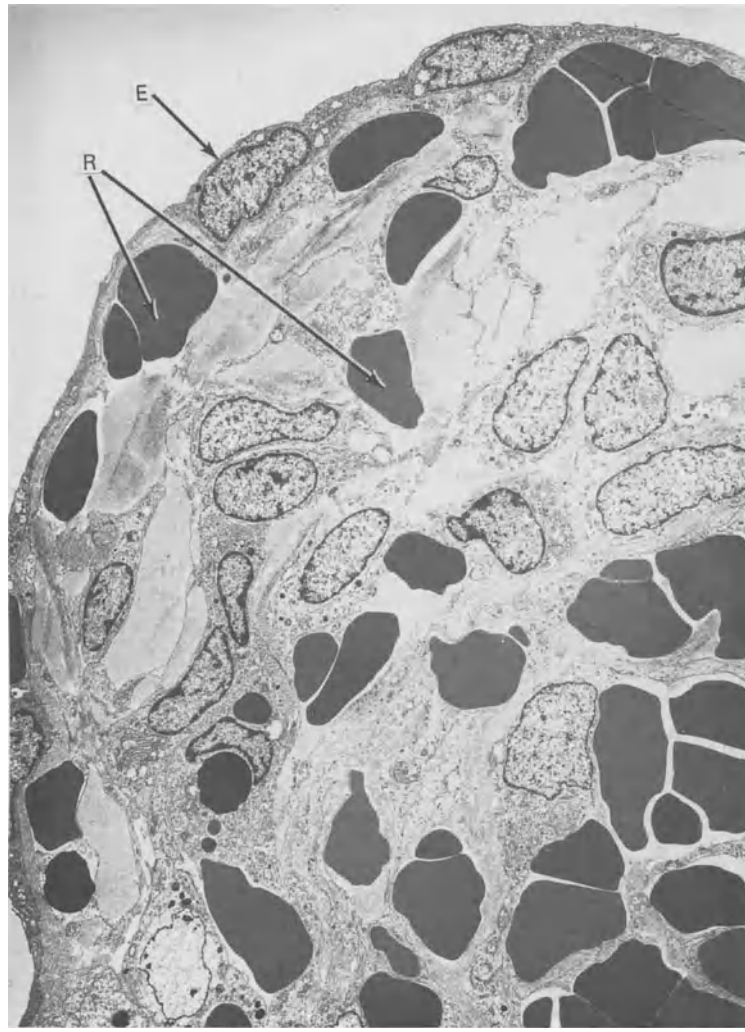


Figure 3.16. Transmission electron micrograph of an arachnoid granulation following a recent subarachnoid hemorrhage. Erythrocytes (R) are seen in channels within the arachnoid cap and under the endothelium (E). (×2,800.) (Reproduced with permission from Kida et al.[27])

granulations in order to discover whether blockage of the arachnoid granulations is instrumental in the impedance of CSF flow and the development of the hydrocephalus. Although some early studies[36] suggested that fibrosis occurred in arachnoid granulations following subarachnoid hemorrhage, this has not been substantiated in later reports.[37] Despite the presence of red blood cells within the granulations, there appears to be little fibrin,[28,29,34] and it is not known whether the erythrocytes alone can be eliminated from the granulations or indeed whether they do become blocked after subarachnoid hemorrhage.

Transendothelial Passage of CSF

Kida and colleagues[28,34] have emphasized the problems of adequate fixation in the ultrastructural study of human arachnoid granulations. They are not structures that can be biopsied, so that postmortem tissue has almost invariably been used. Although the basic

organization of the arachnoid granulations appears to be well preserved, few valid conclusions can be drawn regarding the dynamic processes occurring in endothelial cells in these preparations. There is still discussion with regard to whether the surface coating of arachnoid granulations through which CSF finally drains back into the blood of the venous sinus is coated by endothelial cells[29] or by arachnoid cells.[28] We must rely, to a large extent, therefore, on the findings of experimental studies in which tracers can be used to identify pathways of transendothelial drainage and in which immediate fixation by perfusion can be employed in the preparation of the tissue.

Arachnoid villi in most experimental animals are much simpler in their organization than the villi and granulations seen in man. Nevertheless, it is probably valid to draw conclusions from experimental studies regarding the functions of endothelium on human granulations. Direct observation of the endothelial covering of arachnoid villi in animals has indicated that there are a number of mechanisms for the bulk flow of CSF from villi into the venous sinus.[32,38–43] Numerous pinocytotic vesicles have been described in the endothelium in the dog[38] and it is suggested that this may be a major mechanism for transendothelial bulk drainage of CSF. In the monkey, on the other hand, there are large vacuoles 2 to 10 μm in diameter within the endothelium, and Tripathi and Tripathi[39] have proposed that such a macrovacuolar system could account for the passage, not only of fluid, but also of particulate matter from the arachnoid villi into the blood. There is some indication that such vacuoles are present in human sinus endothelium.[40] Whatever the mechanism for transendothelial drainage in man is, it seems likely that it is a bulk flow mechanism that completes the drainage of CSF.

Summary

Histological, ultrastructural, and tracer studies in man and experimental animals suggest that interstitial fluid (ISF) from the brain drains into the cerebrospinal fluid (CSF). Tracers injected into the cerebral white matter flow between nerve fibers and drain into the ventricles. This pathway of ISF drainage is reversed in hydrocephalus with consequent CSF edema of the periventricular white matter. When tracers are injected into cerebral gray matter, they drain along perivascular spaces to enter the CSF in the subarachnoid space over the surface of the brain. Thence tracers may drain into cervical lymph nodes mainly via nasal lymphatics in several animal species.[44] In man, it appears that the majority of the CSF produced by the choroid plexus and derived from ISF drains through arachnoid villi and granulations back into the blood of the venous sinuses. Arachnoid villi and granulations are formed by the extension of arachnoid through the dural wall of the sinus. They are composed of a central core in which there is a network of channels and collagenous trabeculae through which CSF drains into channels within an apical arachnoid cap. As the apical channels extend right up to the endothelial lining of the venous sinus, it is suggested that the final stage of bulk drainage of CSF into the blood is by the transendothelial microvesicular or macrovacuolar mechanisms described in experimental animals.

Acknowledgments

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CHAPTER 4

Dynamics of Intracranial Cyst Formation and Expansion

Ercole Galassi and Giulio Gaist

Introduction

Intracranial arachnoid cysts are benign extra-axial cerebrospinal fluid (CSF)–filled cavities that are bounded by a membrane with the histological appearance of arachnoid mater.[1–3] They can arise at any location intracranially adjacent to and variously communicating with the subarachnoid spaces, the temporosylvian region, and the infratentorial compartment being the sites of predilection[1–9] (Figure 4.1).

Since the first classic report by Bright,[10] the origin and the pathological significance of arachnoid cysts have represented for years matter of speculation and considerable controversy. The difficulties found in the interpretation of this anatomicoclinical entity are borne out by the numerous and sometimes confusing labels coined in the early neurosurgical literature: "benign brain cysts," "meningitis serosa circumscripta," "chronic cystic arachnoiditis," "external hydrocephalus," "arachnoid diverticula or pouches."[3,11–19]

In 1971, Robinson[9] provided a comprehensive review and classification of arachnoid cysts, maintaining their basically developmental nature and approximately estimating their incidence on the order of 1% of all intracranial space-occupying processes. More recently the advent and widespread use of neuroimaging technologies has greatly facilitated the diagnosis and markedly increased the incidence of arachnoid cysts in neurosurgical practice,[1,4–6,20,21] thus contributing to a better insight of the entity.

The salient clinical and neuroradiological features have become sufficiently elucidated to the extent that these lesions do not usually raise special diagnostic problems at the present time. On the other hand, the developmental substrate of their formation and the pathophysiological mechanisms of their expansion as well as their lifelong biological behavior remain incompletely understood. This chapter is primarily devoted to the fundamental etiopathogenetic theories advanced to explain the origin and progression of arachnoid cysts; a treatise about other abnormal cystic collections of CSF or CSF-like fluid of different nature such as ependymal or porencephalic cysts will be found elsewhere in the volume.

Etiology and General Principles of Classification

Based upon etiologic criteria, Weinman[22] classified intracranial arachnoid cysts into two main categories:

1. acquired cysts, secondary to well-defined etiological factors, and
2. primary cysts, when definite causal agents cannot be identified.

Head traumas, intracranial bleedings, and infectious conditions have been proposed as the most plausible causes of secondary cysts, which have been also currently designated as "leptomeningeal".[3,11,13,19,23,24] Adhesive scarring of the leptomeninges promoted by the

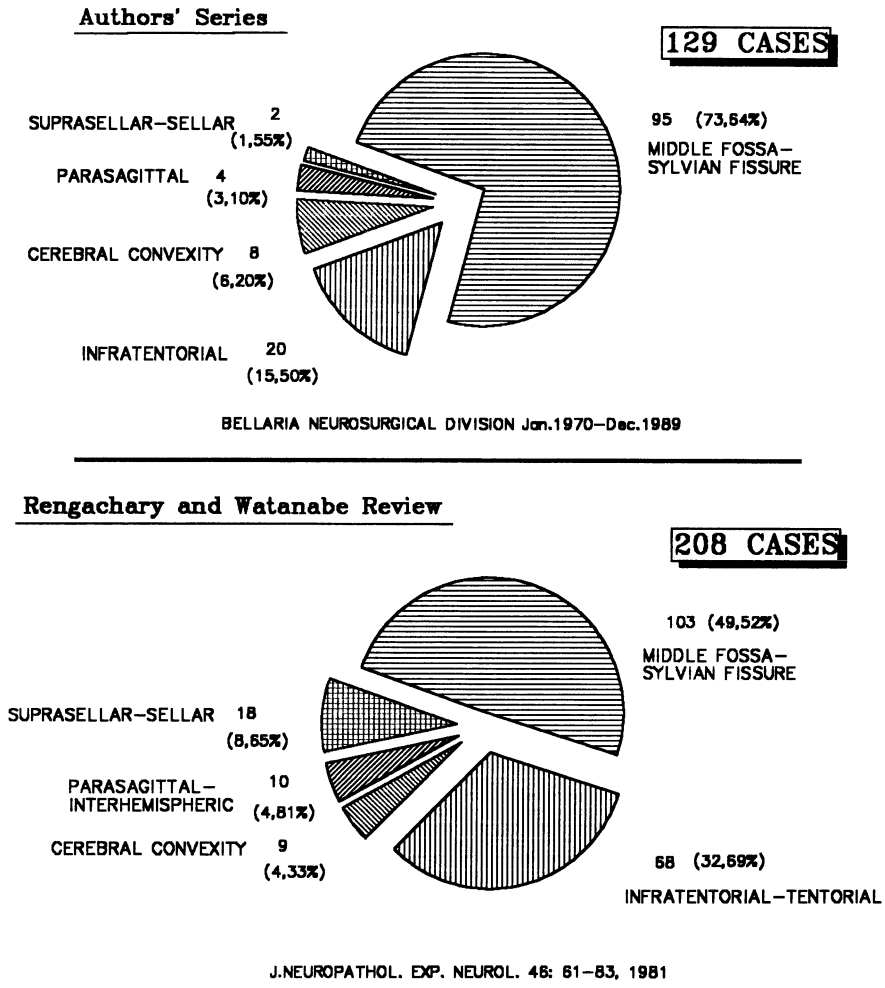


Figure 4.1. Anatomical distribution of intracranial arachnoid cysts. The remarkable predilection for the temporosylvian and infratentorial areas are deducible from both the authors' series (129 cases) and from the tabulated data of the Rengachary and Watanabe[2] review (208 cases).

presence of blood or inflammation would seemingly result in loculation of the subarachnoid space and localized entrapment of CSF, thus supposedly providing a common basis for the formation of the acquired lesions.

Some of the earlier authors have postulated as possible the propagation to the intracranial leptomeninges of infectious processes from the middle ear[13,25] or from extracranial foci[11] to explain a number of acquired infratentorial arachnoiditic cysts. As a matter of fact it is now widely accepted that previous head traumas play a certain role in the production of a rare type of leptomeningeal cysts associated with enlarging calvarial defects.[23,26,27] Such traumatic pockets of the subarachnoid space would take origin from diastatic skull fractures in infancy and early childhood, typically involving the parietal bone, associated with dural tears, pulsating herniation of the arachnoid, and localized damage of the subjacent brain.[27]

It is noteworthy, however, that acquired leptomeningeal CSF collections merely represent sequestrations and localized enlargements of the subarachnoid space, bordered by more or less altered pia and arachnoid mater and, in some posttraumatic cases, by gliotic cerebral

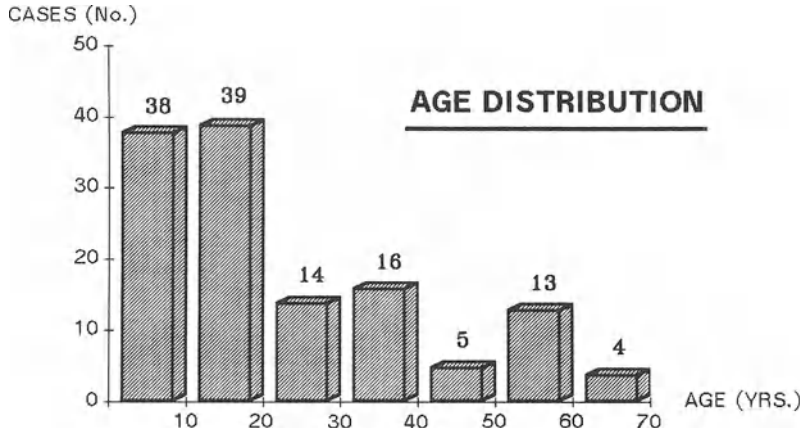


Figure 4.2. Age distribution in the authors' series of 129 cases of intracranial arachnoid cysts. Definite prevalence in the first two decades of life is evident.

tissue.[27,28] This situation is at strong variance with the typical histopathologic pattern of true primary arachnoid cysts that are actually intra-arachnoid in location, as conclusively demonstrated by detailed light and electron-microscopic studies.[2,3,9,15,23,29–31] The pathologic cavity in this latter category is well distinct from the subarachnoid space and contained between inner and outer arachnoid walls that merge together at the periphery of the cyst as a splitting of surrounding normal arachnoid.[2,3,15,31,32]

Primary cysts are far more common than their acquired counterpart and make up the vast majority of extra-axial CSF cystic collections; they are also universally assumed to be congenital in origin and developmental in nature.[1–3,5,9,15,29,31,32] The following arguments attest to the malformative genesis of primary arachnoid cysts:

1. Definite prevalence in infancy and childhood. Most of these lesions have been diagnosed within the first two decades of life[3,4,6,9,21,28,33–38] (Figure 4.2).
2. Exceptional reports of familial occurrences in siblings[39] and sporadic association with genetic diseases such as Marfan syndrome,[15,16,40] chromosomal abnormalities,[41] and with other intra- and extracranial developmental anomalies.[1,19,34,36,42–46] In the series by Menezes et al.,[44] 30% of the cases were found to harbor additional malformations either within the brain or extracranially.
3. The lack of traumatic, hemorrhagic, and inflammatory antecedents in the majority of the past histories. The causal role of previous head injuries, occasionally elicited in patients with middle fossa cysts (22 out of our 95 cases), seems questionable since most of these traumatic events are mild in degree and have occurred shortly before the onset of clinical manifestations.[4,6,47–50] It seems likely that these traumas only act as factors for decompensation of pre-existing, although occult, pathologic conditions.[4,6] Indeed the potentially dangerous vulnerabilty of middle fossa cysts to traumatic insults has been widely recognized and related to the peculiar propensity to develop intracranial hematomas, subdural hygromas (Figure 4.3), and loculated expansion of the pathologic cavity.[4,21,47–55]

The possibility of a causal relationship between a number of infratentorial arachnoid cysts and old birth injuries is more intriguing and difficult to determine.[1,19,25,45,46,56–60] It has been

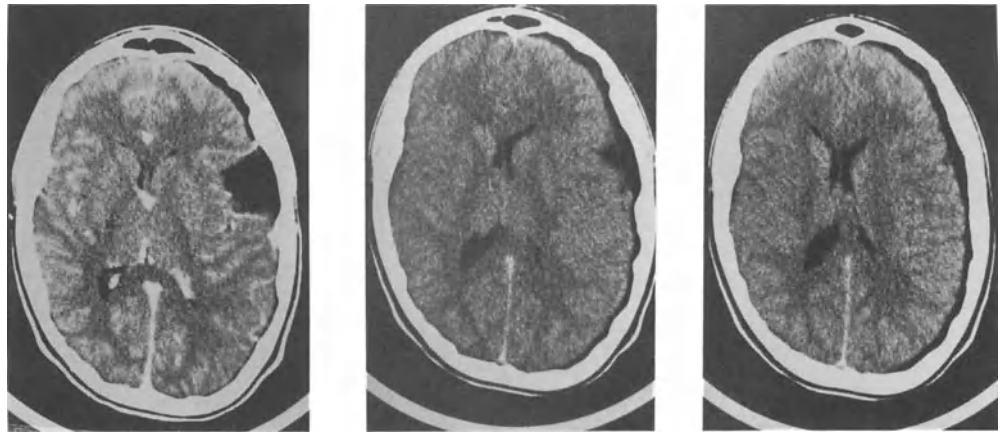


Figure 4.3. Sylvian arachnoid cyst complicated by posttraumatic subdural hygroma due to laceration of the cyst dome and escape of CSF into the subdural space.

hypothesized that traumatic deliveries and related intracranial bleedings might reasonably provide a probable etiology in some instances. Williams,[19] while describing three cases of "subarachnoid pouches" of the posterior fossa associated with cervical syringomyelia, concluded that both anomalies might be attributed to a basal arachnoiditis at the level of the foramen magnum secondary, in turn, to past birth traumas and subsequent meningeal bleeding. The resultant craniospinal pressure dissociation and misdirection of CSF in response to periodic venous pressure fluctuations would theoretically account for the enlargement of both the infratentorial pouch and the cervical syrinx.[19]

Galassi and associates[1] called analogous

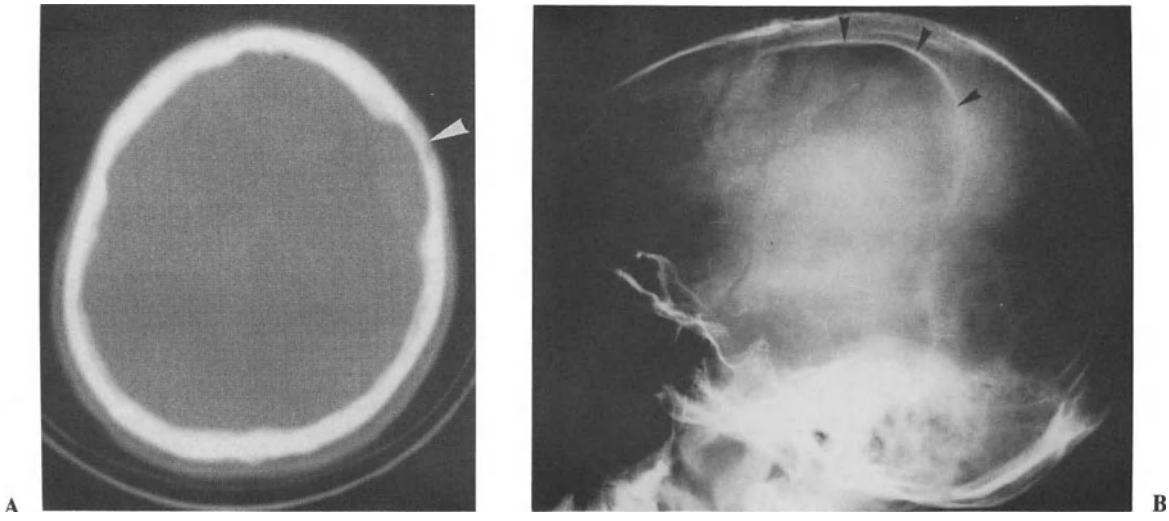
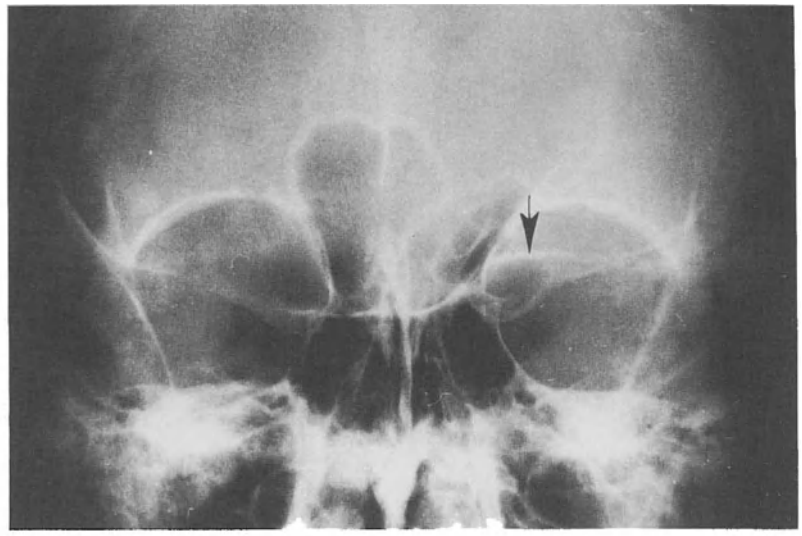


Figure 4.4. Examples of bony changes induced by congenital arachnoid cysts. (A) Focal expansion of the cranial vault (white arrowhead). (B) Localized erosion of the calvarium demarcated by a rim of increased density (black arrowheads).



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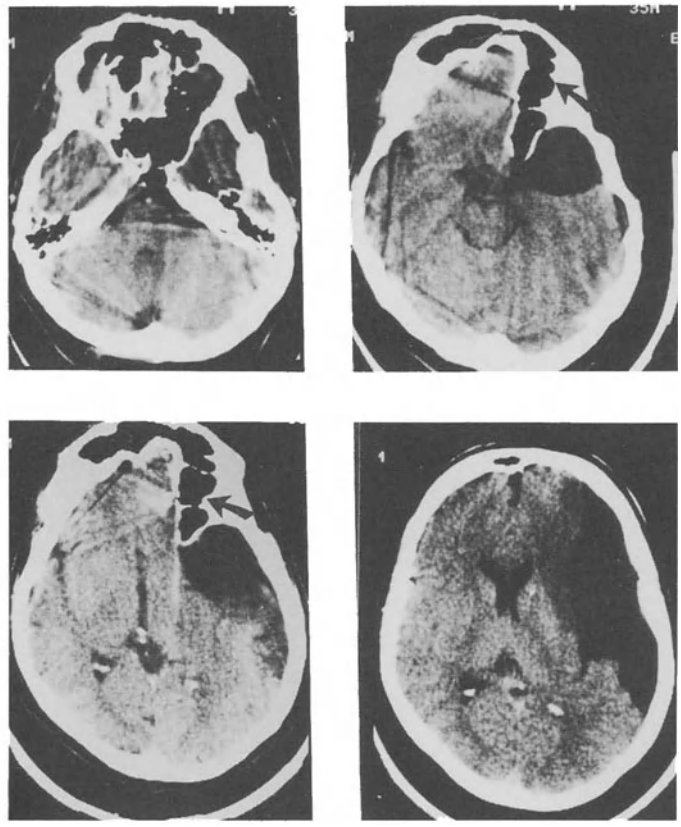


C: Elevation and pneumatization of the lesser sphenoid wing (straight arrow). D: Excessive pneumatization and expansion of the sphenoid and frontal sinuses and anterior cranial base (curved arrow).

attention to the frequency (50% of the cases) of dystocic events recorded in their series of infratentorial arachnoid cysts but advanced the divergent belief that dystocia might simply result from the fetal macrocranium due to the prenatal malformation and attendant hydrocephalus. Reports of newborns having large heads since birth.[1,25,34,44,59,60] and occasionally mentioned ultrasound demonstrations "in utero"[8] would substantiate this latter assumption.

4. Structural deformities of the skull reflecting chronic molding of the plastic fetal and infantile calvarium. Interestingly, sylvian cysts exhibit bony changes dependent on long-standing localized pressure and CSF pulsations, including bulging and thinning of the temporal squama, elevation of the lesser wing, and forward projection of the greater sphenoid wing, in conjunction with other paradoxical modifications, such as elevation of the middle fossa floor and excessive pneumatization and expansion of the sphenoid sinus, which frequently accompany cerebral hemiatrophy and are seemingly related to an absence of cerebral counterpressure* (Figure 4.4).

   With respect to infratentorial locations, the occipital bulging and increased volume of the posterior fossa bear obvious similarities with the congenital abnormalities found in the Dandy–Walker malformation.†

5. Anomalies of the venous vasculature are also frequently observed and logically speak in favor of a developmental origin. Absence of the sylvian vein and of the sphenoparietal sinus in cases of middle fossa cysts[37,67] and dystopia or absence of the transverse sinuses in cases of infratentorial locations belong to this category.[1,43,64]

Mechanisms of Cyst Formation

At the present state of knowledge, the exact developmental error initially leading to the formation of primary arachnoid cysts remains incompletely understood. Robinson,[16,61] in reviewing a series of middle fossa-sylvian cysts, formerly hypothesized that the basic disorder was a primitive agenesis of the perisylvian region of the brain with lack of migration of the frontotemporal opercula ("temporal lobe agenesis syndrome"), probably occurring by the last 3 months of fetal life. In this view the so-called cyst would merely represent a secondary passive dilation of the subarachnoid space ("external hydrocephalus") occupying the place of absent brain. Although subsequently held also by others,[52,55,62,67] this theory of a primary failure of encephalic growth as well as that of a prenatal or early postnatal cerebral infarction of the perisylvian region[68] both seem untenable, if one considers the essentially normal histologic structure of the brain subjacent to the cyst,[3,8,15,28,69] the identical weight of the affected and contralateral hemispheres,[28] the comparatively low incidence of focal neurological deficits,[6,51,70] and the high rate of cerebral reexpansion and cyst collapse following surgical excision or CSF shunting.* The marked reduction in cyst size or even total obliteration frequently observed at postoperative computed tomography (CT) controls support the belief that anatomical distortion and eventual atrophic changes of the brain are not primary in nature but only secondary to the presence and active compression by the cyst.[5]

Therefore, increasing consensus has emerged in the literature that these lesions should actually be regarded as true malformations of the arachnoid evolving from a primitive derangement of the embryonal mechanisms by which the leptomeninges and the subarachnoid space take origin. This assumption has been convincingly supported by de-

*Refs. 3, 4, 9, 16, 37, 48, 50, 51, 61, 62.
†Refs. 9, 36, 37, 42, 43, 46, 59, 63–66.

*Refs. 4, 5, 6, 21, 28, 29, 33, 38, 46, 48, 52, 60, 71, 72.

tailed postmortem gross and microscopic anatomical studies that have definitely documented the intra-arachnoid location of the pathologic cavity[2,3,9,15,30–32,37,73] and by the fine ultrastructural features of the lining walls partially differing from the organization of the normal arachnoid mater.[2,57,69,74]

However, the mode of occurrence of the hypothesized embryological anomaly of the developing leptomeninges has not been fully clarified. One theory has postulated a focal aberration in the formation processes of the subarachnoid space from the primordial "perimedullary mesh" (endomeninx) after the perforation of the rhombic roof and egress of CSF into the loose mesenchymal tissue surrounding the primitive neural tube.[3,15,31,32,73] A minor misdirection of the fluid flow would cause the constitution of an accessory blind pocket within the arachnoid that might be subsequently closed off from the remainder of the subarachnoid spaces and enlarge by virtue of internal CSF accumulation.[3,15,31,32,73]

Although attractive, the above theory does not offer a satisfactory answer as to why arachnoid cysts show an almost constant anatomical relationship with the site of a normal arachnoid cistern and cannot account for the striking predilection for the middle cranial fossa and sylvian fissure[1,2,5,75] (Figure 4.1). This observation would more seemingly argue in favor of a later disorder affecting the development of the subarachnoid cisterns and fissures which, in turn, is influenced by the complex foldings of the growing encephalon.[1,2,75]

An alternative hypothesis has recently put forward by Go and coworkers[69,76] based upon the close electron-microscopic morphological similarities between the elements bordering the cyst walls and the subdural neurothelium, or arachnoid mesothelium, which constitutes the outer layer of the arachnoid, subjacent to the dura, and which lines the arachnoid granulations. Furthermore, the presence of microvilli and the enzyme ultracytochemical results, consistent with the presence of fluid secreting and transporting functions, in the cells bordering the cyst cavity as well as in the lining of arachnoid villi and granulations stimulated the concept of a possible derivation of arachnoid cysts from the subdural neurothelium differentiating toward arachnoid villus mesothelium.[69,76] An ectopic villus failing to find its physiological connection with a dural sinus would progressively collect its secretory product into a closed cyst cavity.[69]

Pathophysiology of Cyst Enlargement

Whatever the primary developmental disorder causing the formation of intracranial arachnoid cysts, a more important issue from a practical standpoint concerns the pathogenetic pathways possibly leading to the expansion of these CSF-filled cavities. Conceivably a better understanding of the pathophysiology of altered fluid kinetics responsible for potential cyst enlargement may offer useful clues to solve clinical questions and related therapeutic problems. This seems particularly valuable if one considers that the natural history of the entity is enigmatic and that the lifelong clinical behavior cannot be reliably ventured.

There is no doubt that, despite their connatal presence and prevailing tendency to give rise to symptoms within the first two decades, an undetermined number of arachnoid cysts remain stable and clinically silent throughout a long period of life; some become manifest only at an adult or advanced age,* some are fortuitously discovered in individuals who prove virtually symptom-free even at thorough neurological and psychological testing,[78] whereas others merely represent incidental autoptic findings.[16,31,73,79] Such curious and unpredictable qualities have been additionally confirmed by the spontaneous "self cure" and regression demonstrated in exceptional circumstances.[80]

In general, there is sufficient evidence that arachnoid cysts actually behave as "active" space-occupying lesions that do compete for

*Refs. 4–7, 9, 15, 29, 32, 48, 50, 52, 53, 77.

space with the brain and can progressively increase in size. Such potentially harmful properties seem indisputably confirmed by reported cases of cyst enlargement verified at serial CT controls,[24,48] by the common association with evident, and sometimes striking, mass effects seen at neuroradiological investigations, as well as by the remarkable incidence of clinical manifestations of intracranial hypertension recorded in many series.*

Conceivably, the development of the arachnoid cyst is usually very slow and allows the brain to find a sort of chronic accommodation;[53] however, the balance is delicate and unstable and may be altered either idiopathically or by ensuing precipitating traumas of varying intensity. Once initiated, the process of clinical decompensation may rapidly progress and eventually lead to irreversible, and even fatal, neurological consequences.[31,48,50,53,56]

Multiple pathogenetic theories have been advanced to explain the internal fluid accumulation under pressure, possibly producing the progressive distension of the pathologic cavity:

1. Active fluid secretion directly by the cyst walls.
2. Fluid filtration through the lining membranes by virtue of an osmotic gradient between the intracystic content and the normal CSF.
3. Internal fluid trapping most likely due to unidirectional ball-valve mechanism working at the site of communication between the cyst and the subarachnoid pathways.† Repetitive CSF waves in response to either arterial pulsations[81] or to venous pressure fluctuations[70,75] would force the displacement of fluid into the arachnoid cavity.
4. Transcortical leak of CSF from the ventricles, through compressed white mater and cortex, into the cyst in cases of convexity lesions.[82]

Especially helpful information in order to elucidate these pathophysiological issues became available with the introduction of more sophisticated examination of the lining arachnoid membranes by scanning and transmission electron microscopy and enzyme ultracytochemistry, as well as by dynamic evaluation of the CSF circulation and of the functional relationships between the cyst and the neighboring CSF pathways by means of radionuclide[60,62,63,67,75] or metrizamide CT cisternography.†

The ultrastructural and ultracytochemical investigations by Go et al.[69,76] have clearly demonstrated that the cells bordering the cyst walls are capable of active fluid secretion and transport toward the internal cyst lumen. On the other hand, CT cisternographic findings have indicated different patterns of contrast penetration inside the cyst, implying variable degrees, and sometimes absence, of communication between the arachnoid malformation and the remainder of the subarachnoid space.‡ Galassi and associates[5,6] found an inverse correlation between the existence and ease of this functional communication and the expanding behavior and size of middle fossa cysts; it was therefore suggested that the enlargement of the pathologic cavity was strictly linked to its gradual segregation from the basal arachnoid cisterns.

Based upon the appearance at CT and the dynamic assessment at CT cisternography, three subtypes of middle fossa cysts have been classified reflecting anatomicophysiological conditions of increasing severity.[5] The mildest cysts, type 1, are small, biconvex or semicircular in shape and confined to the anterior aspect of the temporal fossa. Mass effects, if any, are negligible, whereas a free and rapid communication with the basal cisterns is evident since early cisternograms (Figures 4.5 and 4.6).

Intermediate malformations, type 2, are medium sized and roughly triangular or quadrangular; they involve the anterior and middle parts of the temporal fossa, upward extending and opening the sylvian fissure. Mass effects

*Refs. 3–6, 8, 9, 21, 28, 33, 37, 38, 51.
†Refs. 1, 3, 5, 29, 30, 35, 50, 62, 69.
†Refs. 1, 4, 5, 35, 37, 70, 83, 84.
‡1, 4, 5, 6, 35, 37, 70, 83, 84.

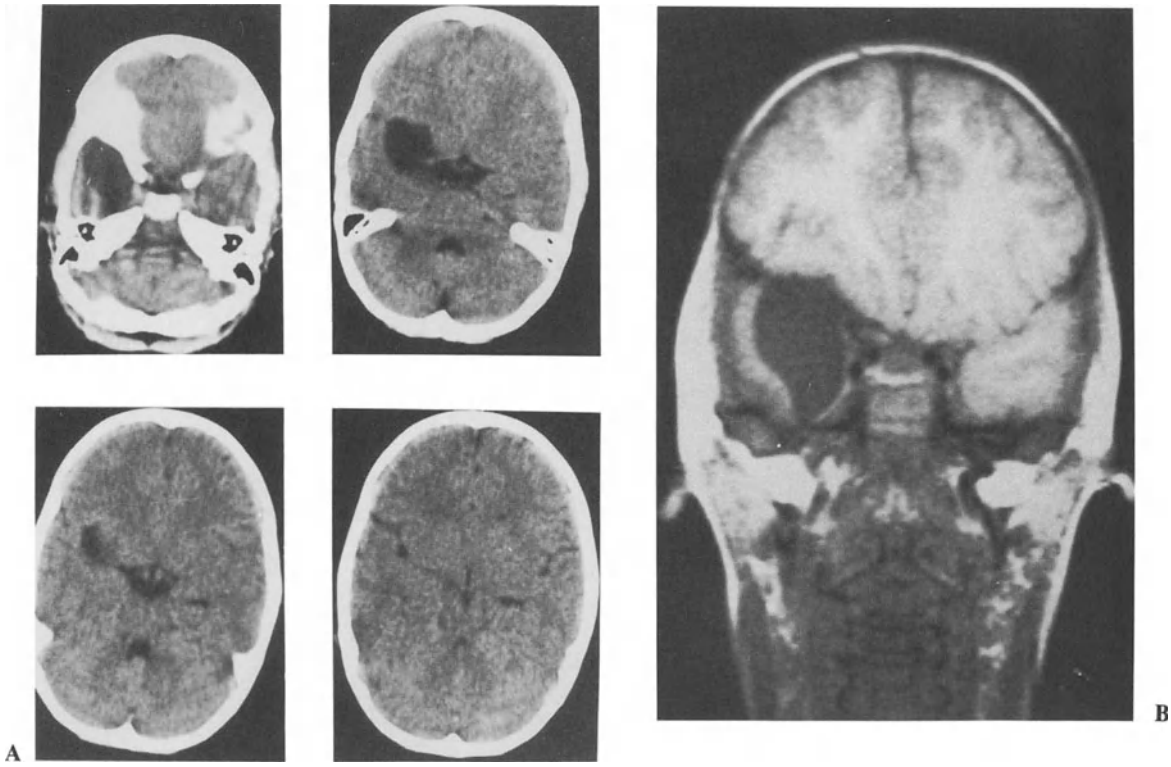


Figure 4.5. Type 1 middle fossa cyst at axial CT scans (A) and coronal T1-weighted MR image (B). The CSF cavity is small and confined to the anterior part of the temporal fossa. Mass effects are negligible.

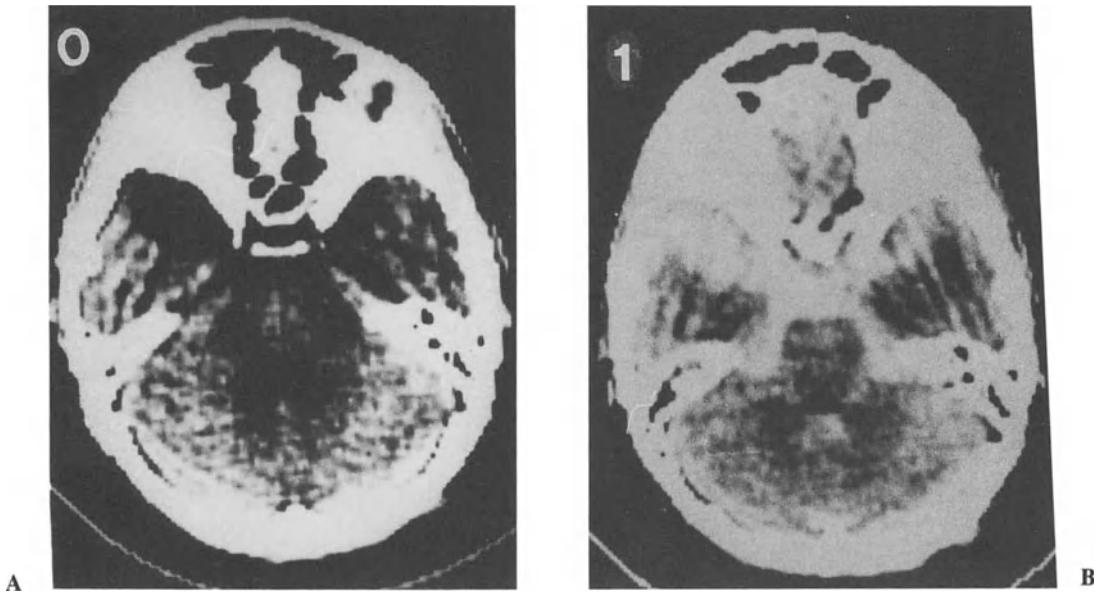


Figure 4.6. Rapidly communicating type 1 middle fossa cyst at metrizamide CT cisternography. A: Baseline axial CT scan. B: Massive contrast filling at the first (1 hour) cisternogram indicates a free communication with the basal cisterns.

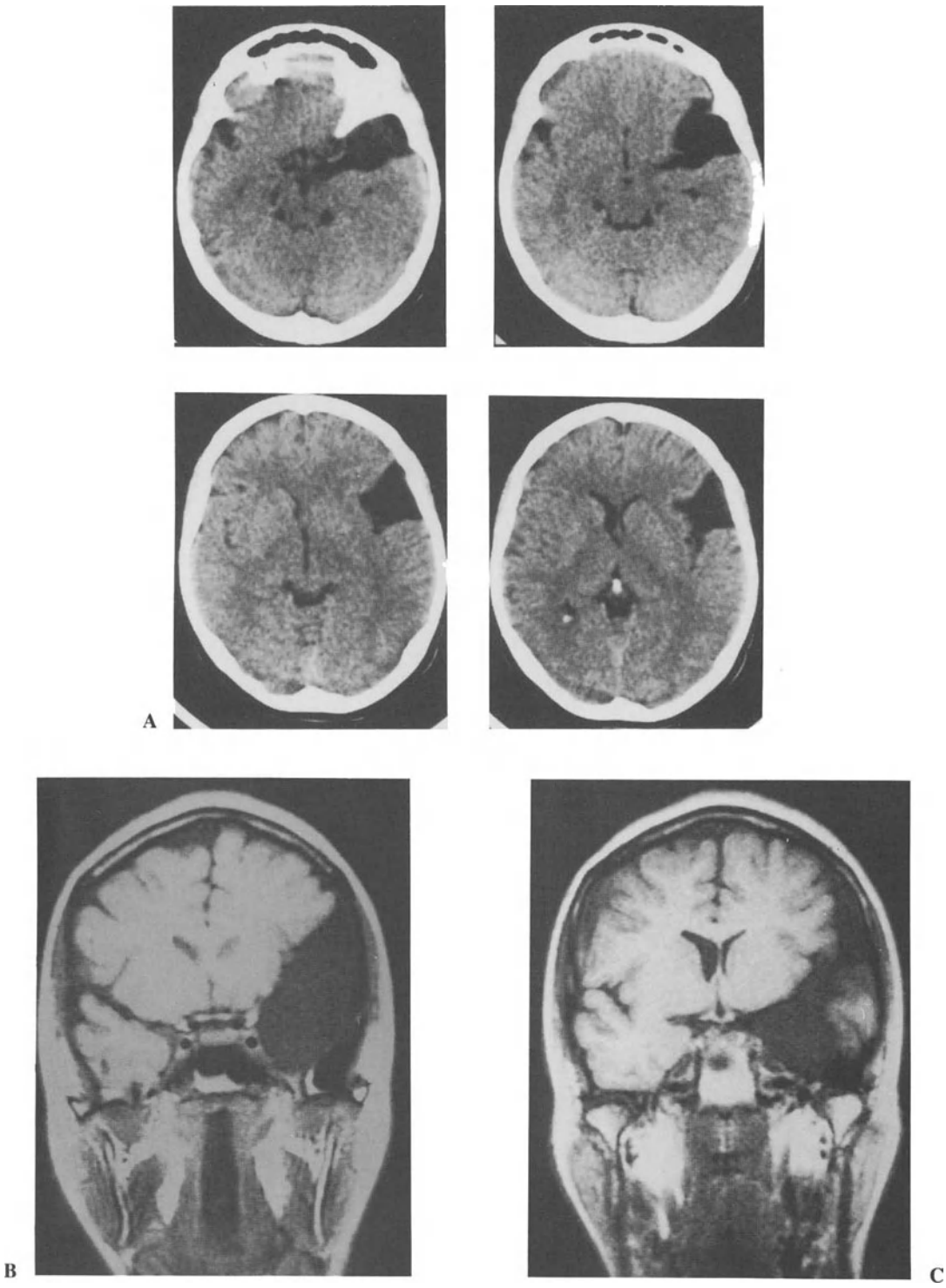


Figure 4.7. Intermediate type 2 middle fossa cyst at axial CT scans (A) and coronal T1-weighted MR images (B and C). The lesion upward extends from the anterior part of temporal fossa largely involving and opening the sylvian fissure. Compression over the ipsilateral ventricle is clearly visible.

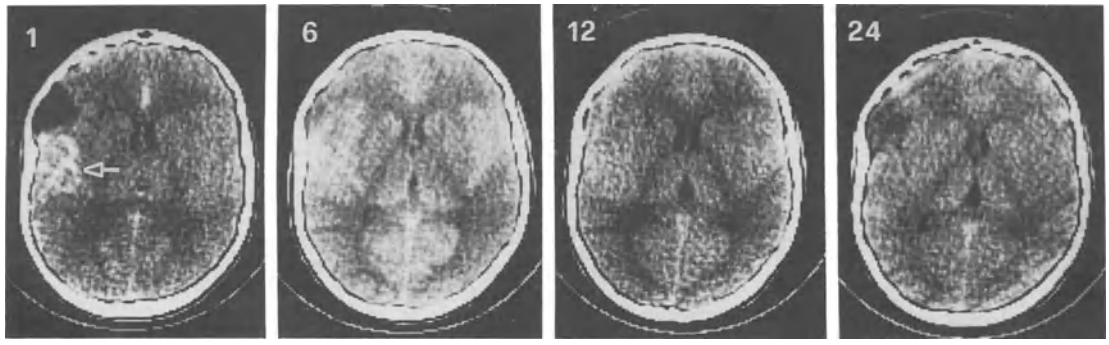


Figure 4.8. Metrizamide CT cisternograms (1, 6, 12, and 24 hours) of a type 2 middle fossa cyst. The initial (1 hour) cisternogram reveals no penetration of the contrast. Maximum opacification occurs later (6 hours) compared to the rapidly communicating type 1. Intracystic density remains slightly higher than the standard values at 24 hours, suggesting a somewhat delayed drainage from the lesion. Arrow points to an early prominent staining of the adjacent extracystic subarachnoid spaces. [Reprinted with permission from Galassi et al.[5]]

are frequent, although usually moderate (Figure 4.7). A comparatively later filling and clearance of water-soluble contrast at CT cisternography document a less adequate connection with the subarachnoid spaces (Figure 4.8).

The largest, roundish or oval, cysts, type 3, occupy almost entirely the temporal fossa and widely expand over the hemispheric surface exerting constant and severe compressive effects with relevant ventricular displacements and midline shifts (Figure 4.9). Sequential CT cisternograms of these large malformations reveal an absent (Figure 4.10) or noticeably delayed injection and washout of contrast (Figure 4.11). This is compatible with lacking or incomplete, and functionally inadequate, connection with the normal CSF pathways. The delayed passage of contrast into some large noncommunicating type 3 lesions would presumably imply either an intermittent and small communication or diverse functional ways of intracystic access, through the lining walls, mediated by passive osmotic or active

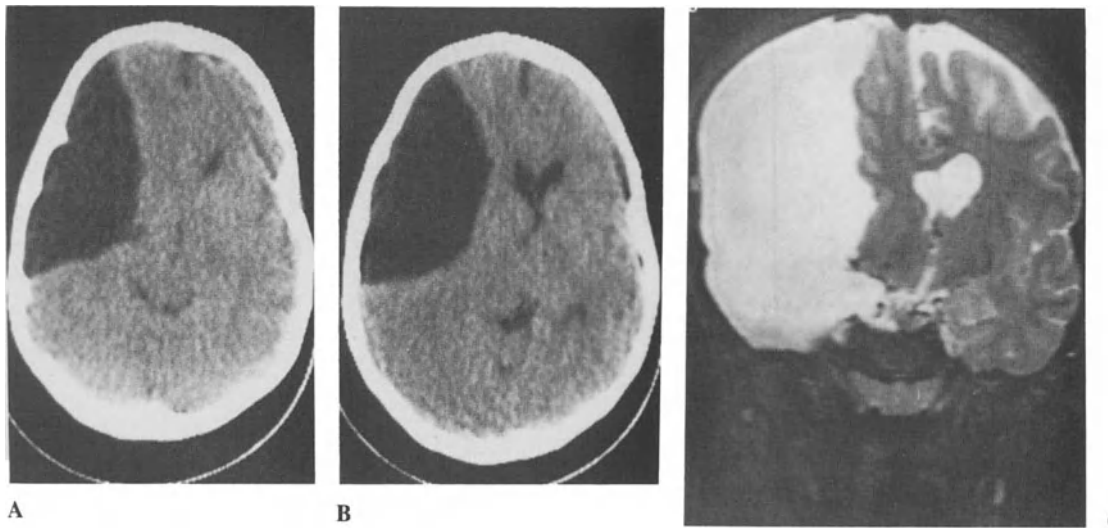


Figure 4.9. Axial CT scans (A and B) and coronal T2-weighted image (C) of a huge type 3 middle fossa cyst show the severe dimensions with striking cerebral compression and ventricular displacement.

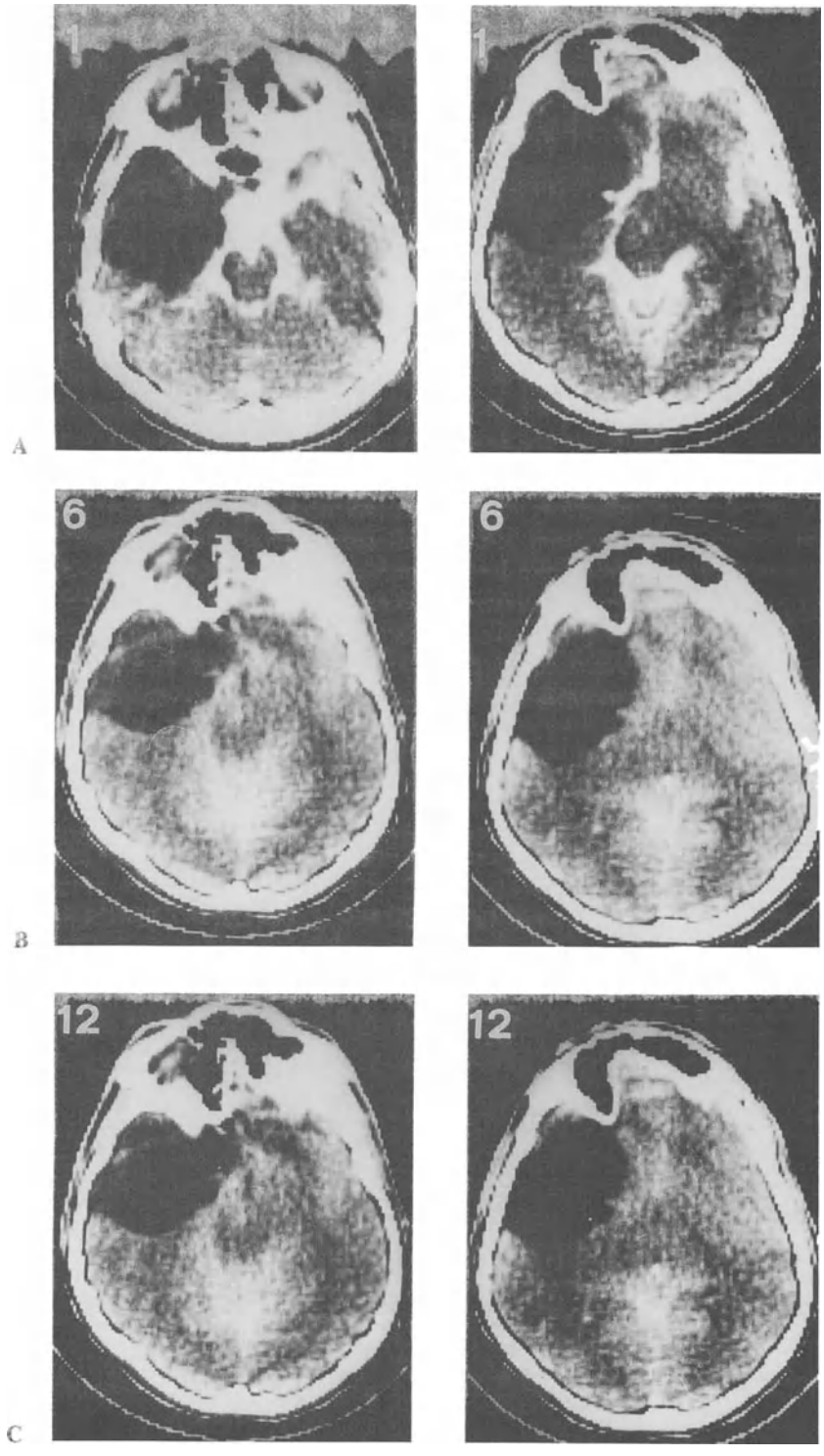


Figure 4.10. Metrizamide CT cisternograms at 1 (A), 6 (B), and 12 (C) hours of a noncommunicating type 3 middle fossa cyst. The intracystic content remains lucent at sequential controls documenting the absence of a functional communication with the subarachnoid spaces.

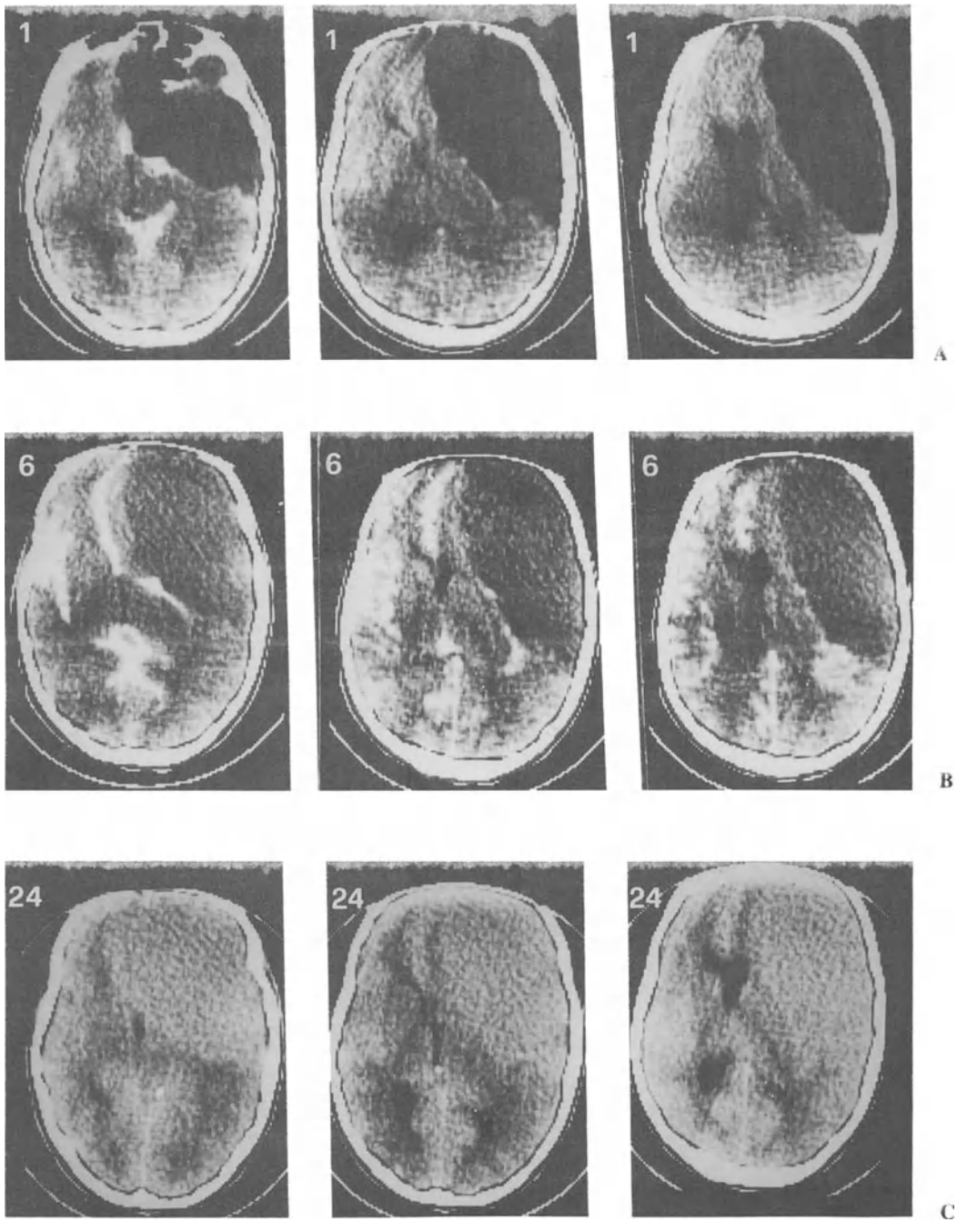


Figure 4.11. Metrizamide CT cisternograms at 1 (A), 6 (B), and 24 (C) hours of a large type 3 middle fossa cyst. No staining of the lesion is detected at the early (1 hour) cisternogram, but slow and progressive contamination occurs later. The peak of intracystic contrast concentration is reached at very delayed control (24 hours), conceivably implying a different mechanism of internal access.

membrane processes.[5,35,70,84] From these data there is reason to assume that the gradual narrowing of the connection with the subarachnoid cisterns is of critical importance from the pathophysiological standpoint and that its occlusion may lead to intraluminal fluid accumulation under pressure, due to active secretion or ball-valve trapping, and ultimately to the expansion of the cystic cavity.

Operative findings lend further support to this view, frequently showing the deeper floor of the largest malformations to be occluded, toward the base of the brain, by a thick arachnoid membrane, preventing any effective communication with the main basal cisterns[4,69] (Figure 4.12). CT cisternography using water-soluble iodinated contrast was performed in 10 out of our 95 cases of middle fossa cysts (two type 1, three type 2, and five type 3 cysts) without finding any significant objection to the above-described rule.

Four infratentorial cysts underwent dynamic evaluation of the fluid kinetics by means of CT cisternography in our series: two of them proved to be noncommunicating (Figure 4.13) and two communicating. It is worth noticing, however, that even in the communicating forms persistence of intense staining of the cyst, compared to the remaining subarachnoid spaces, at the late cisternograms suggested a stasis and delayed drainage of the intracystic CSF.[1]

A noteworthy, although uncommon, cause for acute cyst expansion is the development of concurrent intracystic hemorrhages; such an occurrence was encountered in three out of our 95 cases of middle fossa malformations and readily produced dramatic increases in intracranial pressure and sudden neurological deterioration (Figure 4.14). The peculiar proneness of sylvian cysts to develop intracystic and, particularly, subdural hematomas has been widely recognized* and conceivably attributed to the disruption of tenuously supported bridging vessels frequently coursing inside the cavity or along the outer dome of the cyst or of bridging cerebromeningeal veins crossing the neighboring subdural space[3,4,27,29,49,54,85,87] (Figure 4.15). Transmission of abnormal stretching and tearing stresses to these vascular structures in response to head traumas of varying degree, and often of trivial intensity, would be enhanced by the cranioencephalic disproportion, turbulent fluid movements within communicating cysts, or the lack of deformability of non-communicating lesions.[49,85,87]

Therapeutic Implications of Altered CSF Dynamics

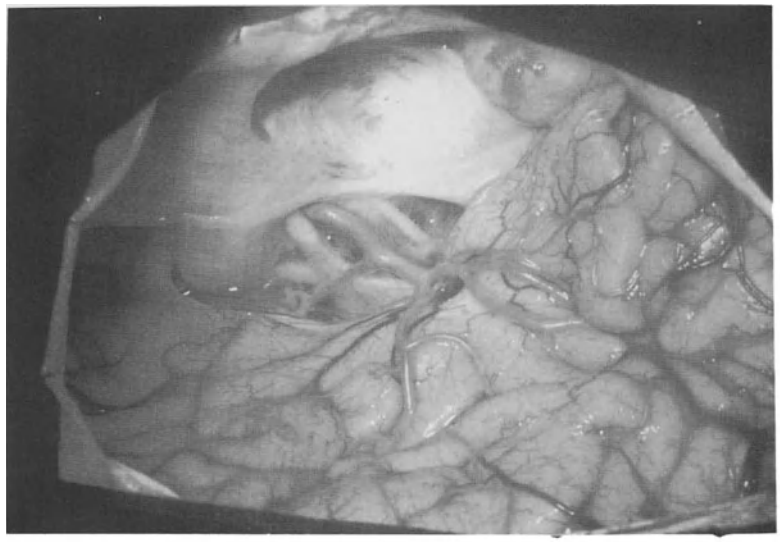
Treatment of intracranial arachnoid cysts remains a debated and problematic topic in the current neurosurgical literature; controversy mainly concerns the indication for surgery in asymptomatic cases and the choice of the optimal surgical method. As for the latter issue, two fundamental operative procedures have been traditionally adopted and variously recommended: (a) craniotomy, direct cyst excision, and fenestration of the cavity into the basal subarachnoid pathways; and (b) cyst-peritoneal shunting alone or in combination with ventriculoperitoneal CSF diversion in cases of complicating hydrocephalus.†

Even though this particular topic will be addressed in detail in later chapters, we feel it

*Refs. 3, 4, 6, 9, 16, 21, 28, 37, 49–52, 54, 55, 62, 67, 85, 86.

†Refs. 1, 3–8, 21, 28, 33, 38, 46, 48, 50, 52, 60, 67, 69, 71, 72, 74, 88.

Figure 4.12. Operative view, of a large noncommunicating type 3 middle fossa cyst. (A) The large pathologic cavity after excision of the outer cyst wall; there is impressive compression of the brain and wide exposure of the temporal fossa and tentorium. (B) At magnification, the inner floor of the cyst, adjacent to the tentorial edge and toward the basal neural and vascular structures, is occluded by semiopaque, thicker arachnoid, which is perforated (C) into the basal cisterns at surgery. The optic nerves and chiasm, the internal carotid artery, and the middle cerebral artery are well identifiable.



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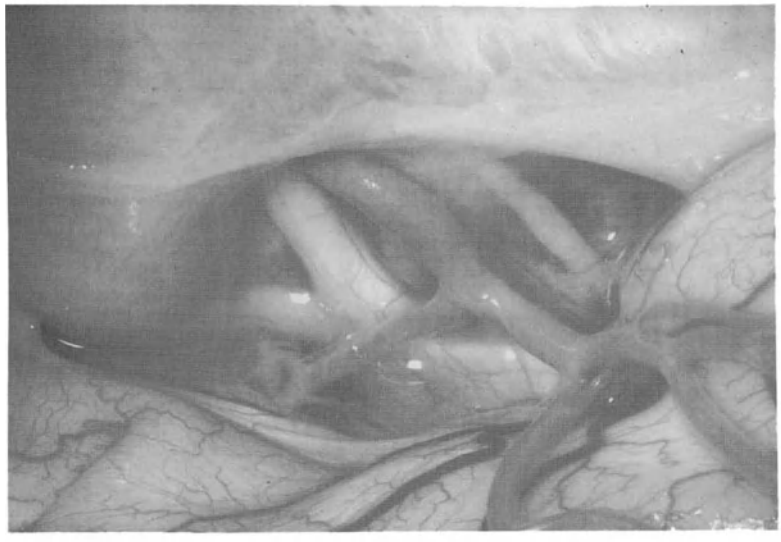

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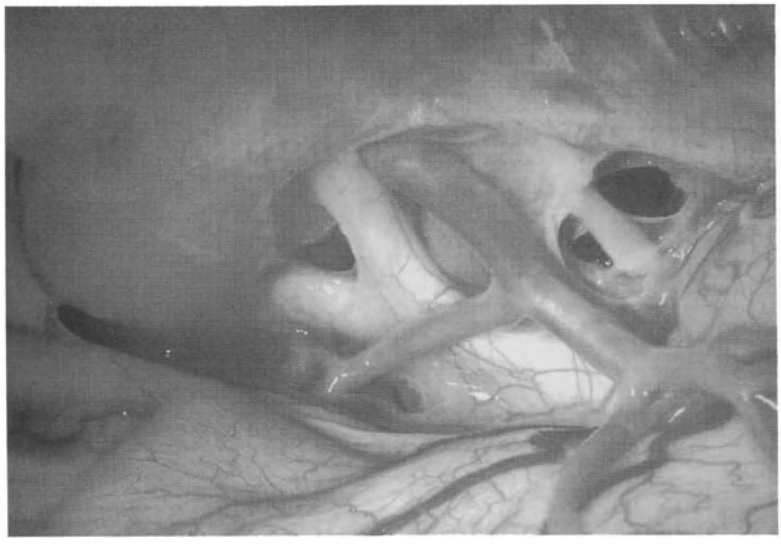

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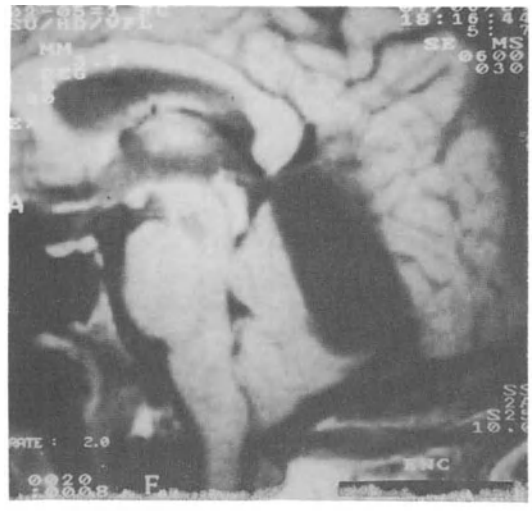

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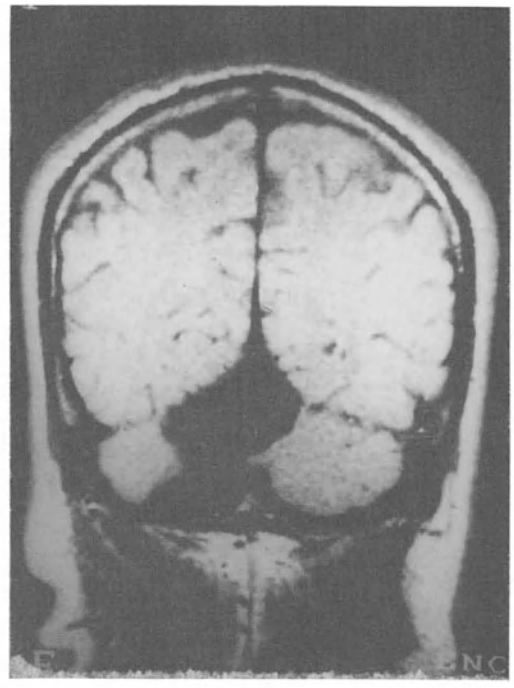

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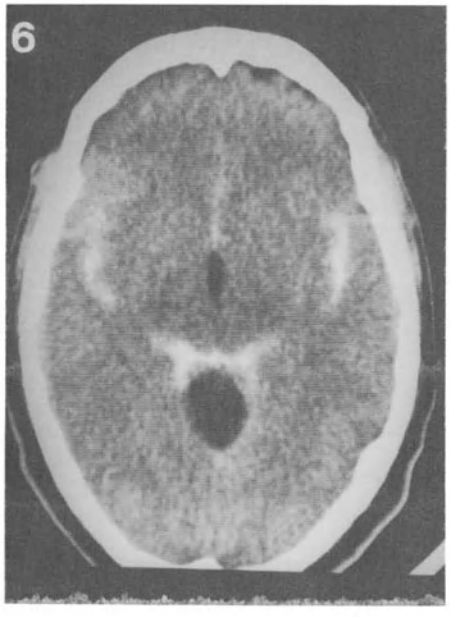

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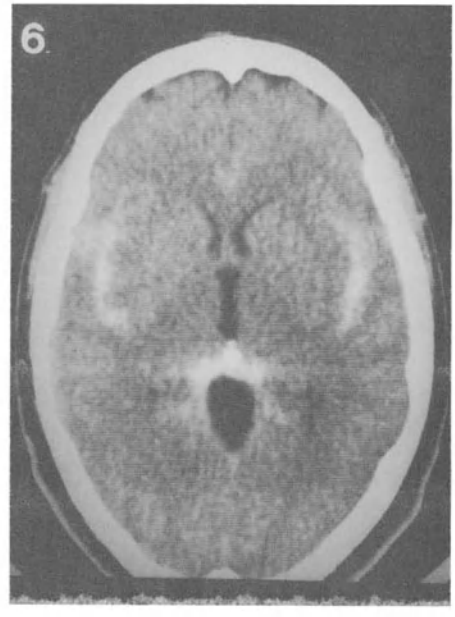


D

Figure 4.13. Supracerebellar and incisural arachnoid cyst at sagittal and coronal T1-weighted MR images (A and B). Water-soluble CT cisternograms at 6 hours (C and D) document no contrast injection with absence of an adequate connection with the subarachnoid spaces.

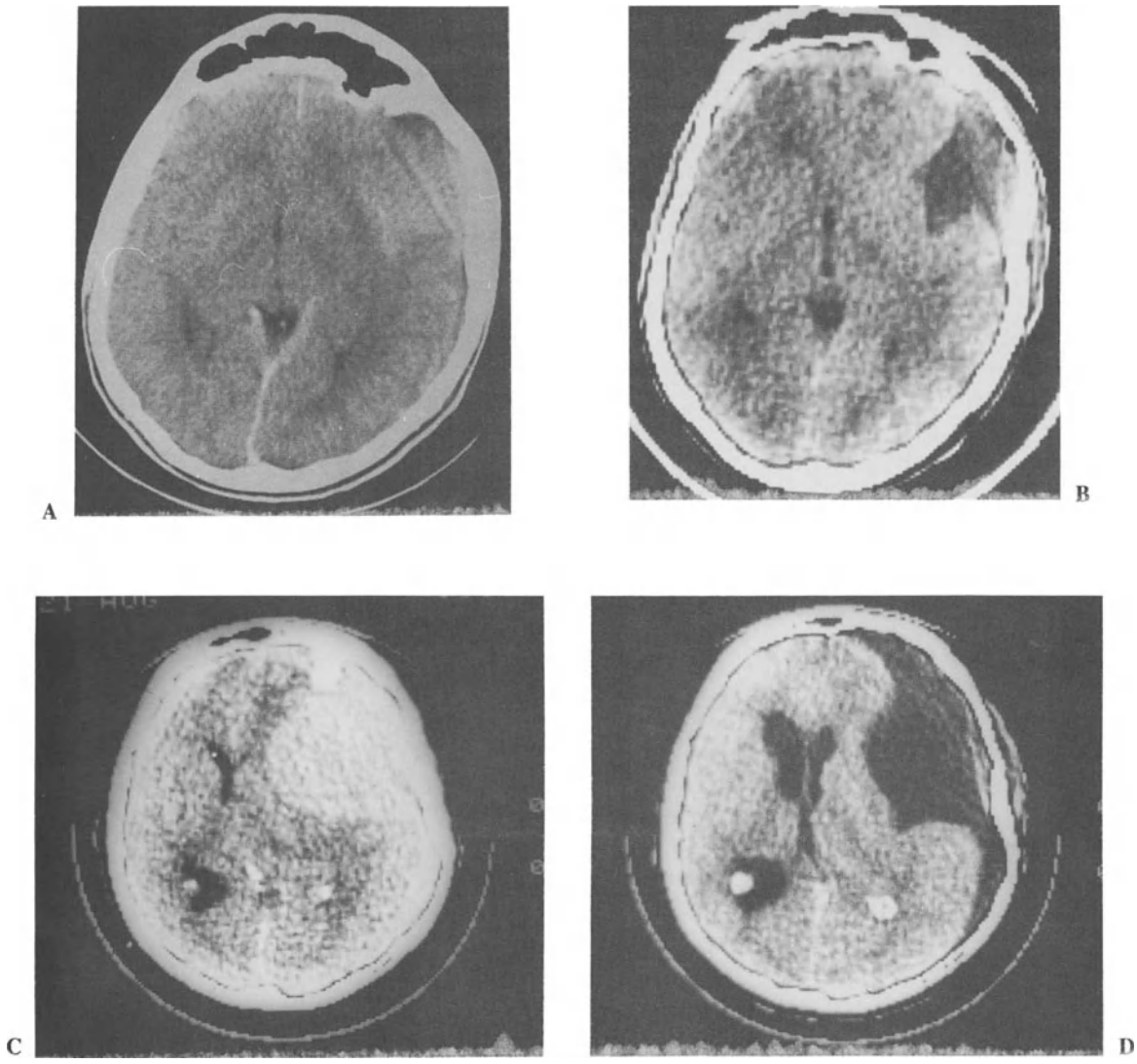


Figure 4.14. Two cases of middle fossa cysts, (A and B) and (C and D), complicated by intracystic and subdural bleedings. At preoperative CT scans (A and C) the hyperdense hematomas mask the presence of the CSF collection. At early postoperative CT scans (B and D) the evacuation of the bloody content discloses the appearance of the fluid-filled cavity.

is appropriate to underscore here the critical value of pathophysiological information in the management of these lesions, since a better understanding of the altered CSF dynamics related to arachnoid malformations can positively guide the selection of the ideal treatment modality. Indeed, if the most likely pathogenetic mechanisms (secretion by the lining walls and ball-valve internal trapping of the CSF) are taken into account, the direct approach, when feasible, would theoretically seem the most realistic and curative therapy, since it allows extensive removal of the secreting membranes and establishment of a wide fenestration into the basal and adsorbable CSF pathways. The demonstration of a com-

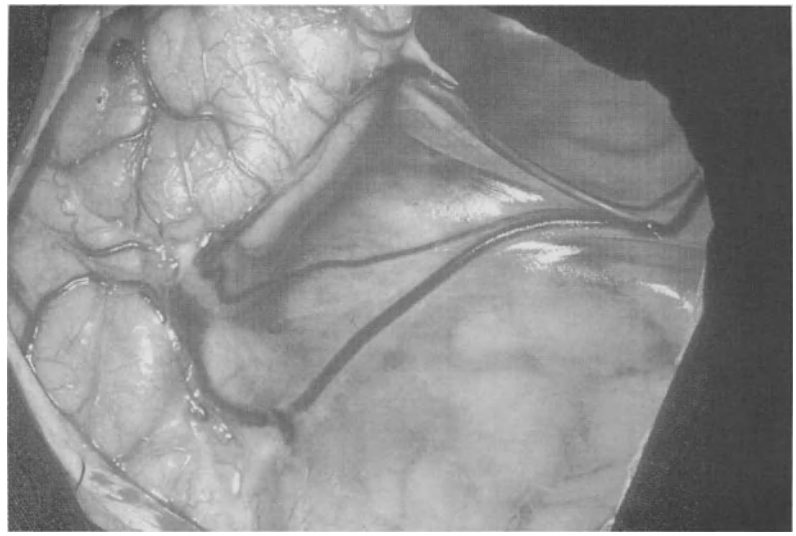


Figure 4.15. Operative view showing multiple bridging veins coursing along the dome of a sylvian cyst. These vessels are the most likely cause of complicating bleeding.

