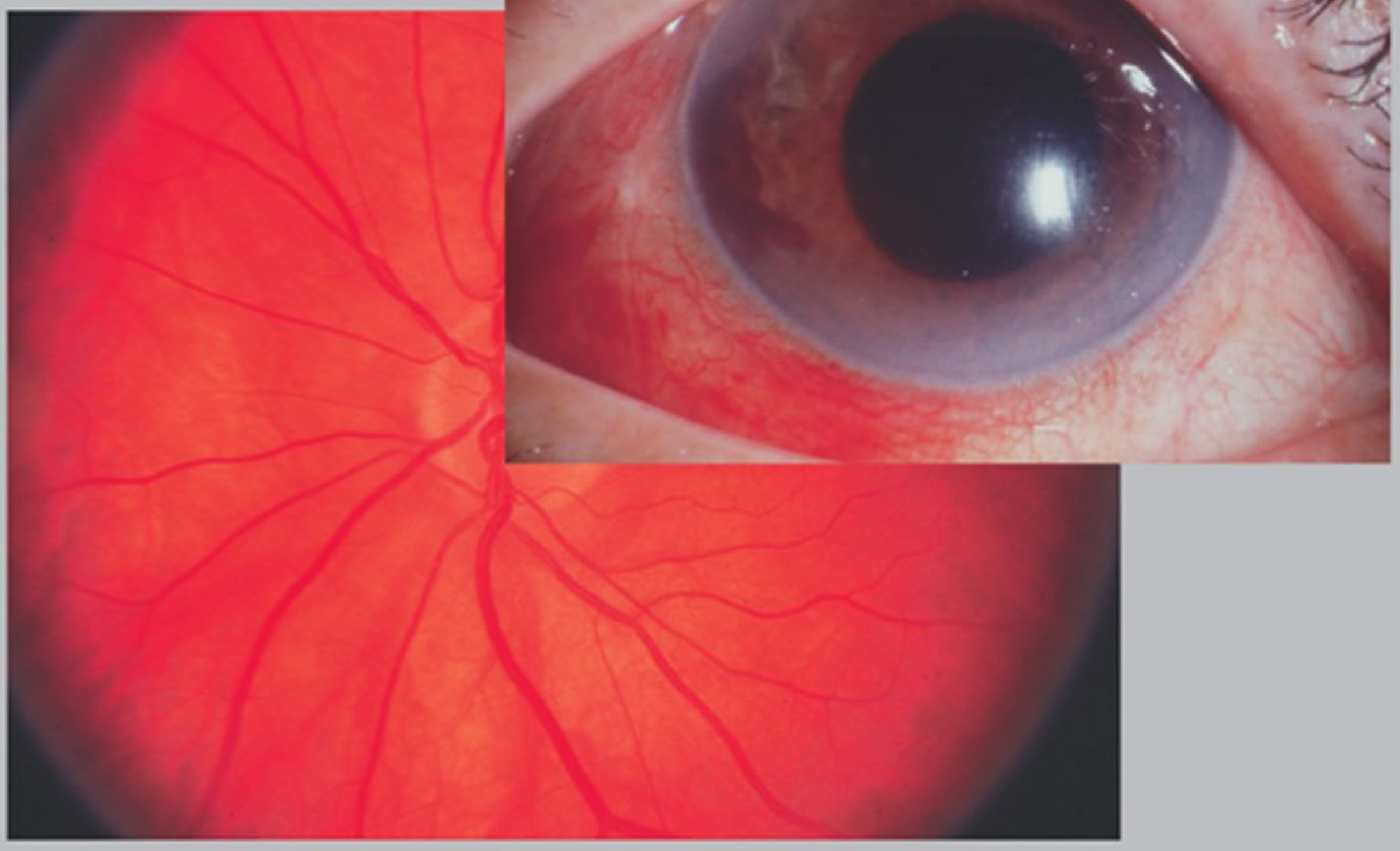
Ophthalmology Review

A Case-Study Approach

Kuldev Singh
William E. Smiddy
Andrew G. Lee



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Ophthalmology Review

A Case-Study Approach

Thieme

To

my parents, Mandev and Kanti Singh
—K. S.

my most patient and loving wife, Hilary A. Beaver, M.D.,
who has been a pillar of strength, support, and constancy
in an ever-changing and unpredictable world
—A. G. L.

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A Case-Study Approach

Edited by

Kuldev Singh, M.D., M.P.H

Associate Professor
Department of Ophthalmology
Director
Glaucoma Service
Stanford University Medical Center
Stanford, California

William E. Smiddy, M.D.

Professor
Department of Ophthalmology–
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

and

Andrew G. Lee, M.D.

Associate Professor
Departments of Ophthalmology
Neurology, and Neurosurgery
University of Iowa Hospitals and Clinics
Iowa City, Iowa

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Director, Production and Manufacturing: Anne Vinnicombe
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Preface

This textbook is aimed at medical students, residents, and comprehensive ophthalmologists who have an interest in general ophthalmologic problems. The format is designed to be easy to use, case-driven, and a basic introduction to clinical problems, evaluation, management, and treatment. It is not our intention to provide a complete, all-inclusive, detailed, or heavily referenced text. Instead, it is our goal to present real-world case examples of common clinical conditions and to discuss the work-up and management in a simple and easy-to-read manner.

We hope that the reader will be able to use this text in the clinic to guide the management of patients. The reader is encouraged to reference more detailed literature and texts for elements or less-common disorders that are not covered in our book.

Dr. Singh would like to thank his teachers at the institutions where he trained: The Johns Hopkins University School of Medicine, Oregon Health Sciences University, and The Bascom Palmer Eye Institute–University of Miami School of Medicine. He is particularly grateful to Alfred Sommer, E. Michael Van Buskirk, Alana Grajewski, Richard Parrish, Elizabeth Hodapp, Paul Palmberg, and Douglas Anderson. He would like to acknowledge his colleagues and mentors in the field of ophthalmology—too numerous to mention individually—who are a constant source of inspiration and guidance. He thanks the ophthalmology residents, glaucoma fellows, colleagues, technicians, and assistants at Stanford who have helped make his work so enjoyable. Finally, he would like to acknowledge his mentors at the Stanford University School of Medicine, especially R. Brooke Jeffrey, M.D., who have been so generous with their time.

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Kuldev Singh, M.D., M.P.H.
William E. Smiddy, M.D.
Andrew G. Lee, M.D.

Contributors

Richard L. Abbott, M.D.
Professor of Ophthalmology
University of California, San Francisco
San Francisco, California

Arezo Amirikia, M.D.
Department of Ophthalmology–
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Scott R. Anagnoste, M.D.
Retina Vitreous Consultants
Ft. Lauderdale, Florida

Antonio V. Aragon II, M.D.
Department of Ophthalmology
Eye Institute of Albuquerque
Albuquerque, New Mexico

V. Nicholas Batra, M.D.
Turner Eye Institute
San Leandro, California

Milton Boniuk, M.D.
Professor of Ophthalmology
Baylor College of Medicine
Houston, Texas

Paul Brazis, M.D.
Associate Professor of Neurology
and Ophthalmology
Mayo Clinic–Jacksonville
Jacksonville, Florida

Donald L. Budenz, M.D.
Associate Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Terry E. Burris, M.D.
Associate Clinical Professor
of Ophthalmology
Casey Eye Institute
Oregon Health Sciences University School
of Medicine
Portland, Oregon

Sally Byrd, M.D.
Clinical Assistant Professor
of Ophthalmology
Stanford University Medical Center
Stanford, California

Lourdes A. Casuso, M.D.
Instructor
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

David F. Chang, M.D.
Clinical Professor of Ophthalmology
University of California, San Francisco
San Francisco, California

Nauman A. Chaudhry, M.D.
New England Retina Associates
New London, Connecticut

David K. Coats, M.D.
Assistant Professor of Ophthalmology
and Pediatrics
Baylor College of Medicine
Houston, Texas

Anne L. Coleman, M.D., Ph.D.
Associate Professor of Ophthalmology
Jules Stein Eye Institute
University of California, Los Angeles
Los Angeles, California

Ghassan J. Cordahi, M.D.
Associate
VitreoRetinal Foundation
Memphis, Tennessee

Scott A. Cory, M.D.
Lake Eye Associate
Porter Memorial Hospital
Portage, Indiana

Peter R. Egbert, M.D.
Professor of Ophthalmology
Stanford University Medical Center
Stanford, California

Sherif M. El-Harazi, M.D.
Hermann Hospital
Department of Ophthalmology
University of Texas–Houston
Houston, Texas

Robert M. Feldman, M.D.
Hermann Hospital
Clinical Associate Professor of Ophthalmology
University of Texas–Houston
Houston, Texas

I. Howard Fine, M.D.
Associate Clinical Professor of Ophthalmology
Casey Eye Institute
Oregon Health Sciences University School
of Medicine
Portland, Oregon

Paul E. Finley, M.D.
Hillsboro Eye Clinic
Hillsboro, Oregon

Alana L. Grajewski, M.D.
Clinical Associate Professor
of Ophthalmology
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Weldon W. Haw, M.D.
Assistant Professor of Ophthalmology
Stanford University Medical Center
Stanford, California

Andrew J.W. Huang, M.D., M.P.H.
Associate Professor of Ophthalmology
Director of Cornea Service
University of Minnesota
Minneapolis, Minnesota

Rick S. Huo, M.D.
Department of Ophthalmology
Kaiser Permanente
Vista, California

Matthew R. Jones, M.D.
Clinical Instructor
Stanford University Medical Center
Stanford, California

Byron L. Lam, M.D.
Associate Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Andrew G. Lee, M.D.
Associate Professor of Ophthalmology,
Neurology, and Neurosurgery
University of Iowa Hospitals and Clinics
Iowa City, Iowa

Martha Motuz Leen, M.D.
Clinical Assistant Professor
of Ophthalmology
University of Washington
Seattle, Washington

Stephen A. Lin, M.D.
Assistant Clinical Professor
of Ophthalmology
Stanford University Medical Center
Stanford, California

Medhat M. Mady, M.D.
El Mohandseen
Cairo, Egypt

Edward E. Manche, M.D.
Assistant Professor of Ophthalmology
Director of Corneal and Refractive Surgery
Stanford University Medical Center
Stanford, California

Cathleen M. McCabe, M.D.
Indiana Lasik Centers
Fort Wayne, Indiana

Stephen D. McLeod, M.D.
Assistant Professor of Clinical Ophthalmology
University of California, San Francisco
San Francisco, California

Mozart de O. Mello Jr., M.D.
Assistant Professor of Ophthalmology
Fundacao Banco de Olhos de Goias
Goiania-Goias, Brazil

Timothy G. Murray, M.D.
Associate Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Peter A. Netland, M.D., Ph.D.
Associate Professor of Ophthalmology
University of Tennessee Health Science Center
Memphis, Tennessee

Evelyn A. Paysse, M.D.
Assistant Professor of Ophthalmology
and Pediatrics
Baylor College of Medicine
Houston, Texas

Renato T.F. Pires, M.D.
Instituto de Olhos de Goiania
Goiania-Goias, Brazil

James C. Robinson, M.D.
Assistant Professor of Ophthalmology
Medical College of Wisconsin
Milwaukee, Wisconsin

Thomas W. Samuelson, M.D.
Associate Clinical Professor of Ophthalmology
University of Minnesota
Minneapolis, Minnesota

Ingrid U. Scott, M.D., M.P.H.
Assistant Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Debra Shetlar, M.D.
Assistant Professor of Ophthalmology
Baylor College of Medicine
Houston, Texas

Magdalena F. Shuler, M.D., Ph.D.
Retina Fellow
Wills Eye Hospital
Philadelphia, Pennsylvania

Kuldev Singh, M.D., M.P.H.
Associate Professor of Ophthalmology
Director of Glaucoma Service
Stanford University Medical Center
Stanford, California

William E. Smiddy, M.D.
Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Stephen U. Stechschulte, M.D.
Clinical Faculty
Department of Ophthalmology
University of Kansas School of Medicine
Kansas City, Kansas

Christopher N. Ta, M.D.
Assistant Professor of Ophthalmology
Stanford University Medical Center
Stanford, California

Scheffer C.G.Tseng, M.D., Ph.D.
Professor of Ophthalmology
Bascom Palmer Eye Institute
University of Miami School of Medicine
Miami, Florida

Richard G. Weleber, M.D.
Professor of Ophthalmology
Casey Eye Institute
Oregon Health Sciences University School
of Medicine
Portland, Oregon

Pongmas Wichiensin, M.D.
Rajavithi Hospital
Bangkok, Thailand

Section I

CORNEA AND EXTERNAL DISEASE

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2. Chronic Follicular Conjunctivitis
3. Acute Bacterial Conjunctivitis
4. Pterygium
5. Recurrent Erosion/Epithelial Basement Membrane Dystrophy
6. Fuchs' Corneal Dystrophy
7. Keratoconus
8. Microbial Keratitis
9. Keratoconjunctivitis Sicca—Dry Eye
10. Postsurgical Corneal Edema
11. Dellen
12. Graft Rejection Following Penetrating Keratoplasty
13. Blepharitis

Case 1

ACUTE FOLLICULAR CONJUNCTIVITIS

Terry E. Burris, M.D.

HISTORY

A 37-year-old female office worker has a 2-week history of photophobia, discomfort, and headache centered around the right eye. A week previously, she developed sudden onset of redness and watering of the right eye the first day back at work, having returned several days earlier from a vacation in Hawaii. She also noted a swelling in front of her right ear. She saw her eye-care practitioner who found unilateral follicular conjunctivitis with a mildly tender preauricular node. He treated her with a 2-week course of topical Tobramycin-Dexamethasone; her node became slightly smaller, but 2 days after cessation of the topical Tobramycin-Dexamethasone, she had epithelial infiltrates in the cornea and persisting follicles.

Visual acuity is 20/20 in each eye. There is a right-sided nontender preauricular node. At penlight examination, the right eye shows a 1 to 2 mm ptosis of the upper lid, and mild injection of the bulbar conjunctiva; the left eye appears quiet. Biomicroscopy reveals a moderate number of medium sized pretarsal follicles and papillae in the right eye (Fig. 1–1); the left eye demonstrates substantially fewer follicles in the inferior fornix. The right cornea shows diffuse midperipheral and a few central epithelial infiltrates, with no stromal involvement or other anterior segment findings. The left cornea and anterior segment are normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Acute follicular conjunctivitis is commonly encountered in the general ophthalmologic setting, and less commonly so as unilateral disease. The patient's history is particularly remarkable in that she was recently on vacation, possibly increasing the risk of encountering infectious agents either from acquaintances or from fomites she may have contacted. She specifically denies any possible sexual contact, but stayed in hotel rooms and used swimming pool facilities.

The differential diagnosis in this case can be narrowed to include adenoviral keratoconjunctivitis, chlamydial disease (adult inclusion conjunctivitis), primary herpes simplex or Epstein-Barr (EB) keratoconjunctivitis, and Molluscum contagiosum. Toxic and allergic reactions should also be considered in previously treated or self-medicating patients, although lymphadenopathy is not a common feature.

2. Adenovirus is a leading cause of follicular conjunctivitis and can present in milder forms, such as seen in the present case, to more fulminate forms with substantial ocular morbidity. It is generally acquired by fomite–hand-eye contact or from swimming pools. These can be visually significant. Clinical symptoms and signs generally occur about a week after exposure to the virus. Its more severe forms include epidemic keratoconjunctivitis (EKC) caused by several adenoviral serotypes including 8 and 19; EKC routinely demonstrates a hemorrhagic and membranous conjunctivitis, which may be accompanied by prominent lid edema and erythema and even preseptal cellulitis. Systemic symptoms may include fever and malaise. Pharyngoconjunctival fever (PCF) is generally a milder condition and includes an antecedent or simultaneous pharyngitis, fever, and upper respiratory symptoms, and demonstrates relatively mild or absent corneal infiltrates. In both conditions, the acute onset is in one eye, followed by the

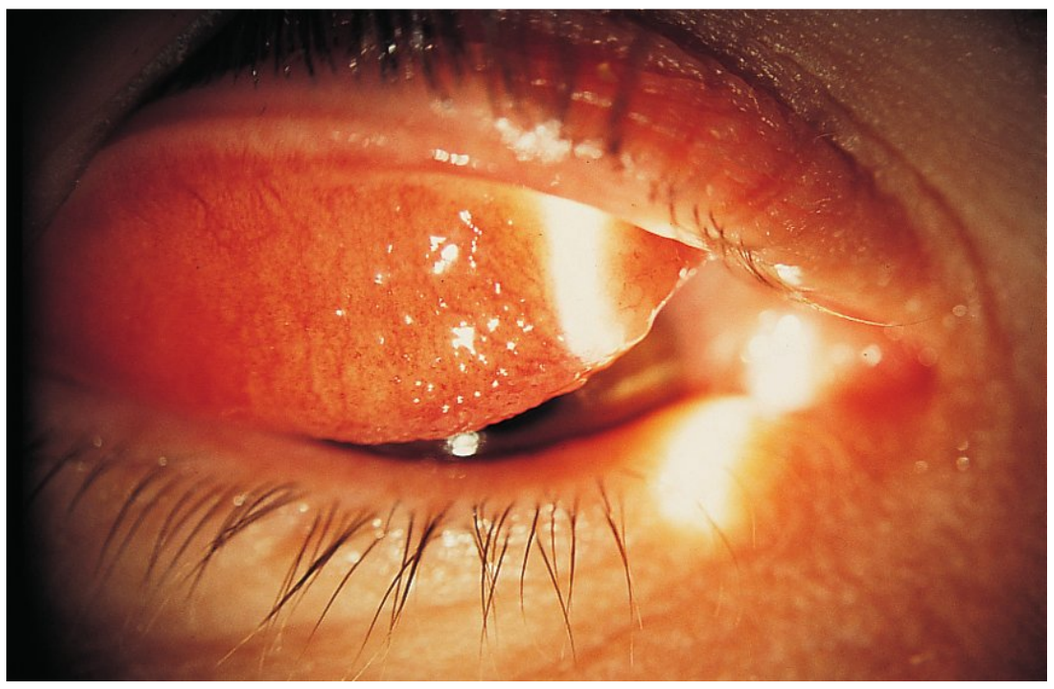

FIGURE 1–1 Superior pretarsal mixed follicular and papillary conjunctivitis.

second eye a few days later; the latter eye is generally less involved with symptoms and signs.

This patient has no antecedent or concurrent systemic symptoms. She developed epithelial infiltrates only after cessation of topical Tobramycin-Dexamethasone; topical corticosteroid usage early in the course of acute conjunctivitis can mask this helpful diagnostic corneal finding. Typically, within a week of onset of EKC, fine diffuse punctate epithelial infiltrates develop; these coalesce into larger, coarse epithelial infiltrates about a week later. These are replaced by focal subepithelial infiltrates, which become more intense by a month after onset and typically reside in the central and pericentral cornea.

3. Adult chlamydia inclusion conjunctivitis is caused by Chlamydia trachomatis; it is an oculogenital disease generally found in younger, sexually active adults, but it can also be contracted from fomites including toilet seats and swimming pools or hot tubs. Onset of first symptoms may be more difficult to pinpoint, but is likely within 2 to 3 weeks of exposure. It is commonly unilateral, and involves mild lid swelling and a minimal mucopurulent discharge. A minimally tender preauricular node may develop as well as pseudoptosis, both features presenting with this patient. Small epithelial infiltrates as seen in this patient can develop 2 to 3 weeks after onset of the conjunctivitis. A superior micropannus may develop. Corticosteroid use again may have altered the clinical presentation of this patient. The patient denies any systemic or genital symptoms, but the clinician must remain circumspect in this regard.

Chlamydia psittaci, an infection of birds, is rarely transmitted to humans. The infection can inhabit cats, but this patient had not knowingly been exposed to birds or cats. Clinical findings are similar to inclusion conjunctivitis except that no pannus is seen; the disease is often accompanied by a mild influenza-like illness or frank pneumonia. Presentation of a Parinaud's oculoglandular syndrome would also invoke another possible chlamydial condition, lymphogranuloma venereum, a venereal disease accompanied by lymphadenitis and febrile illness. The conjunctiva would classically demonstrate follicles and one or more granulomas. Newcastle disease infection (a paramyxovirus) of poultry workers may present similarly as in this patient, but the follicles are generally prominent only in the lower lid, and any epithelial infiltrates are more scant.

4. Primary herpes simplex and EB viruses may present as an acute follicular conjunctivitis, with possible mild conjunctival hemorrhages or even membranes. Primary herpes simplex infection in adults is often accompanied by vesicular lid lesions, with watery discharge and a preauricular node. The cornea may develop a fine punctate epitheliopathy or small fine dendritic figures. EB virus keratoconjunctivitis may manifest subepithelial infiltrates similar to adenovirus, and patients may present with no systemic manifestations or with the more classic spectrum of fever, sore throat, and lympadenopathy of mononucleosis.

5. Molluscum contagiosum is now the most commonly encountered pox virus and can cause a unilateral follicular conjunctivitis. The lid must be carefully examined. Corneal infiltrates are not seen. Preauricular lymphadenopathy is also not a characteristic feature, unlike the vaccinia pox virus, which

may be encountered when administered as a smallpox vaccination.

TEST INTERPRETATION

Clinical suspicion is usually a valuable indicator for testing required to confirm certain etiologies of acute follicular conjunctivitis. Simple observation for 1 or 2 weeks is reasonable if adenovirus is highly suspected. Patient counseling is important regarding the infectious nature of the condition. Her social history was convincing that she was not at high risk for chlamydia, other than possibly through fomite exposure. Her epithelial infiltrates were consistent with chlamydia or adenovirus, although the clinical picture was possibly altered by use of topical corticosteroids before referral. Cultures and other tests were performed to rule out viral and chlamydial disease. Cultures may not be helpful in certain health systems or hospitals if performed infrequently or if the clinician has found recurring spurious results.

To rule out continued shedding of adenovirus or primary herpes infection, a conjunctival scraping for tissue culture on human fibroblasts was performed; however, at 2 to 3 weeks post onset, a positive culture is more difficult to obtain. For chlamydia, conjunctival scrapings for direct fluorescent antibody (DFA) testing and McCoy cell culture were performed. These tests are fairly sensitive and highly specific. These scrapings are effectively obtained with small wire Dacron swabs.

Kits for DFA testing have an indefinite shelf life and are provided by a properly equipped laboratory with personnel properly trained to do the analysis. The conjunctiva is anesthetized with proparacaine, and the Dacron swab is rubbed across the fornix or pretarsal conjunctiva with firm strokes sufficient to harvest epithelial cells. The swab is rolled over the glass slide provided in the kit, and a smudge of material should be apparent by the naked eye when the slide is observed in reflected light. The slide is preserved with a fixative and transported to the laboratory. The same swab used for the glass slide can then be inoculated into suitable tissue culture transport medium by cutting or breaking off the top portion of the handle to allow the Dacron portion to be fully immersed in the medium. Alternatively, polymerase or ligase chain reaction testing is becoming increasingly available but these tests are not FDA-approved for use with the eye at the time of this writing. Giemsa or Wright-Giemsa staining was not ordered because this test is infrequently performed now that more sensitive and specific testing is available; in our heavily penetrated managed care environment, fewer experienced laboratory technicians are available who can reliably identify inclusions by this traditional technique. For this case study, test results were negative for adenovirus and herpes simplex as well as for chlamydia.

DIAGNOSIS

Acute follicular conjunctivitis, likely adenoviral.

MEDICAL MANAGEMENT

Observation and symptomatic treatment with unpreserved lubricants were initiated. The patient was counseled regarding the potential infectious nature of the condition. Had she demonstrated a positive adenoviral culture (which takes 1 to 2 weeks of culture incubation), she would be further counseled, again emphasizing possible infectivity to others for another week or two (or longer), with viral shedding possibly being prolonged by previous use of corticosteroids. Keeping personal soiled tissues, washcloths, and pillowcases isolated from others is recommended. Cidofovir, a promising broad-spectrum antiviral, may soon be available which may substantially shorten the morbidity of adenoviral keratoconjunctivitis and reduce the period of viral shedding. If the patient develops visually significant subepithelial infiltrates that prevent her from driving or doing her job, a mild dose of topical corticosteroid, such as loteprednol, may be indicated; the goal is to obtain usable vision and not to totally eradicate the subepithelial infiltrates. A positive herpes culture (available after 2 days of culture

incubation) would suggest initiation of topical trifluridine therapy, or, in the presence of prominent central corneal epithelial infiltrates, systemic acyclovir 400 to 800 mg 5 times a day for 1 to 2 weeks. Acyclovir offers the advantage of reducing epithelial toxicity in an irritated eye.

A positive chlamydia culture would require initiation of systemic therapy for adult inclusion conjunctivitis, due to the relatively high incidence of genital tract and other nonocular involvement. Treatment of sexual partners would also be mandatory. The traditional therapy includes tetracycline 250 mg orally 4 times daily for 3 weeks, taken on an empty stomach and avoiding milk products and antacids, which reduce absorption. A simpler regimen is doxycycline, 100 mg daily for 2 to 3 weeks; this can be taken with food and is usually better tolerated. Pregnant or breastfeeding women may take erythromycin 250 mg 4 times daily for 3 weeks, or sulfisoxazole, 0.5 to 1 g 4 times daily for 3 weeks if tetracycline is contraindicated. Azithromycin 1 g as a single dose may also prove effective for adult inclusion conjunctivitis.

REHABILITATION AND FOLLOW-UP

The patient should be examined in 4 to 6 weeks to ensure that symptoms have improved and the follicles nearly regressed. A careful history should be obtained to make certain that the prescribed medications have been taken properly.

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Case 2

CHRONIC FOLLICULAR CONJUNCTIVITIS

Terry E. Burris, M.D.