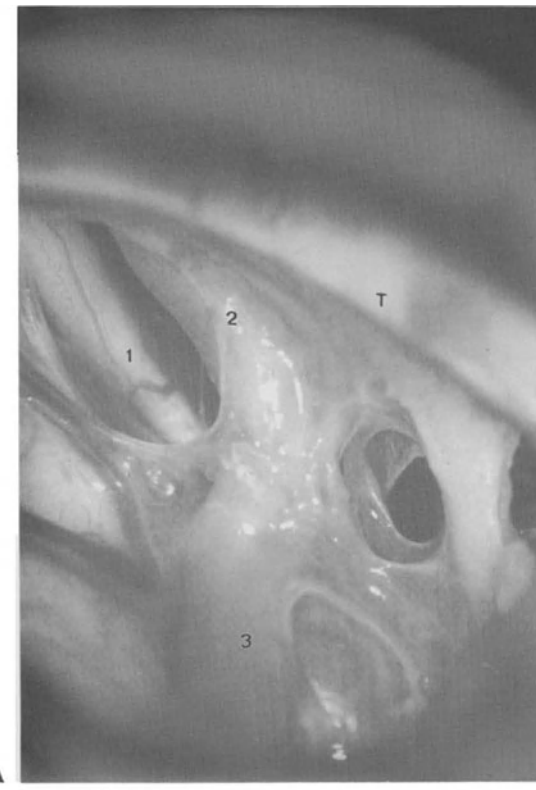
munication with the subarachnoid spaces at neuroradiological workup does not preclude the indication for this radical approach in symptomatic cases. In fact, as revealed by intraoperative observations, a small anatomical communication may be considerably enlarged at surgery in order to prevent its closure or a valvular mechanism[1,5,6] (Figure 4.16).

With respect to middle fossa lesions, the efficacy of the direct, open attack has been confirmed by our experience as judged by the high rate (72.5%) of marked reduction in size or even total collapse of the cysts on postoperative CT scans (Figures 4.17 and 4.18) and from the satisfactory alleviation of symptoms achieved in a sizable proportion of cases.[6] This more common and favorable category of arachnoid cysts is characterized by only a local alteration of fluid kinetics, limited to the cavity itself and immediate periphery, which can be permanently normalized by radical excision and fenestration, making unnecessary any indefinite shunt-dependency with its related risks.[6]

Conversely, other kinds of intracranial arachnoid cysts, namely infratentorial, suprasellar, and quadrigeminal locations, may eventually cause a more complex impairment of the CSF circulation due to a permanent obstruction of the intra-axial or extraventricular pathways or to a defect of the fluid absorption mechanisms rostral to the cyst[1,9,28,34,35,38,57] easily leading to associated hydrocephalus.

In such circumstances, a fenestration into occluded and incompetent subarachnoid spaces would be reasonably useless[60] and the direct approach may yield unsuccessful results, whereas serious consideration should be given to extrathecal shunting as the initially advisable surgical option. Based on these considerations CSF diversions to the peritoneum have become increasingly adopted and recommended in the management of cysts associated with hydrocephalus and located in the suprasellar and infratentorial areas.[28,38,46,71,72]

Nevertheless, we feel that the presence of concurrent hydrocephalus and the location of the cyst per se do not simply represent determinant criteria that can always reliably identify which cysts should undergo craniotomy and which should preferably receive the insertion of a shunt. In a previous study on infratentorial arachnoid cysts,[1] we laid stress on the importance of the direct mechanical influence exerted by the cyst itself in the pathogenesis of associated obstructive hy-



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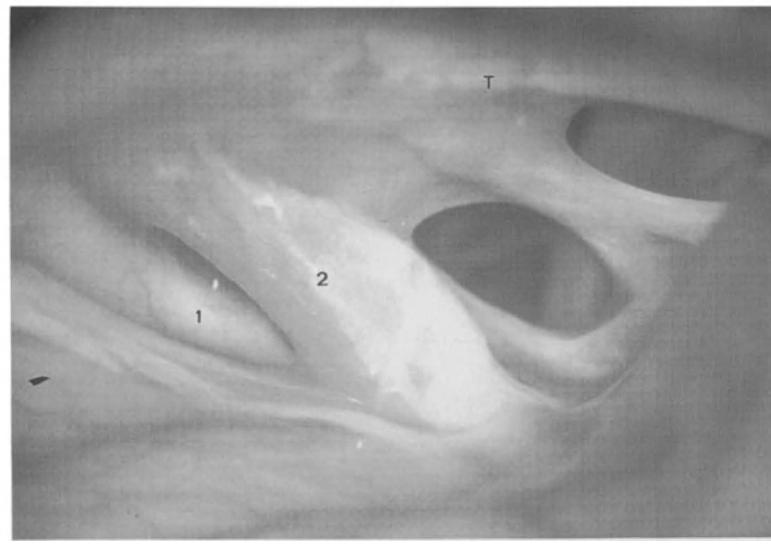

B

Figure 4.16. Perforation of the inner arachnoid lining into the basal cisterns is accomplished with the aid of the surgical microscope in order to establish or enlarge a patent communication with the subarachnoid pathways; operative view in two different cases (A and B). 1, optic nerve; 2, internal carotid artery; 3, middle cerebral artery; T, tentorial edge.

drocephalus. This contention was substantiated by the constant correlation between the presence, or absence, of hydrocephalus and the eventual existence of a cisternoventricular block as revealed either by lumbar encephalography or ventriculography.[1] These data would seem to underscore the direct obstructive effects played by posterior fossa arachnoid cysts; compression and distortion of the aqueduct, fourth ventricle, and basal cisterns,

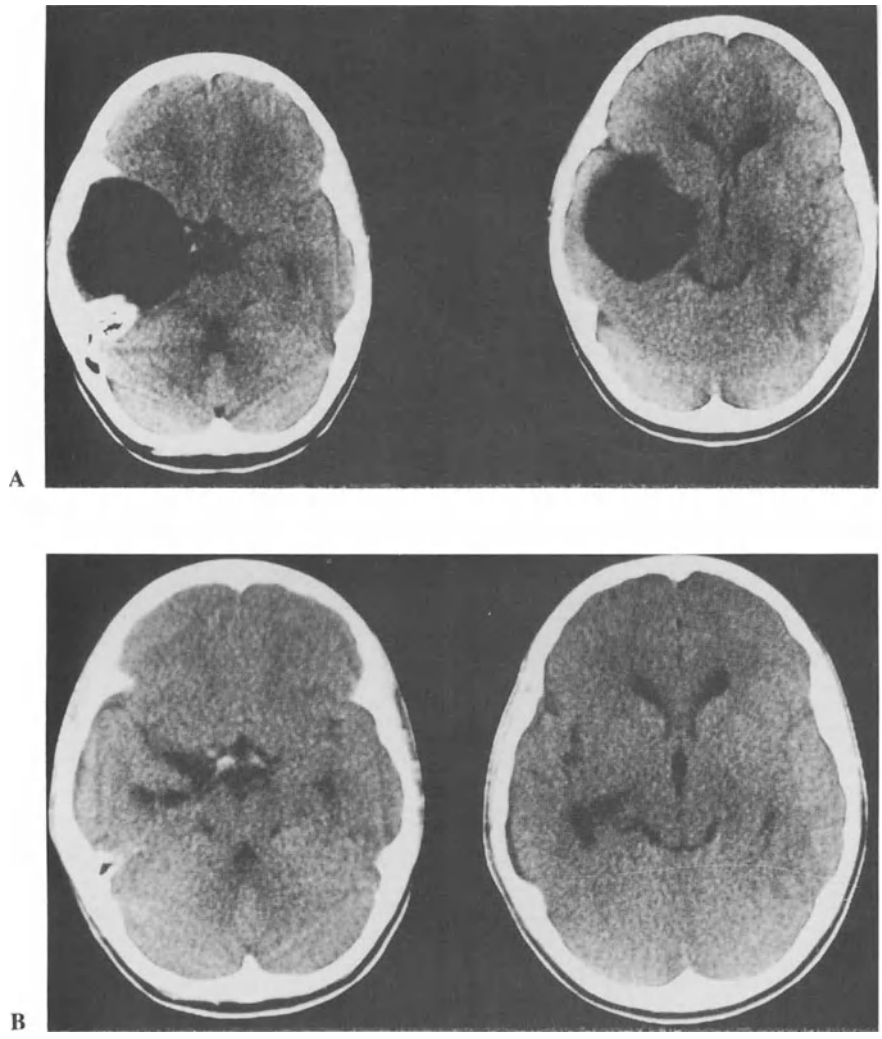

Figure 4.17. Axial preoperative CT scans of large middle fossa cyst (A). Follow-up CT control (B) shows postsurgical obliteration of the cyst, confirming the efficacy of direct excision and fenestration procedures.

and occlusion of the outlet foramina by cyst membranes are the most likely factors in this regard.[1]

In accordance with this view, the direct attack with resection and fenestration of the cyst proved beneficial in our infratentorial series, affording complete clinical remission in the majority of the cases; reduction in cyst size was achieved in 10 of the 12 cases that were submitted to follow-up postoperative CT controls (Figure 4.19). In no case was a subsequent insertion of a CSF shunt needed for progressing hydrocephalus.

It seems therefore appropriate to conclude that the removal and the fenestration of an infratentorial arachnoid cyst causing the block deal directly with the pathogenetic mechanisms of eventually associated obstructive hydrocephalus and can provide the chance to permanently restore an adequate CSF circulation and to achieve the ideal goal of leaving a shunt-independent patient.

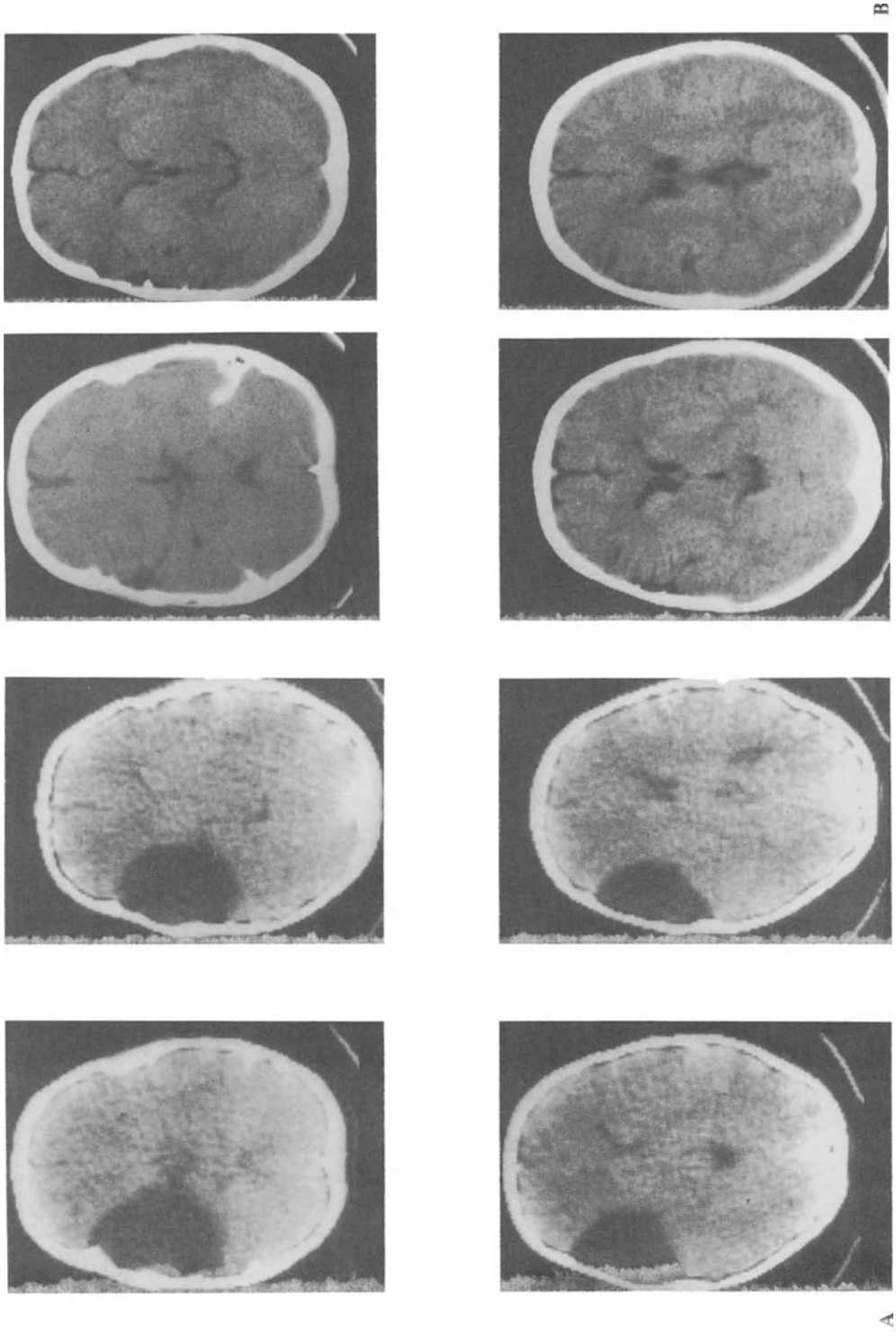

Figure 4.18. Axial preoperative CT scans of a type 3 middle fossa cyst (A). Postoperative CT scans after radical cyst resection and fenestration into the basal cisterns (B) reveal total collapse of the CSF cavity and regression of mass effects.

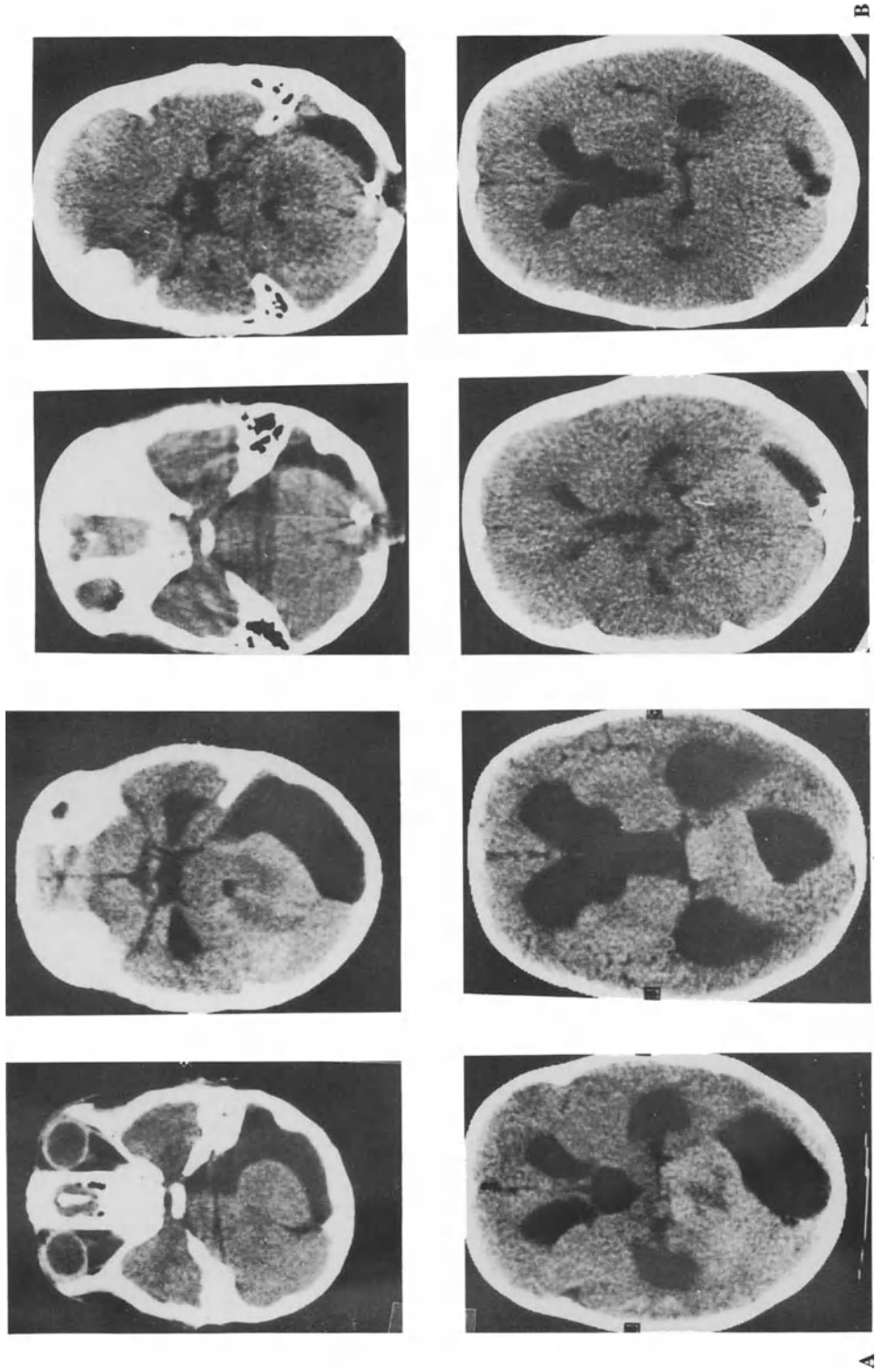

Figure 4.19. Axial CT scans of a large infratentorial arachnoid cyst associated with marked obstructive hydrocephalus (A). At follow-up CT control, after direct approach, removal of the cyst membranes, and fenestration procedure, a steady decrease in size of the cyst and satisfactory regression of hydrocephalus have been achieved (B).

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CHAPTER 5

Pathogenesis of Arachnoid Cysts in Relation to the Mechanism of Cerebrospinal Fluid Absorption

K. G. Go

Introduction and Definitions

The history of our evolving knowledge of arachnoid cysts illustrates the misconceptions that have existed about their nature and pathogenesis. In the past, arachnoid cysts were confused with pockets of the true subarachnoid space, which have been sequestered by arachnoid adhesions following trauma or infection, and which are presently known as leptomeningeal cysts or false arachnoid cysts.[1] It may presumably explain the persisting belief in the existence of arachnoid cysts that originate from trauma. Contrary to arachnoid cysts, these leptomeningeal cysts are readily accessible from the subarachnoid space, as demonstrated by radioisotope cisternography studies.[2] Moreover, leptomeningeal cysts have shown a smooth wall surface when viewed by scanning electron microscopy,[3] whereas the walls of arachnoid cysts tend to show fenestrations and microvilli of diverse shapes (Figure 5.1).

Another misconception that tended to persist until recent times is the interpretation that sylvian arachnoid cysts are secondary to agenesis of the temporal lobe.[4–6] Although preferential, the sylvian location is, however, only one of the possible locations of arachnoid cysts. Others include the cerebral convexity with transitions to the sylvian location, the suprasellar location, and the quadrigeminal with transitions to the posterior fossa location (Figure 5.2). Also, the reported normal weight of the brain on autopsies of cases of arachnoid cysts[7,8] argues against the relevance of a primary developmental defect of the brain such as agenesis.

Pathophysiological Considerations on Maintenance of Cyst Volume

In contrast to cysts associated with brain tumors, arachnoid cysts contain a fluid that is indistinguishable from cerebrospinal fluid (CSF). Notable is its low protein content, like that of CSF. This might indicate that the cyst fluid is in extensive communication with the CSF spaces or with the extracellular fluid of brain tissue. It is well known that cavities in the brain parenchyma, like those resulting from surgical resections, tend to collapse and eventually obliterate in due time, with the fluid within the cavity being resolved as a consequence of reabsorption and drainage of the fluid to the CSF spaces, in accordance with the mechanisms for the resolution of brain edema fluid. Cyst cavities can only persist when they are lined with a cell layer that resists fusion of the cavity walls following collapse. Alternatively, cyst cavities may persist when the fluid withstands reabsorption, e.g., on account of a high protein content, or when by some mechanism the fluid is replenished. A high protein content may counteract reabsorption of fluid on account of the Starling fluid flux equation:

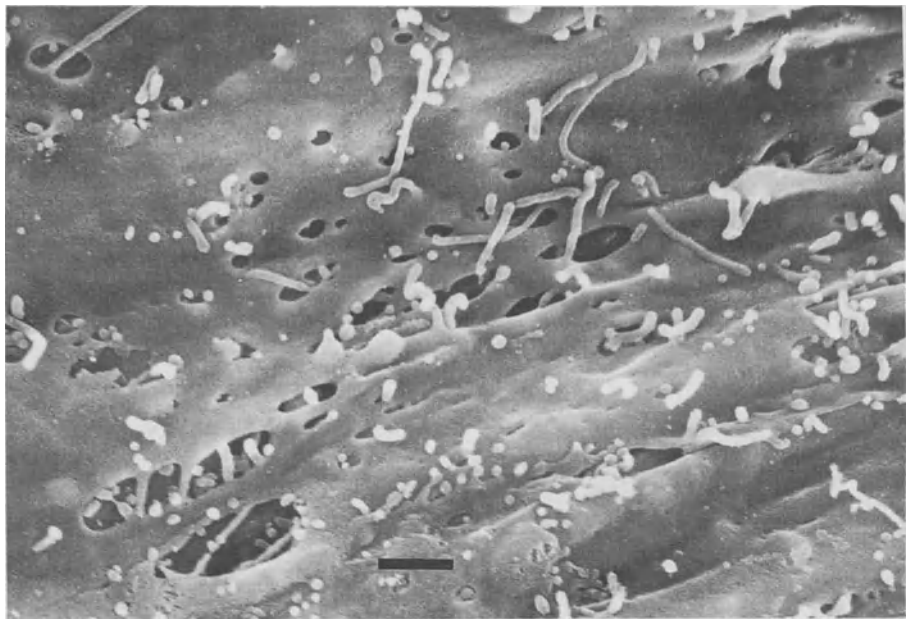

Figure 5.1. Scanning electron-microscopic view of the luminal surface of arachnoid cyst wall, showing microvilli of 1 to 2 μm in length, next to fenestrations of 0.1 to 1 μm in diameter. Bar = 1 μm.

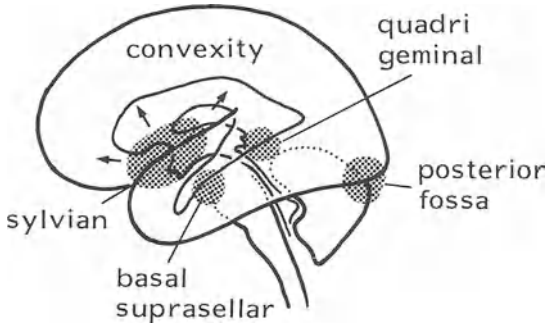

Figure 5.2. Intracranial locations of arachnoid cysts.

$$J_v = L_p(\Delta P - \sigma\Delta\pi)$$
$$\Delta P = P_a - P_{if}$$
$$\Delta\pi = \pi_{if} - \pi_{pl}$$

in which J_v is the net amount of fluid moving in or out of the capillary; L_p is the so-called hydraulic conductivity of the capillary wall for the movement of fluid; ΔP is the hydrostatic pressure gradient, i.e., the difference between intracapillary blood pressure (P_a) forcing the fluid out, and tissue pressure (P_{if}) favoring fluid absorption into the capillary; σ is Staverman's reflection coefficient of the capillary wall for protein, denoting the amount of protein leakage across the capillary wall that reduces the effect of $\Delta\pi$, which is the colloid-osmotic pressure gradient, i.e., the difference between the colloid-osmotic pressure exerted by the plasma proteins (π_{pl}) favoring fluid absorption, and that exerted by the protein present in the interstitial space (π_{if}).[9] Thus, reabsorption is retarded when the fluid is rich in proteins (exerting an increased π_{if}), as in the case of brain tumor–associated cysts or vasogenic brain edema. With the low protein content of normal extracellular fluid or arachnoid cyst fluid, the colloid-osmotic pressure of the plasma proteins prevail and the interstitial (or cyst) fluid tends to be reabsorbed.

Arachnoid cysts belong to the variety of cysts that contain little protein but that may resist obliteration and fusion of the cyst walls

on account of their possession of a special cell lining. The similarity of the arachnoid cyst fluid to CSF might also suggest communication of the cyst cavity with the subarachnoid space. However, many observations have refuted this contention.[7] During surgical explorations one may entirely empty arachnoid cysts and observe that no fluid is flowing in from adjacent subarachnoid spaces that are separated from the cyst cavity by the translucent cyst walls. According to early studies, air or dyes that had been introduced into the cyst, did not enter the CSF spaces.[10]

Radioisotope cisternography and computed tomography (CT) cisternography using intrathecal contrast agents clearly demonstrate retarded filling of arachnoid cysts from adjacent subarachnoid spaces.[11] Moreover, sequential studies using the latter technique, with measurements of contrast density in the cyst and the surrounding subarachnoid spaces, have facilitated distinguishing slowly filling from rapidly filling cysts. In the slowly filling cysts, which initially showed no contrast enhancement at all upon the lumbar injection of contrast, density progressively increased until at 24 hours a maximum was reached. The rapidly filling category showed immediate entrance of contrast agent into the cyst, although to a lesser extent than into the surrounding subarachnoid spaces, while the contrast density further increased until a maximum at 6 hours, whereupon it showed a decrease that paralleled that of the surrounding subarachnoid spaces. Clinically, the slowly filling types behaved like expanding lesions and corresponded to symptomatic cases that improved upon surgery, whereas the fast-filling category was found by chance and occasionally showed no improvement upon treatment[12] The fast-filling types probably represented arachnoid cysts, which showed minute perforations of their walls as a result of pressure-induced atrophy and therefore already possessed rudiments of outlets that otherwise should be provided by surgery. Arachnoid cysts in the posterior fossa which in the literature have been reported to exhibit communication with the ventricular system, presumably represent confusion with the Dandy–Walker malformation.[13]

The Significance of Arachnoid Cysts with Regard to the Pressure/Volume Relationship

The segregation of the arachnoid cyst cavity from surrounding CSF spaces may even be considered as the justification for surgical intervention, as the segregation prevents the cyst from emptying its contents when it is compressed by surrounding brain structures upon movement of the head. Thus, the cyst content does not behave as a displaceable volume of fluid that easily shifts to and fro into the CSF spaces upon movement or postural changes, but constitutes an incompressible mass that may exert pressure upon the adjacent brain during decelerations or accelerations of the head. Moreover, in terms of pressure/volume relationships, an incompressible arachnoid cyst may be considered to cause a reduction of craniospinal compliance, although it per se does not have to raise intracranial pressure. To remedy the condition, it would suffice to establish communications to the surrounding subarachnoid spaces or basal cisterns by perforating the enclosing membranes. Although large cysts will conceivably not completely collapse on account of the ex vacuo situation, in which the missing brain tissue finds no replacement, the created outlets to the CSF spaces will turn the lesion from an incompressible mass to a displaceable volume of fluid.

Evidence of intracranial pressure elevation is an obvious indication for surgical intervention. Causes may be obstruction of CSF pathways, in particular with the suprasellar and quadrigeminal locations,[14–19] hemorrhage within the cyst occasionally developing into subdural hematomas,[20,21] and enlargement of the cyst. The advent of noninvasive imaging such as CT and MRI scanning have documented enlargement, but also shrinking of arachnoid cysts during their evolution.[22]

Mechanisms of Formation of Arachnoid Cysts

Expansion of the cyst, indentation, and displacement of adjoining (developing) brain structures, or at least the failure of the cyst to collapse, all point to the existence of a mechanism that maintains or increases its fluid volume. It has been proposed by Starkman et al.[7] that at an early stage in its development there may be an open communication with the subarachnoid space, allowing inflow of fluid, whereas sequestration may follow at a later stage by closure of the opening. This mechanism would, however, not explain long-term maintenance or expansion of fluid volume.

Valvular mechanisms have also been suggested, e.g., by way of a single small opening serving both as an entrance and an exit for fluid,[23] presumably with the CSF pulse pressure being the driving force. It is, however, difficult to envision how the CSF pulse pressure can act as a driving force and achieve fluid accumulation when the latter may cause an elevated intracranial pressure that exceeds the driving force.

Finally, there is the possibility of secretion of fluid by the cyst walls, which may occur by a mechanism similar to that of CSF absorption, as has been considered by Krawchenko and Collins[24] in a significant analysis of conceivable mechanisms.

Similarity to Mechanism of CSF Absorption

By virtue of several characteristics (Figure 5.3), such as the possession of desmosomal junctions, tonofilaments in their cytoplasm (of the type of vimentin-positive intermediate filaments,[25] interdigitating cytoplasmic pro-

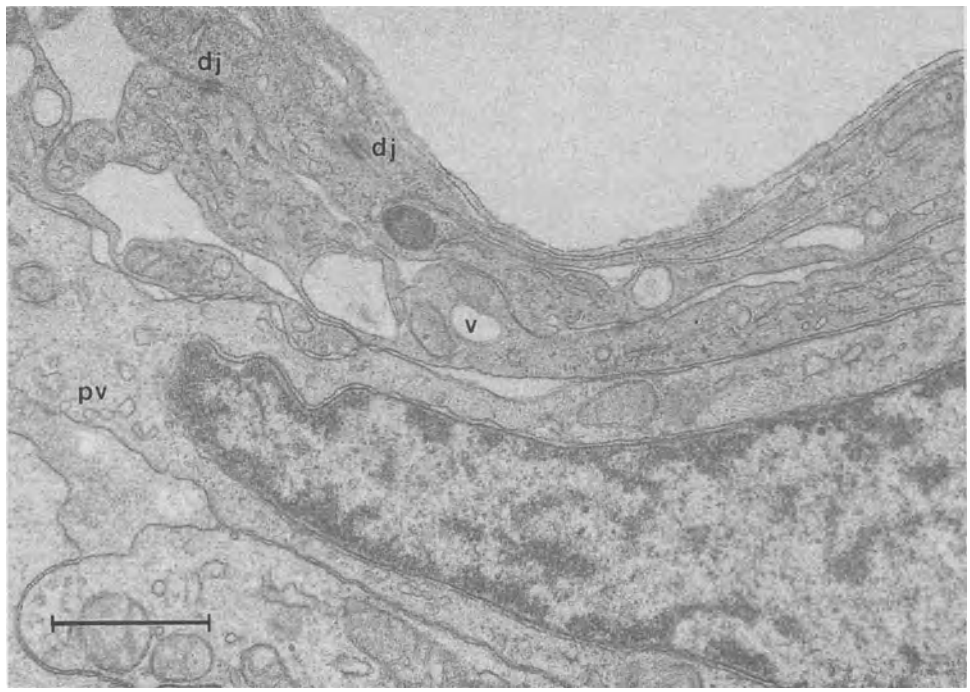

Figure 5.3. Transmission electron micrograph of the luminal lining of same arachnoid cyst as in Figure 5.1, showing the cellular elements with their interdigitating processes, separated by tortuous and locally dilated intercellular clefts. The cytoplasm contains vacuoles (v), pinocytotic vesicles (pv), and tonofilaments abutting the desmosomal junctions (dj). Bar = 1 μm.

cesses, large cytoplasmic vacuoles and pinocytotic vesicles. and an underlying basal lamina,[26] it has been recognized that the cells lining arachnoid cysts morphologically resemble those of the outer layer of the arachnoid mater bordering the dura, designated as the subdural neurothelium.[27,28]

Furthermore, subdural neurothelium has been observed as constituents of arachnoid villi and granulations. Arachnoid villi are small, macroscopically hardly visible mushroom-like protrusions of the arachnoid mater into the dura, which abut dural or subdural veins, whereas arachnoid granulations are macroscopically visible protrusions of the arachnoid mater through the dura, which essentially are similar in structure to the villi but exhibit a more complex cauliflower-like surface and usually abut dural sinuses. Both have a core of spongious arachnoid mesothelium containing CSF, which in fact is a protrusion of the subarachnoid space. The core is surrounded by a layer of subdural neurothelium, which is to be regarded as a continuation of the subdural neurothelial layer in the arachnoid mater bordering the dura.[29,30] The outermost layer covering the villus and granulation is an endothelial layer that is continuous with the endothelium of the vessel upon which the villus abuts, but which has been observed to show morphological similarities to the underlying arachnoid layers.[25,31,32] It contains vacuoles, which are envisaged as being formed from invaginations of the abluminal plasma membrane of the cells (i.e., the side facing the villous core). After traversing the cytoplasm of the cell they evacuate into the vessel lumen, thus constituting a dynamic fluid transporting chain of vacuoles.[31–33] In the arachnoid villus, which exhibits a continuous endothelial layer,[29,34,35] it may be the mechanism underlying CSF absorption. Arachnoid granulations, however, have been reported to contain tubules lined by endothelium, constituting open (static) channels from the CSF space in the core of the granulation to the vessel lumen.[36–38] Small animals seem to possess arachnoid villi only, whereas larger mammals, such as humans, possess both villi and granulations.

Next to the aforementioned mechanisms of CSF transport at the arachnoid villus, there is the possibility of a mechanism of fluid secretion that is based upon Na^+K^+-ATPase. Na^+K^+-ATPase, which is also called transport ATPase, is implicated in the transport of sodium as the basis of fluid transport. Using the K-NPPase reaction (a reaction that is based upon the conversion of K-nitrophenylphosphate (K-NPP) by Na^+K^+-ATPase into an electron-dense reaction product that can be visualized by electron microscopy), enzyme ultracytochemistry has shown the presence of Na^+K^+-ATPase in the luminal plasma membrane of the cells lining arachnoid cysts (Figure 5.4) as well as those covering arachnoid granulations.[39,40]

Alleged Cellular Mechanisms Involved in Fluid Secretion by the Arachnoid Cyst Lining

In addition to the membrane Na^+K^+-ATPase, usually other mechanisms are involved in processes of fluid transport and cell volume regulation, such as ion-exchange and cotransport mechanisms in the cell membrane, although the Na^+K^+-ATPase is generally regarded as the mechanism that provides the driving force of the transport. It may thus be envisaged that in the process of fluid secretion allegedly the Na^+K^+-ATPase of the cyst wall transports Na^+ from the cell contents into the cyst lumen; the Na^+ then attracts osmotically obliged water to form the secreted fluid. The efflux of Na^+ proceeds at the expense of ATP and in exchange with K^+, in a ratio of 2 K^+ entering against 3 Na^+ leaving the cell. It results in depletion of cellular Na^+, i.e., it creates a Na^+ gradient, that can be used to supply Na^+ in exchange with H^+ by an Na^+/H^+ ion-exchange mechanism. The H^+ may be provided by the carbonic anhydrase reaction: $H_2O + CO_2 \longleftrightarrow H^+ + HCO_3^-$, in which H^+ and HCO_3^- are formed from H_2O and CO_2. The HCO_3^- concomitantly formed with H^+ may be exchanged against Cl^- by way of a Cl^-/HCO_3^- anion-exchange mecha-

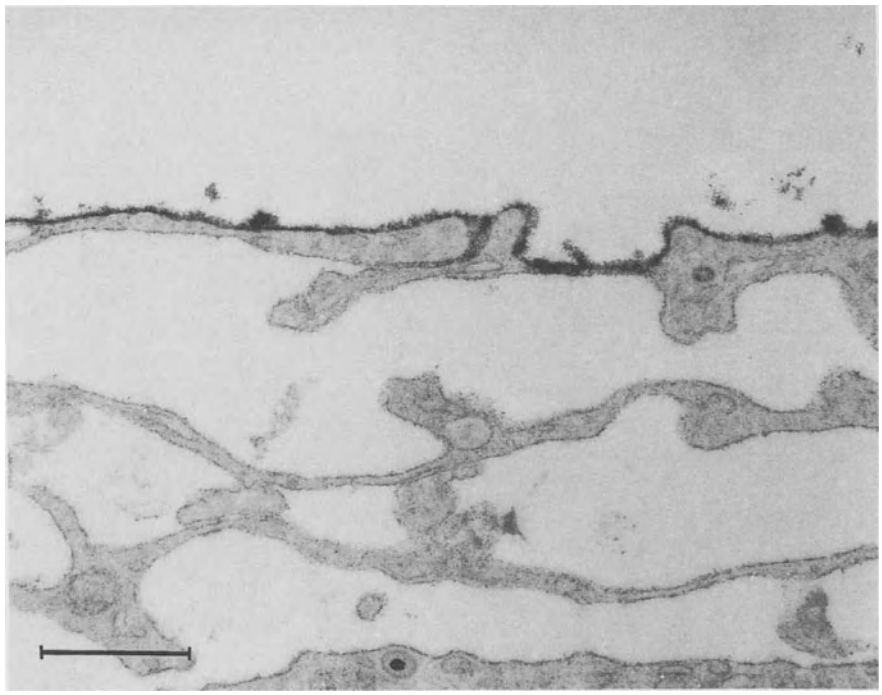

Figure 5.4. Transmission electron micrograph of the luminal lining of an arachnoid cyst, showing electron-dense reaction product of the K-NPPase reaction on the luminal plasma membrane of the lining cells; it denotes the presence of Na^+K^+ ATPase in the luminal plasma membrane. Bar = 1 μm.

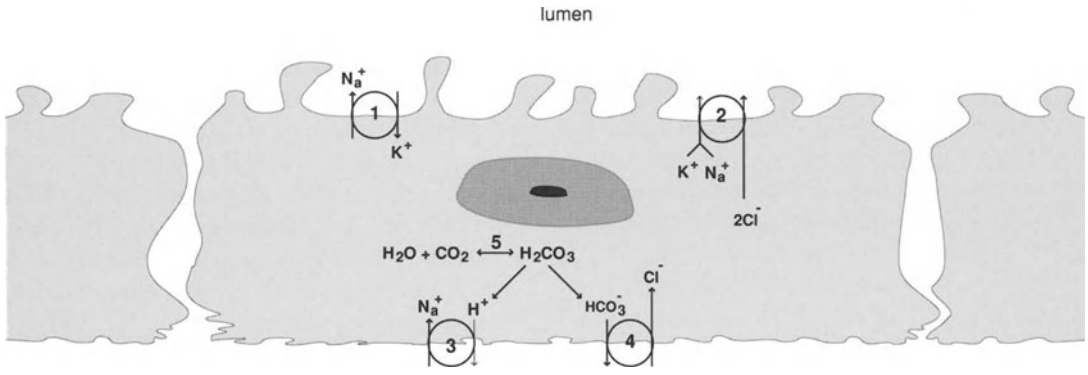

Figure 5.5. Schematic representation of the ion-transport mechanisms, which are allegedly involved in fluid secretion. 1: Na^+K^+ ATPase; 2: $K^+Na^+/2$ Cl^- cotransport mechanism; 3: Na^+/H^+ exchange mechanism; 4: Cl^-/HCC_3^- exchange mechanism; 5: carbonic anhydrase reaction.

nism. This provides Cl^- that (for the sake of electroneutrality) accompanies the Na^+ efflux, or is associated with both an Na^+ and K^+ efflux by way of an Na^+, $K^+/2\ Cl^-$ cotransport mechanism (Figure 5.5).

A biochemical mechanism of fluid secretion that is inherently independent of pressure may well account for the development of fluid accumulations that may eventually result in elevation of intracranial pressure.

In contrast to the morphological situation in arachnoid villi or granulations, in which CSF is transported from the subarachnoid space into the lumen of a venous vessel, arachnoid cysts lack the blood circulation as the drainage pathway, and therefore the transported fluid accumulates in the cyst cavity in the same way as epidermoid cysts are formed by accumulation of secretion from sequestered epithelium. The situation may arise as a developmental defect of the leptomeninges, in the sense that rudiments of arachnoid villi are developing without the establishment of a connection to draining vessels.

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CHAPTER 6

Cysts Originating from a Defect in the Hemispheric Cleavage (Cavum Septi Pellucidi, Cavum Vergae, Cavum Veli Interpositi)

Akira Yokota

Cavities formed in the interhemispheric cleavage (cavum septi pellucidi, cavum vergae, and cavum veli interpositi) develop as normal structures in the intrauterine period, and are usually developmentally obliterated during postnatal life. Remnants of these cavities are regarded as nonmalformative structures and have no clinical significance in the majority of cases. Abnormally expanded cavities that do not have free communication with the lateral ventricles or subarachnoid space are called *cysts*. The terms *symptomatic cysts* and *pathological cava* may be preferred for cavities that produce neurological symptoms by compressing the neighboring structures or cause hydrocephalus by obstructing the CSF pathways.[1] Symptomatic or pathological cysts arising from the cava septi pellucidi, vergae, and veli interpositi are considered to be very rare.[1]

Embryology

Cava arising in the telencephalic hemispheric cleavage develop in close contact with the corpus callosum and fornix. At 11 to 12 weeks of gestation, the corpus callosum originates in the commissural plate, dorsal to the hippocampal (fornical) commissura. With the dorsocaudal growth of the corpus callosum, the fornices are pushed below and to the side of the corpus callosum, and the hippocampal commissura shifts posteriorly subjacent to the posterior end of the corpus callosum. During the caudal growth of these structures, the septum pellucidum is formed to span longitudinally the corpus callosum and the columns of the fornix between the lateral ventricules.[2,3] Formation of the cavity (cavum) of the septum pellucidum has been controversial in terms of whether it is derived from necrosis within the commissural plate, which is mechanically stretched by the rapid expansion of the cerebral vesicles,[4] or whether the cavity arises as a pocket between the walls of the infolded hippocampal primordium, which is at first open to the interhemispheric fissure but is later sealed by the development of the corpus callosum.[5]

With development, the cavum septi pellucidi narrows in the caudorostral direction from its posterior end, and its posterior portion (cavum vergae) begins to disappear at about 6 months of gestation. The cavum septi pellucidi begins to close just before term.[6]

The cavum veli interpositi is also formed in relation to the development of the corpus callosum; as the corpus callosum extends posteriorly, it carries on its undersurface the roof of the diencephalon with a fold of pia mater by 18 to 20 weeks of gestation. The fold of pia mater, the superior leaf of which clings to the fornix and the inferior leaf of which follows the roof of the third ventricle, constitutes the velum interpositum or the transverse choroidal fissure (Figures 6.1 and 6.2). When the sac-like fold is open, it forms the cistern of the velum interpositum; if dilated, it is properly called the cavum veli interpositi.[7]

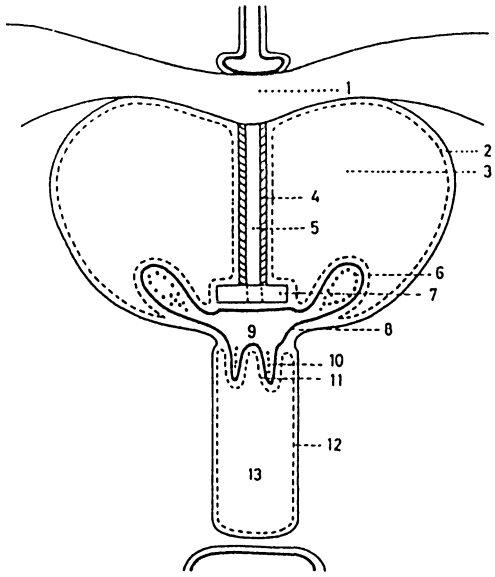


Figure 6.1. The formation of cavum veli interpositi. Coronal section behind the foramen of Monro. Cavum veli interpositi is located between the fornix above, the roof of the third ventricle below, the plexuses of the ventricles laterally. It is entirely surrounded by pia mater. 1, corpus callosum; 2, ependymal epithelium; 3, lateral ventricle; 4, wall of septum pellucidum; 5, cavum septi pellucidi; 6, choroid plexus of the lateral ventricle; 7, fornix; 8, pia mater; 9, cavum veli interpositi; 10, choroid plexus of the third ventricle; 11, tela choroidea; 12, ependymal epithelium of the third ventricle; 13, third ventricle. [Reprinted with permission from Robertson[22] and Larroche and Baudey.[6]]

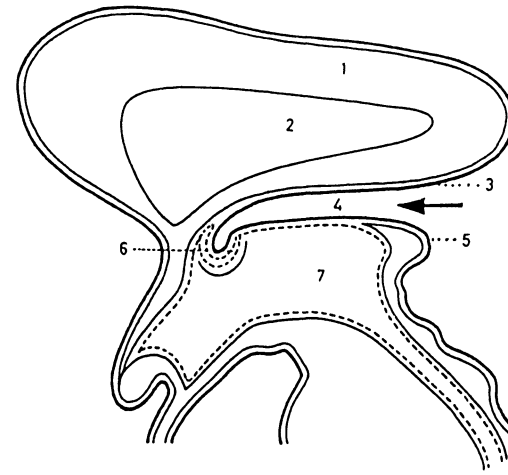


Figure 6.2. The formation of cavum veli interpositi. Median sagittal section. Cavum veli interpositi is located between the fornix above and the roof of the third ventricle below. Anteriorly, it extends to the foramen of Monro. Posteriorly, it opens in the cistern of the vein of Galen. It is lined with pia mater which is invaginated between the fornix and the roof of the third ventricle. 1, corpus callosum; 2, septum pellucidum; 3 and 5, pia mater; 4, cavum veli interpositi; 6, foramen of Monro; 7, third ventricle. [Reprinted with permission from Robertson[22] and Larroche and Baudey.[6]]

Anatomy and Incidence

Cavum Septi Pellucidi

The cavum septi pellucidi, which is formed between the two leaves of the septum pellucidum, is bounded anteriorly and superiorly by the genu and the body of the corpus callosum, respectively, and inferiorly by the columns of the fornix. Its anteroinferior portion attaches to the rostrum of the corpus callosum and the anterior commissura. The posterior portion of the cavum septi pellucidi becomes narrower as the columns of the fornix approach the corpus callosum. It comes to a point with the fusion of the fornix and corpus callosum, or it forms an isthumus, called "aqueduct septi," when the cavity extends further posteriorly to form the cavum vergae.[1,6]

The cavum septi pellucidi is essentially a closed cavity, isolated either from the ventricle or the subarachnoid space, but it often communicates with one or both lateral ventricles through small openings where the septal laminae are ruptured or perforated.[8,9] Cerebrospinal fluid (CSF) fills the cavity in a communicating cavum, but the source of fluid within the noncommunicating cavum is not known since the cells lining the inner wall of the septum pellucidum are considered to be nonsecreting.[10] The cells lining the cavity have been assumed to have the morphologic and functional characteristics of ependyma,[11] but a monolayer of flat, cylindrical, or cuboidal cells occasionally covering the glial wall of the

cavum is now regarded as having neither cilia nor blepharoblasts.[8,12]

The incidence of cavum septi pellucidi varies with age and with whether the patients are examined radiologically or by autopsy. Age-dependent prevalence of the cavum is well established; the cavum is present in all fetuses and premature neonates, but its prevalence drops sharply shortly after full-term birth.[1,6] According to Shaw and Alvord,[1] the incidence of cavum septi pellucidi is 97% at term, 85% under 2 months of age, 41% at 2 to 3 months, 15% at 3 to 6 months, and 12% at 6 months to 16 years. In autopsy studies several authors[13–15] found cavum septi pellucidi at rates exceeding 60%, but this high incidence is accounted for by the fact that these authors included small triangular clefts in the septum subjacent to the corpus callosum that were ignored by others.[1,16] Sarwar[10] considered a reasonable prevalence rate of the cavum in adults as 12% to 20%, citing the reports of Schwidde[16] and Shaw and Alvord.[1]

The incidence of cavum septi pellucidi in neuroimaging studies is less than in autopsy studies. The incidence surveyed by pneumoencephalography has been reported as 0.3% to 1.7%.[8] Recently Sarwar[10] found the computed tomography (CT) prevalence of cavum septi pellucidi to be 43.3% under 1 year of age, 5.1% at 1 to 20 years, and 1.9% in adults over 20 years. Another CT series reported an incidence of 2.2% in infants and children,[17] and 0.15% in all age groups.[18]

The decreased prevalence of cavum septi pellucidi in neuroimaging studies in comparison with autopsy studies is explained by the limited resolution of CT, which fails to reveal cava less than 3 mm in width.[10,18] Another explanation that has been given is that the media walls of the cerebral hemispheres are approximated more closely in the living due to expansion of the ventricular system than at autopsy when CSF is drained from the ventricles.[10]

Cavum Vergae

The cavum vergae originally coincides with the cavum septi pellucidi, and the two cavities usually communicate freely without any noticeable isthmic portion between them. Therefore, the cavum vergae is limited superiorly and posteriorly by the body and splenium of the corpus callosum, respectively, and laterally and inferiorly by the columns of the fornix and hippocampal commissure, respectively (Figure 6.3). The cavum vergae is almost invariably associated with the presence of the cavum septi pellucidi, and only rare instances of isolated cavum vergae in the absence of the septum pellucidum have been reported.[8]

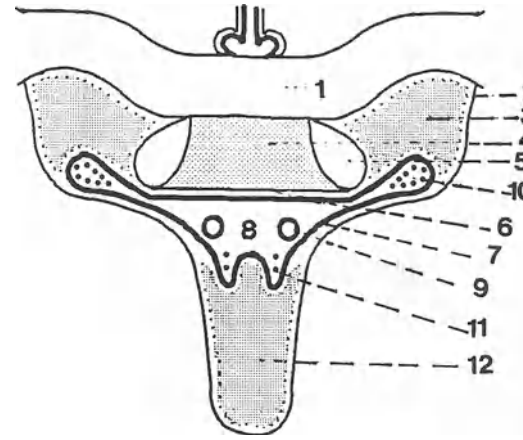


Figure 6.3. Anatomical correlation between cavum vergae and cavum veli interpositi. 1, corpus callosum; 2, ependyma; 3, lateral ventricle, 4, cavum vergae; 5, column of the fornix; 6, hippocampal commissure; 7, pia mater; 8, cavum veli interpositi; 9, internal cerebral vein; 10, choroid plexus; 11, tela choroidea; 12, third ventricle.

Cavum vergae is found in almost every fetus at the age of 6 months, but in only 30% at full term.[6] Its prevalence decreases with age after birth, as with the cavum septi pellucidi. Schwidde[1] found cavum vergae in 2.33% of 1,032 autopsied brains, and in no instance did cavum verage exist alone. Studied by CT, Sarwar[10] found 1.6% of cavum vergae concurrent with cavum septi pellucidi in 633 cases of all age. As shown in the reports cited above, cavum vergae is invariably associated with cavum septi pellucidi, and its occurrence by itself is considered exceptional.[8] However, Nakano et al.[17] found cavum vergae in 35 (3.3%) of 1,050 children examined by CT, 4

(0.4%) of which were cavum vergae alone. Among 10 pediatric cases of cavum vergae diagnosed by CT, 2 cases were unaccompanied by cavum septi pellucidi, according to Miller et al.[19] These two reports pose the question of whether the presence of cavum vergae alone is actually as exceptional as has been believed. Rather, 10% to 20% of cases with cavum vergae may not be associated with cavum septi pellucidi. Radiological differentiation of cavum vergae from cavum veli interpositi is difficult in horizontal cuts of conventional CT, particularly when cavum septi pellucidi, whose concurrence is said to be a hallmark in diagnosing cavum vergae, is absent. Also in the era of pneumoencephalography, Zellweger and Van Epps[20] maintained that some earlier cases of cavum veli interpositi were erroneously reported as cavum vergae. Further evidence is needed to resolve the question of whether it is possible for cavum vergae to exist alone.

Cavum Veli Interpositi

Cavum veli interpositi is the enlarged cistern of the velum interpositum, which consists of two leaves of pia mater. The velum interpositum forms the tela choroidea of the third ventricle and continues laterally to the insertion of the tela choroidea of the lateral ventricles. Therefore, the cavum is bounded superiorly by the fornix (columns and the hippocampal commissure) and inferiorly by the roof of the third ventricle. Its anterior extension is limited by the foramina of Monro, where the body of the lateral ventricles converge from posteriorly, so that the cavum forms a triangle with the apex pointing anteriorly (Figures 6.1 and 6.2).

The cavum veli interpositi is seen much more frequently in infants than in children and adults.[21,22] According to Storother and Harwood-Nash,[47] the cavum is found in 60% of children under 1 year, but in 30% of those from 1 to 10 years. Picard et al.[21] showed the incidence of the cavum as 30% in children less than 2 years and 2.75% in those over 2 years. These figures were obtained by pneumoencephalographic findings, and we see the cavum much more frequently even in adults on CT or magnetic resonance imaging (MRI) if a small cistern of the velum interpositum is included. Cavum veli interpositi is defined as enlarged cistern of the velum interpositum, but their differentiation is not clear. Apart from age-dependent prevalence, the cavum veli interpositi is also known to be much more common among those whose brain is hypoplastic, atrophic, or degenerative.[20,22,23]

Clinical Aspects of the Cava

As cava septi pellucidi, vergae, and veli interpositi develop in tissue that has no neurological function, they should remain asymptomatic unless they are transformed into cysts, which, in turn, exert pressure on neighboring structures to cause neurological signs or obstruct the CSF pathway to cause hydrocephalus. However, noncystic cava are sometimes controversial when they are associated with functional neurological abnormalities.

Bruyn,[8] reviewing cavum septi pellucidi in the German literature, found that epileptic seizures were reported in 31% to 55% of cases, and psychiatric disorders such as psychosis, dementia, and personality changes in about 15%. The association of these neurological dysfunctions with the cavum is considered principally due to a common underlying developmental aberration of the brain.[18] Nevertheless, there is a view that the impact of the cava on the anatomical relationship between the fornix, hippocampus, corpus callosum and stria terminalis may cause neuropsychiatric symptoms.[8] An alternative explanation for the associated symptoms have been suggested in relation to trauma, since head trauma is frequently observed in patient histories.[8] Repeated craniocerebral trauma exerted on susceptible midline structures is assumed to a factor in the development of cavum septi pellucidi.[24] In this connection, increased prevalence of cavum septi pellucidi is well known among boxers. According to Corsellis et al.[25] cavum septi pellucidi was found in 92% of 13 brains of ex-boxers, com-

pared with 28% of 500 brains in the control population. They considered that the detachment of the fornix from the undersurface of the corpus callosum, which was observed as septal fenestration in association with septal cavum, was responsible for the neurological symptoms relating to the septal region.[25]

Since cavum vergae coexists with cavum septi pellucidi in almost all instances, the clinical significance of the former cavity has not been discussed properly. Recently Miller et al.[19] reported 10 children with cavum vergae alone or together with cavum septi pellucidi. Of the 10, 5 had delayed development, 4 had macrocephaly, 2 had learning disabilities, and 2 had abnormal electroencephalograms. However, the causal relationship between the cavum vergae and associated neurological symptoms remains unclear.

The clinical manifestations of cavum veli interpositi are even more obscure than those of the other two cava. Raimondi et al.[26] proposed a new clinical syndrome of infants with cavum veli interpositi in which large head, sunken fontanel, developmental delay, failure to thrive, and seizures are included together with normal or low-pressure hydrocephalus. High prevalence rate of mental retardation and epilepsy have been reported in association with cavum veli interpositi by others.[8,20] However, cavum veli interpositi is more common among infants whose brain is atrophic or degenerative, and it does not seem to have any relationship with clinical symptoms.[20–23]

Neuroimaging of the Cava

Cavum septi pellucidi is readily diagnosed on conventional CT. In axial sections the cavum is seen as an oblong or oval cavity of CSF density between the frontal horns and bodies of the lateral ventricles. When not associated with cavum vergae, it forms a slender triangle, with its apex pointing posteriorly. The cavity may be called "cyst" when it is rounded and displaces the lateral ventricles laterally, but no criteria exist that allow differentiation between a dialted cavum and a cyst[7] (Figure 6.4).

Cavum vergae is seen as a posterior extension of the cavum septi pellucidi between the body of the lateral ventricles and forms a flask shape in the axial plane, with its bottom pos-

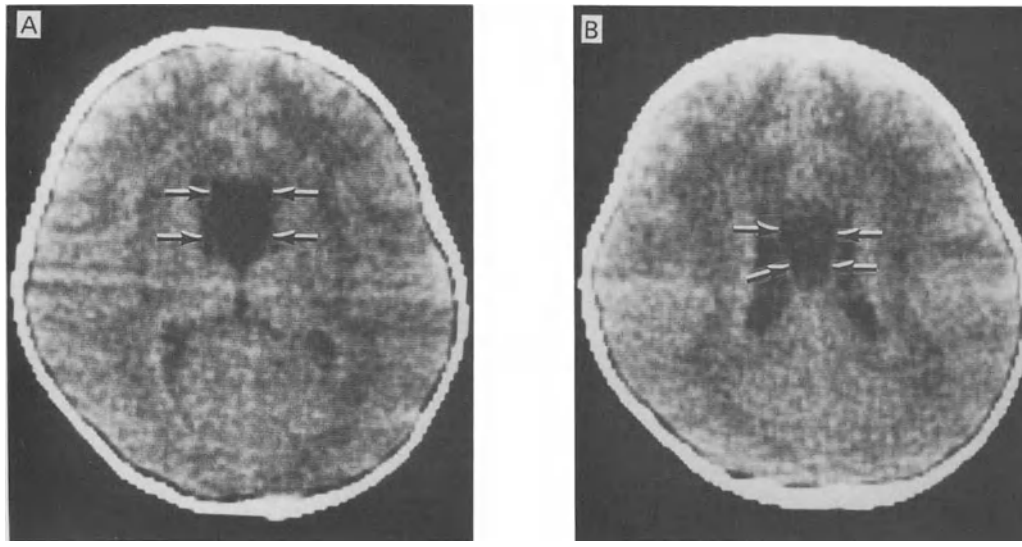


Figure 6.4. Cystic cavum septi pellucidi in a 4-year-old boy. A and B: CT scans show a rounded cyst (arrows) displacing laterally the frontal horns and bodies of the lateral ventricles. Cystic cavum of the septum pellucidum does not extend posteriorly beyond the level of the foramen of Monro.

teriorly bounded by the splenium of the corpus callosum.[10,19] In the coronal plane it takes a trapezoidal or hexagonal configuration, with its flat roof formed by the corpus callosum and its lateral walls bounded by the columns of the fornix from the body of the lateral ventricle. Its floor abutting the velum interpositum usually forms a wider base of the trapezoid, but may project inferiorly to form the lower half of the hexagon (Figure 6.3 and 6.5). Boundary between the cavum anterius (septi pellucidi) and posterius (vergae) is defined as the isthmus produced by the approximation of the columns of the fornix when the cavum takes an hourglass configuration on the axial plane.[7,27] But when the cavum is rounded without constriction in the midpoint, the cavum anterius and posterius are roughly demarcated by the level of the foramen of Monro (Figure 6.6).

Cavum veli interpositi shows a triangular configuration on the axial plane, with its apex pointing anteriorly and being limited by the foramina of Monro, with its bilateral posterolateral extremities continuing to the choroid plexus of the lateral ventricle, and with its posterior border being bounded by the splenium of the corpus callosum superiorly but opening into the qnadrigeminal cistern inferiorly. In the coronal plane it assumes a tentlike configuration roofed by the columns of the fornix and lying on the roof of the third ventricle[7] (Figures 6.5 and 6.7).

The cavum veli interpositi can be differentiated from the cavum vergae by the following characteristics: the cavum veli interpositi lies under the fornix, converges at the interventricular foramina, and does not extend into the septum pellucidum.[7] However, the cavum veli interpositi is sometimes difficult to distinguish from the isolated cavity of vergae. In this instance, the two internal cerebral veins seen on MRI may help to distinguish the two cava: the cavum vergae lies above these veins, whereas the cavum veli interpositi encloses the two vessels[19] (Figure 6.7).

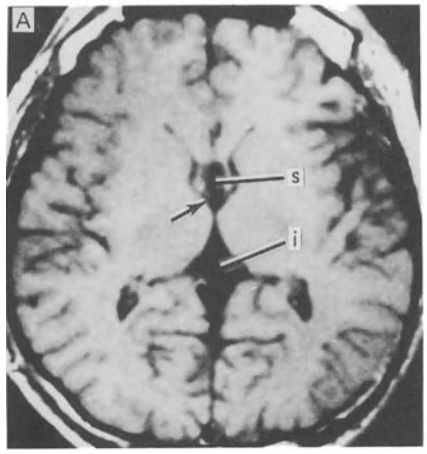
Cysts of the Septum Pellucidum, Cavum Vergae, and Velum Interpositum

The distinction between a dilated cavum and cyst is arbitrarily defined. When the cavum is larger than usual, it may be called a cyst, but the actual size distinguishing the cavities has not been established.[1] A noncommunicating cavum has been called a cyst,[7] but the proof of communication is becoming more difficult since dynamic diagnostic studies such as pneumoencephalography are not currently employed in routine neuroimaging. Cyst of the septum pellucidum was defined by Sarwar[10] as a cavity on CT and MR imaging having a width of 10 mm or more and walls bowing laterally.

A radiologically defined cyst does not necessarily produce clinical symptoms, but a larger cyst is more likely to be symptomatic than a smaller one, since neurological symptoms are attributed to the pressure effect of the cyst.[1] Symptoms are presented as being due either to obstruction of the CSF pathway at the foramina of Monro or at the aqueduct by the cyst, or to direct compression of the cyst against the neighboring neuronal structures. However, symptomatic cyst is considered to be extremely rare.[1,10]

Symptomatic cysts are almost invariably confined to those arising in the septum pellucidum. Shaw and Alvord[1] found 15 cases of symptomatic cyst of the septum pellucidum in

Figure 6.5. Cava septi pellucidi and vergae in a 27-year-old man. T1-weighted MR images. Axial (A–C) and coronal (D–F) sections. Cavum septi pellucidi (s) and its posterior extension, cavum vergae (v) are demarcated by the level of the foramen of Monro (arrows). Lateral ventricles are separated by the cava, but not compressed. In C and F, cavum vergae is bounded superiorly by the corpus callosum (c), laterally by the columns of fornix (f) and posteriorly by the splenium of the corpus callosum (c-s), but its inferior boundary is ill-defined by the superimposed cavum veli interpositi (i). In A, cavum veli interpositi is seen as a triangular fluid space converging toward the foramina of Monro. E and F shows the third ventricle.[3]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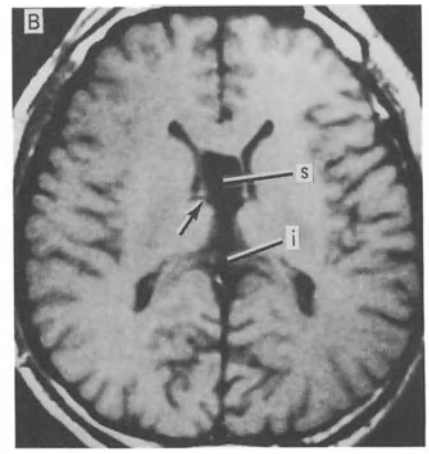
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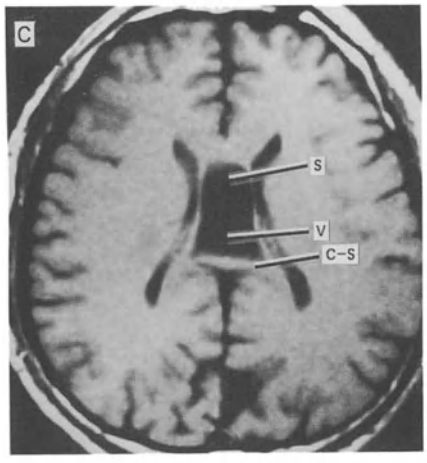
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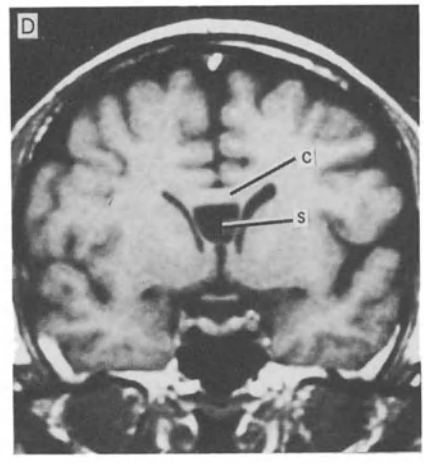
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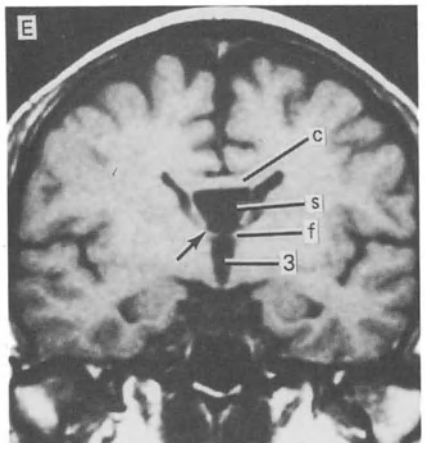
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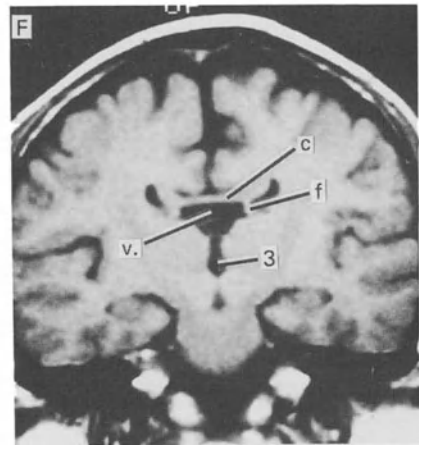
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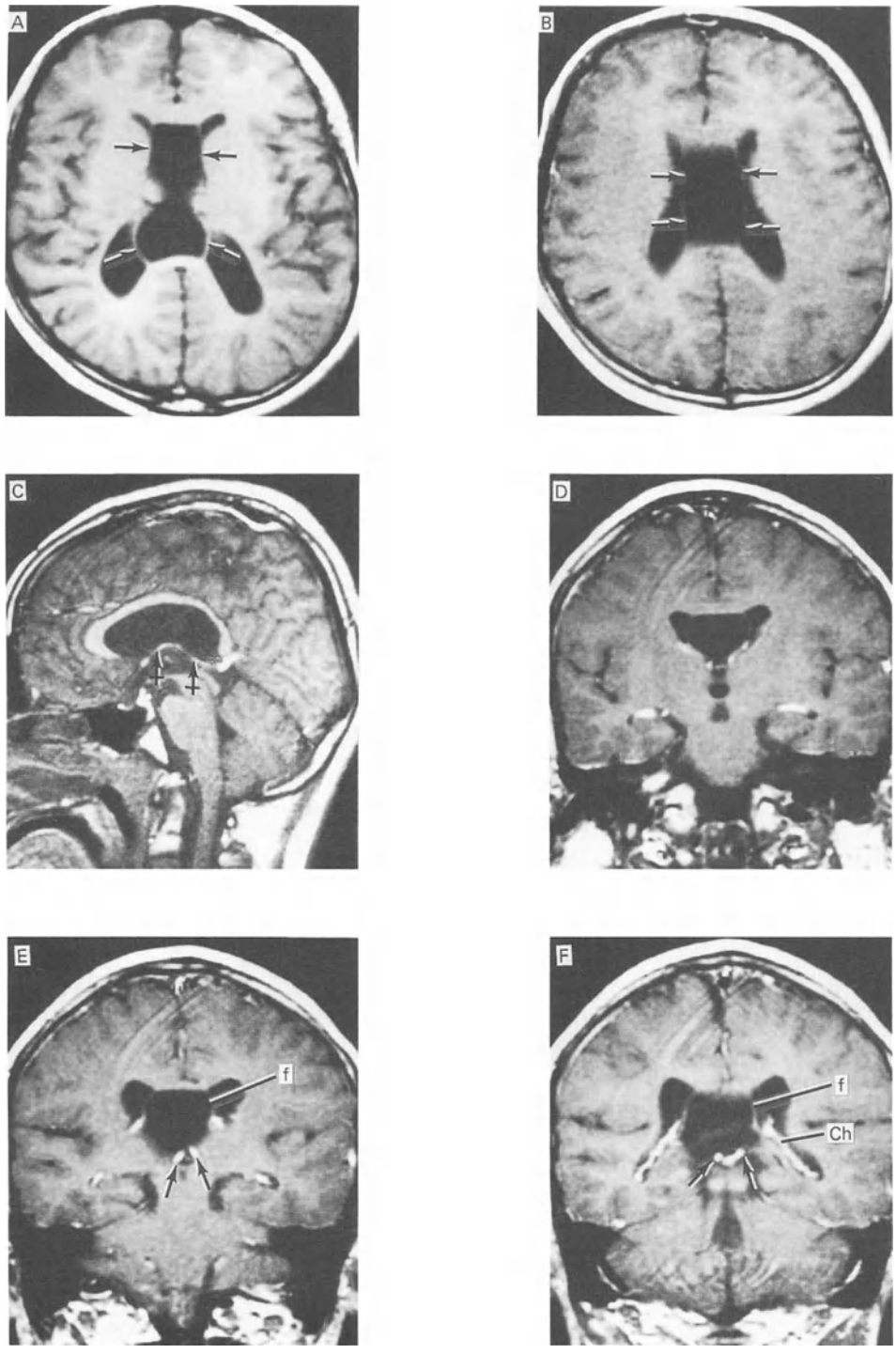

Figure 6.6. Cystic cava septi pellucidi and vergae in a 15-year-old boy. T1-weighted MR images. A and B: Axial sections show lateral bowing of walls of the cava (arrows), and moderate enlargement of the lateral ventricles. C: Sagittal section, gadolinium enhancement shows the cystic cava surrounded by the corpus callosum and the internal cerebral veins (crossed arrows). D–F: Coronal sections, gadolinium enhancement shows a rounded, cystic cava located above the internal cerebral veins (arrows). f, fornix; ch, choroid plexus.

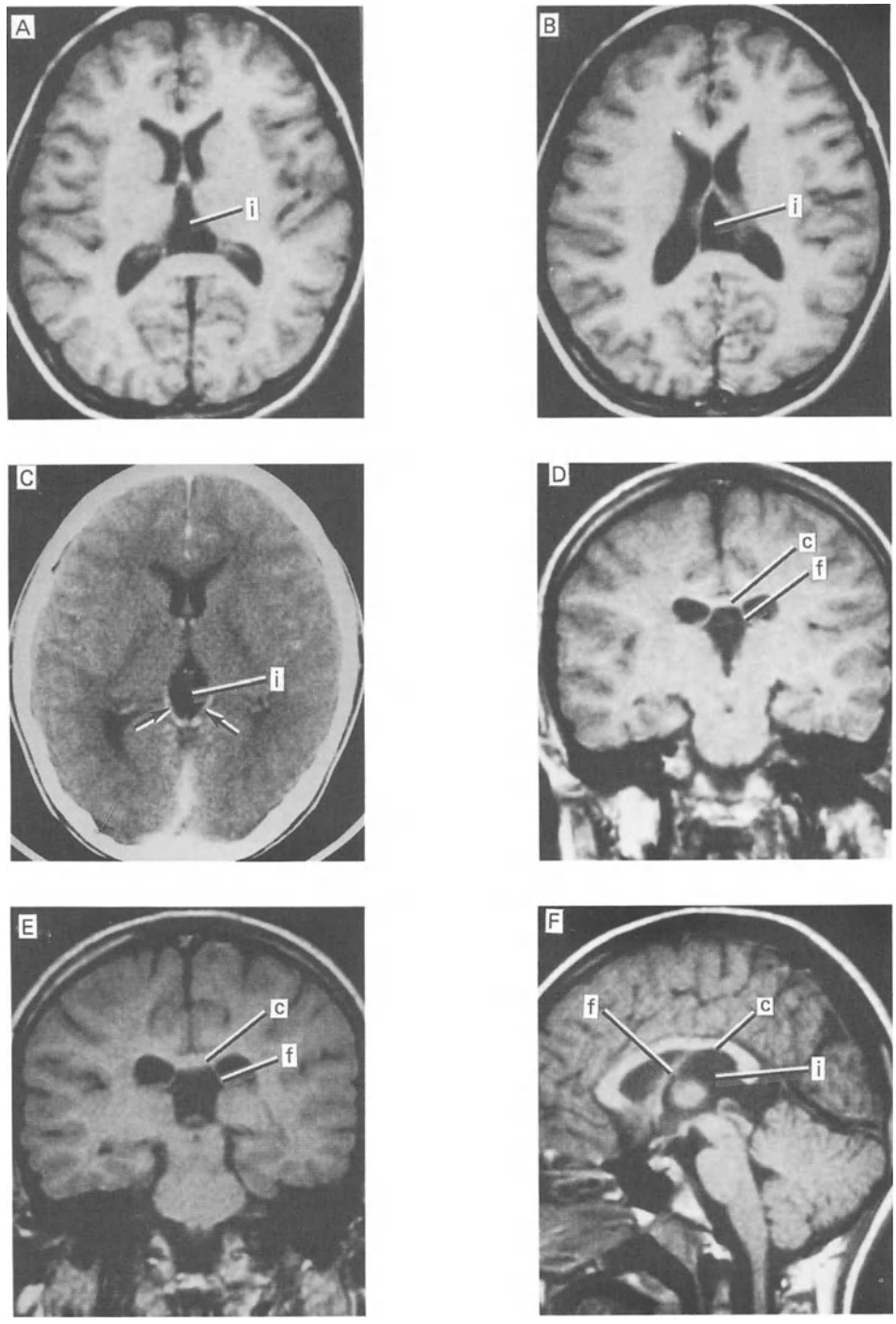

Figure 6.7. Cavum veli interpositi in a 12-year-old girl. A and B: Axial T1-weighted MR images show the expanded cavum veli interpositi (i). The cavum does not extend into the septum pellucidum. C: Enhanced CT scan allows the differentiation of this cavity from cavum vergae by the internal cerebral veins (arrows), which enclose the cavum. D and E: Coronal T1-weighted MR images show that the columns of fornix (f) roofing the cavum veli interpositi are unusually separated. Distinction between the cavum veli interpositi and cavum vergae is difficult on these images. F: Sagittal T1-weighted MR image shows the cavum bounded anteriorly by the fornix (f) and opening posteriorly into the quadrigeminal cistern. c, corpus callosum.