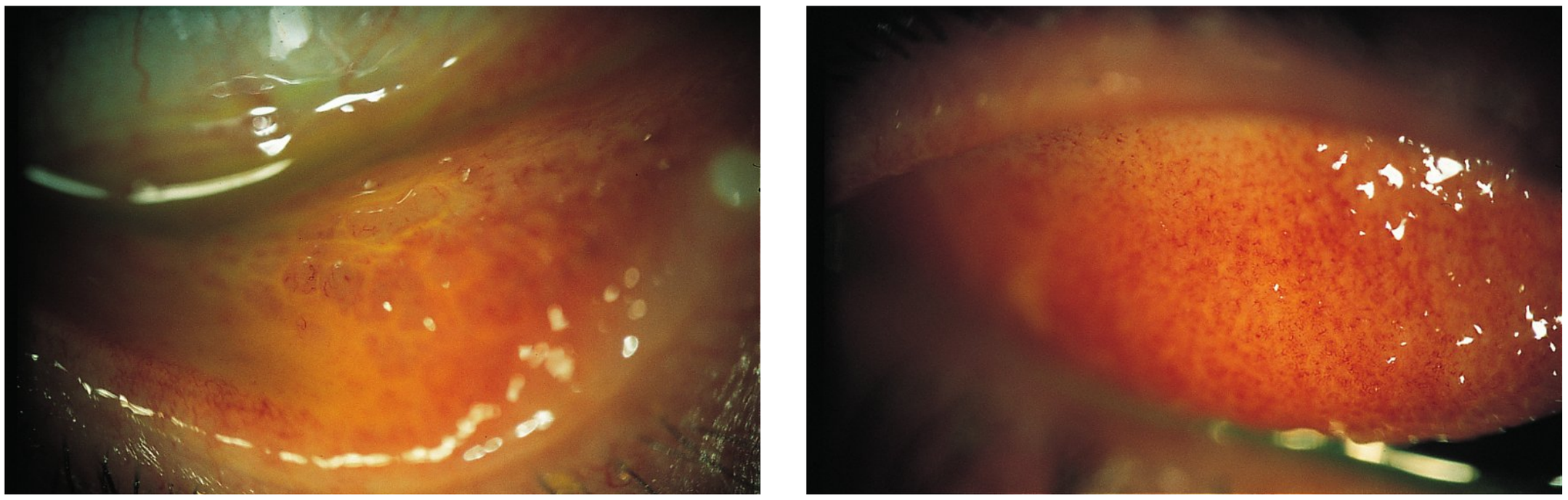
HISTORY

A 38-year-old female patient presents for a routine follow-up visit 15 months after penetrating keratoplasty and anterior segment reconstruction for traumatic injury. Her eyes are comfortable but she complains of mild right-sided preauricular discomfort and swelling. She recalls that 6 weeks previously she developed a fever and swollen glands, particularly on the right side of her face, and her internist suspected "strep throat" or "mononucleosis." She had no ocular symptoms at that time. Throat culture and Epstein-Barr (EB) virus serology were taken and were negative. She was treated with penicillin (14 days) and she recovered symptomatically, except for the persisting preauricular node.

The patient is otherwise healthy with a negative review of systems. Her past ocular history is also significant for medically treated traumatic angle recession glaucoma of her right eye, with normal left eye. Her ocular medications for the right eye were loteprednol etabonate 0.5% twice daily, brimonidine 0.2% twice daily, timolol gel forming solution 0.5%, and methyl cellulose at bedtime. She had last been seen 3 months previously, and no ocular inflammation was seen. Her current examination reveals a visual acuity of 20/60+ with pinhole to 20/40. Intraocular pressure was 28 mm Hg in the right eye, 14 mm Hg in the left eye. She has a slightly tender right preauricular node. External exam reveals slight puffiness of the lids, right worse than left. Biomicroscopy of the right eye shows mild lid scurf and no other lesions; the conjunctiva reveals prominent follicules and papillae in the inferior fornix and superior pretarsal area (Fig. 2–1); no granulomas are present. The keratoplasty has mild diffuse epitheliopathy; the anterior segment exam is otherwise non-contributory. The left eye shows mild pretarsal papillae and an otherwise normal exam.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. A presumed presence of unilateral follicular conjunctivitis for the previous 3 or more weeks is inferred due to the associated 6-week history of preauricular lymphadenopathy associated with febrile illness. Chronic follicular conjunctivitis can manifest either after an acute onset, as in this case, or after insidious onset.
2. A detailed history is necessary to encompass the period since the patient's last examination. This should include onset of symptoms and presence of ocular redness, discharge, discomfort, or photophobia. The use of prescribed or over-the-counter ocular medications, irrigants, or herbal preparations must be ascertained. Patients frequently will not recall, or admit to, over-the-counter, herbal, or home remedies, or naturopathic or homeopathic preparations unless directly and specifically questioned. She denied close contact with animals, including cats and birds. She had not traveled to potentially endemic areas for other infectious etiologies.
3. The differential diagnosis for this case included EB virus, herpes simplex, and adenoviral keratoconjunctivitis. A viral etiology was suggested by the febrile prodrome. Mitigating against these diagnoses were unilaterality and lack of corneal signs (though the latter could be masked by the use of topical corticosteroid [loteprednol]). Additionally, with EB virus or adenovirus, at least some degree of follicular involvement is generally noted in the other eye. She had no lid



A B

FIGURE 2–1 Medium-sized "buried" pretarsal follicles in midst of papillary response. (A) Inferior tarsal. (B) Superior tarsal.

lesions or chronic blepharitis that might suggest molluscum, or chronic bacterial infection, such as Moraxella. Her history and findings were not consistent with oculoglandular syndrome (Parinaud's).

4. The patient was a sexually active, monogamous but unmarried female. She denied any gynecologic complaints, but the presence of unilateral chronic follicular disease raised suspicion of adult inclusion conjunctivitis as a cohabiting opportunistic illness.
5. Toxic follicular conjunctivitis must be considered, particularly with the patient's history of chronic topical medication usage. Hurricane epitheliopathy, a punctate keratitis with a swirling configuration inside the keratoplasty wound margin, is consistent with a toxic effect of her preserved medication usage. The preservatives utilized included benzalkonium chloride and benzododecinium bromide, which are known to contribute to punctate keratitis but are unlikely to contribute to follicle formation. Timolol is rarely associated with toxic conjunctival effects but can contribute to epithelial keratitis. Brimonidine tartrate (Alphagan®), a selective alpha-2-adrenergic agonist, is a potential offender since the related product, apraclonidine hydrochloride (Iopidine®), is known to cause a follicular conjunctivitis in some cases.
6. Masquerade syndrome: Subconjunctival lymphoma can appear as a cluster of follicles. They generally have a salmon appearance and may encroach onto the globe. Examination in sunlight may help accentuate and delineate the involved area of conjunctiva.

TEST INTERPRETATION

Bacterial cultures are not initially indicated in this case given the absence of lid or conjunctival signs of infection. Conjunctival scrapings reveal polymorphonuclear leukocytes and lymphocytes, with no eosinophils, suggesting a chronic inflammatory response. Viral cultures were negative for herpes (determined by 2 days' incubation on human fibroblast cells) and adenovirus (determined by 2 weeks' incubation). Chlamydia culture on McCoy cells and conjunctival smear for direct fluorescent antibody (DFA) staining are negative. Conjunctival biopsy can be considered in cases of protracted follicular conjunctivitis where masquerade syndrome is suspected.

DIAGNOSIS

Unilateral toxic chronic follicular conjunctivitis.

MEDICAL MANAGEMENT

Pending culture results, observation is a reasonable approach to determine the natural history

of follicle development or improvement. In this case, the follicles persisted and the eye actually became more symptomatic, with mild redness and irritation developing while culture results were pending. When toxic follicular conjunctivitis became the primary diagnostic possibility, brimonidine was stopped since it was the most likely offending agent. Addition of more frequent corticosteroids is not indicated, and these would have little effect on the conjunctival response when the toxic agent is still being utilized.

Failure to recognize toxic follicular conjunctivitis can result in progressive punctal stenosis and subconjunctival scarring, ie, pseudopemphigoid. This can be a self-limiting disorder, or can continue to progress, with eventual dry eye and keratopathy.

REHABILITATION AND FOLLOW-UP

The patient should be followed every 2 to 3 weeks until improvement is noted, observing for any signs of occult infective involvement. In this case, the patient's symptoms rapidly improved, and by 3 weeks after cessation of the brimonidine, her follicles were improving. The follicles completely resolved by 2 months post cessation of the offending agent, as did the hurricane epitheliopathy.

Toxic follicular conjunctivitis is most commonly caused by antiviral agents, cycloplegic agents, and glaucoma drugs. Of the latter, pilocarpine and carbachol, echothiophate, epinephrine and dipivefrin, and apraclonidine are classically associated. Brimonidine is rarely reported to cause follicles, and, in this case, the viral prodrome may have predisposed the patient to developing this response through a subclinical irritated conjunctiva.

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Case 3

ACUTE BACTERIAL CONJUNCTIVITIS

Stephen U. Stechschulte, M.D.

HISTORY

A 60-year-old woman presents with complaints of decreased vision, irritation, and discharge in her right eye over the past 3 days. She reports that her eye has been stuck shut for the past 2 days, requiring a warm, wet washcloth to open the eye. She denies any trauma or surgery. Her past medical history includes hypertension and a hysterectomy 10 years ago. She reports no allergies to medications and uses metoprolol for hypertension. She denies any family history of eye disease.

The patient is healthy with a negative review of systems other than her ocular complaints. She is wearing glasses. On examination her corrected visual acuity with glasses is 20/40 OD and 20/25 OS. Manifest refraction OD is −2.50−1.00 × 85 and corrects her to 20/30. Her manifest refraction OS is −2.00 −0.75 × 90 which corrects her vision to 20/20. There is no afferent pupillary defect. Slit-lamp examination of the left eye is normal. The right conjunctiva is injected and edematous. There is mucopurulent discharge from the lower lid (Fig. 3–1). The inferior fornix is covered with a fibrin–mucus pseudomembrane (Fig. 3–2). The inferior and superior palpebral conjunctiva show a 2+ papillary reaction. The corneas are clear and with no evidence of scarring or inflammation. The anterior chambers are quiet. The right lens demonstrates mild cataractous changes. The left lens is clear. The posterior poles of the right and left eyes are normal. The cup to disk ratio is 0.4 in both eyes. Intraocular pressures are 18 and 15 mm Hg, respectively. Mucus from the right eye is submitted for immediate Gram stain, and cultures are plated on blood and chocolate agar.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The sudden onset of redness with irritation and discharge is a typical feature of infectious conjunctivitis. Bacterial conjunctivitis is uncommon and accounts for only a small percentage of cases but the presence of purulent discharge that crusts and seals the eyelids makes the diagnosis more likely. A rapid onset of symptoms over the course of hours or days with copious discharge must alert one to the possibility of more virulent genera such as Neisseria, Haemophilus, or Streptococcus.
2. It is tempting in a busy clinical setting to treat suspected bacterial conjunctivitis with a broad spectrum antibiotic without first culturing the conjunctiva. In acute and hyperacute cases it is helpful, if not mandatory, to take Gram stains and cultures prior to initiating therapy. These initial tests are the only objective diagnostic information to identify causative organisms and are the best guide for treatment.
3. Bacterial conjunctivitis can be classified by rapidity of onset, useful for clinical diagnoses (Table 3–1), or morphologic characteristics, which determine laboratory differentiation.
4. The formation of inflammatory membranes or pseudomembranes is characteristic of several types of conjunctivitis, such as Clostridium diphtheriae, Neisseria gonorrheae, or beta-hemolytic Streptococci, viral conjunctivitis, or ligneous conjunctivitis. These membranes consist of fibrin and mucus and may be easily peeled from the conjunctiva in the case of pseudomembranes or may cause bleeding when removed in the case of true membranes. Membranes are seen in more severe cases.

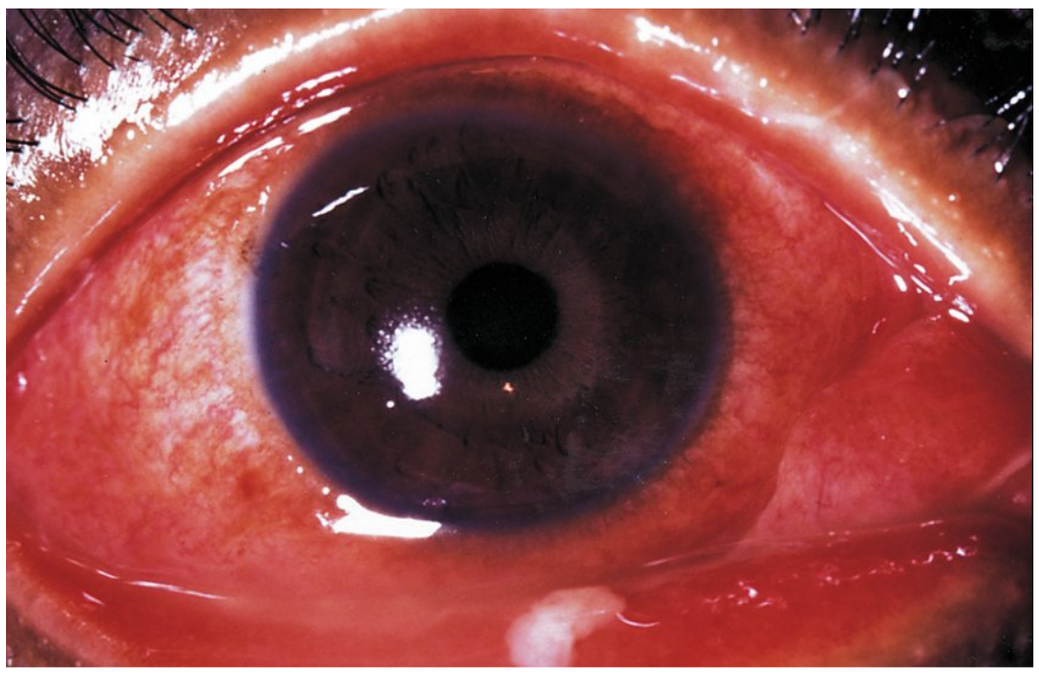

FIGURE 3–1 The right eye shows hyperemia and discharge from the lower lid.

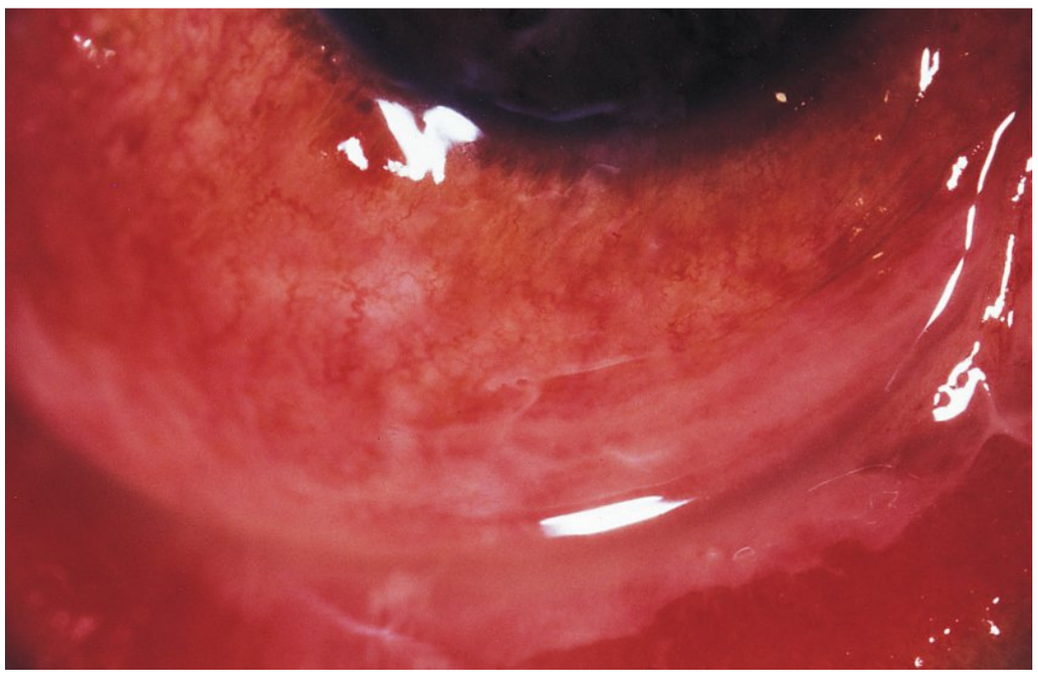

FIGURE 3–2 The inferior fornix of the right eye demonstrating an inflammatory pseudomembrane covering the tarsal conjunctiva.

TEST INTERPRETATION

The Gram stain showed numerous gram-positive cocci in pairs and numerous polymorphonuclear lymphocytes. Cultures grew Streptococcus pneumoniae that was sensitive to penicillin, ciprofloxacin, vancomycin, and trimethoprim/sulfamethoxazole.

DIAGNOSIS

Streptococcal pneumoniae bacterial conjunctivitis with the formation of inflammatory pseudomembrane membranes.

MEDICAL MANAGEMENT

This patient can be managed medically with topical antibiotic drops. She was treated with trimethoprim sulfate-polymixin B drops 4 times a day for 7 days. After 2 days her symptoms had improved significantly. Most cases of bacterial conjunctivitis are self-limited; however, infections can occur in epidemics, and appropriate antibiotic therapy not only helps relieve the individual's discomfort and lessens the severity of the infections but treatment may prevent further spread of the organism. Patients should be cautioned to avoid touching their eyes or sharing towels or washcloths. Hyperacute conjunctivitis, that which occurs within hours and is characterized by conjunctival hemorrhage and copious mucous discharge, mandates quick diagnosis and more aggressive therapy. A Gram stain that shows gram-negative diplococcus is highly suggestive of gonococcal conjunctivitis. Treatment consists of a one-time intramuscular dose of ceftriaxone if the cornea is not involved and intravenous therapy in combination with topical bacitracin or erythromycin if the cornea is affected. Neisseria gonorrhoeae may lead to

TABLE 3–1 **Bacterial Conjunctivitis**

ONSET	Hyperacute	Acute	Slow
ORGANISMS	Neisseria gonorrhoeae Neisseria meningitidis	Haemophilus influenzae Staphylococcus aureus Streptococcus pneumoniae	Enterobacteriaceae Moraxella lacunata Pseudomonas Staphylococcus aureus

cornea perforation and these patients must be monitored closely.

SURGICAL MANAGEMENT

There is almost no role for surgery in acute bacterial conjunctivitis. Membranes may be debrided but at the risk of bleeding and scar formation. Pseudomembranes can be removed without bleeding.

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Case 4

PTERYGIUM

Weldon W. Haw, M.D.
Edward E. Manche, M.D.

HISTORY

A 32-year-old lifeguard presents with intermittent symptoms of bilateral red eye, dryness, irritation, and foreign body sensation. Visual acuity is 20/20 in both eyes. Examination reveals a fibrovascular overgrowth of the bulbar conjunctiva extending onto the cornea of both eyes (Fig. 4–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

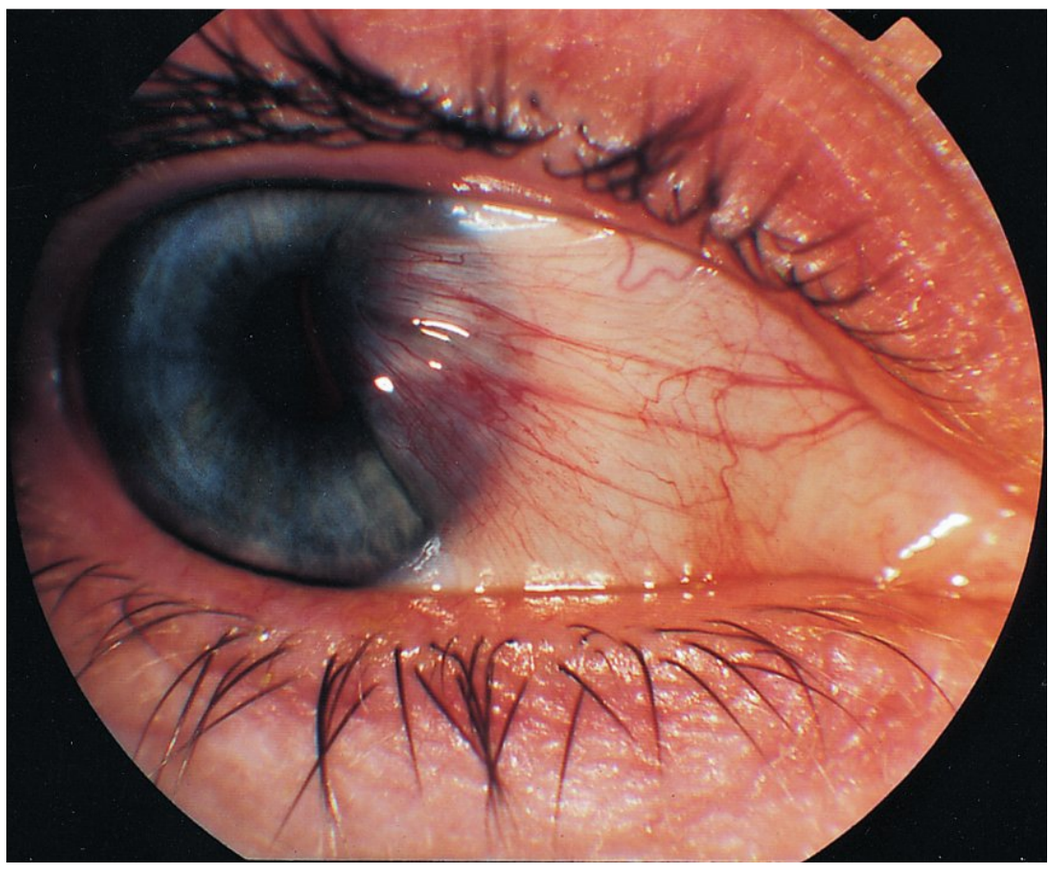
1. A pterygium is a fibrovascular overgrowth of the bulbar conjunctiva typically located in the interpalpebral fissure. It is a common finding among individuals 20 to 40 years of age with exposure to ultraviolet radiation and wind. The incidence is higher in patients living closer to the equator. It occurs more commonly in males than females.
2. A pterygium in its earliest stages is indistinguishable from a pinguecula. A pinguecula is a benign, elevated, yellowish, perilimbal lesion of the interpalpebral fissure. It may arise from degenerative factors similar to pterygia. By definition, however, pingueculae do not involve the cornea. Pingueculae are believed to be precursors of pterygia.
3. A pterygium should be differentiated from a pseudopterygium. Pseudopterygia result from nonspecific inflammation from chemical injuries, trauma, burns, and infections. The resulting injury leads to a fibrovascular, bulbar conjunctival scar that extends over the cornea. A probe may be placed between the body of a pseudopterygium and the globe, whereas it may not be placed between a true pterygium and the globe. In addition, pseudopterygia differ from true pterygia as they may occur outside the interpalpebral fissure.
4. It is also important to distinguish a pterygium from a malignant lesion. Conjunctival intraepithelial neoplasia (CIN) may be mistaken for an atypical pterygium. CIN usually appears in the interpalpebral limbal area. It may appear as a gelatinous elevated lesion with varying degrees of keratinization, as a small elevated vascularized papillomatous lesion, or as a white plaque (leukoplakia). Although it is difficult to differentiate squamous cell carcinoma from CIN, squamous cell carcinoma tends to involve more of the limbal circumference and may be more elevated.
5. A pterygium may be associated with a pigmented iron line at its leading edge, the "Stocker's line"; that is, a nonspecific associated finding with no clinical value.
6. Most pterygia either grow very slowly or enter a quiescent phase. Occasionally, pterygia may either become actively inflamed or grow rapidly and progressively. Epithelial irregularity, opacification of Bowman's layer, and prominent and inflamed vessels may be predictive of an active phase.

TEST INTERPRETATION

Diagnosis is based on typical clinical presentation. Corneal topography is rarely indicated but may be useful in documenting topographic changes and induced astigmatism resulting from a pterygium. Histologic examination reveals subepithelial fibrovascular tissue with disruption of Bowman's layer, increased fibroblasts, and elastoid degeneration of the underlying collagen.

DIAGNOSIS

Pterygium, bilateral.



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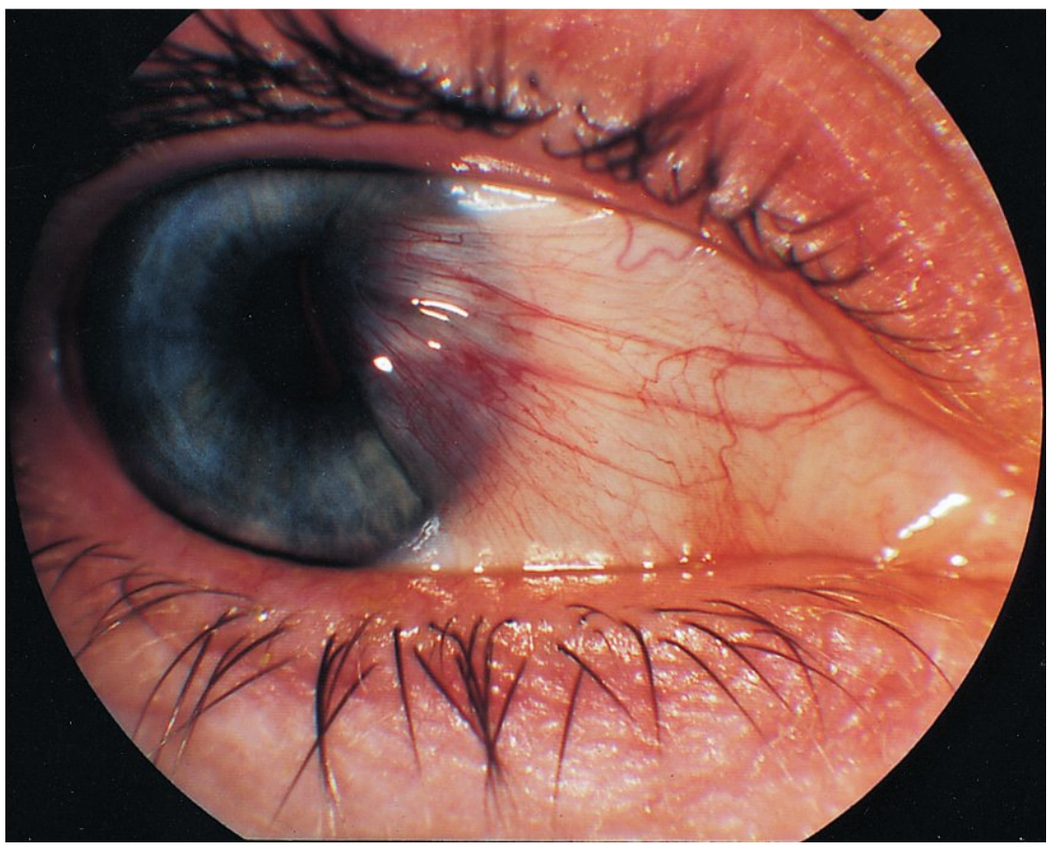

B

FIGURE 4-1 Pterygium. (A) Right eye. (B) Left eye.

MEDICAL MANAGEMENT

A small, nonactive, symptom-free pterygium may simply be observed. A small, minimally inflamed pterygium with mild symptoms may often be managed with frequent use of preservative-free artificial tears or vasoconstrictors. For active exacerbation of symptoms or inflammation, a short course of a mild topical steroid may be useful in controlling the symptoms. Some physicians have suggested that the use of ultraviolet blocking sunglasses may play a role in limiting progressive pterygium growth.

SURGICAL MANAGEMENT

Indications for pterygium excision include interference with vision from progressive growth over the visual axis, induced against the rule astigmatism, unacceptable cosmesis, and severe symptoms. Restriction of extraocular motility has also been reported. However, patients should be counseled on the published recurrence rates, which may be as high as 40%. These recurrence rates tend to be higher for fleshy, actively growing lesions. Recurrent pterygia may also demonstrate more aggressive growth as compared to the primary pterygia. Subsequent removal of recurrent pterygia may also be challenging because of fibrovascular scarring. Several techniques have been reported to diminish the recurrence rates. These include the use of irradiation, application of antimetabolites such as mitomycin-C, and conjunctival autografts. These adjunctive maneuvers may decrease recurrence rates to less than 5%. Complications of mitomycin-C (0.02%) include persistent epithelial defects and scleral necrosis. Therefore, the concentration and duration of mitomycin-C must be titrated to the appearance and aggressiveness of the pterygium and used judiciously to prevent these complications.

A pterygium is usually excised under local, subconjunctival anesthesia. Anesthetic infiltration with lidocaine in the correct plane will result in "tenting" up of the pterygium. This will facilitate the dissection of the pterygium and will provide adequate anesthesia for its removal. Multiple methods exist for pterygium excision. One method involves a 69 Beaver blade and Westcott scissors which are sufficient for undermining the body of the pterygium and anterior lamellar dissection of the corneal component of the pterygium. The pterygium should be sent to an appropriate ocular pathology laboratory for histopathologic examination. Primary conjunctival anastomosis, rotational flaps, and various conjunctival autograft techniques have been used to close the conjunctival defect created by pterygium

excision. Following the surgery, patients may be started on a topical antibiotic 4 times a day for 1 week and a topical corticosteroid tapered according to the severity of the postoperative inflammatory response.

REHABILITATION AND FOLLOW-UP

Follow-up for medically managed pterygia is dictated by the severity of symptoms. If topical steroids are used for inflammatory pterygia or during the postoperative period, earlier follow-up is indicated to assess response and to evaluate the intraocular pressure.

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Case 5

RECURRENT EROSION/ EPITHELIAL BASEMENT MEMBRANE DYSTROPHY

Weldon W. Haw, M.D.

HISTORY

A 35-year-old woman awoke from sleep with sudden onset of unilateral pain, foreign body sensation, lacrimation, photophobia, and blurred vision immediately upon opening her eyes. The patient had a previous history of multiple, similar episodes occurring in either eye. The patient's mother has also been affected with similar episodes. She had no history of prior ocular trauma.

Visual acuity is 20/400 in the involved eye and 20/20 in the fellow eye. Slit-lamp examination of the involved eye revealed a large, discrete area of epithelial sloughing (Fig. 5–1). The edges of the epithelial defect were remarkable for a "heaped up" appearance. No infiltrate was apparent. Fluorescein dye revealed pooling over the epithelial defect. Examination of the fellow eye was remarkable for diffuse, superficial gray-white opacities in a "map" and "dot" configuration (Fig. 5–2).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Onset of symptoms was sudden and noted by the patient upon opening her eyes while awakening. The prior day, the patient had not noticed any premonitory symptoms. This is the classic presentation of recurrent erosion syndrome. As the patient opens his or her eyes, the corneal epithelium that is loosely adherent to the underlying abnormal basement membrane may be pulled off, causing a discrete epithelial defect.
2. Notably, there was no acute, inciting event such as trauma. The epithelium was shed spontaneously. Also, the patient had a history of multiple spontaneous episodes. Thus, the examiner should note that the diagnosis is not a simple corneal abrasion.
3. On examination, discrete roughening of the corneal epithelium is noted with a "sloughed off" appearance. The dislodged epithelium appears to be shed in a single large "sheet." This is also the typical appearance of a recurrent erosion resulting from pathological adherence of the epithelium to the underlying basement membrane. Occasionally, symptoms may have improved by the time the patient is examined as the epithelial changes may resolve rapidly if the defect is small.
4. Recurrent epithelial erosion is usually noted among one of two populations. The first population consists of patients with a prior history of abrading trauma or surgery in the affected eye. The second population consists of patients with an underlying corneal dystrophy. Map-dot-fingerprint dystrophy is the most common, accounting for an estimated 50% of patients with recurrent epithelial erosion syndrome. However, other basement membrane dystrophies may also present with recurrent erosions. These include Meesmann's and Reis-Buckler dystrophies. Anterior stromal corneal dystrophies such as lattice, macular, and granular dystrophies may also cause recurrent epithelial erosion.
5. In order to differentiate between these causes, the examiner should inquire about a past history of corneal trauma or injury and whether

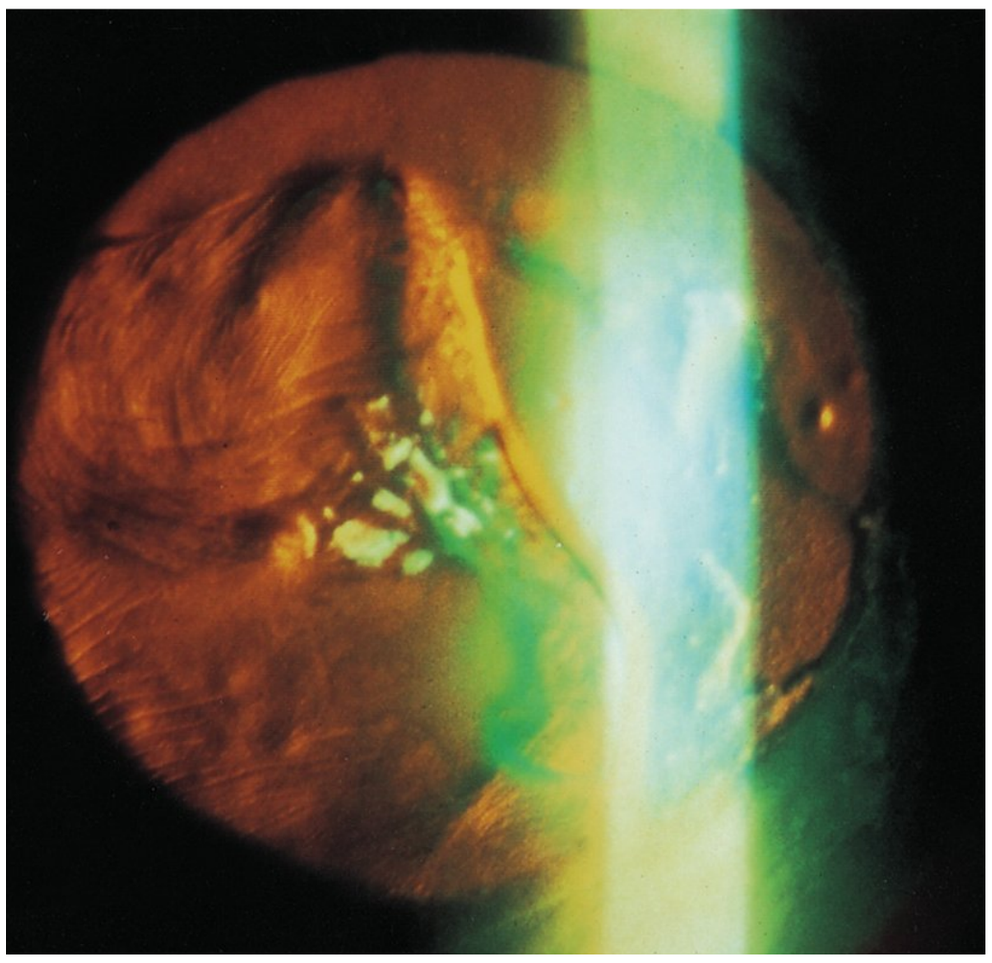

FIGURE 5–1 Recurrent erosion: Red reflex examination demonstrates diffuse sloughing of the epithelium as a large sheet.

recurrent episodes are unilateral or bilateral. Our patient denied a history of corneal injury (although the patient may often forget about a minor ocular injury in the past, as recurrent erosion may occur many years after the initial injury). Our patient also noted that her recurrent episodes occurred in either eye. These historical features suggest an underlying corneal dystrophy rather than a past traumatic event as the underlying etiology.

6. Family history may also be positive in a patient with corneal dystrophies. Our patient had a mother who reports similar episodes. Map-dot-fingerprint dystrophy may be inherited in a dominant pattern, usually with incomplete penetrance.

7. Examination of the contralateral, noninvolved eye is also important as it may reveal evidence of dystrophic changes. Examination of this patient's fellow eye demonstrated a typical pattern of map-dot-fingerprint changes. Fingerprint lines are thin concentric lines arranged in a pattern that resembles the prints on the end of a finger. Thicker geographic lines surrounded by a faint haze are called map lines. Dots are discrete, gray-white circular or oval lesions of varying sizes. These corneal changes may be variable and can change over time within the same individual. These changes may be quite subtle and may require careful examination. Map lines, dots, and fingerprint lines may be identified at the slit lamp with a broad, tangential beam or through a red reflex (Tables 5–1, 5–2).

TABLE 5–1 **Differentiation of Etiology of Recurrent Erosion**

Traumatic	Map-dot-*fi*ngerprint
History of corneal trauma/injury in affected eye	No history of trauma
Unilateral recurrent episodes	May be bilateral recurrent episodes
No family history	May have positive family hx (autosomal dominant with incomplete penetrance)
Contralateral eye—normal examination	Contralateral eye—may have evidence of map-dot-fingerprint changes

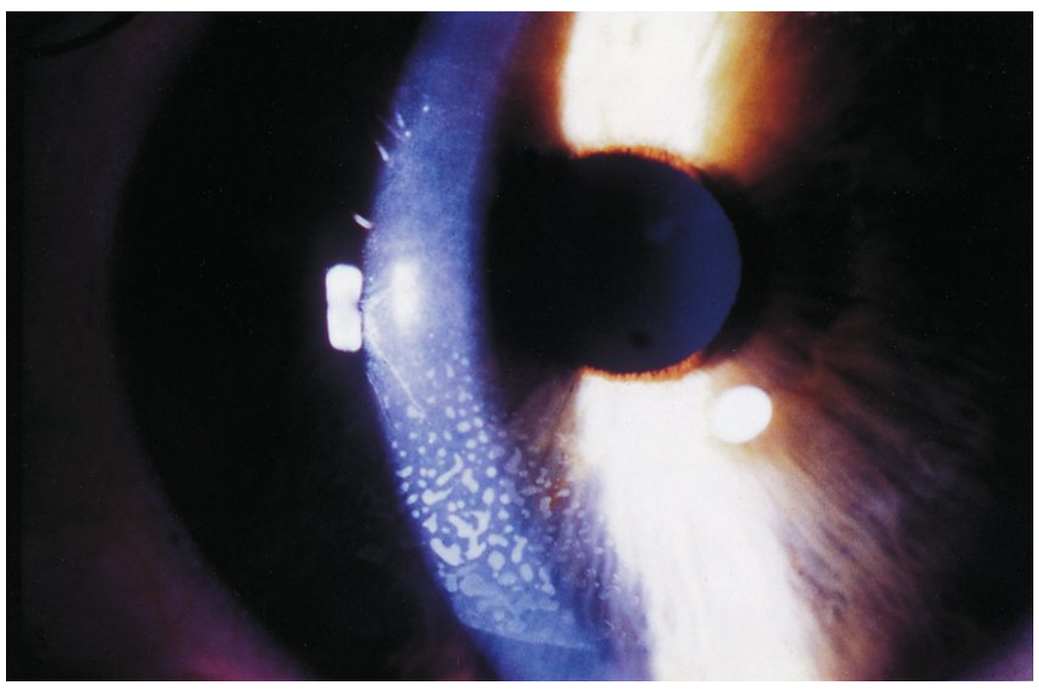

FIGURE 5–2 Epithelial basement membrane dystrophy: Careful slit-lamp examination reveals superficial gray-white opacities characteristic of "map" and "dot" changes.

TABLE 5–2 **Summary of Epithelial Basement Membrane Dystrophy**

Most common corneal dystrophy
Estimated 2% of population may have dystrophy
May represent an estimated 50% of recurrent erosions
Autosomal dominant—female predominance
Map lines, fingerprint lines, and dots

TEST INTERPRETATION

Diagnosis is made by careful slit-lamp examination of the involved and fellow eyes. The ocular and family history may also be useful. No ancillary tests are required for diagnosis.

DIAGNOSIS

Recurrent epithelial erosion syndrome, basement membrane dystrophy type.

MEDICAL MANAGEMENT

Medical management during the acute stage is directed at safely promoting epithelial healing while maximizing patient comfort. The application of a prophylactic topical antibiotic ointment in conjunction with a pressure patch for 24 to 48 hours may achieve both of these goals. Cycloplegia may also be useful in relieving discomfort for those patients with a significant associated anterior chamber reaction or ciliary spasm. Some clinicians have recommended the use of a soft bandage contact lens for 2 or more months to facilitate epithelial readhesion. However, the use of a contact lens may lead to complications of a "tight lens syndrome" or secondary infectious keratitis.

SURGICAL MANAGEMENT

In more severe or recurrent cases, it may be necessary to pursue more aggressive therapeutic interventions. These include the use of total epithelial debridement, anterior stromal micropuncture, or excimer laser phototherapeutic keratectomy (PTK).

Epithelial debridement is most appropriately performed during the acute phase and is done by gently scraping the edge of the epithelial defect with a moist Q-tip® or cellulose sponge under topical anesthesia. Performing this procedure during the acute phase is appropriate as it may cause considerable ocular discomfort. The remaining involved epithelium may then be peeled off with a nontoothed forceps. The involved eye is then managed as described above (antibiotic ointment, patch, or bandage contact lens). Since epithelial basement membrane dystrophy is a diffuse disease, gentle epithelial debridement should be performed over the entire surface of the cornea. Bowman's membrane should not be violated as this may result in subepithelial scarring. Following this procedure, patients may remain symptom free for 1 or 2 years. However, recurrences are possible.

Anterior stromal micropuncture involves making between 15 and 25 anterior stromal micropunctures with a bent 25-gauge needle. This induces a cicatricial adhesion between the epithelium and anterior stroma. This technique is most useful in patients with posttraumatic recurrent erosions localized outside the visual axis. Following anterior stromal micropuncture, topical antibiotic ointment, cycloplegia, and a pressure patch are applied.

The newest development in the management of recurrent erosions involves the use of the excimer laser in a procedure labeled PTK or phototherapeutic keratectomy. This procedure involves removing the epithelium either manually or by laser scrape and subsequent superficial photoablation of the cornea. The entire cornea should be treated in patients with underlying anterior corneal dystrophies. This wide superficial ablation is particularly useful in the treatment of an underlying anterior corneal dystrophy associated with significant visual impairment due to scarring or recalcitrant, recurrent erosions. Initial studies on PTK for recurrent erosion syndrome are promising. Complications of excimer laser PTK include delayed corneal wound healing and refractive changes.

REHABILITATION AND FOLLOW-UP

Daily follow-up until resolution of the epithelial defect is recommended. After the resolution of the epithelial defect, it may be important for patients with recurrent epithelial erosions to maintain adequate lubrication with nonpreserved artificial tears 4 to 8 times per day and with artificial tear ointment prior to bedtime. The lubrication

may prevent the lid from applying traction to epithelium loosely adherent to the underlying basement membrane. In addition, hypertonic solutions such as 5% sodium chloride have the theoretical advantage of osmotically drawing fluid from the epithelium and promoting adherance to the underlying basement membrane. Thus, 5% sodium chloride drops during the day and 5% sodium chloride ointment prior to bedtime may be useful as an alternative to artificial tears for 3 or more months following the acute episode.

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Case 6

FUCHS' CORNEAL DYSTROPHY

Matthew R. Jones, M.D.

HISTORY

A 60-year-old woman presented with a history of slowly progressive loss of vision in the left greater than the right eye. Initially her vision was worse upon awakening and gradually cleared as the day went on; more recently, however, her vision remained poor throughout the day.

Examination revealed corrected visual acuities of 20/200 in the right eye and counting fingers at 4 feet in the left eye. Intraocular pressure was 14 mm Hg in each eye. Slit-lamp examination of the cornea revealed central microcystic epithelial edema and stromal edema with folds in Descemet's membrane in the left greater than the right eye (Fig. 6–1). Corneal guttatae and endothelial pigmentation extended over the central portion of the cornea in both eyes. The anterior chamber was deep and quiet and the iris was normal in both eyes. Moderate nuclear sclerotic cataracts were present bilaterally, and dilated fundus examination revealed normal posterior poles through a hazy view. B-scan ultrasonography of the posterior poles was unremarkable.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Corneal edema can be divided into congenital and acquired causes. Congenital causes include dystrophies such as posterior polymorphous dystrophy, congenital hereditary endothelial dystrophy (CHED), congenital glaucoma, and forceps injury. Acquired causes include pseudophakic/aphakic bullous keratopathy, Fuchs' corneal dystrophy, angle closure glaucoma, herpes simplex stromal keratitis, varicella zoster keratitis, iridocorneal endothelial (ICE) syndrome, posterior polymorphous dystrophy, corneal hydrops (as in keratoconus), and trauma.
2. Endothelial dysfunction causes secondary stromal edema that is worse in the morning. Eyelid closure while sleeping decreases surface evaporation and maximizes corneal edema upon awakening.
3. Corneal edema is a necessary component of Fuchs' corneal dystrophy. Patients with guttata but without corneal edema are considered to have "endothelial dystrophy."
4. In addition to complaints of decreased vision, patients with advanced Fuchs' dystrophy often complain of episodes of sharp pain due to rupture of epithelial bullae. Clinical examination readily distinguishes these patients from those with recurrent erosion syndrome, who may have similar complaints.

TEST INTERPRETATION

The diagnosis of Fuchs' corneal dystrophy is usually made on the basis of the classic slit-lamp findings of epithelial and stromal edema, endothelial guttata, and endothelial pigmentation, all of which are most prominent in the central cornea.

Ultrasonic pachymetry can sometimes be helpful in detecting early subclinical corneal thickening in endothelial dystrophy. This information is useful in determining the likelihood of corneal decompensation following cataract extraction. A general rule of thumb is to proceed with cataract extraction alone if central pachymetry is less than 600 microns, and to proceed with combined penetrating keratoplasty (PK) and cataract extraction if central pachymetry is greater than 600 microns. This rule of thumb is

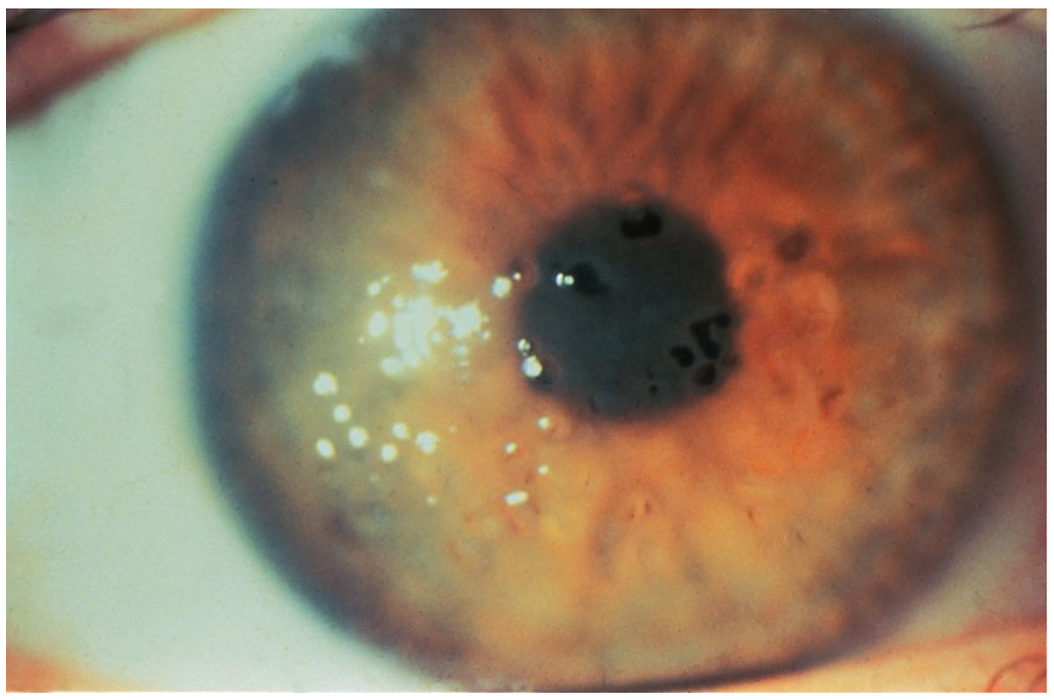

FIGURE 6–1 Advanced Fuchs' corneal dystrophy with severe stromal and epithelial edema. (Courtesy of Peter R. Laibson, M.D., Philadelphia, PA)

only loosely applicable, however, as trauma to the endothelium during cataract extraction varies greatly depending upon the degree of skill of the surgeon, as well as upon the density of the nucleus.

Specular microscopy can be useful in further elucidating the status of the endothelium in early Fuchs' corneal dystrophy. Guttata are seen as dark spots within the mosaic of endothelial cells. Increased variability in cell shape (pleomorphism) and size (polymegathism) are typically present, and overall cell density is diminished when compared to normal. As Fuchs' corneal dystrophy progresses, specular microscopy becomes more difficult to perform due to increasing corneal edema.

DIAGNOSIS

1. Fuchs' corneal dystrophy OU.
2. Cataract OU.

MEDICAL MANAGEMENT

In endothelial dystrophy, the patient is usually asymptomatic and no treatment is necessary. In early Fuchs' corneal dystrophy, "morning blur" secondary to corneal edema can be reduced through the use of hypertonic sodium chloride (eg, NaCl 5%) drops. Initially, these may be required only upon awakening, but as the disease progresses they may be required throughout the day. Hypertonic sodium chloride ointment at bedtime may also reduce morning blur. Another approach to reducing corneal edema involves using a hair dryer to dehydrate the cornea. The hair dryer is placed on the lowest setting and is directed toward the cornea at arm's length for several minutes. Eventually progressive endothelial failure overwhelms such measures and PK is necessary to rehabilitate vision.

SURGICAL MANAGEMENT

When corneal edema advances to the point where visual function is significantly affected, PK is indicated. As visual rehabilitation after PK can be as long as 6 to 12 months after surgery, the patient will, for a period of time, be dependent on the less involved "better" eye for visual function in the postoperative period. Therefore, when indicated, PK should be performed as soon as possible in the worse eye, while the patient still has functional vision in the better eye.

PK is performed using standard techniques. Simultaneous cataract extraction and intraocular lens (IOL) placement should be strongly considered if any significant lenticular opacity is present, as cataracts tend to worsen after PK. Furthermore, cataract extraction after PK will traumatize the endothelium and shorten graft survival. The determination of the appropriate IOL power is problematic in these patients, as postoperative keratometry cannot be predicted with great accuracy. Variations of surgical technique, the amount of oversizing of the graft, wound healing, the keratometric power of the recipient corneal rim and donor button all contribute to the final power of the grafted cornea. Ultimately, each surgeon must develop his or her own algorithm for determining IOL power based on experience.

Suturing techniques are determined by surgeon preference and the degree of preoperative corneal edema. In cases where diffuse limbus-to-limbus edema exists, a 16-bite interrupted pattern allows for individual suture removal in the early postoperative period if necessary for suture

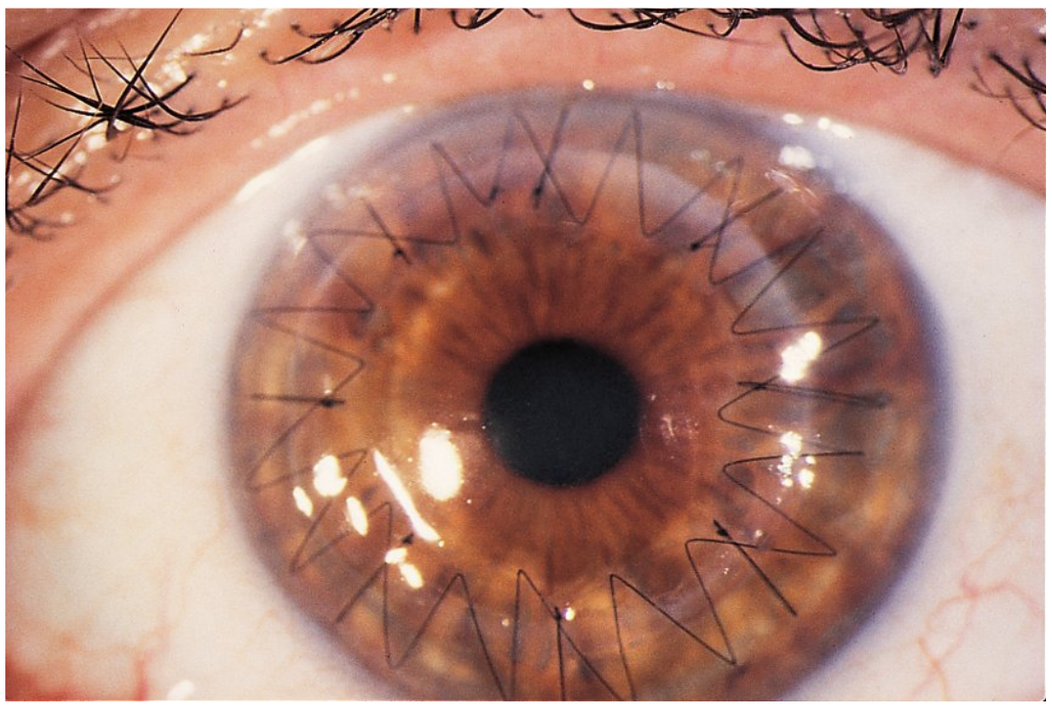

FIGURE 6–2 Six weeks after penetrating keratoplasty.

loosening or vascularization. If the peripheral cornea is nonedematous, premature suture loosening is less of a concern, and a running or combined running–interrupted suture technique can be considered (Fig. 6–2).