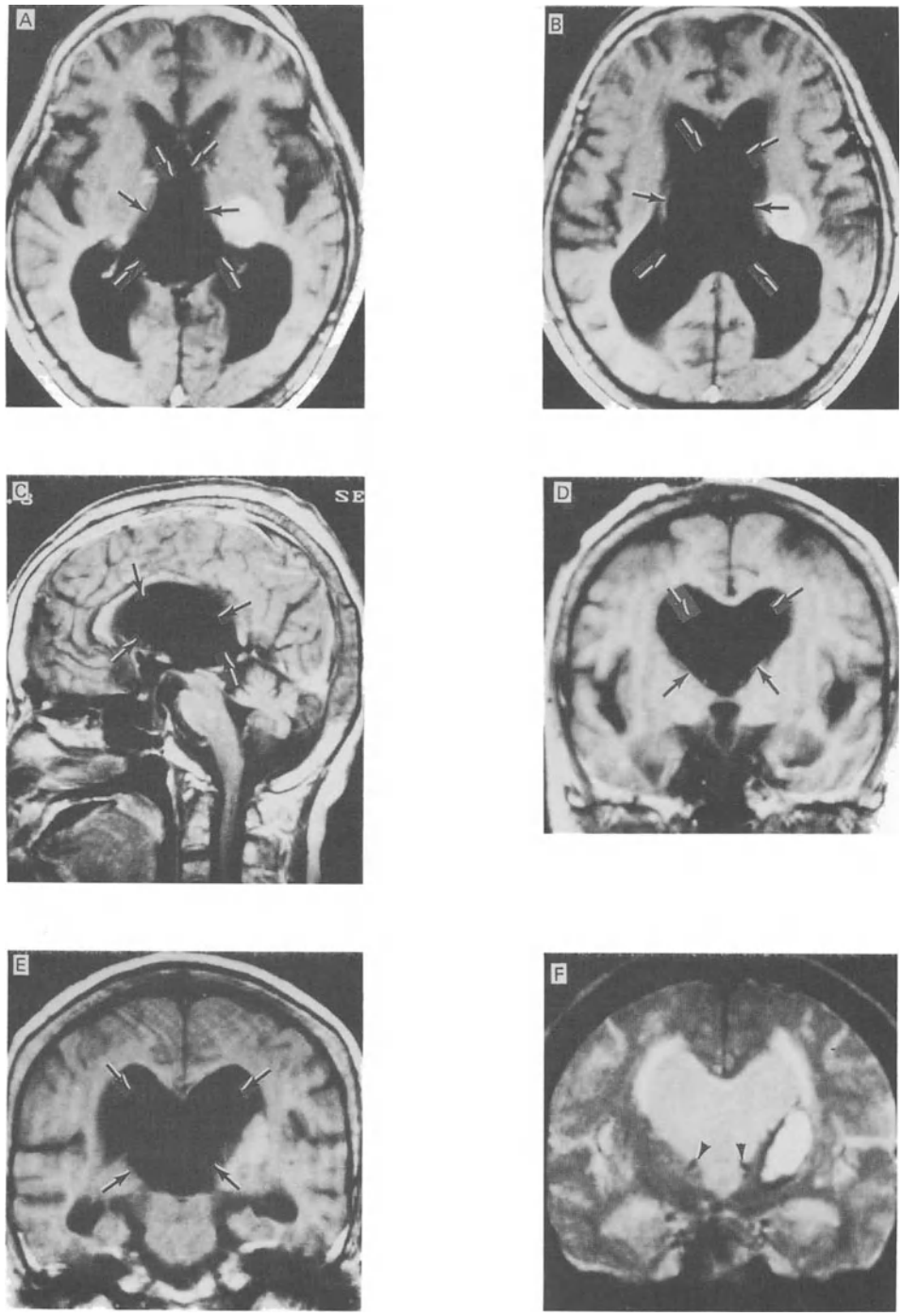

Figure 6.8. Cyst developing probably in the cavum veli interpositi in a 71-year-old woman with left thalamic hemorrhage. A–E: T1-weighted MR images show a large central cystic cavity (arrows). F: Coronal T2-weighted MR image demonstrates the two internal cerebral veins (arrowheads) enclosing the cyst. This may indicate that the cyst is not of the cavum vergae, but arises in the cavum veli interpositi. (Courtesy of Dr. I. Fuwa.)

the literature and described their own two cases in 1969. Since then, 11 such symptomatic cases have been reported in the literature.[28–38] The literature cited above suggests that symptomatic cysts occur almost equally in children under the age of 15 and in adults, in contrast to the age-dependent prevalence of nonsymptomatic incidental cavum of the septum pellucidum. The most common symptoms produced by the cyst are caused by the increased intracranial pressure, which causes headaches[13,15,28,39] and hydrocephalus in pediatric cases.[31,32,34] Convulsions, mental disturbances such as behavioral changes or amnestic syndromes, and motor disturbances were also been reported as presenting symptoms of the cyst.[30,37,38] In the absence of hydrocephalus, symptoms probably caused by the direct compression of the neighboring structures were also described in cases with bitemporal hemianopia,[35] acute Korsakoff syndrome,[33] or hemiparesis.[29]

Cyst of the cavum vergae, though rare, has been reported as a posterior extension of septum pellucidum cyst.[40] Isolated cyst of the cavum vergae, if present, is exceptional, as discussed in the section Cavum Vergae, above. In the 1940s, two cases were reported by Leslie[3] and Scott[41] and described as "cyst of the cavum vergae." These two cases presented problems regarding their location and the nature of the cyst wall, as briefly reviewed by Shaw and Alvord.[40] Recently four cases of cavum vergae cyst diagnosed by CT were reported by Donauer et al.[42] However, the examples of cavities presented in their paper should be distinguished from cavum veli interpositi. As reviewed here, isolated cyst of the cavum vergae should be thoroughly examined before it is diagnosed, since the presence of isolated cavum vergae is hard to accept from the embryological viewpoint.

True cyst of the velum interpositum has not been described. Cystic, huge dilation of the cavum veli interpositi is occasionally observed as an anterior extension of the dilated cistern of the quadrigeminal plate.[43] Arachnoid or neuroepithelial cyst developing in the cistern of the velum interpositum should be differentiated from cyst of the cavum vergae[43–45] (Figure 6.8).

Surgical treatment of the cyst is simple. Since Dandy[39] advocated excision by craniotomy, fenestration of the cyst wall to establish communication with the ventricular system is now widely employed.[32,34,38] Some neurosurgeons punctured the cyst through a burr hole either under radiographic control[46] or by the stereotaxic approach.[42] These surgical results were reportedly successful in the majority of cases, but the symptoms recurred in some cases. When fenestration is occluded, shunting from the cyst is the alternative.[30,47]

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CHAPTER 7

Incidence, Anatomical Distribution, and Classification of Arachnoidal Cysts

Concezio Di Rocco, Massimo Caldarelli, and Antonello Ceddia

Introduction

Out of the wide variety of intracranial benign cystic lesions, those developing within the arachnoid membrane, apparently because of a splitting or duplication of this membrane,[1–10] remain a puzzling phenomenon to the neurosurgeon, even nowadays. Several aspects of these cysts are still relatively obscure: the physiopathogenesis has not been completely clarified, the natural history is not well known, the surgical indication as well as the choice of surgical modalities are often difficult, and the results of the surgical treatment appear relatively unpredictable in a significant proportion of cases. Though the recognition of arachnoid cysts has been greatly facilitated, even in asymptomatic subjects, by the modern diagnostic tools for neuroimaging, the differential diagnosis with other intracranial fluid collections may still offer some problems.

As the term *cyst* refers to a closed cavity of abnormal character, the definition of arachnoid cyst implies the absence of any communication with the natural pathways of cerebrospinal fluid circulation, thus excluding the localized dilations of the subarachnoid space, which freely communicate with this space. Indeed, most of the authors agree on denominating such cavities as pouches, sacs or diverticula of the arachnoid space. Also to be excluded are the cavities that result from various cavitation processes of the brain, namely the porencephalic cavities and the cavities secondary to vascular infarction, where the fluid accumulation substitutes a localized loss of brain tissue.

The adjectives *primary* and *true* have been proposed by several authors to describe arachnoid cysts that appear as collections of fluid surrounded by a membrane resembling the arachnoid mater, formed indeed by various layers of arachnoid cells and eventually reinforced by collagen fibers, as distinct from the "secondary" or "false" arachnoid cysts. The latter are acquired accumulations of cerebrospinal fluid deriving from postinflammatory loculation of the subarachnoid space in subjects who have undergone head injury, intracranial infection, or hemorrhage.[1–12] Inflammatory cells or hemosiderin deposits within the lining membrane characterize this second type of arachnoid cyst and allow the differential diagnosis; in the same way, the presence of glial tissue and epithelial cells differentiates the less frequent glioependymal cysts, which also may develop in rare instances within the subarachnoid space.[8,13,14]

Primary or true arachnoid cysts should then be regarded as "arachnoid malformations." Consequently, their origin must lie in a disorder in the development of the arachnoid mater. Unfortunately, very little information is known about the process that could lead to a defective development of the arachnoid membrane, and eventually to an associated abnormality of the underlying brain. Among the various theories that have been propounded to explain the formation of arachnoid cysts, the most credited hypothesis postulates that

these lesions represent a minor aberration of the formation of the subarachnoid space. Under normal conditions, this space is formed by the action of the cerebrospinal fluid flowing from the cerebral ventricles, when the roof of the fourth ventricle becomes permeable, through the loose primitive mesenchyme that surrounds the developing nervous system of the embryo. This loose primitive mesenchyme, by means of a change in the nature of the ground substance within its extracellular spaces and under the pulsatile forces of the cerebrospinal fluid driven by the choroid pulsation, gives rise to the subarachnoid space and the pia, the inner layer of the arachnoid. Part of the primitive mesenchyme condenses into a distinct cellular layer, which forms the outer layer of the arachnoid and the dura.[4,6–8,15–17] At the end of the process the cerebrospinal fluid has replaced the ground substance, by filling a space (subarachnoid space) crisscrossed by arachnoidal cells and connective tissue (arachnoid trabeculae), and lined by an inner wall (pia mater) and an outer wall (arachnoid mater). The arachnoid cysts, as well as the arachnoid diverticula, would originate either by abnormalities in the condensation of the mesenchyme in the layer that forms the arachnoid, or because of variations in the flow of the cerebrospinal fluid in the earliest stages of the embryogenesis.[18]

The malformative origin of arachnoid cysts is supported by several observations, such as the relatively similar incidence in both adult and pediatric populations, the relationship with the cisternae, the direct demonstration of a splitting of the arachnoid membrane at the margin of the cyst which has occurred in some cases, the association with other congenital anomalies (namely, agenesis of the corpus callosum and Marfan syndrome), and the occasional occurrence in siblings and in both the sylvian fissures.[2,19–28]

Incidence, Heredity, and Age Distribution

Among the major factors that impede a reliable evaluation of the actual incidence of arachnoid cysts are the difficulties in reaching a histological diagnosis on specimens obtained from operated on subjects or on brains and spinal cords removed for postmortem studies. In surgical specimens, the entire cystic wall is only available for a histological investigation in exceptional cases; the fragments that are usually examined often present important artifacts due to their difficult preservation. Only in very rare instances is the site of the origin of the arachnoid malformation obtained for the laboratory diagnosis, which facilitates the correct recognition. Further difficulties in the diagnosis derive from the possible presence of glial tissue in the cystic wall, which might represent attenuated cerebral or cerebellar cortex englobed in a "true" arachnoid cyst. On the other hand, arachnoid cells may be detected extending over the nonspecific fibrous wall lining cystic lesions of a different nature.[29] In autoptic investigations, the thin cystic wall of an arachnoid cyst is easily torn when the brain is removed and, especially in case of small lesions, the cyst may easily escape detection. A clinical history, negative for trauma or inflammation, does not exclude the possibility of a secondary, acquired cyst, as the fragility of the arachnoid membrane may favor its focal rupture and laceration, following even a minor insult that may remain clinically ignored.

If the pathological event occurs early in life when the phagocytic processes are particularly active, any eventual necrotic tissue could have been removed by macrophages at the time of the surgical diagnosis, so that the absence of any trace of hemorrhage or infection does not necessarily give license to ascribe the lesion to a developmental error.[29] A further factor that impedes the assessment of the actual incidence of arachnoid cysts is their possibility to remain asymptomatic for several years or for an entire lifetime depending on their size and location.

Bearing in mind the above-mentioned limitations, a review of the literature seems to demonstrate that arachnoid cysts are relatively rare, as they have usually been reported to account for only 1% of all intracranial space-occupying lesions.[11,18,19,21,22,30] In recent

years, however, an apparent relative increase in the frequency of this type of lesion and a shift toward the left in the age distribution have resulted from the wide application of computed tomography (CT), magnetic resonance imaging (MRI), and ultrasonographic techniques. In several instances, in fact, arachnoid cysts are detected incidentally in subjects examined for head injury (Figure 7.1) or undergoing investigation because of an aspecific macrocrania, suggesting an underlying hydrocephalus (Figure 7.2). Thus, in clinical practice, especially in pediatric neurosurgical centers, arachnoid cysts may be present in a large proportion of patients; for example, 12% of the children treated in our institution for a space-occupying lesion were operated on for an arachnoid cyst.

However, this apparently high incidence in our opinion reflects the impact of the new diagnostic tools for neuroimaging and the concentration of cases in specialized institutions. Such an opinion is supported by the correlation of data between the low incidence observed in clinical practice before the introduction of CT, MRI, and ultrasonography and that obtained from autoptic observations. In 1960, for example, Cassinari and coworkers[31] found only 13 arachnoid cysts out of 3,706 expansive intracranial lesions, i.e., 0.4%. Similar figures were reported by Shuangshoti[32] and Tamaki and coworkers,[33] who also found an incidence of around 0.4% of all intracranial tumors. Nagoulitch and Perovitch[34] calculated that 0.7% of their infants with intracranial space-occupying lesion had an extracerebral fluid collection that could be identified as an arachnoid cyst.

When based on autoptic material the studies seemed to demonstrate an even minor incidence. In 1977, Shaw and Alvord,[29] for example, observed only 5 arachnoid cysts in 5,000 human brain and spinal cord specimens, i.e., 0.1%. In fetal and neonatal autopsies, Adams and coworkers[35] reported only 5 arachnoid cysts in a total of 3,000 consecutive examinations, i.e., an incidence of 0.17%.

Arachnoid cysts are nearly always sporadic and occur as single lesions. Males are more commonly involved[1,11,23,36–47] (Table 7.1) The bilateral, more or less symmetrical, occurrence of an arachnoid cyst is a rare event that, however, has been observed by various authors.[1,48–52] Although these bilateral cysts may be present in subjects showing a normal psychomo-

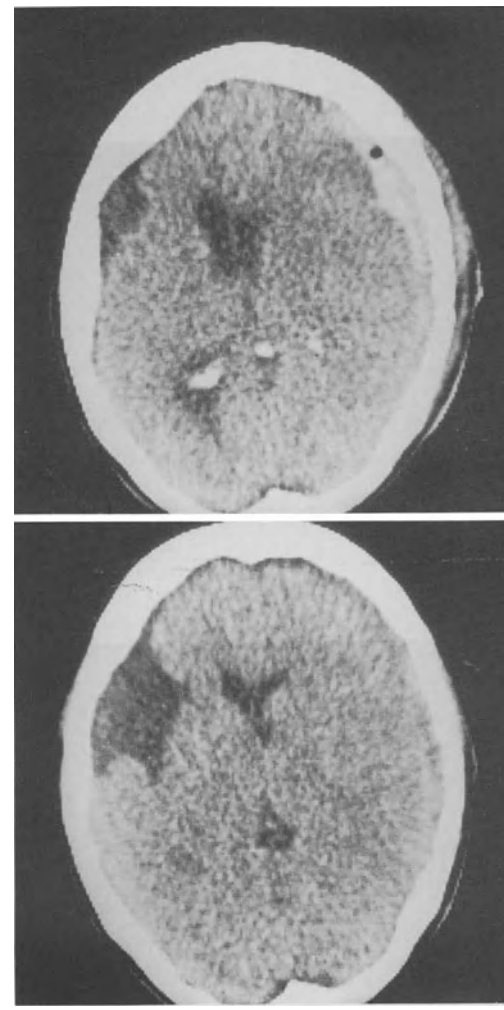


Figure 7.1. CT scan examination performed immediately after a head injury (above) and repeated at a 2-week interval (below). Note the presence of a right epidural hematoma that compresses the underlying brain contralaterally, the acute ventricular dilation, and the cystic area corresponding to the left temporal region (above). After the removal of the hematoma the shift of midline structures toward the left has disappeared and the left temporal cystic area is increased in size, showing the morphological characteristics of a temporal region cyst (below).

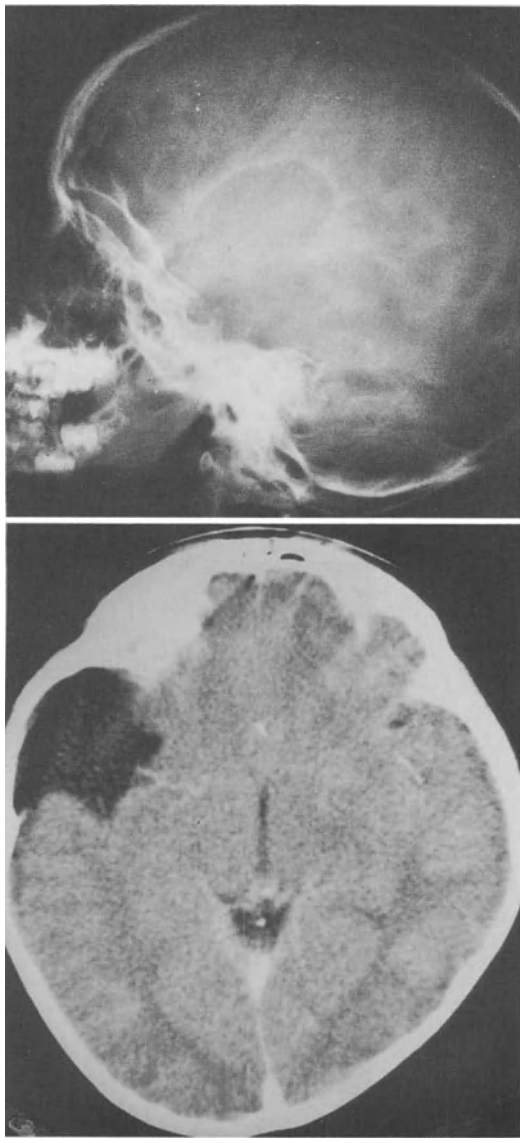


Figure 7.2. An 8-year-old child with macrocrania. The skull x-ray examination demonstrates signs of chronically increased intracranial pressure as well as an osteolytic area above the temporal region (above). The CT scan examination reveals the presence of an underlying temporal arachnoid cyst (below).

Table 7.1. Sex distribution of arachnoidal cysts.

Author (reference no.)	Males	Females
Anderson and Landing, 1966[23]	7	2
Harrison, 1971[36]	8	6
Danziger and Bloch, 1975[37]	12	1
Aicardi and Bauman, 1975[38]	10	2
Choux et al., 1978[1]	27	9
Leo et al., 1979[39]	7	5
Galassi et al., 1982[40]	29	6
Sato et al., 1983[41]	14	6
Cilluffo et al., 1983[11]	16	10
Crisi et al., 1984[42]	14	7
Locatelli et al., 1987[44]	15	15
Galassi et al., 1988[45]	60	17
Garcia-Bach et al., 1988[46]	14	8
Ciricillo et al., 1991[47]	26	14
Personal series	53	32
Total	312 (69%)	140 (31%)

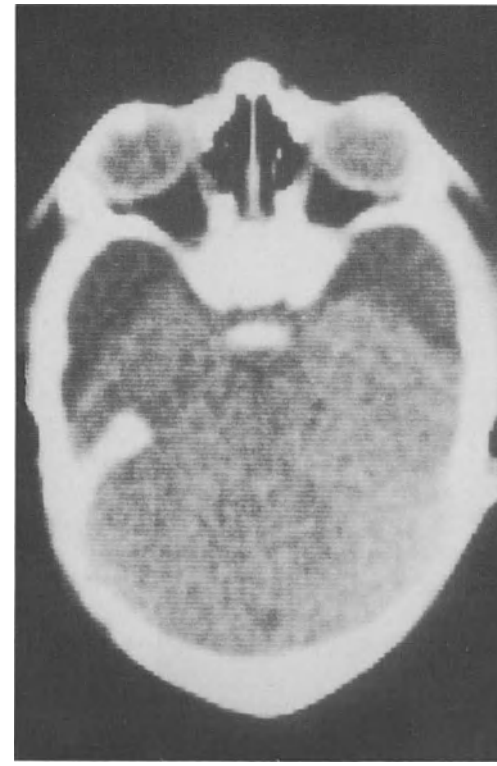


Figure 7.3. A 3-year-old child with severe psychomotor retardation. The CT scan examination shows bilateral temporal arachnoid cysts.

tor development, most of these patients, (as well as the only child who came to our attention) (Figure 7.3) exhibit various degrees of mental retardation. Rossitch and Oakes in 1989,[50] described an 11-year-old boy with

Table 7.2. Anatomical distribution of arachnoid cysts.

	1		2		3	
	No. cases	%	No. cases	%	No. cases	%
Supratentorial	161	77%	289	78%	62	73%
Sylvian fissure	103	50%	137	37%	18	21%
Suprasellar region	18	9%	58	16%	14	16%
Cerebral convexity	9	4%	59	16%	9	11%
Interhemispheric fissure	10	5%	18	5%	15	18%
Quadrigeminal region	21	10%	17	5%	6	7%
Infratentorial	47	23%	83*	22%	23	27%
Median	19	9%	59	—	15	18%
Cerebellar hemisphere	22	11%	10	—	8	9%
Clival	6	3%	2	—	—	—
Total	208		372		85	

Column 1: Cases from literature collected by Rengachary and Watanabe (7).
Column 2: Pediatric cases from literature from 1962 through 1991 (1,11,21,23,36–39,43,44,47,53–73); this series shares some cases with the above-reported series.
Column 3: Personal series.
*Twelve cases reported by Ciricillo et al. (47) have not been anatomically classified by the authors; thus the anatomical distribution of posterior fossa cysts refers to only 71 cases and the relative percentages have not been calculated.

bitemporal arachnoid cysts, whose symptomatology (inappropriate sexual conduct, associated with placidity, passivity, blunted affect, memory and language dysfunction, and precocious puberty) expressed the clinical picture of the Klüver–Bucy syndrome. It is possible that a few of these bilateral temporal cysts may escape detection, being interpreted as a result of perinatal cerebral hypoxia. Most of the arachnoid cysts are detected in the first two decades of life. In children, the great proportion of these lesions is recognized during the 1st year of life, the majority within the first 2 years (Figure 7.4).[11,23,36–39,42–44,53–70]

Anatomical Distribution and Classification

The nearly constant anatomical relationship of arachnoid cysts with the cistern of the sylvian fissure, the chiasmatic cistern, the cisterna magna, the quadrigeminal cistern, and the prepontine cistern seems to suggest that these lesions may actually represent a developmental anomaly of the cisternal spaces in the great majority of cases. In fact, the cysts of the cerebral convexity, especially those that reach a huge size, also might correspond to an extension of the cistern of the sylvian fissure or of the interhemispheric cistern. Table 7.2 shows the distribution of 208 subjects of all ages with arachnoid cysts, collected by Rengachary and Watanabe[7] from papers published from 1831 through 1980, as well as of 372 pediatric cases reported in the literature from 1962 through 1991,* and 85 personal pediatric cases operated on in the period 1979 through 1990.

From the table it is well apparent that the sylvian fissure represents the most common site, whereas the clival region corresponds to the less frequent localization. There are some obvious differences between adults and children, such as the relatively high incidence of the cerebellopontine angle cysts in the former, and the relatively high proportion of cysts of the chiasmatic region in the latter. Even though the regions in anatomical relationship with the cisterns are those bearing almost all the arachnoid cysts, in rare instances these lesions may develop in sites anatomically unrelated to the cerebral cisterns. Obviously,

*Refs. 1, 11, 21, 23, 36–39, 43, 44, 47, 53–73.

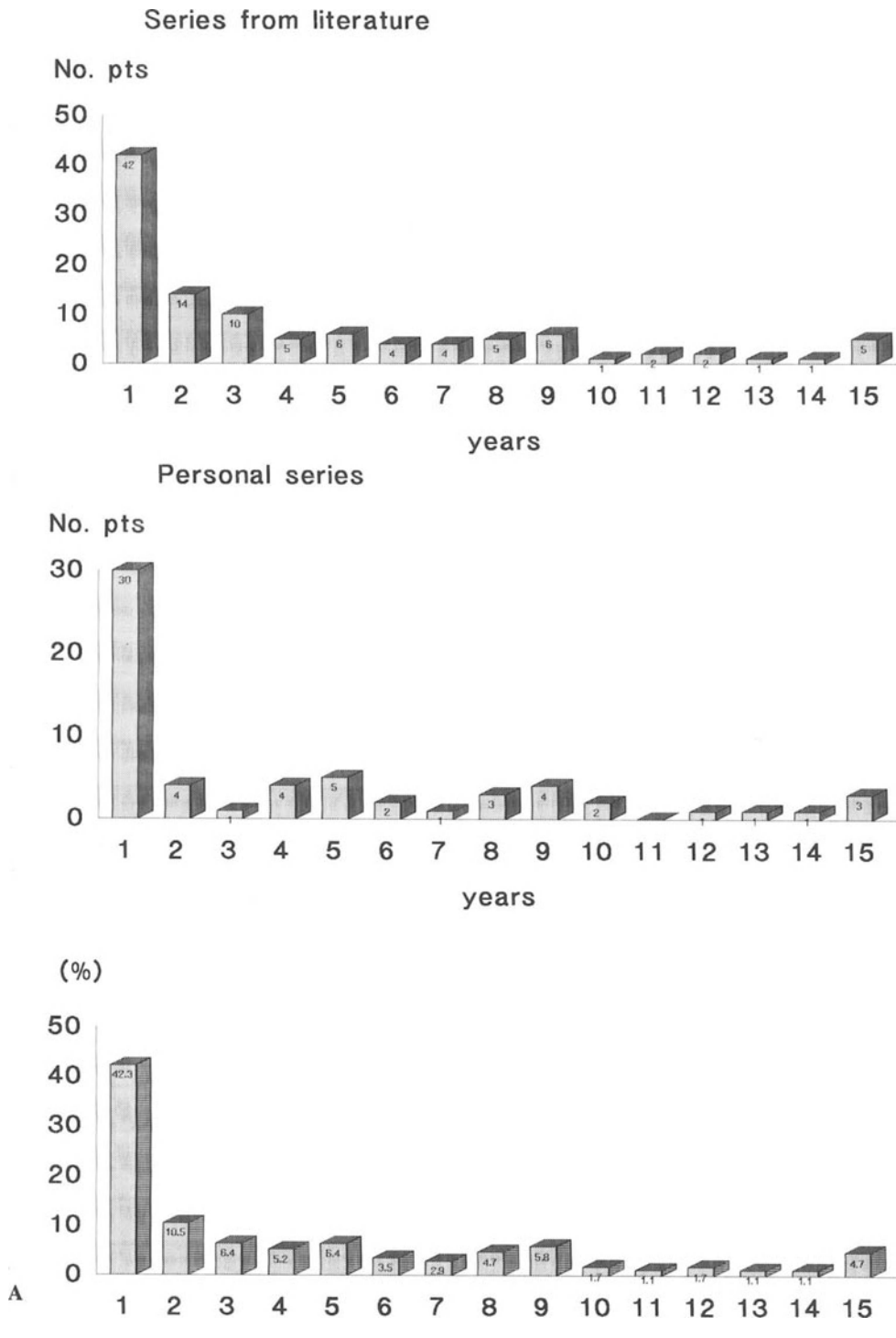
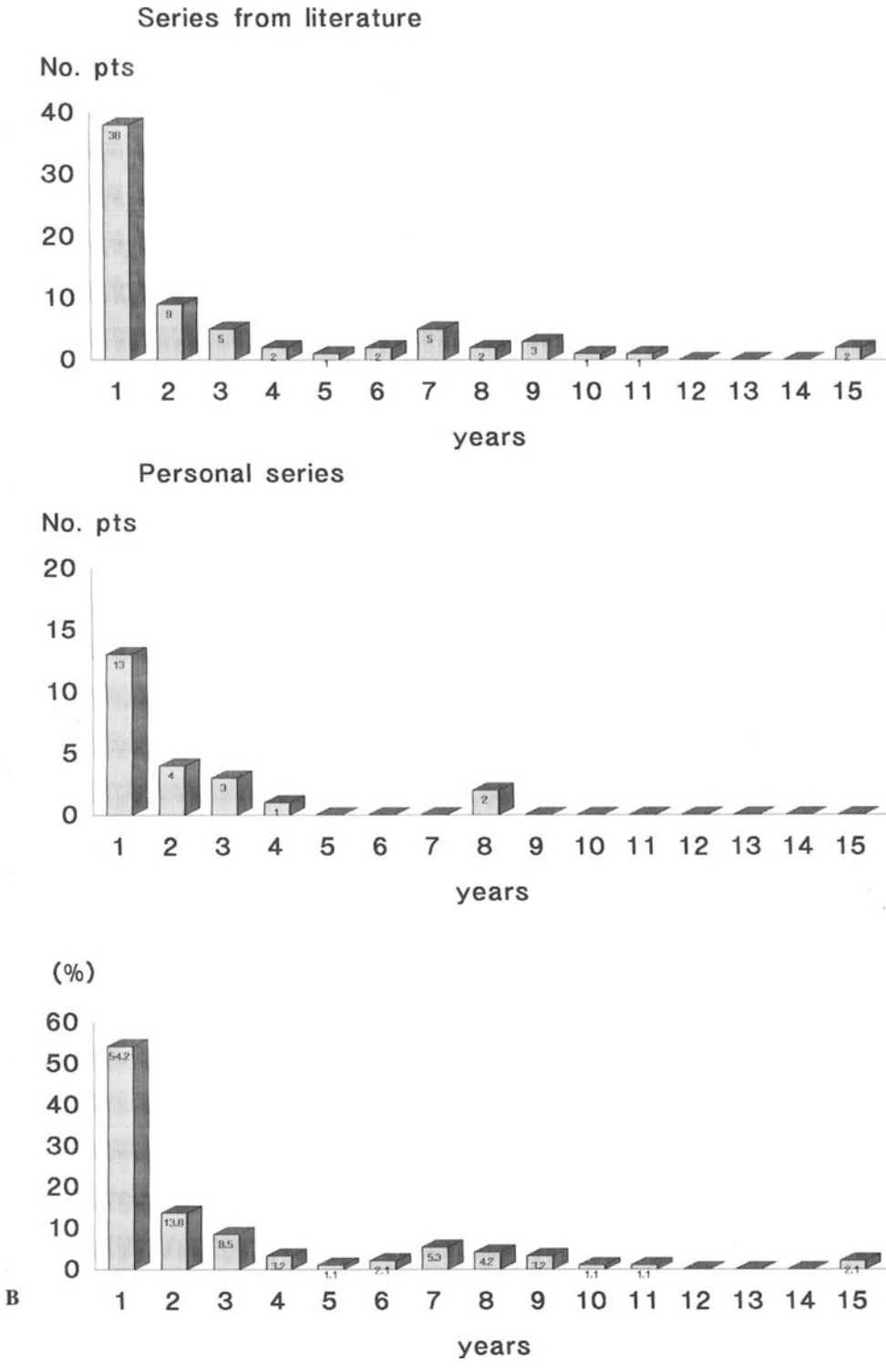


Figure 7.4. Age distribution of supratentorial (A) and infratentorial (B) arachnoid cysts.


Series from literature
No. pts
40
30
20
10
0
38
8
5
2
1
2
5
2
3
1
1
2
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
years
Personal series
No. pts
20
15
10
5
0
13
4
3
1
2
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
years
(%)
60
50
40
30
20
10
0
54.2
13.8
8.5
3.2
1.1
2.1
5.3
4.2
3.2
1.1
1.1
2.1
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15
years

B

Table 7.3. Anatomical classification of intracranial arachnoid cysts.

1. Extradural intradiploic arachnoid cysts
a. Supratentorial
b. Infratentorial
2. Intradural arachnoid cysts
a. Supratentorial
Sylvian fissure
Sellar and suprasellar region
Interhemispheric fissure
Cerebral convexity
Intraventricular
b. Tentorial
Quadrigeminal plate
c. Infratentorial
Cerebellar
Cerebellopontine angle
Clival

these rare cysts offer further difficulties for the physiopathogenetic interpretation. In 1971, for example, the hypothesis of an internal meningocele was propounded by Faris and coworkers[74] for a unusual case of an arachnoid cyst that developed within the the third ventricle. In 1979, Yeates and Enzman[75] described a case of intraventricular arachnoid cyst and postulated its origin from the vascular mesenchyme of the choroid plexus of the lateral ventricle. This hypothesis was supported 8 years later by Seike and coworkers.[76] On the other hand, Nakase and coworkers[77] reported a further case of intraventricular arachnoid cyst and hypothesized that the lesion could arise from the arachnoid layer carried along by the vascular mesenchyme when it invaginates via the choroidal fissure. A further case of an arachnoid cyst within one lateral cerebral ventricle was also reported by Yoshida and coworkers in 1984.[78]

The development of an arachnoid cyst within the fourth ventricle in a 7-year-old boy with a history of so-called arrested hydrocephalus was first described by Di Rocco and coworkers in 1979.[79] In adults, Korosue and coworkers[80] observed a similar occurrence in a patient who also presented with the clinical picture of an intermittently evolving ventricular dilation.

Finally, even at the cranial level arachnoid cysts may develop extradurally, like the analogous congenital extradural cysts of the spine, presenting as lytic lesions. For these cysts the definition of "intradiploic" arachnoid cysts has been proposed and the congenital nature recently confirmed in contrast with other previous interpretations that postulated a traumatic etiology ("traumatic arachnoid cysts without fracture").[81]

As the intracranial cysts give clinical signs and symptoms according to the site of their development, these lesions can be classified on the basis of their anatomical localization.

Thus, the two principal categories of supratentorial and infratentorial arachnoid cysts can be further divided into main subgroups, as shown in Table 7.3. From among these subgroups, the intraventricular arachnoid cysts and intradiploic arachnoid cysts have relatively little value from a practical point of view, due to their rare occurrence. The other subgroups fall into typical clinical patterns, each requiring a specific treatment and so warranting a separate discussion.

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CHAPTER 8

Suprasellar Arachnoidal Cysts

Concezio Di Rocco and Massimo Caldarelli

Introduction

Arachnoid cysts occurring in the chiasmatic region have been the subject of controversial scientific contributions, most of the discussions being centered on their complex physiopathogenetic interpretation. Further difficulties have been added by the complex anatomy and relatively undefined anatomical boundaries of the chiasmatic cistern, which has been variably described in the different classifications propounded through the years (Table 8.1). According to Key and Retzius' work,[1] for example, the chiasmatic cistern consisted only of the space behind and below the optic chiasma, as far as the hypophysial stalk and the area between the two diverging optic nerves. The space in front of the optic chiasma was termed by these authors "cisterna laminae cinerae terminalis."

The extension given to the cistern by Locke and Naffzinger[2] was relatively similar. The authors, however, considered the chiasmatic space only as a portion of the cisterna basalis. Spatz and Stroescu[3] also had the same belief and added that the cisterna basalis, in their opinion, ended as far anteriorly as the posterior surface of the chiasma. Other investigators, however, opined that the chiasmatic cistern extended also laterally to the chiasm as far as the uncus of the hypocampal gyrus and up to posterior surfaces of the frontal lobes, the gyrus rectus; this was, for example, the definition of the "cisterne opto-chiasmatique" given by Dilenge.[4]

With the introduction of air encephalography more practical classifications were proposed, based on the results of the roentgenographic examinations and the various pathological processes of the region, namely the "opto-chiasmal arachnoiditis." In this direction, in 1959, Liliequist[5] simplified the classifications of the cisterns by recognizing three groups: the cisterns in the posterior cranial fossa, the suprasellar cisterns, and the cisterns in the tentorial notch including the cisterna corporis callosi. It is easy to appreciate how the current classification of arachnoid cysts (see Chapter 7) corresponds well to Liliequist's concepts, with the exception of the cisterna Sylvii. The sylvian fissure cistern, in fact, was not regarded by the author as a true cistern, but rather a transitional type of subarachnoid space between the sulci on the brain surface and the cisterns. In this publication devoted to illustrating the anatomy of the subarachnoid cisterns, Liliequist[5] stressed that "in the first stage of an encephalographic examination the flow of air is sometimes stopped by an obstruction at the level of the dorsum sellae" and that other parts of the subarachnoid space of the sellar region could be visualized only following a further injection of air. The obstacle to the passage of air (which was, however, noticed in only 25 subjects out of the 54 men and 66 women, aged from 15 to 68 years, considered by the author for his study) was seen in the presence of a membrane—subsequently designed as Liliequist's membrane—extending between the two oculomotor nerves and between the dorsum sellae and the posterior hypothalamus. Actually, such a membrane, which represented the boundary between the interpeduncular and chiasmatic cisterns, had been already identified by Key and Retzius[1] by

Table 8.1. Classifications of cisterns.

Key and Retzius, 1875 (ref. 1)
1. Cisterna cerebellomedullaris
2. Cisterna pontis with a pars medialis and partes laterales
3. Cisterna intercruralis
4. Cisterna chiasmatis
5. Cisterna laminae cinerae terminalis
6. Cisterna corporis callosi or spatium subarachnoidale corporis callosi
7. Spatium subarachnoidale corporum quadrigeminorum
8. Cisterna ambiens
9. Cisterna fossae Sylvii
10. Velum triangulare

Locke and Naffzinger, 1924 (ref. 2)
1. Cisterna magna cerebellomedullaris
2. Cisterna basalis with a pars pontis, pars interpenduncularis, and pars chiasmatis
3. The paired cerebrocortical channels
4. The paired internal channels
5. The paired lateral cerebellocortical channels
6. The single sagittal channels: the cerebrosagittal and cerebellosagittal channels

Spatz and Stroescu, 1934 (ref. 3)
1. Cisterna magna cerebellomedullaris
2. Cisterna pontocerebellaris
3. Cisterna basalis
4. Cisterna fissurae lateralis
5. Cisterna fissurae interhemisphericae
6. Cisterna fissurae transversae

Liliequist, 1959 (ref. 5)
1. The cisterns in the posterior cranial fossa
2. The suprasellar cisterns
3. The cisterns in the tentorial notch including the cisterna corporis callosi

gross anatomical dissection, and has been described more recently in papers devoted to the microsurgical anatomy of the chiasmatic region.[6,7]

The role of the membrane of Liliequist in the genesis of the cystic lesions of the chiasmatic region is still a subject of debate. For some authors, the arachnoid cysts of the sellar region should be actually regarded as false arachnoid cysts, being rather a diverticulum or an outpouching of Liliequist's membrane, when the permeability of this structure is lessened by previous hemorrhage, infection, or maldevelopment.[8] The observations of suprasellar and/or retrosellar cysts in children with a known history of trauma and meningitis, as well as of cysts filling with air via the interpeduncular cistern at pneumoencephalography,[9–11] have been advocated in support of the aforementioned hypothesis.[8] Also the direction of the expansion of suprasellar cysts, mainly upward, is indicative for some authors[12] that these cysts do actually represent progressively enlarging arachnoid pouches. In fact, although Binitie et al.[12] deny that presence of an identifiable anatomical structure, such as the membrane of Liliequist, is necessary in order to explain the occurrence of suprasellar cysts, they do believe that this type of lesion results when the pulsatile energy of the cerebrospinal fluid (CSF), brought about by repeated alterations in venous pressure, is "entrapped upward by any kind of membrane adhesions in the sellar region, secondary to hemorrhage, infection, or some variety of maldevelopment".[12]

However, noncommunicating suprasellar arachnoid cysts have been unequivocally described by various authors, both in operated on subjects and in postmortem studies.[10,13–17] Nevertheless, in some of these cases, the presence of glial elements on the cystic walls has thrown some doubts on the purely leptomeningeal nature of the lesion. In fact, Harrison[10] in 1971 first questioned whether these cysts could arise from glial cell rests in the leptomeninges, but other authors[16] have suggested that the glial component represents merely a secondary invasion of the cyst wall following a break in the pia caused by the pressure of the arachnoid cyst against the neighboring neural structures.

As opposed to the suprasellar, retrosellar, or parasellar arachnoid cysts, the existence of true or primary intrasellar arachnoid cysts has been denied, on the grounds of anatomical observations that indicated that the leptomeninges surround only the infundibulum and do not usually extend into the sella turcica.[16,18] Even in normal subjects, however, neuroimaging studies often demonstrate that the basal cistern may protude into the sella via the central opening in the dura mater of the diaphragma sellae, which allows the infundibulum to pass through into the pituitary fossa. This endosellar "physiological" protrusion of the basal cistern, which has been denominated

as "intrasellar arachnoid diverticulum" or "intrasellar subarachnoid space,"[19] does not act as a space-occupying lesion. In cases of necrosis or atrophy of the pituitary gland, such as occurs in patients with so-called empty sella syndrome, or in subjects who have undergone the surgical extirpation of the gland or its irradiation for pituitary tumor, the protrusion of the basal cistern may occupy practically the whole sellar cavity.[20]

In other cases, the abnormal protrusion of the basal cistern into the pituitary fossa may depend on a low attachment of the diaphragma sellae or a herniation of the arachnoid membrane through an excessively large central opening in the diaphragma sellae.[21,22] Though this kind of phenomenon has been improperly described by some authors under the denomination of arachnoid cyst,[23] the currently available diagnostic tools may easily demonstrate the communication of the herniated intrasellar space with the subarachnoid space of the skull base in the majority of subjects, thus ruling out any possible confusion. A similar observation could be made for those intrasellar arachnoid diverticula that tend to progressively enlarge under the effect of a relative increase in intracranial mean and/or pulse pressure, probably through a flap-valved mechanism involving the arachnoid that has herniated through the aperture in the diaphragma sellae.[24,25] The differential diagnosis could be more difficult when the communication between the intracranial and intrasellar spaces closes, for example, because of arachnoid bridges or inflammatory adherences that seal the neck of the diverticulum,[26] so that the typical, empty sella apparently becomes an enclosed "arachnoid" cyst.[27–32]

Undoubtedly, true intrasellar arachnoid cysts are very rare and their pathogenesis remains unclear. Probably, these cysts could be likened to those developing extradurally at the spinal level,[32] rather than explained on the basis of the most credited mechanism that gives rise to the endocranial intradural arachnoid cyst, i.e., the duplication of the arachnoid membrane. However, this latter mechanism has been propounded by some authors even in recent years, together with the possibility of an origin from aberrant arachnoid remnants below the diaphragma sellae.[23,33,34]

Incidence and Age and Sex Distribution

Arachnoid cysts occurring in the chiasmatic region are usually divided into two groups: the suprasellar cysts developing above the diaphragma sellae, and the intrasellar cysts that are found within the sellar cavity. The latter are far less frequent than the former, and practically absent in children. Indeed, the mean age at clinical presentation for this type of lesion has been evaluated to be around 42.2 years.[35] On the other hand, the suprasellar variety may be regarded as a typical condition of the pediatric age. In 1982, for example, Hoffman and coworkers[36] reported on a personal series of eight cases, and on 46 cases (34 of which were prior to the era of com-

Table 8.2. Age distribution of suprasellar arachnoid cysts.

Author (Reference no.)	No. of cases	1 year	1–5 years	6–10 years	11–15 years	16–20 years	Over 20 years
Hoffman et al., 1982[36]	54*	18.5%	29.6%	|←	38.9%	→|	13%
Gonzalez et al., 1982[37]	3	66.6%			33.4%		
Harsh et al., 1986[69]	4	25.0%	25.0%	50.0%			
Pierre-Kahn et al., 1990[40]	20	20.0%	50.0%	25.0%	5.0%		
Personal series	14	78.6%	14.3%	7.1%			

*46 cases collected from the literature (the relative percentage does not represent the actual distribution in children, as they comprise also adolescents and adults).

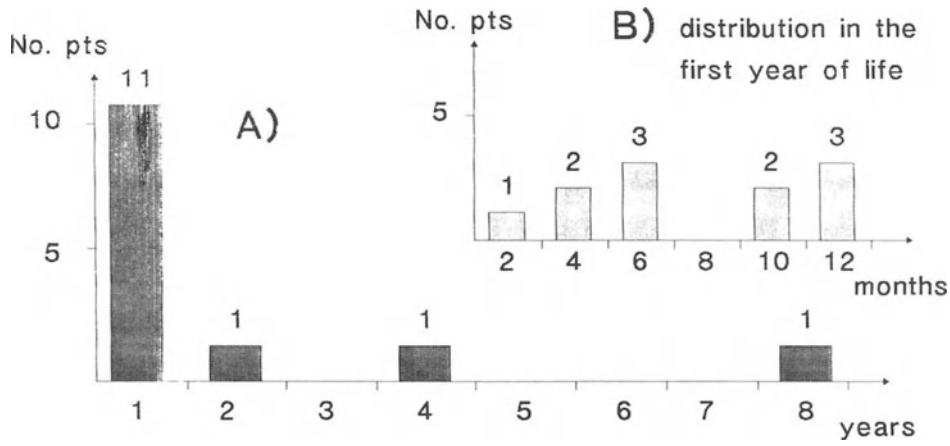

Figure 8.1. Age distribution of suprasellar arachnoid cysts in children (personal series).

puted tomography) collected from the literature. The authors found the following distribution: 18.5% in infants under 1 year old; 29.6% in children ranging in age between 1 and 5 years; 38.9% in children between 6 and 20 years; and 13% in subjects older than 20 years of age (Table 8.2). With the advent of computed tomography and ultrasonography, the mean age at diagnosis has become significantly lower, so that in our series of 14 children operated on in the last 10 years the great majority of cases (78.6%) were treated under 1 year of age (Table 8.2 and Figure 8.1). It is worth noting that in 2 of our 14 cases the diagnosis was made in utero.

A second consequence of the wide use of

Table 8.3. Relative incidence of suprasellar arachnoid cysts among supratentorial arachnoid cysts in children.

Author (Reference no.)	No. supratentorial cysts	No. suprasellar arachnoid cysts	%
Anderson and Landing, 1966*[23]	8	0	—
Harrison, 1971[10]	9	5	56
Danziger and Bloch, 1975[11]	10	2	20
Aicardi and Bauman, 1975[59]	12	0	—
Choux et al., 1978*[1]	36	5	14
Leo et al., 1979[63]	4	2	50
Menezes et al., 1980*[66]	18	2	11
Stein, 1981[67]	7	0	—
Gonzales et al., 1982[37]	20	3	15
Cilluffo et al., 1983*[11]	9	1	11
Serlo et al., 1985*[71]	10	0	—
Lodrini et al., 1985*[70]	18	6	33
Choux et al., 1987*[21]	49	15	31
Locatelli et al., 1987*[44]	20	0	—
Raffel and McComb, 1988[70]	27	5	19
Marinov et al., 1989*[73]	42	11	26
Ciricillo et al., 1991*[47]	28	5	18
Personal series	62	14	23
Total	389	76	20

*These reference are in Chapter 7.

modern diagnostic techniques for neuroimaging is the apparently relative increase in incidence of suprasellar cysts compared with the other localization of supratentorial arachnoid cysts; in fact, suprasellar cysts once regarded as rare,[14,36–39] currently represent the second group in incidence (Table 8.3).

Both in literature [106 cases collected by Pierre-Kahn and coworkers[40]] and in our experience, males slightly outnumber females (male to female ratio 1.6 and 1.3, respectively).

Clinical Presentation

Due to their prevalently extracerebral location, suprasellar arachnoid cysts may remain in some cases clinically silent, even when they have increased to a relatively large volume within the chiasmatic cistern. In such cases, a diagnosis may be accidentally reached during routine ultrasonographic examinations performed during the prenatal period (Table 8.4), or just after birth, if neuromorphological investigations are carried out because of head injury. However, in most children the presence of the lesion is suggested by signs of increased intracranial pressure, endocrinological disturbances, abnormal ocular movements, and visual impairment[10,15,32,36,37,40–42] (Table 8.4).

The major clinical manifestations may appear as only isolated occurrences in a given patient, or else combined in different clinical pictures, depending on the prevalent direction of growth of the cyst as well as on the rapidity of its enlargement.

Usually, suprasellar arachnoid cysts expand in all directions; laterally, they can grow into one or both temporal fossae and posteriorly into the interpeduncular and prepontine cisterns, behind the clivus. When the suprasellar arachnoid cysts develop upward in the direction of the third ventricle, they gradually replace the space occupied by this structure by pushing its floor upward (Figure 8.2). Hydrocephalus, which frequently accompanies the arachnoid cysts developing in the region of the chiasmatic cistern, is believed to ensue when the foramina of Monro and/or the basal cisterns are obstructed because of the cyst expansion.[10,32,42] In fact, when upward expansion into the third ventricle occurs, the ventricular floor together with the fornices and the septum pellucidum are pushed up against the corpus callosum, thus obstructing both foramina of Monro. Furthermore, the rostral mid-

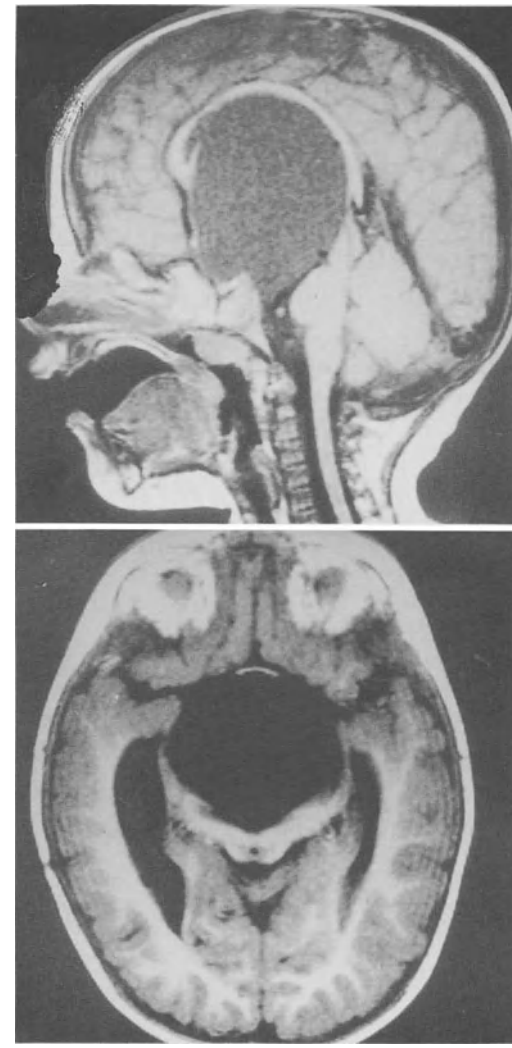

Figure 8.2. MRI of a suprasellar arachnoid cyst. Note the huge extension of the cyst into the region of the third ventricle (sagittal view) and interpeduncular cistern (axial view). The presence of the associated hydrocephalus is suggested by the dilated temporal horns.

Table 8.4. Clinical manifestations of suprasellar arachnoid cysts (literature and personal series).

Author (Reference no.) [No. cases]	Series summarized by Hoffman et al.[36] (up to 1981) [46]	Hoffman et al.[36] [8]	Gonzalez et al.[37] [3]	Albright[53] [1]	Cilluffo et al.*[11] [1]	Giroud et al.[73] [1]	Pierre-Kahn et al.[40] [20]	Ciricillo et al.*[47] [5]	Personal series [14]	Total [99]
Hydrocephalus	40	7	3				16	3	8	77
Increased HC	23	8	3				13	2	9	58
Symptoms of ↑ ICP	14		3				5	3	4	29
Endocrine dysfunction	13	1			1		9	1	7	32
growth retardation	8	1			—		4	—	7	20
precocious puberty	5	—			1		4	1	—	11
ACTH deficiency	—	—			—		1	—	—	1
Ocular manifestations	11	5	1	1	1		7	1	3	30
↓ visual acuity	11	5	1	1	1		5	1	1	26
nystagmus	—	—	—	1	—		—	—	2	3
strabismus	—	—	—	—	—		—	—	1	1
Neurological signs	11	4	1	1	1		11		7	36
ataxia	11	4	1	1	1		6		5	29
pyramidal signs	—	—	—	—	—		11		2	13
Bobble-headed doll syndrome	9			1		1	3	1		15
Psychomotor retardation			1	1	1		2	4	6	15
Epilepsy			1			1		1	1	4
Prenatal diagnosis									2	2

*These references are in Chapter 7.
HC, head circumference; ICP, intracranial pressure.

brain is dislocated dorsally and posteriorly, thus compressing the aqueduct of Sylvius.

For some authors,[12] however, the relationship between suprasellar arachnoid cysts and hydrocephalus is more complex than the mere result of an obstruction in the CSF pathways. A common pathogenetic cause, for instance some generalized defect of development accounting for both the phenomena, has been advocated as well as the possibility that a hydrocephalus preceding the formation of the cyst could favor its origin and further expansion. This would occur by means of three main mechanisms: an inpushing of the floor of the third ventricle, an obstacle in the CSF movement created by the tendency of the enlarged temporal horn to become jammed into the incisura, and an increase in the energy of CSF pulse pressure, transmitted to the arachnoid cysts, when the dampening effect of the intrathecal veins is diminished because of the flattening of these collapsible structures due to the ventricular dilation. The superior and posterior expansion of suprasellar arachnoid cysts may induce a stretching and eventual disruption of the pituitary stalk and a compression of the inferomedial portions of the thalami, the tuber cinereum, and mammilary bodies, thus explaining the endocrinological dysfunction that may be demonstrated in a significant percentage of the affected subjects. Hypopituitarism, growth retardation, and isosexual precocious puberty represent the most common clinical manifestations of the endocrinopathy induced by a suprasellar arachnoid cyst.[14,36,43,44]

The optic nerve and the chiasma may be stretched over the cyst wall, with variable effects on visual function. In most cases the visual impairment is characterized by the unilateral or bilateral decrease in visual acuity and/or bitemporal hemianopsia. A typical, though rare, presentation is the so-called bobble-headed doll syndome, which was first described by Benton and coworkers in 1966,[45] and subsequently reported by other authors,[46–54] in subjects with suprasellar arachnoid cysts or enlarged third ventricle and hydrocephalus. The syndrome derives its definition from the typical nodding or bobbing motion of the head, which consists of irregular involuntary movements in the anteroposterior direction, occurring two or three times per second and resembling those of dolls with a weighted head resting on a coiled spring.[32]

The to-and-fro bobbing of the head (and, in some cases, of the trunk) characterizes the subjects when standing, whereas it is usually absent during sleep. The rhythmic movements can be interrupted voluntarily only for short periods of time. The syndrome has been nearly always described in the pediatric age group: 16 out of the 17 cases collected by Jensen and coworkers[52] were children, with a mean of age of 7 years. Males predominated over females with a 2:1 ratio. Some affected subjects present a variable degree of mental retardation. The physiopathogenesis of the bobble-headed doll syndrome is still not understood, even though it has been believed to depend on the abnormal pressure exerted by the cyst on the enlarged third ventricle and on the dorsomedial nucleus of the thalamus.[55] The clinical manifestations are found only in chronic cases; in fact, an acute onset of the syndrome has been never reported.[52]

Finally, as in other subjects with hydrocephalus, ataxia of gait is also a relatively common presenting sign in children with suprasellar arachnoid cysts.[36]

Diagnosis

In the late 1970s and early 1980s, various papers appeared in the literature emphasizing the role of computed tomography (CT) in the diagnosis of suprasellar arachnoid cysts, and their differentation from an enlarged third ventricle in cases with an associated hydrocephalus.[7,36,41,56–58] Prior to this type of examination, the presence of the lesion could be only indirectly detected by investigations such as plain skull x-ray films (J-shaped sella turcica), isotopic brain scan (silent area or area of increased uptake), ventriculography (upward displacement of the floor of the third ventricle, upward and backward displacement of the aqueduct), air encephalography (lack of visualization of the suprasellar portion of the

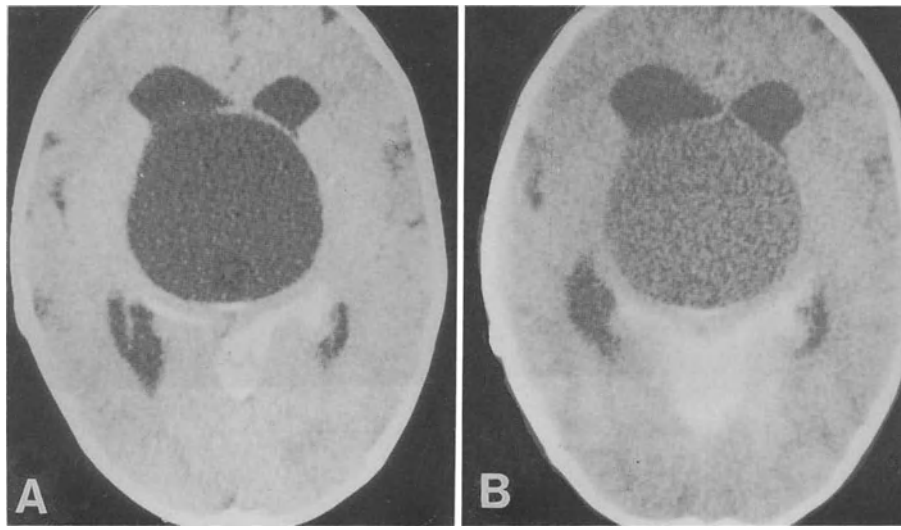

Figure 8.3. Metrizamide-enhanced CT scan of a suprasellar arachnoid cyst in a 12-month-old boy. Following metrizamide injection into the subarachnoid lumbar space, the contrast medium diffuses within the subarachnoid space and outlines the "negative" image of the cyst (A). In the late phase of the examination the contrast medium penetrates partially the cyst wall and the density of the cyst fluid increases (B).

chiasmatic cistern), and cerebral angiography (elevation of the horizontal portions of the anterior cerebral artery, lateralization of the internal carotid arteries, enlargement of the circle of Willis, elevation and backward displacement of the internal cerebral vein, elevation of the basal vein of Rosenthal).[11,15,37,43,59]

Since Kasdon and coworkers in 1977,[56] first reached the preoperative diagnosis of a suprasellar arachnoid cyst by means of CT, the examination has been substituted for practically all the other diagnostic tools. The most prominent findings on CT in cases of suprasellar arachnoid cysts is the presence of an oval-to-round, large, midline cystic lesion in the region of the third ventricle, containing fluid of CSF density (Figure 8.3A). The lucency of the cyst, when seen combined with the images of the dilated frontal horns of the lateral cerebral ventricles in children with an associated hydrocephalus, may give rise to radiological images similar to the head of a "bunny," or resembling the silhouette of the cartoon character Mickey Mouse[41] (Figure 8.3A).

Though CT is an excellent method for detecting a suprasellar arachnoid cyst, some authors have stressed its limit in two conditions: in the presence of a dilated third ventricle or in the presence of other cystic lesions of the region such as Rathke's cleft cysts, cystic craniopharyngiomas, epidermoid cysts, and cystic gliomas.[60,61] In the latter, additional radiological findings such as density differences of the fluid content, presence or absence of enhancement after contrast medium injection, and calcifications in the cystic wall may facilitate the differential diagnosis in several instances.

On the other hand, the differential diagnosis with a dilated third ventricle may remain difficult, as demonstrated by cases in which the cyst is recognized only after having shunted the coexisting hydrocephalus.[40,62] Although the size and shape of the lesion as well as the secondary changes induced on the ventricular conformation may often favor the correct diagnosis, the most practical method of differentiation is the injection of contrast medium (metrizamide) directly into the lateral ventricles or into the lumbar subarachnoid spaces. Metrizamide ventriculography may be necessary when the aqueduct is functionally obstructed by the pressure exerted by the cyst; following the injection of contrast medium,

there is an opacification only of the lateral cerebral ventricle because of the impairment in the CSF circulation at the foramina of Monro.[36,63] Also metrizamide cisternography may be utilized for the diagnosis; following the injection at the lumbar level, the contrast medium diffuses rapidly within the subarachnoid spaces and penetrates the ventricular system, when the aqueduct is not completely obstructed, outlining the negative image of the cyst (Figure 8.3A). In the final stages of the examination (8 to 12 hours) there is a kind of inversion of the CT image, as the contrast disappears from the subarachnoid spaces while the density of the fluid inside the lesion increases (30 to 40 units). This finding corresponds to a partial penetration of the cyst by the metrizamide (Figure 8.3B). After 24 hours the contrast agent also disappears from the interior of the cystic cavity.[64,65]

Besides its high reliability in differentiating arachnoid cysts from other intracranial cystic lesions, magnetic resonance offers the great advantage of multiplanar images. In particular, the sagittal images provide the best evaluation of the relationship between a suprasellar cyst and the third ventricle, to be utilized for planning the surgical treatment (Figure 8.2). During prenatal life and in the neonatal period and infancy, ultrasound technique may further contribute to the diagnosis (Figure 8.4A). The same examination may also be utilized in order to control the result of the surgical treatment as well as the evolution of the associated ventricular dilation (Figure 8.4B).

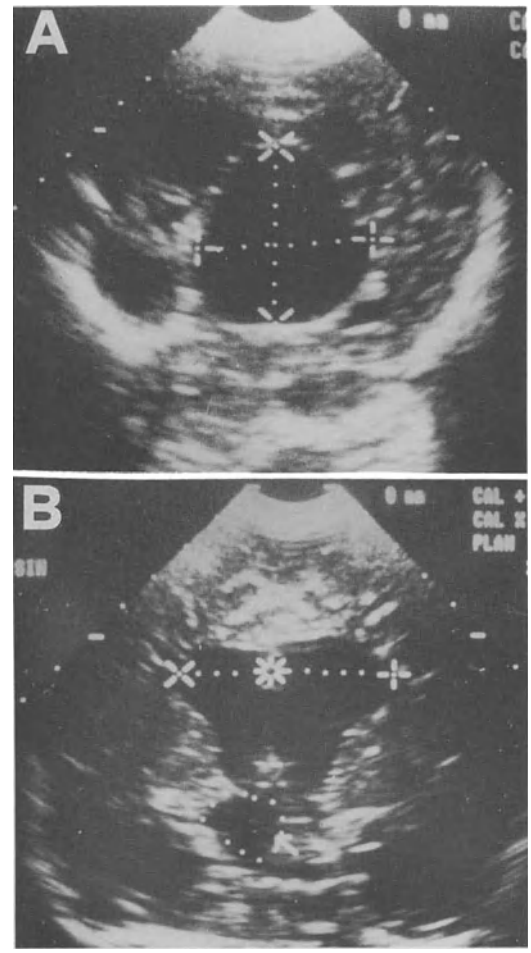

Figure 8.4. A 4-month-old baby with suprasellar arachnoid cyst diagnosed by means of ultrasound examination, performed through the anterior fontanel (A). The same investigation repeated 3 weeks after surgery (B) demonstrates the marked reduction of the size of the cyst and the relative increase of the ventricular volume.

Management and Results

The surgical treatment of suprasellar arachnoid cysts includes a variety of options, from the simple bypass shunting of the cyst and/or the associated hydrocephalus, to the resection of the cyst wall by means of craniotomy (Table 8.5). The lack of reliable preoperative criteria that may predict the result of any one specific surgical procedure in a given patient accounts for the various approaches that have been proposed for the treatment of the lesion. For the same reason, it can be easily understood, why most surgeons have experienced a change in their attitude toward this type of lesion during the course of their professional career.

The shunting only of the associated hydrocephalus has been practically abandoned, since in several cases the procedure was seen to determine the reduction in size of the cerebral ventricles, without altering the volume and the shape of the cyst itself.[60] In some cases, a worsening in clinical condition was

Table 8.5. Surgical options in the management of suprasellar arachnoid cysts.

1. Bypass shunting of the associated hydrocephalus
2. Bypass shunting of the cyst
3. Bypass shunting of the cyst and associated hydrocephalus by means of two independent devices
4. Bypass shunting of the cyst and associated hydrocephalus by means of a unique device
   - 4.1 Two intracranial catheters: one from the cyst, the second from one cerebral ventricle connected with a Y connector
   - 4.2 One intracranial catheter, draining simultaneously the cyst and the ventricular system
5. Direct excision of the membrane by means of craniotomy
   - by subfrontal route
   - by transventricular-transcortical route
   - by transcallosal route
   - by temporal route
     - (a) opening of the cyst into the chiasmatic cistern
     - (b) opening of the cyst into the third ventricle
6. Excision of the cyst membrane and placing of a shunt catheter in the cyst bed ending into one lateral ventricle (or connected to an extrathecal catheter)
7. Excision of the cyst membrane and shunting of the associated hydrocephalus (also, in the reverse order)

observed after the ventricular drainage, due to the progressive enlargement of the cyst.[40] However, the shunting of the associated hydrocephalus, nearly always by means of a ventriculoperitoneal shunt, is required in a large percentage of cases where the wall of the cyst has been excised or fenestrated. The phenomenon may be given a dual interpretation. The persistence of the hydrocephalus may depend on the incomplete removal of the cystic membrane, with a residual obstacle in the CSF circulation sufficient to maintain the ventricular dilation. On the other hand, the need for CSF drainage may reflect a generalized defect in the CSF absorption; in such cases the suprasellar arachnoid cyst would be merely an epiphenomenon of a more complex pathologic event, and the removal of the cyst wall would not assure the complete cure of the affected subjects.

The main advantage of shunting the cyst is that it is a relatively safe surgical procedure compared with the more difficult operations requiring craniotomy[66–69] (Figure 8.5). The disadvantages consist in the known complications of the CSF shunting devices (mechanical and infective complications) that may require one or more revision procedures. For example, 41.7% of the subjects reported by Raffel and McComb[70] in 1988 who underwent

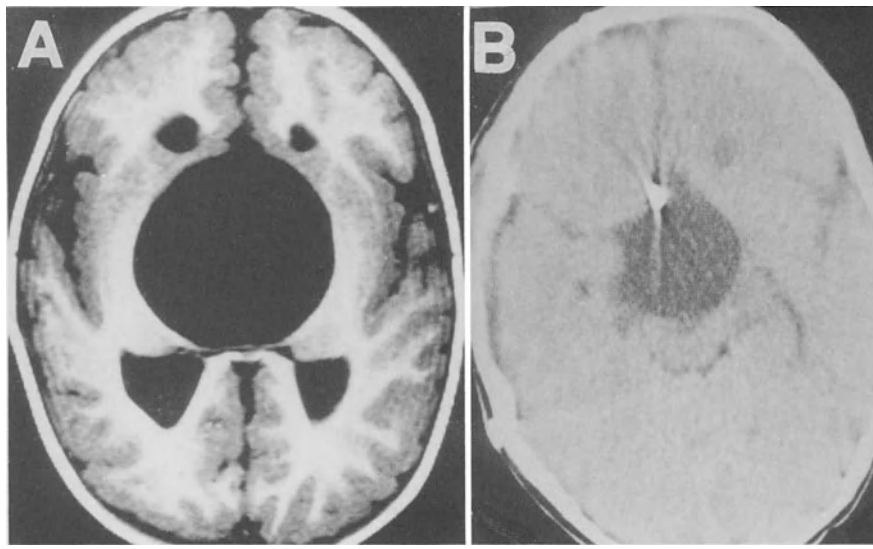

Figure 8.5. A 6-month-old boy with suprasellar arachnoid cyst. Preoperative MRI (A) shows the huge extension of the cyst. A cystoperitoneal shunt insertion has been followed by a marked reduction in the size of the cyst, as demonstrated by the postoperative CT scan (B).

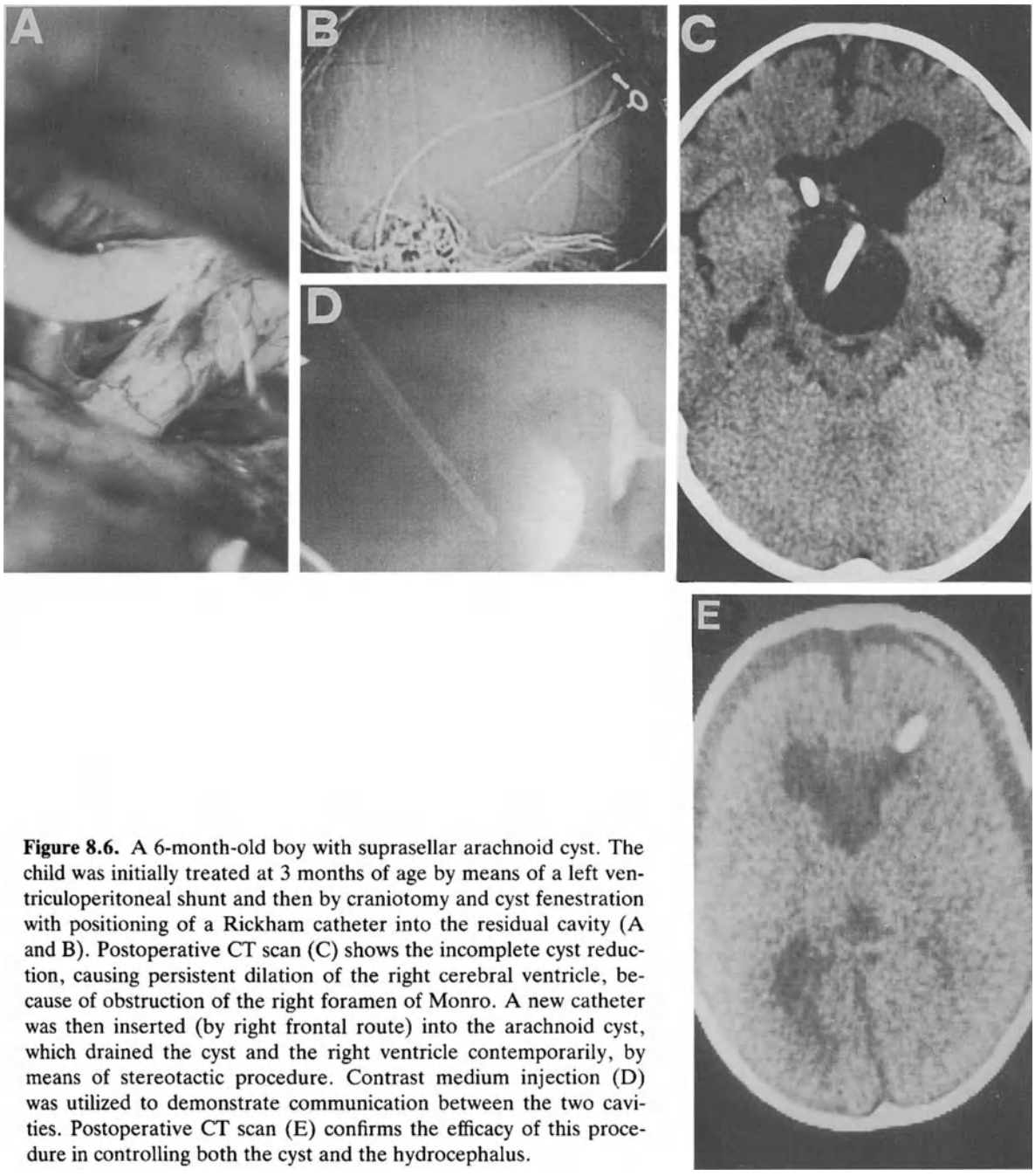

Figure 8.6. A 6-month-old boy with suprasellar arachnoid cyst. The child was initially treated at 3 months of age by means of a left ventriculoperitoneal shunt and then by craniotomy and cyst fenestration with positioning of a Rickham catheter into the residual cavity (A and B). Postoperative CT scan (C) shows the incomplete cyst reduction, causing persistent dilation of the right cerebral ventricle, because of obstruction of the right foramen of Monro. A new catheter was then inserted (by right frontal route) into the arachnoid cyst, which drained the cyst and the right ventricle contemporarily, by means of stereotactic procedure. Contrast medium injection (D) was utilized to demonstrate communication between the two cavities. Postoperative CT scan (E) confirms the efficacy of this procedure in controlling both the cyst and the hydrocephalus.

a shunting operation because of an arachnoid cyst necessitated one further procedure of revision of the CSF shunt assembly, and 25% required more than three revisions. In our series 3 (23%) out of our 13 children with suprasellar arachnoid cysts who have been treated through a direct surgical attack of the lesion with excision or fenestration of its wall required a subsequent operation of CSF shunting either of the associated hydrocephalus or both the cystic lesion and the hydrocephalus. One child was treated directly

by means of a cystoventriculoperitoneal drainage using the stereotactic technique, as suggested by Harsh and coworkers[69] (Figure 8.6). In fact, owing to the relatively high proportion of children with suprasellar arachnoid cysts who subsequently need the insertion of a CSF shunt device, these authors have proposed proceeding directly to a combined cystoventriculoperitoneal shunt, a procedure that can be facilitated by using ultrasound guidance or the stereotactic technique.

A variant of this approach is that proposed by Kasdan and coworkers[56], who indicated the advantage of leaving a separate tube in the residual cavity of the cyst when adopting a direct approach to the lesion, to be then connected to the subscalp area for later conversion to a definitive extrathecal shunt, if necessary. This suggestion requires careful attention when considering that the wall of suprasellar cyst may be thicker and more rigid than that of arachnoid cysts in other intracranial regions (Figure 8.7), so that the cyst may not collapse even after a wide fenestration of its wall.