REHABILITATION AND FOLLOW-UP

Postoperatively topical antibiotic and corticosteroid drops are prescribed. Ointments and/or nonpreserved artificial tears can be employed to rehabilitate the ocular surface as needed. The antibiotics are discontinued after 1 week. Topical steroids are slowly tapered over 6 to 12 months. The surgeon should minimize the number and frequency of preserved topical eye drops to prevent surface toxicity. Postoperative astigmatism is managed initially by selective suture lysis and/or running suture adjustment, guided by topography. Glasses or rigid gas permeable contact lenses are prescribed when appropriate. Occasionally, high degrees of astigmatism will require surgical intervention such as astigmatic keratotomy, compression sutures, wedge resection, or rarely, repeat PK. Laser in situ keratomileusis (LASIK) may be useful in selected cases with large refractive errors. LASIK should be performed only after all sutures have been removed and in the presence of a secure wound.

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Case 7

KERATOCONUS

Stephen U. Stechschulte, M.D.

HISTORY

A 19-year-old man presents with complaints of gradual decreased vision in his right eye over the past year. He has worn glasses and contacts for 9 years and despite a recent change in his prescription and new contact lenses, he doesn't "see clearly." He denies any trauma, surgery, or recent eye infection. He reports his vision in both eyes was clear as a child and young adult and until last year was correctable to 20/20. His past medical history is significant for seasonal allergies. He reports allergies to penicillin and uses occasional acetaminophen. He denies any family history of eye disease.

The patient is healthy with a negative review of systems. He is wearing contact lenses. On examination his corrected visual acuity with contacts is 20/50 OD and 20/25 OS. Manifest refraction OD, −2.00 −7.50 × 60, only corrects him to 20/100. His manifest refraction OS is −2.25 −1.00 × 28, which corrects his vision to 20/40. There is no afferent pupillary defect. On slit-lamp examination the lids and lashes are normal. He has an adequate tear lake and tear breakup time. The corneas are clear and with no evidence of scarring or inflammation. The anterior chamber is quiet, the lens clear, and the posterior pole viewed after dilation is normal with a healthy foveal light reflex. The cup-to-disc ratio is 0.3 bilaterally and the intraocular pressures are 12 and 14, respectively.

On careful inspection of the cornea, mild thinning is evident centrally, Vogt's striae are visible on Descemet's membrane (Fig. 7–1), and a partial Fleischer ring is visible more prominently with cobalt blue illumination. Ultrasound pachymetry measures the corneal thickness at 450 micrometers in the right eye and 480 micrometers in the left. Computerized topography with the EyeSys system showed steepening inferiorly in the right eye (Fig. 7–2). A hard contact lens overrefraction corrects the vision to 20/30 in the right eye.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Individuals who present with unexplained visual deterioration must be examined carefully with attention to the cornea, anterior chamber, lens, nerve, and macula. Unexplained visual loss or deterioration must be explained by the examining ophthalmologist, otherwise subtleties such as mild cystoid macular edema and pars planitis, a slightly swollen nerve and pseudotumor cerebri, or corneal thinning and early keratoconus will be missed.
2. There are few conditions that cause decreased vision in a young healthy patient secondary to astigmatism, ectasia, and thin corneas.
   a. Pellucid marginal degeneration may cause peripheral thinning in a quiet uninflamed eye. It is a rare, idiopathic, bilateral condition and results in thinning inferiorly with clear overlying stroma. It can produce large amounts of irregular astigmatism usually correctable with spectacles or contacts. Topography may show a bow-tie configuration.
   b. Terrien's marginal degeneration is the most common cause of peripheral thinning. It is usually seen in patients older than 40 years and causes gradual thinning and ectasia beginning superiorly. This thinning is often accompanied by lipid deposition and pannus formation. If the ectasia becomes severe enough and uncorrectable with contact lenses, focal lamellar keratoplasty may be indicated.
   c. Keratoglobus is a rare bilateral condition consisting of diffusely thinned corneas with ectasia and enlarged corneal diameter. It may be seen in association with

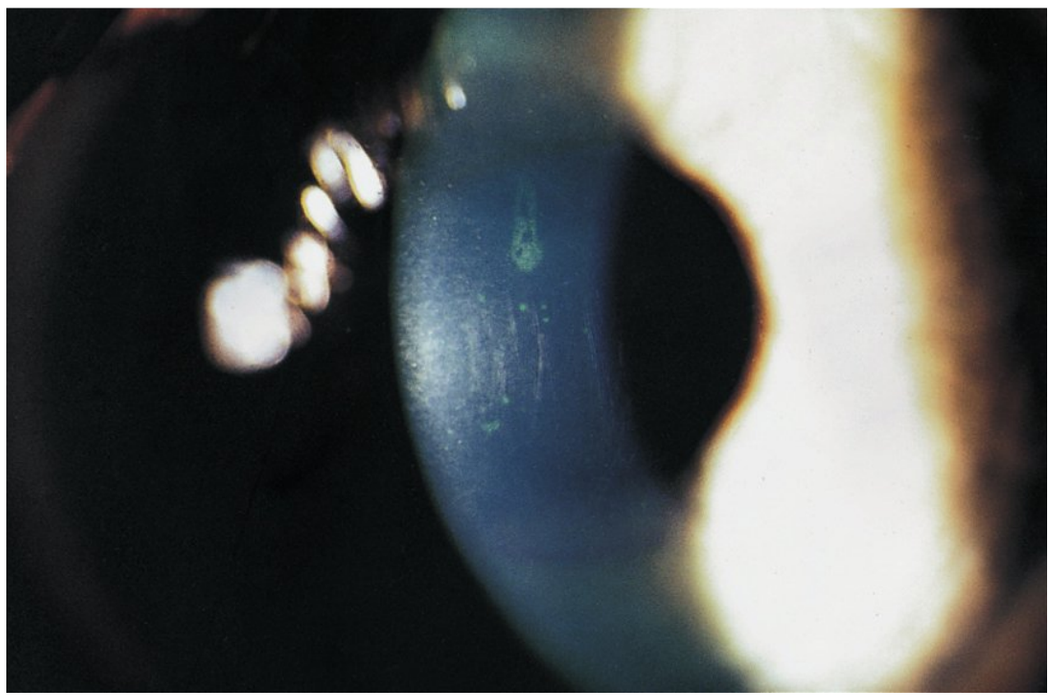


FIGURE 7–1 Slit-lamp photograph of the right eye showing fine striae of Descemet's membrane, Vogt's striae, at the thinnest point in the right cornea.

connective tissue disorders. Patients with keratoglobus are prone to hydrops and perforation. Because the most pronounced thinning may be peripheral, surgical management is challenging and may require limbus-to-limbus lamellar keratoplasty or epikeratoplasty.

d. Rheumatoid arthritis may cause peripheral ulcerative keratitis in association with scleritic processes. Central thinning, however, seen in an otherwise quiet eye, is thought to be secondary to keratoconjunctivitis sicca or upregulation of collagenases.

TEST INTERPRETATION

The major diagnostic consideration in this patient stems from unexplained visual loss in what at first appears to be a normal exam. Careful examination reveals few striae in Descemet's membrane and central thinning.

The cornea is normally thickest nasally and inferiorly and thins centrally to approximately 550 micrometers. Corneal thickness is best measured with an ultrasound pachymeter. Using sound waves calibrated to travel in the cornea, ultrasound pachymetry gives reliable, reproducible measurements. This patient's right cornea measured 450 microns, outside the normal range of central corneal thickness.

Cobalt blue illumination highlights iron deposition in the epithelium, which frequently occurs over irregular surfaces or a change in curvature. In keratoconus hemosiderin accumulates in the epithelium around the base of a cone.

Computer-assisted videokeratoscopy or topography is one of the most helpful tests when corneal abnormalities are detected or suspected. Computerized topography most commonly employs a placido disk nose cone and a computer-based keratoscope to capture the image and rapidly analyze the data. The computer examines topographic data points across the placido rings and generates a color-coded map that corresponds to corneal curvature. In this case the asymmetry between the curvature above and below the horizontal meridian and the difference in cornea power between the right and left eyes are highly suggestive of keratoconus.

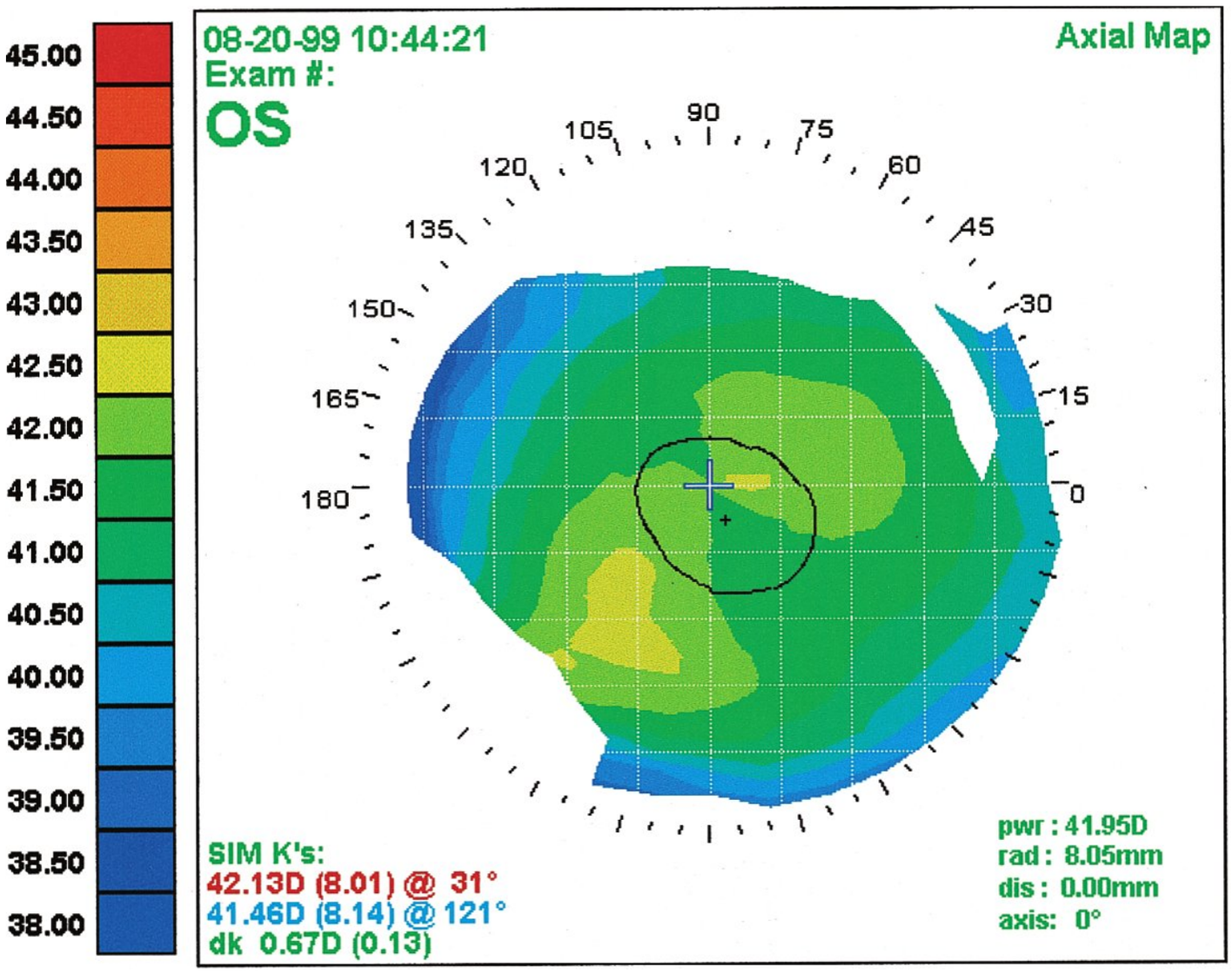
All of the findings taken together indicate that this patient has unilateral keratoconus.

DIAGNOSIS

Keratoconus in the right eye with no signs in the left eye.

MEDICAL MANAGEMENT

Keratoconus is a noninflammatory corneal ectasia of unknown etiology. Its well-described findings include thinning, iron deposition in the epithelium, and breaks in Bowman's membrane. The incidence of keratoconus is approximately 1 in 2000 and is almost always bilateral. Cases that appear to be unilateral will often progress over time to include the other eye. Most patients, as in the case here, can be managed medically with glasses or contact lenses. If spectacle or soft contact lens correction fails to yield good visual results then a rigid gas permeable lens or a toric lens may be used to maximized visual acuity. When seen soon after diagnosis almost all patients with keratoconus can be treated successfully with contact lenses.



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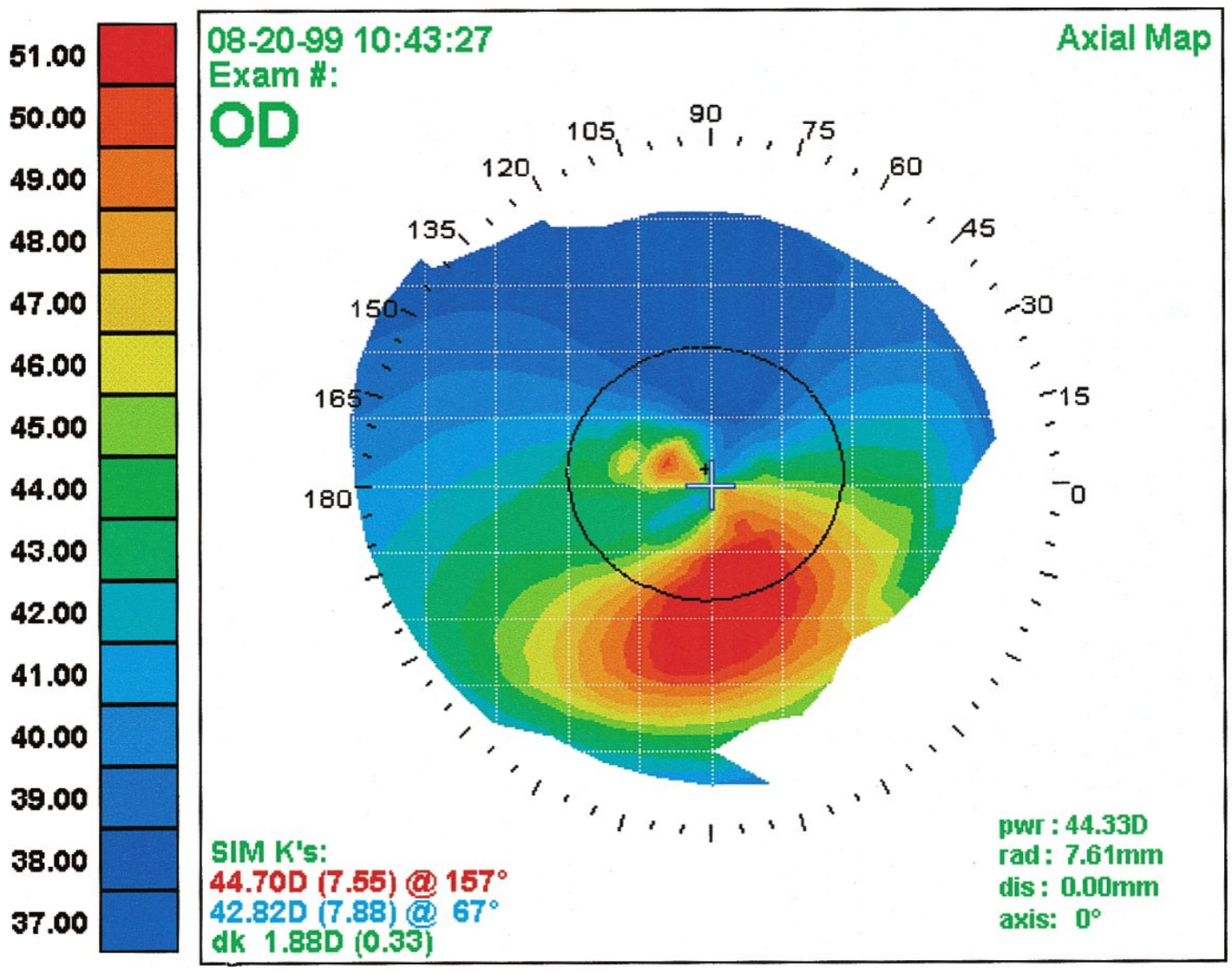

B

FIGURE 7–2 (A) Computerized videokeratoscopy using the EyeSys system demonstrates in the left eye inferior steepening and superior–inferior dioptric asymmetry. (B) The right eye appears normal.

This patient presented with mild keratoconus and was not correctable with glasses or soft contacts but was able to see 20/30 with rigid gas permeable lenses. The probability of avoiding surgical intervention 20 years after diagnosis is greater than 80%. Were this patient not able to see well with hard contacts and if the thinning were to progress, surgical treatment might be necessary.

SURGICAL MANAGEMENT

There are two possible methods for surgical correction of keratoconus, penetrating or lamellar keratoplasty. Penetrating keratoplasty is the procedure of choice and has several advantages. In the United States and many countries with active eye banks, there is a surfeit of healthy donor corneas making

penetrating keratoplasty an elective procedure. Surgical techniques and newer sutures have helped make penetrating keratoplasty a successful operation and particularly so for patients with keratoconus. Five-year success rates for penetrating keratoplasty in patients with keratoconus approach 95%. Nonetheless, after penetrating keratoplasty, patients are forever at risk for rejection and must be followed closely. Patients are treated with topical corticosteroids, which are tapered over time. Other complications include residual astigmatism, myopia, glaucoma, cataract, and mydriasis.

An alternative to penetrating keratoplasty, lamellar keratoplasty, has some advantages. Because Descemet's membrane and the endothelium are left intact, the eye is structurally more secure both during and after surgery. Importantly, the patient is free from most problems associated with transplant rejection and the need for long-term topical medication. Technically, however, lamellar keratoplasty is a challenging procedure when the goal of surgery includes maximizing visual acuity.

REHABILITATION AND FOLLOW-UP

This patient has done well in a rigid gas permeable contact for the right eye. One would expect the left eye to eventually show changes consistent with keratoconus.

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Case 8

MICROBIAL KERATITIS

V. Nicholas Batra, M.D.
Richard L. Abbott, M.D.

HISTORY

A 39-year-old woman with a history of contact lens wear presented complaining of decreased vision, pain, photophobia, redness, and discharge in her left eye for the previous 48 hours.

Visual acuity was 20/20 OD and 20/CF 3'OS. Examination of the right eye was unremarkable. Left eye external examination showed mild lid and conjunctival edema, a papillary conjunctival reaction, and a purulent discharge. The corneal stroma showed a central, dense, gray-white, necrotic-appearing infiltrate with loss of the overlying corneal epithelium (Fig. 8–1). The edges of the infiltrate were indistinct and extended beyond the stromal opacity. The anterior chamber showed 2+ cell and flare and a 1-mm hypopyon. The iris, lens, and retinal examination were unremarkable.

Subsequent examination 4 days later showed vision of 20/20 OD and 20/400 OS. Left eye examination showed minimal lid and conjunctival edema and scant purulent discharge. The cornea showed a condensing gray-white opacity with defined borders. The corneal epithelium was filling in the edges of the opacity. Examination 11 days after initial presentation showed vision of 20/20 OD and 20/400 OS. The gray-white stromal opacity had condensed further with continued corneal re-epithelialization (Fig. 8–2). Subsequent examination 1 month later showed vision of 20/20 OD, 20/50 OS, and a central corneal stromal opacity (Fig. 8–3).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. In a patient with a history of contact lens wear and the above symptoms and clinical findings, the likely diagnosis is microbial bacterial keratitis. It is important to identify risk factors that predispose to bacterial corneal ulcers. Contact lens wear was found to be a predisposing factor in 56% of patients in the Olmstead County study. This was followed by ocular trauma (25%), lid dysfunction, conjunctival dysfunction, and lacrimal dysfunction.

2. Differentiation from other causes of keratitis (such as viral, protozoal, inflammatory, hypersensitivity, or immune-mediated keratitis) can be challenging. The history of contact lens wear, lack of epithelium overlying the infiltrate, central site of the ulceration, and the presence of a supporative reaction are all factors that point to a likely diagnosis of bacterial keratitis in this patient.

3. Bacteria that cause microbial keratitis can be divided into types that typically affect different clinical conditions of the cornea. Staphylococcus, Streptococcus, Pseudomonas, Enterobacteriacae, Moraxella, and Kleibsiella have all been isolated from healthy corneal tissue. Staphylococcus aureus, Staphylococcus epidermidis, alpha-hemolytic and beta-hemolytic Streptococcus, Pseudomonas, and Proteus have more commonly been isolated from compromised corneas. Pseudomonas, Staphylococcus, and fungi have been isolated from pediatric corneas.

4. Some bacteria produce a characteristic clinical appearance. Pseudomonas typically has a yellowish-green discharge that sticks to the corneal surface. The gram-positive cocci, such as Staphylococcus aureus and Streptococcus pneumoniae, often produce round or oval ulcers with distinct borders that are gray-white and dry in appearance. There is frequently a severe anterior chamber reaction that may include a sterile hypopyon. Gram-negative rods usually produce a wet, soupy

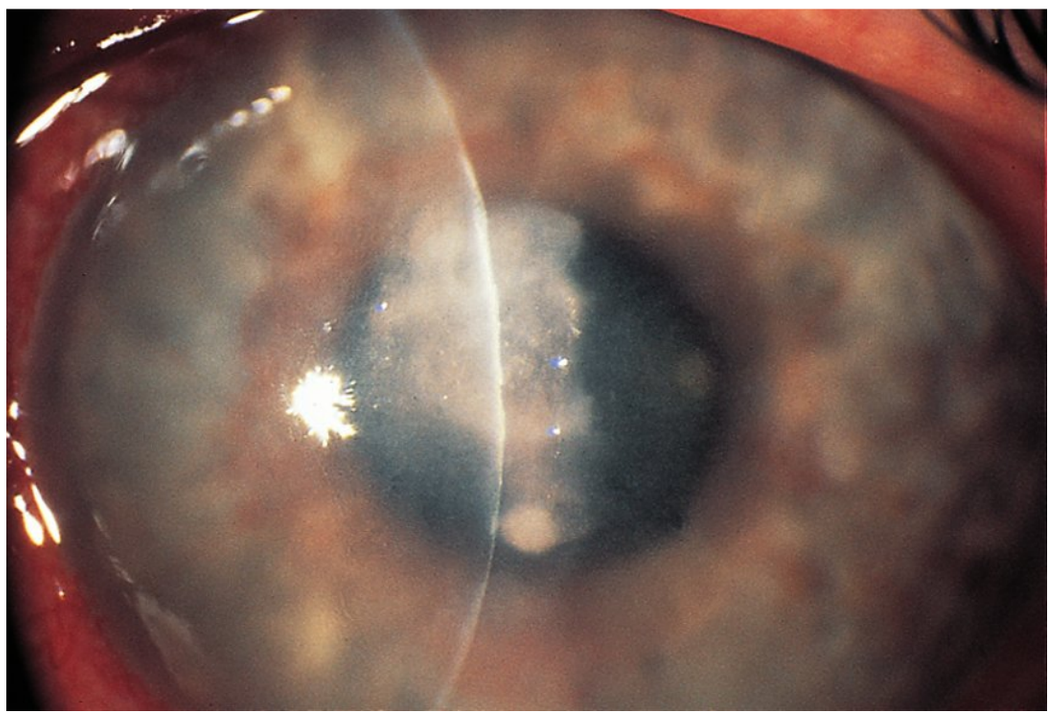

FIGURE 8–1 Corneal stroma with a central, dense, gray-white, necrotic-appearing infiltrate and loss of the overlying corneal epithelium.

infiltrate that may spread to involve the entire cornea and typically is associated with a severe anterior chamber reaction with hypopyon formation.

5. When bacterial keratitis is suspected, appropriate laboratory workup is indicated. This usually consists of scraping the ulcer margins and sending the specimen for bacterial (and in some cases fungal) cultures.

TEST INTERPRETATION

The diagnosis of bacterial keratitis is generally made by taking a thorough history and performing a clinical examination. Accurate laboratory

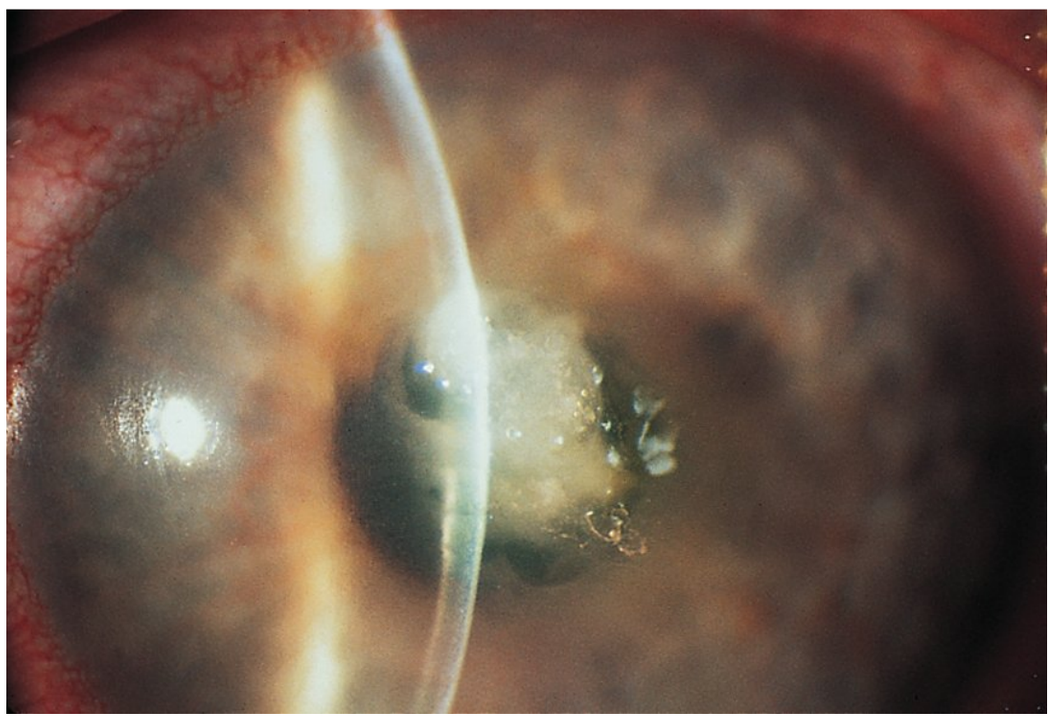

FIGURE 8–2 Condensation of gray-white stromal opacity and partial corneal re-epithelialization.

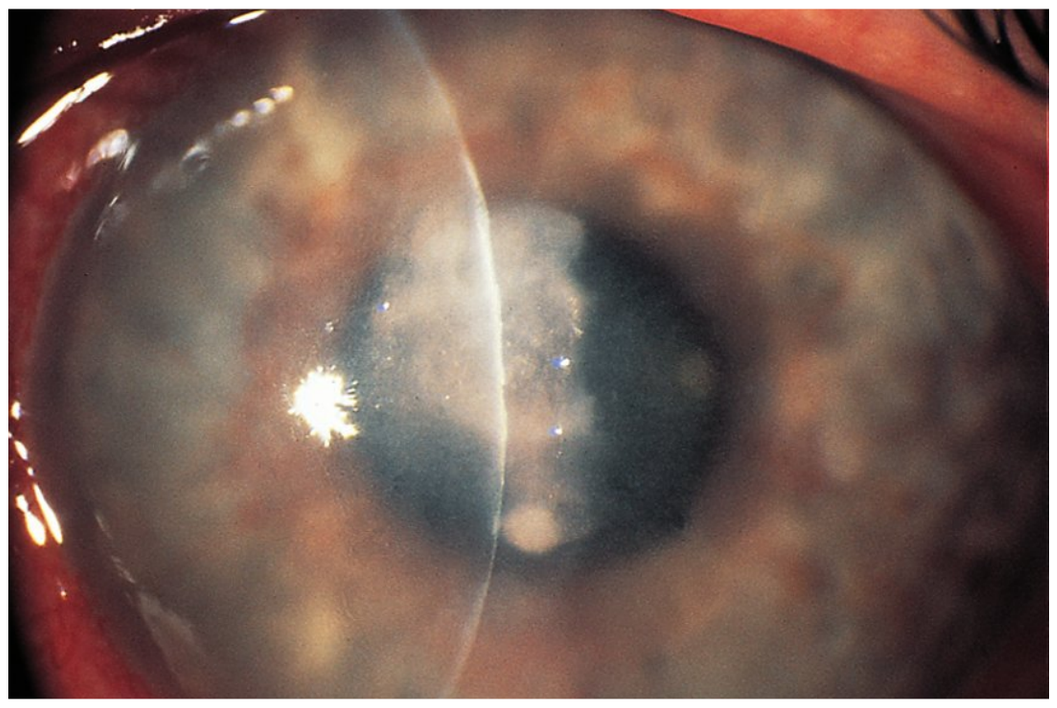

FIGURE 8–3 Residual central corneal stromal opacity.

studies can aid in proper diagnosis and appropriate antimicrobial therapy. Culture swabs from the lids and conjunctivae of both eyes should be plated directly onto culture media. Calcium alginate swabs that contain inert materials are preferable to cotton-tipped applicators that contain fatty acids, which may inhibit bacterial growth.

The cornea of the affected eye should then be anesthetized and a flame-sterilized spatula (Kimura) or calcium alginate swab used to take a corneal specimen. Multiple scrapings from affected areas should be performed to increase the yield of live organisms. The specimens should be plated on blood agar, chocolate agar, Sabourad's agar, Thioglycolate broth, brain-heart infusion broth, and glass slides. The bacteria typically begin to grow within 24 to 48 hours and sensitivities to antimicrobial agents can be examined usually 24 hours later. In this case the cultures grew out a Streptococcus species.

DIAGNOSIS

Streptococcal corneal ulcer left eye.

MEDICAL MANAGEMENT

The prognosis for a central Streptococcal corneal ulcer is fair. The mainstay of treatment is

antimicrobial therapy consisting of broad-spectrum topical fortified antibiotics or topical antibiotic therapy tailored to the Gram stain. Caution should be exercised when the Gram stain is used alone as there has been only a 60% correlation between the Gram stain and the organisms that are later cultured. The severity of the keratitis should be used as a guide to the intensity and frequency of treatment. Topical fortified antibiotics or fluoroquinolones may be used on peripheral ulcers. Central ulcers usually require a combination of topical fortified antibiotics and fluoroquinolones. Severe cases, including imminent perforation, may require subconjunctival injection of antibiotics as well as hospitalization for IV antibiotics.

Antibiotic choices include aminoglycosides, cephalosporins, fluoroquinolones, penicillins, synthetic penicillins, erythromycin, bacitracin, polymyxin, chloramphenicol, vancomycin, tetracycline, sulfonamides, and rifampin. Typical therapy includes gram-positive and gram-negative coverage with two topical fortified agents every hour for 36 hours. Often a fluoroquinolone may be substituted for one of the fortified antibiotics. If there are signs of clinical improvement then the frequency of the antibiotic may be reduced. After 48 to 72 hours coverage may be switched to every 3 to 4 hours and to regular-strength drops after 96 hours. Once sterility has been achieved, adjunctive agents such as corticosteroids, cycloplegics, and enzyme inhibitors may also be used. Corticosteroid drops may be cautiously started 72 hours after antibiotic therapy has begun in selected cases. Their role is to reduce damage produced by invading polymorphonuclear leukocytes and their destructive enzymes and to decrease visual loss from postinflammatory scarring. Corticosteroids should be avoided in cases of pseudomonas and gram-negative infection until the cornea is sterilized. Subconjunctival injections of antibiotics can be used in patients with suboptimal compliance. Unfortunately they can be associated with pain and scarring of the conjunctiva.

Other therapeutic modalities include collagen shields and bandage contact lenses. Collagen shields can be impregnated with a variety of antibiotic solutions. They can then deliver antibiotics in a sustained release fashion usually over a 24-hour time period. They can be useful in cases of noncompliance. Unfortunately, they can be dislodged and lost. Bandage contact lenses may be used in nonhealing epithelial defects once the cornea is sterile or as a temporary measure to prevent total chamber collapse as the patient awaits definitive surgical intervention.

SURGICAL MANAGEMENT

Surgical management should be reserved for cases of medical failure. Structural integrity of the anterior segment should be maintained with surgical glue if possible. If perforation has occurred then a lamellar patch graft or penetrating corneal transplant can be performed to retain the structural integrity of the globe. Every attempt to sterilize the cornea should be made prior to surgical repair in order to prevent reinfection of the graft. A conjunctival flap is not indicated in cases of perforation.

Corneal scarring is a common sequela of bacterial keratitis. When in the central visual axis, it can lead to significant ocular morbidity. Contact lenses can be used to regularize the corneal surface. Phototherapeutic keratectomy (PTK) can be used to remove anterior stromal scarring. Penetrating keratoplasty (PKP) can be used to remove deep central scarring. As much healthy corneal tissue should be preserved as possible.

REHABILITATION AND FOLLOW–UP

Once bacterial keratitis has been successfully treated the patient should have any risk factors for the development of recurrence evaluated and corrected if possible. Discontinuation of contact lenses or modification of wearing habits may be suggested. Lid, lacrimal, or conjunctival dysfunction should be treated. In cases of

severe scarring surgical modalities may be considered.

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Case 9

KERATOCONJUNCTIVITIS SICCA—DRY EYE

Renato T.F. Pires, M.D.
Scheffer C.G. Tseng, M.D., Ph.D.

HISTORY

This 56-year-old man with a history of diabetes mellitus and a chief complaint of ocular irritation in both eyes was referred by an ophthalmologist for a second opinion under the impression of an unstable ocular surface due to dry eye in his right eye. He complained of burning, foreign body sensation, sandy-gritty feeling, and redness, more in his right eye. These symptoms were worse in the morning and also in the later part of the day and made him unable to read or drive comfortably. He still preserved emotional lacrimation. He stated that he slept on his stomach, preferring his right side.

While taking the history, it was noted that his blink rate was reduced in both eyes. His best-corrected visual acuity was 20/40 in the right eye and 20/20 in the left eye. External examination did not reveal features suggestive of rosacea. There were no palpable preauricular nodes. The lid position and relationship to the globe were normal, while the lid tension was loose and floppy. Lid tension was graded as 2+ in the right eye and 1+ in the left eye.

On slit-lamp examination, the meibomian secretion was normal as its fluid appeared clear and was easily expressible. The height of the tear meniscus was low, ie, less than 0.3 mm in the upper and lower lids of both eyes. Both tarsal and bulbar conjunctivae were diffusely injected with the tarsal conjunctiva showing a mixed papillary and follicular response. Ocular sensitivity was markedly reduced as measured by a Cochet-Bonnet anesthesimeter. The tear break-up time was less than 2 seconds (abnormal) each eye. Fluorescein showed superficial punctate staining and rose bengal staining was positive over the exposure zone, more prominent in the right eye. Intraocular pressure was 15 and 16 mm Hg, in the right and left eye, respectively. Fluorescein clearance test (FCT) revealed marked delayed dye clearance and decreased tear secretion (Fig. 9–1) in both eyes. The lens and the fundus were unremarkable in both eyes.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

Anatomically, the ocular surface comprises corneal and conjunctival epithelia spreading from the upper to the lower eyelid mucocutaneous border. Physiologically, to maintain the ocular surface health it is important to have a stable preocular tear film, which requires functioning external adnexae and neuroanatomic feedback control. Ocular surface epithelia and the preocular tear film work as a unit to provide clear vision, maintain comfort, and serve as the first line of defense against microbial infections during open eye conditions (for a review, see Tseng and Tsubota, 1997; Table 9–1).

The preocular tear film is composed of lipids, electrolyte- and protein-containing aqueous fluid, and mucins. Under normal circumstances, aqueous tears are primarily secreted by the main lacrimal gland, spread over the entire ocular surface by lid blinking, and then cleared from the eye into the nose through the nasolacrimal drainage system, which includes superior and inferior puncta and canaliculi, the lacrimal sac, and the nasolacrimal duct. It has long been recognized that decreased tear secretion by lacrimal glands results in the disease state of aqueous tear deficiency (ATD), ie, keratoconjunctivitis sicca. However, based on the fact that a stable tear film depends not only on necessary tear components but also on other hydrodynamic elements, which include tear spread and tear clearance or turnover, it has now been recognized that deficiency in other aspects of

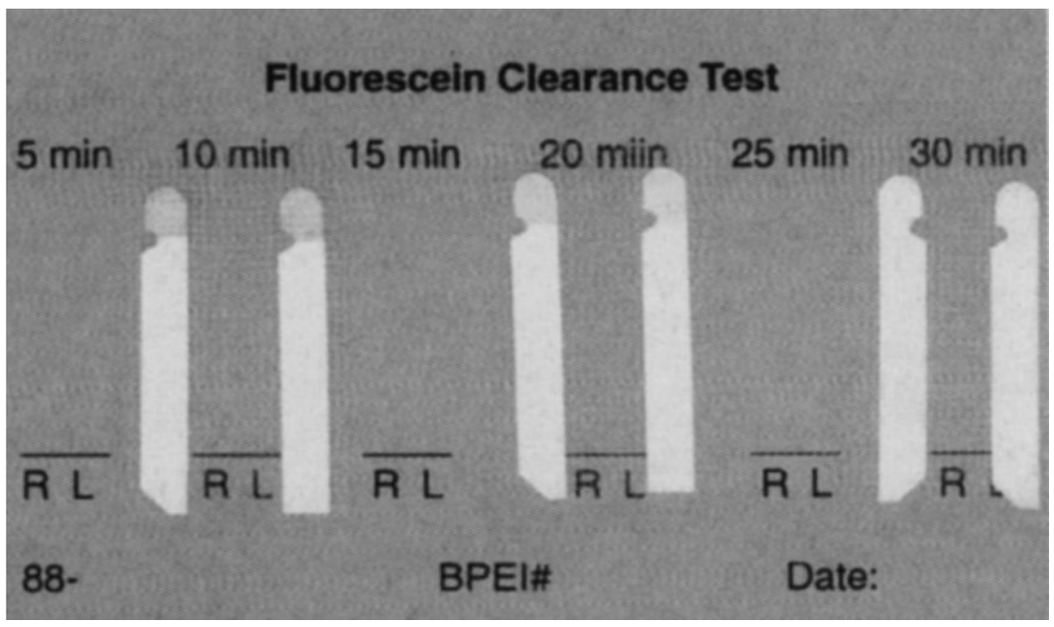

FIGURE 9–1 Fluorescein clearance test.

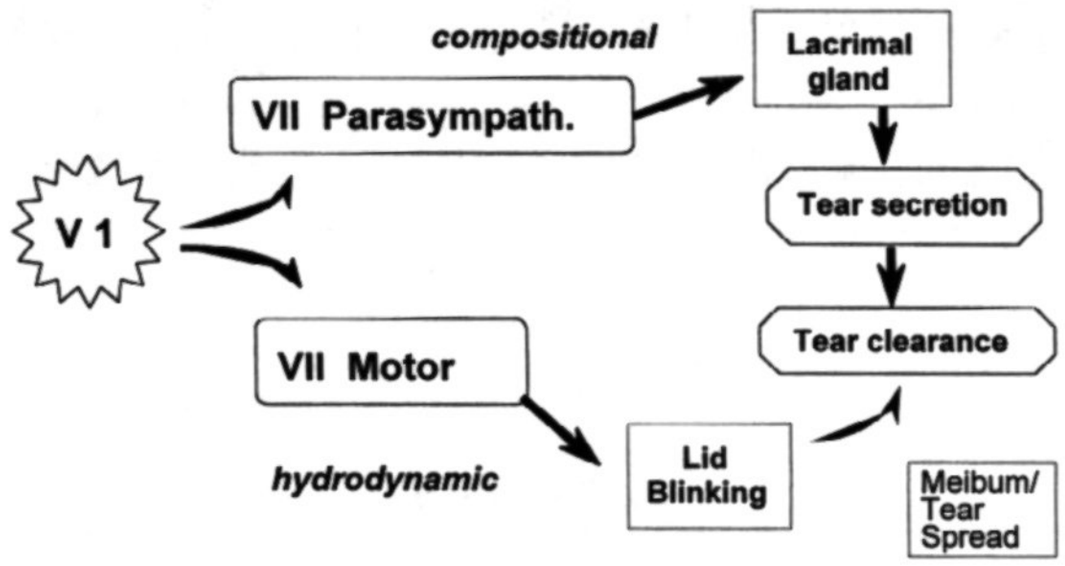

FIGURE 9–2 Neuroanatomic integration.

tear dynamics can also affect dry eye, of which the hallmark is an unstable tear film.

It is important to point out that both compositional and hydrodynamic factors of the ocular surface defense are integrated with the status of ocular surface epithelia via two neuronal reflex arcs. Both reflexes are triggered by the sensory drive of the first branch of the trigeminal nerve (V_1) and operated by connecting to the parasympathetic branch and the motor branch of the facial nerve (VII) as the efferent output, respectively (Fig. 9–2). Such a neuroanatomic integration explains how different tissue parts of the ocular surface including external adnexal glands and eyelids can be integrated with ocular surface epithelia for the purpose of maintaining a stable tear film.

ATD in this case was aggravated by a neurotrophic state caused by diabetes mellitus that affects the corneal sensory nerve. Once corneal anesthesia, together with reduction of ocular sensitivity in the eye such as conjunctiva, lid margins, and lashes, sets in and persists, other sequelae on the ocular surface can develop due to insufficient aqueous tear secretion and exposure as a result of interruption of two corneal nerve–mediated reflex arcs (Fig. 9–2). This phenomenon explains why the patient suffered from punctate keratitis on the exposure zone as a result of keratoconjunctivitis sicca. Because prolonged exposure tends to be worse in the latter part of the day and during reading and driving, this patient's symptoms of unstable tear film (dry eye) such as burning and foreign body sensation were more pronounced in the evening.

Because of decreased secretion of aqueous tear fluid and reduced eyelid blinking, the tear clearance was also delayed (Fig. 9–1). It has been recognized that delayed tear clearance is further aggravated by floppy eyelids (Prabhasawat and Tseng, 1998) (Fig. 9–3). Floppy eyelids are known to be associated with papillary conjunctivitis and

TABLE 9–1 **Important Concepts Governing Mechanisms by Which Ocular Surface Health Is Maintained**

The ocular surface epithelium and the tear film function as a unit.
A stable tear film is maintained by external adnexae and by eyelid blinking and closure.
The intact protective mechanism is controlled by effective neuroanatomic integration.
Corneal epithelial stem cells are located at the limbus.
Ocular surface epithelial cell function is supported by stromal fibroblasts and matrix.

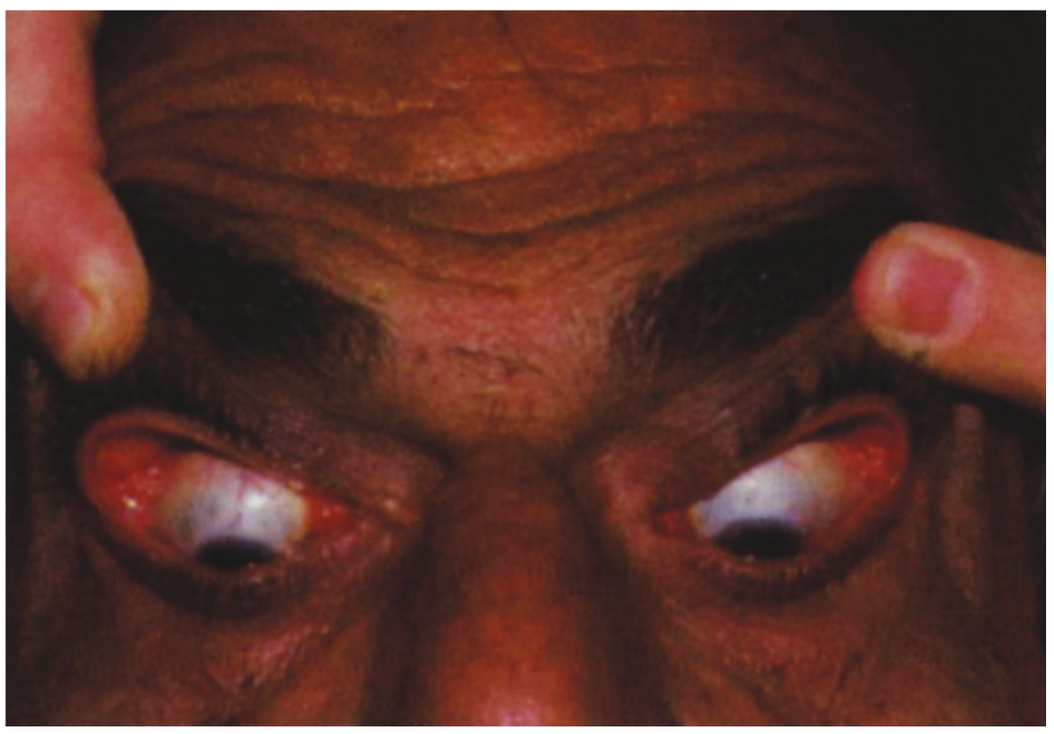

FIGURE 9–3 External examination showing floppy eyelids.

ocular inflammation, which are also worse in the eye that corresponds with the side the patient sleeps on; and ocular symptoms tend to be worsened upon awakening (for a review, see Culbertson and Tseng, 1994). Because of the underlying delayed tear clearance (DTC), symptoms of ocular inflammation such as redness tend to be worse in the morning, especially in the eye corresponding with the side of sleep (Prabhasawat and Tseng, 1998).

Tear production is reduced during regional and general anesthesia, sleep, and pathological neurotrophic keratitis. These observations coupled with the lack of demonstrable specific innervation of the accessory lacrimal glands suggest that basal (or basic) and reflex lacrimation are controlled by neuronal reflexes under minimal and maximal sensory stimulation, rather than by discrete participation of the accessory and principle lacrimal glands, respectively. Furthermore, it has been proposed that the stimulation of lacrimation is dependent upon summed V_1 stimulation (from cornea, conjunctiva, lid margin, and nasal mucosa) (Jordan and Baum, 1980) and modified by cortical influences, eg, emotional lacrimation. The presence or absence of reflex tearing under maximal sensory stimulation of V_1 has been regarded as a reliable index of the capability of the lacrimal gland to produce aqueous fluid (Tsubota, 1994). Loss of reflex tearing is the hallmark of Sjörgren syndrome (SS)-type ATD and can be used to distinguish this from non–SS-type ATD (keratoconjuntivitis sicca). SS-type ATD also manifests more intense rose bengal staining and squamous metaplasia, indicative of severe ocular surface damage, and it correlates with the extent of lymphocyte infiltration in the lacrimal glands (Tsubota, Xu, Fujihara et al, 1996). Based on the findings that there was emotional tearing and that the FCT test showed reflex tearing, we concluded that this patient's ATD was not of SS-type and that his lacrimal glands were not destroyed.

TEST INTERPRETATION

The diagnosis of an unstable tear film was made based on a short tear breakup time. Because the entire spectrum of tear dynamics includes secretion with or without stimulation, ie, basal or reflex tearing, and clearance, and because both unstable tear film and DTC are pathogenic, we advocate the use of FCT for precise diagnosis (Prabhasawat and Tseng, 1998). Tables 9–2 and 9–3 describe the performance and interpretation of the FCT test. For patients with normal tear secretion and clearance, each strip should have a wetting length equal to or greater than 3 mm. The intensity of fluorescein dye fades with time under the blue light and becomes invisible to the naked eye after 15 minutes (ie, from the second pair of strips on). After 15 minutes (ie, the second pair of strips), the wetting length should increase because of waning of topical anesthetics. If this does not happen, the wetting length can be further increased at the final interval of 30 minutes (ie, the third pair of strips) by nasal stimulation. Therefore, FCT allows one to measure basal tearing, reflex tearing, and clearance at the same time.

Because the wetting length was zero, ie, less than 3 mm, in the first and second pairs of strips from this patient (Fig. 9–1), we made the diagnosis of ATD. A wetting length of the last strip greater than the first two sets (Fig. 9–1) also supported this diagnosis. The fact that the dye was clearly visible in the last two sets (Fig. 9–1) further supported the presence of DTC. Based on these diagnostic criteria, we made the diagnosis of ATD and DTC. The underlying cause for ATD was neurotrophic keratopathy secondary to diabetes mellitus and that for DTC was floppy eyelids.

TABLE 9–2 **How to Perform Fluorescein Clearance Test**

Instill one drop of 0.5% proparacaine in the fornix then dry.
Instill 5μ 1 of 0.25% Fluress®.
Allow normal blink.
Perform the Schirmer test for 1 minute after each 10-minute interval.
Perform nasal stimulation after 30 minutes to elicit maximal sensation and repeat the Schirmer test for 1 minute.

TABLE 9–3 **Interpretation of Fluorescein Clearance Test**

	Tear Dynamics		
State	Basal secretion Wetting length of first two strips	Reflex secretion Wetting length of last strip vs. first two strips	Tear clearance Dye visible after 15 minutes
Normal	≥3 mm	Last strip > First two strips	No
DTC	≥3 mm	Last strip > First two strips	Yes
ATD with Reflex	<3 mm	Last strip > First two strips	May be delayed
ATD without Reflex	<3 mm	Last strip > First two strips	Usually delayed

DIAGNOSIS

Keratoconjuctivitis sicca due to ATD secondary to diabetes mellitus–induced neurotrophic keratitis, associated with DTC due to floppy eyelids.

MEDICAL MANAGEMENT

The following are the therapeutic strategies for treating patients with unstable tear film (dry eye) associated with DTC. First, it is essential to eliminate all causes that generate intrinsic irritation, eg, ocular inflammation due to floppy eyelids in this case. This is particularly important if such intrinsic irritation is associated with DTC because the former is exacerbated by the latter in a vicious cycle (Prabhasawat and Tseng, 1998). We propose treatment with topical 1% nonpreserved methylprednisolone drops, which can be prepared by diluting the intravenous preparation of Solumedrol® (UpJohn of Kalamazoo, MI) with normal preservative-free saline. The standard regimen is 1 drop to each eye 3 times a day for 3 weeks. Written and verbal instructions are also given to advise patients to refrigerate this medication between uses and to avoid direct contact of the dropper with the eye or the skin during application. For this patient, we noted a significant improvement with reduced symptoms at a follow-up visit in 3 weeks.

If intrinsic irritative stimuli and ocular inflammation are controlled or eliminated, concomitant DTC should be preserved, as it serves as "punctal occlusion." We can then begin to treat unstable tear film (dry eye). The patient will start with frequent application of preservative-free replacement drops.

SURGICAL MANAGEMENT

For moderate and severe ATD, punctal occlusion with thermal cauterization or temporary plugs is the mainstay of therapy. The consideration of the former over the latter for punctal occlusion is based on the absence of reflex tearing. The use of permanent occlusion is generally reserved for patients with proven SS-type ATD. To maximize punctal fibrosis the use of topical steroid preparations should be avoided immediately after treatment. As the neurotrophic state may result in severe dry eye, punctal occlusion should be considered before being contemplated for tarsorrhaphy or conjunctival flap. With punctal occlusion, artificial tear substitutes become relatively more effective. Because punctal occlusion invariably induces DTC, intrinsic inflammatory irritation has to be eliminated first. Preservative-free tear substitutes are preferred to avoid potential medicamentosa from then on. Because tear fluids contain complex factors, supplementation of

TABLE 9–4 **Therapeutic Management for Treating Dry Eye**

Goal	Modality	Treatment
Replace aqueous fluid	Topical treatment	Artificial tears, autologous serum
Conserve aqueous fluid	Punctal occlusion	Punctal plugs, thermal cautery
Reduce evaporation	Cover Reinforce lipid layer	Eye shields or goggles Meibomian lipid replacement
Reduce exposure	Reduce palpebral aperture Increase blink	Tarsorrhaphy/botox induced ptosis Encouragement
Increase lacrimal gland secretion	Parasympathetic stimulation Suppress lacrimal gland inflammation	Pilocarpine Cyclosporin A

conventional tear substitutes may not be adequate. Therefore, in severe ATD, especially those with SS type, eye drops prepared from a patient's autologous serum may be necessary (Fox, Chan, Michelson, et al, 1984; Tsubota, Goto, Fujita, et al, 1999). Other surgical therapies are directed to reducing exposure by inducing ptosis with botulinum toxin injections or tarsorrhaphy. Newer treatments for SS-type ATD include the T-cell suppressant, cyclosporin A, which is thought to act principally by reducing lacrimal gland lymphocyte infiltration (Table 9–4).