The possibility of avoiding shunt-dependency is the main advantage of procedures involving cyst wall excision, fenestration, or marsupialization, through either a subfrontal, transventricular, or transcallosal, and less often, temporal route, (Figure 8.8), which have been proposed by various authors.[36,57,58,71,72] In fact, findings of as high as 75% of children with arachnoid cysts, and without associated hydrocephalus, have been reported to benefit from this type of procedure, without any need for further operations.[70] However, in cases of suprasellar arachnoid cysts, the recurrence of the lesion after marsupialization or fenestration of its wall is quite common. Even though the subfrontal approach has been considered more reliable than the transcortical-transventricular approach, on the basis of an analysis of cases published in the literature up to 1980,[58] the subfrontal route is also weighted by a high recurrence rate of the cyst.

This complication has been given various interpretations Raffel and McComb,[70] for example, have hypothesized a direct role of the surgeon, as they correlated the success rate to the aggressiveness of the operation and to the ability to perform definitive resection and fenestrations of the cyst wall. On the other hand, Hoffman and coworkers[36] believe that

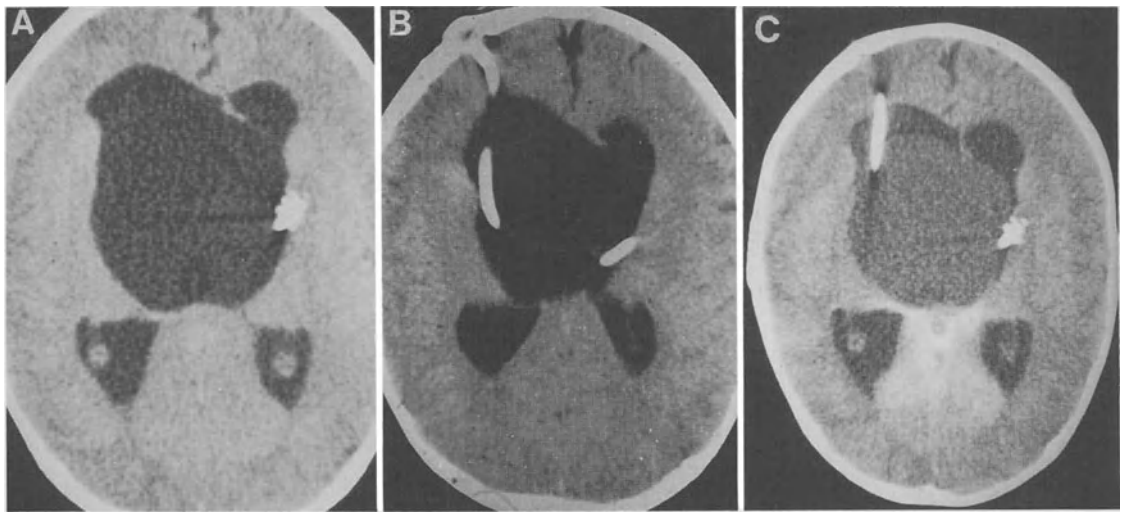

Figure 8.7. An 8-month-old boy with suprasellar arachnoid cyst. The attempt to drain the cyst into the peritoneal cavity through percutaneous route was unsuccessful. In fact, the cranial catheter failed to penetrate the thick cyst wall, penetrating into the lateral cerebral ventricle (A and B). The surgical failure is further demonstrated by metrizamide cisternography (C).

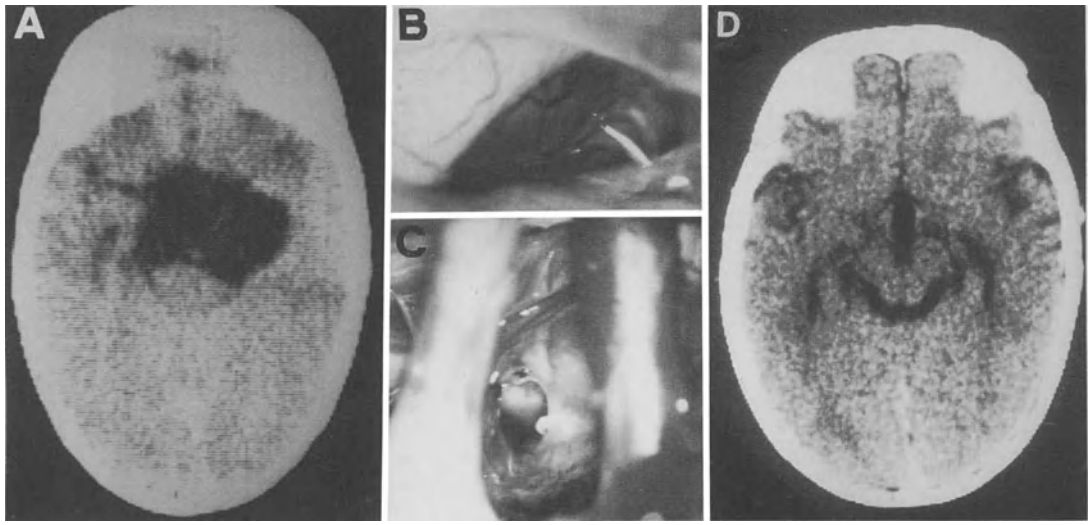

Figure 8.8. A 1-year-old boy with suprasellar arachnoid cyst. The preoperative CT scan (A) shows the cyst extending into the right temporal region. The cyst was directly excised by means of a pterional approach (B and C). The postoperative CT scan (D) demonstrates the efficacy of the surgical procedure.

the main cause of failure is the relative inability of the chiasmatic region to accommodate the diversion of fluid from inside the cyst, thus opposing the view of Fox and Al-Mefty,[8] and Raimondi and coworkers,[58] on the role of an imperforated membrane of Liliequist in the genesis of the lesions. Hoffman and coworkers[36] have stressed the good results obtained by using a transcallosal approach to open the dome of the cyst into one lateral ventricle. This view has been confirmed in recent years by Pierre-Kahn and coworkers[40] who have described a procedure of percutaneous ventriculocystostomy under ventriculoscopic guidance, which in their hands has assured a high rate of success. The operation is carried out by means of a leukotome introduced through a paramedian coronal burr hole; the dome of the cyst is reached and perforated using monopolar coagulation, via the frontal horn and the foramen of Monro, after having visualized the ventricles by metrizamide. According to these authors, the intracranial pressure is normalized and the patient's IQ or DQ improved after the operation, in spite of the fact that the cyst is only partially reduced in size and the cerebral ventricles remain larger than normal. It is worth noting that most authors agree on the limited possibility of curing the symptoms of the bobble-headed doll syndrome by means of the surgical detension of the cyst, even though some success has been reported in single cases.[52,53,73]

Conclusions

Suprasellar arachnoid cysts should be considered separately from the intracranial arachnoid cysts occurring in other regions. First of all, this type of cyst is becoming relatively frequent; nowadays, the diagnosis is usually reached prenatally or in the very early days of life. Besides detecting the lesion in a larger number of subjects, modern neuroimaging techniques facilitate a precise evaluation of the anatomical relation of the cyst with the vitally important surrounding neural and vascular structures. However, in spite of the improvement in diagnosis and the numerous surgical options nowadays available,the management of the lesion still justifies controversial attitudes. The difficulties experienced by

the surgeon in planning the best possible care depend mainly on the uncertain relationship between the cyst and a frequently accompanying hydrocephalus. Although the two conditions may be corrected by only one operation in some children, in others they each require a specific and separate treatment. Unfortunately, at the present time neither of the two categories of patients can be detected preoperatively with sufficient reliability.

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CHAPTER 9

Infratentorial Arachnoidal Cysts

Concezio Di Rocco, Massimo Caldarelli, and Antonello Ceddia

Introduction

Owing to the wide variety of cystic malformations occurring within the posterior cranial fossa, the recognition of arachnoid cysts in the region may still be difficult even when the modern diagnostic tools for neuroimaging are available. An appropriate knowledge of the developmental morphology of the nervous structures and of the ventricular and subarachnoid spaces of the posterior fossa is required for the neuroradiological diagnosis as well as for the therapeutic indications.

Definition, Incidence, and Age and Sex Distribution

For most authors, posterior fossa arachnoid cysts represent an abnormal expansion of the subarachnoid space within the cisterna magna,[1] which depends on the defective development of the roof of the fourth ventricle and adjacent meningeal structures. This malformative process takes place between the 7th and 10th week of embryonic life, in the same way as other cystic malformations of the posterior fossa, namely the Dandy–Walker malformation and the Dandy–Walker variants. Posterior fossa arachnoid cysts are not, however, associated with any vermian abnormality. On the other hand, the Dandy–Walker malformation and the Dandy–Walker variants are characterized by the partial agenesis of the vermis, which is accompanied by the absence of the foramen of Magendie in the former and by a normal communication between the fourth ventricle and the subarachnoid spaces in the latter.[1]

Correctly, the term *arachnoid cyst* should be reserved for those cases in which the cyst does not communicate with the subarachnoid spaces, with a possible compression of the surrounding anatomical structures. Such are the closed diverticula that develop within the cisterna magna when the roof of the fourth ventricle fails to become entirely permeable, and splits into two layers between which the cerebrospinal fluid (CSF) is "trapped" during the embryonic development.[2,3] This type of cystic lesion, however, cannot be morphologically distinguished from other posterior evaginations of the tela choroidea, which occur without gross abnormalities of the cerebellar vermis[1] and communicate with the perimedullary subarachnoid spaces. This second type of cystic malformation of the posterior fossa is often referred to as "retrocerebellar arachnoid cyst" or "cyst of the cisterna magna," though it is correctly distinguished from "true" arachnoid cysts by some authors, who use different definitions, such as "Blake's pouch" and "subarachnoid pouches."[4,5] The differentiation between the two entities is important as far as the actual incidence of arachnoid cysts of the posterior cranial fossa is concerned, taking into account that retrocerebellar arachnoid pouches are fairly common whereas arachnoid cysts are relatively rare. The distinction is far less important for the physiopathogenic interpretation, as the two entities are regarded by some authors to be basically different aspects of the same nosographic entity.[1,6,7] In fact, even in cases where the incomplete perforation of the

roof of the fourth ventricle is followed by the forming of a diverticulum within the cisterna magna, a later outward flow of CSF could still form a subarachnoid space enclosing the diverticulum, and may possibly exhibit a kind of communication with it.[8,9]

If the caudal evagination of the fourth ventricle fails to dissolve, thus forming a persistent Blake's pouch that extends into region of the cisterna magna, eventually pushing the caudal vermis rostrally (rhombencephalic roof "cyst"), the failure of the lateral recesses to perforate (the process that leads to the formation of the foramina of Luschka) may form a "cyst" in the cerebellopontine angle, which also maintains a free communication with the fourth ventricle and may clinically mimic an arachnoid cyst in this region. As for the equivalent midline lesion (persistent Blake's pouch), the presence of the choroid plexus and ependyma inside the cystic wall should allow the differential diagnosis from a "true" arachnoid cyst. However, the differentiation may be difficult or even impossible when this type of cystic malformation reaches a relatively large size; in such cases, in fact, the cystic wall becomes so stretched and thin as to be more or less denuded of its ependymal cells.

With the above-mentioned limitations in mind concerning the difficulties that may be experienced in the differential diagnosis, an analysis of the literature indicates that posterior fossa arachnoid cysts are rather uncommon compared to the more frequent supratentorial lesions (see Tables 7.1 and 7.2, Chapter 7), and relatively more rare in adults than in infants and children.[10–12] Concerning the pediatric age, in particular, out of 372 cases with intracranial arachnoid cyst collected from the literature, 83 children (22.3%) had the cyst localized within the posterior fossa. In our series, the proportion was 27% i.e., 23 cases, within the posterior fossa, and 73%; i.e., 62 cases, within the supratentorial compartment. Though posterior fossa arachnoid cysts may give symptoms at any age, in most instances they become symptomatic during infancy and childhood. More than half the cases, in fact, are already recognized during the first year of life (Figure 9.1) and the mean age at diagnosis in the pediatric series described in the literature is 38.5 months.[6,7,11,13–32]

Table 9.1. Sex distribution of infratentorial arachnoid cysts (from literature and personal series).

Author (reference no.)	No. of cases	Male	Female
Haller et al., 1971[19]	2	1	1
Conway et al., 1971[17]	3	0	3
Harrison, 1971[18]	5	3	2
Gilles and Rockett, 1971[6]	3	2	1
La Torre et al., 1973[20]	3	1	2
Little et al., 1973[21]	20	8	12
Williams and Guthkelch, 1974[22]	2	0	2
Danziger and Bloch, 1975[23]	2*	0	1
Mori et al., 1977[11]	10	8	2
Ito et al., 1977[24]	1	0	1
McCullough et al., 1980[26]	1	1	0
Vaquero et al., 1981[28]	6	3	3
Roach et al., 1982[29]	1	1	0
Galassi et al., 1985[7]	10	7	3
Harsh et al., 1986[31]	5	3	2
Locatelli et al., 1987[32]	10	3	7
Personal series	23	13	10
Total	107	54	52

*One case not specified.

With regard to sex distribution (Table 9.1) no clear prevalence of males or females can be established on the grounds of the analysis of the literature.

Variants

In papers dealing with patients of all ages, three main patterns of anatomical distribution are recognized: the cerebellopontine angle cysts, which represent about a third of cases; the midline region cysts (Figures 9.2 and 9.3), which account for about another third of cases; and the cerebellar hemisphere cysts (Figure 9.4), which correspond to about 20% of all the localizations.[21,33] In rare instances, arachnoid cysts of the posterior cranial fossa may extend at the level of the tentorial notch, into the cisterna of the superior cerebellar vermis, within the internal auditory canal, or may remain confined within the fourth ventricle.[10,21,33–36]

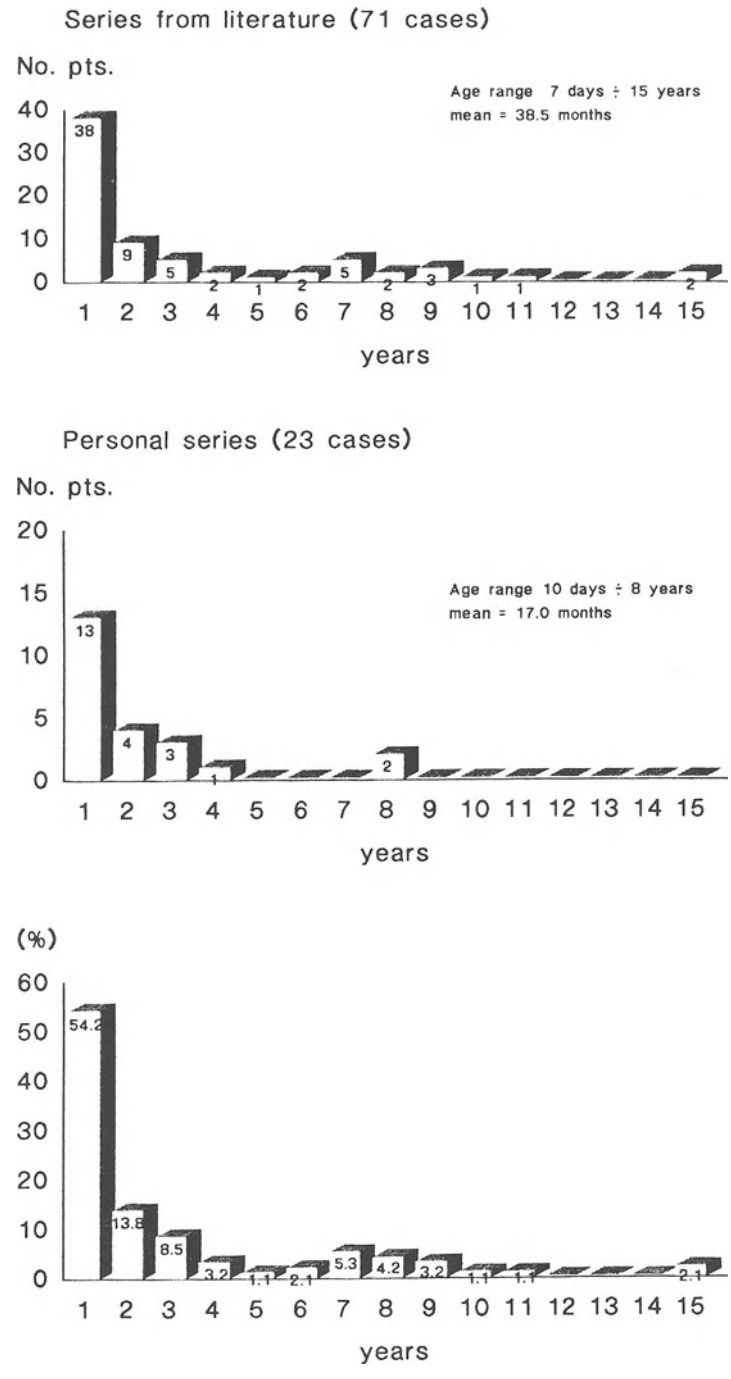

Figure 9.1. Age distribution of infratentorial arachnoid cysts.

Even though cerebellopontine angle cysts have also been described in the pediatric age group, including lesions localized within the internal auditory canal in children presenting with facial palsy,[37,38] this type of localization is considerably less frequent in the pediatric population than in adults. In children, infratentorial arachnoid cysts develop more commonly on the midline, between the two cerebellar hemispheres or at the level of the cisterna

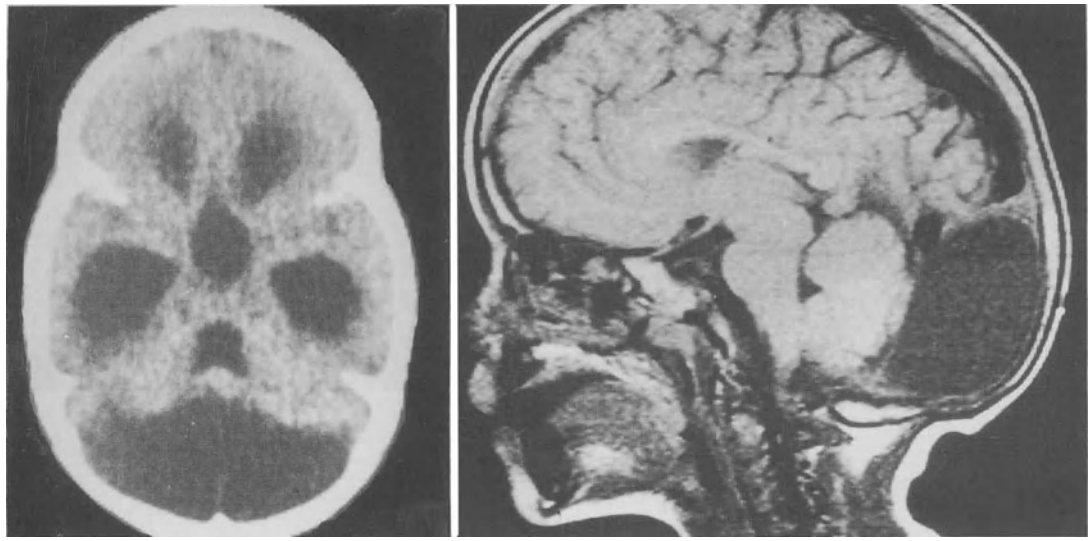

Figure 9.2. An 8-month-old boy with a midline posterior fossa arachnoid cyst. CT scan (left) and MRI study (right) demonstrate the mass effect of the lesion, which displaces the fourth ventricle and the cerebellar structures anteriorly.

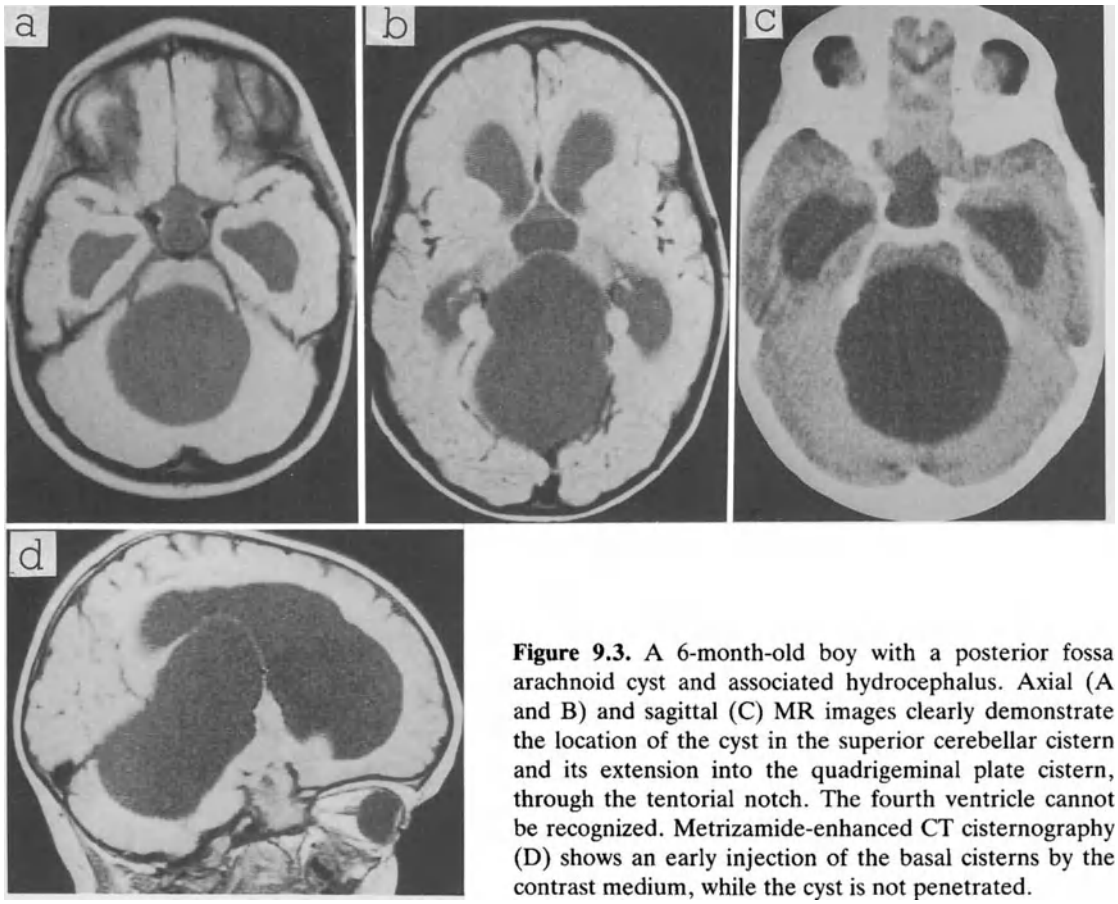

Figure 9.3. A 6-month-old boy with a posterior fossa arachnoid cyst and associated hydrocephalus. Axial (A and B) and sagittal (C) MR images clearly demonstrate the location of the cyst in the superior cerebellar cistern and its extension into the quadrigeminal plate cistern, through the tentorial notch. The fourth ventricle cannot be recognized. Metrizamide-enhanced CT cisternography (D) shows an early injection of the basal cisterns by the contrast medium, while the cyst is not penetrated.

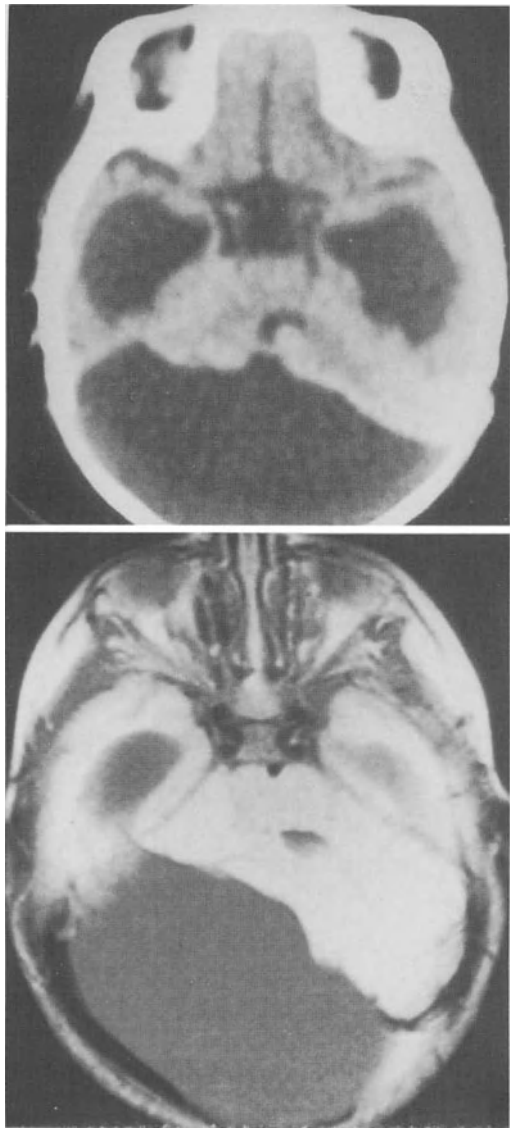

Figure 9.4. A 1-year-old girl with a posterior fossa arachnoid cyst. The CT scan (above) and MRI study (below) show the location of the cyst over the left cerebellar hemisphere; the fourth ventricle and the cerebellar structures are displaced forward and to the right; hydrocephalus is also present.

magna, and above one of the cerebellar hemispheres. In general, in the pediatric age group, the midline localization is found in a little more than two-thirds of the cases, whereas the lateral localization in a little less than one-third (Figure 9.5).

Clinical Presentation and Diagnosis

The great majority of cases of posterior fossa arachnoid cysts occurring in the pediatric population present with macrocrania and signs and symptoms of increased intracranial pressure, in most cases due to the common association with obstructive hydrocephalus (Tables 9.2 and 9.3).* Although hydrocephalus typically characterizes the cysts localized on the midline, this type of complication is frequently found also in patients in whom the lesion develops over the cerebellar hemispheres. In the latter, however, nystagmus and cerebellar signs may become essential features of the clinical presentation. Only rarely do posterior fossa arachnoid cysts induce a localized, unilateral, or bilateral bulging of the occipital squama, which brings to mind the more commonly observed bulging in children with Dandy–Walker syndrome. A significant proportion of the affected subjects exhibits a variable degree of psychomotor retardation; epilepsy is relatively rare.†

By evaluating the diagnostic procedures described in the literature as being utilized for the recognition of posterior fossa arachnoid cysts, the declining role of cerebral angiography is well apparent. This type of investigation, which is rarely performed nowadays, was thought in the early 1970s to provide key information for the diagnosis.[16,20,42] The main vascular changes associated with a posterior fossa arachnoid cyst were those suggesting an extra-axial retrocerebellar mass. Thus, the authors pointed out the anterior displacement of the posteroinferior cerebellar and the superior cerebellar arteries, the elevation of the torcular Herophili and the transverse sinuses, the oblique descent across the posterior cranial fossa of the transverse and sigmoid sinuses, the inverted angulation—from the normal posteroanterior to an abnormal anteroposterior direction—of the cerebellar cortical veins entering the superior sagittal sinus,[42] the elevation and posterior displacement of the choroidal point of the posteroinferior cerebellar artery, the inverted convexity of the vein

*Refs. 6, 7, 11, 17–20, 22–32, 39, 40.
†Refs. 7, 11, 18, 20, 32, 35, 39, 41.

Table 9.2. Clinical manifestations of infratentorial arachnoid cysts (from literature and personal series).

Author (reference no.) [No. of cases]	Haller et al.[19] [1]	Conway et al.[17] [3]	Harrison[18] [5]	Gilles and Rockett[6] [3]	La Torre et al.[20] [3]	Williams and Guthkelch[22] [2]	Danziger and Bloch[23] [2]	Mori et al.[11] [6]	Ito et al.[24] [1]	Menezes et al.[25] [9*]
Increased HC	1	2	5	3	3	1	2	3	1	3
Increased ICP	1		3	2	3	2	1	4	1	4
Developmental delay	1	1	3	1		1	2	3	1	1
Cerebellar signs			2			1		2		4
Cranial nerve deficits			1			1				2
Pyramidal signs				2						1
Epilepsy	1	2			1					
Nystagmus										2
Occipital bulging							1			
Other						1 PP	1			1 PP + DI

*HC, Head circumference; ICP, intracranial pressure; PP, precocious puberty; DI, diabetes insipidus.

Table 9.3. Relative incidence of clinical manifestations among midline and lateral infratentorial arachnoid cysts (from literature and personal series).

	Midline		Lateral	
Clinical manifestations	Personal series (15 cases)	Series from literature (73 cases)	Personal series (8 cases)	Series from literature (13 cases)
Increased head circumference	73%	75%	63%	38%
Increased intracranial pressure	60%	68%	38%	38%
Developmental delay	53%	40%	25%	31%
Cerebellar signs	33%	25%	63%	46%
Cranial nerve deficits	33%	7%	25%	8%
Pyramidal signs	33%	8%	13%	8%
Nystagmus	20%	5%	38%	8%
Epilepsy	20%	5%	13%	8%

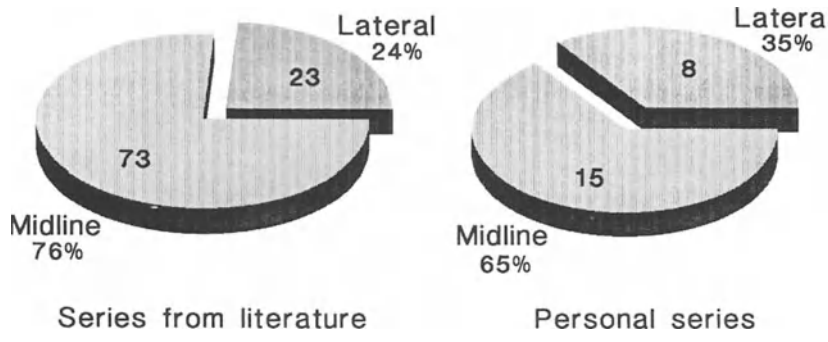

Figure 9.5. Anatomical distribution of infratentorial arachnoid cysts.

McCullough et al.[26] [1]	Stein[27] [5]	Vaquero et al.[28] [3]	Roach et al.[29] [1]	Serlo et al.[30] [2]	Galassi et al.[7] [4]	Harsh et al.[31] [5]	Locatelli et al.[32] [10]	Marinov et al.[39] [18]	Sweasey et al.[40] [1]	Personal Series [23]	Total [108]
1	5	2	1	1	4	2	4	14		16	75
1	5	2	1	1		4	3	14		12	64
		1			4	2	2	10		10	43
		2				1	1	8		10	31
					1					7	12
1		1			1					5	11
					1		1	1		4	11
		1						1		6	10
								5		2	8
		1			1		2		1 PP		8

of Rosenthal, resulting from the transtentorial displacement of the culmen monticuli,[16] and the forward and upward displacement of the vermian branches of the posterior cerebellar artery and vermian veins.[20] The diagnostic value of the above-mentioned changes was stressed by the evaluation of the vascular landmarks corresponding to either a normal or compressed fourth ventricle, as indicated by the vermian arteries and the veins of the lateral recesses.[24]

Pneumoencephalography and ventriculography were commonly utilized prior to the advent of the computed tomography (CT) scan. These examinations allowed a reliable diagnosis when the contrast medium penetrated into the cyst. On the other hand, the differential diagnosis with a posterior fossa tumoral mass could remain uncertain in cases of a noncommunicating cyst, when only the associated hydrocephalus or the forward displacement and/or partial occlusion of the aqueduct and fourth ventricle was demonstrated.[11]

At the present time, CT scan and magnetic resonance (MR) imaging represent the first-choice diagnostic procedures. The former examination clearly defines the extra-axial situation of the cystic lesion, with the same attenuation values of the CSF, and permits a precise definition of its size and anatomical relationship with the surrounding structures. A similar conclusion may be drawn with regard to MR imaging. Both techniques usually allow a relatively easy differentiation with other cystic anomalies of the posterior cranial fossa, namely the Dandy–Walker cyst, by demonstrating a normal-sized fourth ventricle, anatomically separated from the pathological cystic cavity, with a possible deformation of its wall due to the mass effect exerted by the lesion. In doubtful cases, metrizamide CT cisternography may contribute to the diagnosis by means of a dynamic assessment of the CSF circulation[43] (Figures 9.3 and 9.6). The penetration of the pathological cavity by the contrast medium and its clearance demonstrated by subsequent scans are the main criteria of the evaluation of the communicating or noncommunicating nature of the cyst and its dynamic relationship with the surrounding CSF spaces.

As with the Dandy–Walker cyst,[44,45] the diagnosis of a posterior fossa arachnoid cyst may be obtained by means of ultrasonography in utero or in the neonatal period through the anterior fontanel[29,32]; in the first months of life the technique may be utilized to monitor the evolution of the lesion and the possible concomitant hydrocephalus, as well as the effects of an eventual surgical treatment.

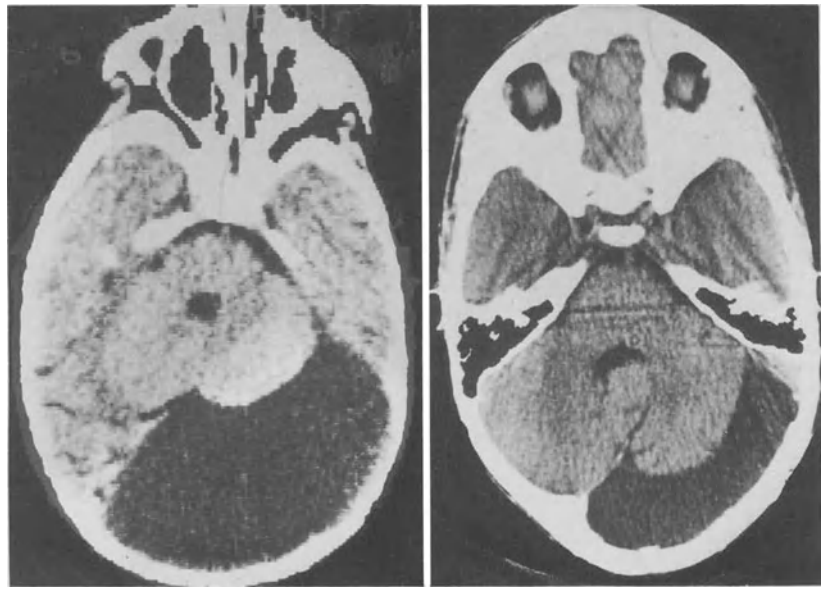

Figure 9.6. Lateral posterior fossa arachnoid cyst compressing and pushing the cerebellum upward (left). Following suboccipital craniotomy and cyst membrane excision, the volume of the cyst is reduced and the cerebellum is returned in a lower position (right).

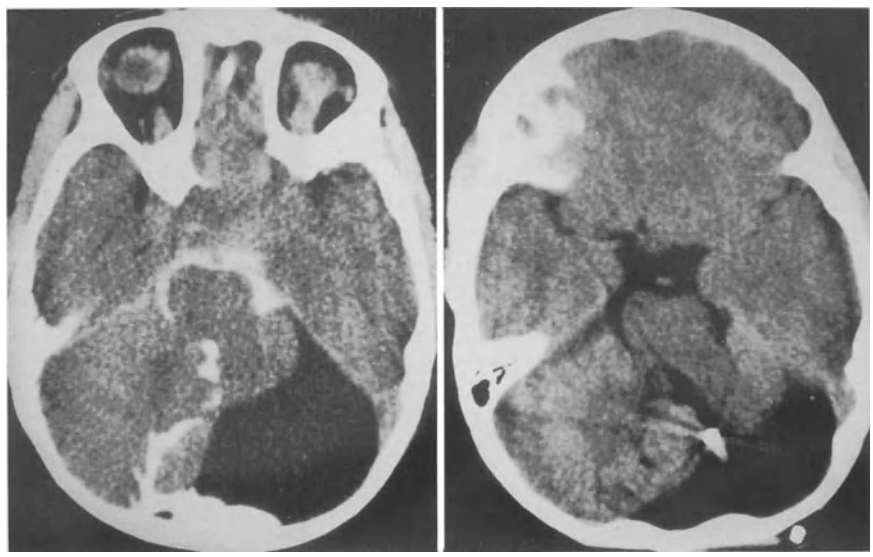

Figure 9.7. A 5-year-old girl with a posterior fossa arachnoid cyst, psychomotor retardation, and epilepsy. The cyst is not penetrated by the contrast medium at the CT cisternography (left). Following the insertion of a cystoperitoneal shunt, the volume of the cyst appears to be reduced with a concomitant reexpansion of the right cerebellar hemisphere.

Surgical Treatment and Results

Posterior fossa arachnoid cysts may occur as a solitary lesion and produce symptoms because of a compression/distortion of the surrounding parenchymal structures. In the majority of children, however, this type of lesion is accompanied by an associated ventricular dilation. In this second instance, the surgical management cannot be limited to merely eliminating the mass effect of the pathological cavity, with the aim of achieving the cerebellar parenchymal reexpansion, but it should also be directed at treating the accompanying hydrocephalus, by reestablishing the normal CSF dynamics.

Thus, the surgical options available for managing posterior fossa cysts include craniotomy with excision of the cyst membrane (Figure 9.6), shunting procedures of the cyst (Figure 9.7) and/or associated hydrocephalus, and lastly, a combination of craniotomy and shunting operations (Figure 9.8 and Table 9.4). In the latter instance, opinions may diverge concerning the time sequence and the order to be followed in planning the surgical procedures. In fact, some authors prefer to shunt the cerebral ventricles or residual cystic cavity after the craniotomy (Figure 9.8) and the resection of the cystic membranes, whereas others maintain that results are better when shunting precedes craniotomy.[6,12,28,30,39,41]

Table 9.4. Surgical options for infratentorial arachnoidal cysts (from literature and personal series).

	Series from literature (96 cases)	Personal series (23 cases)
1. C	17	4
2. C + VP shunt	16	4
3. C + CP shunt	1	1
4. VP (or VA) shunt	6	4
5. CP (or CA) shunt	18	7
6. VP + CP shunt	13	3
7. LP shunt	1	—
8. Not indicated	24	—

C, craniectomy + cyst membrane excision; VP, ventriculoperitoneal; VA, ventriculoatrial; CP, cystoperitoneal; CA, cystoatrial; LP, lumboperitoneal.

The preoperative evaluation of the mass effect exerted by the cyst is relatively easy, by taking into consideration the findings provided

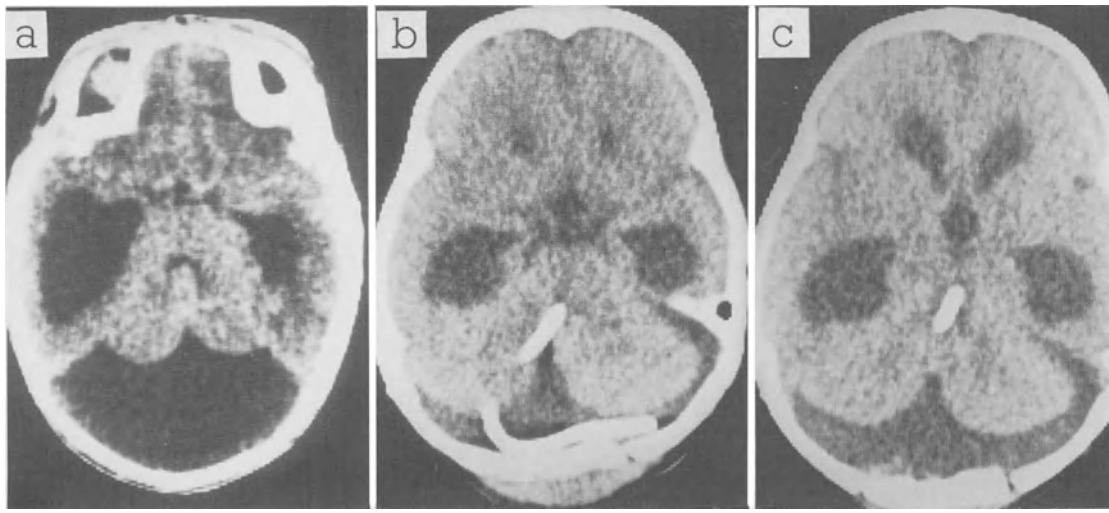

Figure 9.8. A 1-year-old girl with hydrocephalus and posterior fossa arachnoid cyst (A). The child was treated initially by means of a ventriculoperitoneal shunt, which controlled the supratentorial ventricular dilation but failed to reduce the size of the cyst. A reduction of cyst volume was obtained through a wide excision of the cystic lining, after suboccipital craniotomy, and placement of a cyst–3rd ventricle shunt (aqueduct cannulation) (B,C).

by neuroimaging studies, such as the compression, distortion, and controlateral deviation of the underlying cerebellar hemisphere in cases of lateral cysts (Figure 9.4), or the anteroposterior displacement of the fourth ventricle in cases of midline cysts (Figures 9.2 and 9.3). The evidence of neurological signs and symptoms indicating a dysfunction of the posterior fossa parenchymal structures, directly exposed to the pressure of the expanding cystic lesion, may further support the surgical indications.

In infants without hydrocephalus, the excision of the cyst membrane by means of a direct surgical approach through craniotomy appears theoretically the most appropriate managment. In a high proportion of subjects this type of approach is followed by the disappearance of the lesion, and cerebellar reexpansion. In some cases, however, the excision of the cystic lining is not sufficient to prevent the recurrence of the lesion; in others, the procedure may be followed by the sudden appearance of an unexpected postoperative hydrocephalus. An insufficient circulation and absorption of CSF within the peripheral subarachnoid space of the cerebral convexities probably accounts for this second type of complication. Thus, an accurate preoperative investigation of the CSF dynamics by means of cisternography or CSF infusion test[35,41] is recommended in order to reduce the rate of unsatisfactory outcomes, following the direct surgical approach in children with a posterior fossa arachnoid cyst, even when the lesion is not accompanied by hydrocephalus.

For some surgeons,[7,39] the excision of the cystic membrane through craniotomy is the first-choice surgical option even in cases where the posterior fossa arachnoid cyst is associated with a ventricular dilation. At the base of such a policy is the conviction that the accompanying hydrocephalus is secondary and obstructive in nature. Nevertheless, although in some cases an obstruction in the CSF circulation due to the presence of the cyst might be hypothesized on the grounds of examinations that demonstrate the blockage of the aqueduct or the outlet foramina of the fourth ventricle,[19,46] in several instances metrizamide CT cisternography may clearly demonstrate some kind of communication with the ventricular system or the subarachnoid spaces, in the same way as air encephalography or radionuclide cisternography did in the past, thus ruling out the merely obstructive nature of the phenomenon.[5,7,28,39,41,47]

The need for a direct surgical approach with excision of the cystic membrane, even in infants whose cysts appear to be communicating with the neighboring CSF spaces, is postulated by various authors who propose a mechanism of "ball-valve" obstruction, possibly associated with a secretion of fluid by the cystic lining, which accounts for a progressive accumulation of fluid within the cyst in spite of the communication existing between its inner space and the CSF spaces.[7,43,48] Various observations in favor of such a hypothesis have been reported in the literature, such as the delayed clearance of the contrast media penetrating the cyst after having been injected into the CSF stream,[7,42,49] the difference between protein concentrations in the fluid of the cyst and in the CSF,[19] and even the intermittent clinical symptomatology, possibly related to episodic fluctuations in cyst volume.[7]

In fact, the relationship between the posterior fossa arachnoid cysts and the accompanying hydrocephalus is too complex to be explained on the grounds of a simple obstruction in the CSF circulation such as that caused by a space-occupying lesion. A developmental anomaly of the subarachnoid space resulting in a decreased CSF absorption and/or defective circulation seems to be suggested in several patients by the results of dynamic examinations, such as cisternography and lumbar spinal subarachnoid infusion test.[35,39] At the cisternography, findings characteristic of both obstructive and communicating hydrocephalus have been found to be intermingled in the same subject.[39] A further confirmation to the above-mentioned hypothesis is provided by the relatively large number of subjects requiring a CSF shunting procedure, either from the residual cystic cavity or from the cerebral ventricles, after an apparently successful operation of craniotomy and a wide excision of the cyst lining.[11,35,39,50,51] The placement of an ex-

Table 9.5. Algorithm for the treatment of posterior fossa arachnoid cysts.

POSTERIOR FOSSA ARACHNOID CYST

a) Without hydrocephalus

↓

Subarachnoid infusion test, metrizamide CT cisternography

Impaired CSF absorption/ circulation (at the level of peripheral CSF spaces)	Normal CSF absorption/ circulation (at the level of peripheral CSF spaces)
↓	↓
1. Craniotomy, cystic membrane excision plus Cystoperitoneal shunt	1. Craniotomy, cystic membrane excision

b) With hydrocephalus

↓

Subarachnoid infusion test, metrizamide CT cisternography

Lateral and third ventricles communicating with the cyst	Ventricular system noncommunicating with the cyst	
	Impaired CSF absorption/ circulation (at the level of peripheral CSF spaces)	Normal CSF absorption/ circulation (at the level of peripheral CSF spaces)
↓	↓	↓
1. Ventriculoperitoneal shunt or 2. Cystoperitoneal shunt	1. Ventriculoperitoneal shunt plus Cystoperitoneal shunt or 2. Ventriculoperitoneal shunt plus Cystoventricular shunt (aqueductal cannulation)	1. Craniotomy, cystic membrane excision or 2. Craniotomy, cystic membrane excision plus Ventriculoperitoneal shunt or 3. Ventriculoperitoneal shunt plus Cystoventricular shunt (aqueductal cannulation)

trathecal shunting device from the pathological cystic cavity has been proposed by various authors[28,32] as the only treatment to be performed in this type of lesion. The advantage of this approach consists essentially in the simplicity of the operation; disadvantages include the possiblility of a shunt malfunction, which has been reported with a frequency ranging from 10%[32] to 26%.[39] Such a relatively high proportion of shunt malfunction characterizes, in general, all the cystic lesions of the posterior fossa, including Dandy–Walker cysts and cysts associated with a hindbrain developmental anomaly.[52] The finding has been explained on the grounds of the limited amount of choroidal tissue available for CSF production within the posterior cranial fossa.[52] Although sufficient in some patients for inducing a life-threatening cyst distension, this reduced CSF production would not be adequate to maintain the CSF shunting system patent, without an additional flow from the lateral and third cerebral ventricles through a pervious aqueduct of Sylvius. By taking into account all the possible surgical options available for the treatment of the lesion, and the findings provided by dynamic diagnostic investigations, we have elaborated an algorithm that can be utilized when planning the surgical treatment (Table 9.5).

With regard to results, it is worth noting that, in spite of the wide range of surgical options and the various surgical modalities that have been adopted by the different authors, in the great majority of cases the surgical management of posterior fossa arachnoid cysts is followed by satisfactory results (Table 9.6). However, although in nearly all cases the

Table 9.6. Results of the surgical treatment of infratentorial arachnoid cysts (from literature and personal series).

	Series from literature (96 cases)			Personal series (23 cases)		
	No. of cases			No. of cases		
Clinical manifestations	Pre-op	Post-op	% of success	Pre-op	Post-op	% of success
Increased intracranial pressure	62	6	90%	12	1	92%
Developmental delay	43	13	70%	10	4	60%
Cerebellar signs	37	9	76%	10	2	80%
Cranial nerve deficits	12	3	75%	7	1	86%
Pyramidal signs	13	4	69%	6	1	83%
Nystagmus	7	2	71%	6	0	100%
Epilepsy	7	5	29%	4	1	75%

symptoms and signs of increased intracranial pressure appear to be fully under control, some children continue to exhibit variable degrees of psychomotor retardation and focal neurological signs. Further experience will indicate whether this partial failure in the treatment of posterior fossa arachnoid cysts results from a still inadequate or late treatment, or, on the other hand, if the simple arrest in progression of neurological symptoms coupled with the normalization of CSF dynamics should be considered the maximum result possible, at least in a certain percentage of subjects with this type of lesion.

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CHAPTER 10

Cortical Cysts

Concezio Di Rocco and Massimo Caldarelli

Introduction

The arachnoid cysts that develop over the cerebral convexity differ from those localized in other intracranial regions, because of the apparent lack of any anatomical relationship with a cisternal space. In fact, the scissura of Sylvius, an extension of which has been hypothesized as giving rise to at least those arachnoid cysts overlying the cerebral cortex, which reach considerable proportions, is classed among the sulci rather than the cisternae by the majority of authors.[1] The cysts of the cerebral convexity should not be confused with focal accumulations of cerebrospinal fluid (CSF), which are frequent in the sulci of the medial frontoparietal convexities in the form of lakes or pockets, freely communicating with the subarachnoid space.[2] On the other hand, arachnoid cysts of the cerebral convexities do not usually show any communication with the surrounding fluid spaces, both in cases of small-sized lesions and huge cysts extending all over the cerebral hemisphere.

Varieties, Incidence, and Age and Sex Distribution

The arachnoid cysts overlying the cerebral convexities may be grossly subdivided into two main varieties that differ considerably for morphology, age distribution, and clinical symptomatology, even though intermediate forms between the two entities could be found in rare cases.

The first variety, *hemispheric cysts*, is constituted by huge fluid collections between the dura and the brain, which extend over most, or all, of the surface of one cerebral hemisphere. The cerebral parenchyma and the lateral cerebral ventricle are compressed and contralaterally dislocated (Figure 10.1). The hemispheric cysts have been considered to be a massive extension of temporal lobe arachnoid cysts; the hypothesis, however, cannot be accepted for those cases in which a hemispheric cyst is not accompanied by any signs of temporal lobe aplasia, and the scissure of Sylvius appears to be compressed rather than enlarged.

The second variety, *focal cysts*, corresponds to small-sized lesions, the presence of which is usually suggested by a localized bulging of the skull (Figure 10.2). In this type of lesion, the localized bone deformity indicates a long-standing process, which began in early infancy, even though the interval of time before the diagnosis may be surprisingly long because of the relatively small size of the lesion. In the absence of a generalized increase in intracranial pressure, the bulging of the calvarial bone and its erosion may be explained by the water-hammer effect of cerebral pulsations.

Arachnoid cysts of the cerebral convexities are rare (Table 10.1).[3–22] In our series, they correspond to an incidence of about 10% of all intracranial localizations, without any significant difference between the hemispheric and the focal varieties (Table 10.1). It is worth noting, however, that the latter variety tended to be clinically eloquent in relatively older children (all of our cases were detected be-

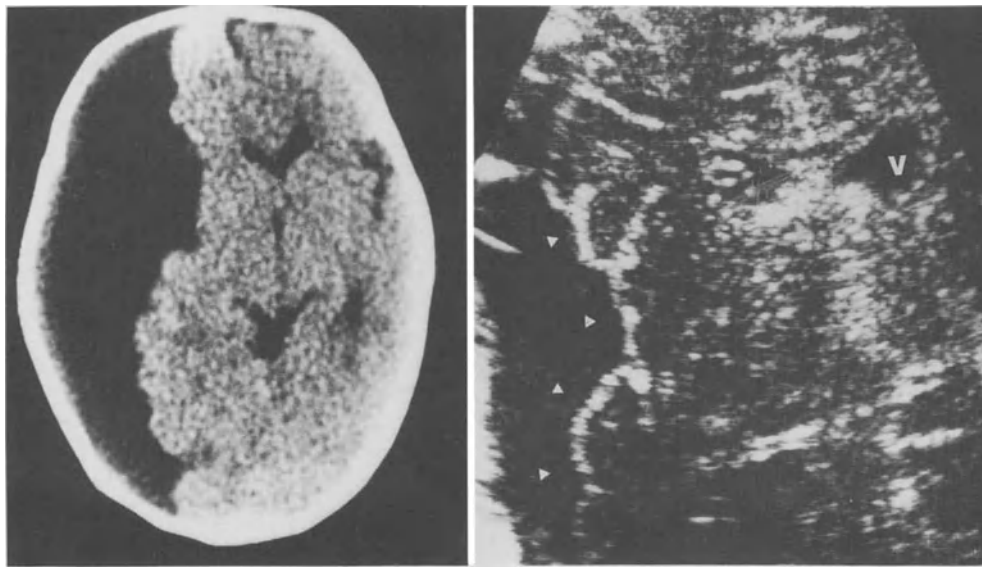

Figure 10.1. A 4-month-old girl with hemispheric arachnoid cyst. Note the huge extension of the fluid collection all over the cerebral hemisphere, which is compressed and dislocated toward the opposite side together with the midline structures. The normal outline of the cortical gyri and sulci is preserved, a finding that is well demonstrated also by the ultrasonographic examination. Arrows: outline of the cerebral cortex; v, lateral cerebral ventricle.

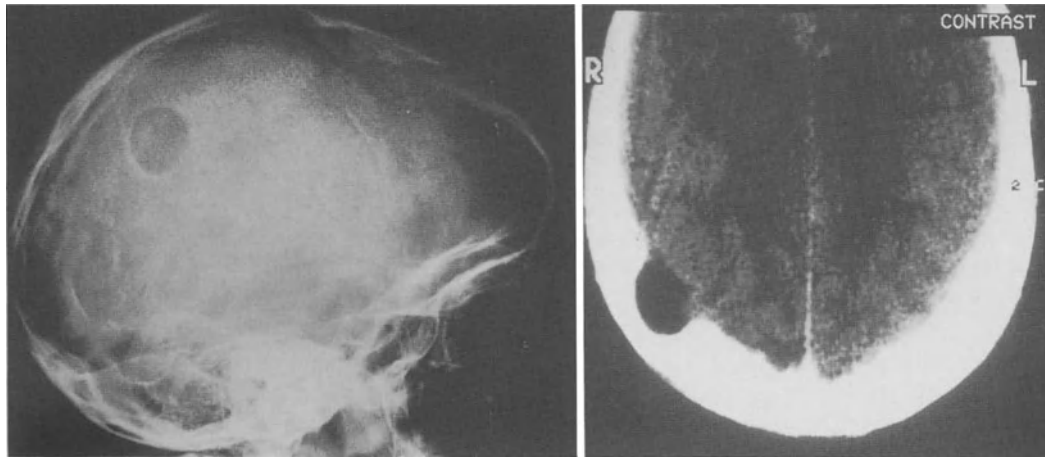

Figure 10.2. A 14-year-old girl presenting with seizure disorder and a localized bulging in the right parietal region. The skull x-ray shows a localized area of bone erosion. The CT scan confirms the presence of an osteolytic area occupied by a CSF density lesion.

Table 10.1. Relative incidence of cerebral convexity arachnoid cysts among supratentorial arachnoid cysts in children.

Author (reference no.)	No. supratentorial arachnoid cysts	No. cerebral convexity arachnoid cysts	%
Anderson and Landing, 1966[3]	8	2[1]*	25
Harrison, 1971[4]	9	0	—
Danziger and Bloch, 1975[5]	10	1[1]	10
Aicardi and Bauman, 1975[6]	12	2	17
Choux et al., 1978[7]	36	18[9]	50
Leo et al., 1979[8]	4	1	25
Anderson et al., 1979[9]	20	8[8]	40
Menezes et al., 1980[10]	18	5[1]	28
Kato et al., 1980[11]	4	2[2]	50
Markakis et al., 1981[12]	9	1[1]	11
McCullough et al., 1980[13]	2	1[1]	50
Stein, 1981[14]	7	4	57
Cilluffo et al., 1983[15]	9	2[1]	22
Serlo et al., 1985[16]	10	0	—
Lodrini et al., 1985[17]	18	4	22
Harsh et al., 1986[18]	11	2	18
Choux et al., 1987[19]	49	6	12
Locatelli et al., 1987[20]	20	6	30
Raffel and McComb, 1988[21]	27	5	19
Marinov et al., 1989[22]	42	4	10
Personal series	62	9[5]	14
Total	387	83[30]	21

*No. of *huge* convexity arachnoid cysts.

tween 5 and 15 years of age), whereas the former seemed typical of the very young (the oldest child in our population being 4 years old) (Figure 10.3). Females appear more frequently involved than males.

Clinical Presentation and Diagnosis

The long-standing nature of the hemispheric arachnoid cysts of the cerebral convexities is usually demonstrated by the unilateral cranial enlargement, with a flattening of the calvarial bones overlying the cyst. In spite of the impressive dislocation of the nervous structures, these lesions may be found in otherwise normal children presenting only with cranial asymmetry. In some infants, a delayed psychomotor development may be noticed, which, however, is not specific (Table 10.2).*

Except for being compressed, the cerebral hemisphere underlying a hemispheric arachnoid cyst is normal, a finding that differentiates this type of condition from the so-called hemiaplasia cerebri and from partial, more or less extensive, congenital defects in the development of the brain, which also can be accompanied in some cases by fluid accumulation under tension.

Cerebral angiography is the best diagnostic tool demonstrating the normal architecture of the cerebral hemisphere in cases of hemispheric arachnoid cysts (Figure 10.4), in contrast with the hypoplasia or even complete absence of the carotid artery and/or its main subdivision branches (especially, the middle cerebral artery) that are found in patients with an arrest in cerebral development (Figure 10.5). In the latter, the involved hemisphere may simulate a cystic cavity at computed tomography, and at surgery will appear as a thin-walled cyst, the lining of which consists of the atrophic-dysplastic cortex made up by glial cells and eventually a few immature glial cells. Seizure disorder is not a rare manifestation of the condition; contralateral motor deficits are common, even though this anomaly may be found in apparently asymptomatic subjects as in the case of hemispheric arachnoid cysts.

*Refs. 3, 5, 6, 11, 13–15, 18, 20, 23–27.

Table 10.2. Clinical manifestations of cerebral convexity arachnoid cysts (from literature and personal series).

Author (reference no.) [No. cases]	Nagoulitch and Perovitch[23] [1]	Freeman and Gold[25] [1]	Gruszckiewicz and Peyser[26] [1]	Anderson and Landing[3] [2]	Mishkin and Truksa[27] [1]	Robinson[24] [1]	Danziger and Bloch[5] [1]
Increased HC		1	1	2	1	1	1
Cranial bulging*		1	1	1		1	1
Increased ICP	1			1	1		1
Neurological signs	1	1	1		1		
hemiparesis		1	1				
ptosis	1				1		
hypertonia							
hypotonia							
Epilepsy						1	1
Developmental delay		1					
Asymptomatic (besides cranial bulging)				1			

*Localized or hemicranial. HC, head circumference; ICP, intracranial pressure.

The differential clinical diagnosis of hemispheric arachnoid cysts with unilateral subdural hygromas and hematomas can be difficult, especially when the lesions are characterized by the formation of neomembranes around the fluid collections and the overlying skull is bulging.[25] Infants with chronic subdural hematoma are commonly symptomatic, though the clinical picture can be rather aspecific: failure to thrive, irritability, seizures, and psychomotor retardation associated with macrocrania. Also a history of head injury or an intracranial inflammatory condition may help in correctly recognizing the lesion. Only in a few cases is the diagnosis reached after a histological examination of the cystic wall. In fact nowadays, the modern diagnostic tools for neuroimaging differentiate the two pathological entities in nearly all cases, already in the preoperative phase. The flattening of the cerebral cortex in cases of chronic subdural hematoma in contrast with the normal outline of this structure, is the most typical ultrasound finding (Figure 10.1). On computed tomogra-

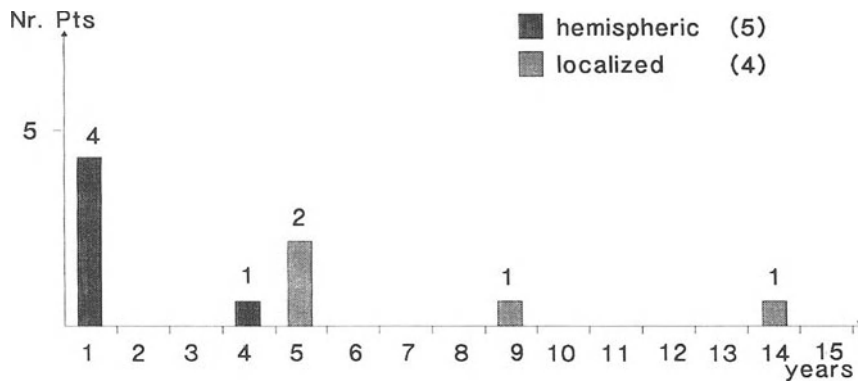

Figure 10.3. Age distribution of convexity arachnoid cysts (personal series).

Aicardi and Bauman[6] [2]	McCullough et al.[13] [1]	Kato et al.[11] [2]	Stein[14] [4]	Cilluffo et al.[15] [2]	Harsh et al.[18] [2]	Locatelli et al.[20] [6]	Personal series [9]	Total [36]
2	1	2	4	2	1		5	24
1		2		1			9	18
			2	1	1	1	1	10
2				1			3	10
				1			2	5
								2
1							1	2
1								1
						1	3	6
					1	1	1	4
	1	2	2	1		3	3	13

phy, the density of the hematoma, inferior or equal to that of the cerebral parenchyma, corresponds to the increased protein content of the lesion as compared to the water-like density of the arachnoid cyst. The high signal intensity of the hematoma on recovery sequence characterizes this type of fluid collection rather than the arachnoid cyst, the signal of which maintains the same characteristics as the cerebrospinal fluid. At the present time, brain scanning, once widely utilized for the differential diagnosis of intracranial cystic lesions,[27] has been practically abandoned.

The second variety, the focal arachnoid cyst of the cerebral convexities, is usually recognized because of a local bulging of the skull.

On skull x-ray examination, the localized area of bone changes does not present any differential characteristics with other osteolytic calvarial lesions that might contribute to the correct diagnosis. Even after the advent of computed tomography, the differential diagnosis with grade I or II cerebral gliomas may remain difficult, especially when considering that both the conditions may be clinically revealed by seizure disorder. Magnetic resonance imaging, however, does generally allow the correct diagnosis. One characteristic finding of these lesions on cerebral angiography is that the venous vessels corresponding to the cyst are usually in a "normal" peripheral position, lying over the cystic wall, while the arterial vessels are pushed centripetally together with the cerebral parenchyma.

Surgical Management and Results

The treatment of focal arachnoid cysts of the cerebral convexity consists essentially in the excision of the outer layer of the cyst. Usually, it is not necessary to attempt removing the medial cystic wall, which is intimately connected with the underlying cerebral cortex. Generally, the operation suffices in eliminating the lesion and allowing the local reexpansion of the cerebral parenchyma (Figure 10.6).

The management of the hemispheric arachnoid cysts is much more complex. The surgical excision of the cystic membrane requires, in fact, a large craniotomy and, in spite of the multiple communications that can be made at the borders of the cyst, where there is the apparent reflexion or splitting of the arachnoid membrane, the circulation of cerebrospinal fluid may remain relatively impaired with a consequent reaccumulation of fluid over the cerebral hemisphere. The phenomenon is favored in some cases by the incomplete reexpansion of the compressed cerebral

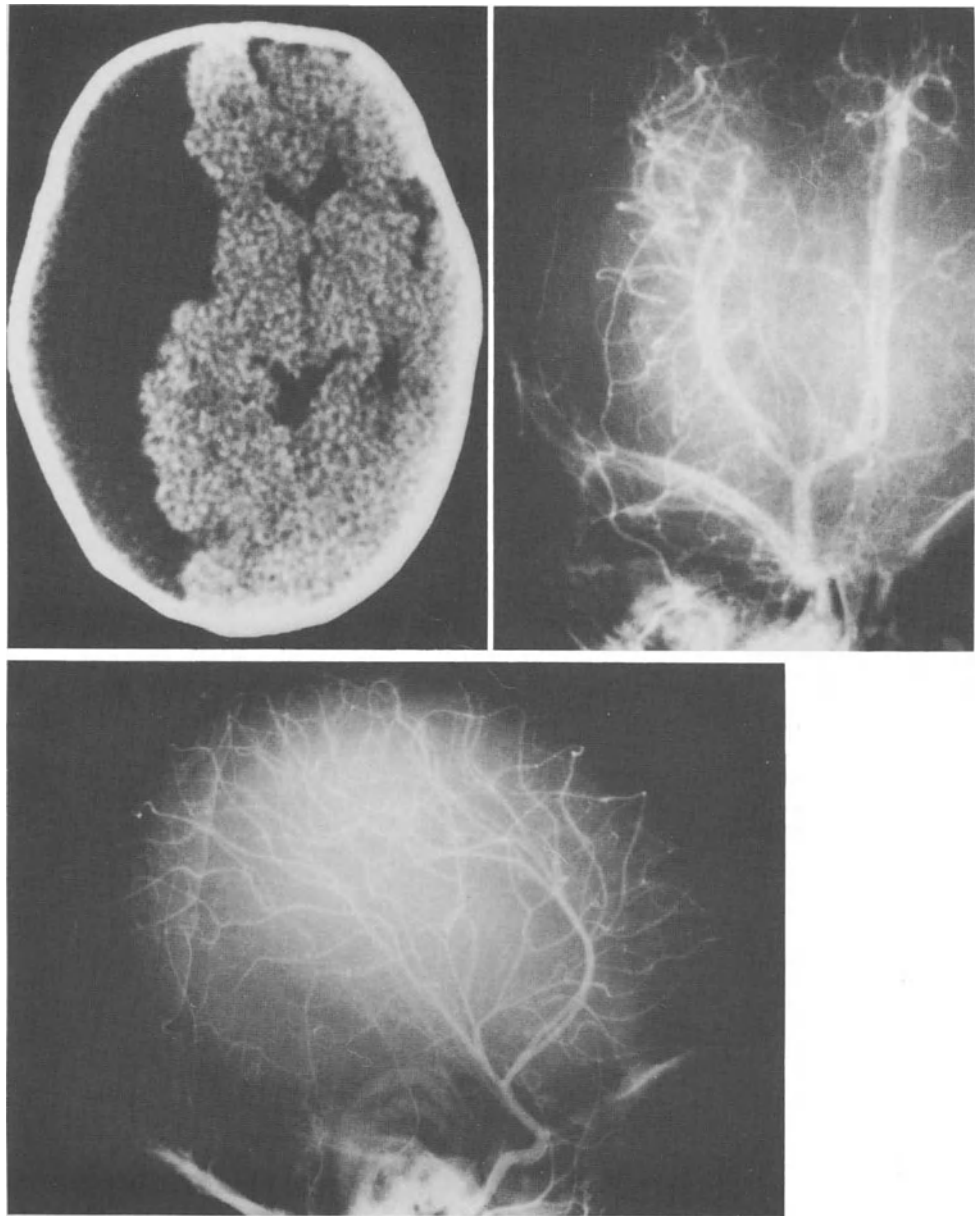

Figure 10.4. A 5-month-old infant with a right hemispheric arachnoid cyst. The R-carotid angiography demonstrates a normal cerebrovascular architecture. The main vessels appear dislocated from their normal position by the cystic lesion.

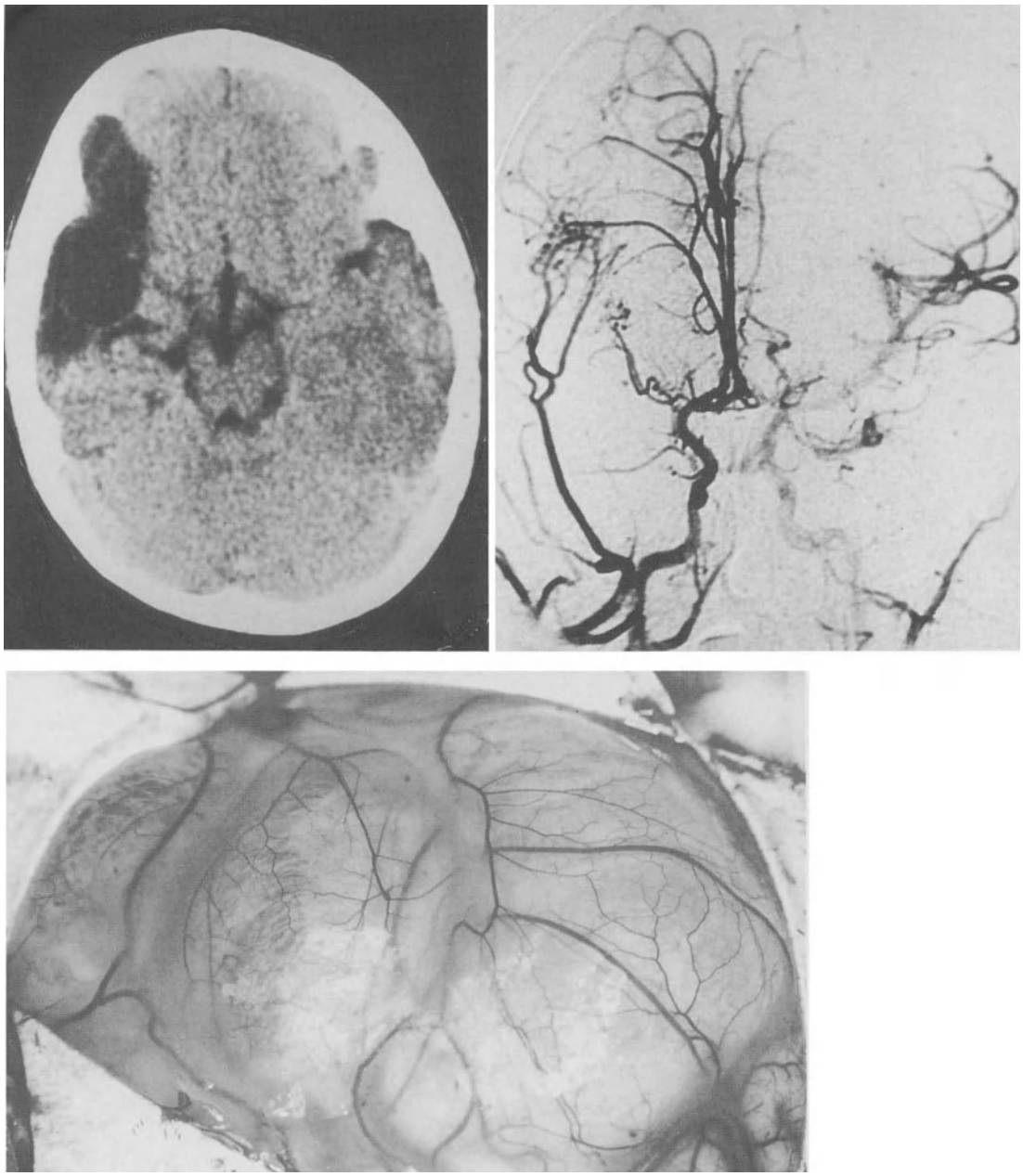

Figure 10.5. A 3-year-old boy with seizure disorder. The CT scan shows a hypodense lesion in the fronto-temporal region. The R-carotid angiography demonstrates the complete occlusion of the middle cerebral artery, responsible for the ischemic insult to the cerebral parenchyma. At the operation, the dysplastic cortex appears so thinned as to simulate the wall of a cyst, although it can be easily differentiated from an arachnoid cyst.

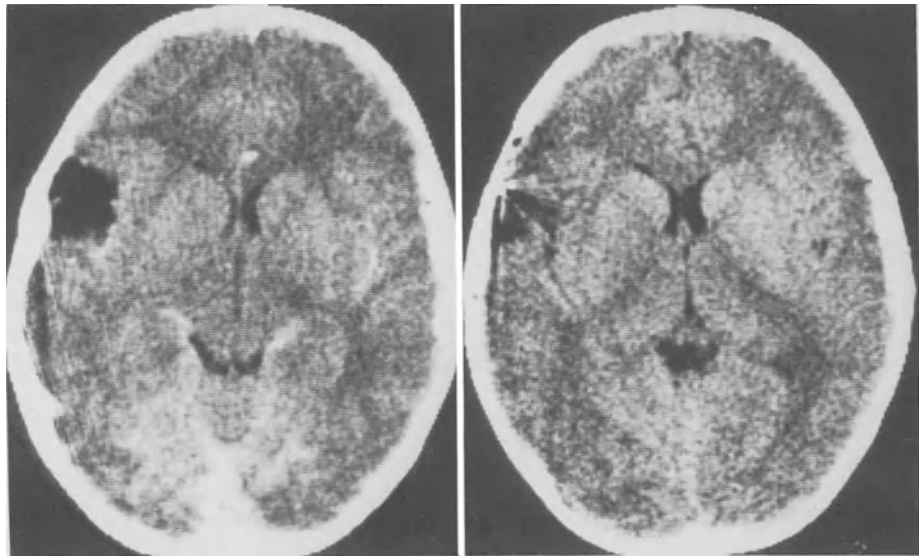

Figure 10.6. "Focal" arachnoid cyst of the right frontal cerebral convexity in a 5-year-old girl, presenting with chronic headache and focal spikes on the EEG. Note the reexpansion of the cerebral parenchyma following craniotomy and cyst excision, which has been accompanied by the disappearance of the clinical and electroencephalographic abnormalities.

parenchyma (Figure 10.7), thus suggesting the need to complete the treatment by inserting a cerebrospinal fluid shunting device from the residual cystic cavity to the peritoneal cavity.

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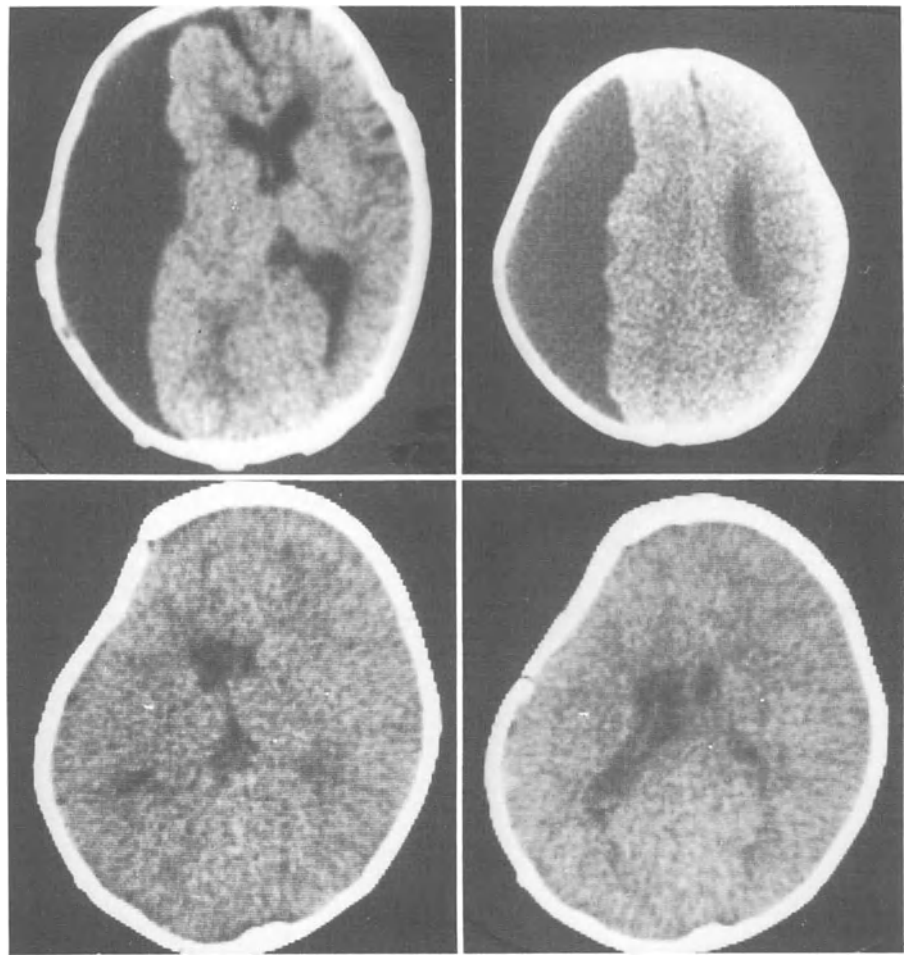

Figure 10.7. Preoperative (top) and postoperative CT scan studies (bottom) of a hemispheric arachnoid cyst treated by means of craniotomy and excision of the outer wall of the cyst. On the postoperative control the midline structures are in a relatively normal position, whereas the calvarial bone corresponding to the lesion appears depressed, following the normalization in intracranial pressure.

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CHAPTER 11

Supratentorial Interhemispheric and Pineal Region Cysts

Concezio Di Rocco and Massimo Caldarelli

Introduction

The group of cisterns anatomically related to the tentorial notch represents a critical space for the cerebro spinal fluid (CSF) circulation; these cisterns are also a preferential site for a variety of cystic lesions, of which the arachnoid cysts constitute only a minor fraction.[1,2] In fact, the two main cisterns of the group—the cisterna corporis callosi and the cisterna corporum quadrigeminorum—together with the satellite subarachnoid cisterns around the brain stem (cisterna ambiens), above the roof of the third ventricle (cisterna veli interpositi), and around the superior vermis of the cerebellum (cisterna cerebelli superior), form a large and complex space that is often involved in the developmental anomalies of the midline structures of the brain. On neuroimaging investigation the resulting malformations may assume various configurations; the differential diagnosis, especially in newborns and infants, may be particularly difficult, even though a careful evaluation of the corpus callosum, as well as of the shape and position of the lateral and third ventricles, may usually facilitate the correct recognition of the lesion (Figure 11.1).

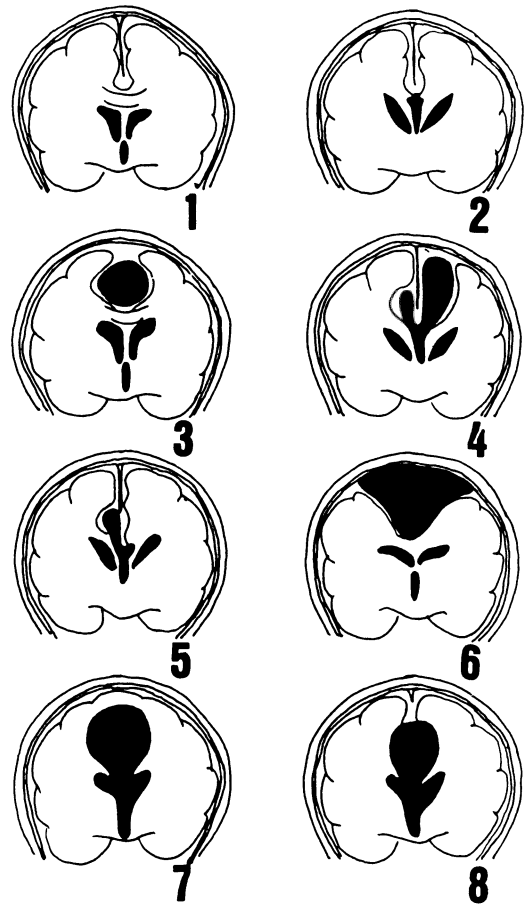

Figure 11.1. Schematic representation of different midline cystic lesions. 1: Normal coronal section of the brain. 2: Agenesis of the corpus callosum. 3: Interhemispheric cyst. 4 and 5: Agenesis of the corpus callosum with "secondary" interhemispheric cyst. 6: Intradural cyst. 7: Alobar holoprosencephaly. 8: Lobar holoprosencephaly. (Modified from refs. 1, 2.)

Varieties, Incidence, and Age and Sex Distribution

The anatomical relationship of arachnoid cysts that develop in the tentorial notch with the corpus callosum constitutes the main factor

for their definition. In fact, the partial or complete agenesis of the corpus callosum is the only element that justifies the classification of the cysts arising in the interhemispheric fissure into two main varieties: *interhemispheric cysts*, associated with a partial or complete agenesis of the corpus callosum (Figure 11.1, parts 4,5); and *parasagittal cysts*, which are not associated with a defect in the formation of the corpus callosum (Figure 11.1, part 3). Whether the occurrence of an interhemispheric cyst and the agenesis of the corpus callosum are causally related remains unclear,[3,4] as the hypothesis of a mechanical interference exerted by the presence of the cyst in the development of the midline commissure seems to be denied by cases where the complete agenesis of the corpus callosum is accompanied only by interhemispheric cysts of minimal size.[5,6] On the other hand, when the main interhemispheric commissure is normally developed, its presence determines the direction of growth of the cystic lesions, thus allowing their subdivision into the *anterior*, *middle*, and *posterior* varieties. The anterior cysts expand toward the cisterna laminae terminalis and the space between the falx and the medial surface of the cerebral hemisphere (Figure 11.2), and the posterior cysts extend into the quadrigeminal cistern, or around the splenium, into the cistern above the roof of the third ventricle, or the cisterna veli interpositi. In several cases, the cysts of the interhemispheric fissure involve both the supra- and infratentorial compartments, growing also in the cistern of the superior vermis of the cerebellum within the posterior cranial fossa (Figure 11.3).

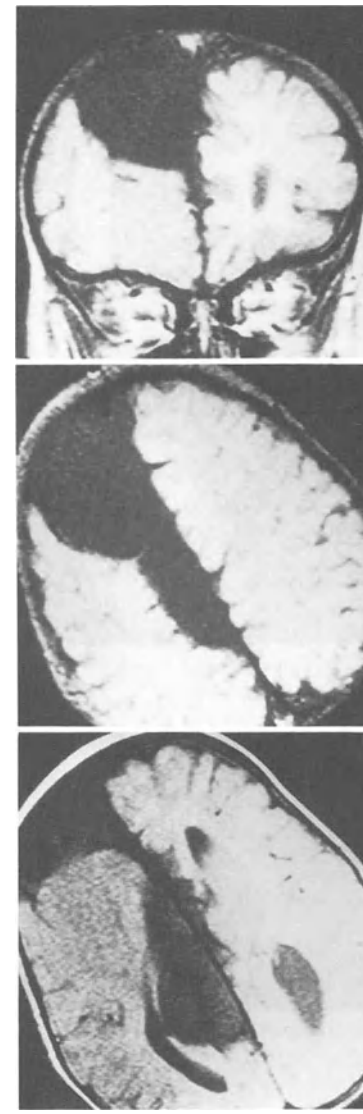

Figure 11.2. MRI study of an interhemispheric cyst in a 4-month-old boy (coronal and sagittal views). Note the prevalently anterior extension of the right paramedian cystic lesion between the falx and the medial aspects of the right hemisphere, which is compressed and laterally dislocated.

A very rare variety of interhemispheric arachnoid cyst is that developing between the two folds of the dura that form the falx cerebri, which has been termed *interhemispheric intradural cyst* (Figure 11.1, part 6).[2,7] In the case described by Rao and coworkers in 1982,[2] the lesion arose between the two cerebral hemispheres, widely separating the anterior cerebral arteries, compressing the cortical mantle and the cerebral ventricles, and interfering with the normal position of the sagittal sinus and anterior falx. The authors hypothesized that this type of cyst originates from the arachnoid, which penetrates the dural venous sinuses at various places in the form of arachnoid villi.

The *epicranial arachnoid cysts*, which occur in the midline of the skull, usually in the parietal region, should be excluded from the

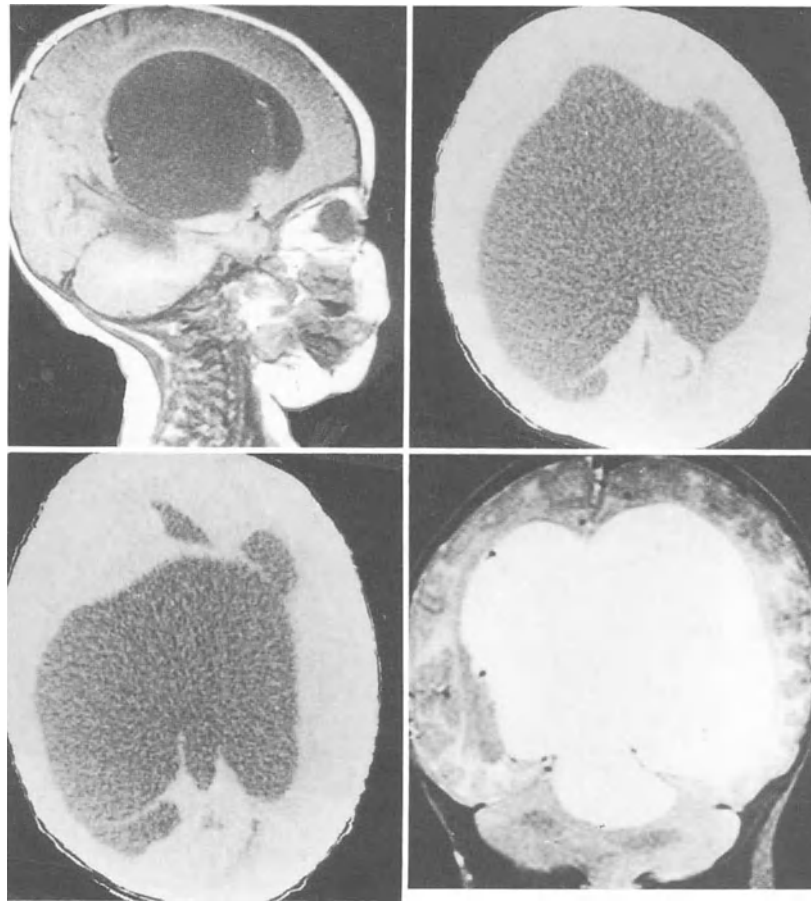

Figure 11.3. A 2-month-old boy presenting with macrocrania and symptoms and signs of increased intracranial pressure. The MRI examination reveals a huge arachnoid cyst of the posterior two-thirds of the cerebral midline, extending into the posterior fossa through the tentorial notch. The ventricular system is compressed and laterally dislocated.

group of interhemispheric cysts. Though histologically these lesions are true arachnoid cysts, as their wall is constituted by arachnoid cells reinforced by fibrous tissue,[8] most authors prefer to consider them a variant of meningocele.[9] It is worth noting that associated abnormalities include agenesis of the corpus callosum as well as dermal sinus. The incidence of interhemispheric cysts is not known, although in most series this localization seems rather rare. In the series of 208 patients of all ages collected by Rengachary[5] from the literature, the interhemispheric cysts accounted for only 5%. In 352 pediatric cases collected from the literature[5,10–24] (Table 11.1), the incidence of this type of localization ranged from 0% to 38% of the supratentorial cases, with a mean of 8%.

In our series of 85 intracranial arachnoid cysts in children, we observed 15 cases of cysts localized in the interhemispheric fissure, an incidence of 18%; when considering only 62 supratentorial cases, this incidence increases to 24% (Table 11.1). Twelve of these 15 children were males and three females, for a ratio of males to females of 4:1. The age distribution in our series is reported in Figure 11.4.

The arachnoid cysts arising within the cistern of the lamina quadrigemina—*quadrigeminal cistern arachnoid cysts*—are

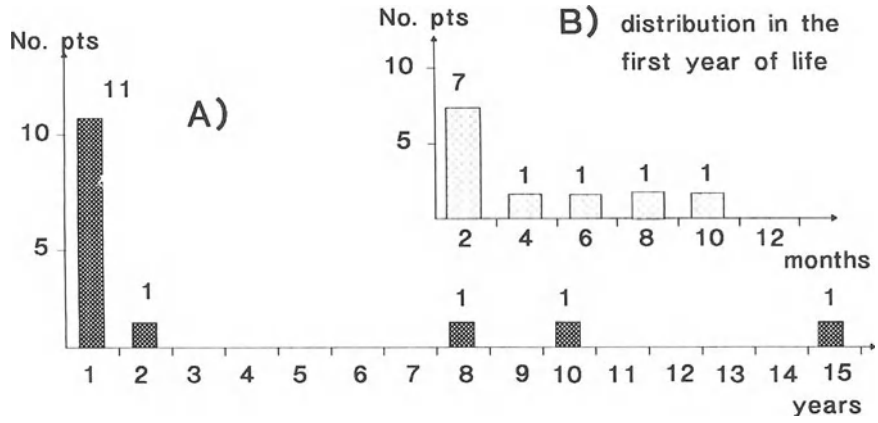

Figure 11.4. Age distribution of interhemispheric fissure arachnoid cysts (personal series).

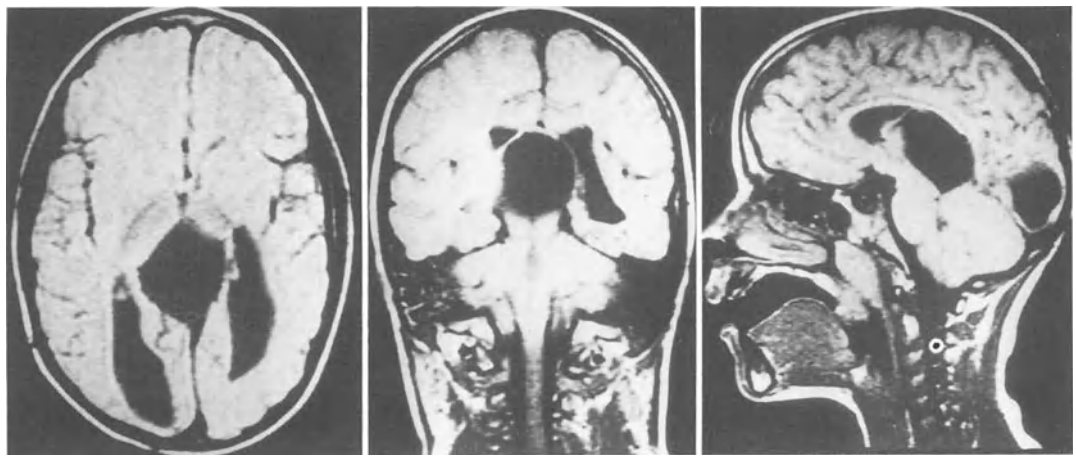

Figure 11.5. MRI study of a quadrigeminal plate arachnoid cyst in a 3-year-old boy. The cyst pushes forward the posterior wall of the third ventricle, pushes the splenium upward, and divaricates the pulvinars. The tectum of the midbrain and the upper vermis are compressed. Note also the associated moderate dilation of the lateral cerebral ventricles, more obvious in the occipital horns.

typically located below the splenium of the corpus callosum, behind the third ventricle, between the pulvinars and the medial aspects of the temporal lobes, and above the lamina quadrigemina itself (Figure 11.5). However, a considerable variety in configuration of these cysts is determined by the irregular anatomy of the cistern and by the various directions of expansion of the cysts occurring at this level. The direction of growth of the lesion can be, in fact, lateral into the cisterna ambiens (Figure 11.6), downward into the cisterna of the superior cerebellar vermis, upward into the posterior part of the interhemispheric fissure, and anterior toward the posterior part of the third ventricle. Thus, it is not surprising that arachnoid cysts in the quadrigeminal cistern have been given various denominations, such as "supracollicular," "collicular," "paracollicular," "incisural," "paramesencephalic," and "cysts of the cisterna ambiens." [25–29]

Quadrigeminal cistern arachnoid cysts are rare, even though their actual incidence is not known; in our series of 85 children with in-

Table 11.1. Relative incidence of interhemispheric arachnoid cysts among supratentorial arachnoid cysts in children (from literature and personal series).

Author (reference no.)	No. supratentorial arachnoid cysts	No. interhemispheric fissure arachnoid cysts	%
Anderson and Landing, 1966[10]	8	3	38
Harrison, 1971[11]	9	0	—
Danziger and Bloch, 1975[12]	10	0	—
Aicardi and Bauman, 1975[13]	12	2	17
Choux et al., 1978[14]	36	0	—
Leo et al., 1979[15]	4	0	—
Menezes et al., 1980[4]	18	2	11
Stein, 1981[16]	7	0	—
Cilluffo et al., 1983[17]	9	1	11
Serlo et al., 1985[18]	10	0	—
Lodrini et al., 1985[19]	18	1	6
Harsh et al., 1986[20]	11	1	9
Choux et al., 1987[21]	49	0	—
Locatelli et al., 1987[22]	20	2	10
Raffel and McComb, 1988[23]	27	2	7
Marinov et al., 1989[24]	42	0	—
Personal series	62	15	24
Total	352	29	8

Table 11.2. Relative incidence of quadrigeminal plate arachnoid cysts among supratentorial arachnoid cysts in children (from literature and personal series).

Author (reference no.)	No. supratentorial arachnoid cysts	No. quadrigeminal plate arachnoid cysts	%
Anderson and Landing, 1966[10]	8	0	—
Harrison, 1971[11]	9	4	44
Danziger and Bloch, 1975[12]	10	2	20
Aicardi and Bauman, 1975[13]	12	0	—
Choux et al., 1978[14]	36	0	—
Leo et al., 1979[15]	4	0	—
Menezes et al., 1980[4]	18	2	11
Stein, 1981[16]	7	0	—
Cilluffo et al., 1983[17]	9	2	22
Serlo et al., 1985[18]	10	3	30
Lodrini et al., 1985[19]	18	0	—
Choux et al., 1987[21]	49	0	—
Locatelli et al., 1987[22]	20	1	5
Raffel and McComb, 1988[23]	27	1	4
Marinov et al., 1989[24]	42	2	5
Ciricillo et al., 1991[30]	28	1	4
Personal series	62	6	10
Total	369	24	7

tracranial arachnoid cysts they accounted for 7% of all the localizations and for 9% of the supratentorial cases (Table 11.2). The relative incidence that can be drawn from the literature is about 7% (Table 11.2).[4,10–19,21–24,30]

Even though arachnoid cysts in the cistern of the lamina quadrigemina can be found at all ages they are more often detected in the pediatric age group. In 1980, Hayashi and coworkers[31] reported on 25 cases collected from the literature since 1950; 22 of them (88%) were children under 15 years of age, and 10 (40%) were infants under 12 months. The age distribution in our series is shown in Figure 11.7.

In our experience, the arachnoid cysts of

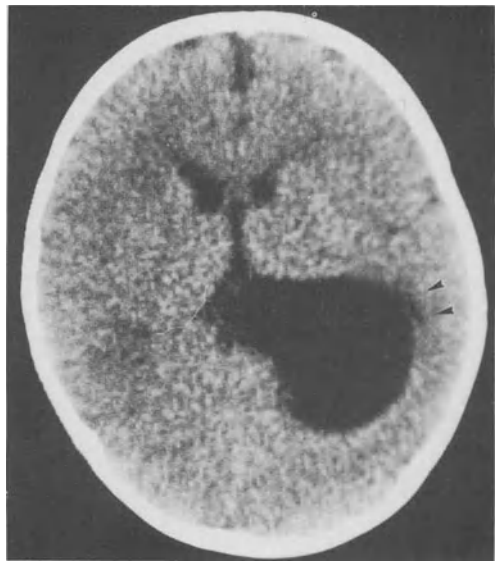

Figure 11.6. A 8-month-old boy presenting with macrocrania. The CT scan reveals a cyst of the quadrigeminal plate cistern extending laterally, displacing the medial surface of the hemisphere and compressing the trigone of the lateral ventricle (arrows), via the cisterna ambiens. The ventricular system is not dilated.

the quadrigeminal cistern share with those of the suprasellar region the lowest mean age at diagnosis (24 months and 17 months, respectively), as compared with values of 29 months, 51 months, and 89 months for the cysts localized in the interhemispheric fissure, over the cerebral hemispheres, and in the sylvian fissure. The apparent prevalence in the very young may be explained on the basis of the common association with an obstructive hydrocephalus and the early appearance of neurological deficits that might prompt the diagnosis, similarly to what can be noticed for the suprasellar arachnoid cysts, which also occur in a restricted space and induce an early impairment in the CSF circulation. Both in the literature[31] and in our series a higher incidence in females was noticed (ratio of females to males 1.5:1 in the literature, 2:1 in our series).

Clinical Presentation and Diagnosis

In spite of the large dimension that interhemispheric cysts may reach in the course of time, the clinical symptomatology may remain surprisingly poor (Table 11.3).[2,10,13,17,20,22] Actually, in a significant proportion of cases the diagnosis is obtained incidentally in otherwise asymptomatic subjects.

In most cases, macrocrania is the presenting sign; when the head is enlarged at birth, a diagnosis of compensated or arrested hydrocephalus can be subsequently made on the basis of the rather slow growth rate of the skull.[5] In our series, 80% of the patients exhibited an abnormally large head (Table 11.3); nevertheless, only in 66% of them was

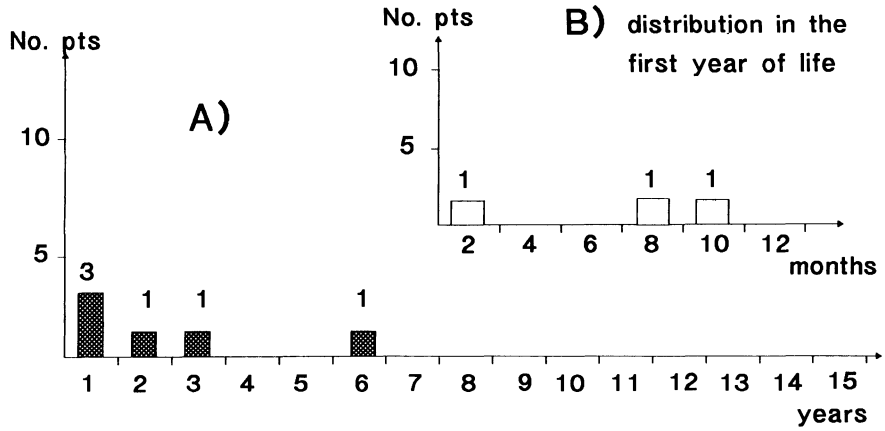

Figure 11.7. Age distribution of quadrigeminal plate arachnoid cysts (personal series).

Table 11.3. Clinical manifestations of interhemispheric arachnoid cysts (from literature and personal series).

Author (reference no.) [no. of cases]	Anderson and Landing[10] [3]	Aicardi and Bauman[13] [2]	Cilluffo et al.[17] [1]	Rao et al.[2] [1]	Harsh et al.[20] [1]	Locatelli et al.[22] [2]	Personal series [15]	Total [25]
Increased head circumference	3	2	1	1	1		12	20
Cranial bulging	3	1					7	11
Increased intracranial pressure	1		1		1		8	11
Neurological signs				1			3	4
hypertonia							2	2
hemiparesis							1	1
tremor				1				1
Developmental delay				1			2	3
Epilepsy							2	2
Prenatal diagnosis							6	6

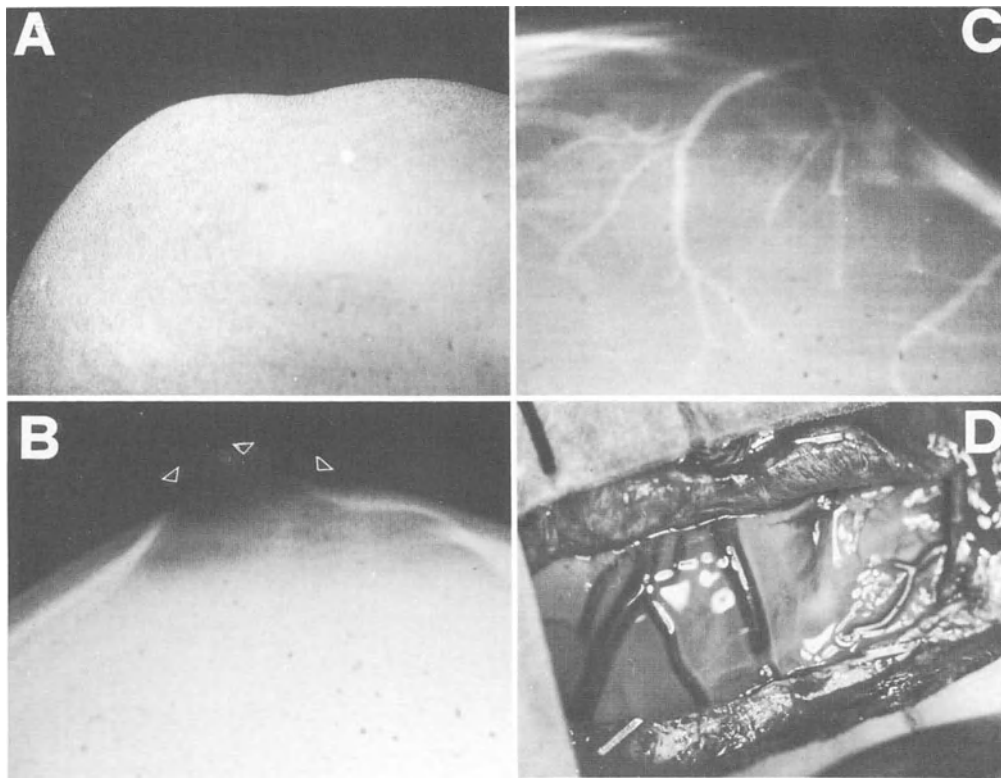

Figure 11.8. An 8-year-old girl harboring an arachnoid cyst of the interhemispheric fissure the presence of which is suggested by the overlying bulging of the skull at the vertex (A). Plain x-ray film (B) confirms the skull deformity and shows a thinning of the calvarial bone. The cerebral angiography (venous phase) (C) and the intraoperative view (D) demonstrate that the bridge veins are elevated along with the external wall of the cyst.

the macrocrania accompanied by signs of increased intracranial pressure. In most cases, the displacement of the superior sagittal sinus from its normal position and a thinning of the calvarium overlying the lesion suggested a long-standing process. Of our children with interhemispheric arachnoid cysts, 49% showed a localized cranial bulging, corresponding to the underlying cystic lesion (Figure 11.8); however, the bone deformity was usually not so apparent (and radiologically so sharply defined) (Figure 11.9) as in cases of cyst localized over the cerebral convexities and within the scissura of Sylvius.

In most patients with parasagittal cysts the hydrocephalus is mild or even absent. The association with a ventricular dilation is, however, more common in cases where the corpus callosum is absent or defective. In such an instance, it may be difficult to establish the relative role exerted in the genesis of the disturbance in CSF circulation by the cerebral maldevelopmental process or by the mere presence of the cyst, resulting in obvious limits to establishing the surgical indication and choosing the most appropriate surgical procedure. The absence of neurological deficits in the great majority of patients even in those with an interhemispheric cyst associated with the absence of the corpus callosum, can be understood when considering that in the agenesis of the corpus callosum, fibers that normally pass the midline at the third month of fetal life are not interrupted, but rather spread over the medial side of the homolateral cerebral hemisphere.

Both varieties of arachnoid cysts occurring in the interhemispheric fissure—the parasagittal form and the interhemispheric form—present considerable difficulties in the diagnosis, though to a different extent. In fact, the recognition of the parasagittal form appears relatively facilitated by its unilaterality and by the absence of accompanying cerebral malformations; however, by no means may this type of lesion be distinguished preoperatively from other cystic lesions that also may develop along one side of the falx in the callosal cistern, such as glial, ependymal, choroid, and epithelial cysts (Figure 11.10). Clinically, parasagittal arachnoid cyst are usually suggested by the asymmetrical enlargement of the head and local bulging of the calvarium. The standard x-ray examination of the skull may reveal localized bulging and thinning of the cranial vault in the midline region of the skull, usually at the vertex. The bone findings are confirmed by computed tomography, which also demon-

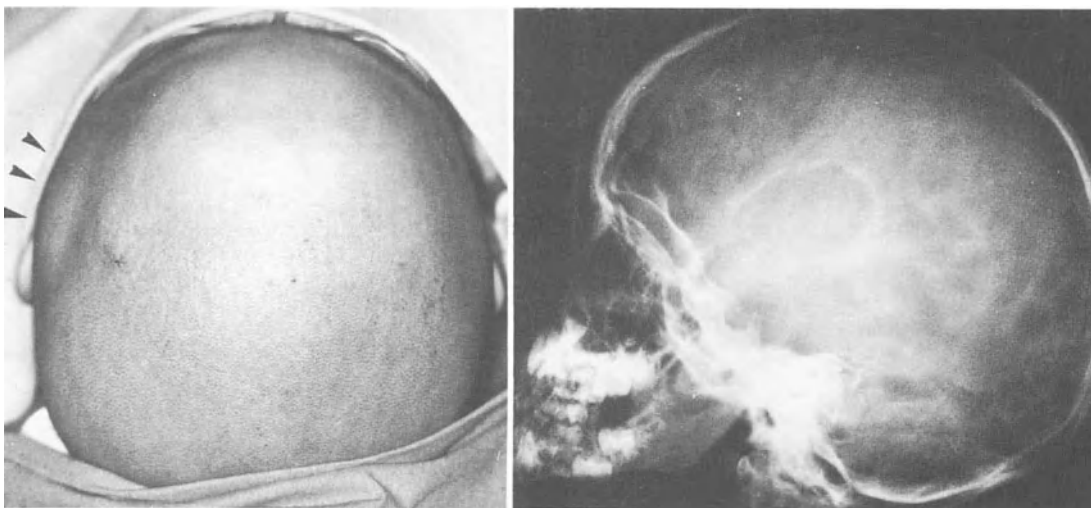

Figure 11.9. Localized bulging (arrows) of the left temporal bone in 5-year-old boy with L-sylvian fissure arachnoid cyst. Note the osteolytic appearance of the calvarium overlying the lesion.

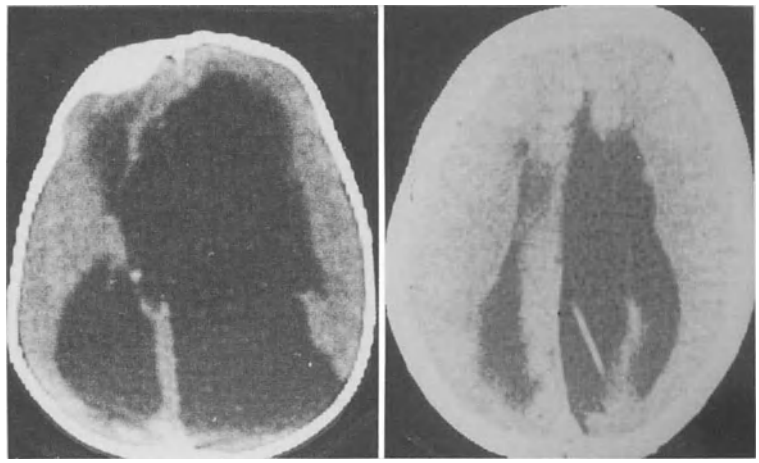

Figure 11.10. CT scan appearance of an interhemispheric ependymal cyst in a 15-year-old boy. Preoperative CT scan (left) shows the huge cystic lesion dislocating laterally the dilated right lateral ventricle. Postoperative CT scan (right) shows the separation of the cyst from lateral ventricle and demonstrates a good reexpansion of the cerebral parenchyma, as an affect of the shunting of the cyst.

strates the underlying unilateral lesion of a density comparable with that of water and with no enhancement after contrast medium administration. On the coronal section, the interhemispheric cyst, sharply defined by the falx on one side and relatively more expanded on the other side because of the minor resistance offered by the cerebral hemisphere and the compliant cerebral ventricle, tends to assume a wedge-shaped configuration on the coronal view (Figure 11.11). The lateral ventricle on the side of the maximal expansion of the lesion is usually laterally and downwardly dislocated and compressed. Similar results may be obtained using magnetic resonance imaging.

When examined by means of dynamic radionuclide cisternography or computed tomogra-

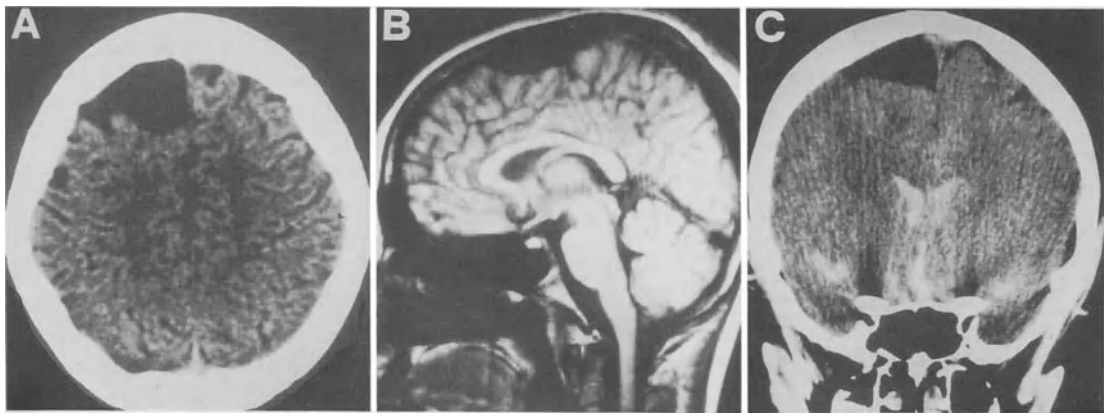

Figure 11.11. A 10-year-old boy presenting with a history of moderately increased intracranial pressure and seizure disorder. The CT (A) and MRI studies (B) define the relationships of the cyst with the surrounding structures. CT scan taken about 5 hours after metrizamide injection into the lumbar subarachnoid space (C), fails to demonstrate cyst opacification, whereas the ventricular system is penetrated by the contrast medium. On the coronal view the cyst assumes a wedge-shaped configuration.

Table 11.4. Clinical manifestations of quadrigeminal plate arachnoid cysts (from literature of personal series).

Author (reference no.) [no. of cases]	Alexander[26] [1]	Dott and Gillingham[34] [1]	Lourie and Berne[35] [1]	Dvorak and Zapletal[36] [1]	Kruyff[27] [5]	Huckman et al.[37] [1]	Harrison[11] [4]
Increased HC	1		1			1	4
Increased ICP			1	1	3	1	1
Neurological signs		1	1			1	1
hypertonia		1	1				
gait disturbance						1	
hemiparesis							1
Developmental delay					2		1
Ocular signs					3		2
↓ visual acuity							2
nystagmus					2		
Parinaud's syndrome							
"wandering" eyes					2		
Epilepsy							1
Precocious puberty							

HC, head circumference; ICP, intracranial pressure.

phy cisternography the parasagittal cysts are usually penetrated by the contrast medium, in a relatively short time; however, the clearance of the agent from the interior of their cavity is surprisingly slow. The phenomenon has received multiple explanations, the most credited of which postulate a kind of unidirectional valvular communication with the subarachnoid space, favoring the penetration of fluid into the cyst rather than its outflow, or take into account the scarce elasticity of the cystic wall which is provided mostly by collagen fibers and lacking elastic fibers.[5]

The differential diagnosis of interhemispheric arachnoid cysts with other midline cystic lesions, certain forms of agenesis of the corpus callosum, and in particular with type I-C prosencephaly, as described by Probst,[3] is practically impossible on the basis of neuroradiological findings alone.[32]

Twenty-five percent of children with agenesis of the corpus callosum have associated midline cysts and approximately 30% of subjects with holoprosencephaly have a dorsal cyst.[33] In almost all malformations resulting in a defect of the corpus callosum, there is some degree of elevation, and even "cystic" distension, of the roof of the third ventricle, which may extend upward between the two cerebral hemispheres, thus simulating an interhemispheric cyst. This "secondary" cyst is often indented in the midline by the free edge of the falx, bulging more or less symmetrically on both sides. Primary interhemispheric cysts are usually less indented in the midline because of a certain degree of hypoplasia of the falx cerebri, but maintain a "batwing" appearance on the coronal computed tomography view of the lateral ventricles, with a dorsally displaced third ventricle. Hydrocephalus may be present in both conditions; however, in cases of interhemispheric arachnoid cysts the occipital horns of the lateral ventricles are recognizable, though laterally displaced (Figure 11.3). The posterior part of the ventricular system is barely identifiable in children with type C prosencephaly. Another distinguishing finding is the normal separation and the lateral dislocation of the basal ganglia in the presence of an interhemispheric arachnoid cyst, whereas the same structures may be undivided or showing only varying degrees of division in porencephalic subjects.

The subarachnoid space, which lies above the quadrigeminal plate, usually indicated as the cisterna venae magnae Galeni, represents

Danziger and Bloch[12] [5]	Grollmus et al.[25] [1]	Handa et al.[38] [1]	Hayashi et al.[31] [1]	Cilluffo et al.[17] [2]	Locatelli et al.[22] [1]	Marinov et al.[24] [2]	Ciricillo et al.[30] [1]	Personal series [6]	Total [34]
5	1	1	1	1	1	1		3	21
	1		1	2	1	1	1	2	16
								2	6
								1	3
								1	2
									1
2				1		1		4	11
			1	1				2	9
1				1				1	5
									2
			1						
								1	2
									2
								5	6
				1					1

a critical area for the cerebrospinal fluid circulation. Arachnoid cysts developing in this relatively restricted space behave as any other space-occupying lesions in the region of the pineal gland, causing an obstructive hydrocephalus and determining the early impairment of the adjacent neural structures (Table 11.4).* The most common clinical presentation is that of an obstructive hydrocephalus, with enlargement of the head, abnormally high growth rate of the cranial perimeter, late milestones or regression of development in infants and young children, and with headache, nausea, vomiting, lethargy, and papilledema in other patients. Impairment of pupillary reactions, limb weakness, ataxia, and bilateral deafness due to damage to the inferior colliculus have been occasionally reported.[26,28,31,35,39] It is worth noting that impairment of the upward conjugate gaze as seen in pinealomas is relatively rare in this pathological condition.

In some of our patients epilepsy dominated the clinical pictures. In one of these subjects treated with a cystoperitoneal shunt (Figure 11.12) the frequency of the seizures seemed to be related to the volume (and/or inner pressure) of the cyst, as the seizures became more frequent whenever shunt malfunction occurred. When considering the relative aspecificity of the clinical manifestations of arachnoid cysts in the quadrigeminal cistern, it is well apparent that the diagnosis cannot rely on the clinical picture alone. In fact, similar manifestations can be observed in patients with an obstructive hydrocephalus, due to a heterogeneous group of expansive processes in the region apt to induce a compression of the aqueduct and fourth ventricle, such as pinealomas, third ventricle tumors, gliomas of the brain stem, and arterovenous malformations.

In cases where ultrasonography, computed tomography, and magnetic resonance imaging have established the "cystic" nature of the lesion, the differential diagnosis is to be made with various congenital and acquired cystic lesions that can be found at the level of the quadrigeminal plate. A dilated suprapineal recess of the third ventricle, or atrial diverticula of the lateral cerebral ventricles in cases of severe hydrocephalus secondary to aqueductal stenosis, are usually easy to recognize. In

*Refs. 11, 17, 22, 24–27, 29–31, 34–38.

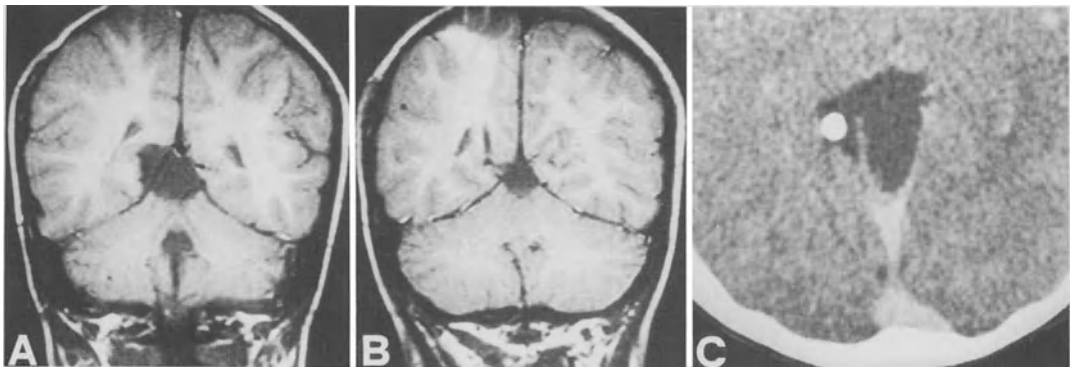

Figure 11.12. A 4-year-old girl with quadrigeminal plate arachnoid cyst, presenting with seizure disorder (A). Postoperative MRI study (B) demonstrates the reduction in size of the lesion following the insertion of a cystoperitoneal shunt. The operation was accompanied by the disappearance of seizures which, however, recurred when the cyst reexpanded because of a shunt malfunction 2 years after the first operation (C).

doubtful cases, the demonstration of a communication between the "cyst" and the ventricular system by means of computed tomography cisternography, or following the injection of contrast medium within the cerebral ventricles, allows the correct recognition of the lesion. The differential diagnosis with "cysts" of the cavum vergae is made possible by the typical configuration of the cavum, even when its dilation extends downward and posteriorly to the splenium of the corpus callosum.

In cases of dilated subarachnoid pouches developing in the region of the quadrigeminal cistern, because of postinflammatory loculations of this space,[34] a differential diagnosis may be practically impossible. On the other hand, the evidence of a posterior fossa tumor may easily differentiate the subarachnoid pouches or dilated cisterns—the so-called cyst-like lesion of Kruyff[27]—described by several authors as an accompanying finding of a space-occupying lesion within the posterior cranial fossa.[40–43] A similar consideration may be made for the dilation of the cavum veli interpositi, which can be observed in more than one-third of the subjects with posterior fossa tumors.

A neuropathological examination is required in order to differentiate arachnoid cysts of the cistern of the lamina quadrigemina from congenital cystic lesions that have the same morphological and radiological characteristics, such as ependymal cysts, neuroglial cysts, and intracranial neuroencephalocele.[27,39,44] In such an occurrence, however, the limit in diagnosis does not have any practical influence, as these lesions when behaving as symptomatic quadrigeminal arachnoid cysts require the same surgical treatment, with similar operative risks and long-term outcomes.

Surgical Management and Results

There are usually two main surgical procedures in the treatment of interhemispheric arachnoid cysts: the insertion of a cystoperitoneal shunt device or the wide excision of the cystic membrane, by means of craniotomy. The two procedures may possibly be associated in a given subject.[5]

Although the shunting of the cyst has the great advantage of being a low-risk operation, the direct surgical attack on the lesion offers the possibility of reestablishing a "natural" pathway of the cerebrospinal fluid circulation. As for arachnoid cysts localized in other intracranial regions, the "recurrence" of the cyst is the main limit of the procedure of direct ex-

Table 11.5. Symptoms, signs, treatment, and result of cysts, as reported in the literature.

Author (reference no.)	No. of cases		Age	Location of cyst	Symptoms and signs	Treatment	Results
Alexander, 1953[26]	1		18 mo	Quadrigeminal cistern	Hydrocephalus	Cyst excision; communication with the third ventricle	Improvement
Katagiri et al., 1960[28]	2	a	Adult	Quadrigeminal cistern	—	Cyst excision	Operatory death
		b	Adult	Cisterna ambiens	—	Puncture of cyst	Improvement
Lourie and Berne, 1961[35]	1		13 mo	Quadrigeminal cistern with supratentorial and infratentorial extension	Hydrocephalus	1) Communication between the cyst and the superior cerebeller cistern	Recurrence
						2) Communication between the cyst and both the third and lateral ventricles	Improvement
Lewis, 1962[45]	1		7 mo	Tentorial notch	Hydrocephalus	Cyst excision	Death
Kruyff, 1965[27]	2	a	1 mo	Quadrigeminal cistern	Hydrocephalus	Cyst excision	?
		b	13 mo	Quadrigeminal cistern	Wandering eyes; nystagmus	Cyst excision	?
Huckman et al., 1970[37]	1		9 yr	Quadrigeminal cistern	Hydrocephalus	Cyst excision	Improvement
Harrison, 1971[11]	3	a	4 mo	Quadrigeminal cistern	Hydrocephalus; ↑ ICP; ↓ visual acuity	VA shunt	Dead 7 mo later
		b	3 mo	Quadrigeminal cistern	Hydrocephalus; ↑ ICP	Craniotomy, aspiration of fluid and Torkildsen procedure	Fair improvement
		c	9 mo	Quadrigeminal cistern	Hydrocephalus; ↑ ICP	Cyst fenestration followed by VA shunt	Arrest of hydrocephalus; severe mental retardation; spasticity
Danziger and Bloch, 1975[12]	4	a	7 mo	Quadrigeminal cistern	Hydrocephalus; developmental delay	Cyst drainage followed by VA shunt	Initial improvement; recurrence of hydrocephalus
		b	9 mo	Quadrigeminal cistern	Hydrocephalus	Cyst drainage	?
		c	10 mo	Quadrigeminal cistern	Hydrocephalus	Cyst drainage	?
		d	13 mo	Quadrigeminal cistern	Hydrocephalus	Cyst drainage	?
Handa et al., 1977[38]	1		4 mo	Quadrigeminal cistern	Hydrocephalus	Craniotomy and cyst excision	Improvement

Table 11.5. (cont.)

Author (reference no.)	No. of cases	Age	Location of cyst	Symptoms and signs	Treatment	Results
Hayashi et al., 1980[31]	1	22 mo	Quadrigeminal cistern	Hydrocephalus	Communication between the cyst, the cisterna ambiens, and the third ventricule	Improvement
Cilluffo et al., 1983[17]	2 a	7 yr	Quadrigeminal cistern	↑ ICP; mentally retarded; ↓ visual acuity (optic atrophy); precocious puberty	VP shunt	Improvement; L-eye blindness
	b	15 mo	Quadrigeminal cistern	Hydrocephalus; ↑ ICP; bilateral 6th nerve palsy	Craniotomy and cyst excision followed by VA shunt	Mild ataxia; Parinaud's syndrome; otherwise normal
Serlo et al., 1985[18]	3 a	3 yr	Quadrigeminal cistern	Precocious puberty	Cystoatrial shunt	Normal (precocious puberty)
	b	$1\frac{1}{2}$ yr	Quadrigeminal cistern	Hydrocephalus	Cyst fenestration and VA shunt followed by cystoventriculoatrial shunt	Ataxia
	c	6 mo	Quadrigeminal cistern	Hydrocephalus	VA shunt followed by cystoventriculoperitoneal shunt	Ataxia

ICP, intracranial pressure; VA, ventriculo-atrial; VP, ventriculo-peritoneal.

cision of the cystic wall. In our experience, variable results have ensued from the removal of the cystic membranes, from the adequate reexpansion of the parenchymal structures to the persistence of midline cystic cavities, even though reduced in size and apparently communicating with the normal subarachnoid spaces. As the surgical correction—either shunting of the cyst or excision of its wall—is nearly always aimed at controlling the increased intracranial pressure and the abnormally growing head, successful results, i.e., the normalization of intracranial pressure, are usually obtained in the large majority of affected subjects.

Also, for the cysts localized within the quadrigeminal cisterns the two main surgical options available—the shunting of the cyst and the excision of its wall by means of craniotomy—present obvious limits in their practical utilization. The shunting of the cyst to the peritoneal cavity by means of the catheter can be more difficult than the usual operations of CSF shunting, because of the central location of the cyst, the resistance of its wall, the relatively small size in several patients, and the close proximity to ventricular structures, which may lead to the incorrect position of an intrathecal shunt device when using the percutaneous technique. In very young children—or in older children in whom a craniotomy has been performed—the application of the preoperative ultrasound technique has been suggested in order to facilitate the recognition of the cyst from the adjacent ventricular system.[33] The stereotactic technique may be

particularly helpful in performing the shunting procedure, especially when the establishing of a communication between the cyst and the lateral cerebral ventricle by means of one intracranial catheter is desirable. The direct attack on the lesion by the excision of its wall is weighted by a significant surgical risk (Table 11.5)* Furthermore, the recurrence of symptoms because of refilling of the cyst is quite common, unless a permanent fistula between the residual cavity and the third or lateral cerebral ventricle (less commonly, the fourth ventricle) has been created. The operation can be performed from above or from below the tentorium, depending on the main direction of expansion of the cyst.[26,37]

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CHAPTER 12

Ependymal and Paraphyseal Cysts

Arthur E. Marlin and Sarah J. Gaskill

Paraphyseal cysts, more commonly called colloid cysts and ependymal cysts, are benign developmental lesions of presumed neuroepithelial origin. The colloid cyst is a well-defined pathological entity but considered by some to be part of the spectrum of ependymal cysts. Ependymal cysts are poorly defined in the literature and thus will be considered separately.

Colloid (Paraphyseal) Cysts

Colloid cysts were first described by Wallerman[1] in 1858. They are now recognized to represent between 0.5% and 1% of all brain tumors and 15% of all third ventricular tumors.[2] However, with the advent of improved neuroimaging, colloid cysts are being diagnosed with increasing frequency.

Origin

The origin of these lesions has been the subject of some debate. Although colloid cysts appear to have a neuroepithelial origin the exact mechanism of development remains controversial.

The paraphysis cerebri develops in the midline as a pouch from the diencephalic roof rostral to the telencephalic border.[3] It is present in embryos 17 to 100 mm in size and regresses by the time the embryo is 145 mm in size.[4] It is during this same point in development, and within the same region, that the diencephalic ependymal pouches develop. The paraphysis and ependymal pouches are each capable of "pinching off" and developing as separate entities. Thus, a colloid cyst could arise from either a paraphyseal or ependymal source.

In 1909, Sjovall[5] suggested that colloid cysts were in fact derived from anlagen of the paraphysis. The name *paraphyseal cyst* came into common usage at that time and persisted for the next 50 years. This concept was further explored by Bailey[6] who in 1916 studied the paraphysis in human embryos as a possible precursor to these tumors. He emphasized the midline location of the paraphysis and the (then) constant midline appearance of these lesions in support of their derivation from the paraphysis. Many have agreed with this,[7,8] and it has been further supported by Zeitlin and Lichtenstein,[8] who noted that the microscopic tubules in the walls of the cysts obtained from their patients were identical to the tubules seen in the paraphysis of lower vertebrates and human embryos.

A number of investigators feel that colloid cysts are derived from ependymal epithelium and favor ependymal pouches as the primary source of these lesions[4,9,10] This is supported by electron microscopic studies of colloid cysts[4,10,11] Kappers[4] emphasized the variety of cellular organelles and cell types as consistent with an ependymal origin. Cysts considered to be of ependymal origin are characterized by low columnar epithelium, goblet cells, cilia, and blepharoplasts.[3] As both cilia and

blepharoplasts are seen only in fetal ependymal cells,[8] these findings support the concept of an ependymal origin.

An alternative theory based on developmental and comparative anatomy has been proposed by Shuangshoti et al.[12,13] They propose that cysts can develop in any part of the neuroepithelial-lined ventricular system through invagination or evagination, resulting in a connective tissue layer forming outside or inside (respectively) the neuroepithelial layer. They present evidence that the paraphysis is in fact extraventricular choroid plexus and that choroid plexus and ependyma are derived from a common neuroepithelium.[12–14] They suggest that a colloid cyst can develop anywhere along the neuroepithelial-lined central nervous system from choroid plexus or ependyma.[12] the histological variations in cell types and the presence or absence of organelles by the normal regional variation in neuroepithelium can be thus justified. A case of a combined colloid cyst and xanthogranuloma is offered as evidence that these entities arise from proliferated neuroepithelium.[15] Similar mixed lesions have been confirmed by other authors[16] and a series of cases reported by Palacios et al.[3] also supports the concept of a broad neuroepithelial origin of "paraphyseal cysts." This strengthens the concept that colloid cysts and ependymal cysts are part of the spectrum of neuroepithelial cysts.

A few authors subscribe to a non-neuroepithelial origin of these lesions. This is primarily based on comparison with Rathke cleft cysts and neurenteric or entogenous cysts in conjunction with electron-microscopic findings. An endodermal origin of these cysts has been based on electron microscopy demonstrating features of upper respiratory epithelium—a coating material of the surface of nonciliated cells and a prominent basement membrane.[17,18] Proponents of this theory place these lesions in the same category as other midline congenital anomalies.

Although the exact mechanism of development of colloid cysts remains a controversial issue, their embryological origin is unquestioned. A case of colloid cysts occurring in identical twins is an interesting confirmation.[19]

Presentation

Although colloid cysts are thought to be congenital in origin they do not usually present until the fourth to sixth decades. There is no sex predilection.[16,20–23] Isolated cases have been reported in the pediatric age group.[15,22,24–27] All of these cases presented with signs of progressive hydrocephalus, the cause of which was later diagnosed through ventriculograms, pneumoencephalograms, computed tomography, or autopsy.

The clinical significance of these lesions is based primarily on their strategic location within the foramen of Monro. This results in an obstructive hydrocephalus. It has been suggested that this occurs in a ball-valve fashion, explaining the intermittent nature of symptoms in some patients.[8] Hydrocephalus is present in 93% of patients—severe in 43% moderate in 36%, and mild in 14%.[20]

The most common presenting signs and symptoms are headache, change in mental status, ataxia, papilledema, nausea, and vomiting.[16,20–23] The headaches have been classically described as positional in nature, with improvement in symptoms in the horizontal position,[10,28] although this is certainly not always the case.[16,29,30] Less frequent presenting signs and symptoms include diplopia, seizures, incontinence, motor weakness, and nystagmus.[16,21–23,31] Sudden deterioration and death is not an uncommon presentation.[22,30,32–35] Sudden death is thought to occur in up to 10% of cases.[22]

With improved neuroimaging there has been an increasing number of incidental colloid cysts diagnosed.[20] The appropriate management of incidental colloid cysts is debated. A recent series described the nonsurgical management of 24 patients with colloid cysts,[20] 71% of these patients demonstrated a normal ventricular size. The authors recommended close follow-up with periodic neuroimaging. Brun and Egund,[29] based on autopsies in four patients with colloid cysts with diameters of 1.5 to 1.7 cm, recommended that patients with lesions approaching this size undergo surgical therapy. Although it will be some time before the natural history of these

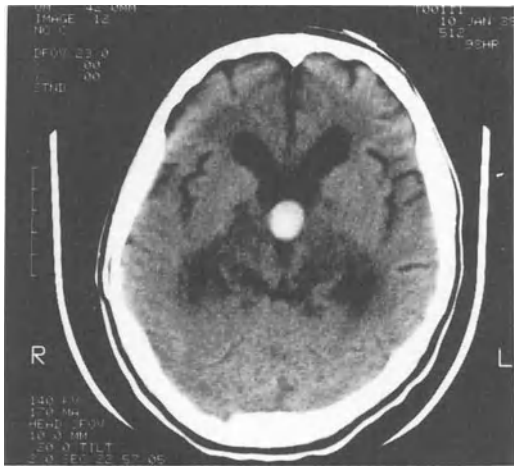

Figure 12.1. CT showing a homogeneous, hyperdense round colloid cyst at the level of the foramen of Monro.

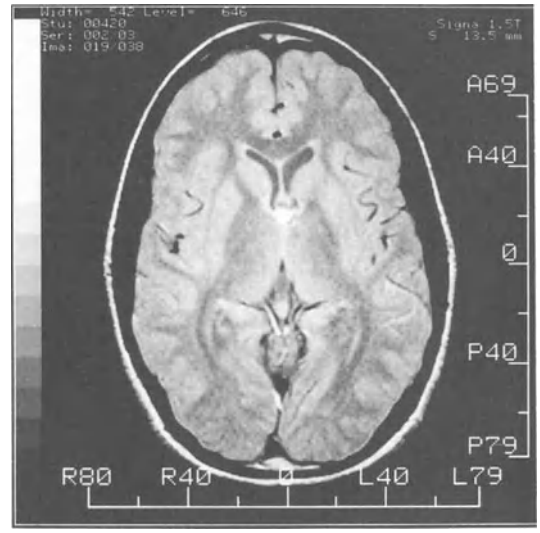

Figure 12.2. MRI image of a colloid cyst without hydrocephalus.

lesions is more clearly defined, it seems reasonable that small lesions not causing hydrocephalus are closely observed with magnetic resonance imaging (MRI). Because of the incidence of sudden death, larger lesions and those causing hydrocephalus should be removed.

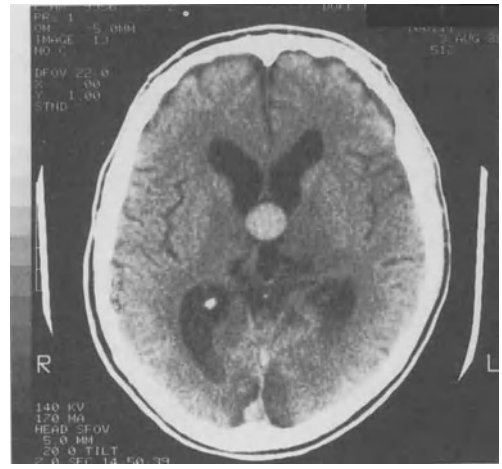

Figure 12.3. CT image of obstructive hydrocephalus due to a colloid cyst.

Radiographic Appearance

The "characteristic" computed tomography (CT) appearance of colloid cysts is a homogeneous, hyperdense, round lesion within the foramen of Monro (Figure 12.1). Colloid cysts will often show some enhancement with the administration of intravenous contrast material. Obstructive hydrocephalus may or may not be present (Figures 12.2 and 12.3). In practice the appearance of colloid cysts on CT is highly variable[36–39] Colloid cysts may be isodense or hyperdense lesions with or without change with contrast enhancement. There may even be ring enhancement on CT[36] Definite calcification has been noted in pathological material.[38] This may explain the increased radiodensity noted in some cases.

The differential diagnosis includes aneurysms of the basilar tip projecting anteriorly and superiorly, meningiomas, ependymomas, intraventricular gliomas, choroid plexus papillomas, craniopharyngiomas, cysticercosis, tuberous sclerosis, pituitary tumors, and teratomas.[40]

Magnetic resonance imaging has provided the ability to make more accurate radiographic diagnosis of these lesions. Experience with the MRI appearance of these lesions is still limited.[41–43] Colloid cysts are more heterogeneous on MRI than on CT (Figure 12.4).

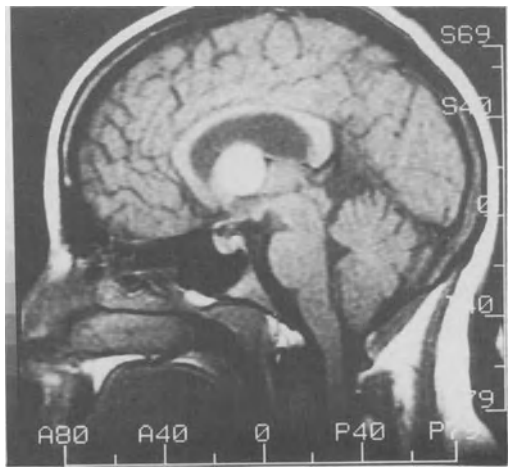

Figure 12.4. Sagittal T1-weighted MRI showing a heterogeneous colloid cyst.

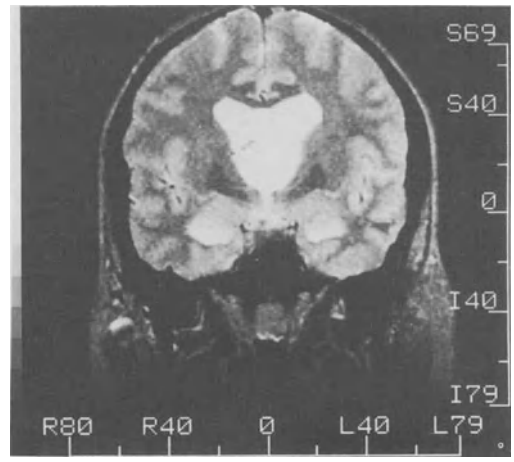

Figure 12.6. Coronal T2-weighted MRI image of a colloid cyst.

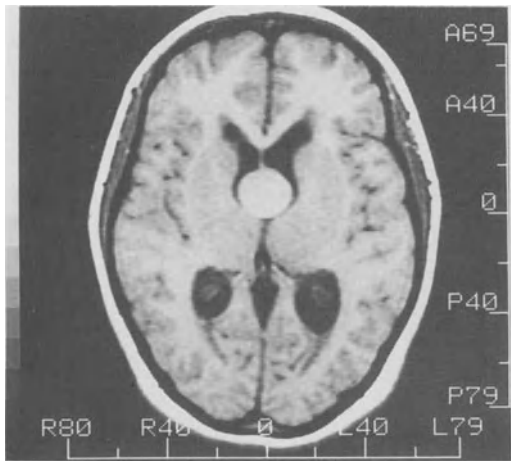

Figure 12.5. Axial T1-weighted MRI of a colloid cyst.

On Tl-weighted images colloid cysts are usually homogeneously hyperintense (Figure 12.5), although examples of isointensity have been reported in the literature.[43] The T2-weighted images are characterized by a strongly hypointense center with a hyperintense rim (Figure 12.6). A high degree of density on CT and a high MRI signal have been correlated with a high cholesterol content.[41]

It should also be noted that colloid cysts may occur at locations other than the anterior third ventricle. Indeed, they may be found throughout the ventricular system[15,44–45] and even in extraventricular locations.[26,46]

Surgical Technique

Colloid cysts are particularly important as they are benign lesions that can be completely removed with favorable operative outcomes. The fact that they have very minimal attachments to the surrounding anatomy makes them readily amenable to surgical extirpation.[47]

The first successful surgical removal of a colloid cyst was by Dandy[28] in 1921 using the pineal approach. Dandy went on to recommend a transcortical transventricular approach to these lesions as he gained further experience with them. In 1949, Greenwood,[47] who felt the risks of traumatic epilepsy were too great with the transcortical approach, successfully removed four colloid cysts via a transcallosal approach. A variation on Dandy's approach was later suggested by McKissock.[48] A variety of surgical approaches have thus been proposed and today there are six commonly used approaches to the third ventricle: (a) subfrontal, (b) subtemporal, (c) anterior transventricular, (d) anterior transcallosal, (e) posterior transcallosal, and (f)

transtentorial.[49] The operative mortality rate of 20% in Dandy's series has been reduced to near zero.[50] The authors prefer a transcallosal approach.

In 1975, Gutierrez-Lara et al.[51] reported the successful evacuation of five colloid cysts by needle aspiration using standard external landmarks to the third ventricular region. They reported no complications with this method, and all five of their patients returned to work within 1 month. The first successful stereotactic aspirations of colloid cysts were described by Bosch et al.[50] Since then, this has become the treatment of choice for a number of authors.[52–57] The problems that can be encountered with this approach are, however, not insignificant. The contents of a colloid cyst are more likely to be viscous or semisolid than liquid.[20] This necessitates the use of a larger cannula than is utilized for routine stereotactic brain biopsy and may result in a failed aspiration attempt.[58] Obviously this increases the risk for hemorrhage or parenchymal damage. Further, the capsule of the colloid cyst is often tenacious and difficult to puncture even in an open surgical approach. The risk of spilling the contents of the cyst into the ventricular system is increased with this approach. The irritative nature of this substance could result in an aseptic meningitis or accelerate the development of hydrocephalus based on scarring. Finally, as the natural history of these lesions remains unclear, the effective duration of this therapy is not known. Further information regarding the correlation between the radiographic appearance of these lesions and their chemical content would be useful in deciding whether or not a stereotactic approach should be attempted.

Three other techniques for the management of these lesions should be mentioned. One is the use of ventriculoscopy as a diagnostic and therapeutic tool for the management of isodense third ventricular lesions.[59] This combines the advantages of the stereotactic approach with limited visualization. Intraoperative ultrasound with open approaches can be used as a means of assisting in the localization, especially in patients without ventriculomegaly.[60] This can reduce the amount of unnecessary surgical dissection. The cyst is readily identified using this technique (Figure 12.7). Alternatively, a catheter can be placed stereotactically to the cyst and the lesion can be found following the catheter tract.

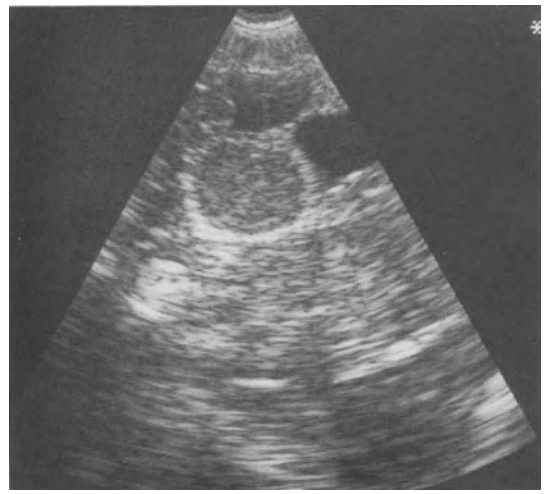

Figure 12.7. Intraoperative ultrasound demonstrating the location of a colloid cyst.

Ventricular drainage by external or internal means may or may not precede operative intervention, depending on the individual circumstances. Cerebrospinal fluid (CSF) diversion, however, is not to be considered the definitive treatment for a colloid cyst.

Pathology

The pathological diagnosis of colloid cysts is clear. Grossly, these lesions have smooth, spherical capsules ranging in size from 0.3 to 4 cm (Figure 12.8). Their contents are usually a viscous, cloudy material, or a more solid hyaline material resembling soft cartilage. Histologically they show an outer collagenous capsule lined by cuboidal or columnar epithelium (Figure 12.9) with goblet cells and ciliated cells (Figure 12.10). The contents of the cyst are an amorphous, periodic acid-Schiff (PAS)–positive debris composed of eosinophilic filamentous masses, degenerating leukocytes, and cell ghosts.[61] Hyphae-like structures have been noted (Figure 12.11) and are

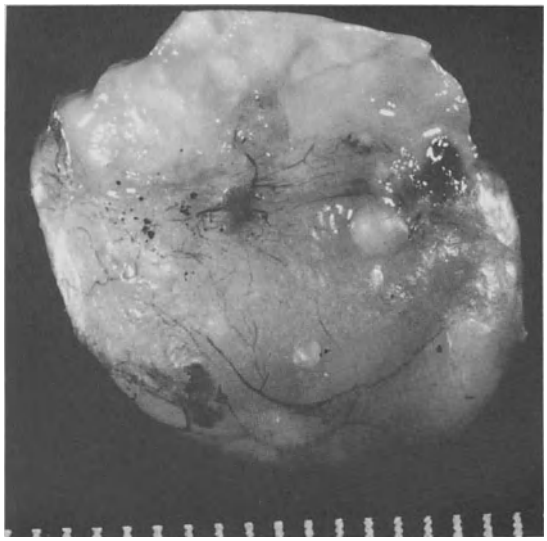

Figure 12.8. Gross specimen of a colloid cyst measuring approximately 1.7 cm.

thought to represent degenerated nuclear protein and phospholipid.[62] New or old hemorrhage may be present.[63]

Prognosis

The prognosis for these lesions is excellent. Survival with return to normal neurological status is the rule. The morbidity and mortality associated with colloid cysts should be minimal. Persistent memory loss has been reported in patients undergoing an anterior transcallosal approach to these lesions.[49] This has been attributed to sectioning of the anterior fornix.[64] Seizures are a common sequela of a transcortical, transventricular approach, but are readily managed with anticonvulsants.[22] As mentioned previously, sudden deaths do occur in a minority of patients. Most of these patients had symptoms for days to months.[30]

Ependymal Cysts

Ependymal cysts are rare. These lesions are poorly defined from multiple single case reports. This is most likely due to the fact that cysts within the ventricular system containing CSF-like contents are frequently treated by shunting or establishing internal communication, many times without actual biopsy. They are a developmental lesion whose unique characteristics distinguish them from other fluid-filled cysts within the central nervous system. As discussed above, colloid cysts may be a variety of ependymal cysts.

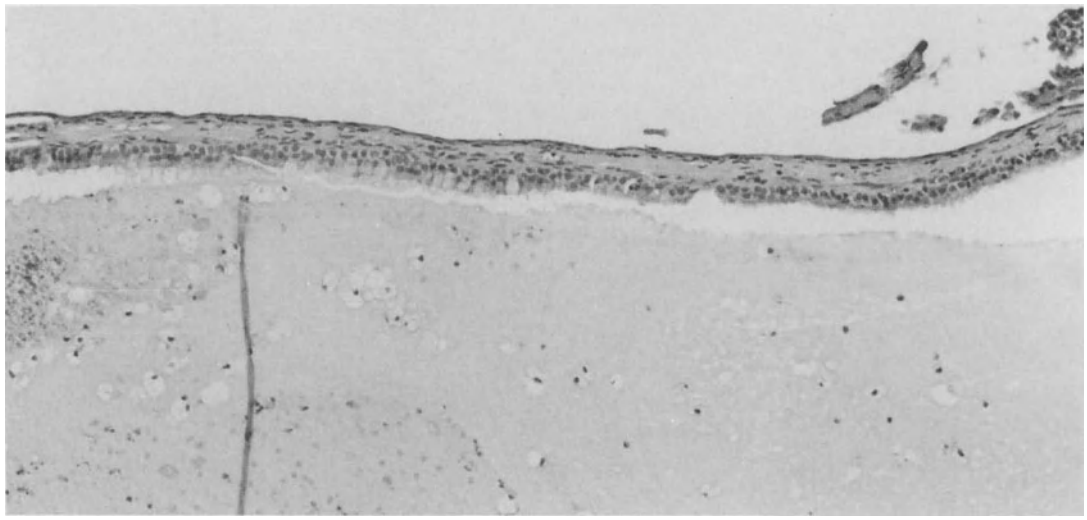

Figure 12.9. A histological section of the cyst wall demonstrating its outer collagenous wall with a cuboidal epithelium.

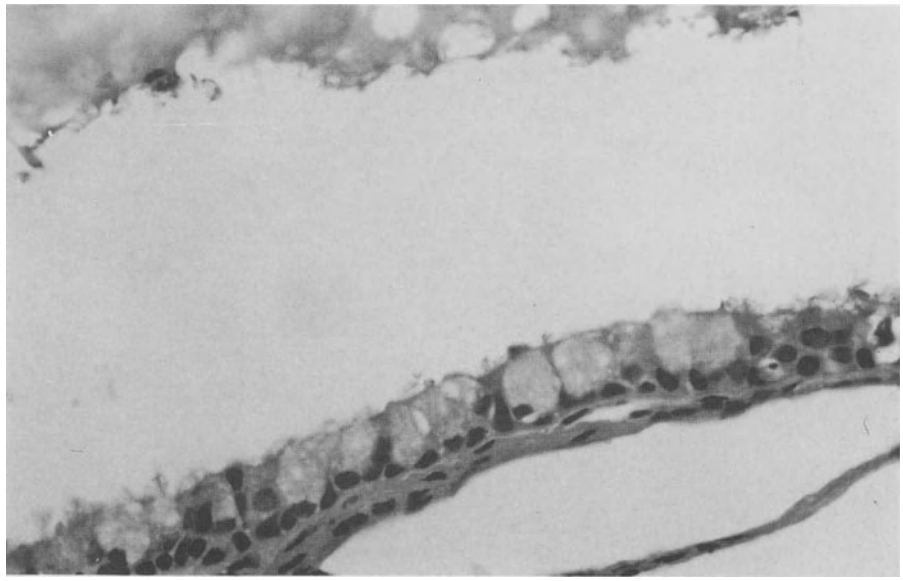

Figure 12.10. A higher power showing the goblet cells and cilia characteristic of colloid cysts.

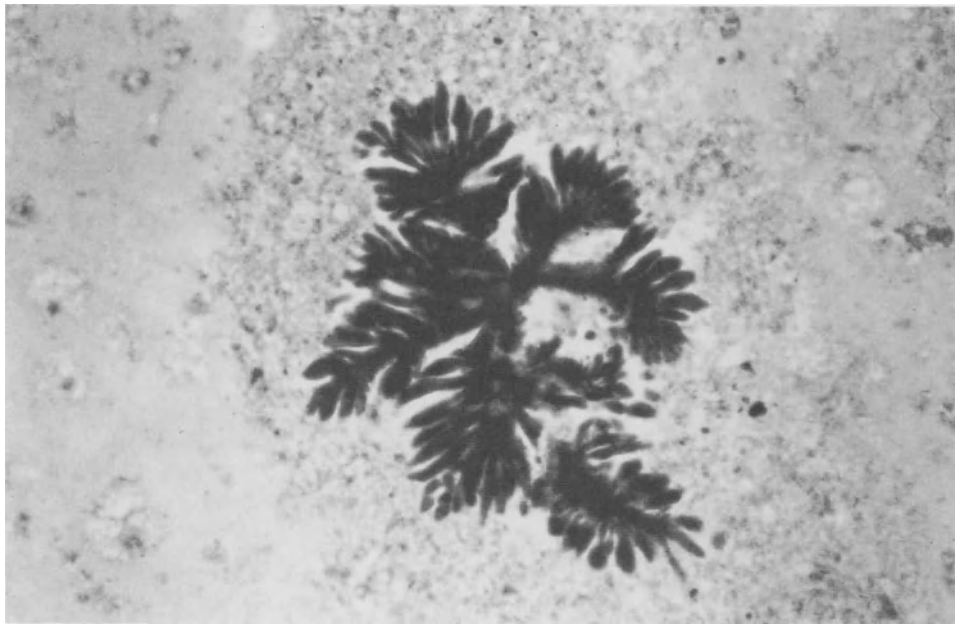

Figure 12.11. Hyphae-like structures within the colloid cyst. These represent degenerated nuclear protein and phospholipids.