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Case 10

POSTSURGICAL CORNEAL EDEMA

Pongmas Wichiensin, M.D.
Andrew J.W. Huang, M.D., M.P.H.

HISTORY

A 55-year-old man presented with a chief complaint of decreased vision (especially at night) in both eyes for 1 year. Past medical history was remarkable for diabetes mellitus for 10 years, which had been well controlled with oral medications. Past ocular history was unremarkable. There was no family history of systemic or ocular diseases.

Best corrected visual acuity was 20/50 in the right eye and 20/100 in the left eye. Pupillary examination and ocular motility were unremarkable. The intraocular pressures (IOPs) were 12 mm Hg and 13 mm Hg in the right and left eyes, respectively. There was no visual field loss by confrontation finger counting. Slit-lamp examination was normal other than moderate nuclear sclerosis of the crystalline lens in both eyes, left worse than right. Fundus examination did not show any evidence of diabetic retinopathy. Potential acuity testing revealed a visual potential of 20/25 in each eye. A clinical diagnosis of cataract in both eyes was made and cataract surgery of the left eye was recommended for visual rehabilitation.

The patient underwent an uncomplicated phacoemulsification via temporal clear corneal incision with implantation of a posterior chamber acrylic intraocular lens in the left eye. The visual acuity was 20/100 with an IOP of 18 mm Hg on the first postoperative day. Slit-lamp examination revealed diffuse corneal edema in the central cornea as well as around the incision site (Fig. 10–1), and the patient complained of persistent blurred vision without major discomfort.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

The patient is experiencing poor visual outcome immediately after cataract extraction secondary to corneal edema. The differential diagnosis should include the following:

1. Preexisting endothelial disease or dysfunction.

a. Low endothelial cell density without the presence of corneal guttata can occur in a small portion of the population.

b. Corneal guttata and Fuchs' corneal endothelial dystrophy are relatively common preexisting corneal endothelial disorders. These conditions usually occur after 50 years of age with a female preponderance. Corneal guttatae are initially evident centrally and spread toward the corneal periphery. The corneal endothelial cells of Fuchs' corneal endothelial dystrophy are larger and more polymorphic than those of normal individuals. Descemet's membrane is usually thickened. Diurnal fluctuation of vision is common in patients with advanced corneal edema.

c. Past ocular history of an acute rise of IOP such as that seen with acute angle closure glaucoma resulting in reduction of corneal endothelial cell density should also be considered as a cause of low preoperative endothelial cell counts.

d. Abnormality of endothelial cell morphology and function has also been reported in diabetic patients with no known corneal dystrophy.

2. Surgical trauma.

a. Direct injury to the corneal endothelium by instruments or intraocular lens can cause diffuse or discrete patches of edema. This type of edema usually occurs in the central or temporal cornea around the incision site.

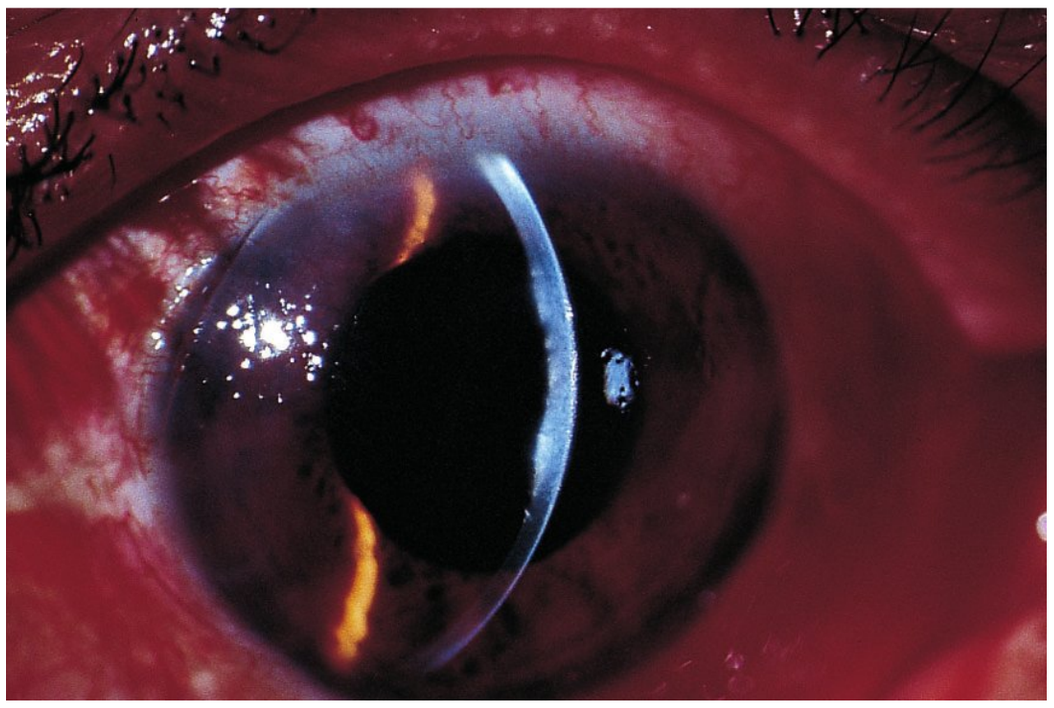

FIGURE 10–1 Postsurgical corneal edema: A diffuse corneal edema was noted in the central cornea and at the temporal incision site.

b. Detachment of Descemet's membrane by incisional blades or misdirection of the surgical instruments intraoperatively can also cause corneal edema. It is usually most visible at the entry wound.

c. Prolonged endothelial exposure to the ultrasound and/or irrigating solutions during phacoemulsification can also cause diffuse corneal edema. This is especially common in patients whose pupils are not fully dilated such as some diabetics and pseudoexfoliation syndrome patients.

d. Other surgical complications, such as a vitreous strand to the wound, vitreous prolapse with corneal endothelial contact, malpositioning of the intraocular lens, wound leaks with shallow anterior chamber, or hypotony with choroidal effusion, may result in corneal edema.

e. Thermal injury to the corneal endothelium may be caused by phacoprobe or cryoprobe (in intracapsular cataract extraction).

3. Toxicity.

a. Various chemical contaminants may result in diffuse endothelial damage. This is frequently accompanied by other evidence of intraocular toxicity such as a fixed and dilated pupil.

b. Antibiotics in high concentrations are common offending agents. Errors in diluting medications may occur. Perioperative topical or subconjunctival antibiotics may enter the anterior chamber through an unsealed wound.

c. Intracameral epinephrine is occasionally used for patients with inadequate pupillary dilatation such as is seen with pseudoexfoliation syndrome. Endothelial toxicity and corneal edema may be caused by sodium bisulfite, which is used as an antioxidant for epinephrine. Preservative-free epinephrine is recommended for intracameral use.

d. Intracameral injection of lidocaine HCL, one of the anesthetic methods used for phacoemulsification, may also cause endothelial toxicity by its preservative (methyl-paraben). Preservative-free preparations of lidocaine are recommended to avoid endothelial toxicity.

e. Detergents used for cleaning ophthalmic instruments, such as ethoxylated fatty acid (a cleaning solution in ultrasonic bath), benzalkonium chloride (a preservative solution), or chlorhexidine (an antiseptic used for preparing facial skin prior to surgery), can cause direct damage to the corneal endothelium. Ethylene oxide used for gas sterilization of ophthalmic instruments is also potentially toxic to the corneal endothelium.

4. Excessive postoperative inflammation.

a. Inflammation may lead to short-term endothelial dysfunction and long-term endothelial cell loss. Active inflammation can compromise endothelial cell functions, especially in older patients who may already have marginal corneal function before inflammation.

b. The degree of postoperative inflammation is dependent on many factors: preexisting conditions, surgical technique, fluids and instrumentation, intraocular lens choice, and medications used.

c. Patients with a history of uveitis such as juvenile rheumatoid arthritis, Vogt Koyanagi Harada or recurrent granulo-matous uveitis are at increased risk of excessive postoperative inflammation.

5. Postoperative IOP elevation.

a. Under normal conditions, the IOP tends to counterbalance the swelling pressure of the cornea. The difference between these two values is termed imbibition pressure. The endothelial pump plays a major role in keeping this dynamic balance of corneal hydration. If the increase of IOP postoperatively exceeds the swelling pressure in the presence of compromised endothelial function, the net flux of water is into the cornea resulting in corneal edema.

b. The use of viscoelastic substances for corneal endothelial protection during surgery has been associated with elevation of postoperative IOP.

c. Pupillary block glaucoma due to iris–intraocular lens adhesion can also cause postoperative IOP elevation.

6. Long-term use of topical ophthalmic medication.

Preoperative ocular conditions requiring long-term use of topical ophthalmic medications may be associated with compromised endothelial function. Preservatives such as benzalkonium chloride or thimerosal found in the ocular medications have been associated with progressive corneal endothelial cell damage.

TEST INTERPRETATION

1. Specular microscopy of the fellow eye.

a. This patient presented with unexpected corneal edema after apparently atraumatic cataract surgery. In the absence of preoperative specular microscopy in the operated eye, the status of the corneal endothelium in the fellow eye is the best parameter of preoperative endothelial cell function.

b. The minimum corneal endothelial cell density required to maintain corneal deturgescence varies from person to person. A cornea with endothelial density less than 1000 cells/mm^2 is known to be at increased risk of corneal decompensation. The routine use of preoperative specular microscopic examination to screen patients for unexpected low endothelial cell counts has been controversial.

c. Noncontact specular microscopy is generally more comfortable for patients than contact microscopy. The latter, however, gives a wider field of view, though with less resolution.

d. One less expensive method of estimating endothelial cell counts is by inserting a reticule in the eyepiece of the slit-lamp biomicroscope and comparing the endothelial mosaics with diagrams of cells with known density. Although convenient and inexpensive, this method is difficult to master and time consuming.

2. Pachymetry.

a. Corneal pachymetry is a useful method of estimating endothelial function.

b. The normal cornea measures 0.52 ± 0.02 mm centrally and approximately 0.65 mm in the periphery.

c. Corneal pachymetry can be helpful in identifying patients with a central corneal thickness greater than 0.6 mm. These patients may have marginal corneal endothelial function and are more susceptible to postoperative corneal decompensation than normal individuals.

d. Corneal pachymetry can also be used postoperatively to monitor the recovery of endothelial function.

DIAGNOSIS

After a detailed examination of the fellow eye, a low endothelial cell density in the absence of

guttata was noted by specular microscopy in this patient. The unexpected postoperative corneal edema in the operated eye was attributed to a preexisting low endothelial density of undetermined etiology.

MEDICAL MANAGEMENT

The goals of management of early postsurgical corneal edema are to maximize visual function and to minimize patient discomfort.

Control of Inflammation

Because persistent inflammation can have a detrimental effect on the corneal endothelial barrier functions, it is essential to control inflammation as soon as possible. Most clinicians treat patients with strong topical steroids such as prednisolone acetate 1% as often as every 1 hour for acute postoperative corneal edema. Subconjunctival corticosteroid injection may be considered for severe inflammation.

Control of IOP

If there is a documented elevation of IOP, topical antiglaucoma medications or systemic carbonic anhydrase inhibitors should be used to control it.

Topical Hypertonic Solution

Topical hyperosmotic agents can facilitate removal of fluid from the edematous cornea. A 5% sodium chloride solution or ointment is commonly used.

Therapeutic Hydrophilic Contact Lens

In patients with early corneal decompensation and mild edema, a thin hydrophilic lens, fitted flat to allow maximum contact between the lens and the irregular epithelium, may be helpful in restoring vision and maximizing patient comfort.

SURGICAL MANAGEMENT

Penetrating Keratoplasty (PK)

Restoration of vision in an eye with irreversible corneal edema requires PK to replace the damaged endothelial cells. A final decision about proceeding with PK should be deferred for 2 to 3 months after postoperative corneal decompensation is noted. In some patients with temporary corneal endothelial dysfunction, clarity can be regained within this time frame.

The prognosis for PK in this type of patient is generally very good with a success rate better than 85%. The long-term success of PK, however, often depends on the quality of postoperative care.

Postoperative Care of PK Eyes

A. Postsurgical complications. The following postsurgical complications may occur following penetrating keratoplasty: wound leak, flat anterior chamber, iris incarceration in the wound, IOP, primary endothelial failure, endophthalmitis, epithelial defect, or downgrowth.
B. Evaluation of postoperative astigmatism by corneal topography. Astigmatism is the most frequent complication of PK. Severe astigmatism can adversely affect postoperative visual outcome. Using a surgical technique that may reduce the occurrence of postoperative astigmatism should be considered. In patients with a moderate to severe degree of astigmatism, relaxing incisions or wedge corneal resection may be considered.
C. Differential diagnosis of graft rejection vs acute graft failure. Acute graft failure usually occurs shortly after PK. It may be related to poor preservation of, or surgical trauma to, the donor tissue. In this situation, corneal edema persists despite medical treatment.

Corneal allograft rejection can occur at any time after transplantation but rarely occurs within 2 weeks of surgery. One should carefully look for signs of graft rejection such as severe anterior segment inflammation, corneal stromal

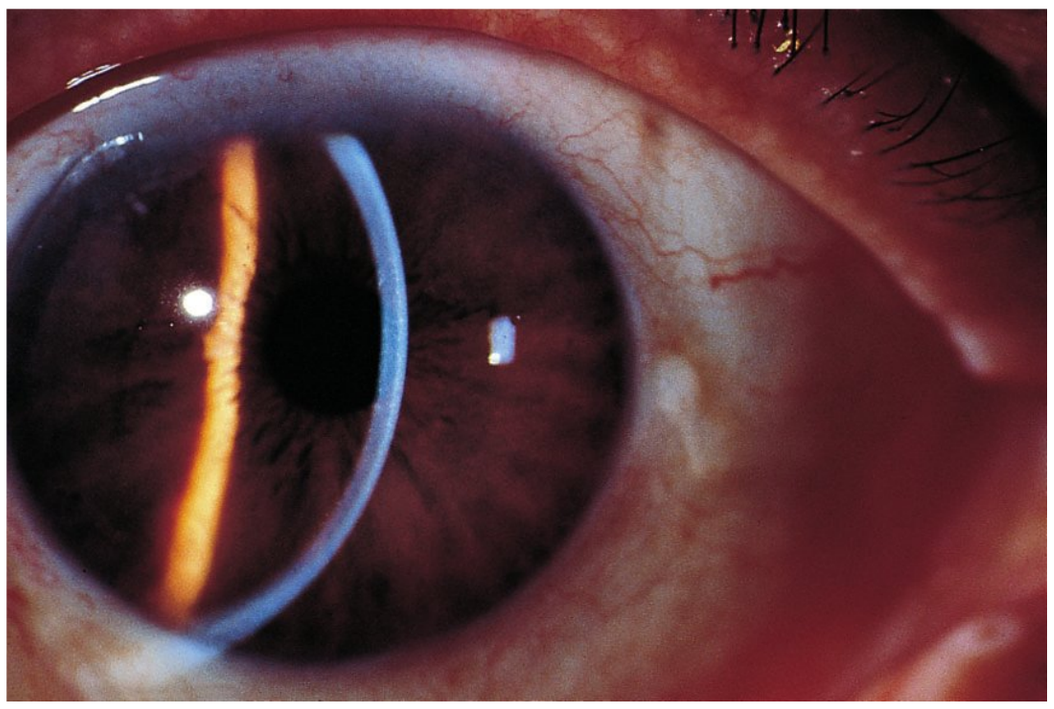

FIGURE 10–2 Complete recovery of corneal edema: After 1 week of medical treatment, the cornea was clear with complete resolution of corneal edema.

infiltrates or edema, keratic precipitate, or rejection line. Frequent topical corticosteroid is the mainstay of treatment for corneal allograft rejection. Periocular or systemic steroids may be considered for severe rejection or in noncompliant patients. Systemic immunotherapy with cyclosporin-A may be needed in selective patients.

REHABILITATION AND FOLLOW-UP

The patient was managed with topical corticosteroids and hypertonic saline solution q.i.d. for 1 week. The corneal edema resolved completely after the treatment and the final best corrected visual acuity was 20/20 (Fig. 10–2).

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Case 11

DELLEN

Stephen D. McLeod, M.D.

HISTORY

A 55-year-old man with a history of glaucoma that required multiple filtration procedures in the right eye was found to have elevated intraocular pressure on maximal medical therapy. A repeat trabeculectomy procedure was performed. In order to avoid the previous surgical site, the trabeculectomy flap was established at the 7-o'clock position, which resulted in a moderately elevated filtering bleb extending from the 5- to 8-o'clock positions.

Two weeks after surgery, peripheral corneal thinning was noted adjacent to the filtering bleb (Fig. 11–1). Fluorescein instillation revealed pooling with a small area of epithelial cell loss.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. A delle represents an area of localized corneal thinning due to desiccation that results from poor tear coverage over a specific area (Fig. 11–2). This localized interruption in the tear film is most commonly due to some form of limbal elevation (eg, filtering bleb, dermoid, conjunctival elevation following muscle or scleral buckling surgery), which therefore tends to produce desiccation and delle formation at the periphery of the cornea, especially in the setting of dry eye. Because of the location, the correct diagnosis is often not considered, and inflammatory causes of peripheral corneal thinning are invoked.

2. While delle formation is a relatively benign process, inflammatory causes of peripheral corneal thinning can have disastrous consequences for the eye and might be associated with severe systemic diseases. These should therefore be considered in the differential diagnosis, along with degenerative causes of peripheral corneal thinning.

3. Inflammatory causes of peripheral corneal thinning include Mooren's ulceration, thinning associated with scleritis of various causes, and autoimmune processes such as rheumatoid arthritis, systemic lupus erythematosus, relapsing polychondritis, inflammatory bowel disease, and vasculitis syndromes such as Wegener's granulomatosis, temporal arteritis, polyarteritis nodosa, and Churg-Strauss Angiitis. Systemic evaluation is required to rule out inflammatory disease in those cases that are often accompanied by significant ocular inflammation and corneal infiltration. While noninfiltrated, relatively quiet peripheral corneal melting can occur in association with disorders such as rheumatoid arthritis, systemic lupus erythematosus, or relapsing polychondritis, an epithelial defect is almost always present in active disease, and an adjacent mass that could disturb tear distribution is unlikely to be present.

4. Degenerative causes of localized peripheral corneal thinning include Terrien's marginal degeneration, pellucid marginal degeneration, and Fuchs' superficial marginal keratitis. Terrien's marginal degeneration is characterized by superficial vascularization of thinned peripheral cornea preceded by a distinct lipid line. As opposed to the typically well-circumscribed area involved in dellen, pellucid marginal degeneration extends over a narrow arcuate band and is not associated with any adjacent elevation that might impede tear distribution. Fuchs' superficial marginal keratitis is characterized by intermittent, recurrent episodes of ocular irritation accompanied by marginal infiltrates that result in progressive marginal superficial stromal thinning, and in advanced cases, pseudopterygium over the area of thinning.

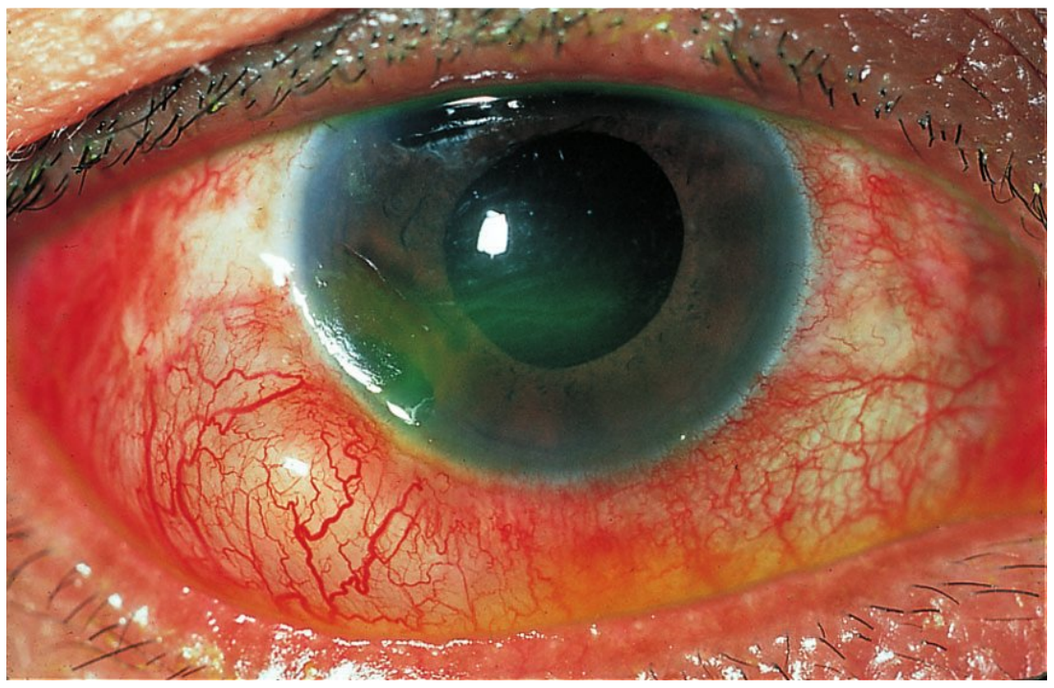
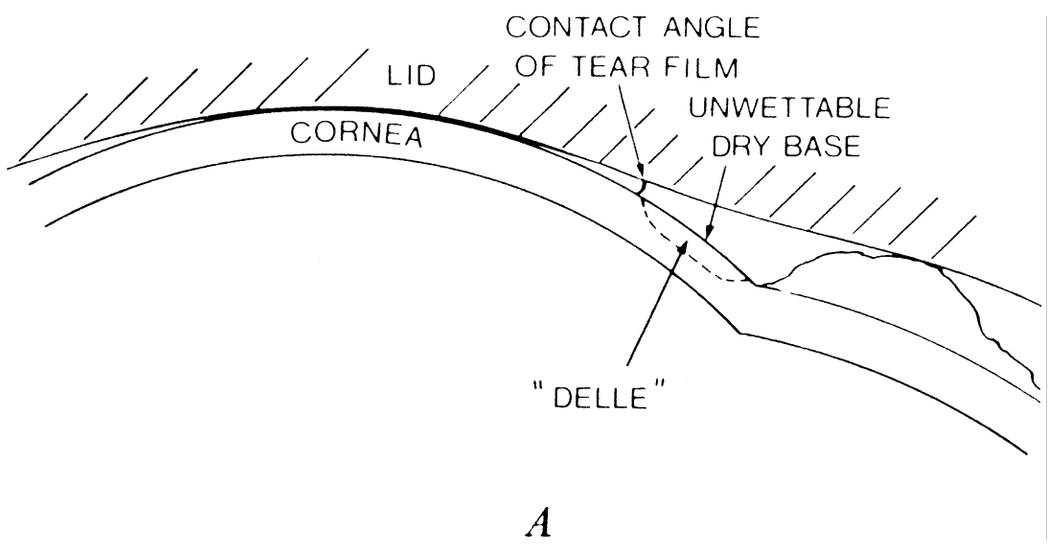


FIGURE 11–1 A filtering bleb is evident extending from the 5-o'clock to the 8-o'clock positions. Note the pooling of fluorescein in the peripheral corneal delle that has developed adjacent to the filtering bleb. (Courtesy of John P. Whitcher, M.D., San Francisco, CA)

TEST INTERPRETATION

Dellen are typically associated with the following clinical characteristics. Underlying dry eye or meibomian gland dysfunction may be present. The area of thinning is usually well circumscribed with sloping edges. There is often an obvious adjacent elevation responsible for the localized interruption in tear distribution. As the patient blinks, the tear film is disrupted over the area of thinning. This can often be demonstrated more clearly by highlighting the tear film with a drop of fluorescein. If too much fluorescein is instilled, it will often pool in the depression giving the appearance that an epithelial defect is present. The epithelium, however, is usually intact along the base of the delle, and this can be demonstrated by gently removing the excess fluorescein from the excavation with a spear-tip cellulose sponge. It should be recognized, however, that due to the epithelial trauma that might accompany chronic desiccation, epithelial breakdown, scarring, and true tissue loss can occur, so that a delle evolves into a true noninfectious corneal ulcer.

The definitive diagnostic test for a delle is to rehydrate the area, which will result in thickening of the corneal stroma and resolution of the localized thinning. This is best achieved by applying a generous quantity of a viscous lubricating agent such as a 1% methylcellulose solution or ophthalmic lubricating ointment, and patching the eye shut for 15 to 30 minutes. Under these conditions, a delle should rapidly rehydrate, so that the cornea returns to near normal thickness. Usually, because of the relative localized stromal edema, the cornea appears mildly opacified in the former area of the delle.



A

FIGURE 11–2 This schematic illustrates the formation of a delle: In this case, the mass acts as a spacer that disturbs the continuity of contact between the lid and the cornea. This leads to an area consistently devoid of tear film, resulting in desiccation and thinning.

DIAGNOSIS

Delle in right eye due to dry eye in the setting of a filtering bleb.

MEDICAL MANAGEMENT

Dellen are due to inadequate tear distribution, dry eye, and lid disease such as meibomitis and blepharitis. These risk factors should be treated. Dry eye treatments include supplementation with artificial tears, bland ophthalmic lubricating ointment, punctal occlusion, or in the most severe cases, limited tarsorraphy. The stability of the tear film is affected by the health of the oil layer produced by the lid's meibomian glands: lid treatments such as heat compresses and gentle massage directed to the meibomian glands might be helpful in relieving meibomian gland inspissation and reduced tear break-up time.