Origin

It is presumed that ependymal cysts represent an embryologic maldevelopment. Several different theories have been proposed to explain their development.

The diencephalic roof consists of two layers: an external, vascular pia mater, which is derived from mesenchyme, and the ependymal roof. Together these two layers form the tela choroidea. With active proliferation of the vascular pia mater the tela choroidea invaginates to form the choroid plexus of the fourth ventricle. These same developmental events occur in the roofs of the third ventricle and medial walls of the lateral ventricles.[65] One theory is that ependymal cysts arise from a small segment of the tela choroidea that becomes displaced either into the cerebral tissue (to form an intracerebral ependymal cyst) or into the subarachnoid space (to form a subarachnoid glioependymal cyst).[66] This concept is based on studies of the ultrastructure of ependymal cysts that show a basement membrane and pinocytosis—both characteristics of choroid plexus.[67]

Ependymal cysts in the subarachnoid space in particular have been attributed to the cystic degeneration of subarachnoid glial heterotopias with an ependymal element[68] Ectopic glial tissue has been found in a variety of locations, including two cases of ependymal cysts in close relation to the vertebral column.[69–72] The first, by Connor[71] in 1965, discussed a subcutaneous ependymal cyst at the level of the first lumbar spinous process with no connection to the spinal canal. A second case was reported by Jacobs and McKinnell,[72] who noted an ependymal cyst in the neural arch of the second lumbar vertebra, again without a connection to the spinal canal. These cases implicate ectopic glial tissue in the formation of ependymal cysts. Other authors have suggested that they are remnants of an ependymal-lined diverticulum (Blake's pouch), which embryologically projects dorsally from the roof of the fourth ventricle.[73]

Ependymal cysts occurring in conjunction with other developmental anomalies have been reported.[74–77] Harrist et al.[75] reported two sacrococcygeal neuroepithelial heterotopias that occurred in children with an epidermal nevus and a lipomeningocele. Oral-facial-digital syndrome has been associated with a number of central nervous system anomalies including a large number of intracranial ependymal cysts.[74,76,77] These reports support the notion that the lesions have a maldevelopmental origin.

Shuangshoti et al.[78] maintain that ependymal cysts fall within the category of neuroepithelial cysts. They have supported this hypothesis with immunohistochemistry, and they cite as evidence a case of an ependymal cyst occurring in a 2-year-old child with glial fibrillary acidic protein (GFAP)-positive epithelium. They contend that ependymal cysts and colloid cysts belong in a continuum of lesions derived from neuroepithelium, and they should be classified merely as "neuroepithelial cysts."

Ependymal cysts of the spinal cord have unique characteristics and are thought by some to have an enterogenic origin based on electron-microscopic studies showing ciliated epithelium.[79–81] The primitive entodermal lining of the foregut goes through a transient stage of ciliation before it reaches its final stratified squamous state and the respiratory tract is ciliated throughout most of its development.[82] These embryological findings support an enterogenic origin for spinal ependymal cysts. Hyman et al.[83] have suggested an alternative theory. They believe that spinal ependymal cysts arise from an embryonic connection between the cyst and the central canal in the form of evaginated cells that separate from the neural tube. There have been very few cases of spinal ependymal cysts in the literature, making it difficult to support one theory over another.[79,81,83–90]

In summary, the origin of ependymal cysts remains debatable and there has been much confusion regarding the definition. Various nomenclatures have been applied to ependyma-lined cysts and this further complicates the issue. This is in part because of the variety of cell types that have been described in the cyst wall. Both nonciliated cuboidal or columnar epithelial cells have been described,[86] as

well as mixtures of ciliated and nonciliated cells.[90] This variation in the cyst linings has been explained by the regional variations of cilia and microvilli seen on electron-microscopic studies of ventricular walls.[91] Ependymal cysts include a spectrum of ependyma-lined cysts with a variable histological picture from nonciliated low-cuboidal epithelium to ciliated columnar epithelium resting on a thin collagen membrane or glial tissue.[66]

Presentation

The clinical presentation of ependymal cysts is nearly as varied as the number of cases.[92–108] Some patterns do emerge. In children, presentation is that of increased intracranial pressure either from the cyst or cysts or obstructive hydrocephalus caused by them (Figure 12.12). Gilles and Rockett[73] document this in their series of retrocerebellar cysts. Most cases in the literature are in adults, with the most common location in or near the frontal lobes or the frontoparietal region. Other locations include the temporal and temporoparietal. The majority of cysts are over 4 cm at the time of presentation.[66]

Over 50% of patients will present with seizures and/or headaches.[66] Other presenting symptoms include hemiparesis, hypesthesia, hemianopsia, ataxia, personality changes, and memory disturbance. The duration of symptoms varies from hours to many years, with most histories evolving over a 1- to 2-year period.

Radiographic Appearance

The radiographic appearance of ependymal cysts is variable. These lesions are hypodense on CT scan. Various signal intensities occur on MRI and the cysts may or may not follow cerebrospinal fluid depending on the protein content. (Figures 12.12 and 12.13). As a rule ependymal cysts do not communicate with the ventricular system or subarachnoid space.[109] The differential diagnosis includes arachnoid cyst, cystic tumors, and infectious lesions.

Management

Ependymal cysts, in any location, are relatively benign lesions. Treatment options include a variety of surgical approaches. The goal of surgical intervention is to decompress the cyst.

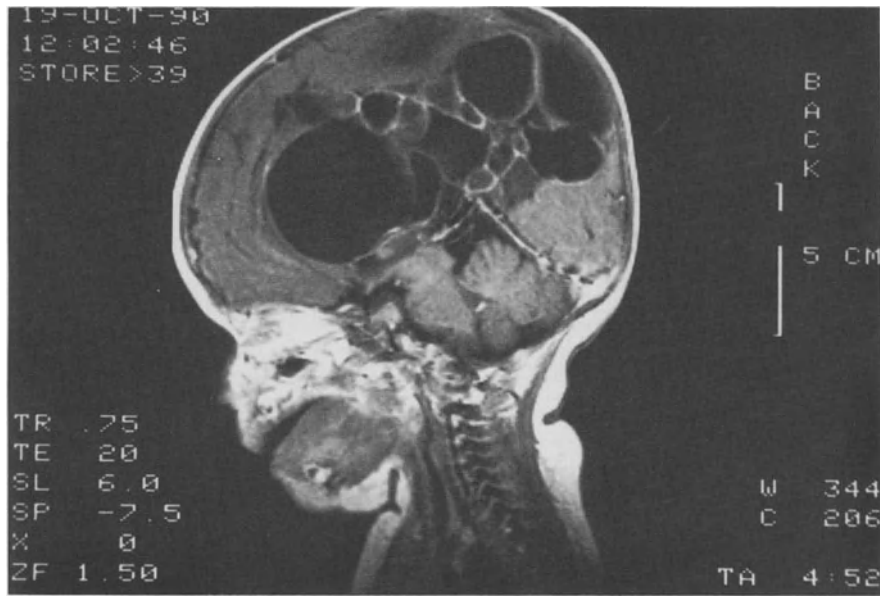

Figure 12.12. T1-weighted MRI image of multiple ependymal cysts.

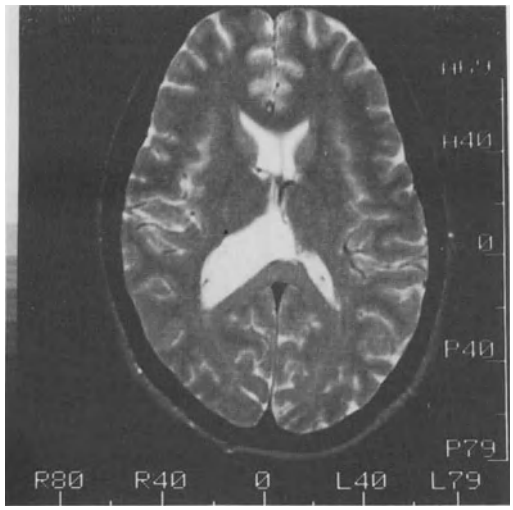

Figure 12.13. T2-weighted MRI image of an ependymal cyst.

This can be accomplished by establishing a communication between the ventricular system or shunting the cyst. Subtotal resection with creation of a communication with the ventricular system[66,97,100,106] and total resection with either cystosubarachnoid shunting or subgaleal shunting have been described.[95,101] The approach taken is partly decided on by the location of the lesion. Frequently, shunting the cyst to the peritoneal cavity is the simplest and most satisfactory approach. Multiple shunts may be required. With multiple cysts or even a single cyst in the ventricular system, ventriculoscopy can be used to communicate the cysts with each other or the ventricular system. The single resulting cavity can then be shunted. This latter approach is the authors' preference. Prognosis is excellent. Periodic postoperative scans should be obtained to insure adequate decompression of the cyst.

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CHAPTER 13

Dandy–Walker Syndrome

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The basic triad of Dandy–Walker syndrome (DWS) is the supratentorial hydrocephalus, the posterior fossa cyst, and dysgenesis of the cerebellar vermis. In this chapter, we review 37 cases of DWS treated at Cook County and Children's Memorial Hospitals in Chicago between 1963 and 1977, and 26 cases of the posterior fossa cyst, including 2 cases of DWS, diagnosed at the Juntendo University Hospital in Tokyo since 1978. On the basis of these investigations, we present clinical, neuroradiological, and surgical features of DWS and offer a review of the literature.

Etiology and Historical Review

In 1914, Dandy and Blackfan[1] reported on a 13-month-old girl with noncommunicating hydrocephalus. The disease had developed after she suffered fever, convulsions, and decerebrate rigidity at the age of 4 months, incurring progressive cranial enlargement and death. Autopsy revealed supratentorial hydrocephalus associated with aqueduct dilatation, cystic dilatation of the fourth ventricle, and atrophy of the rostral part of cerebellar vermis. As neither the foramen of Magendie nor the foramen of Luschka was recognized to be patent, the investigators concluded that obstruction of the cerebrospinal fluid (CSF) pathway had caused hydrocephalus in this patient.

In 1921, Dandy[2] reported on eight infants and two adults with similar noncommunicating hydrocephalus. He classified those cases in which the foramina of Magendie and Luschka congenitally occluded as the congenital type, and those in which such occlusion secondarily resulted from meningitis as the postmeningitis type.

In 1942, Taggart and Walker[3] reported on three infants in whom hydrocephalus was assumed to result from a congenital defect in the foramina of Magendie and Luschka. Their hypothesis of etiology of hydrocephalus was interesting: if fetal development of the foramina of Magendie and Luschka is disturbed, CSF is retained in the fourth ventricle, causing it to bulge on the dorsal side and prevent the formation of vermis cerebelli, especially the posterior vermis which extends from the cerebellar commissure to the caudal side (atresia theory).

In 1941, Sahs[4] reported a case of congenital anomaly of the cerebellar vermis that closely resembled the congenital type of hydrocephalus reported by Dandy, although the foramen of Luschkas was patent.

In 1954, Benda[5] suggested, after pathological study of six hydrocephalus patients, that cystic dilatation of the fourth ventricle is not always induced by the occlusion of the foramina of Magendie and Luschka, but by the congenital malformation of the cerebellar vermis itself. His theory apparently conflicted with the atresia theory proposed by Dandy[2] and Walker.[6] However, Benda praised their achievements and proposed naming the type of hydrocephalus associated with cerebellar vermis hypoplasia and cystic dilatation of the fourth ventricle as Dandy–Walker syndrome.

In 1954, in a report on five cases of DWS, Schreiber and Reye[7] suggested that occlusion of the foramina of Magendie and Luschka is not always indispensable for diagnosis of DWS and its cause. In 1959, Brodal and Hauglie-Hanssen[8] stated in a report on the pathological study of two DWS patients that the pictures of the two cases resembled the 1943 histopathological findings of Bonnevie[9] in murine hydrocephalus (Hy-1). They compared pathological findings of cystic dilatation of the fourth ventricle in Hy-1 with those in human DWS patients and assumed that this had developed before formation of the area membranacea posterior and induced dorsal bulging in the area membranacea anterior, thus arresting the development of the cerebellar vermis. They therefore concluded that occlusion of the foramina of Magendie and Luschka is not directly involved in the maldevelopment of the cerebellar vermis in DWS.

Since 1960, D'Agostino et al.[10] Hart et al.[11] Garder et al.[12] and many other investigators have introduced new ideas on the cause of DWS. Nonetheless, it generally is agreed that the basic picture of DWS is maldevelopment of the inferior vermis associated with cystic dilatation of the fourth ventricle. However, its cause is still unknown. Because, in DWS patients, associated anomalies are found not only in the central nervous system (Table 13.1) but also in other organs (Table 13.2), and because family and hereditary backgrounds[5,10,13,14] are likely to be relevant in connection with this disease, we are of the opinion that more complicated and unknown teratogenic factors are involved in DWS etiology.

Table 13.1. Associated anomalies of the central nervous system in Dandy–Walker syndrome.

Absence of medullary pyramid[10,11]
Agyria[56], aqueductal stenosis[11, 12]
Cavum septi pellucidi[11,35]
Cerebellar folial anomalies[11]
Chiari malformation type-III,[57] cyst of choroid plexus[12]
Diverticular cyst of third ventricle[11]
Dysgenesis of corpus callosum[7,10–12,43,57–60]
Encephalocele,[35,37,61] fused hypothalami[12]
Holoprosencephaly,[62] infundibular hamartoma[11]
Malformation of inferior olivary nuclei[11]
Meningocele,[2,63,64] microcephaly[13]
Neurocutaneous melanosis[65]
Nonspecific cerebral gyral anomalies[11]
Polymicrogyria,[11] specific cerebral gyral anomalies[11]
Syringomyelia[11]

Table 13.2. Systemic anomalies associated with Dandy–Walker syndrome.

Absence of middle lobe of right lung[66]
Bicornuate uterus,[4] cleft palate[11]
Coarctation of aorta[67]
Chondrodystrophia calcificans congenita[40]
Cornelia de Lange's syndrome[11]
Double vagina,[9] dysplastic and hypoplastic kidney[11]
Ellis-van Creveld syndrome[68]
Fetal ovaries,[1] tracheoesophageal fistula[35]
Fryns syndrome,[69,70] hernia of accessory lobe of liver[71]
High arched palate, hypospadia[13]
Hypertelorism,[12] intrahepatic biliary atresia[67]
Klippel-Feil syndrome,[11] laryngomalacia[13]
Lipoma of posterior fossa,[11] low-set ears[66]
Macroglossia,[4] macrogyria,[11] macrostomia[42]
Meckel's diverticulum,[3] micrognathia,[13] microophthalmia[42]
Prognathism,[4] pulmonary stenosis[66]
Six-lumbar vertebra,[11] polydactylia,[11,13,42] polycystic kidney[37]
Rhinencephaly,[56] sclerocornea,[72] tuberous sclerosis[56]
Turner's syndrome,[67] undescended testis[73]
Ventricular septal defect,[74] Walker–Warburg syndrome[75–77]

Recent advances in neuroimaging, especially computed tomography (CT) and magnetic resonance imaging (MRI), have allowed us to see the anatomic architecture of the posterior cranial fossa and to obtain the pathological picture of each disease. Such investigation revealed that DWS includes a variety of similar diseases. In contrast, there is a slight confusion in regard to posterior cranial fossa cystic lesions.

Harwood-Nash and Fitz[15] designated a group of diseases that greatly resemble DWS; milder hypoplasia of the cerebellar vermis was the Dandy–Walker variant (DWV).

Raybaud[16] classified retrocerebellar cystic lesions roughly into true Dandy–Walker malformation, Dandy–Walker variant, and arachnoid pouches of the cisterna magna. He described the first and second types as having

Table 13.3. Classification of retrocerebellar cyst.

With maldevelopment of the rhombencephalic roof
involvement of area membranacea anterior
Dandy–Walker syndome[5]
Dandy–Walker variant[15]
involvement of area membranacea posterior
persistent Blake's pouch[17]
Without maldevelopment of the rhombencephalic roof
retrocerebellar arachnoid cyst[17]
cyst in the cisterna magna[17]
enlarged cisterna magna with communicating hydrocephalus[19]
mega–cisterna magna[20]

Table 13.4. Clinical features of Dandy–Walker syndrome.

	Cook county and children's memorial hospitals in Chicago[22] (37 cases)	Hirsch et al.[23] (40 cases)
Enlargement of head	30	29
Enlarged posterior fossa	6	6
Headache and/or vomiting	4	6
Hypotonia	—	10
Downward-displaced eyeballs	6	6
Pyramidal syndrome and/or motor weakness	12	4
Seizures	3	6
Cranial nerve involvements	6	1
Irritability	2	—
Lethargy	2	—
Respiratory problems	3	—
Cerebellar syndrome	6	4

cerebellar vermis hypoplasia, whereas the third did not. This group of diseases was therefore considered to include retrocerebellar arachnoid cysts, cysts in the cisterna magna, and persistent Blake's pouch.[17] On the basis of the finding of those investigators and ourselves[18] retrocerebellar cystic lesions are classified as shown in Table 13.3.

Among diseases with anomaly in the rhombencephalic roof, those with apparent hypoplasia of the cerebellar vermis were placed in the category of DWS or DWV; the principal pathogenesis was malformation of the area membranacea anterior. Although the clinical concept has not been established, there probably is a disease—in which anomaly is restricted to the area membranacea posterior and in which the cerebellar vermis develops but the tela choroidea alone bulges out like a cyst—that may be called persistent Blake's pouch.[17] On the other hand, we believe there is no anomaly in the rhombencephalic roof in patients with retrocerebellar arachnoid cysts,[17] cysts in the cisterna magna,[17] enlarged cisterna magna with communicating hydrocephalus,[19] or mega–cisterna magna.[20] Of these patients, those with mega–cisterna magna have a basically benign clinical picture, and surgery is not indicated. Their cerebellar vermis, although small, is considered to develop undisturbed.[18,20] Recently, however, Barkovich et al.[21] proposed that, since mega–cisterna magna has the same development anomaly as in DWS and DWV, the three diseases should be included in Dandy–Walker complex. Retrocerebellar cystic lesions, including DWS, are not systematically understood as yet and require further research.

Clinical Features

Table 13.4 shows the clinical picture of 37 cases of DWS that were diagnosed and treated at Cook County and Children's Memorial Hospitals in Chicago during the 15-year period between 1963 and 1977,[22] and 40 DWS cases reported by Hirsch et al.[23] Cranial enlargement is a major symptom of DWS diagnosed before the age of 12 months[22,24,25] and is considered to be induced by the development of hydrocephalus. However, as Hirsch et al. reported, macrocephaly with occipital bulging sometimes precedes the onset of hydrocephalus. Our study of 37 cases indicated that hydrocephalus in infants less than 3 months old progressed slowly and rarely displayed intracranial pressure high enough to require emergency treatment. In fact, hydrocephalus associated with DWS has been reported to de-

velop after birth.[23] Normally, infants are not likely to develop serious hydrocephalus immediately after birth.

Most patients with DWS diagnosed 12 months or more after birth primarily visit hospitals with disturbance of psychomotor development or such symptoms associated with increased intracranial pressure as headaches and vomiting.[22,24,26] The pathological site of DWS directed our attention to such signs of cerebellar dysfunction as nystagmus and ataxia, but the incidence of such signs was unexpectedly low (Table 13.4).

Neuroimaging

Skull Radiography

Bucy[27] studied DWS skull radiographic findings and reported the features of this disease to be abnormal dilatation of the posterior cranial fossa and high position of the sulcus of the transverse sinus. Among the 37 patients in series at Cook County and Children's Memorial Hospitals in Chicago, however, 25 who had undergone skull radiography before age 2 did not demonstrate a sulcus of the transverse sinus even though a dilated and bulging posterior cranial fossa was observed in approximately 80% of them. Because, as Schreiber and Reye[7] indicated, skull radiography often fails to disclose the sulcus of the transverse sinus in infants, the diagnosis of DWS is not assisted by any effort to determine its presence. Furthermore, we determined radiologically the interorbital distance as described by Hansman[28] in 16 of the 37 patients in our series, and statistically detected significant abnormal extension of the distance in more than half the patients.[22]

Sinography

In 1956, Matson[29] reported that sinography could disclose high position of the torcular Herophili and transverse sinus, which would be useful for diagnosis of DWS. However, such findings also are obtained in regard to arachnoid cysts and congenital tumors of the posterior cranial fossa. Because such abnormalities of the venous sinus can be revealed by less invasive techniques, including radionuclide brain scan,[30] venophase of serial cerebral angiography, and digital subtraction angiography, sinography is no longer used for DWS diagnosis.

CT/Radioisotope Cisternography and Ventriculography

A number of DWS studies using (radioisotope) cisternography and ventriculography have been reported.[31,32] Recently, CT cisternography and CT ventriculography using a water-soluble contrast medium, such as metrizamide, have been introduced in the diagnosis of DWS.[18,22,24,33,34] In selecting a method of DWS therapy, it is important to determine whether there is communication in the aqueduct or between the cyst and the subarachnoid space. Examination of intracystic CSF circulation examined by RI and CT cisternography is essential for diagnosing retrocerebellar cystic lesions, including DWS, and particularly for determining surgical indication.[18] Findings obtained through these techniques are classified into three groups, depending on how the tracer fills and clears (Figure 13.1): early filling and early clearance (Figure 13.1A), delayed filling and delayed clearance (Figure 13.1B), and nonfilling (Figure 13.1C). The latter two groups are considered to indicate some disturbance in intracystic CSF circulation that, whatever the diagnosis, would call for some surgical procedure such as shunt operation.[18]

Cerebral Angiography

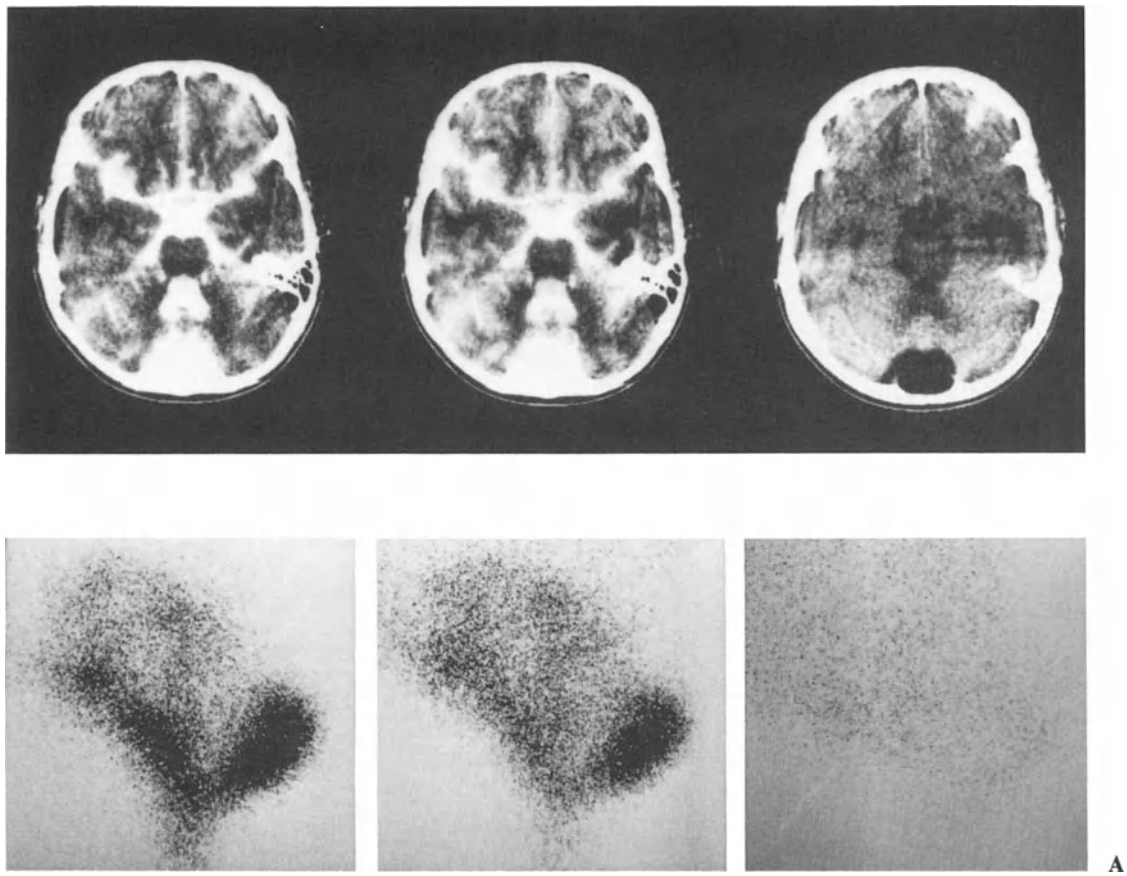
Angiographical findings in DWS have been reported by Juhl and Wesenberg[35] Geilfuss and Puckett[36] Raimondi et al.[37] Wolpert[38] LaTorre et al.[39] and Harwood-Nash and Fitz et al.[15] The findings are as follows:

1. Nonspecific angiographic findings in the supratentorial hydrocephalus[35]
2. Elongation of the great vein of Galen[36]
3. High position of the torcular Herophili

associated with the straight sinus draining to the superior sagittal sinus situated more to the rostal side[36]

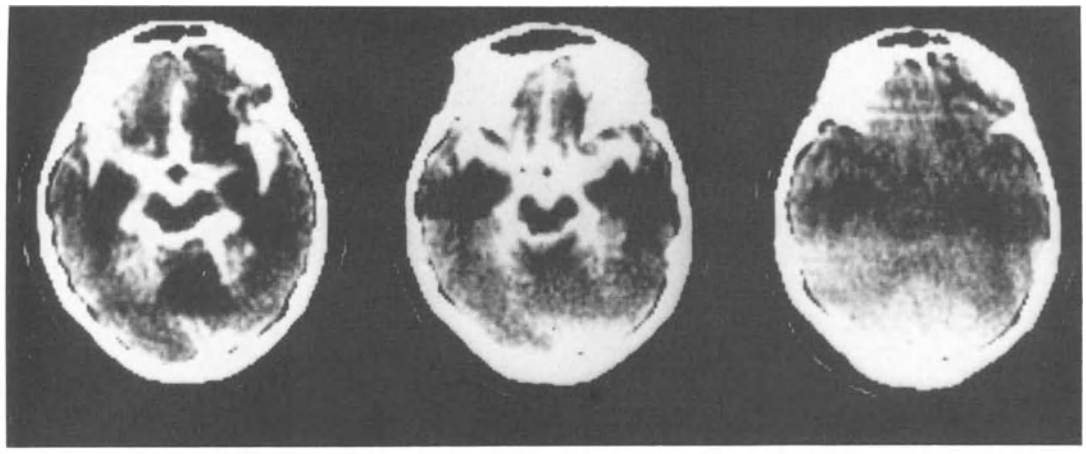
4. Lateral displacement of the right and left posterior cerebral arteries by upward herniation (Figure 13.2)[37] and the hypoplastic superior cerebellar artery crossing over the posterior cerebral artery[38]
5. An avascular area in the posterior cranial fossa, suggestive of cystic dilatation of the fourth ventricle (Figure 13.2)[38]
6. High position of the torcular Herophili and lateral sinus (Figure 13.3)[38]
7. Cerebellar hypoplasia disclosed in the capillary phase and early venophase[37,40]
8. Hypoplasia or a defect of the posteroinferior cerebellar artery (PICA),[38,41,42] or a defect of the vermian branch of the PICA[15,39]
9. Caudal displacement of the PICA[15,39]
10. Defect of the inferior vermian vein[42,43]

The angiographic findings in 25 children with DWS at Cook County and Children's Memorial Hospitals in Chicago were studied in detail with reference to the above findings,



A

Figure 13.1. Computed tomography (CT) (upper) and radioisotope (R1) (lower) cisternograms obtained 3 (left), 6 (middle), and 24 (right) hours after simultaneous intrathecal injection of metrizamide and ^{111}indium-diethyltriaminopentacetic acid (^{111}In-DTPA). A: A case of mega–cisterna magna. The tracers simultaneously filled both the cyst and the subarachnoid space in the posterior fossa. Persistence of tracers within the cyst was not observed in either CT or RI cisternograms taken 24 hours after their administration. B: A case of retrocerebellar arachnoid cyst. Note retention of tracers in the cyst (right) in cisternograms taken 24 hours after their administration. C: A case of retrocerebellar arachnoid cyst. Neither tracer has entered the cyst.



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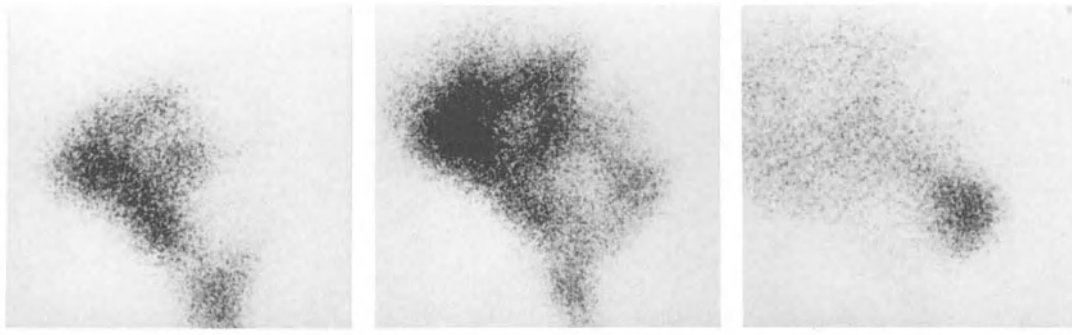

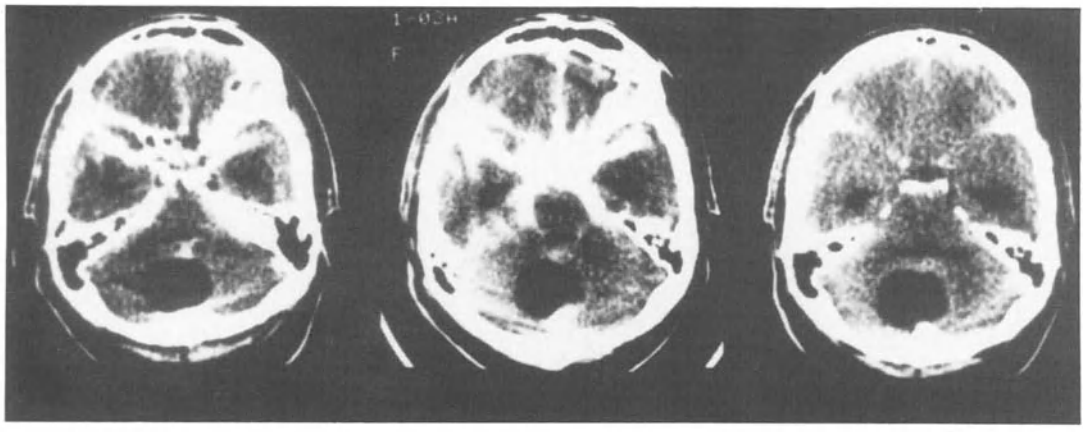

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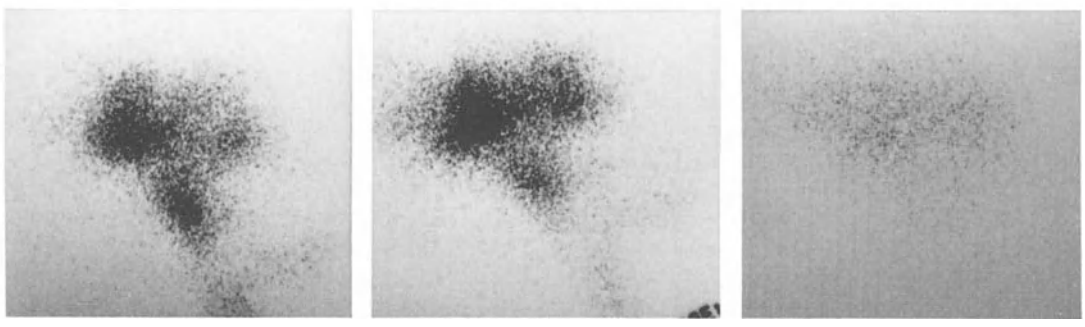


Figure 13.1 (cont.)

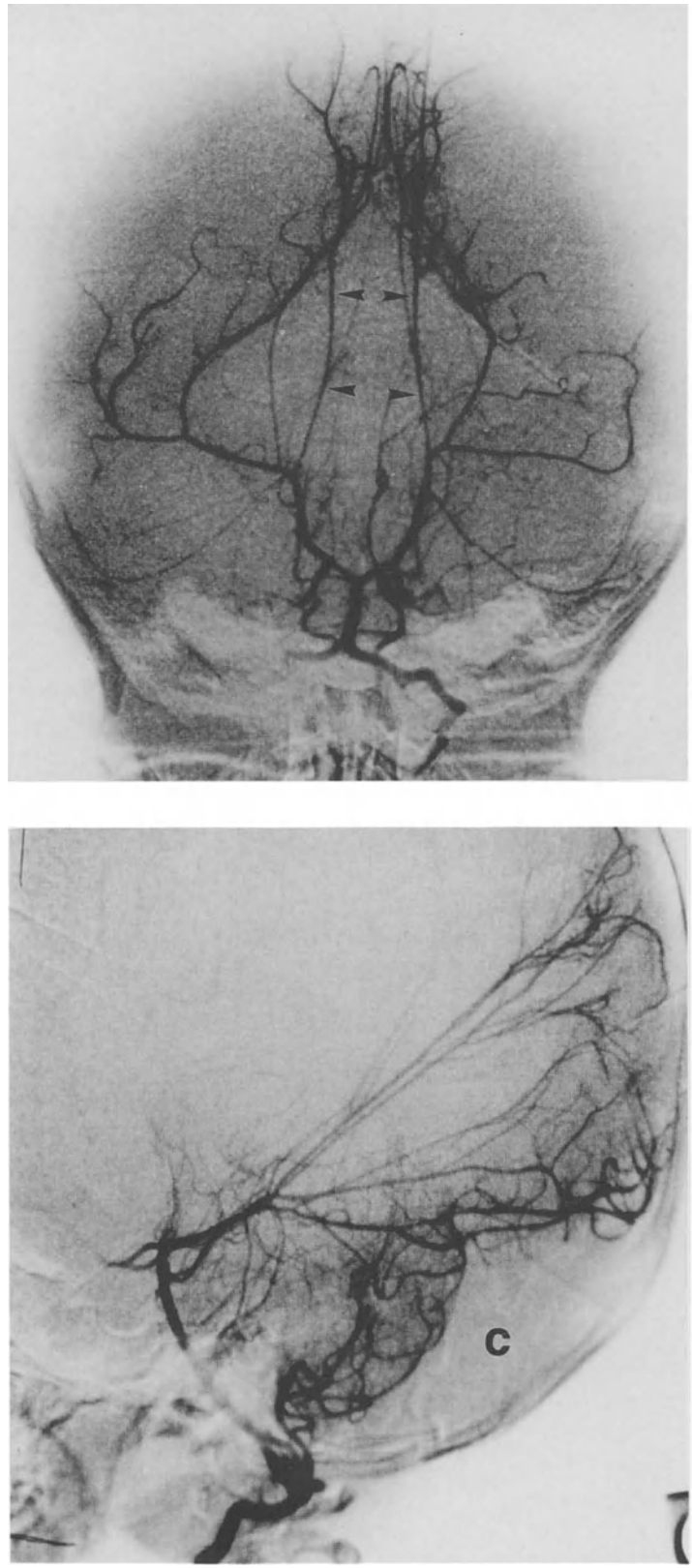
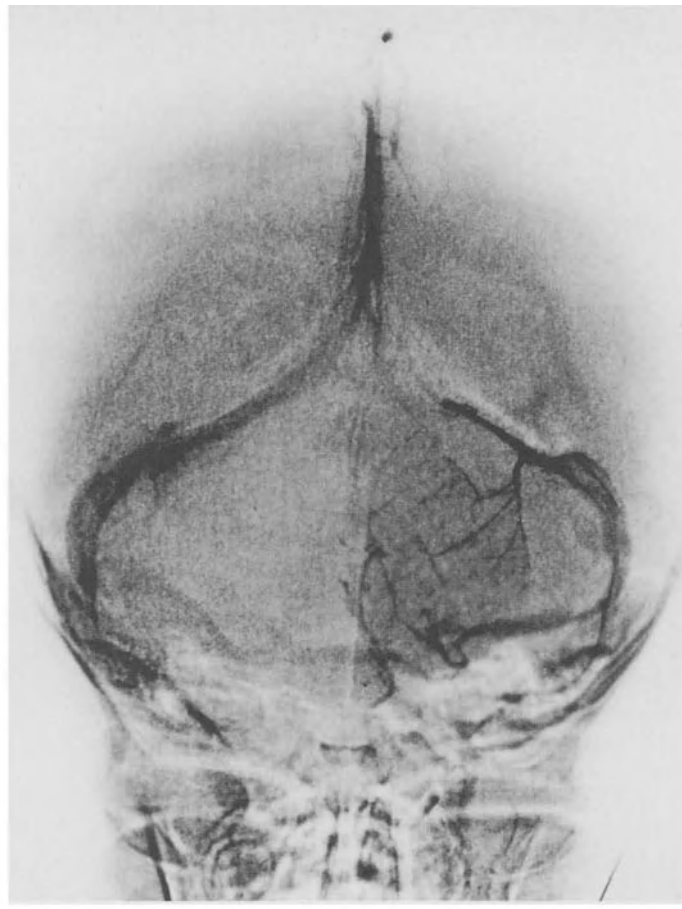
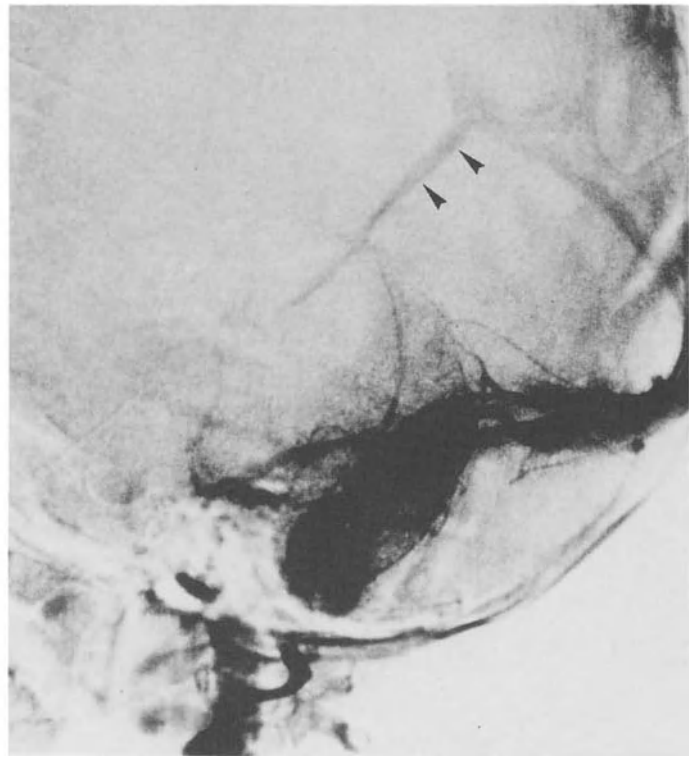


Figure 13.2. Vertebral angiograms in a case of Dandy–Walker syndrome. A: Anteroposterior view of arterial phase. Right and left posterior cerebral arteries (arrowheads) deviate laterally and ran in parallel. B: Lateral view of arterial phase. C indicates an avascular area that likely is a fourth ventricle cyst. Posteroinferior cerebellar arteries and their vermian branches are clearly disclosed.



A



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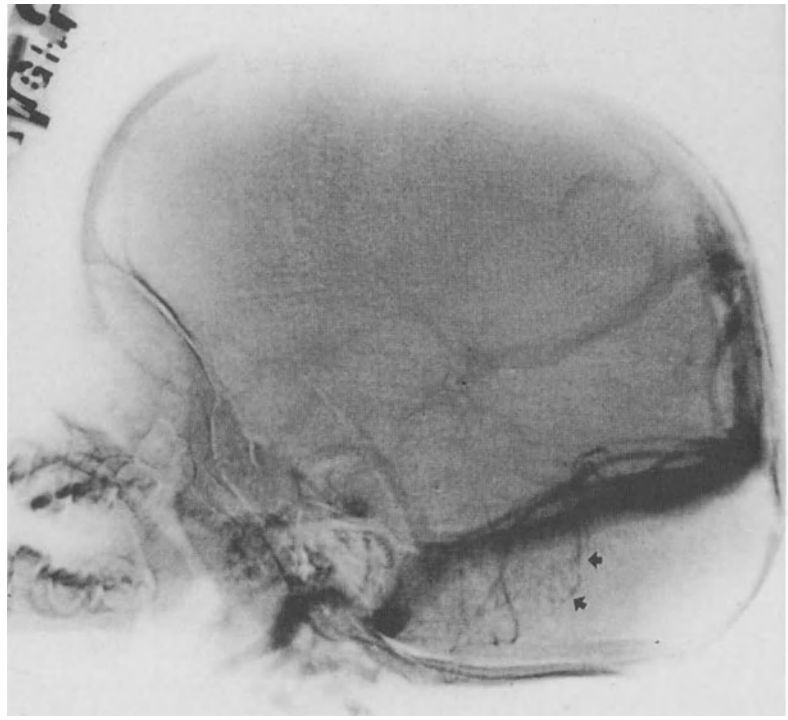


Figure 13.3. Vertebral angiograms in cases of Dandy–Walker syndrome. A: Anteroposterior view of venophase. B: Lateral view of venophase in the same patient as a. Note high position of the torcular Herophili and lateral sinus. Arrowheads indicate elongation of the great vein of Galen. C: Lateral view of venophase in a different patient. Note elongation of straight sinus and high position of the torcular Herophili and lateral sinus. Inferior vermian vein is disclosed (arrows).

none of which seemed to be specific to the disease. Only 5 of the 25 patients showed either a lack of or a very rudimentary PICA, it being clearly demonstrated in the others (Figure 13.2). Whether or not this artery was disclosed depended on size of the cerebellar blush in the capillary phase. Thus, there was no or only rudimentary filling of the PICA in children with a small cerebellar blush. As the cerebellar blush increased in size, the PICA developed sufficiently to be filled. In patients with a clearly disclosed PICA, examination of the course of its vermian branch revealed no uniform finding specific to DWS. Moreover, we checked the presence of the inferior vermian vein and found that defects in it were rare (Figure 13.3).

LaTorre et al.[39] and Harwood-Nash and Fitz[15] reported that a defect in the inferior vermian vein was specific to DWS and used in arriving at a definite diagnosis because this vein is disclosed in an arachnoid cyst of the posterior cranial fossa. They suggested that differentiation of these diseases was based on whether there is an inferior vermian vein. However, as pointed out above, angiographical findings alone are not sufficient to arrive at a definite diagnosis of DWS or to differentiate diagnoses.

Cisternal Pneumoencephalography

Cisternal pneumoencephalography offers findings specific to DWS in a midsagittal section of the brain stem (Figure 13.4). These images, however, are apparently inferior in resolution to those of CT and MRI,[44] and thus it is rarely used in DWS diagnosis.

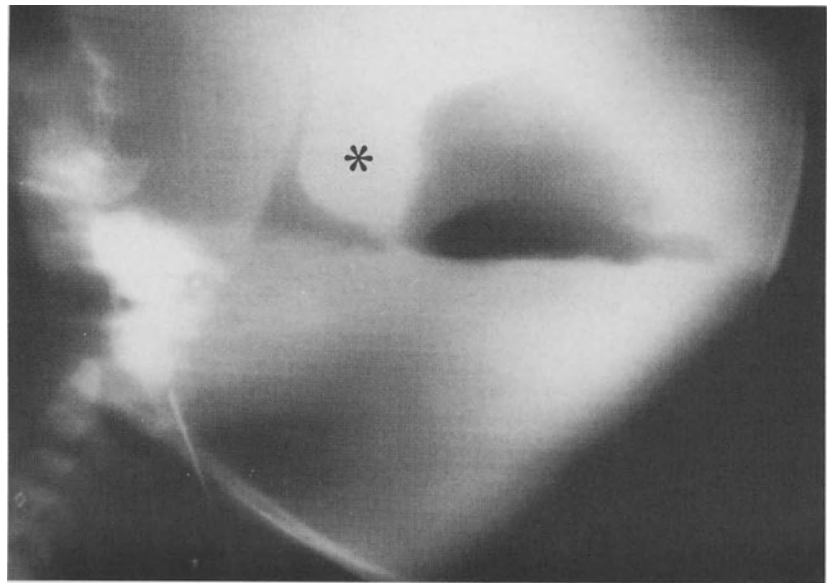


Figure 13.4. Pneumoencephalogram in a case of Dandy–Walker syndrome. Fourth ventricle cyst is disclosed. Asterisk indicates a superior vermis.

Computed Tomography

After CT was introduced to this area, Harwood-Nash and Fitz[15] and Archer et al.[45] reported DWS CT findings and presented the view that it is hard to differentiate DWS from arachnoid cyst of the posterior cranial fossa and mega–cisterna magna.

Some investigators, however, have reported that CT, which can disclose a midsagittal section of the posterior cranial fossa, allows fairly definite DWS diagnosis and differentiation from other diseases.[24,45] Figure 13.5 shows CT findings of a 5-year-old boy with DWS. In the left of upper row, the picture of the midsagittal section clearly discloses the hypoplastic superior vermis and the fourth ventricle cyst. Neither the inferior vermis nor inferior medullary velum are detected.

Figure 13.5 b–f shows axial CT sections of the posterior cranial fossa extending from the rostal to the caudal side. A cyst extending to the rostral side (Figure 13.5b), and the anterior lobe of the vermis (Figure 13.5c,d) are disclosed. An inferior vermis is not revealed at the caudal end, and only a cyst (Figure 13.5d,e) directly communicating with the fourth ventricle is disclosed.

Magnetic Resonance Imaging

The usefulness of MRI in DWS diagnosis is indisputable.[21,46,47] In particular, the MRI of the midsagittal section clearly reveals defects in the inferior vermis and cystic dilatation of the fourth ventricle, providing evidence of basic lesions in DWS. Moreover, MRI facilitates diagnosis of central nervous system anomalies, such as dysgenesis of corpus callosum, which coexists with DWS. MRI diagnosis of fetal DWS was recently reported.[47] It should be emphasized that MRI is an indispensable diagnostic procedure for DWS. Figure 13.6 A shows an MRI finding of the midsagittal section in a 3-month-old boy with DWS. It discloses a defect of the inferior vermis, cystic dilatation of the fourth ventricle, and dysgenesis of the corpus callosum.

Figure 13.6B illustrates a MRI finding of the midsagittal section in a patient diagnosed with mega–cisterna magna. MRI revealed a low-intensity area similar to that of the CSF

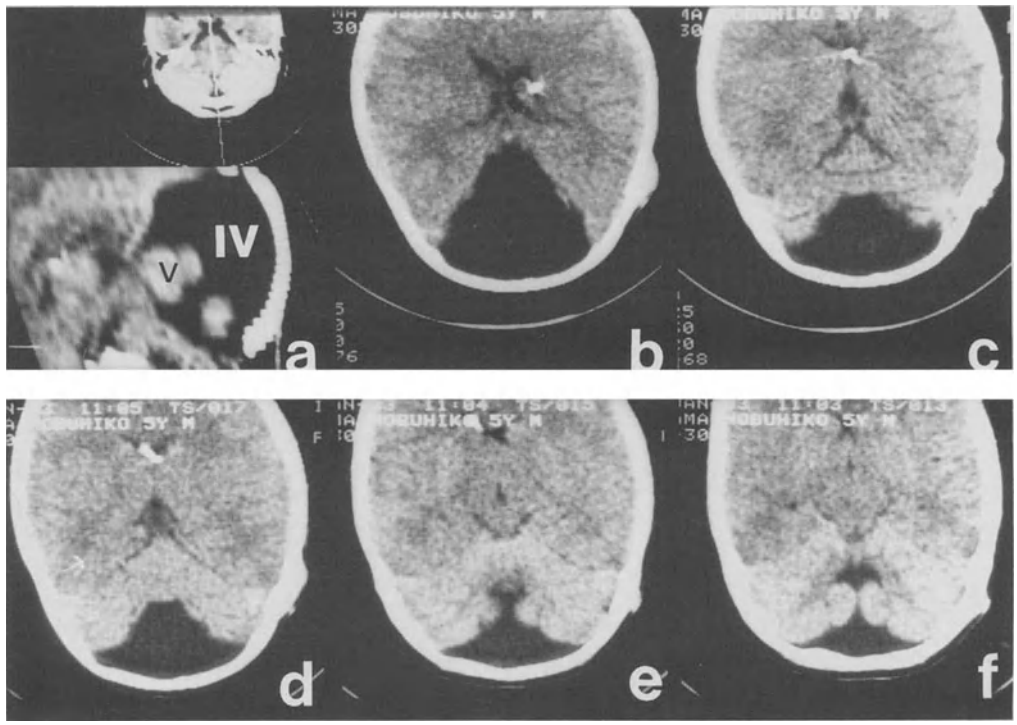


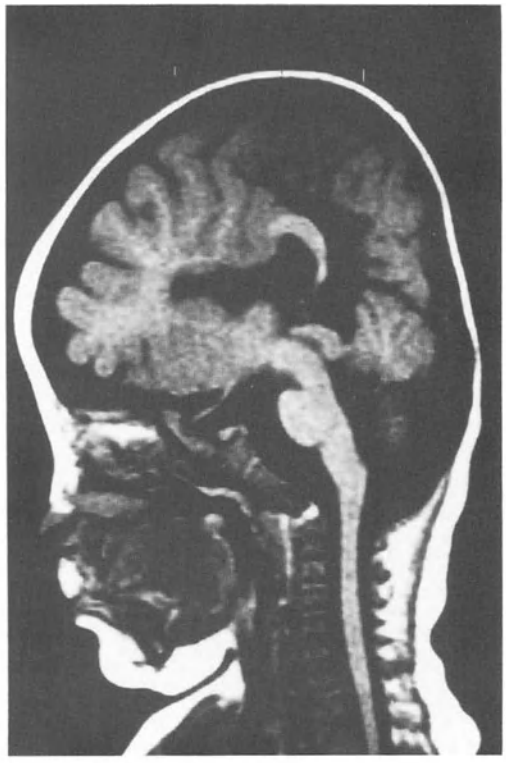
Figure 13.5. CT findings in a case of Dandy–Walker syndrome. a: CT, midsagittal section of posterior fossa. b–f: Serial CT scans of axial section. V, Cerebellar vermis; IV, Fourth ventricle cyst.

on the dorsal side of the cerebellar vermis, but a normally shaped vermis. In this case, RI and CT cisternography revealed no disturbance of CSF circulation on the retrocerebellar area (early filling and early clearance). Surgical treatment was therefore not indicated for this patient.

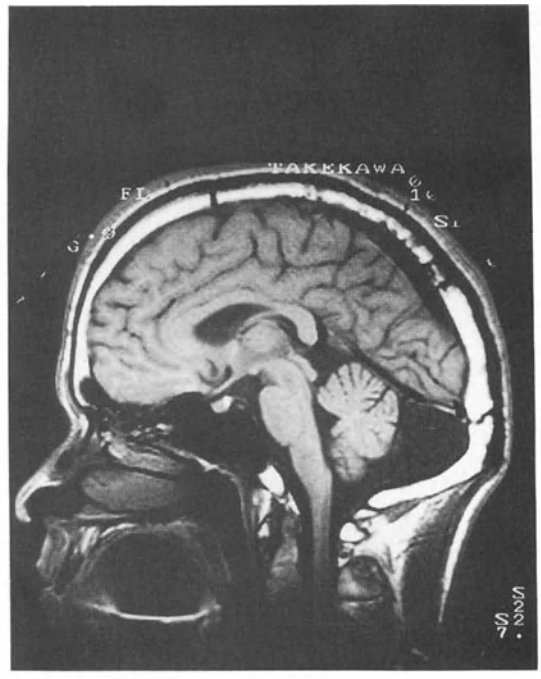
Figure 13.6C shows MRI of the midsagittal section in a $1\frac{1}{2}$-year-old girl with persistent Blake's pouch who visited the Juntendo University Hospital owing to cranial enlargement. This picture discloses supratentorial hydrocephalus and cystic dilatation of the fourth ventricle, which apparently differs from MRI findings in the case of arachnoid cyst of the posterior cranial fossa. Development of the cerebellar vermis in this case is considered to be relatively good as compared to that shown in Figure 13.6B. RI and CT cisternography performed for this patient revealed a noncommunicating cyst. The ventricle and cyst were markedly reduced following ventriculoperitoneal shunt and cystoperitoneal shunt operations (Figure 13.7).

Figure 13.6D shows a midsagittal MRI finding of a 19-month-old boy who visited the Juntendo University Hospital owing to psychomotor retardation. Axial CT of this patient revealed that the floor and lateral wall of the fourth ventricle were normal, but the vermis is hypoplastic (Figure 13.8). Midsagittal MRI, however, shows a considerably hypoplastic vermis and helps to visualize the fastigium of fourth ventricle. From these findings, diagnosis of this patient is considered to be DWV.

Recently, Barkovich et al.[21] reviewed findings regarding retrocerebellar cystic lesions, especially those of MRI. They did not mention the concept of persistent Blake's pouch but proposed that the group including DWS, DWV, and mega–cisterna magna should be designated the Dandy–Walker complex. Although typical DWS can be diagnosed



A



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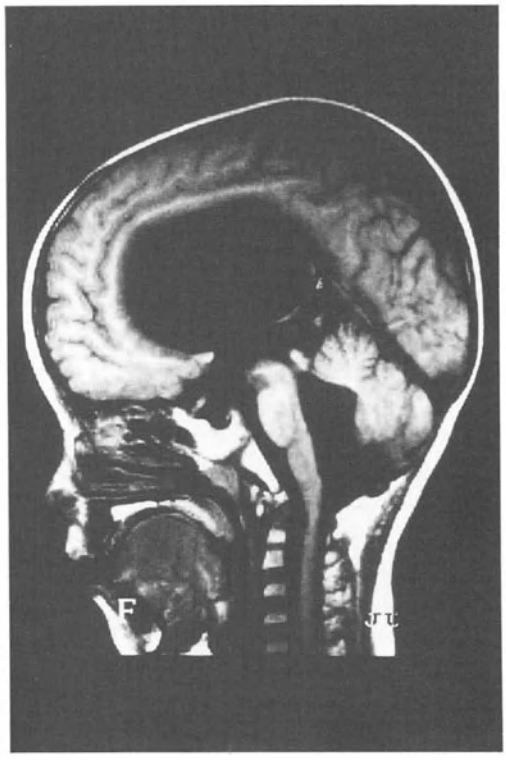

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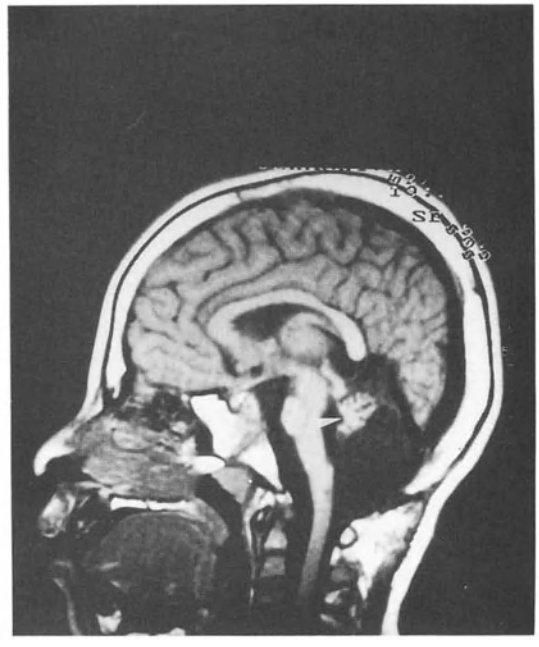

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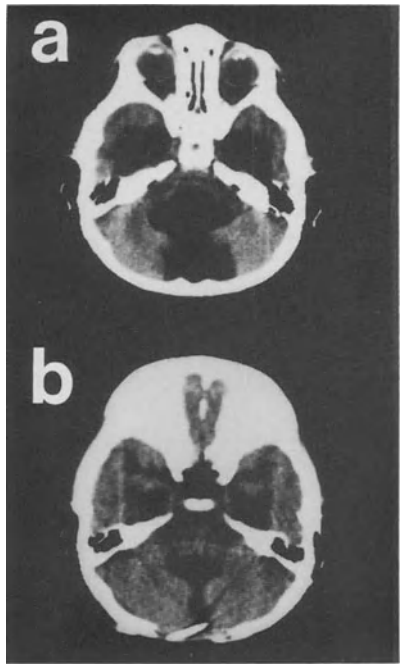

Figure 13.7. Axial CT scans in a case of persistent Blake's pouch. a: Preoperative CT. Fourth ventricle cyst is disclosed. Floor and lateral wall of the fourth ventricle are recognizable. b: Postoperative CT. Note postoperative disappearance of cyst.

with the introduction of MRI, differential diagnosis of closely similar diseases, including DWV, requires further investigation.

Echography

Although the usefulness of echography in diagnosing DWS in neonates has been reported,[48] echography primarily is for diagnosis involving fetuses.[49–51] Such diagnosis is based on dysplasia of the cerebellar vermis and cystic dilatation of the fourth ventricle. However, as Hirsch et al.[23] indicated, hydrocephalus is not the prime manifestation in

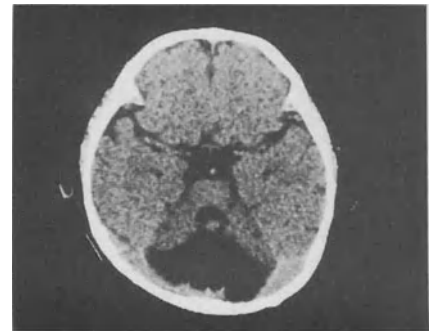

Figure 13.8. Axial CT scan in a case of Dandy–Walker variant. Although cerebellar vermis is hypoplastic, floor and lateral wall of the fourth ventricle are recognizable.

fetal DWS. Differential diagnosis of DWS is based on accurate observation of abnormalities in the posterior cranial fossa. A key point in prognosis of DWS is whether the patient presents associated anomalies of the central nervous system or systemic anomalies. Some investigators have indicated that if complications of these anomalies could be accurately diagnosed, the abortion of fetuses with serious anomalies should be considered.[50] We believe, however, that the ethical issues involved and the doubtful accuracy of fetal echography make it too early for this idea to be accepted.

Associated Anomalies of the Central Nervous System

Of the 37 children with DWS at Cook County and Children's Memorial Hospitals in Chicago, 89% had the complication of hydrocephalus. Only a fourth ventricle cyst was observed in the remaining 11%. However, increasing cystic dilatation in size of the fourth

Figure 13.6. Midsagittal magnetic resonance imaging (MRI). A: A case of Dandy–Walker syndrome. A retrocerebellar cyst communicating with the fourth ventricle is associated with agenesis of lower half of vermis and dysgenesis of corpus callosum. B: A case of mega–cisterna magna. Note the normally developed fourth ventricle and vermis. C: A case of persistent Blake's pouch. Cystic dilatation of the fourth ventricle and relatively well-developed superior and inferior vermes are observed. D: A case of Dandy–Walker variant. A considerably hypoplastic vermis is disclosed. Arrowhead indicates fastigium.

Table 13.5. Associated anomalies of the central nervous system in 37 cases of Dandy–Walker syndrome.

Dysgenesis of corpus callosum	14 (38%)
Aqueductal stenosis	8 (22%)
Chiari malformation type III	2 (5%)
Porencephaly	1 (3%)
Dermoid cyst	1 (3%)
None	17 (46%)

Table 13.6. Mortality rate in Dandy–Walker syndrome.

	Total cases	Mortality rate (%)
Raimondi et al.[37]	8	50
Fischer[53]	27	41
Udvarhelyi and Epstein[55]	6	0
Carmel et al.[40]	18	28
James et al.[54]	10	40
Sawaya and McLaurin[25]	23	26
Tal et al.[78]	12	33
Hirsch et al.[23]	40	12.5
Maria et al.[24]	20	10

ventricle may cause functional aqueductal stenosis, which afterward induces supratentorial hydrocephalus.

Table 13.5 lists complications of the central nervous system in the 37 cases in our series. Such central nervous system anomalies in DWS, which have been reported to occur in 25% to 70% of cases[11,23–25,52] were seen in 54% of our cases.

Dysgenesis of the corpus callosum was the most frequently associated central nervous system anomaly in our series. Although Golden et al.[52] reported that no case with dysgenesis of the corpus callosum was found in their DWS series, it is considered that about 10% to 20% of DWS cases present dysgenesis of the corpus callosum.[11,23–25]

Surgical Treatment and Prognosis

Dandy,[2] Walker,[6] and Matson[29] indicated that, in surgical treatment of DWS, excision of the cyst wall and reestablishment of the CSF pathway between the fourth ventricle and the subarachnoid space were essential. However, as Raimondi et al.[37] and other investigators[40,53] pointed out, reestablishment of normal CSF circulation could not, in many cases, be achieved solely by excision of the cyst wall, and additional ventriculoperitoneal (V-P) shunt operations were required for the purpose of decompressing the supratentorial hydrocephalus. Thus, in cases of DWS complicated by supratentorial hydrocephalus, V-P shunt operation is the first therapy selected. To prevent upward herniation from occurring after a V-P shunt, Raimondi et al.[37] and James et al.[54] recommended simultaneous uniform V-P and cystoperitoneal (C-P) shunt operations, connecting the two with a Y-shaped connector. However, Fisher[53] and Carmel et al.[40] stated that C-P shunt should be added to V-P shunt only in selected cases. Udvarhelyi and Epstein[55] reported that excision of the cyst wall was sufficient to cure DWS occurring at the age of 3 years or more. Maria et al.[24] claimed that C-P shunt alone was sufficient for DWS patients with a favorably communicating aqueduct. V-P and C-P shunts are the basic surgical therapies at the present time (Figure 13.9).

Table 13.6 lists the DWS mortality rates reported by various investigators. A rate of around 10%, as reported by Hirsch et al.[23] and Maria et al.,[24] is considered to be the current DWS mortality rate.

Raimondi and Soare[41] reported, on the basis of their study, that the mean full-scale IQ of DWS patients was 48.3 ± 26.1. They reported the prognosis for mental development in DWS infants to be markedly worse for those with simple hydrocephalus or Chiari malformation type II. Sawaya and McLaurin[25] found similar prognoses.

Analyzing the findings in 27 DWS infants, Fisher[53] suggested that the treatment of hydrocephalus alone did not determine the prognosis of DWS infants. Udvarhelyi and Epstein[55] and Maria et al.[24] stressed the importance of coexistent serious anomalies in other organs or the central nervous system in DWS prognosis. In the diagnosis and treatment of DWS, therefore, we should fully investigate coexisting anomalies in not only the

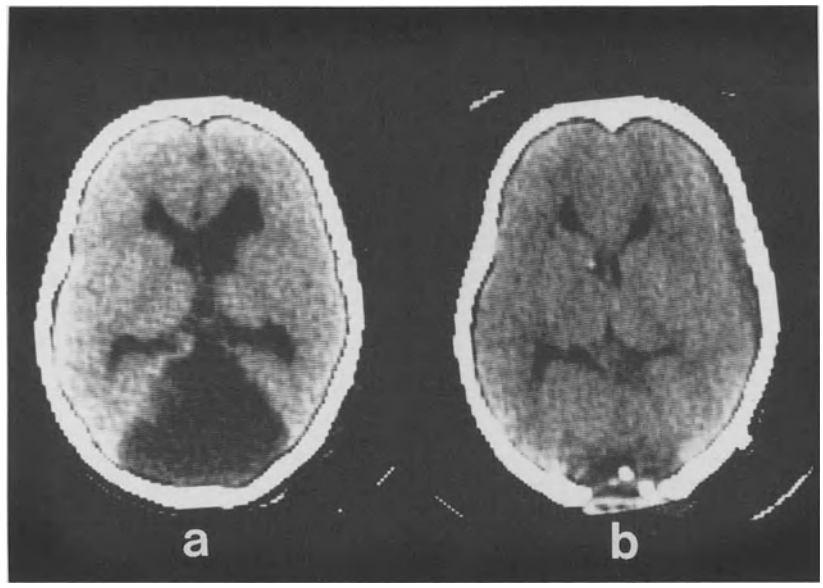

Figure 13.9. Preoperative (a) and postoperative (b) CT scans in a case of Dandy–Walker syndrome. Postoperatively, the size of the fourth ventricle cyst has decreased and the cerebellum is considerably enlarged in size.

central nervous system but also in other organs in order to gain a comprehensive view of the lesions before arriving at a prognosis.

Conclusion

The basic picture of DWS is maldevelopment of the inferior vermis associated with cystic dilatation of the fourth ventricle. Although typical DWS and its associated anomalies of the central nervous system can be diagnosed clearly with the introduction of MRI, differential diagnosis of closely similar diseases, including DWV, requires further investigation.

Treatment of DWS has changed evolutionarily since the entity of this disease was recognized, and V-P and/or C-P shunt operations are considered to be the basic surgical therapies at the present time.

Because the presence of associated anomalies in the central nervous system and other organs correlates with poor prognosis, we believe that DWS is not limited to a simple disturbance of CSF circulation but is a more complicated disorder involving the central nervous system.

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CHAPTER 14

Post-traumatic Cysts

Padraic O'Neill

Introduction

Although post-traumatic intracranial cysts are relatively rare lesions, the literature pertaining to these entities is quite extensive. Its value is somewhat limited, however, by the use of a multitude of different terms to describe the same pathological process. The embodiment of a hypothetical concept of pathogenesis in a particular descriptive term has frequently been a confusing influence and although custom appears to have justified certain usages, it has frequently been at the expense of clear understanding. For the purposes of this chapter a cyst is defined as a fluid-filled space surrounded by a membrane. The most generally accepted terminology will be used for each cyst type.

Subepicranial Hydroma

The term *subepicranial hydroma* was first coined by Soloman in 1949[1] although Brozsan and Grennan[2] had previously published a comprehensive review of the same entity, which they had termed *transient flase meningoceles*.

Subepicranial hydroma is a benign complication of head trauma and appears as a soft, fluctuant swelling within hours or more often days following head injury. The injury itself is frequently mild with no apparent immediate reaction. Signs of serious cerebral dysfunction, such as unconsciousness or focal neurological deficits, are infrequent. Transient drowsiness and vomiting may occur but usually subside before the hydroma is evident.

The swelling once apparent may increase with alarming rapidity. The area of swelling having no confines other than those of the subgaleal space may cover the entire cranium, although it is more frequently unilateral. Skull x-rays frequently demonstrate a linear fracture in the parietal region traversing a suture line. The dura is maximally adherent at the various sutures and consequently is torn as a fracture occurs. The laceration extends into the subarachnoid space and cerebrospinal fluid escapes through the dural defect, transverses the fracture line and tear in the pericranium, and accumulates in the epicranial space. These patients do not go on to develop growing fractures (vide infra).

No active treatment is required for subepicranial hydroma, which usually settles spontaneously in from 2 to 28 days. Aspiration is contraindicated because of the risk of infection.

Growing Skull Fracture

The term *growing skull fracture* was first coined following publication of a German study in 1953 by Pia and Tonnis[3] entitled "Die Wachsende Schadelfraktur Des Kindesalters." Previously the same entity had been described under a variety of different terms including cephalohydrocele,[4,5] meningocele spuria,[6] traumatic ventricular cyst,[7] osteitis fibrosa cystica,[8,9] subdural hygroma,[9] craniocerebral

erosion,[10] traumatic meningocele,[11] and leptomeningeal cyst.[12–15]

The first clinical description of this condition was by John Howship in 1816,[16] who noted "partial absorption of the parietal bone arising from a blow on the head in a nine month old child." The pathological features were first presented by Rokitansky in 1856,[17] when he detailed the autopsy findings in an 8-month-old child who had died of meningitis following puncture of the "cephalohydrocele." He described a fluid-filled sac above the cranial defect, and beneath it was a dural defect and an underlying brain injury. Dyke[12] in 1937, without reference to previous pathological or clinical descriptions, outlined the radiological features and coined the term *leptomeningeal cyst.* The features that he stressed included (a) widening of an old fracture, (b) scalloping of the bordering inner table of the skull and, (c) localized increase in the vascularity of the bone.

The precise incidence of growing skull fracture is difficult to elucidate. The condition occurs only in infancy or childhood with more than 50% occurring within the first year of life and 90% in children under 3 years of age.[18] In a series of 3,447 head injuries reported by Ramamurthi and Kalyanaraman,[19] there were 620 skull fractures of which only 4 (0.6%) demonstrated evidence of growing fracture. No analysis for age was given. In contrast Vas and Winn,[20] reported an incidence of 3.8% (1 out of 26) in children under 10 years and an incidence of 16.6% in children under 3 years of age.

The factors involved in the etiology and pathogenesis of this condition have been extensively studied and reported. In 1941, Penfield and Erickson[10] proposed that the cranial erosion was similar to that of a pacchionian granulation burrowing into the skull. They suggested that brain rather than a leptomeningeal cyst between the edges of the skull defect produced the cranial cerebral erosion.

In 1953, Taveras and Ransohoff[15] postulated the following mechanism, which gained widespread acceptance and was frequently quoted verbatim in other publications:

> "Trauma produces a skull fracture and an underlying dural tear. At the same time there is probably sufficient subarachnoid haemorrhage to hinder the local circulation of cerebrospinal fluid. The arachnoid membrane projects out through the dural tear into the fracture site. The trapped arachnoidal hernia, aided by the normal pulsations of the brain, gradually erodes the edges of the bone and at the same time compresses the underlying cortex. There must be some degree of a ball valve mechanism at work also, with cerebrospinal fluid having easier ingress into than egress from the cyst. Arachnoidal adhesions about the margin of the lesion probably also play a part in trapping the fluid locally. It seems probable that the dural tear is the single most important factor in the pathogenesis of these lesions and that without it the fractures would heal as expected.[15]"

Support for this concept was obtained from a number of experimental studies. Keener in 1959[21] demonstrated that repair of a dural defect does not occur by growth outward from the dural edges but rather by the proliferation of fibroblasts from adjacent fascia and muscle. He stressed that dural regeneration adjacent to bone was "inadequate," whereas that adjacent to soft tissue was "adequate." Lende and Ericson[18] pointed out that frequently in cases of growing skull fracture the dural edge was retracted and underlies bone. The same authors further postulated that damage to the dura disrupts to some degree its periosteal functions, including formation of new bone in repair of skull fractures.

Goldstein et al.[22] in an experimental study on dogs, showed that a dural tear with interruption of the arachnoid was essential for the formation of a growing skull fracture. Furthermore they found that additional pial, brain, or ventricular damage did not increase the incidence of growing fractures and that these lesions were therefore of secondary importance. They also stressed the important role of pulsation in the development of the bony erosion and in particular reported that not a simple pulsation of the fluid against the

bone but rather a fluid pulsation in a cyst or pouch produces a higher incidence of bone erosion.

While accepting the findings of Goldstein et al., Stein and Tenner[23] emphasized the importance of cerebral herniation and the perpetuation of cerebral involvement in growing fractures, a factor that they felt Goldstein's group had underrated. Other authors had postulated that raised intracranial pressure secondary to the underlying brain injury and occurring close to the time of injury may be another factor in the pathogenesis of this lesion but thus far the evidence provided does not appear convincing.[24] Several authors, however, point out the coincidence of the age of injury with the period of most active brain growth.

The most common symptom and sign is a scalp mass usually in the parietal region. There is nothing unique in the manner of the initial cranial trauma. The scalp overlying the fracture is almost never broken at the time of injury. A collection of cerebrospinal fluid (CSF) beneath the scalp commonly follows the head injury. This may occur rapidly or be delayed in onset, and its course is frequently transient. There is then a latent period until the fracture has enlarged sufficiently to allow a pulsating mass to be seen or felt. Other symptoms are those that can be attributed to an associated brain injury, the most common being seizures or focal weakness or atrophy.

The initial fracture line is diastatic (inital width greater than 4 mm) (Figure 14.1). There is frequently a rapid increase in the size of the fracture within the first 2 months following injury and this can be followed by a long period of either stability or a very much slower rate of enlargement. It can be noted that a fracture line with an initial width of less than 4 mm is unlikely to proceed to a growing skull fracture. There can, however, be transient enlargement of such fractures, a phenomenon termed pseudogrowth by Sekhar and Scarff.[25] These authors postulated that in pseudogrowth of a skull fracture the dura is torn but the arachnoid remains intact, although this was questioned by Page,[26] who felt that the most practical distinguishing feature between "pseudogrowth" and "growth" of a skull fracture is the absence of a palpable mass beneath the scalp in the former.