SURGICAL MANAGEMENT

In many cases, the localized elevation precipitating delle formation (such as with filtering blebs or following conjunctival surgery) cannot easily be resolved. Removal of the offending structure is not a reasonable option in such cases. However, a mass such as a pyogenic granuloma or dermoid may be amenable to surgical excision.

REHABILITATION AND FOLLOW-UP

Since delle formation represents a relatively benign process, little is usually required in the way of visual rehabilitation. However, patients should be observed and treated over the long term for signs and symptoms of dry eye that are contributing factors to dellen formation.

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Case 12

GRAFT REJECTION FOLLOWING PENETRATING KERATOPLASTY

Matthew R. Jones, M.D.

HISTORY

A 30-year-old man presented with complaints of redness, photophobia, and blurred vision in his right eye for 1 week. Past ocular history included keratoconus, for which he had undergone penetrating keratoplasty (PK) in the right eye 5 months earlier. At his examination 1 month earlier a visual acuity of 20/60 in the right eye with improvement to 20/30 with pinhole had been recorded.

Examination revealed a visual acuity of 20/400 in the right eye without improvement with pinhole. Visual acuity was 20/20 in the left eye with a rigid gas permeable contact lens. Intraocular pressure was 17 mm Hg in both eyes. Slit-lamp examination was notable for 2+ ciliary flush in the right eye. A broken, exposed interrupted suture with a surrounding infiltrate was noted in the graft at the 11-o'clock meridian. Marked stromal edema extended 2 mm into the graft from the site of the broken suture. A line of keratic precipitates demarcated the central edge of the stromal edema. The anterior chamber showed 1+ cell and flare. The left eye was quiet with a well-positioned rigid gas permeable contact lens, with thinning and mild protrusion of the central cornea. A Fleischer ring was present.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. New symptoms in a patient with a PK (foreign body sensation, decreased visual acuity, photophobia, red eye) should be evaluated immediately. The chances of a graft-threatening problem in a patient with such symptoms are high, and successful management depends upon timely presentation and intervention.
2. Broken sutures in the postoperative period after PK are common. If not removed immediately they can lead to vascularization, suture abscess, or rejection.
3. After PK, patients may present with the signs and symptoms of iritis without signs of graft rejection. Such patients may or may not have a previous history of uveitis. Iritis should be treated as a "form fruste" of allograft rejection.
4. Rejection after PK may take one of three major forms: epithelial rejection, subepithelial rejection, or endothelial rejection.

Epithelial rejection presents with a slightly elevated gray-white epithelial ridge inside the graft host junction that stains with fluorescein and may extend for 360 degrees. The ridge represents sensitized lymphocytes that are rejecting the donor epithelium (Fig. 12–1). The host stem cells replace the epithelium behind the advancing ridge. Epithelial rejection occurs most commonly within the first year after PK.

Subepithelial rejection consists of multiple round subepithelial infiltrates scattered over the graft, similar in appearance to postadenoviral subepithelial infiltrates.

Endothelial rejection may present with one or more of the following features: ciliary injection, keratic precipitates, stromal edema, anterior chamber cell, and flare. Signs of advanced rejection include superficial and deep vascularization of the graft or a linear deposit of keratic precipitates (Khodadoust line) (Fig. 12–2). Endothelial rejection is the most common cause of graft failure.

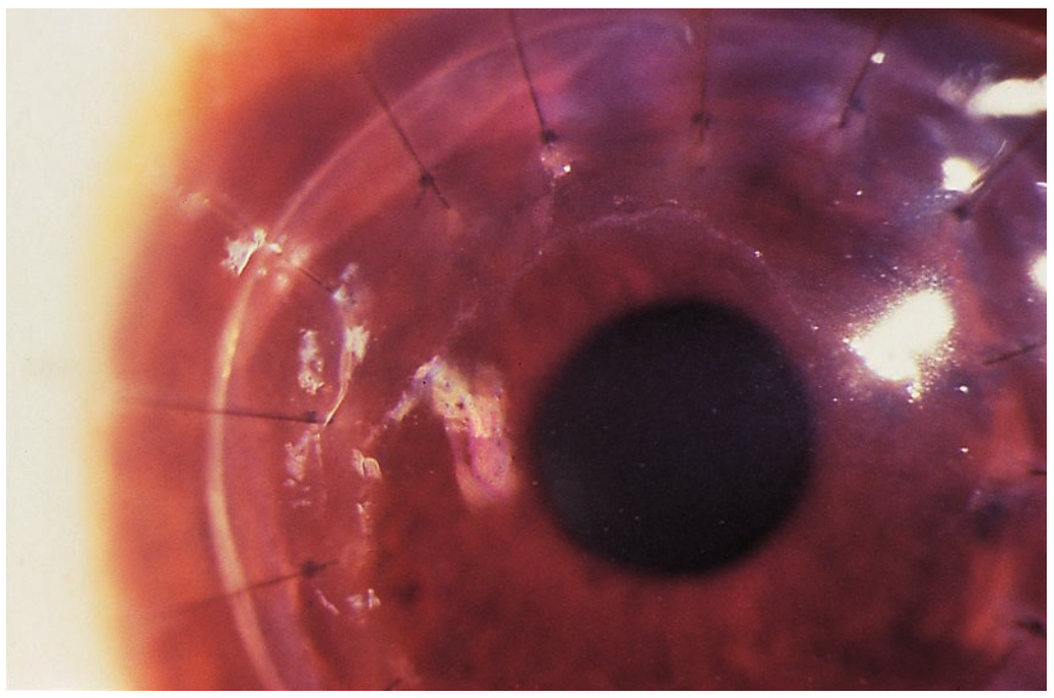

FIGURE 12–1 Epithelial rejection 3 months after penetrating keratoplasty. Note centrally advancing epithelial rejection line.

5. Risk factors for endothelial rejection include stromal vascularization, large-diameter grafts, eccentric grafts, and repeat grafts. Any cause of inflammation in the postoperative period including iritis, mild trauma, epithelial or subepithelial rejection, or broken sutures can trigger endothelial rejection.

TEST INTERPRETATION

The diagnosis of graft rejection after PK is made predominantly by slit-lamp examination. Occasionally in questionable cases ultrasonic pachymetry can be helpful in detecting a subclinical increase in graft thickness suggestive of endothelial dysfunction. Similarly, a decrease in corneal thickness can be a useful early sign that a severe rejection episode is responding to treatment even if the edematous graft appears unchanged.

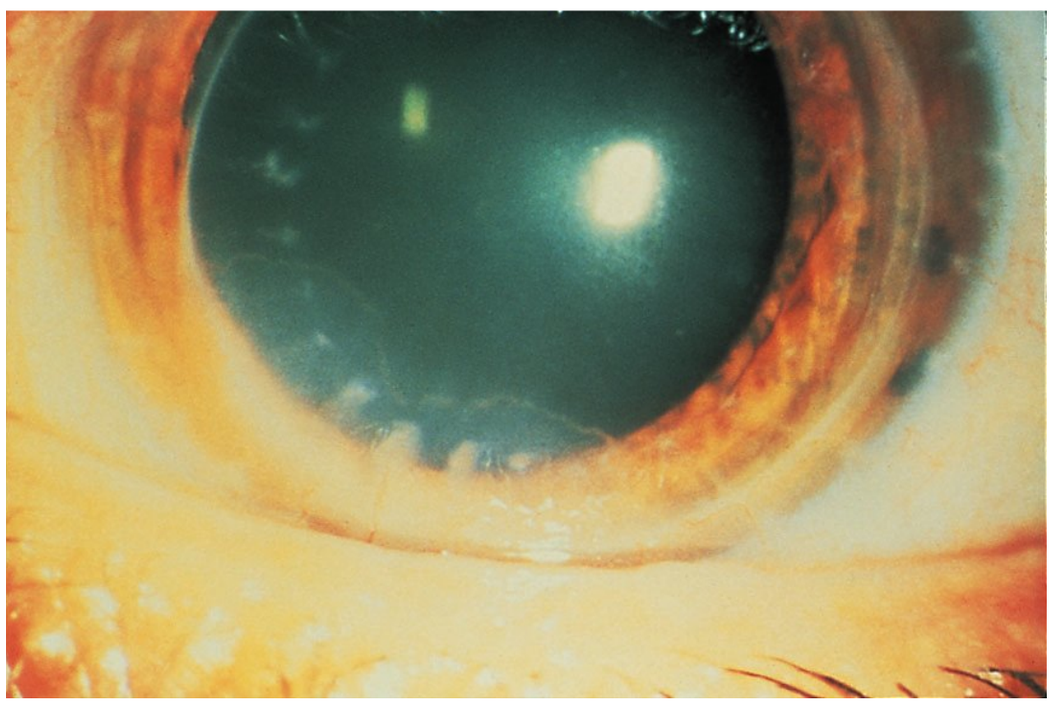

FIGURE 12–2 Endothelial rejection with inferior corneal edema and Khodadoust line.

DIAGNOSIS

OD: (1) Broken suture with suture abscess. (2) Endothelial corneal graft rejection.

OS: Keratoconus.

MEDICAL MANAGEMENT

Timely intervention in the management of endothelial rejection is critical to prevent irreversible endothelial damage. As such, patients must be educated to seek evaluation within 24 hours of any new symptom of photophobia, foreign body sensation, red eye, or decreased vision.

Broken sutures should be removed at the slit lamp. If no infiltrate exists, prophylactic treatment with a broad spectrum antibiotic in drop or ointment form should be instituted (eg, Polytrim q.i.d. for 2 to 3 days; bacitracin ointment t.i.d. for 2 to 3 days). If a suture abscess is present, culturing should be considered and the frequent application of a broad-spectrum fluoroquinolone or other fortified antibiotic (eg, ciprofloxacin every hour around the clock) may be necessary. In the presence of an abscess, topical corticosteroid frequency is typically reduced or discontinued for the first several days. After control of the abscess is achieved, the steroid can be increased judiciously to treat excessive inflammation or rejection if present.

While epithelial and subepithelial rejection do not significantly effect the health of the graft directly, they can trigger endothelial rejection if left untreated. Both epithelial and subepithelial rejection typically respond quickly to moderate doses of topical corticosteroids (eg, prednisolone acetate 1% q.i.d. for 1 week, with subsequent tapering to baseline corticosteroid levels).

Endothelial rejection should be managed aggressively by using frequent topical corticosteroids. The initial frequency of topical steroid

depends upon the severity of the rejection episode. For mild rejection consisting of one to several keratic precipitates and a mild anterior chamber reaction, application of a topical steroid such as prednisolone acetate 1% 4 to 6 times daily and tapered over 6 weeks may be sufficient. For more severe episodes with the presence of many keratic precipitates and corneal edema, hourly application of topical steroids should be instituted. A cycloplegic agent (eg, scopolamine 0.25% t.i.d.) can be used to help stabilize the blood–aqueous barrier and increase patient comfort in more severe cases. In severe or recalcitrant cases of endothelial rejection, systemic steroids (eg, prednisone 80 mg PO q.d.) and/or subconjunctival steroids (eg, triamcinolone 40 mg/ml) can be used to supplement topical therapy.

SURGICAL MANAGEMENT

If no improvement is noted in the amount of edema after several weeks of therapy, the steroids should be tapered and consideration given to repeat PK. Although repeat PK is often successful in these cases, repeat grafts have a higher risk of failure. This is particularly true if deep stromal vessels are present, which is often the case after severe or prolonged rejection episodes. Perioperatively, prophylactic systemic steroids or, less commonly, cyclosporin A can be considered in particularly high risk cases. HLA matching of donor tissue to the recipient has not been convincingly demonstrated to reduce graft rejection in high risk patients. There is, however, some evidence that ABO blood type matching may be of some benefit and can be considered in high risk patients.

REHABILITATION AND FOLLOW–UP

Scheduling of follow-up care during the treatment of endothelial rejection varies depending on the severity of the episode, but typically ranges from 2 to 4 days in more severe cases to 1 week in less severe cases. As it becomes apparent that the rejection process is under control, the frequency of the follow-up visits can be decreased as topical steroids are tapered. Attention can then be returned to visual rehabilitation of the eye. Residual astigmatism is addressed via suture lysis, glasses, or rigid contact lens fitting as is appropriate.

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Figures courtesy of Peter R. Laibson, M.D.

Case 13

BLEPHARITIS

Weldon W. Haw, M.D.

HISTORY

A 42-year-old woman with no past ocular history presents with complaints of bilateral itching, burning, foreign body sensation, and crusting eyelids in the morning. Although she has experienced these symptoms intermittently over the last 2 years, her symptoms have recently become worse. She denies taking any ocular medications. Her symptoms are unrelated to any systemic illness including allergy, rosacea, or flu-like symptoms.

Her visual acuity is 20/20 in both eyes without correction and her intraocular pressures are normal. Slit-lamp examination reveals mild erythema of the eyelid margin associated with scaling, crusting formations around the base of the eyelashes (Fig. 13–1). Evidence of trichiasis (misdirected eyelashes), madarosis (loss of eyelashes), poliosis (whitening of the eyelashes), and ulceration of the eyelid is also seen (Fig. 13–2). There is mild conjunctival hyperemia associated with mild papillary reaction of the inferior tarsal conjunctiva. The tear lake in both eyes is diminished. Rose bengal dye examination of the cornea was remarkable for inferior, superficial punctate epithelial erosions. A Schirmer test was performed and revealed mild aqueous tear deficiency in both eyes.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The differential diagnosis for this set of nonspecific symptoms is extensive and includes a variety of conditions such as allergic conjunctivitis, dry eye syndrome, giant papillary conjunctivitis, pediculosis, atopic and vernal conjunctivitis, medicamentosa, and many other disease entities. Therefore, important historical features include contact lens wear, recent exposure to infected individuals, presence of dermatologic conditions (ie, eczema, rosacea), seasonal component, unilateral vs bilateral symptoms, and use of ocular medications.

2. There are multiple classifications of blepharitis. Marginal blepharitis is most commonly classified according to etiology. This includes blepharitis from staphylococcal colonization (Staphylococcal aureus and Staphylococcal epidermis), seborrhea, meibomian gland dysfunction, or a combination of any of the above. Seborrheic blepharitis is characterized by oily, greasy deposits of the anterior eyelid usually associated with seborrheic dermatitis. There may be mild conjunctival infection and inferior punctate epithelial erosions. Patients with meibomian gland dysfunction (posterior blepharitis) have pouting or metaplastic meibomian gland orifices, prominent vasculature crossing the mucocutaneous junction, foamy or turbid meibomian secretions, eventual atrophy of the meibomian glands, and rosacea. There may be mild to moderate conjunctival infection, papillary reaction of the tarsal conjunctiva, and inferior punctate epithelial erosions with occasional scarring and neovascularization.

This patient has the characteristics of staphylococcal blepharitis. Staphylococcal blepharitis has more potential to demonstrate structural damage. There may be evidence of poliosis, madarosis, and lid ulceration. Examination of the cornea may also reveal inferior punctate epithelial erosions, infiltrates, neovascularization, thinning, and phlyctenules. Staphylococcal blepharitis may lead to several forms of keratitis including marginal infiltrates and phlyctenules. Marginal infiltrates are sterile gray-white infiltrates along the peripheral cornea at the 2-, 4-, 8-, and 10-o'clock positions. Phlyctenules are focal, triangular, elevated,

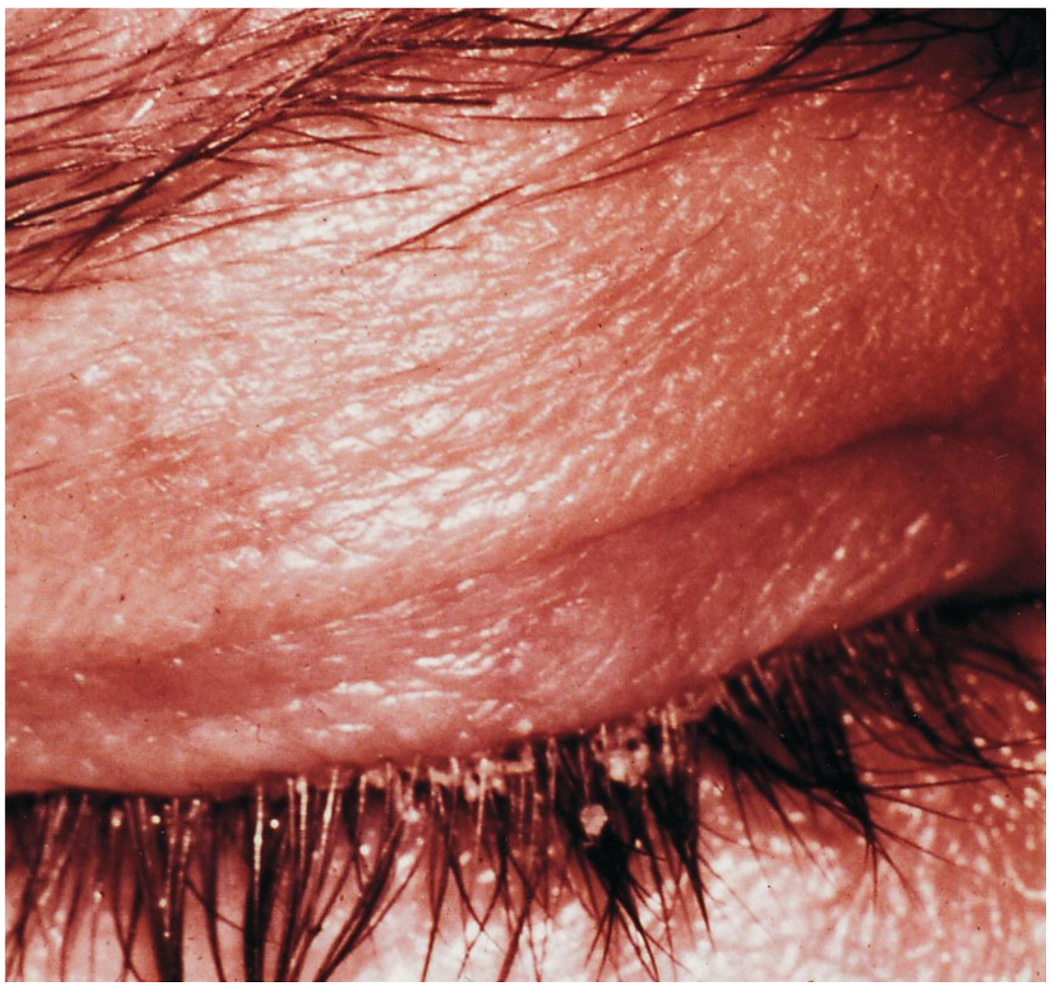

FIGURE 13–1 Blepharitis: Note the crusting debris at the base of the eyelashes.

inflammatory nodules occurring on the limbus, cornea, or conjunctiva.

3. In cases of severe unilateral or asymmetric disease resistant to therapy, it is always important to consider the possibility of an underlying malignancy. Rarely, sebaceous cell carcinoma, basal cell carcinoma, or squamous cell carcinoma may masquerade as blepharitis. The presence of a nodular mass, extensive fibrosis or ulceration, and localized dermal crusting should lead to careful reevaluation of the diagnosis. However, our patient had a history, exam, and course typical of blepharitis.

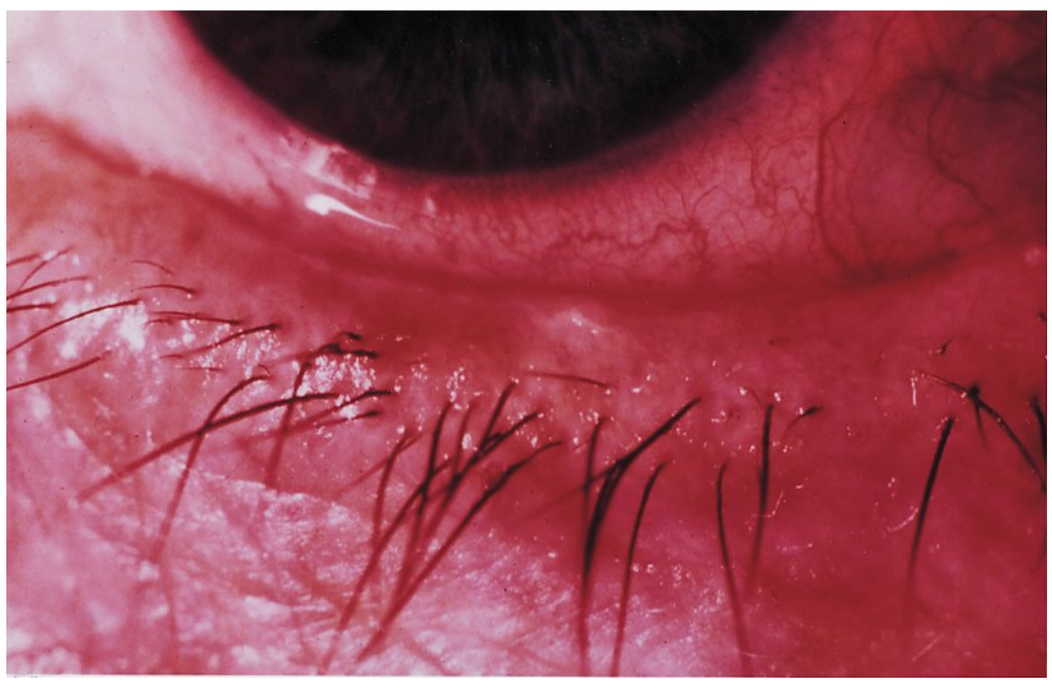

FIGURE 13–2 Blepharitis: Note the disruption of normal eyelid margin architecture and the loss of eyelashes (madarosis).

4. Multiple conditions may be associated with blepharitis. Aqueous tear deficiency is common in patients with seborrheic blepharitis or meibomian gland dysfunction and may be present in as many as 50% of patients with staphylococcal blepharitis. Seborrheic dermatitis may affect 95% of patients who also have a seborrheic blepharitis. Meibomian gland dysfunction is also associated with seborrheic dermatitis (74%) and acne rosacea (51%). These conditions should be identified and addressed during the treatment regimen. Our patient did have symptoms related to dry eyes and on clinical examination revealed evidence of an associated aqueous tear deficiency (inferior punctate keratopathy, diminished tear lake, and a positive Schirmer test).

TEST INTERPRETATION

Clinical examination is paramount in the diagnosis of blepharitis. However, specific diagnostic tests may be useful in selected patients. Eyelid cultures may be useful in patients with recurrent or persistent anterior inflammatory blepharitis refractory to medical management. In this same population aqueous tear deficiency may be detected by a positive Schirmer test or characteristic fluorescein or rose bengal corneal staining pattern. An unstable tear breakup time of less than 10 seconds may help confirm meibomian gland dysfunction.

DIAGNOSIS

Anterior blepharitis, staphylococcal type.

MEDICAL MANAGEMENT

It should be emphasized to the patient that blepharitis is a chronic and relapsing condition that requires repetitious and fastidious maintenance of eyelid hygiene. The primary goals of treatment include minimizing structural damage and controlling symptoms. In staphylococcal blepharitis,

the eyelid bacterial colonization may be reduced by meticulous mechanical debridement of eyelid scales with a cotton-tip applicator or lid scrub with a mild shampoo once or twice a day. Frequent or rough handling of the eyelids is to be avoided as this may lead to mechanically induced lid inflammation. The application of topical antibiotic ointment before bedtime with activity against Staphylococcus aureus may also be appropriate (ie, erythromycin, sulfacetamide, bacitracin) in severe cases. In refractory cases, eyelid bacterial culture and sensitivity testing may be useful in directing antibiotic therapy. A brief course of topical steroids may help to reduce hypersensitivity and sterile inflammatory reactions to staphylococcal antigens (ie, marginal keratitis and phlyctenular conjunctivitis). Artificial tears administered 4 to 8 times per day may be useful in treating an associated aqueous tear deficiency in these patients. Warm compresses may also help relieve discomfort during active phases and soften adherent eyelid debris.

Gentle massage of the eyelids may help mechanically express meibomian secretions in patients with meibomitis. In patients with recurrent meibomitis, the addition of doxycycline 50 to 100 mg PO b.i.d. or tetracycline 250 mg PO q.i.d. for 4 weeks may also be useful in providing symptomatic relief for severely affected patients. Indefinite use of doxycycline may be required to maintain control over blepharitis symptoms. It should be noted that doxycycline and tetracycline are contraindicated in young children as this may lead to dental staining. Erythromycin may be safely used as an alternative.

SURGICAL MANAGEMENT

In cases of atypical, refractory unilateral cases, an eyelid biopsy may be indicated to evaluate for malignancy. Basal cell carcinomas and squamous cell carcinomas are the most common malignancies mistaken for blepharitis. Rarely, sebaceous cell carcinoma may masquerade as chronic, unilateral blepharitis or as a recurrent chalazion. Melanoma has also rarely been reported to masquerade as blepharitis. Patients may also require surgical management of eyelid or eyelash malposition from progressive structural damage and scarring.

REHABILITATION AND FOLLOW-UP

Patients with mild blepharitis may be followed as needed or at their next routine visit. In more severe cases, initial follow-up may require a return visit in 3 to 6 weeks depending on the severity of the symptoms. If patients are prescribed topical steroids, earlier initial follow-up may be indicated in order to evaluate response and to measure intraocular pressure. Often, patients require a maintenance regimen of lid hygiene, artificial tears, and warm compresses. However, this regimen may be tailored to the severity of the patient's symptoms. During follow-up, it is important to emphasize to the patient the relapsing and chronic nature of the disease. Reinforcing the maintenance regimen may also prevent exacerbations in the disease process.

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Section II

LENS

14. A Nearly Mature Cataract in a Patient with Glaucoma
15. Retained Lens Material After Cataract Extraction
16. Fibrin Deposition on Intraocular Lenses
17. Subluxated Crystalline Lens
18. Congenital Cataract

Case 14

A NEARLY MATURE CATARACT IN A PATIENT WITH GLAUCOMA

I. Howard Fine, M.D.

HISTORY

A 34-year-old white woman, working full-time as a stock broker, was referred by a glaucoma specialist for evaluation of a nearly mature cataract in her right eye. Her history included congenital glaucoma, a phthisical left eye, and a history of multiple previous surgical procedures in the right eye including goniotomies, peripheral iridectomies, filtering surgery, and a revision of the filtering bleb associated with sphincterotomies and multiple peripheral iridectomies.