At the time of diagnosis of a growing skull fracture, the skull x-ray demonstrates a characteristic bony defect lying in the course of a previous diastatic skull fracture. The bony defect is irregular with saucerized margins. Sometimes the edges are everted and there appears to be greater erosion of the inner than the outer table of the skull. Computed tomography (CT) scan usually demonstrates dilatation of the ipsilateral ventricle as well as defining the contents within the growing fracture and underlying brain injury.

Early and aggressive surgical treatment of growing skull fractures has been generally advocated with the aim of (a) debriding and removing necrotic brain, (b) communicating subarachnoid loculations, (c) reconstructing the leptomeninges, and (d) repairing the cranial defects. Thompson et al.[27] recommended early surgery in cases of diastatic skull fractures with associated marked swelling of the scalp and a contralateral neurological abnormality. Stein and Tenner[23] also support an aggressive policy. They describe six cases in which brain tissue was found within the defect by arteriography and argue that in the absence of surgery such brain tissue would be liable to further trauma and scarring. Ramamurthi and Kalyanaraman,[19] on the other hand, reported four patients who did well without surgery. They felt that surgery was unnecessary in the absence of a large defect or bulging of the scalp. Although the same authors point out that air studies almost invariably show enlargement of the lateral ventricle on the side of the fracture, thereby indicating cerebral atrophy resulting from brain damage at the time of the injury rather than subsequent compression by a cyst, it is noteworthy that two out of the four patients reported by them suffered progressive neurological deficit during their period of follow-up.

Improvement in seizure control has been reported following surgery. Neurological deficit is unlikely to be improved but progressive deterioration can be arrested.

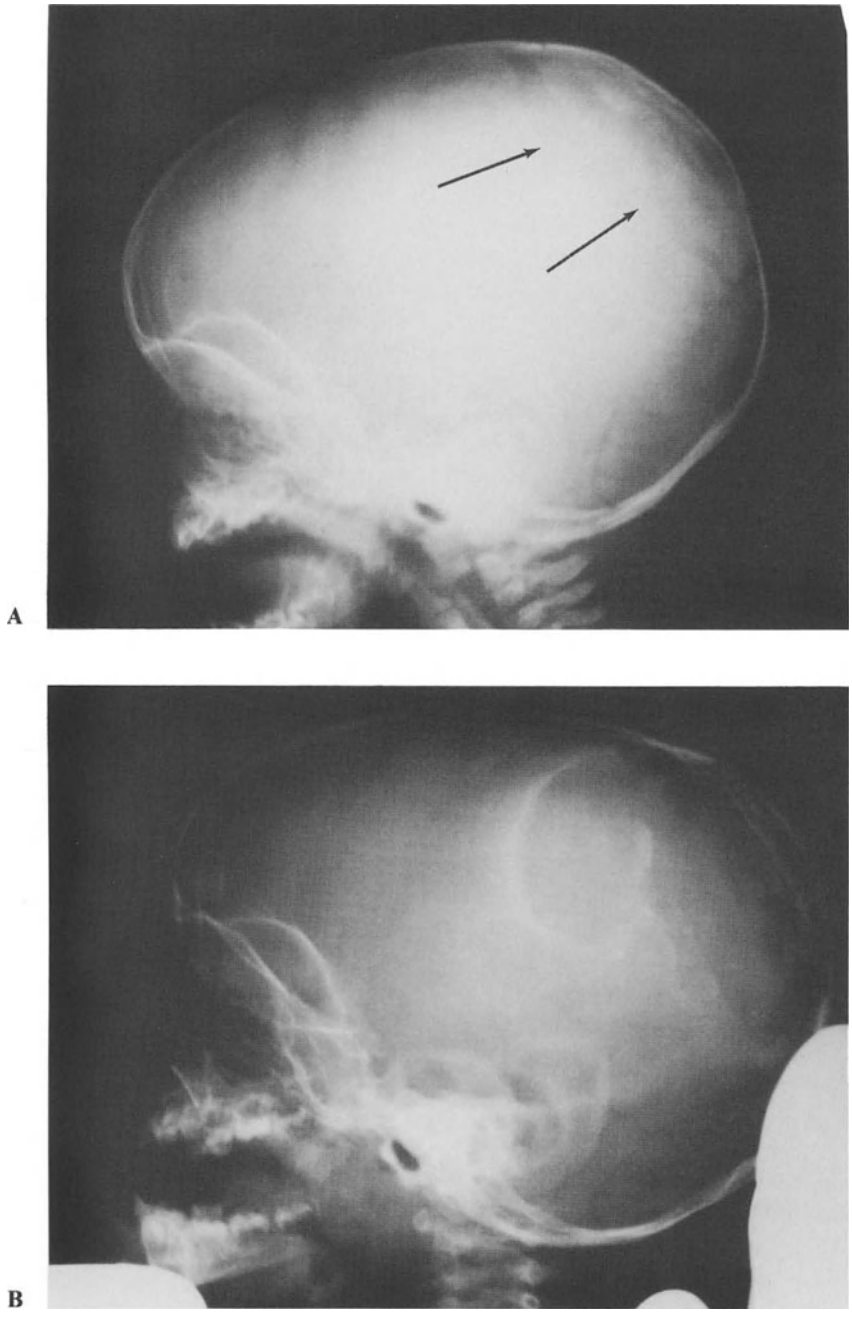

Figure 14.1. A: Lateral view of skull demonstrating diastatic fracture of posterior parietal bone (arrows). B: Lateral view of skull 6 months later demonstrating growing skull fracture. C: CT sections through growing skull fracture demonstrating its contents.

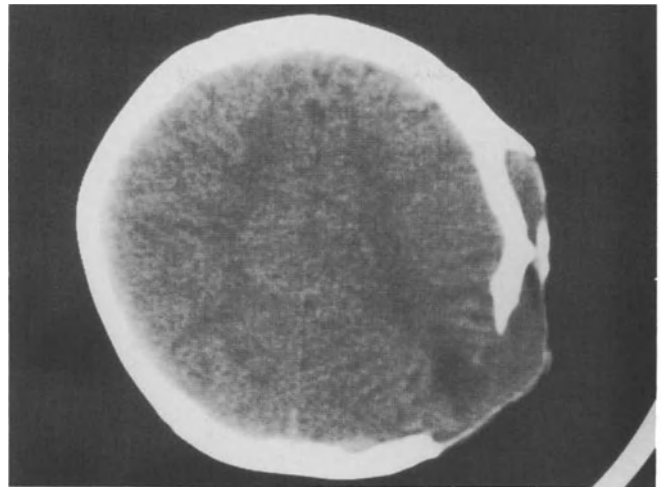

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Figure 14.1 (cont.)

Intraosseous Leptomeningeal Cyst

A variant of growing skull fracture is found in the occipital region and has been termed an intraosseous leptomeningeal cyst. In this lesion the "cyst" expands between the tables of the occipital bone rather than extending completely through the external table and presenting as a soft tissue mass under the scalp. Although the initial head injury occurs in childhood, several further years are required (10 to 50 years) for the development of the cyst. Dunkser and McCreary[28] postulated that because of the greater thickness of the occipital bone near the midline, the arachnoid at the time of injury does not herniate through the entire thickness of the bone, but only through the inner table. Another possible factor suggested by Hillman et al.[29] is that the thick musculature behind the inferior portion of the occipital bone may cushion the force of the trauma so that only the inner table fractures. With time the pulsation of arachnoid trapped between the inner and outer tables results in the formation of an intraosseous cyst. All of the described cases had retained a communication with intracranial CSF spaces. It is interesting that Sartawi et al.[30] reported a case of intraosseous cyst in a 44-year-old man who did not have a demonstrable skull fracture at the time of the initial injury.

Intracranial Posttraumatic Arachnoid Cyst

In 1946, Thompson[31] described the posttraumatic "cystic accumulation of fluid at the site of the cisterna magna," an entity that he termed "cystic cerebellar arachnoiditis." He made reference to a previous review by Horrax in 1924.[32] The pathogenesis was suggested to be the development of an inflammatory reaction of the leptomeninges in the region of the cisterna magna following trauma, which in turn causes scarring and thickening of the meninges in this region and results in partial obstruction to the flow of CSF from the cisterna magna to the remainder of the basal cisterns and subarachnoid spaces over the hemispheres. As a result of this partial obstruction the cisterna magna gradually becomes dilated, resulting in an arachnoid cyst. The presenting symptoms are those due either to the obstruction of flow of CSF with resultant hydrocephalus or to local pressure effects of the cyst.

Although Thompson desribed a midline posterior fossa cyst, it is of course clear that a similar-type cyst could develop following trauma at any site within the CSF pathways.

A traumatic origin for intracranial arachnoid cysts has been considered by several authors.[33,34] Tiberin and Cruszkiewicz[35] felt

that a traumatic subarachnoid hematoma may encapsulate, and that subsequently these cysts enlarge due to changes in osmotic pressure caused by local blood breakdown.

The majority of current opinion, however, suggests that the sylvian fissure/temporal lobe arachnoid cysts represent congenital malformations rather than posttraumatic cysts. However, the associated variations in drainage of the superficial middle cerebral veins[36] may lead to subdural or intracystic bleeding following relatively minor trauma, and these lesions are therefore not infrequently first diagnosed on investigations of minor head injuries.

In 1953, Nichols and Manganiello[37] described a posttraumatic arachnoid cyst in the cerebellopontine angle in an 18-year-old man that simulated the presentation of an acoustic neurinoma, whereas in 1967, Jelsma and Ross[38] described a traumatic intracranial arachnoid cyst involving the gasserian ganglion.

Porencephalic Cysts

Various definitions have been proposed for the term *porencephaly* first described in 1859 by Heschl.[39] The definition proposed by LeCount and Semerak[40] of "a defect communicating with the ventricles or separated from them by a thin layer of brain tissue and covered on the outside by arachnoid" has become generally accepted. Porencephalic cysts may be congenital or acquired. The pathogenesis of acquired porencephaly is varied but may result from the destruction of cerebral tissue by trauma. Courville[41] observed that the immature infant brain was susceptible to cavitation and that this tendency diminished with age. The progressive development of porencephalic cysts in areas of cerebral softening and hemorrhage in infants with birth trauma was described by Schwartz in 1927.[42] Jaffe[43] noted that porencephaly occurred more frequently in infants who were premature or the product of a prolonged labor or an instrumental delivery. Since then, only a few cases of posttraumatic porencephalic cysts in infancy have been recorded. In the series of Drew and Grant[44] only 2 of the 30 cases were in this category, whereas in two other series the incidence was only 2 in 22[41] and 1 in 32.[45]

In 1965, Barrett and Mendelsohn[46] reported three unusual cases of posttraumatic porencephaly in infancy. They speculated regarding the incidence of traumatic porencephalic cyst formation secondary to a hemorrhagic loss of brain substance following subdural and ventricular punctures and suggested that this complication might occur more often than is recognized as the location of such cysts is predominantly in the frontal lobes where large lesions may be present with only minimal clinical findings. In 1969, Williams[47] reported a 10-month-old child in whom bilateal porencephalic cyst formed over a 6-month period following a severe head injury. The cysts were unusual in that they caused pressure erosion and eversion of the overlying skull. It is noted that at the time of the original injury this child had repeated bilateral subdural taps performed.

In 1982, Grant et al.[48] reported 13 low birth weight neonates who were found on ultrasound examination to have intraparenchymal hemorrhage beyond the area of the germinal matrix. Weekly follow-up sonograms revealed progression to porencephaly in every surviving infant and the size of the mature porencephalic cyst correlated directly with the size of the intraparenchymal hemorrhage.

Chronic Subdural Hematoma

There is an extensive literature on subdural fluid collections in the pediatric age group and it is not within the scope of this chapter to comprehensively review it. However, as a chronic subdural hematoma constitutes a fluid-filled space enclosed by a membrane and can thus be regarded as a "traumatic cyst," it does require some mention.

Chronic subdural hematomas in children occur with greater frequency in the first 2

years of life, with a peak incidence in the first 6 months. It must be stressed, however, that such lesions as a complication of closed head injury occur throughout the balance of childhood and can present with headache, vomiting, mental obtundation, and papilledema without focal neurological signs.

In infancy, however, there are different diagnostic and indeed therapeutic problems. In this age group there is no clinical picture pathognomonic of this lesion. The most common symptoms include convulsions, vomiting, irritability, and failure to thrive, and on physical examination fever, bulging anterior fontanel, enlargement of head, and retinal hemorrhages are common findings.

Although chronic subdural hematoma in infants is by no means rare, nevertheless several important features of the condition remain conjectural or controversial. In many cases the cause and mode of formation of the fluid is unclear and there is controversy over the best method of treatment. In addition, there is a relative paucity of reports with documented long-term follow-up.

Trauma is an important etiological factor in chronic subdural hematoma of infancy and a significant proportion of those hematomas that occur in the first 6 months of life are thought to be associated with trauma at the time of birth or in the early postnatal period. A negative history does not exclude trauma as the cause.

The evolution of the hematoma has several features of interest. Within a week to 10 days after subdural bleeding, a membrane begins to form from the inner surface of the dura.[49] In a well-developed hematoma this outer membrane can be from 0.5 to 2 mm in thickness. An inner membrane between hematoma and the pia-arachnoid also forms eventually and this tends to be thinner and more transparent than the outer membrane. Histological examination of the membranes demonstrates large abnormal capillaries with a single endothelial cell-thick wall and some surrounding proliferative fibroblasts.[50,51] With time the membranes become increasingly less vascular, a fact attributed by Collins and Pucci[52] to effective drainage of the hematoma.

Gardner[53] demonstrated that the membranes formed around the hematoma are semipermeable and subsequently the increase in the size of the fluid collection was ascribed to the osmotic effect of the hemolysing red cells. However, Gitlin[54] demonstrated a high protein content in the subdural fluid relative to serum and a high ratio of albumin to gamma globulin and total protein. He commented that capillary filtrates are normally very low in protein content, and he felt that it was therefore difficult to explain the source of the additional albumin on the basis of osmotic pressure alone. He suggested that an effusion occurs through damaged capillary walls. Rabe et al.[55] demonstrated the passage of serum albumin labeled with radioactive iodine into the subdural collection of a 5-month-old infant, thus confirming that the source of the protein is the plasma and not significantly local red cell breakdown.

The optimum treatment for chronic subdural hematoma in infants remains controversial. Since the report of Peet and Kahn,[56] several authors have recommended fontanel puncture for diagnosis and relief of acute symptoms, followed by exploratory burr holes and craniotomy with removal of subdural membrane. This regimen evolved from earlier experience with documented, uniformly poor results in patients treated by puncture of the fontanel alone.

Although constriction of the rapidly developing brain by enveloping membranes was predicted as a possible complication early in the present era of surgical treatment,[49,56] this has not subsequently been documented in the literature as posing a significant problem, and the necessity of excising membranes has been questioned.[50,57] Ransohoff[58] suggested a shunting procedure so that continuous drainage could occur over a period of time during which disproportion between brain and skull could be corrected. Till[59] felt that a subdural-pleural shunt was a superior procedure to craniotomy.

It is generally agreed, however, that it is the degree of underlying cortical damage rather than the method of treatment that has the greatest prognostic significance.

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CHAPTER 15

Neoplastic Cystic Lesions, Types, Theory Regarding Formation, and Treatment

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Cyst formation in brain tumors is not uncommon. Associated pathological features in brain tumors are readily disclosed by advanced neuroimaging studies such as computed tomography (CT) and magnetic resonance imaging (MRI). Direct visualizations of these pathological conditions were not possible by angiography or pneumoencephalography, which provided only indirect images shown by displaced cerebral blood vessels or cerebrospinal fluid (CSF) spaces. Predicting the histological nature of the intracranial mass may be possible when it is accompanied by a cyst. Intravenous contrast agents for CT or MRI provide further information as to whether or not the cyst wall consists of neoplastic cells. Although the term *cystic tumor* is commonly used in clinical practice, it would be more appropriate to classify these lesions into two groups: one, mural tumor with cyst, and another, cyst within tumor. The former does not contain neoplastic cells in the cyst wall, whereas the cyst wall of the latter is composed of neoplastic cells. On neuroimaging, contrast-enhancing cyst walls have neoplastic cells; therefore, this observation is important in planning resection of these tumors (Figures 15.1 and 15.2).

Cystic tumor can occur anywhere in the central nervous system, and cystic formation or cystic degeneration can develop in any tumor types. The origin of cyst formation and cyst fluid remain controversial. In 1977, Murray et al.[1] published a study of six patients with tumor cysts. They analyzed the immunoproteins present in cyst fluid of patients with medulloblastoma and hemangioblastoma and concluded that these cysts are not likely due to hemorrhage into the tumors, since immunoglobulins such as IgM were present in lesser concentration in the cyst than in the serum. Nor did they feel that the proteins present in the cyst were due to a secretory process, because these tumors are not known to secrete immunoglobulins nor do they contain significant concentration of plasma cells. Loculation of the CSF may be possible but it is

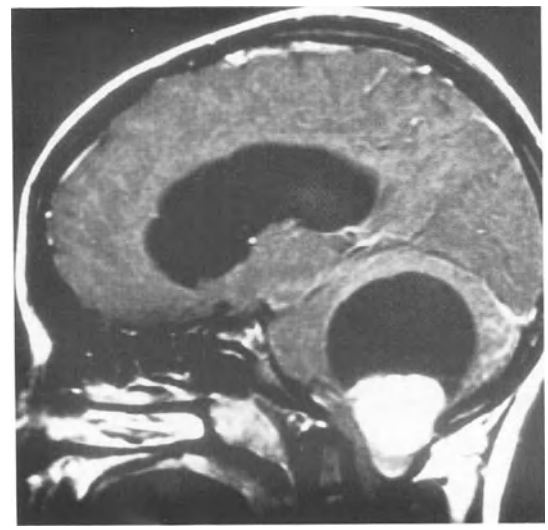

Figure 15.1. Sagittal MRI after intravenous gadolinium injection showing a mural tumor with cyst in the cerebellar hemisphere. Note the cyst wall is not enhanced by contrast, and does not consist of neoplastic cells. (Histology: benign astrocytoma.)

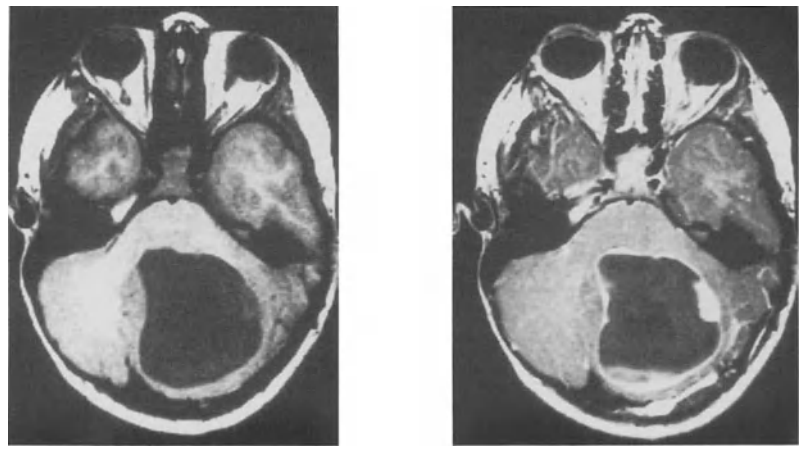

Figure 15.2. Axial MRI before (left) and after (right) intravenous gadolinium injection showing a large cystic tumor in the cerebellar hemisphere. Note the cyst wall enhances after contrast injection, and indicates the presence of neoplastic cells in the wall. (Histology: benign astrocytoma.)

unlikely due to the high protein content of these cysts, and their lack of communication with the CSF. Murray et al. considered the major protein content of the brain tumor cyst fluid to be consequential to a transudative process from serum, as the quantitative values for total protein, albumin, complement, and three immunoglobulins all more closely parallel serum than CSF.

Posterior Fossa

Cerebellum

One of the most representative cystic tumors in childhood occurs in the cerebellum. Benign cerebellar astrocytomas often present with cyst formation.[2,3] However, typical mural tumors with cyst make up only 32% of our cases,[3] whereas they are 61% of cases reported by Lapras et al.[2] Other astrocytomas in the cerbellum are either of the solid type or the cyst within tumor type. Solid astrocytomas, particularly those in the posterior fossa midline, are often difficult to distinguish from medulloblastomas on neuroimaging studies. Although medulloblastoma may present with cystic changes, a typical mural tumor with nonenhancing cyst is usually indicative of a benign astrocytoma. Cysts within tumor, in which cyst walls enhance after contrast infusion, were more common in our experience (39%). Due to the relatively low incidence of the occurrence of medulloblastoma in the cerebellar hemisphere, solid benign astrocytomas are more likely if the lesion occupies the cerebellar hemisphere. Cerebellar astrocytomas with cyst within tumor may show various appearances; some may have thick, irregular walls or multiple cysts in spite of their benign histological nature. Therefore, tumors that occur in the midline, either solid or partially cystic, can be any of the common pediatric tumors such as medulloblastoma, ependymoma, or benign astrocytoma. Although all of our patients with mural tumors in the cerebellum were diagnosed as having benign astrocytoma, one should also rule out hemangioblastoma, which, while rare in childhood, shows much denser contrast enhancement of the mural tumor due to the increased vascularity.

Surgical resection of these cerebellar or fourth ventricle tumors is warranted. Posterior fossa craniotomy is done through a midline vertical skin incision. The craniotomy is extended more to the ipsilateral side if the tumor is located in the unilateral hemisphere. If the posterior fossa dura is tight, one can decompress coexisting hydrocephalus by means

of a ventriculostomy, which can be converted to postoperative external ventricular drainage for the purpose of intracranial pressure monitoring and drainage of CSF. If the ventricles are small but the posterior fossa dura is tight, one can open the dura at the foramen magnum and drain CSF from the cisterna magnum. Another way to decompress the posterior fossa content prior to the dural opening is by puncturing the cyst. Intraoperative ultrasound is helpful for this.

For benign astrocytomas, all enhancing portions on neuroimaging studies should be resected. The cyst wall of the mural tumor does not require resection if it does not enhance by contrast.[2–4] Mural tumor can be present in various locations in relation to the cyst. Careful review of the obtained neuroimaging tests provides precise location of the mural nodules. The mural tumor of an astrocytoma is grayish and distinctly identifiable at surgery. But the intracystic surface of the mural tumor may be covered by whitish, gliotic tissue and may not be well recognized. These mural nodules do not necessarily protrude into the cyst cavity. It is therefore wise to maintain the cyst with little or no drainage of the cystic fluid so that one can identify these mural nodules according to the information given by neuroimaging.

Cyst within tumor needs resection of the entire cyst wall. Once the cyst is drained and the plane between the neoplastic cyst wall and the underlying white matter is identified, the resection is straightforward. Multiple cyst formation is not uncommon, and it is important to resect the entire tumor.

Brain Stem

A great majority of pontine tumors are malignant. It may be confusing as to whether the central hypodense lesion within the contrast-enhancing ring represents a necrotic center of the tumor or a true fluid-filled cyst. When the tumor is located in the pons and neuroimaging studies show a cyst within tumor, these lesions are almost always malignant astrocytoma.[5,6] On the other hand, mural tumor with nonenhancing cyst, even though the lesions are located in the pons, are most likely benign astrocytomas. Histology of the lesion and the nature of the central hypodensity can be confirmed by CT-guided stereotactic biopsy and evacuation of the cystic lesion. It is our impression that pontine lesions with thick and irregular ring-like enhancement are invariably glioblastomas. Surgical resection of these lesions are often complicated by neurological morbidity. Nonetheless, resection of the necrotic center of a glioblastoma may enhance the radiosensitivity of the tumor. If the lesion undergoes cystic degeneration, particularly after radiation therapy, one may consider placing an indwelling catheter connected to an Ommaya reservoir for percutaneous drainage if the cyst reaccumulates and the patient becomes symptomatic. The catheter can be placed safely under CT-guided stereotaxy.

As opposed to tumors in a pontine location, tumors affecting the midbrain, medulla oblongata, and cerebellar peduncle may be benign astrocytomas.[5] Some may present as mural tumors with cysts or cysts within tumors. These tumors probably warrant histological confirmation and surgical debulking. The drainage of the cyst fluid often causes symptomatic improvement of these patients. Benign astrocytomas of the brain stem respond to radiation therapy and a prolonged remission may be achieved, whereas malignant astrocytomas or glioblastomas almost always lead to fatal outcome.

Cerebellopontine Angle

Primary tumors in the cerebellopontine angle are rare in childhood. Meningiomas or acoustic neurinomas can occur, but are invariably associated with neurofibromatosis. Epidermoids may occur and be cystic. More frequent tumors in this location are secondary tumors, either by direct extension from the brain stem or cerebellar peduncle, or direct extension from the fourth ventricle through the lateral recess (notably ependymomas), or subarachnoid seeding of malignant tumor from other sites. Cystic components of benign astrocytomas from the cerebellar peduncle can distort the brain stem or may extend to the

cerebellopontine angle.[7] These lesions are surgically resectable.

Pineal Region

Common tumors in the pineal region are germ cell tumors and pineoblastomas. Our data show that the incidence of these tumor is about equal.[8] Germ cell tumors occur in male and older children, whereas pineoblastomas do not have any sex predilection and affect younger individuals. These tumors are often calcified in the center but cyst formation is unusual. Among the germ cell tumors, benign teratoma may present mixed appearance on neuroimaging studies, and a glandular component may secrete and form a cyst. Pineoblastomas are usually solid but may have peritumoral cystic components or necrotic centers. These tumors should be surgically resected. This may restore the CSF circulation and allow better response to adjuvant therapy such as radiation therapy and/or chemotherapy. The only exception to this would be pure germinomas, which are extremely radiosensitive.

Cerebral Hemisphere

The most common tumors in the cerebral hemisphere of children are benign astrocytomas. As in the cases of the cerebellar astrocytomas, cerebral astrocytomas present with various appearances: solid, cyst with mural nodules, and cyst within tumor.[9–11] Usually solid portions of astrocytoma enhance by intravenous contrast, but they may not enhance, preserving their hypodense or sometimes isodense appearance. The latter appearance can occur with oligodendrogliomas or gangliogliomas. The mural tumor with a nonenhancing cyst can be cured by resecting the mural tumor alone.[9–12] One should plan the craniotomy and dural opening appropriately to allow access to the mural nodule. Solid tumors or cysts within tumors should be resected in toto, otherwise tumor recurrence is inevitable, though their growth rates are commonly very slow.

Another common tumor in the cerebral hemisphere is the primitive neuroectodermal tumors (PNET). The microscopic appearance is indistinguishable from that of medulloblastomas. On neuroimaging studies, most tumors are solid with focal calcifications or hemorrhage.[13] Some may be accompanied by focal necrotic foci mimicking cyst formation on neuroimaging studies. Cystic formation in cerebral PNET is relatively uncommon.

Other tumors such as ependymoma, oligodendroglioma, and ganglioglioma can present with cyst formation in the fashion of either mural tumor type or cyst within tumor type.[11]

Suprasellar

Common tumors in the suprasellar location of children are craniopharyngioma, astrocytoma, and germ-cell tumor.

Craniopharyngiomas in childhood are invariably associated with cyst formation. Radiographically, cyst formation is found in about 85% of cases, but surgical observation shows the presence of a cyst in almost all cases. Some tumors are predominantly cystic whereas others are solid with small cyst formation. Multiple cyst formation is not unusual. Although the solid portion of a craniopharyngioma is primarily located in an intrasellar and suprasellar location, the cyst can extend in various directions; anteriorly to the subfrontal space, laterally to the subtemporal region, and superiorly to the third ventricle and, on some occasions, to the lateral ventricle. The direction of cyst expansion seems to be toward the direction of least resistance. Therefore, vascular (circle of Willis) or neural (optic chiasm and nerves) structures often dictate the direction of cyst extension. Cyst walls of craniopharyngiomas consist of neoplastic epithelial cells so that surgical resection should include not only the solid portion but the cyst wall as well. The cyst wall varies in thickness and nature. It may be very thin or quite thick, and it may be calcified. On resecting the cyst wall, it is important to maintain its continuity. Otherwise, the deeper portions of

the cyst wall may retract beyond the surgeon's view. Although there are practically no adhesions between the cyst wall and vital neural structures such as the optic pathway and circle of Willis, the tuber cinereum and hypothalamic floor are often severely involved. This portion of the hypothalamus is bordered by gliotic tissue; hence, a separation of the cyst wall from the hypothalamus is possible. In general, craniopharyngiomas are resected through a subfrontal or pterional approach with microsurgical technique. If the cyst extends further into the third ventricle or lateral ventricle, the transcallosal approach may be applied. A strictly intrasellar mass is best removed via a transsphenoidal approach. A controversy exists as to whether patients benefit from aggressive radical resection as opposed to an intentional simple operation like cyst aspiration followed by irradiation.[14,15] Cyst aspiration can produce a dramatic improvement of symptoms, particularly those of acute visual disturbances, but cyst reaccumulation is usually very rapid unless further therapy is initiated. For recurrent cystic craniopharyngiomas, some recommend treatment with installation of bleomycin or radioisotope.

Chiasmal or hypothalamic astrocytomas are common in childhood. These two tumors may not be distinguishable due to the lack of anatomical separation of these neural structures. Therefore, it may be appropriate to categorize these tumors into "suprasellar gliomas." Astrocytomas in this location are usually solid and benign. Contrast-enhancement may vary, but most benign astrocytomas show dense enhancement. Occasionally mural tumor with a cyst can occur, but the mural tumor may be very large, particularly during infancy. Optic pathway gliomas, when associated with neurofibromatosis I, rarely undergo cystic degeneration, and often show a diffuse, bright image along the optic pathway on MRI with or without focal enhancement after contrast administration. Astrocytomas of hypothalamic origin usually extend into the third ventricle. Cyst formation is rare in hypothalamic astrocytomas, though they are invariably benign.

Other common suprasellar tumors in childhood such as germ cell tumors and PNETs may present with focal calcification or cystic degeneration within the tumor. These cases may be similar to those of craniopharyngiomas.

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CHAPTER 16

Epidermoid and Dermoid Cysts

Irena Škodová and Ivana Julišová

Intracranial epidermoid cysts were first recognized as a specific pathological entity by Cruveilhier in 1829, and in older literature they were called by several synonyms, like pearly tumor,[1] cholesteatomas;[2] and sebaceous cysts.

The epidermoids and dermoids now feature as specific entities within malformative tumors and tumor-like lesions in the World Health Organization (WHO) classification.[3] According to Zülch[4] they are sharply separated both from other squamous epithelium–containing tumors, e.g., craniopharyngiomas, and from so-called inflammatory cholesteatomas of the middle ear.

The age curve of intracranial lesions at the time of operation shows a peak between 25 and 40 years of age with equal sex representation; dermoids are more frequent in children.[4] The frequency of both epidermoids and dermoids is 0.7% in Cushing's material and 0.9% in Findeisen's and Tönis's intracranial tumors.[5] Guidetti[6] reports 0.8% for cerebral epidermoids and 0.5% for cerebral dermoids in space-occupying lesions of the brain and spinal canal. According to Raimondi,[7] they are the most frequent skull tumors in children. Dermoids are generally rarer intracranially than epidermoids but somewhat more common in the spinal canal.

Epidermoid cysts originate from epidermis, and dermoids also contain inner dense connective tissue, which is mesodermal in origin. They may arise wherever two ectodermal surfaces fuse together in the developing embryo, provided an ectodermal implant is retained in the deep tissue.

Between the 3rd and the 5th week of gestation the neural tube closes and cutaneous ectoderm separates from the neural ectoderm. According to the "midline" hypothesis, if the primitive medullary plate fails to invaginate properly, an epithelium-lined tube or a fragment of a tube persists between the skin and central canal of the spinal cord or ventricles of the brain.

The "midline" hypothesis does not account for the tumors developing in lateral locations. They could be explained by the misplaced cell rests, associated with secondary vesicles, particularly the optic and otic, which develop at about the 5th fetal week, giving rise to laterally located epidermoid tumors.

Epidermoids are macroscopically well defined with nodular outer surface; the section reveals waxy or flaky material, which can be occasionally softened—the term *epidermoid cyst* is then used. Epidermoids can be firmly attached to the surrounding brain tissue because of focal sterile meningitis. They can "melt" the adjacent parenchyma via irritation, setting up an inflammatory process. Focal calcifications may be present. In the ventricles they can rupture, causing meningeal irritation.

Their histologic appearance is characterized by a wall composed of a thin connective tissue capsule upon which stratified squamous keratinized epithelium rests (Figure 16.1). The content may consist of variable granular material, arranged in layers as in an onion

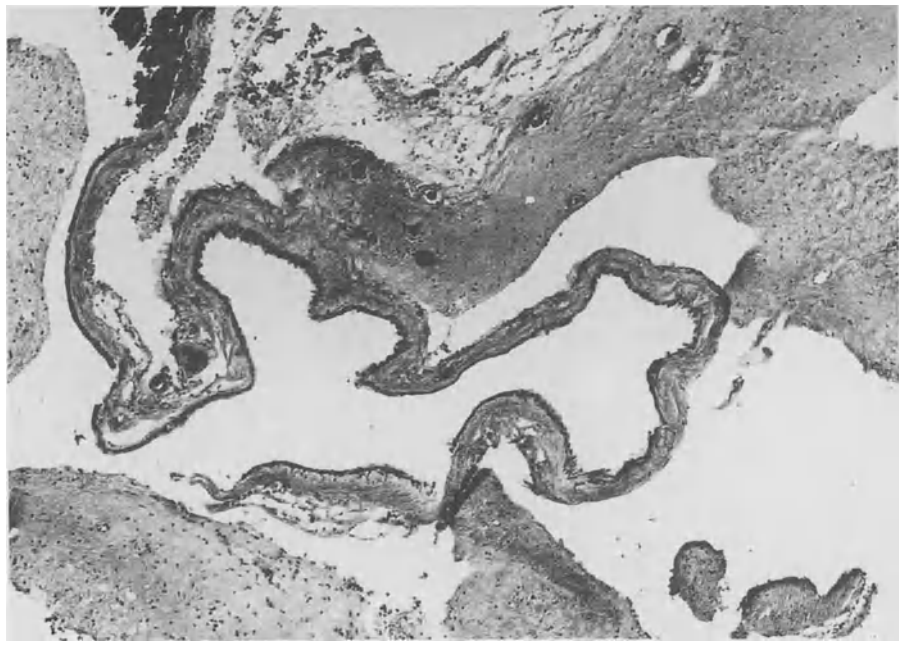

Figure 16.1. Epidermoid cyst of the spinal cord in a 11-year-old girl. Lumen is lined with flattened spinocellular epithelium. Underneath, only the layer of fine fibrous tissue and the neural tissue is visible. (Blue Masson trichrome, ×170.)

bulb, rich in cholesterol crystals formed by the breakdown of keratin from desquamating epithelial cells.

The biological behavior is characterized by slow growth; it corresponds to grade I in the WHO classification. They grow by accumulation of keratin and cellular debris; exceptionally carcinomatous degeneration has been described.[4]

The location of epidermoids intracranially deviates from the midline; often they can be found in the cerebellopontine angle, in the parapituitary region, in the corpus callosum and quadrigeminal plate, in the sylvian fissure, in the third and fourth ventricles, and in other locations. In the spinal canal they may be associated with congenital defects of the spinal canal and with dermal sinus. Intradiploic epidermoids occur most frequently in frontal and parietal bone.

Dermoids macroscopically have a firm shell and are generally filled with a greasy, soapy mass containing numerous short hairs (Figure 16.2) and even teeth. The contents are formed by the continual proliferation of the new cells of the germinal layer, degeneration of these cells, and finally cornification as well as secretion of fatty material. Occasionally, colorless or yellowish fluid can be found inside

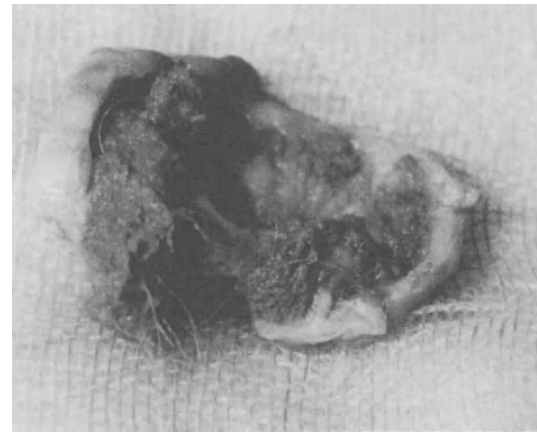

Figure 16.2. Dermoid filled with a soapy mass and hairs.

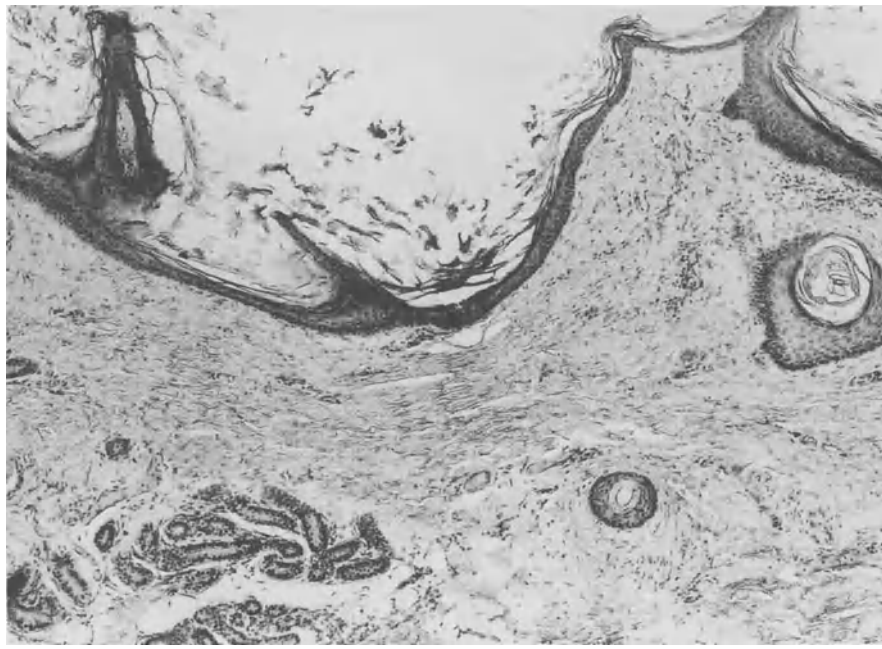

Figure 16.3. Dermoid cyst of the anterior fontanel in a 2-year-old girl. Lumen is filled with layers of keratin. Beneath the stratified spinocellular epithelium in the fibrous tissue there are groups of sweat glands (left lower corner) and a section of the hair follicle (right). (Hematoxylin-eosin, ×70.)

the capsule in children—the term *dermoid cyst* is then used. In adults, the content is more pastry-like and semisolid.

Microscopically, dermoids differ from epidermoids only by the presence of the accessory structures of the skin: the layer comparable to dermis with hair follicles, sweat glands, and sebaceous glands (Figure 16.3). The content includes glandular secretory products, among which hair may be matted.

Dermoids in contrast to epidermoids tend to occur more to the midline and embryonic closure lines,[4] and are frequently associated with defects of overlying bone and skin. Intracranially, they occur frequently in posterior fossa and the pituitary region, and as in the lumbosacral region they can be associated with dermal sinus, dimples, and lipoma overlying. In these cases pyogenic meningitis or abscess may be the manifestation of the disease. The extracranial subgaleal dermoid cyst of the anterior fontanel (Figure 16.4) is a well-known entity in children. These cysts generally do not communicate with the CNS, unlike the dermoid cysts in the occipital area.

Granulomatous meningitis after rupturing of the content into the CSF may occur as in epidermoids.

The biological behavior, possibility of recurrence if subtotally removed, and rare carcinomatous change are the same as in epidermoids.

The clinical manifestation is similar to any other slowly growing space-occupying lesions in the brain. Sometimes infected dimples and neurological symptoms mimicking cerebellar or cerebral abscess and recurrent meningitis are the first symptoms of the disease. Increased intracranial pressure was observed by Guidetti[6] in 50% of the patients with epidermoids and in 80% of those with dermoids. Epileptic manifestation was seen in 11 of 20 patients with intradural epidermoids and in only 1 patient with dermoid. Mental, endocrine, and metabolic disturbances are reported in the literature,[2,5] as is trigeminal

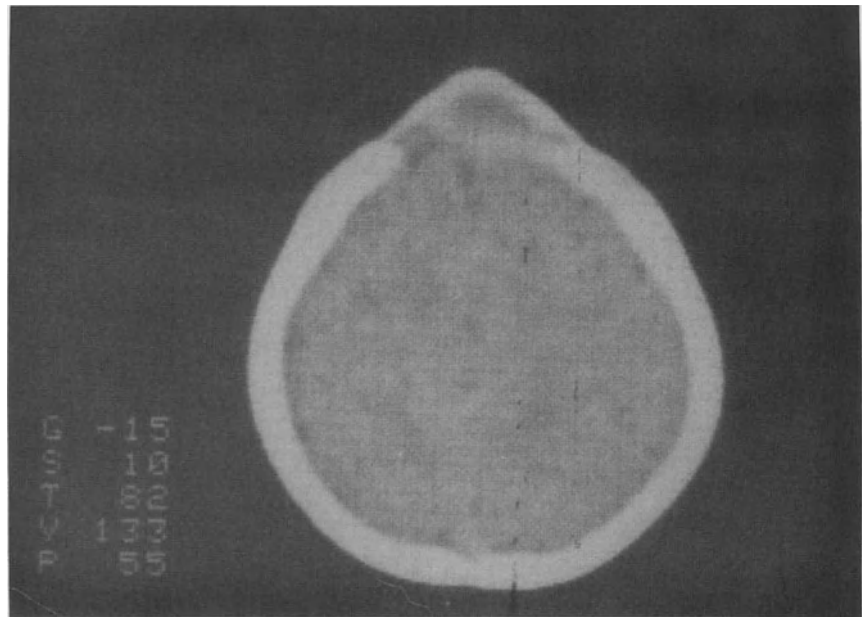

Figure 16.4. CT of the patient in Figure 16.3. No intradural extension can be seen.

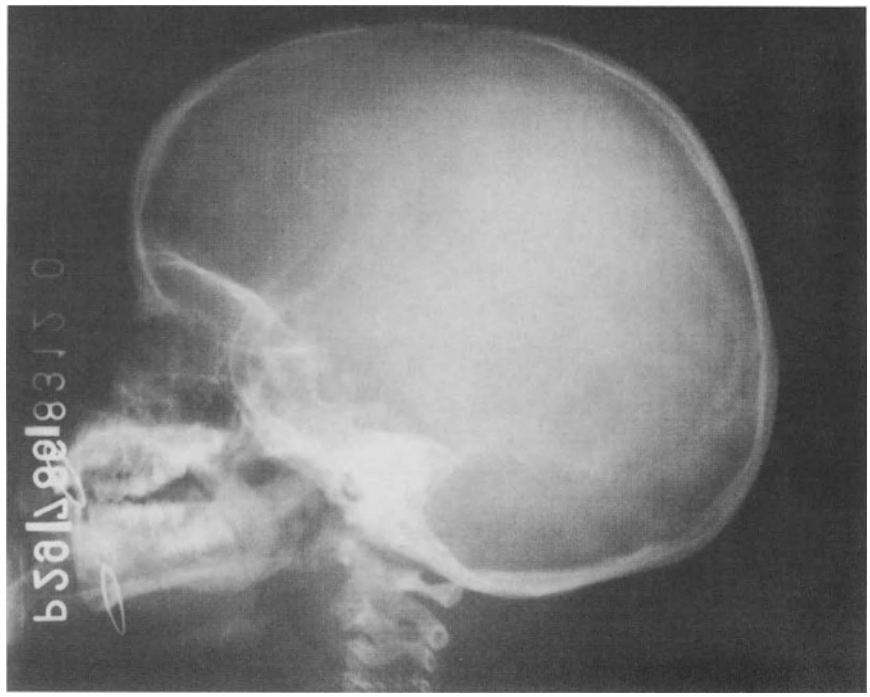

Figure 16.5. X-ray of the patient in Figures 16.3 and 16.4. Thinning of the bone in the bregmatic area is visible.

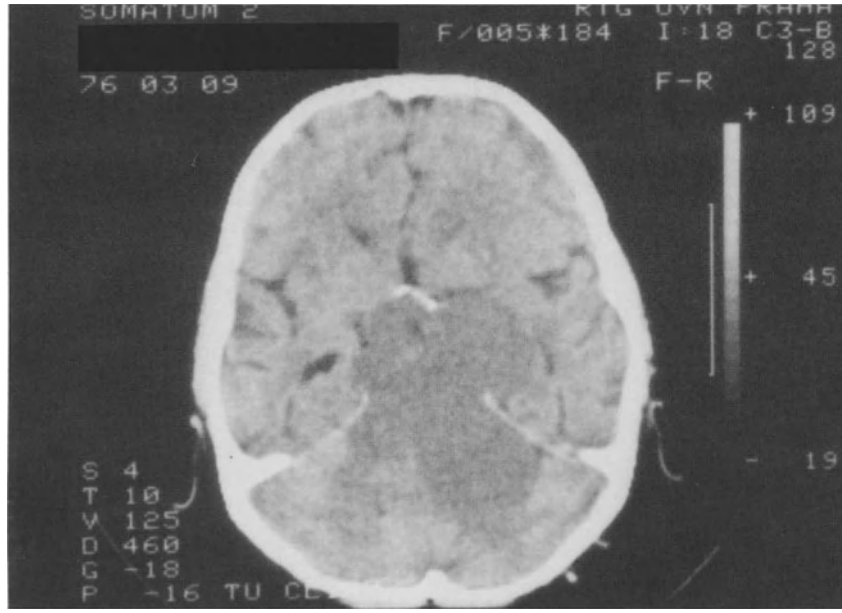

Figure 16.6. CT of a 5-year-old girl with epidermoid cyst at the base of the brain extending from parapituitary region to the right middle fossa and to the posterior fossa. Calcification in parapituitary region is visible.

neuralgia as a symptom of an epidermoid in the cerebellopontine angle.[2]

Bregmatic dermoids present as a swelling in the region of the anterior fontanel with the thinning of the adjacent bone (Figure 16.5). Epidermoids are associated with central radiolucency on the skull x-ray, may destroy one or more layers of the skull, or may be located totally within the subgaleal space.[7] Magnetic resonance imaging (MRI) and computed tomography (CT) (Figure 16.6) disclose an extracerebral mass and should be performed in all asymptomatic patients with dermal sinuses, both in cranial and spinal locations, and in subgaleal dermoids when intracranial involvement is suspected.

Differential diagnosis in intracranial lesions includes other extracerebral tumors (craniopharyngioma, hamartoma, teratoma, lipoma, hemangioma), abscess, and others. Extracerebral mass should be distinguished from eosinophilic granuloma, aneurysmal bone cyst, and meningocele.

Operative treatment consists in radical removal of the tumor without contamination of the cerebrospinal fluid (CSF) by the content of the capsule. Adherence of the capsule to the important structures of the brain can sometimes impede the radical removal, even when microscopic technique is used. Also, in these cases cure can be expected, especially in adults.

Contemporary low rates of mortality—Guidetti[6] reports 3.2%—in intracranial epidermoids and dermoids reflect earlier and more correct diagnosis and advances in surgical techniques, in contrast to previous reports of mortality as high as 30%.[8]

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CHAPTER 17

Postinflammatory Cysts (Loculated Ventricles)

Enrique C. G. Ventureyra and Michael J. Higgins

> It is not necessary to study the different works on hydrocephalus very exhaustively to find that actually observed lesions are much rarer than theories explanatory of the cause of hydrocephalus.
>
> Spiller, 1902[1]

Introduction

Postinflammatory cystic hydrocephalus is an infrequent and perplexing clinical entity that is frustratingly difficult to treat. Typically associated with inflammatory ventricular processes such as meningitis, severe intraventricular hemorrhages, or ventriculitis, it has been variously termed "multiloculated hydrocephalus," "multiloculated ventricles," "ventricular compartmentalization," "septate ventricles," or "polycystic brain disease." Its simpler forms have been designated as "trapped" or "isolated" ventricles. These simpler forms, such as unilateral isolation of the lateral ventricle, present a problem easily remedied; more complex instances often defy the dedicated treatment of a persistent surgeon. These latter instances are seldom discussed in major texts or reviews of hydrocephalus and its treatment and complications.

This chapter reviews the clinical presentation and diagnosis of postinflammatory cystic hydrocephalus, its clinical and experimental pathology, its proposed mechanisms of origin, and the current treatment regimens advocated by various authors. Despite all treatment efforts, cystic hydrocephalus frequently proves to be a recurrent clinical problem, and patients harboring this process are frequently severely neurologically handicapped.

Characteristic Clinical Presentation

Postinflammatory cystic hydrocephalus, despite its varied forms, presents a common clinical picture. Characteristically, a shunted hydrocephalic infant or child presents with a history suggestive of (a) shunt malfunction, (b) prior intracranial inflammatory process (meningitis, ventriculitis, or intraventricular hemorrhage), (c) multiple shunt revisions, and (d) clinical signs indicating possible intracranial hypertension. Such patients may also present focal neurological deficits or altered behavior in addition to this common picture. At times, generalized brain damage, expressed as cerebral palsy or psychomotor retardation, may mask any signs other than those suggesting increased intracranial pressure. Preliminary shunt evaluation often reveals an intact functional shunt system despite the contrasting clinical symptoms signaling inadequate control of the underlying hydrocephalus.

Radiographic evaluation simultaneously clarifies the sometimes confusing clinical picture while disclosing an underlying dilemma. Instead of simple ventriculomegaly consistent with shunt obstruction, or slit-like ventricles suggesting symptomatic overdrainage, computed tomography (CT) demonstrates an asymmetrical ventricular system associated with one or more cystic spaces that may or

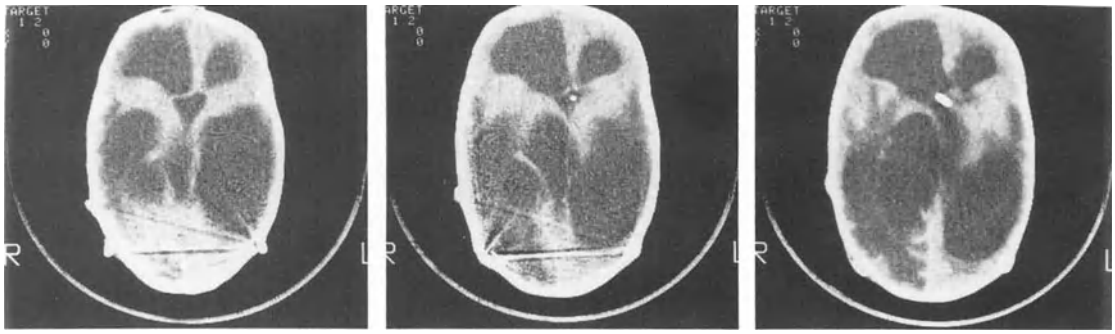

Figure 17.1. Postinflammatory cystic hydrocephalus. Computed tomography (CT) graphically demonstrates multiple asymmetrical cavities, delimiting membranes, and associated parenchymal destruction in this severe example of multilocular hydrocephalus following meningitis-ventriculitis.

may not freely communicate. These alterations in ventricular shape and character may be associated with changes suggesting inflammation of the ventricular system or adjacent cerebral parenchyma. This radiographic picture, typified by Figures 17.1, and 17.2a, is that of postinflammatory cystic hydrocephalus (PICH). Often, evidence of prior treatment is present in the form of one or more ventricular shunt systems.

Ventricular asymmetry, if present, should prompt a search for evidence of membranes delimiting noncommunicating compartments within the ventricular complex. Membranes may be directly visible, may be suggested by indirect signs or clues, or may be seen only with the aid of contrast studies such as ventriculography or cisternography. Indirect clues to the presence of compartmentalized ventricles are the following:

1. Deviated ventricular catheter departing from a normal course or expected position,[2]
2. Asymmetrical hydrocephalus, or asymmetrical ventricular drainage after shunt placement or revision,
3. Small, pointed ependymal projections entering the ventricular lumen, or
4. Unexplained repeated shunt failures after a period of satisfactory shunt function.[2,3]

Diagnosis of postinflammatory cystic hydrocephalus is established by the correlation of the clinical and radiographic presentations. A complex individual instance may require invasive radiographic procedures such as contrast ventriculography or cisternography to fully describe the situation and allow formulation of a detailed treatment plan.

Clinical Spectrum

Ventricular Asymmetries

The varied radiographic presentation of postinflammatory cystic hydrocephalus allows a more specific assessment than does the common clinical presentation, and depicts the pathologic spectrum producing ventricular asymmetries. Until the advent of noninvasive technologies such as CT scanning, visualization of the cerebral ventricular system was a risky procedure often limited to suspected intracranial masses. Today, diagnostic images are easily obtained at minimal risk and afford excellent definition of brain anatomy, which facilitates diagnosis and treatment.

Historically, ventricular asymmetries were postmortem findings. In 1842, Von Mohr[4] described two cases of unilateral ventricular dilation that appeared to be the result of hemispheral atrophy. Cushing[5] in 1908 noted the postmortem finding of unilateral ventricular enlargement resulting in intracranial shift and death in a patient suffering from "brain

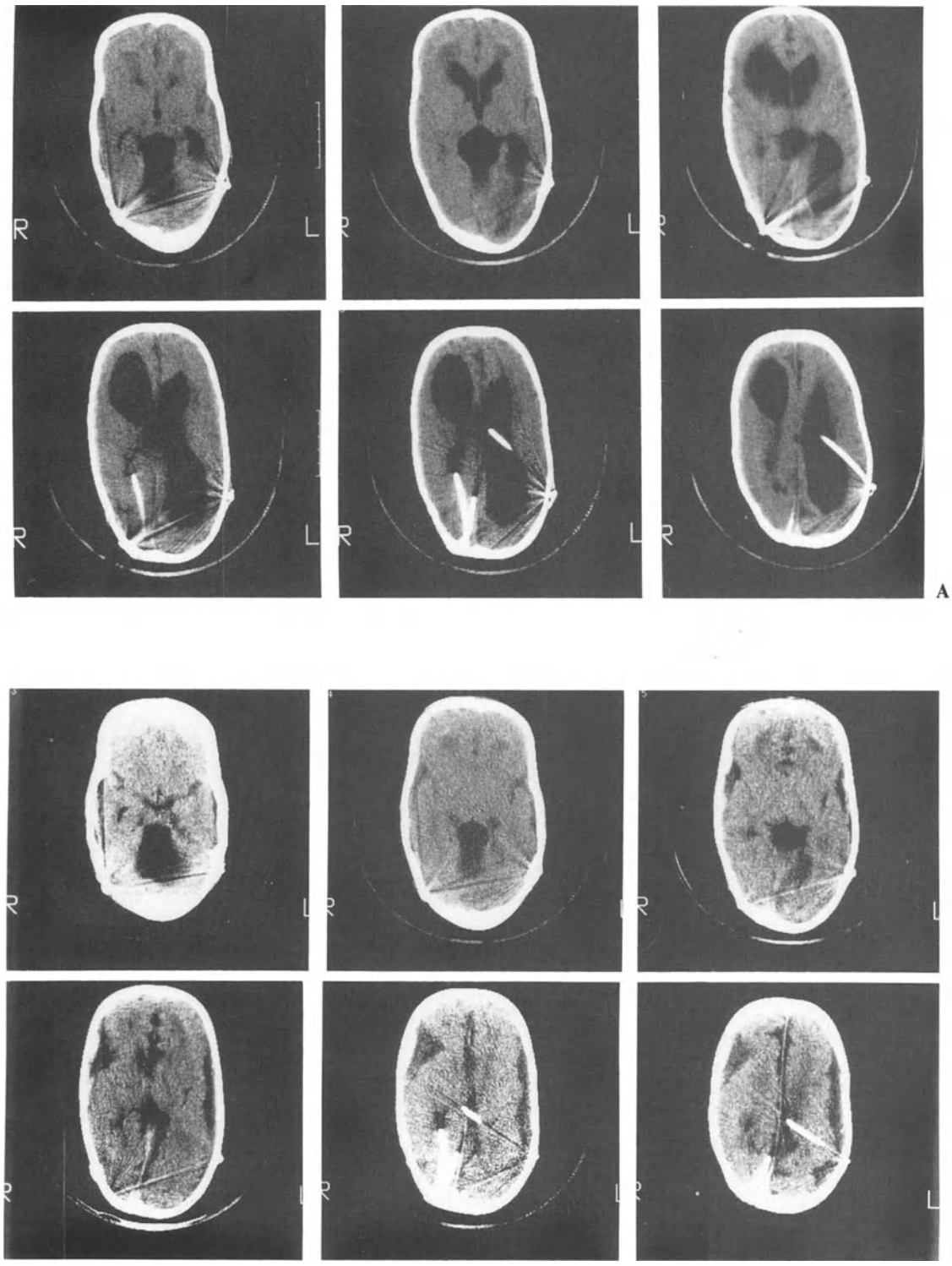

Figure 17.2. Postinflammatory cystic hydrocephalus. CT depicts a severe example of multilocular hydrocephalus following grade IV neonatal intraventricular hemorrhage. CT sequence A is before shunt revision; CT sequence B follows shunt revision. The isolated fourth ventricle presents a distinct "keyhole sign" as it herniates superiorly through the tentorial incisura. Level of consciousness and ataxia rapidly improved after shunt revision. Spastic diplegia improved after shunting of the isolated fourth ventricle.

fever." Dott[6] in 1927 reported a single case of unilateral hydrocephalus cured by fenestration of the septum pellucidum. Cairns et al.[7] subsequently reported three instances of ventricular entrapment, two following penetrating intracranial war wounds, and a single case of an infant with ventricular obstruction following subependymal hemorrhage. In her eloquent monograph detailing the pathology of hydrocephalus, Dorothy Russell[8] reported postmortem findings and a clinical résumé of a pertinent case suggestive of inflammatory origin: Case 29, an infant born prematurely at $7\frac{1}{2}$ months' gestation, developed infantile focal purulent meningitis and presented, at necropsy, a dilated cystic left temporal horn distal to intraventricular adhesions microscopically composed of collagen and glial fibrosis. Local hemorrhage in the choroid plexus at the site of adhesions was considered the initiating event leading to the dilation.

In 1946, Davidoff,[9] spurred by incidental findings of mild frontal horn asymmetries in patients undergoing air ventriculography or pneumoencephalography, described and correlated the radiographic and pathologic characterstics of these anomalies in autopsies within a series of 64 consecutive patients. He termed these asymmetries "ventricular coarctations" and believed them to be the result of a noninflammatory apposition of ependymal surfaces with or without subsequent adhesions. No clinical significance was documented. Davidoff presumed coarctations to be congenital or developmental in origin, despite his expressed impression that they were more frequently seen in older than in younger patients.

With the advent of CT scanning, ventricular asymmetries are more commonly encountered in shunted hydrocephalics than in the general population. Kaufman et al.[10] and Linder et al.[11] each noted shunt-induced ventricular asymmetries and attributed them to diminished ventricular pulse pressures within the shunted ventricle. This interpretation and the proposed mechanism are consistent with the experimental work of Bering[12] relating ventricular size to the presence or absence of choroid plexus within the ventricle. Each author demonstrated diminished pulse pressures in the shunted ventricle. Following shunt revision, both ventricles diminished in volume and the shunted ventricle was always the smaller.[10,11]

Pathologic Ventricular Asymmetries

With few exceptions, postinflammatory cystic hydrocephalus, and its lesser variants arise within the context of intracranial infections or other irritative phenomena causing or complicating symptomatic shunt-compensated hydrocephalus.[2,13–32] Control by simple shunt systems is often inadequate and multiple shunt revisions are the rule.[12,17,21,23,28] These patients are often severely handicapped by brain damage produced by the initial inflammatory insult.* The major geographic variants are the following:

1. The multilocular forms that may follow neonatal meningitis or ventriculitis or significant intraventricular hemorrhages in the newborn,
2. The isolated lateral ventricle (unilateral hydrocephalus),
3. The isolated or trapped fourth ventricle.

Intracranial cysticercosis is the predominant form of parasitic postinflammatory hydrocephalus that may present as "cystic" hydrocephalus, and is discussed in this volume by Dr. Rueda-Franco (Chapter 18).

Multilocular Hydrocephalus

Multilocular hydrocephalus is, in all respects, the most severe form of the disease. This subject of several published reports fortunately remains infrequent and is seldom discussed in any detail in major neurosurgical texts or reviews. Following Salmon's[2] 1970 report of five shunt-dependent children—one of whom demonstrated multiple loculated intraventricular cavities—presenting signs of shunt failure and intracranial hypertension despite the presence of a functioning ventricular shunt,

*Refs. 16, 20, 21, 23, 27, 28, 33–35.

increasing awareness coincident with increasing survival rates in premature infants suffering neonatal meningitis, intraventricular hemorrhages, or both have yielded two major populations distinguished by their underlying inflammatory pathologies: postmeningitic hydrocephalus[3,16,20,23,34,36] and posthemorrhagic hydrocephalus.[37–42] Variously described as "multilocular hydrocephalus",[43] "intraventricular septations",[16] "polycystic brain disease",[20] and "ventricular compartmentalization",[21] both groups present similar clinical and radiographic presentations which we term postinflammatory cystic hydrocephalus (vide supra).

Postmeningitic Hydrocephalus

Schultz and Leeds[16] reported seven infants who developed "intraventricular septation" after surviving neonatal meningitis-ventriculitis and its complicating hydrocephalus. Six of these seven harbored gram-negative infections, and all required parenteral antibiotics in their course of treatment prior to shunting. Four additionally received intraventricular antibiotics. All required multiple revisions after initial shunt placement. Air ventriculography performed prior to shunting to evaluate the extent of hydrocephalus and the site of cerebrospinal fluid obstruction disclosed "intraventricular septations or veils" disrupting communication in all seven patients. In three, demonstration of septa preceded intraventricular therapy; in one, intraventricular instillation of streptokinase-streptodornase failed to deter membrane formation, and in two, serial imaging documented septa formation after clinical resolution of ventriculitis, suggesting proliferation of the process over time.

Outcome in this cohort was distressing: five of seven died by age 34 months, and survivors remained severely neurologically handicapped. Postmortem examination in three of the five infants who succumbed to this disease revealed "filmy, translucent membranes" that randomly compartmentalized the ventricles. Microscopic examination demonstrated evidence of subacute and chronic ventriculitis, denuded ependyma, subependymal gliosis, and "glial tufts" that extended through areas of ependymal loss into the ventricular lumen. The membranes themselves were fibroglial structures infiltrated by round cells and polymorphonuclear cells, and appeared to extend into the lumen from the described "glial tufts." The aqueduct was obliterated by debris and inflammatory reaction. In the opinion of these authors, the intraventricular " . . . septations represent . . . organization of intraventricular exudate and debris accompanying the ventriculitis. A subependymal gliotic process disrupts the ependyma, producing glial tufts that act as a nidus for the formation of the septations within the lateral ventricles." They further suggested this process was not related to a specific bacterial agent, that parenteral corticosteroids were of no clinical benefit, and that the elevated protein present within the ventricles might be an additional factor in the pathogenesis. Although they did consider intraventricular antibiotics a possible causative factor, three of their seven patients had no such treatment prior to documentation of intraventricular membranes.

Brown et al.[20] concurring with prior reports of a much higher incidence of ventriculitis in infants than in older children or adults suffering from meningitis,[2,44,45] described the evolution of "polycystic brain disease" in a well-documented case report. Despite treatment with parenteral antibiotics and dexamethasone, supplemented by intraventricular antibiotics, this infant was neurologically devastated by inflammatory complications of *Escherichia e coli* ventriculitis. Serial CT examinations revealed evolution of the initial communicating hydrocephalus and adjacent periventricular edema and infarction into a progressive compartmentalization of both lateral ventricles by "thin veils" that proved resistant to multiple shunt interventions. Accepting the pathogenesis proposed by Schultz and Leeds,[16] the authors attributed the proliferative nature of the process to persistent ventriculitis, and to the production of cerebrospinal fluid or continued formation of inflammatory exudate within the cysts leading to progressive dilation. Adjacent areas of in-

farction were considered to be the result of induced vasculitis and cerebral edema, arising as a separate complication of the primary infection. Effective treatment, in their opinion, must combine appropriate intraventricular antibiotics and effective drainage of all cavities by shunting. Serial CT was an effective tool simplifying diagnosis and directing therapy as the disease evolved.

Subsequently Kalsbeck and his colleagues[21] reported a series of 13 infants treated for "ventricular compartmentalization" over a 12-year span. In most respects, this series of patients proved similar to those described previously and subsequently in the literature: all had neonatal meningitis—most due to gram-negative organisms—and developed compartmentalization despite appropriate parenteral or intraventricular antibiotic therapy. CT was again the most practical diagnostic intervention. Their investigation disclosed a constant radiographic finding: all patients in their series developed a transverse membrane just posterior to the foramen of Monro, and this membrane was often present bilaterally. Compartmentalization was progressive, was poorly controlled despite multiple shunt systems, and typically led to death or severe psychomotor retardation. Although reluctant to implicate either the presence of a shunt or the intraventricular instillation of antibiotics as contributory factors in this disease process, the authors nevertheless noted a controlled study of 52 neonatal meningitis patients in whom intraventricular antibiotics were associated with increased morbidity.[46] In a short, later publication, Kalsbeck[47] considered these cystic compartments to be the probable result of vasculitis and multiple small infarcts.

Albanese and coworkers[23] presented a paper again confirming the reports of prior authors in a series of five infants with neonatal meningitis. All survived gram-negative meningitis within the first 10 days of life and developed progressive hydrocephalus despite parenteral and intraventricular antibiotics. All subsequently developed progressive septation of the ventricular system, transforming it into an irregularly contoured multicystic cavity. Serial radiologic visualization utilizing air ventriculography, positive contrast ventriculography, and/or CT accurately detailed evolution of the inflammatory process and directed the placement of multiple shunt systems in four patients or, in one case, craniotomy with membrane fenestration. Outcome was dismal: three infants died (one accidental death) and the two survivors were severely or moderately-severely disabled, respectively. This series failed to confirm Kalsbeck's report of a constant membrane synthesis just posterior to the foramen of Monro—a point Kalsbeck[47] contested.

Following review of then-published reports and assessment of their own cases, the authors considered CT adequate to establish a correct diagnosis and advocated treatment by multiple shunt systems (utilizing multiperforated catheters) or by craniotomy with fenestration of membranes in the manner of Rhoton and Gomez.[43] This latter intervention was deemed "most promising" though only five such procedures (including the authors' single operated patient) had been reported at the time of publication. Rhoton,[48] citing his experience with "several" such patients, also favored open fenestration followed by simple shunt placement, declaring " . . . there is no other satisfactory approach to this problem except possibly to attempt lysis of the membrane using a ventriculoscope." Savolaine and Gerber[3] in a concise review and description of two patients with septated ventricles, related the several radiologic clues to the presence of ventricular septations we have cited above.

The pathogenesis of membrane production remains uncertain, encumbered by a lack of well-studied human pathologic specimens. Schultz and Leeds[16] hypothesis, reviewed previously, suggested the inflammatory membranes arose intraventricularly within the milieu of purulent exudate, elevated cerebrospinal fluid protein, and the presence of "glial tufts" exposed by ependymal injury. Although accepted by the authors of earlier reports describing clinical experience, consensus now favors the hypotheses presented by McLone, Raimondi, and their coworkers[25,49–51] based upon their experimental investigations of

both ventriculitis and hydrocephalus in murine models. Both pathogenic processes result in direct ependymal injury and direct or indirect injury to subependymal structures. Induced vasculitis and progressive cerebral edema involving subependymal white matter result in ischemia and infarction, producing cavitary subependymal lesions that coalesce or expand to isolate the remaining scarred ependyma from adjacent tissues. This process, discussed subsequently, produces a series of randomly oriented, poorly communicating cavities deforming both the true ventricles and surrounding tissues. The resultant "cystic" complex is distended by cerebrospinal fluid, yielding the distorted compartmentalized "ventricular" system characteristically seen on CT images (see Figure 17.1).

The combined ischemia and inflammation or subclinical infection, in addition to the presence of a foreign body (shunt), provides a recurring pathologic matrix that allows chronic "smoldering" progression. Further progression is only arrested by adequate drainage of all cavities and prolonged antibiotic treatment, and the resultant gliosis alters periventricular compliance significantly. Such a combined intra- and extraventricular process seems consistent with established pathologic data and clinical experience. Not only is it, as McLone et al.[25] note, " . . . hard to envision the growth of glial or fibrous tissue from the surface of the brain through a pus-filled cavity to form a septum between portions of the ventricular system . . . " but a solely intraventricular process seems less likely to account for the severe neurological and cognitive impairment typical of these children than would a more extensive intra/extraventricular process.

Posthemorrhagic Hydrocephalus

Unlike postmeningitic hydrocephalus, progressive hydrocephalus following significant intraventricular hemorrhage is seldom recognized as producing a significant subpopulation exhibiting the clinical picture of postinflammatory cystic hydrocephalus. Our clinical experiences with several complicated posthemorrhagic hydrocephalic patients, and our review of pertinent literature convinces us that posthemorrhagic hydrocephalus is indeed a major etiologic variant of the postinflammatory cystic hydrocephalus syndrome, sharing many similar or common characteristics with its readily recognized postmeningitic "twin."

Intraventricular hemorrhages commonly complicate the neonatal course of infants born prematurely as determined by gestational age or birth weight,[32,34,37–42] and it is not uncommon in neonates birthed at term.[30] When considered with its closely associated conditions of neonatal respiratory distress syndrome, metabolic disturbance, and the myriad forms of neonatal sepsis, intraventricular hemorrhage, with or without "hemorrhagic hydrocephalus," is a major cause of neonatal death and severe neurological impairment.[38,40,42] In the absence of other difficulties, intraventricular hemorrhage remains a significant neurological insult with the severity of hemorrhage, as classified by Papile et al.,[52] directly related to the likelihood of permanent sequelae.

The incidence of posthemorrhagic hydrocephalus similarly parallels the extent of the hemorrhage, occurring almost without exception in Papile's grades III and IV—92% in grade III and 100% in grade IV as reported by Dykes et al.,[35] who encountered no cases of hydrocephalus following grade II hemorrhages. The majority of intraventricular hemorrhages occur within the first 24 hours of life[34,37,53] and those occurring prior to 6 hours of life often progress to higher grades. Of those surviving their hemorrhages, 4% to 10% in recent series developed posthemorrhagic hydrocephalus requiring shunt placement.[34,35,53]

The rates of shunt revision, shunt infection, poor neurological outcome, and death in this shunted population significantly exceed those of the general pediatric hydrocephalic population[28,35,37,39,53–58] and are themselves exceeded only by the postinfectious population,[58] which we have discussed previously. Posthemorrhagic hydrocephalus is an inflammatory response to intraventricular hemorrhage, generating initially a communi-

cating hydrocephalus. Following shunt decompression, a small number of these patients develop postinflammatory cystic hydrocephalus that is radiographically and clinically indistinguishable from that seen following proven intracranial infection.

The premature neonate subject to intraventricular hemorrhage is also at high risk for infectious complications. Common maneuvers utilized to treat the more severe hemorrhages may substantially increase the already high risk of central nervous system infection. Holt[55] concisely describes the sequence of commonly accepted regimens prescribed in hopes of preventing the development of posthemorrhagic hydrocephalus: (a) medical therapy, (b) serial lumbar punctures, and (c) invasive diversionary treatments.

Acetazolamide, a carbonic anhydrase inhibitor, 15 to 100 mg per kilogram per day, or diuretics, most commonly furosemide 1 to 3 mg per kilogram per day, are frequently prescribed to diminish cerebrospinal fluid production. The significant metabolic acidosis that accompanies medical therapy requires close clinical and laboratory monitoring and concurrent administration of buffering agents.

Serial lumbar punctures have long been advocated and are effective in some infants. Repeated punctures are traumatic, painful, and may expose the patient to a surprisingly high incidence of infection.[33] Indeed, Dykes and colleagues[35] have recently concluded that the risks of serial lumbar punctures or other invasive treatments exceed the potential benefits, and they suggest restricting such interventions to those neonates who, after intraventricular hemorrhage, present overt clinical symptoms of increased intracranial pressure despite aggressive medical management. Progressive but asymptomatic increases in head circumference must, in their opinion, exceed a rate of 2 cm per week to warrant invasive treatment. Failure of medical treatment and a trial of lumbar punctures unfortunately necessitates further more-invasive treatments.

Diversionary measures that require penetration of the cerebral ventricles—ventricular punctures, ventriculostomies, and ventricular shunts—yield notorious risks of complication, infection, or death[27,39,55–59] tolerated only because we lack more effective therapeutic alternatives to prevent continued deterioration or death. Contamination or infection in the wake of ventricular instrumentation, or even the minimal recurrent bleeding that accompanies multiple shunt revisions, may transform simple posthemorrhagic hydrocephalus into postinflammatory cystic hydrocephalus.

Post inflammatory cystic hydrocephalus arising after posthemorrhagic hydrocephalus closely mimics that following postmeningitic forms. The clinical symptoms of increased intracranial pressure are sometimes more apparent because overt meningitis and ventriculitis present such profound neurological impairment prior to the development of hydrocephalus. This notwithstanding, the clinical manifestations are similar: enlarging ventricles preceding enlarging head circumference, split sutures, bulging anterior fontanel, apnea, bradycardia, lethargy, emesis, and feeding intolerance.[27,53,55] Repeated and often frequent shunt difficulties are typical, and symptoms of "shunt malfunction" may occur despite the presence of a functioning shunt.

Focal neurological signs indicative of hemispheral or posterior fossa mass effect may arise with or without concurrent medical evidence of intracranial hypertension. As with postinflammatory cystic hydrocephalus following meningitis, the clinical picture often resolves to a sharper focus under CT scrutiny. The CT image (see Figure 17.2) is distinct and diagnostic of postinflammatory cystic hydrocephalus, revealing compartmentalization of the ventricular system to a greater or lesser degree. The inflammatory insult after hemorrhage may or may not prove progressive. Complicating infection, poorly controlled hydrocephalus, or recurrent insult (for example, frequent shunt revision) may kindle a progressive inflammatory response and continued clinical and CT proliferation. Therapeutic options are the same as those for "infectious" postinflammatory cystic hydrocephalus: multiple shunt catheters, or fenestration procedure by open or endoscopic techniques. Because posthemorrhagic hydrocephalus is largely con-

fined to severe intraventricular hemorrhage accompanied by ischemia and infarction of parenchyma beyond the immediate subependymal structures,[42] outcome is frequently poor, marked by cerebral palsy, psychomotor retardation, and cognitive impairment.

Pathogenesis

Volpe and his many coworkers[38,40–42] have extensively investigated the pathology and pathophysiology of intraventricular hemorrhages. Two specific pathologic features discussed by Volpe are pertinent to the pathogenesis and the diagnostic CT picture of postinflammatory cystic hydrocephalus: periventricular hemorrhagic infarction and periventricular leukomalacia. Sometimes difficult to distinguish, the two respectively represent venous and arterial ischemic complications of intraventricular hemorrhage. Periventricular hemorrhagic infarctions appear directly related to severe intraventricular hemorrhages. Once considered extensions of the initial germinal matrix hemorrhage, these venous infarctions are distinct lesions resulting from stasis and obstruction of regional venous outflow following germinal matrix hemorrhage. Such venous infarction produces extensive necrosis in periventricular white matter in a typically asymmetrical distribution, with the larger lesion ipsilateral to the largest matrix hemorrhage. In contrast, periventricular leukomalacia is a more extensive process that often symmetrically affects both hemispheres. Thought to result from arterial ischemia, this leukomalacia is perhaps a product of the same vascular instability that produces the germinal matrix hemorrhage. These arterial infarcts may undergo secondary hemorrhage following reperfusion or following the venous obstruction that produces the asymmetrical periventricular hemorrhagic infarctions noted above. Thus the two lesions, of disparate origin, frequently coexist, and each disrupts subependymal and periventricular parenchyma, isolating the underlying ependyma. Subsequent to clearance of necrotic debris or the secondary insult of complicating hydrocephalus or infection, subependymal cavitation may occur, yielding in some patients a poorly communicating cystic complex that envelops the ventricular system. The resultant abnormalities of the ventricular system and cerebrospinal fluid (CSF) pathways are consistent with clinical and radiographic postinflammatory cystic hydrocephalus.

The Lesser Variants

The lesser variants of postinflammatory cystic hydrocephalus—double compartment hydrocephalus, unilateral lateral ventricular hydrocephalus, and isolated or trapped fourth ventricular hydrocephalus—arise from inflammatory insults similar to but less extensive than those leading to the severe multilocular forms discussed above. The earliest reports of these variants were, in fact, the initial descriptions of the process we now designate postinflammatory cystic hydrocephalus, and prompted investigation of the pathogenesis of the more complex forms of hydrocephalus.

Double Compartment Hydrocephalus

Foltz and Shurtleff[60] described the clinical conversion of communicating to noncommunicating hydrocephalus in 12 of 27 patients who underwent ventriculoatrial shunting to resolve symptomatic tetraventricular hydrocephalus. The initial air studies documented communicating hydrocephalus with an open aqueduct in all cases; subsequent air studies 1 to 7 years later demonstrated acquired aqueductal stenosis or occlusion. Successful shunting diminished the ". . . pulsating, dilating force of the CSF. . ." leading to ". . . aqueduct and ventricular wall collapse [and] obliteration of the [aqueductal] lumen . . . through fibrosis of the interspaces between ependymal cells." Aqueductal occlusion occurred quickly in one patient, yielding a near-fatal tentorial and tonsillar herniation within 48 hours of shunt revision. Despite admitting that multiple opportunities for inflammation existed, the authors concluded that aqueductal occlusion occurred through a process of fibrosis following apposition of the aqueductal ependyma and that this obstructive ". . . process need not be related

to any inflammatory process *per se*." Close review of this report reveals that infection or inflammation was likely a significant factor: 8 of 12 patients were born prematurely or with bloody CSF: 1 had a documented intracranial infection and another suffered subarachnoid hemorrhage; 6 of the 12 were initially shunted prior to 3 months of age and 10 of the 12 were shunted within the first year of life; and lastly, 11 of the 12 underwent multiple ventricular punctures.

In a later publication extending their concepts, Foltz and DeFeo[61] reported an additional 8 patients and described a new clinical entity: "double compartment hydrocephalus." Two patients, like the previous 12, had communicating hydrocephalus that converted to aqueductal stenosis several years following ventricular shunt; the remaining 6 had persistent aqueductal stenosis from the time of initial evaluation and diagnosis. Three of these 8 were related to known meningitis or bloody CSF, whereas no etiology was apparent for the stenosis in the remaining 5 patients. As with the preceding series, this group of pediatric and adult patients had histories of multiple shunt revisions and complications prior to diagnosis.

Clinical presentation was marked by prominent cerebellar and brain stem impairments: ataxia, altered level of consciousness, diplopia or other cranial nerve dysfunction, and emesis. The seven who were shunted hydrocephalics were frequently assessed as shunt malfunctions, despite the atypical clinical presentation. Diagnostic evaluation demonstrated functional lateral ventricular shunts, decompressed lateral ventricles, and disproportionately large fourth ventricles. Further evaluation demonstrated "veil occlusions" of the proximal aqueduct in six patients, and cannulations of the dilated fourth ventricle with pressure measurements documented increased intracranial pressure and undamped pulse pressures in six. The clinical presentation and diagnostic evaluations in these six patients were considered indicative of progressive fourth ventricular hydrocephalus, and all were found, at suboccipital craniectomy, to harbor "veil occlusion" of the aqueduct. Fenestration or excision of the veil resulted in sustained communication with the rostral ventricular system, and symptoms resolved with continued decompression by the previously placed lateral ventricular shunt in these six patients. The seventh patient had an associated porencephaly without clearly documented veil, and was successfully treated by cystoperitoneal shunt. The eighth patient had "arrested" hydrocephalus with no confirmed evidence of progression or increased intracranial pressure; therefore no treatment was prescribed.

Outcome, not discussed in the previous series, was deemed acceptable: four patients had minimal neurological deficits, two patients were retarded and handicapped, one patient was severely disabled and totally dependent following vermian infarction, and one patient, comatose at operation, remained so and died after discharge from acute care. Prompted by their experience, the authors concluded the aqueductal stenosis, either congenital or acquired, was "eroded" over time by the undamped fourth ventricular CSF pressure and pulsations, resulting in a thinned "veil" obstruction at the junction of the aqueduct and the shunted low-pressure third and lateral ventricles. This condition was, in their opinion, best treated by excision or fenestration of the veil.

Milhorat[15] considered inflammation to be a clear etiologic factor of importance in "almost every case" reported in this series, and preferred the simpler solution of fourth ventricle shunt rather than craniectomy and aqueduct instrumentation, a policy with which O'Brien[62] concurred. Raimondi[31,51] considers virtually all cases of aqueductal stenosis or obstruction to be the result of inflammatory processes. We, too, believe that inflammation is the common factor generating these diverse forms of acquired hydrocephalus. Despite Foltz and DeFeo's contention that their report demonstrates a new clinical entity, we consider their series of patients examples of the common lesser variant of postinflammatory cystic hydrocephalus: the isolated or trapped fourth ventricle.

Fourth Ventricular Hydrocephalus

Multiple reports document the clinical and radiographic presentation of the isolated fourth ventricle.[18,19,22,24,29,63,64] Hawkins and his colleagues[18] in Toronto reported three children who, in the presence of functional lateral ventricular shunts, developed progressive cerebellar signs unaccompanied by evidence of increased intracranial pressure. After benign skull radiographs and shuntography, CT revealing " . . . small slit-like lateral ventricles and an enlarged fourth ventricle led to the diagnosis of an isolated fourth ventricle." They considered this clinical picture the result of an acquired "inflammatory aqueduct stenosis" occurring after successful lateral ventricular shunting, and they thought the presence of a foreign body—the shunt—was significant. The authors cited the reports of Raimondi et al.[65] and Carmel et al.[66] in support of their conclusions that the isolated fourth ventricle was a complication of ventricular shunting. DeFeo et al.[67] similarly reported symptomatic enlargement of the fourth ventricle after lateral ventricular shunting in a case of cysticercosis meningitis, the initial report of a "double compartment hydrocephalus." Subsequent reports have confirmed the trapped fourth ventricle follows successful ventricular shunting of hydrocephalus due to or complicated by an inflammatory process.[24,29,32,63]

Zimmerman et al.[19] reviewed 8,000 intracranial CT examinations, identifying six instances of "trapped fourth ventricle." Four of the six were children who suffered prior CSF infections. Postinflammatory hydrocephalus was initially of the communicating variety, and block of the fourth ventricle outlets occurred after infection or subarachnoid hemorrhage. Aqueductal stenosis, in these authors' opinion, related to internal displacements: ". . . transtentorial downward herniation of the dilated posterior third ventricle, combined with upward displacement of the dilated aqueduct by the enlarging fourth ventricle . . ." occluded the aqueduct. Alternatively, superior and forward displacement of the superior vermis by the progressively enlarging fourth ventricle, as advocated by Raimondi,[68] could compress the aqueduct, thus isolating the fourth ventricle. Minimal clinical details were provided prior to a discussion of the radiologic differential diagnosis of midline cystic posterior fossa lesions which might mimic an isolated fourth ventricle. Four of these six patients (two adults, two children) clinically and radiographically improved after supratentorial shunting, suggesting the aqueduct was patent; in the remaining two, the aqueduct was occluded.

An enlarged fourth ventricle present on CT is not necessarily isolated, and, unless aqueductal obstruction is confirmed by air or contrast ventriculography, it should initially be treated by simple supratentorial shunt. In this situation, further observation and serial radiologic confirmation of resolution of the fourth ventricle enlargement should be pursued to detect possible central herniation of a truly isolated fourth ventricle through the tentorial incisura. The truly isolated fourth ventricle requires direct shunting. Such direct shunting may be complicated by subsequent multiple or variable cranial nerve palsies.[63,69,70]

Scotti and colleagues[22] analyzed a retrospective series of 16 shunted patients with normal-sized lateral and third ventricles and disproportionately enlarged fourth ventricles encountered over a 3-year period. All 16 patients had lateral ventricular shunts placed for control of hydrocephalus, most had prior histories of central nervous system infections, and all had required multiple shunt revisions. Seven (44%) presented signs or symptoms of posterior fossa mass effect without clinical evidence of increased intracranial pressure; 6 had preexisting neurological deficits that perhaps precluded detection of new posterior fossa signs; and the remaining 3 were considered to have incidental fourth ventricular enlargement. Of the 14 patients who underwent direct fourth ventricular shunt, 6 demonstrated rapid significant improvement, 3 showed slight improvement, and 1 who failed to improve after fourth ventricle shunt later responded to posterior fossa decompression.

Occlusion of both the aqueduct and the fourth ventricle outlets isolated the fourth ventricle, which then progressively dilated due to continued cerebrospinal fluid production. Although a distinct "anatomicopathologic entity," the isolated fourth ventricle was, in the authors' opinion, never encountered as a primary condition. It arose only by mechanical or inflammatory changes occurring subsequent to successful shunting of communicating hydrocephalus. Oi and Matsumoto,[71] as discussed later, proposed a similar hypothesis relative to both the isolated fourth ventricle and the isolated lateral ventricle.

Typically, these patients presented a posterior fossa syndrome heralded by recent onset of ataxia, diplopia, and altered level of consciousness, usually in the absence of signs of increased intracranial pressure—a situation not unexpected in the wake of concurrent large, dilated fourth ventricle and a functional lateral ventricular shunt. In some instances, an enlarged isolated fourth ventricle is asymptomatic, or is masked by preexisting neurological deficits. Computed tomography was considered the diagnostic standard, clearly establishing the diagnosis without recourse to other studies as the isolated fourth ventricle was easily distinguished from other cystic posterior fossa lesions. Fourth ventricular shunting, though sometimes technically problematic, afforded effective resolution of the progressive posterior fossa signs. Because this condition is often "potentially curable,"the authors advocated diagnostic CT scanning in all shunted hydrocephalic patients who present new posterior fossa signs or worsening of a preexisting neurological deficit.

Coker and Anderson[32] more recently presented a series of eight posthemorrhagic hydrocephalic patients with CT findings of trapped fourth ventricles and reviewed 14 cases previously reported by others. Only two of their eight patients were treated by direct fourth ventricular shunt, and both improved, as did 13 of the 14 other patients gleaned from the literature. The six untreated patients did not clinically deteriorate, although four of them presented existing neurological deficits capable of masking posterior fossa signs. Citing the prior report of Wolsen et al.,[72] the authors emphasized the "keyhole sign" evident on CT in cases of herniation of the enlarged trapped fourth ventricle through the tentorial notch (see Figure 17.2). Arguing that clinical detection of the isolated fourth ventricle may often prove difficult because most of these infants have preexisting neurological deficits and because clinical evaluations not containing detailed neurological assessments are structured to detect continued shunt function only, Coker and Anderson advised a high index of suspicion and routine follow-up CT examinations, even in asymptomatic patients. Such a course will, in their opinion, detect the trapped fourth ventricle at a relatively acute stage when direct shunting is most likely to improve a patient's status.

In a recent case report, Aoki[29] described a variant of the isolated fourth ventricle which he termed "communicating fourth ventricular hydrocephalus." The clinical picture of this previously shunted hydrocephalic prematurely born infant was that of increased intracranial pressure, suggested by irritability and a tense anterior fontanel in the absence of posterior fossa signs. Computed tomography demonstrated massive fourth ventricular enlargement and dilated basal cisterns accompanied by small lateral and third ventricles. Metrizamide CT ventriculography through the existing shunt proved the proximal and distal shunt limbs patent and the shunt functional, while simultaneously demonstrating aqueductal occlusion. The enlarged fourth ventricle, containing clear CSF under pressure, was shunted to the peritoneum with good results. Subsequent metrizamide cisternography indicated the CSF block was distal to the fourth ventricular outlets. We believe this situation, like the truly isolated fourth ventricle, is a shunt-related complication of successful decompression of communicating posthemorrhagic hydrocephalus. The site of the distal block, presumably at the arachnoid villi, accounts for the clinical presentation of increased intracranial pressure without posterior fossa signs, as if this were an external hydrocephalus asymp-

tomatically enlarging the fourth ventricle by retrograde progression to the site of aqueductal occlusion.

Unilateral Hydrocephalus

Initially described clinically by Cushing[5] in 1908 and then Dott[6] in 1927, Cairns et al. in 1947, and Alexander and Botterell[73] in 1949, and clinicopathologically by Russell[8] in 1949, unilateral hydrocephalus was seldom recognized clinically prior to Salmon's[2] 1970 report of five cases described earlier. Evident as a significant ventricular asymmetry usually associated with mass effect on diagnostic studies, this progressive process involves functional or anatomical obstruction of the foramen of Monro, and has many possible causes: neoplasm or cerebral maldevelopment within or adjacent to the ventricles, focal or intraventricular hemorrhage, infection, vascular malformation, subependymal gliosis, edema or scarring following intraventricular surgery or trauma, the presence of developmentally large choroid plexuses, and overdrainage by lateral ventricular shunt.[2,7,26,71,73–79] Asymmetries that are shunt-induced[10,11] or related to hemispheral atrophy may present no evidence of mass effect or foraminal obstruction. The resultant clinical picture is that of increased intracranial pressure often accompanied by focal neurological deficits: increasing head circumference, full or tense anterior fontanel, progressively split sutures, irritability, impaired consciousness, or emesis, with perhaps hemiparesis, altered muscular tone, or cranial nerve palsies. Catastrophic uncal herniation and respiratory compromise may suddenly occur with dire consequences. CT imaging avoids error in diagnosis of what may clinically appear to be a shunt malfunction. The simultaneous ventricular asymmetry and mass effect with shift of midline structures toward the shunted side present an unmistakable picture of unilateral hydrocephalus. Direct shunting of the dilated ventricle is the simplest effective treatment, regardless of the etiologic process. Fenestration of the septum pellucidum, by either open or endoscopic techniques, is an alternative.

Milhorat and colleagues[74] reported the acute onset of unilateral hydrocephalus following intraventricular resection of a choroid plexus papilloma situated at the foramen of Monro. Forty-eight hours after resection of the small mass via a frontal transcortical approach and closure of the cortical incision by fine silk sutures, sudden uncal herniation occurred with marked impairment of consciousness, complete oculomotor palsy, and contralateral hemiparesis, followed by respiratory arrest. Ventricular puncture, venting cerebrospinal fluid under increased pressure, yielded significant clinical improvement after exploration had revealed no extra-axial or intra-axial mass clot; subsequent pneumoventriculography demonstrated complete obstruction of the foramen of Monro. Repeated study later demonstrated that free communication was reestablished after regional swelling resolved. Six months later, a dense homonymous hemianoposia was the sole persisting deficit. Closure of the frontal corticotomy may have been a contributing factor in the genesis of this symptomatic foraminal obstruction. Similar situations may arise less acutely following intraventricular surgery[14,73,79] or penetrating CNS injury.[7]

Oi and Matsumoto[71] reported four patients with isolated unilateral hydrocephalus associated with slit ventricles. Each had communicating hydrocephalus, and free communication between the lateral ventricles prior to shunting. Overdrainage following shunt placement is usually asymptomatic in children, but in these four patients resulted in obstruction of the foramen of Monro, a slit-like ventricle on the shunted side, and contralateral ventricular enlargement with a degree of midline shift. In one patient, increasing shunt resistance to outflow proved the foraminal obstruction reversible, and the ventricles subsequently evolved to near-equal size. The authors considered slit ventricles a plausible causative factor in the development of isolated unilateral hydrocephalus, though an accompanying figure depicts "reactive inflammation" as the

common pathogenetic factor in the majority of cases.

In a subsequent paper, these same authors discuss the pathophysiology of progressive isolated unilateral hydrocephalus following ventricular shunting.[76] Analysis of the course and response to treatment of 10 children harboring isolating unilateral hydrocephalus allowed the authors to propose a classification schema and a pathophysiological mechanism for this condition. All the children demonstrated clinical symptoms (most often contralateral hemiparesis), progressive unilateral ventriculomegaly on serial CT scans, and then prompt reduction in ventricular size with clinical improvement after shunting of the dilated lateral ventricle. Four of these children, discussed in their previous report, had preexisting low pressure shunts, and rapidly developed unilateral slit ventricle attended by progressive contralateral hydrocephalus. The remaining six children, of whom four demonstrated a patent foramen of Monro, had various other underlying pathologies. The authors classified progressive unilateral hydrocephalus according to the status of the foramen of Monro: category 1, atresia; 2, morphological obstruction; 3, functional obstruction; and 4, patent foramen (no obstruction). Category 1 is congenital in origin, whereas categories 2 and 3 are acquired phenomena.

Intraventricular pressure monitoring demonstrated damped ventricular CSF pulsations within the smaller shunted ventricle. If the shunted lateral ventricle was slit-like, the pulse pressure remained damped, but the absolute intracranial pressure was increased relative to the contralateral side, and then diminished with insertion of a second contralateral ventricular shunt. Compliance testing demonstrated impaired cerebrospinal fluid dynamics. Citing the work of Salmon,[2] Bering,[12] and Kaufman et al.[10] as well as their own investigations, Oi and Matsumoto hypothesized the unilateral shunt damped the ipsilateral ventricular pulse pressure, yielding diminished ventricular volume and altered CSF dynamics. These induced changes impaired communication through the patent foramen of Monro. Such a functional occlusion could be intermittent, or in the presence of other factors could become a permanent morphological obstruction. In the authors' opinion, isolated unilateral hydrocephalus should, in the shunted nontumoral patient, be considered a shunt-related complication.

Maurice-Williams and Choksey[79] report three cases of ventricular trigone obstruction with "entrapment of the temporal horn," considering them representative of a form of focal hydrocephalus " . . . distinct from two other rare but well-recognized forms of partial hydrocephalus: unilateral hydrocephalus caused by obstruction of one foramen of Monro and septation of the ventricular system after infantile meningitis." Although the authors rightly considered their three adult cases distinct from ventricular diverticuli, we disagree with their contention that these cases represent a previously unreported form of hydrocephalus. Arising from varied etiologies like other cases of unilateral hydrocephalus, the three share a common inflammatory response engendered by infection or surgical trauma in which the predominant obstruction occurred in the ventricular trigone. Indeed, they appear very similar to Russell's[8] pediatric case 29 discussed earlier. Thus, in our opinion, they represent an infrequent variation in the spectrum of unilateral hydrocephalus in which the obstructive lesion is at a site other than the foramen of Monro. The effective treatment remains that proven effective in typical unilateral hydrocephalus: simple ventricular shunting of the dilated ventricle.

Another infrequent variant that may be encountered is that of obstruction of the foramen of Monro by developmentally enlarged choroid plexus—"megachoroid"—as reported by Chadduck and Glasier.[77] Having confirmed the report of Netanyahu and Grant[80] that abnormally large choroid plexuses are commonly found in myelodysplastics in an unpublished series of their own patients, Chadduck and Glasier report a neonate who developed unilateral hydrocephalus after ventricular shunting to treat hydrocephalus coincident to lumbar spina bifida aperta. Unilateral ventricular shunting resulted in obstruction of the ipsilateral foramen of Monro by mega-

choroid, attended by contralateral ventricular dilation and deviation of the septum pellucidum. Insertion of a second ventricular shunt promptly decompressed the hydrocephalus. Significantly, abnormal preoperative pulsed Doppler blood-flow measurements returned to normal after the second shunt was placed. The authors chose treatment by simple bilateral ventricular catheters rather than risk hemorrhage from the enlarged plexuses during an attempt to fenestrate the septum pellucidum. The enlarged choroid plexus present in this patient subsequently obstructed a ventricular catheter, requiring revision of the proximal shunt limb. Thereafter, no further operative intervention was required and the child's subsequent development was acceptable over a follow-up period of 12 months.

Conclusions

Despite the varied array of symptoms and settings, postinflammatory cystic hydrocephalus is, in essence, a single clinical entity encompassing the several presentations discussed above: the loculated forms of postmeningitic hydrocephalus and posthemorrhagic hydrocephalus, as well as unilateral hydrocephalus and the isolated fourth ventricle. The inflammatory response common to the postinflammatory cystic hydrocephalus variants clearly accounts for the resulting clinical, radiologic, and pathologic findings.

Inflammation first generates obstruction of the CSF pathways distal to the fourth ventricular outlets, yielding tetraventricular or communicating hydrocephalus. The inflammatory response persists as a bacterial, chemical, or perhaps viral "ventriculitis" or "ependymitis"[31] which is, in our experience and that of others,[43,79] frequently proliferative. The presence of a shunt catheter (foreign body) may be a significant factor favoring proliferation.[18,25] The timing, persistence, and severity of the inflammatory response, a given patient's immune reaction, and the therapy employed to counter the initiating pathologic process all interact to produce postinflammatory cystic hydrocephalus. The isolated fourth ventricle, and those instances of unilateral hydrocephalus resulting from irritative phenomena, occur in the wake of relatively focal inflammatory responses, typically abetted by secondary shunt-induced changes in the already obstructed cerebrospinal fluid pathways.

A more intense inflammatory response, associated with either severe intraventricular hemorrhage or frank bacterial meningitis, extends beyond the ependyma. Indeed, as detailed by Volpe[42] and by McLone and coworkers[25,49–51] in their respective investigations of posthemorrhagic and postmeningitic hydrocephalus, vascular inflammation and ischemia generated progressive destruction of periventricular parenchyma. The recent report of Sande and coworkers[81] confirms that the inflammatory reaction produced by bacterial meningitis elicits ischemia and vasculitis similar to that described by Volpe. This process may also involve other changes induced by shunt decompression of preexisting hydrocephalus.[82] The cavitation thus produced is subependymal and therefore extraventricular, though it may communicate with the ventricular system through gaps in the injured ependyma.

Radiographically, it is difficult, if not impossible, to distinguish the true intraventricular space from the immediately adjacent fluid-filled subependymal cavitary spaces. This compartmentalization process could continue by progressive subependymal ischemia and cavitation, by coaptation and adhesion of ependymal or subependymal structures after decompression by ventricular shunt, or by some as yet undescribed process. Regardless of the extent of the persistent inflammatory response, this secondary obstructive process involves the ventricular system itself, converting the prior communicating hydrocephalus to a noncommunicating hydrocephalus. This loculated "inflammatory" form of noncommunicating hydrocephalus, which we term postinflammatory cystic hydrocephalus, is not a primary process. Compared to the more common forms of hydrocephalus, postinflammatory cystic hydrocephalus remains difficult to

treat and, consequent to its destructive periventricular pathogenesis, is associated with a generally poor outcome.

Multiple other factors related to specific etiologic processes may contribute to the initiation or propagation of the inflammatory response characteristic of postinflammatory cystic hydrocephalus. Serial lumbar punctures, ventriculostomies, or percutaneous reservoir drainage are commonly employed to treat posthemorrhagic hydrocephalus and may introduce complicating infection[33,35,55] into what otherwise might remain a simple clinical situation well controlled by single ventricular shunt. Intraventricular antibiotic therapy, considered by many a standard treatment for bacterial meningitis, may remedy a life-threatening infection, but concurrently intensifies the inflammatory response elicited by that infection.[46,83,84] Such intensification of the inflammatory process is more likely to initiate Volpe's ischemic cascade,[42,81] and thus precipitate postinflammatory cystic hydrocephalus.

The multiple shunt revisions often required in this population increase the risk of recurrent inflammation by evoking infection or minimal intraventricular hemorrhage attendant to manipulation or removal of the obstructed ventricular catheter. Electrocauterization utilizing a stylet introduced into the catheter lumen prior to removal of the embedded catheter may reduce the risk of hemorrhage, but nonetheless produces necrotic debris that may still evoke local inflammation. Even the simple presence of a shunt catheter as a foreign body may enhance or elicit inflammatory response.[85–87] Slit ventricles may, as Oi and Matsumoto[71] suggest, be a contributing factor. This remains unproven as the subsequent experimental evidence offered by these authors[88] is limited and unconvincing. The increased susceptibility to infection shared by all neonates must also be considered a general contributing influence, because any initial inflammatory insult affecting the central nervous system in the presence of neonatal hydrocephalus may evolve into postinflammatory cystic hydrocephalus.

In the course of treating severe forms of postinflammatory cystic hydrocephalus, we have found the peritoneal cavity frequently intolerant of cerebrospinal fluid, despite the documented absence of infection. We cannot identify with certainty any specific reasons for the peritoneal reaction, though it may represent a form of hypersensitivity or immune-related response.[85,87,89] This intolerance has resulted in a ventriculoatrial shunt rate much higher than that of the general population of shunted hydrocephalics treated in our institution. In some patients, this absorptive impairment has proved transient, allowing later conversion of ventriculoatrial shunt to a ventriculoperitoneal shunt. Those patients permanently requiring ventriculoatrial shunt for hydrocephalus control remain at significant risk for specific shunt-related complications in addition to the difficulties and impairments imposed by postinflammatory cystic hydrocephalus. Increased rate of shunt infection, reversible or irreversible cor pulmonale, or shunt nephritis may all complicate or shorten the survival of children with ventriculoatrial shunts.[56,90–94]

Therapy

Limited by currently available technology, the treatments advocated for postinflammatory cystic hydrocephalus are fortunately not as varied as the syndrome itself. Once initiated, postinflammatory cystic hydrocephalus is an irreversible process. All available therapeutic alternatives are essentially salvage operations designed to eliminate or reduce the consequences of the pathologic process. The possibility of "silent" or recurrent infection, or suboptimal shunt decompression in the absence of obvious catheter obstruction, should remain a prominent consideration. Periodic long-term follow-up of these complicated patients should be the rule. A close, open, understanding relationship with each patient and his family is indispensable as the frustration and disappointment encountered in treating postinflammatory cystic hydrocephalus affects everyone involved in the patient's care.

Despite the many revisions that may be required, shunt decompression of all isolated

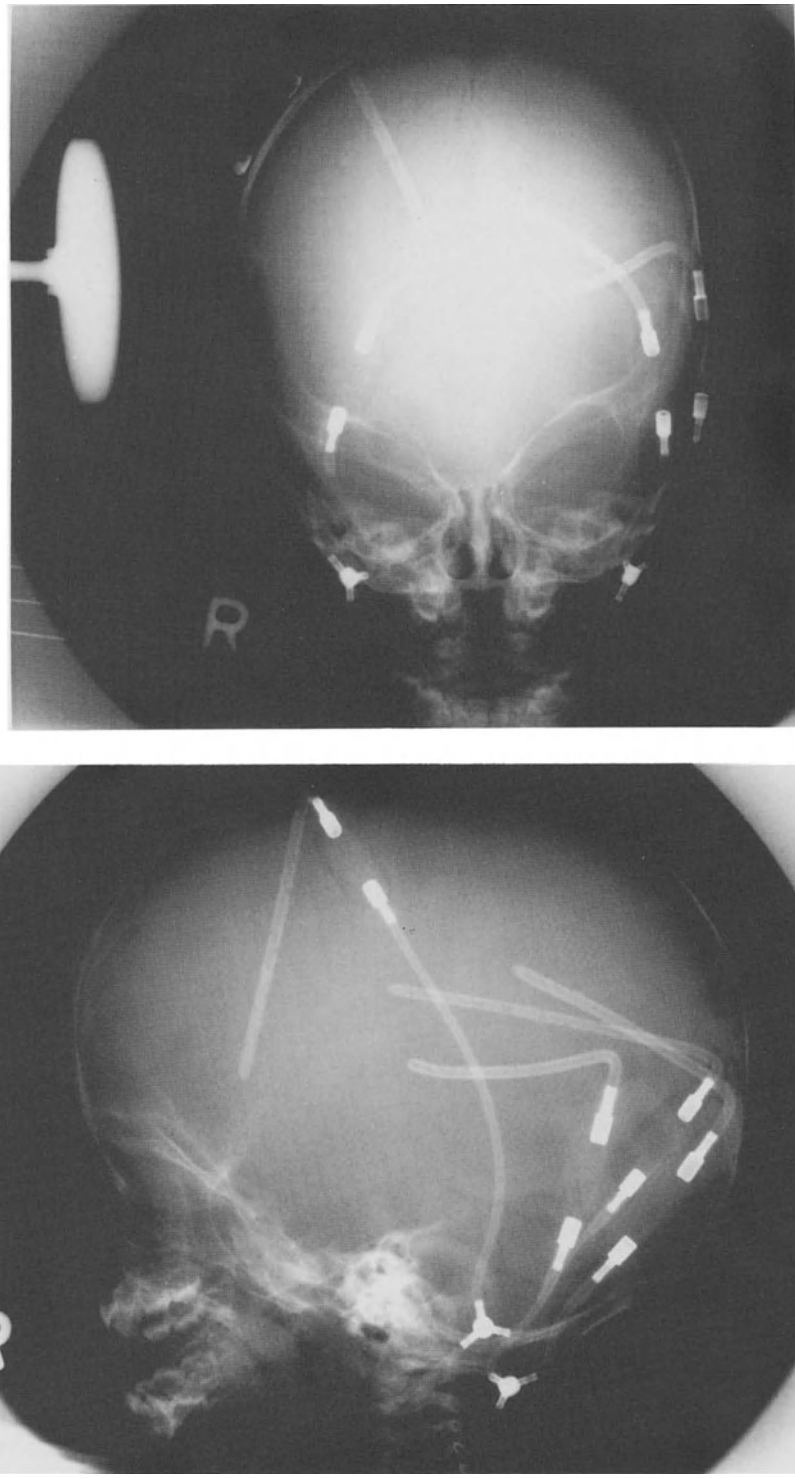

Figure 17.3. Postinflammatory cystic hydrocephalus. Anteroposterior (A) and lateral (B) skull radiographs demonstrate the complex shunt systems often needed to adequately control hydrocephalus in patients with this syndrome.

components of the ventricular complex remains the commonly accepted approach.* We endorse this strategy, though the required "plumbing" may evolve into an intricate system of catheters draining both the supratentorial and infratentorial compartments from multiple points of entry (Figure 17.3). Even an intricate shunt system should be practical: shunt components should be standardized, each major segment of the system should contain its own valve and/or reservoir to diminish regional pressure gradients and allow diagnostic assessment by percutaneous techniques, and drainage catheters should merge to one or two "final common pathways" to peritoneal or atrial sumps. An isolated fourth ventricle (Figure 17.4) should be shunted early, and a fourth ventricular shunt should be integrated into the system draining the supratentorial compartment to reduce the risk of mass shifts across the incisura. The surgeon should be familiar with all the components he implants, and operative principles and techniques should be consistent and standardized.

Therapeutic alternatives to shunting postinflammatory hydrocephalus exist, but do not fully eliminate the need for a functioning shunt. Systemic or intraventricular corticosteroids advocated in hopes of ameliorating inflammation and preventing the onset of postinflammatory cystic hydrocephalus initially showed no benefits.[16,20] Recent studies, including controlled double-blind protocols, now indicate dexamethasone, when administered adjunctively, is clinically beneficial in neonatal meningitis.[81,84,95] Intraventricular streptokinase-streptodornase failed to retard or prevent the development of septations.[16] Open craniotomy with fenestration was advocated by Rhoton[43,48] to convert the compartmentalized ventricular system to a single communicating cavity that may then be drained by a single shunt. Though subsequently encouraged by other[23,61,69] in situations not involving unilateral hydrocephalus secondary to noninflammatory obstruction of the foramen of Monro, only a few isolated cases have been reported.[23,43,48,61,69]

*Refs. 15, 16, 18–24, 26–30, 32, 62–64, 75, 77–79.

More recently, Haines and Nida[96] advocated transcallosal ventricular fenestration followed by placement of a single shunt, based upon their experience with four multiloculated hydrocephalic patients who could not be successfully managed with multiple shunts. Endoscopic fenestration, as reported by Powers,[97] may prove an effective relatively simple therapy once flexible fiberoptic ventriculoscopes incorporating laser technology become readily available. The "saline torch" instrument developed by Manwaring et al.[98] may likewise prove effective in the fenestration treatment of postinflammatory cystic hydrocephalus. If proven successful, fiberoptic endoscopic techniques will convey the obvious advantage of the simple establishment of direct communication through a small skull aperture, thereby allowing simplification of the shunt systems needed to decompress the surgically re-created communicating hydrocephalus.

If the presence of slit ventricles proves to be a significant interim stage in the development of postinflammatory cystic hydrocephalus, various technological improvements in shunting components may allow the surgeon to interrupt or prevent progression to the end-stage clinical presentation now characteristic of the process. Pursuit of a means to prevent overdrainage has resulted in the development of several new devices that alter shunt resistance to cerebrospinal fluid outflow. The developer of each device claims it achieves adequate decompression while lessening the risks of overdrainage complications. The devices promoted include the older antisiphon device (ASD) and reversible occlusion valves developed by Portnoy et al.,[99] a modification of the Portnoy device termed the "siphon-control device" by Horton and Pollay,[100] the Flo-control valve promoted by Foltz and Blanks,[101] and a programmable pressure valve designed by Sophysa of France as reported by Matsumae et al.[102] and Lumenta et al.[103] Clinical experience with newer devices is limited, and significant problems have been encountered when on-off valves or the older ASDs have been utilized in a clinical situation.[104] The Orbis-Sigma valve, initially reported by Sainte-Rose et al.,[105]

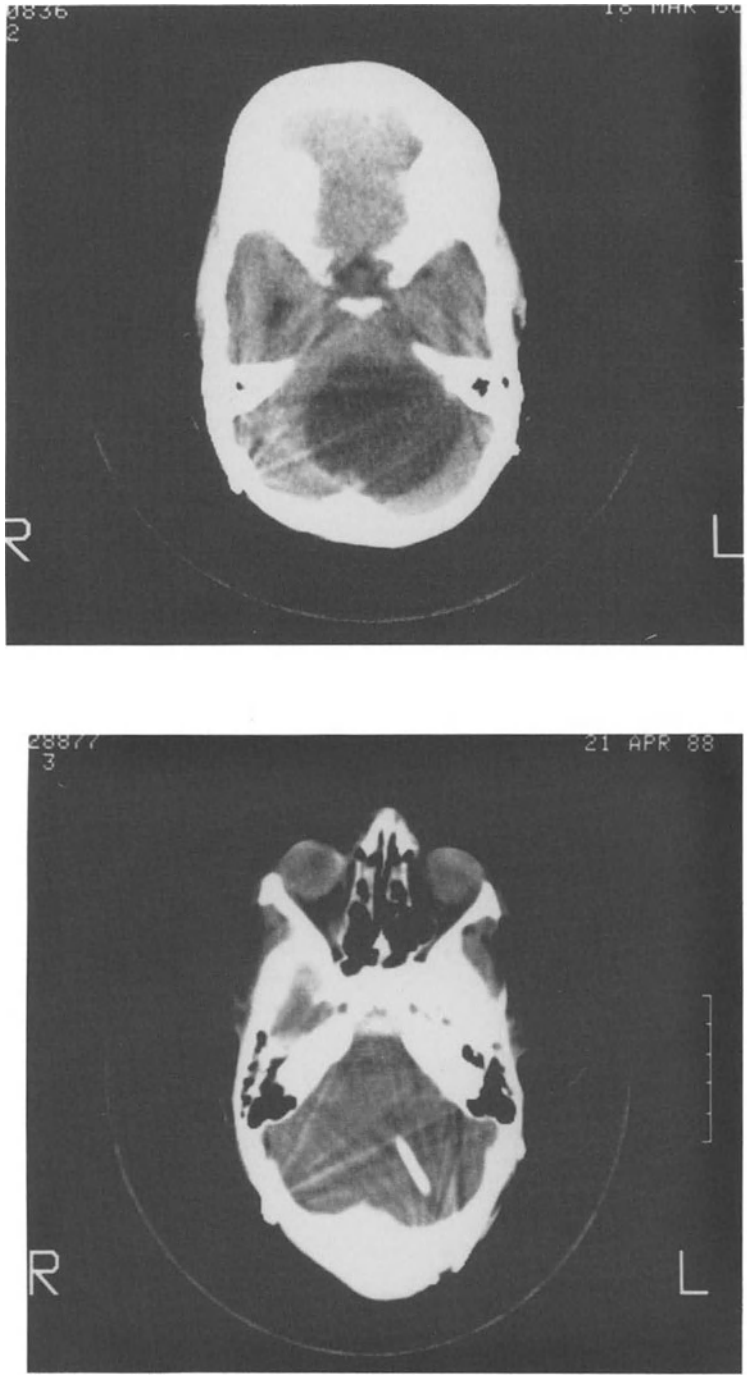

Figure 17.4. Isolated fourth ventricle: preshunt (A) and postshunt (B). Shunt placement in this case allowed rapid significant improvement. Unable to ambulate prior to shunting, this patient ambulated freely without gait disturbance after shunting.

seems conceptually the most innovative and promising with regard to prevention of overdrainage symptoms and complications. Subsequent analysis of the use of this device in 261 pediatric patients revealed moderate success in the prevention of common overdrainage problems.[106]

Summation

We have presented the concept of a common postinflammatory cystic hydrocephalus arising via similar pathogenesis from either infectious or hemorrhagic origins. The process involves similar cerebral regions and generates similar clinical, radiologic, and pathologic presentations. Most readily distinguished by a patient's given medical history, postmeningitic and posthemorrhagic inflammatory cystic hydrocephalus will be increasingly encountered as more premature neonates are saved by aggressive neonatal care. Unfortunately, postinflammatory cystic hydrocephalus constitutes the most severe debilitating form of acquired hydrocephalus. Successful treatment proves difficult and complicated, regardless of the interventions employed. Prolonged periodic follow-up and an open, understanding relationship with the patient and his family are vital to the proper management of the medical, psychological, and social complications that accompany this disease process.

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CHAPTER 18

Neurocysticercosis

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Historical Notes

Some authors state that Hippocrates alluded to cysticercosis, although in the book by Adams[1] entitled *The Genuine Works of Hippocrates*, there is no reference to this effect.[1] However, Aristophanes, in one of his comedies written about 390 B.C., referred to the bladders of cysticerci and how to search for them in pigs' tongues, accurately comparing their appearance to that of hailstones.[2] In his *History of Animals*, Aristotle (384–322 B.C.) described the diseases of pigs, which he classified in three types. The third of these is described as follows: . . . pigs whose meat is tender have bladders which are like hailstones in the region of the thigh, neck, and loin; these are the regions in which they generally appear. If they are few in number, the meat is leaner; if there are many, the meat becomes soft and filled with serous fluid. Pigs affected with this disease are easily recognized; in effect, the bladders can be seen on the inferior surface of the tongue where they are particularly abundant. Furthermore, the sick animals cannot keep their hind legs still. However, pigs do not suffer from this disease while they are nursing. The bladders can be made to disappear with "spelt wheat" (a species of wheat from cold, poor lands), which at the same time serves as fodder.[3]

In an outstanding paper entitled "Die tierischen Parasiten des Zentralnervensystem" written in 1912, Henneberg[4] states that a bibliography on this topic from ancient times to 1862 can be found in the works of Stich (see ref. 4), Davaine (see ref. 4), and Griesinger.[5]

In this historical account (see ref. 4), Paranoli is cited as the first to describe (in 1550) the presence of round, white bladders full of a clear fluid in the corpus callosum of a man. In 1558, Gessner and Rumbler published the first case in which bladders were found in the dura mater of an epileptic. Nevertheless, neither Paranoli nor the latter authors defined the nature of these formations, which were accurately identified as parasites by Redi, Malpighi, and others in 1686. The name "cysticerous" was given to them by Laennec, derived from the Greek words *kystic*, meaning bladder, and *kercos*, signifying tail. In 1809, believing that cysticerci constituted a species of animal, Rudolphi gave them the surname of "cellulosae" due to their great affinity for connective tissue. It appears that Beneden in 1853 was the first to suspect their relationship to taenia, but it was Kückenmeister in 1855 and Leuckart in 1856 (and also Heuber, according to some authors) who conclusively identified these bladders as cysticerci, and demonstrated their biological cycle.

In 1860, Virchow[6] published his famous article "Traubenhydatiden der weichen Hirnhaut," in which he described what today is called racemose cysticercosis at the base of the brain, although he did not define its nature. Virchow's description was later interpreted by Zenker[7] the reknowned German parasitologist: In 1862, the great Berlin psychiatrist Griesinger[5] published his impor-

tant paper entitled "Cysticerken und ihre Diagnose."

Other physicians who made significant contributions to the study of cysticercosis were Lombroso[8] who in 1867 reported a case of a cysticercotic epileptic, Heller,[9] who described cysticercal meningitis in 1874 and Askanazy,[10] who in 1890 reported a case of chronic meningitis that extended to the cervical spinal cord in generally diffuse form although there were some circumscribed lesions, with internal hydrocephalus and ependymitis, thickening of the blood vessels at the base of the brain, and changes typical of endarteritis obliterans. Volovatz's[11] thesis concerning "Ladrerie du cyticercose chez l'homme" appeared in Paris in 1902. In it he described 414 cases of cysticercosis limited to a single organ, 149 of which were located in the nervous system.

Epidemiology

Neurocysticercosis (NCC) has been a major neurological problem for many years in Mexico and Central and South America.[12] In 1979, 1.9% of all general autopsy patients in Mexico were found to be infested with this parasite. Other estimates run as high as 3.3%[13]. In some patients, cysts are resorbed completely, so the number of people in Mexico who are infected at some time during life is presumably much higher than the 1.9% found at autopsy. There have been recent shifts in the geographical areas where the disease is found and increasing numbers of patients are reported from more affluent parts of the world. The personal and socioeconomic costs of this disease are enormous, with mental retardation, epilepsy, and other chronic neurological impairments frequently occurring in affected individuals.

Cysticercosis was until recently a rare disease in the United States because infection in the pig, an intermediate host, is not a problem in this country. As late as 1978, an article describing only three patients with cysticercosis was published in a major neurological periodical.[14] With the immigration of large numbers of people from endemic areas in Mexico and Central and South America to the southwestern United States, the disease has become common in many southern California hospitals.

Cysticercosis is now one of the most common causes of seizures and of hydrocephalus among the Hispanic population in places such as Los Angeles, California.[15,16] However, the incidence of NCC in children is less than in adults. The largest series reported dealt mostly with adult patients, and in the mixed reports, patients younger than 15 years of age constitute only 2% to 10% of the patients. Up to the present time, the largest series published on cerebral cysticercosis in children are the ones by López-Hernández and Garaizar,[17] with 89 cases, and by Thompson and associates,[18] with 61 patients.

Parasitology

In 1947, Stoll[19] estimated that about 2.5 million people in the world were infected with *Taenia solium*. The adult tapeworm lives in the human gut and binds to intestinal mucosa. The adult worm can live only in humans and is inappropriately named the *Taenia solium*, which means pig tapeworm. The gut infestation is generally asymptomatic although patients may develop a mild anemia or gastrointestinal symptoms such as diarrhea due to the adult worm. The adult worm lays eggs that pass out with human feces into the soil. Humans and pigs commonly become infected by the next stage, the larval, or cysticercal stage, by ingesting these eggs in water supplies or vegetables contaminated by human feces. The eggs have a thin membrane that is digested in the gut, releasing an oncosphere that penetrates intestinal venules and spreads to various organ system in pigs and man.

In pigs the major site where the ova or oncospheres encyst is muscle, whereas in humans the major site of infestation is in the brain. When the ova reach their organ of choice they reorganize into the larval form, which consists of a scolex and surrounding trilaminar membrane. This scolex, or head, may live for many years encysted in brain or mus-

cle. When humans eat pig meat with cysts in muscle, the surrounding membrane is digested and the scolex grows into the adult tapeworm in the human gut, completing the cycle.

Once infestation has occurred, the oncosphere (larval form) may invade a variety of tissues, but the central nervous system is the most frequent and important and, in some cases, may be the only tissue invaded. Maturation of the oncosphere into the cysticercus requires 10 to 13 weeks, but symptoms may not appear for several months or years or may never be present at all. Death of the cysticerci occurs approximately 18 months or longer after the initial infestation, and the resulting breakdown products are accountable for the inflammatory response that produces the neurological syndromes.

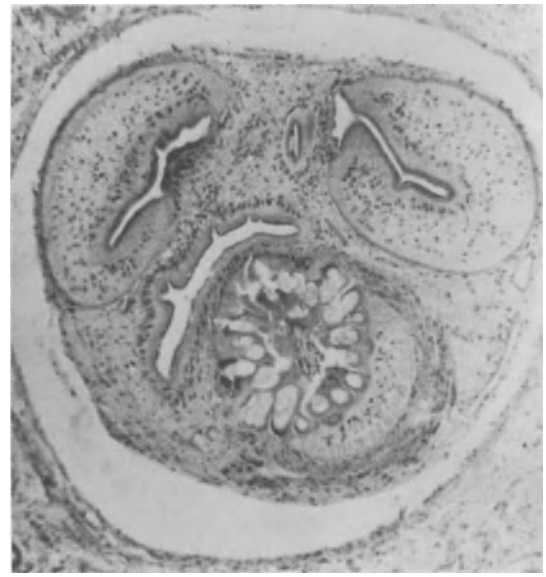

Figure 18.1. Microphotography of a section of a scolex with rostellar hooks and two suckers. (Hematoxylin-eosin, ×200.)

Pathology

The presence of parasites in human tissues triggers an immunologic inflammatory response that varies not only from individual to individual but also from tissue to tissue. A thorough description of the pathology and morbid anatomy of cysticercosis of the central nervous system is important and requires a wide variety of clinical material, studied with all the possible diagnostic methods.

The identification of cysticerci is an important step in the diagnosis, especially when dealing with brain biopsies. A microscopic examination will establish the correct diagnosis in such a case. Light-microscopy examination with a scanning lens allows proper identification of a rudimentary strobila and a scolex formed by a rostellum with four suckers and some 20 pairs of hooks arranged as a crown (Figure 18.1). In order to identify the scolex in a histologic section, serial sections are needed.

Escobar and Nieto[20] had described several stages of the cisticerci. The earliest stage, the *vesicular stage* corresponds to that in which the parasite appears formed by a very thin, friable, translucent whitish membrane. Inside, bathed in transparent fluid, there is an invaginated larva of about 4 to 5 mm in length adopting a curled, spheric shape. The second stage is when the parasite begins to show degenerative changes due either to aging or by immunologic factors and the incapability of the larva to become an adult taenia, the transparent fluid inside the cyst is replaced by a jelly-like whitish material. This is the *colloidal stage* of the vesicular form of cysticercosis. In the next stage, the cyst begins to reduce in size, the walls become thicker, and its contents due to mineralization with calcium salts, are transformed into coarse granules. This is the so-called *granular nodular stage*. The final stage is that in which the granular material seen in the previous one has attained complete mineralization. It has a small size, about one-half or one-fourth of the original live cysticercus, and is of hard consistency, which includes the collagenous capsule that surrounds it. The parasite is then in the *nodular calcified stage*.

Whether all cysticerci follow the sequence described above or pass very rapidly to the late stage cannot be stated with certainty since no one has followed this sequence in experimental material. Also, the length of time spent by a single parasite in each stage is not known. Of prime interest in the understanding of the morbid anatomy and histopathology of NCC is the

inflammatory reaction associated with the presence of the parasites. Generally, it can be said that the inflammatory reaction is present throughout the four stages, but its intensity tends to decline steadily as the parasites reach the last stage when only scattered foci remain. The inflammatory reaction around the parasite itself is always composed of a conglomerate of round mononuclear lymphocytic and plasma cells clumping inside the collagenous strands that constitute the capsule surrounding the membranous structure of the cyst. Some of the inflammatory cells are also found around the perivascular spaces in the adjacent nervous tissue.

It is important in cysticercosis to describe the morphologic characteristics of the arteries, arterioles, and venules because their changes are related to the intensity of the granulomatous immunologic reaction and because significant secondary ischemic lesions may occur subsequent to vascular involvement.

Vasculitis or angiitis is a common finding. The vessels show thickening of the adventitia with fibrosis of the media and endothelial hyperplasia, which is produced by inflammatory cells that may infiltrate all three layers of the vessel. The intensity of this reaction varies but there appears to be no relationship between the intensity of the reaction and the intensity of the changes in the vessels. In the large arteries, atheroma-like deposits appear at the endothelial level and tend to reduce the lumen. In the arterioles and small arteries, the fibrosis of the media replaces this layer and proliferates toward the endothelial layer leading to complete occlusion of the lumen. The adventitia thickens sometimes to a degree that one hardly recognizes the subdivisions of the different layers of the vessels.

In severe cases more intense changes develop, and it is common to find areas of hyaline fibrinoid necrosis, and sometimes all the vessels are completely necrotic in a manner exactly like that seen in immunoallergic reactions. Other times some of the vessels depict clear-cut endothelial hyperplasia that also leads to a reduction or complete occlusion of the lumen. All these changes appear only in the vessels located in the vicinity of the parasites.

Venules are frequently spared, but in severe cases, as in basal meningitis, they are also involved and their walls thicken, but the lumen is rarely occluded.

The most common location of cysticerci occurs at the leptomeningeal level; in most cases the parasites are lodged between two convolutions, and the vesicle tends to displace the adjacent cerebral cortices. The most common pathologic change in the immediate vicinity of the capsule surrounding the parasite is a secondary astrocytic gliosis of variable intensity. The tissue has the appearance of a beehive due to the presence of diffuse edema that constitutes a layer of variable extension. Sometimes one can see a few hypertrophic microglial cells acquiring the rod-cell shape. The neurons in the area are usually affected in variable degrees and tend to undergo degenerative changes.

When the parasites are located in the ventricles, it is common for them to become attached to the ependymal cells lining the ventricular cavities. A common finding in these cases is the presence of astrocytic glial proliferation that tends to engulf the parasite, and sometimes the astrocytic proliferation is so strong that if one is not aware of the presence of the cysticercus, it could easily be mistaken for an astrocytoma. This heavy gliosis is mainly seen in cases of fourth ventricular cysticercosis with blockage of the cerebrospinal fluid (CSF) circulation.

The tissue reaction around the parasites located inside the parenchyma depicts similar features to those described for the meningeal forms. In fact, the inflammatory reaction around the parasite tends to be more circumscribed and less intense. The gliosis is also less marked, and only a small rim of demyelination appears in the vicinity.

Clinical Manifestations

The symptoms of cysticercosis of the CNS are manifold and can vary greatly during the evolution of the disease. In many cases the diagnosis is incidental since the patient's clinical manifestations often do not correspond to the generally accepted symptoms of cysticercosis.

These signs and symptoms are due to irritation, compression, and even to the destruction of the brain tissue, as well as to the sequelae of intracranial hypertension, the reaction to the larvae by host tissue, and the possibility of recurrent bouts of larval infestation or larval breakdown; the diagnosis must be considered in any patient presenting from an endemic area with neurological symptoms.

There have been several attempts to make a classification of NCC[21,22] but inasmuch as all of these papers are based on mixed series that include both children and adults, the author prefers, on the grounds of clinicopathologic correlations, to describe the spectrum of this disease in children as follows.

Parenchymal Infestation

This is the most common form in children and may appear in either an acute or a chronic fashion. The lesion can be single, multiple, or diffuse. *Acute focal parenchymatous disease* presents with localized, patchy edema or a cystic formation. The symptoms depend on the area involved and may manifest as either seizures or signs and symptoms of deficit (e.g., paralysis). The *acute diffuse parenchymatous disease*, the so-called *cysticercotic encephalitic syndrome*[17] presents with generalized cerebral edema, in many cases severe enough to cause an acute rise in intracranial pressure, with deterioration of consciousness, cerebral shifts, and multiple encephalitic symptoms (e.g., seizures). The reason for the higher prevalence of cerebral edema in children is unknown. *Chronic focal parenchymatous disease* presents with intracranial calcifed cysts, which may or may not produce symptoms.

Meningeal Involvement

This form most commonly affects the base of the brain, with the development of the multicystic or racemose form with a basal adhesive arachnoiditis, or both. Usually the patient presents with a syndrome of increased intracranial pressure, obstructive or communicating hydrocephalus, and, eventually, cranial nerve involvement, particularly nerves II, V, VI, and VII. Vasculitic lesions are common in this variety of NCC.

Ventricular Involvement

This form occurs when the parasite reaches the ventricular system via the choroid plexus or ruptures through the ependymal lining and enlarges to become multicystic or racemose. The cysts may be adherent or free-floating. They commonly lodge in the fourth ventricle[23] producing intermittent acute osbtructive hydrocephalus, which may result in loss of consciousness and posture brought on by sudden changes in head position.

Mixed Forms

These are usually a combination of parenchymal and meningeal forms, with a rather protean clinical presentation.

Spinal Involvement

No case has been reported in children as yet, but it may occur and would present as an intramedullary mass lesion or in a form of arachnoiditis and vasculitis of the spinal cord.

Radiologic Diagnosis

The neuroradiologic studies in NCC are of great importance in clinical and surgical neurology. The procedures employed range from simple cranial x-rays to pneumoencephalography, different forms of ventriculography, cerebral angiography, myelography, computed tomography (CT), and finally magnetic resonance image (MRI). Computed tomography is now the most sensitive and reliable method for exploring patients with clinically suspected NCC.

Computed tomography is safe, precise, and noninvasive, and has a high degree of diagnostic certainty—approximately 97%. This procedure has the advantage of clearly establishing the topographic localization of the parasite in a single study. Also, it has permitted the description of a new form of the disease in children,

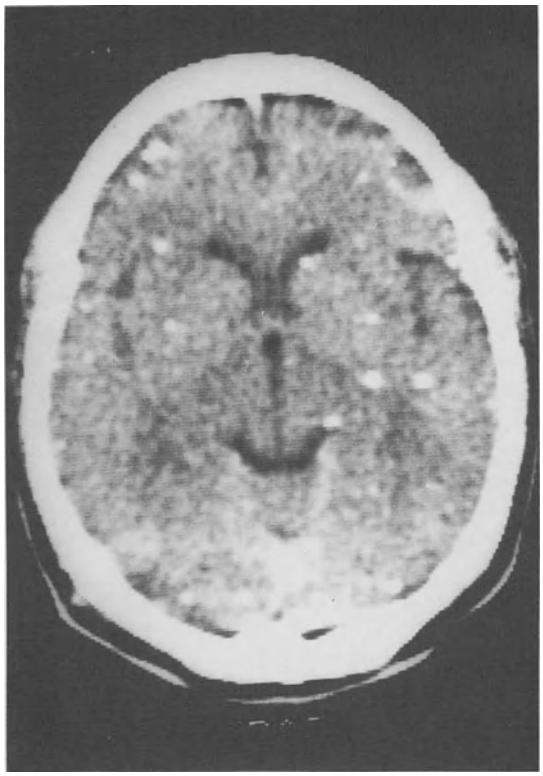

Figure 18.2. CT scan with multiple intraparenchymal calcifications without enhancement in a 7-year-old girl with epilepsy.

called acute encephalitic cysticercosis, as will be discussed later. With CT, one can see the different clinicopathologic varieties of the illness.[24]

Parenchymatous Localization

This is the most common kind of infestation in children. There are three well-identified forms: calcified granulomas; single or multiple intracerebral cysts, mostly in the supratentorial compartment; and the diffuse "encephalitic" form.

Parenchymatous calcifications result from the deposition of calcium salts over the dead larvae. The parasites may be single, but more commonly are multiple and vary in size and location. Due to the higher sensitivity of CT, they can be detected in the scans before they are evident in simple cranial x-rays (Figure 18.2).

Cysts may be single or multiple, occurring predominantly in the supratentorial region, and are of variable size. Single large forms of the racemose variety produce compression and distortion of the cerebral ventricles and midline structures, as do cystic tumors and other space-occupying lesions such as tuberculomas, abscesses, and meningeal cysts. Some have calcifications on their borders, facilitating their identification as parenchymatous lesions due to cysticercosis (Figure 18.3). Cases of multiple lesions generally are associated with pathologic displacement, and the image resembles Gruyère cheese.

Acute encephalitic cysticercosis is an entity found in children.[17] Computed tomography is especially valuable in diagnosing this form of NCC. In our experience, cysticercosis in the acute encephalitic phase commonly manifests in one or two ways: either as multiple nodules of a variable size and distribution, occurring predominantly in the supratentorial region and rarely in the infratentorial area; or as annular lesions, usually localized in the subcortex. Both forms are accompanied by diffuse, generalized edema and small, occasionally collapsed ventricles. In uncontrasted CT scans, the edema appears as irregularly shaped hypodense areas, commonly located in the paraven-

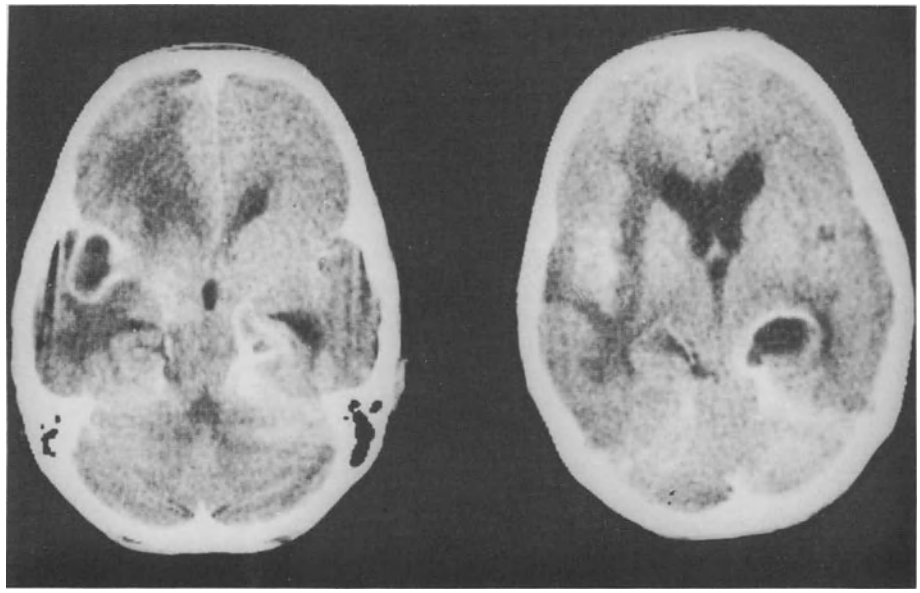

Figure 18.3. CT scan of a 4-year-old boy showing two cystic lesions with enhancement in their periphery and edema in the white matter.

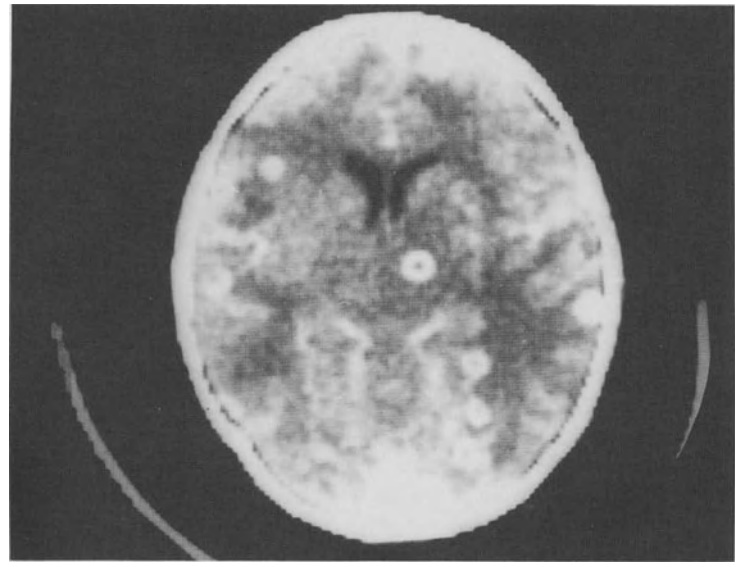

Figure 18.4. Acute encephalitic cysticercosis in a 6-year-old boy. The CT scan with contrast shows multiple ringlike enhanced lesions, edema in the white matter and almost normal ventricles.

tricular white matter and semioval centers, and rarely in the subcortex. Following the intravenous injection of contrast medium, there is enhancement of the nodular and annular images previously described (Figure 18.4).

Computed tomography has been used to follow up these patients during or after medical or surgical treatment. Patients appear to have a maximum clinical improvement 3 to 4 weeks following medical treatment of the increased intracranial pressure syndrome. At this time, the ventricular system returns to its normal size in the majority of cases, and only in some of them will the ventricles become slightly dilated. If the patient survives the acute stage, there is complete disappearance of the cerebral edema and enhancing lesions. The common radiologic sequelae of the encephalitic type of cysticercosis is the presence of calcifications representing the end stage of a granulomatous

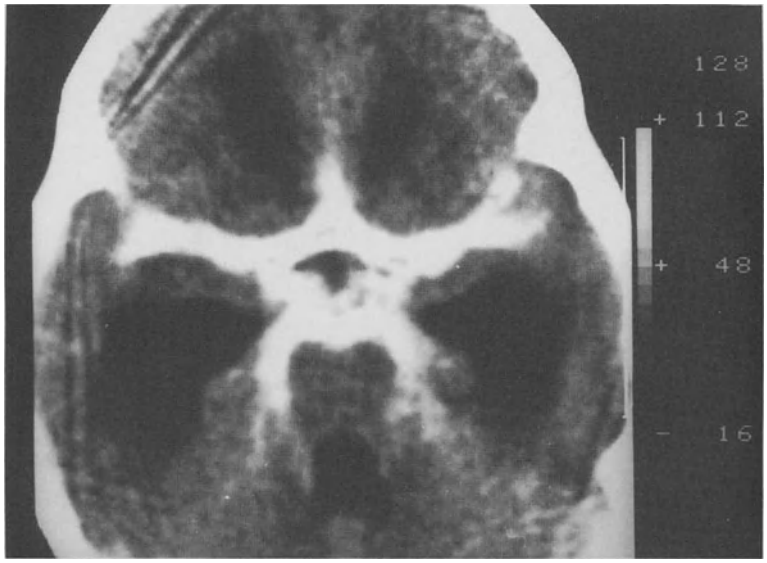

Figure 18.5. A 3-year-old girl with meningeal cysticercosis. The CT scan demonstrates an important inflammatory reaction on the basal cisterns and sylvian fissures.

process of the dead cysticerci. There may be solitary or multiple small, scattered calcifications varying in size and location. The calcifications are more readily detected by computed tomography than with plain radiographs of the skull and may be seen as early as a few months.

Meningeal Localization

In the acute forms of arachnoiditis, enhancement of the basal meninges is evident only in those cases in which there is an inflammatory reaction in the meninges, principally in the sylvian fissures, circumencephalic cistern, and less frequently, in the basal cisterns. This anatomicopathological form of cysticercosis produces hydrocephalus in a large number of cases, due to changes in the absorption of CSF (Figure 18.5).

Intraventricular Localization

Computed tomography is very precise with regard to the intraventricular localization of cysticerci. The cysts can be easily seen, although sometimes it is helpful if the study is complemented with an intraventricular injection of hydrosoluble contrast medium followed by conventional tomography and, in some cases, CT.

The time-honored neuroradiologic contrast studies such as pneumoencephalography, ventriculography, and cerebral angiography are used only when CT is not available or when there is a special indication, e.g., vasculitis of the gross arteries or migrating intraventricular cysts.[25]

Immunologic Tests

The immunologic tests for NCC started with Nieto's test,[26] which used complement fixation with an extract of cisticercosis antigen. A modification of that test, the indirect hemagglutination assay (IHA) was developed in 1962; Mahajan et al.[27] in India, found that 87.5% of patients with cysticercosis had an IHA titer greater than 1:64; the false-negative and false-positive rates were each 12.5%. On the other hand, Percy et al.[28] found that eight out of nine patients with cysticercosis had negative serologic studies in CSF and serum, and McCormick et al.[29] reported that only 66 of 113 patients had positive IHA. In meningitis, the test was positive in 79.6%, but in only 46.9% of patients without meningitis. Immunoelectrophoresis as well as radioimmunoassay has also been used.[30] Miller et al.[31] reported a new radioimmunoassay for NCC, studied in 70 patients. The assay showed nearly 100% sensitiv-

ity for ventricular cyst and meningitis, 86% sensitivity for multiple parenchymal cysts, and a false-positive rate of 7%. Another important test is the enzyme-linked immunosorbent assay (ELISA), which measures specific antibodies to cysticercus antigen, in both serum and CSF. This method, with the modification made by Larralde et al.,[32] yields 90% to 91% sensitivity and 96% to 100% specificity; in addition, the reproductivity of the results is outstanding. In conclusion, as for immunologic diagnosis of NCC, the test developed by Larralde et al. seems the most appropriate at this time.

It is a well-known fact that the CSF in the meningeal and ventricular forms of NCC shows elevation of protein contents, elevation of cells, mostly mononuclear lymphocytes, and, in a few cases, eosinophils; also there is a moderate tendency of glucose levels to decrease.

Treatment

The two treatment approaches to NCC are medical and surgical. Up to 1980, the medical treatment was restricted to alleviating symptoms. Its goal was to control seizures and, in cases of increased intracranial pressure, to reduce edema by the use of steroids and osmotic agents (mannitol or urea). In 1980, Robles and Chavarria[33] in Mexico and Gómez and Mejia[34] in Colombia reported on a beneficial response in NCC with praziquantel, a pyrazinoisoquinoline—2-(cyclohexylcarbonyl)-1,2,3,6,7,11b-hexahydro-4*H*-pyrazino [2,1-a]isoquinolin-4-one. Later these findings were confirmed by other investigators.[35–37] Unfortunately, most of these reports included a variety of forms of NCC, e.g., parenchymal cysts, parenchymal calcifications, hydrocephalus, intracranial hypertension, etc., and for that reason subjective evaluation was the rule.

In 1984 and 1985, Sotelo et al.[38,39] from the National Institute of Neurology and Neurosurgery in Mexico City reported the best-conducted trial for praziquantel. In this study, 91% of patients with parenchymal cysts improved, but only 47% of patients with arachnoiditis or intraventricular forms had remission. The treatment with praziquantel consists of a daily dose of 50 mg/kg of body weight for 2 weeks. Several reports on the use of other drugs in NCC, such as mebendazole, flubendazole, metrifonate, and albendazole has been published.[40–42] Albendazole seems the most appropriate in terms of effectiveness and cost; the dose is 10 to 15 mg/kg body weight daily for 30 days.

The surgical treatment of NCC can be divided into palliative and curative.[16,43–45] Surgical treatment is intended for

1. the relief of increased intracranial pressure in patients with hydrocephalus,
2. the removal of space-occupying lesions (large cysts),
3. the removal of seizuregenic foci.

Hydrocephalus is a common manifestation. The pathologic findings are usually obstruction of the CSF in the cisterns, the ventricular system, or the posterior fossa. A simple shunting procedure is advocated if there is not a mass lesion within or adjacent to the CSF outflow systems.

When there are intraventricular or posterior fossa cysts, they should be removed in addition to shunting, since the cysts in most instances continue to grow, with the strong possibility of increased neurological deficit. The results of shunting procedures in the basal arachnoiditis are encouraging. In patients with intraventricular cysts, there is a preponderance of cysts in the fourth ventricle as compared to those in the third; in this latter instance there is agreement that all third ventricular cysts should be removed, and the same must apply to patients with hydrocephalus and fourth ventricle cisticerci.

The removal of parenchymatous cysts that produce mass effect is strongly recommended, particularly if the cyst is solitary (Figure 18.6).

The removal of multiple cysts is not recommended, except in the very unusual case in which one cysts appears to be, by its large size, primarily responsible for increasing neurological deficits.

In cases of focal seizures, with or without generalization of the fits, that are resistant to medical treatment, the surgical resection of the

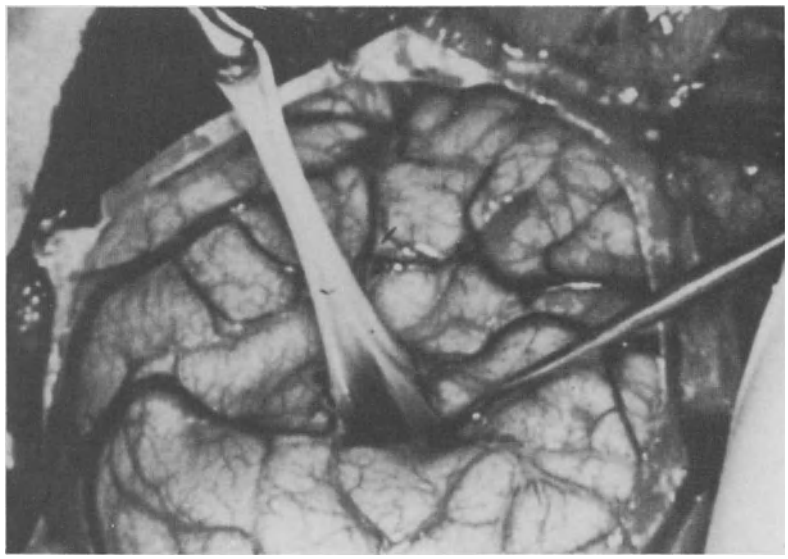

Figure 18.6. Operative photograph. Removal of an intraparenchymatous cysticercus that had a mass-effect. Ten-year-old girl.

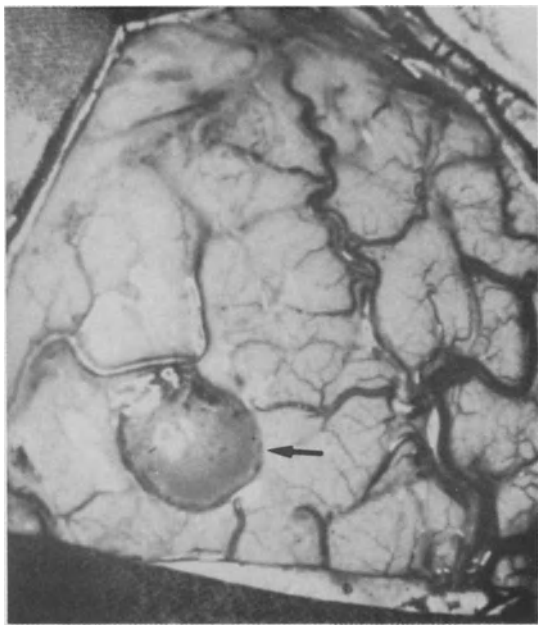

Figure 18.7. Operative photograph. A cortical cysticercus (arrow), in a 9-year-old boy with focal seizures. The cysticercus along with the epileptogenic tissue were removed.

cysticercus or cysticerci may improve or even cure the patient (Figure 18.7).

In cases of acute encephalitic cysticercosis with increased intracranial pressure, slit ventricles, and in which the medical treatment failed, subtemporal decompressive craniectomies are indicated; sometimes, internal decompression involving the thorough resection of brain tissue, mainly in the temporal lobe, is necessary.

In the very rare cases of adhesive arachnoiditis involving the chiasmatic area, a craniotomy to free adhesions or to decompress the structures in the visual pathway is useful. Surgery of course is not always indicated in NCC cases and does not effect a complete cure in every case in which it is performed; occasionally surgery can partially and temporarily relieve intracranial hypertension and sometimes focal epilepsy caused by cortical cysticercus.

In conclusion, the best prognosis for NCC patients in terms of surgical treatment is when there is a single cysticercus, with no meningeal or cerebral inflammatory response, that is located in a site accessible to the surgeon's instruments. At the present time, the sanitary engineering and public health approach will have the widest influence in eliminating this disease.

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