On examination (Fig. 14–1), visual acuity was finger counting in the right and no light perception (NLP) in the left. Examination of the right eye suggested that the patient was using her superior nasal peripheral iridotomy as an entrance pupil. There was a relatively thick-walled but functioning filtering bleb in the superior nasal quadrant. Intraocular pressure (IOP) was 20 mm Hg without glaucoma medications. The cornea was clear but there was some peripheral vascularization and endothelial cell polymorphism and polymegathism. The anterior chamber was clear and deep. The iris was highly atrophic throughout its entire periphery with very little sphincter tissue. The pupil was 3 mm and did not dilate, due to 360 degrees of posterior synechiae. There were multiple sphincterotomies at the pupillary margin and a large radial cut at the 12-o'clock position (Fig. 14–1). There was a dense, nearly mature cataract, an absence of zonules visible through the large superior nasal iridectomy, and questionable zonular status in the areas of broad peripheral iridectomies in two other quadrants. There was no view of the right fundus.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

The diagnosis was obvious, but special and unique challenges existed in the surgical approach to this cataract. The bleb was functional and necessary for IOP control. Corneal endothelial cell loss due to multiple previous surgical procedures indicated a risk for corneal decompensation. The pupil presented perhaps the largest surgical challenge. Any attempt to manipulate or stretch it could result in tearing of the 12-o'clock radial sphincterotomy out to the periphery with loss of entrance pupillary function. In addition, the atrophic nature of the entire iris was such that any thoughts of surgical repair seemed impossible.

There are multiple cataract surgical considerations in this case including: (1) zonular integrity with the risk for potential loss of the cataract into the posterior segment; (2) potential for postoperative inflammation and secondary glaucoma; and (3) difficult and potentially inaccurate preoperative measurements and intraocular lens (IOL) power calculations.

TEST INTERPRETATION

The patient was unable to undergo a reliable refraction. Keratometry measurements showed 7 diopters of astigmatism against-the-rule. Axial length measured 30 mm and the horizontal white-to-white measurement was greater than 14 mm. Corneal topography revealed 6 diopters of astigmatism that did not correlate with keratometry measurements. Endothelial cell count was not performed since surgery was necessary

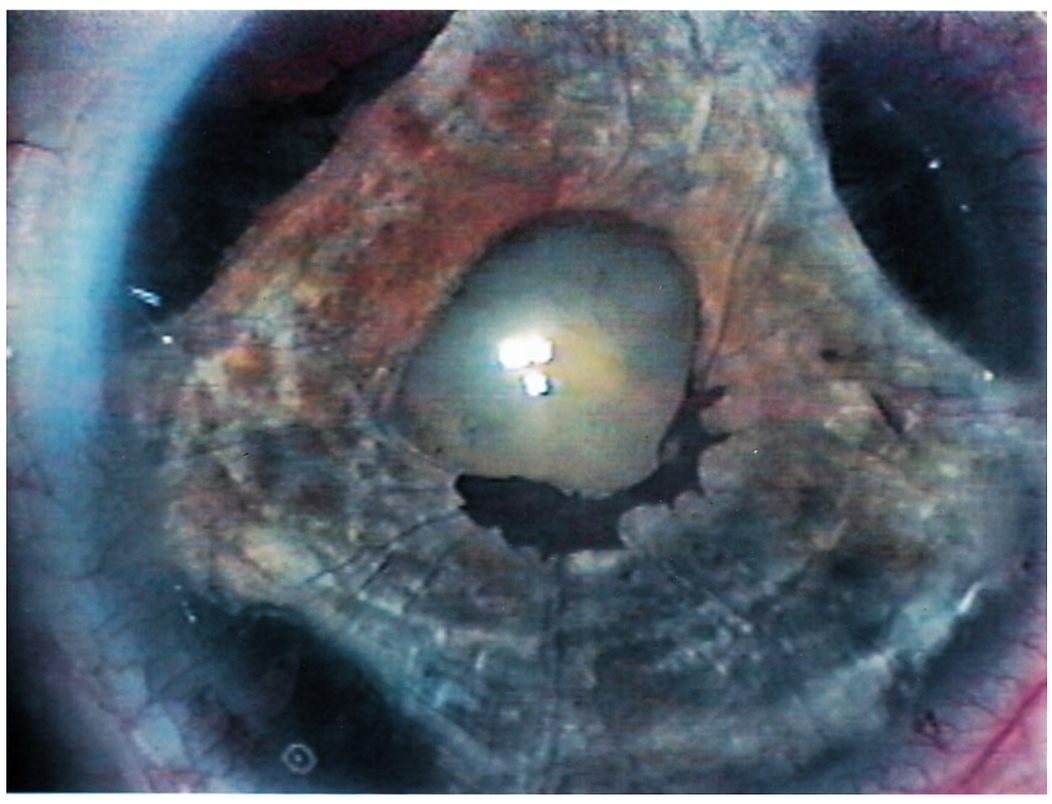

FIGURE 14–1 Appearance of the eye preoperatively with the patient on the operating table.

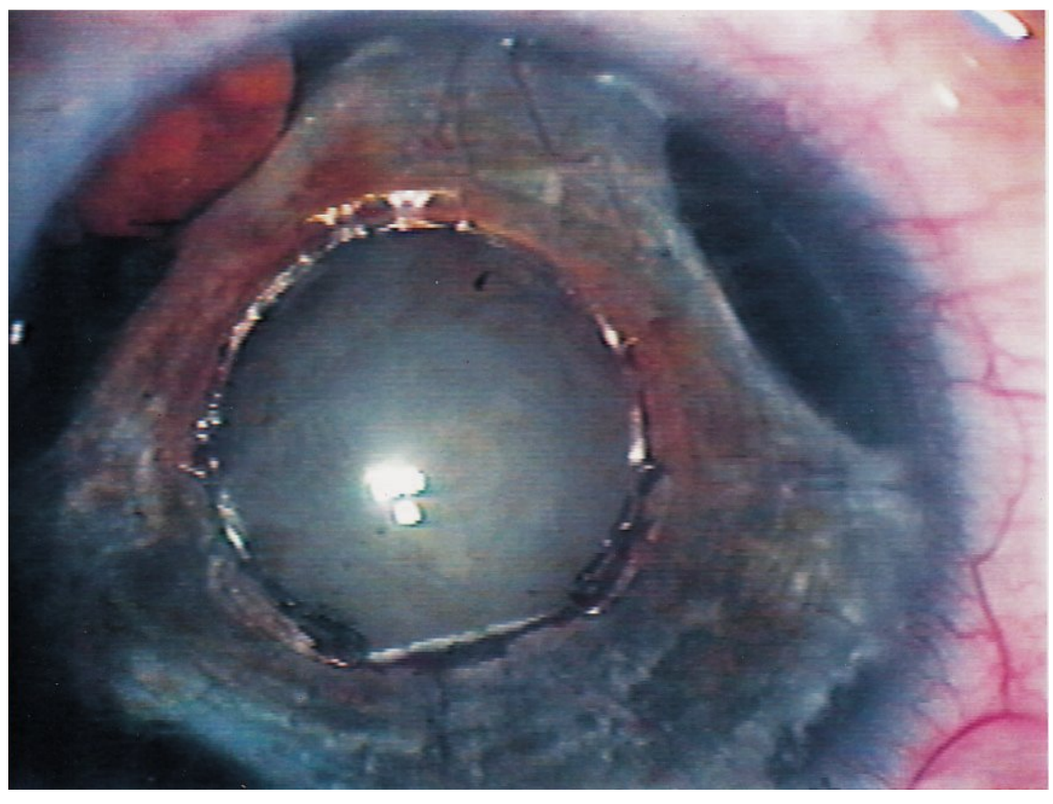

FIGURE 14–2 The iris expander ring in place.

regardless of the status of the endothelium. B-scan ultrasonography revealed that the retina was flat.

DIAGNOSIS

Advanced glaucoma, mature cataract, status post multiple glaucoma surgical procedures, functioning filtering bleb, atrophic iris with radial sphincterotomies, compromised zonular apparatus, blind phthisical fellow eye.

MEDICAL MANAGEMENT

Intermittent use of antiglaucomatous medications and massage of the bleb.

SURGICAL MANAGEMENT

A side-port incision was made and the anterior chamber was partially filled with Viscoat®, a dispersive viscoelastic. The cohesive viscoelastic substance Provisc® was injected directly on the anterior lens capsule, forcing the dispersive Viscoat® to the periphery of the anterior chamber to sequester the area of missing zonules and superiorly in a soft-shell under the endothelium. A 16 mm Fine/Thornton ring was utilized for fixation of the globe as it had a sufficiently large diameter to avoid traumatizing the bleb.

A temporal clear corneal incision was made utilizing a Rhein 3-D diamond blade®, synechiae were lysed, and a Morcher iris expander ring was inserted utilizing two hooks (Fig. 14–2). This device is inserted by compression into the pupillary space, which it then expands. Flanges on the top and bottom allow it to surround a pupil, much as a tire rim surrounds a tire, and holes in the flanges allow for intraocular manipulation. The expander ring maintained a broad angle of contact with the pupil as it was inserted and allowed stretching of the pupil without concentrating forces on the 12-o'clock radial sphincterotomy, thus avoiding extension of the tear.

Following placement of the iris expander ring, a continuous curvilinear capsulorrhexis was performed. A Morcher capsular tension ring was inserted into the capsular bag utilizing a forceps and a Lester hook. This device expands the equatorial zone of the capsule and transmits any focal force on the capsule to the entire zonular apparatus. Without the capsular tension ring, any focal force on the capsule would be transmitted only to the adjacent zonules, with much greater risk of damage. Thus the ring adds a margin of safety when operating on cataracts in the presence of a compromised zonular apparatus. In addition, it facilitates centration of the bag and IOL postoperatively since the outward force of the ring

opposes fibroses of the capsule, unopposed by compromised zonules.

Cortical cleaving hydrodissection and hydrodelineation were performed. Choo choo chop and flip phacoemulsification was done. This is a uniquely safe technique for removing nuclear material because the nucleus is disassembled with mechanical forces in the form of chopping and the resulting pieces are evacuated largely by high vacuum with low-power modulation ultrasound energy. It is an endolenticular technique. Utilizing either a bent Kelman tip or a 30-degree bevel-down straight tip enables one to approach nuclear material from above, pulling it up to the tip rather than getting underneath to mobilize and evacuate it. Ultrasound energy is concentrated at the upper levels of the endolenticular space, remote from the posterior capsule and the corneal endothelium. In addition, the technique allows for fixation of the lens between the two instruments (the chop instrument and the phaco tip) during lollipopping of the nucleus and scoring and chopping. Therefore, no downward force is exerted on the capsule or zonules during lollipopping the nucleus by the phaco tip.

Phacoemulsification took place with an effective phaco time of 6.4 seconds and an average ultrasonic energy of under 13.7%. The cortex, partially held in by the endocapsular tension ring, was carefully irrigated and aspirated. Cortex was stripped tangential to the capsulorrhexis rather than centrally in order to help pull it around the endocapsular tension ring. The capsular bag and anterior chamber were refilled with Provisc® after which a bolus of the dispersive Viscoat® was placed in the center of the capsulorrhexis. A 6-diopter foldable silicone IOL with 6 mm optic and PMMA loops was injected with the Allergan Unfolder into the capsular bag without complication.

During removal of residual viscoelastic, vitreous presented through the superior nasal iridectomy. This was removed with a coaxial vitrector and the iris expander ring was removed utilizing a Lester hook. The remainder of the residual viscoelastic was removed from the

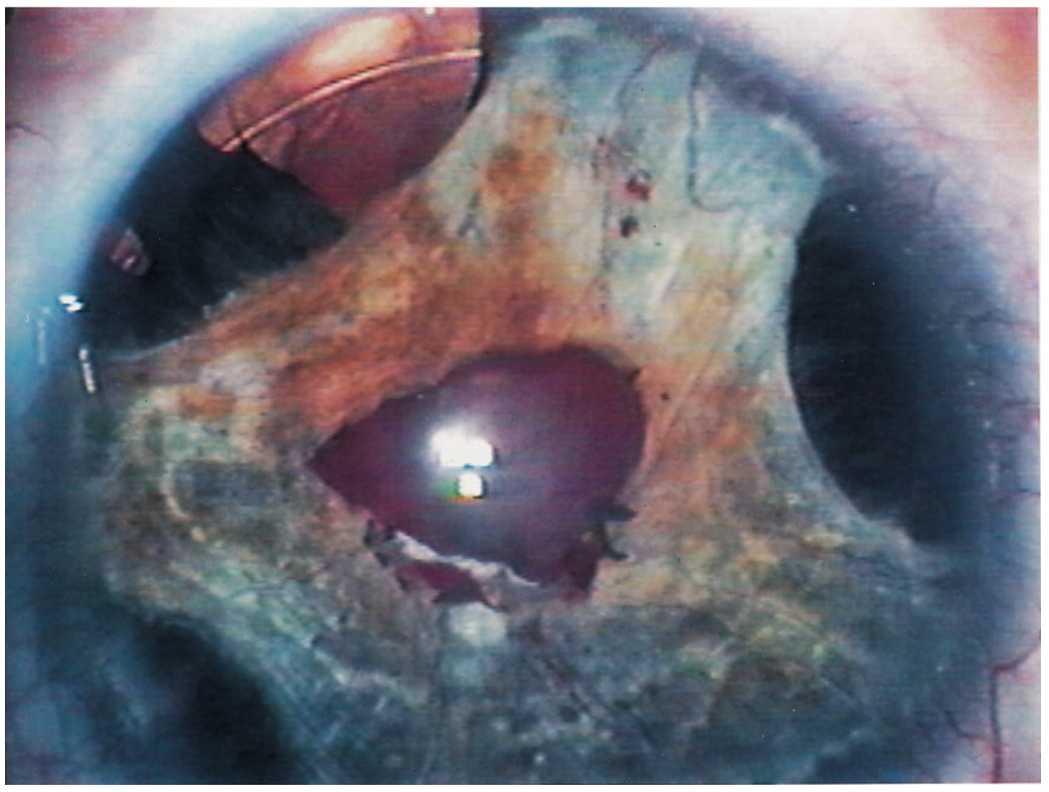

FIGURE 14–3 Immediate postoperative appearance of the eye with the capsular tension ring visible in the superior nasal peripheral iridectomy.

anterior segment with a vitrector to avoid vitreous coming to the incision through the zonular defect in the superior nasal iridectomy. Finally, stromal hydration was performed to seal the incision and the paracentesis. The immediate postoperative appearance of the eye is seen in Figure 14–3.

REHABILITATION AND FOLLOW-UP

The patient was examined twice daily over the next 3 days. The IOP was controlled with antiglaucomatous medicines. She was also treated with Pred Forte, Ocuflox, and Voltaren three times daily. Her IOP remained below 20 mm Hg during the first postoperative day. On the second postoperative day, tonometry revealed an IOP of 34 mm Hg and some mild corneal edema. Her antiglaucomatous medicines were increased, and the IOP came down to 28 mm Hg the next morning and was 17 at the final examination on the afternoon of the third postoperative day.

The postoperative visual acuity without correction was 20/200 in the right eye at each postoperative visit during the first 3 days. She has experienced an enormous increase in correctable acuity to 20/80. She uses a word processor at work, grows flowers, and is very aware of colors

and the brightness of objects. Two years postoperatively, her IOP remains in the low teens on no antiglaucomatous medication.

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Case 15

RETAINED LENS MATERIAL AFTER CATARACT EXTRACTION

Paul E. Finley, M.D.
Richard G. Weleber, M.D.

HISTORY

A 32-year-old man with insulin dependent diabetes mellitus since age 13 presents to an ophthalmologist with the chief complaint of sudden blurred vision and a "stinging" pain in the right eye. He reports an ocular history of uncomplicated bilateral cataract surgery with posterior chamber intraocular lens placement at age 19. At age 23, a traumatic dislocation of the intraocular lens in the right eye occurred secondary to blunt trauma. The patient reports that the lens had spontaneously "relocated" and surgery had not been performed.

Since that time the patient's history is unremarkable. Routine exam 5 months prior to presentation demonstrated 20/20 vision bilaterally, well-placed posterior chamber intraocular lenses with some residual cortex seen in the capsular bag superonasally in the left eye, and an absence of diabetic retinopathy.

Examination reveals 20/25 vision in each eye, normally reactive pupils without an afferent pupillary defect, and applanation pressures of 47 and 15 mm Hg in the right and left eyes, respectively. Slit-lamp biomicroscopy shows mild conjuctival injection in the right eye. Both corneas are clear. Anterior chamber exam of the right eye demonstrates 2+ cell and 3+ flare. Irides are without neovascularization. Gonioscopy of the right eye demonstrates a wide open angle with lens fragments inferiorly (Fig. 15–1). Well-centered posterior chamber intraocular lenses are seen bilaterally with apparently intact posterior capsules. In the anterior vitreous of the right eye a large spiral shaped capsular remnant is seen behind the intraocular lens (Fig. 15–2). Fundus exam shows a cup-to-disc ratio of 0.4 bilaterally and only a few microaneurysms consistent with very mild nonproliferative diabetic retinopathy.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Acute intraocular pressure (IOP) elevation in a diabetic is often a sign of rubeosis iridis and subsequent neovascular glaucoma. Typically this occurs in the setting of long-standing proliferative diabetic retinopathy. The frequency of rubeosis is greatly influenced by surgical intervention. Extracapsular cataract surgery performed without violation of the posterior capsule appears to prevent this complication, but it has occurred following laser capsulotomy. Examination did not demonstrate rubeosis in this instance, although it can sometimes be difficult to appreciate in the acutely inflamed eye. Absence of proliferative retinal disease makes this very unlikely, however.
2. Acute angle-closure glaucoma should be considered in any patient presenting with acute eye pain and blurred vision with a markedly elevated IOP on examination. The ability to visualize the open angle on gonioscopy rules out this diagnosis.
3. Ghost cell glaucoma arising from a vitreous hemorrhage can present with an elevated IOP. This is more likely in the pseudophakic eye where disruption of the anterior hyaloid and zonular apparatus allows forward egress of the degenerated red blood cells, which obstruct the trabecular meshwork. This patient did not have a vitreous hemorrhage, however.

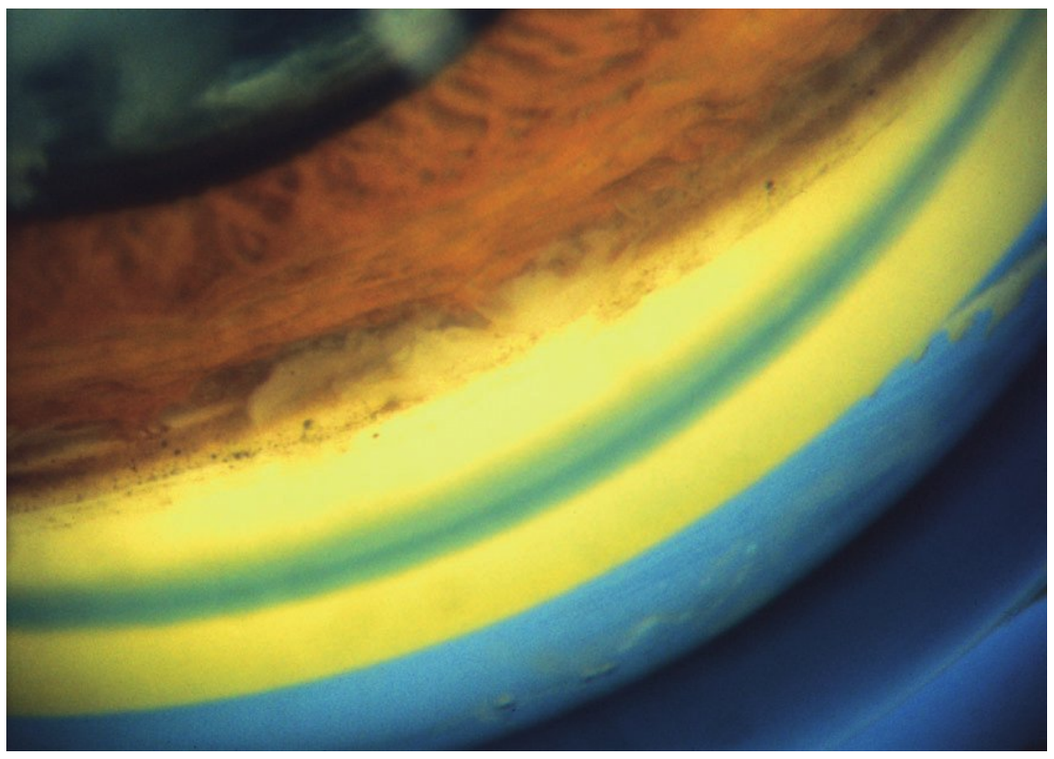

FIGURE 15-1 Gonioscopy demonstrates "fluffy" lens fragments in the inferior angle.

4. Iridocyclitis must be included in the differential when a patient presents with a painful red eye, elevated IOP, and anterior chamber reaction. Typically the IOP is lower than in the fellow eye due to inflammation of the ciliary body, but it can be markedly elevated when inflammatory debris obstructs the trabecular meshwork. Unilateral uveitis in a young male is commonly HLA-B27-positive–related disease. Typically, however, the IOP is reduced with HLA-B27–related anterior uveitis.
5. Lens particle glaucoma is the most likely diagnosis when the patient presents with "fluffy" lens particles in the anterior chamber angle. Outflow through the trabecular meshwork is significantly reduced with small amounts of free particulate lens material. Associated inflammation may also contribute to the elevation of IOP. The large capsular remnant found in the anterior chamber supports the diagnosis of lens particle glaucoma.

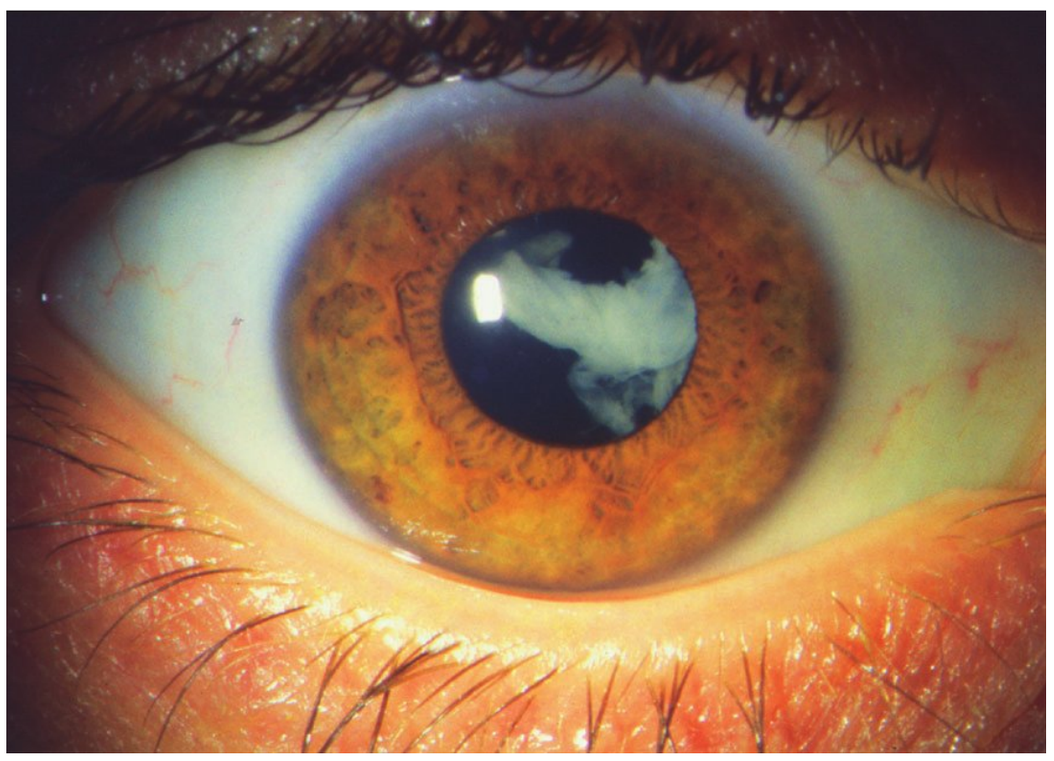

FIGURE 15–2 Anterior vitreous of the right eye demonstrates a large capsular remnant.

TEST INTERPRETATION

Careful clinical evaluation of the acutely inflamed eye can often give clues to the etiology. Markedly elevated pressure implies some disruption of the aqueous outflow tract. Initial evaluation of all patients with glaucoma should include gonioscopy to evaluate the anterior chamber angle, since the mechanism of outflow disruption often affects management. Finding fluffy lens particles in the chamber angle is pathognomonic for lens particle glaucoma. In addition, the finding of a wide open angle, the absence of angle neovascularization, and the lack of degenerated red blood cells rule out most of the etiologies listed above with a single test. The importance of skilled gonioscopic technique cannot be overstated.

If only small amounts of lens material can be seen, or if the setting is otherwise atypical, an anterior chamber tap might be necessary. The aqueous aspirate can be analyzed microscopically for the presence of macrophages and suspected lens material.

A thorough history is often helpful in the uveitis patient. Frequently the diagnosis is not apparent based on examination alone. In this instance, however, the finding of a large cortical lens fragment in the vitreous helped narrow the differential considerably.

DIAGNOSIS

Lens particle glaucoma.

MEDICAL MANAGEMENT

A patient with lens particle glaucoma who presents with an acute pressure elevation must be managed aggressively. Typically this condition

occurs in the immediate postoperative period and in severe cases can be difficult to distinguish from endophthalmitis, but onset can be quite delayed as this case illustrates. Salient issues are control of the IOP and inflammation. Initial treatment should include multiple IOP-lowering agents, frequent corticosteroids, and cycloplegics/mydriatics.

Many authors would advocate multiple IOP-lowering agents as an initial treatment to reduce the pressure into an acceptable range. The duration and magnitude of IOP elevation that can be tolerated depends on the age of the patient, the health of the optic nerve, and the vascular perfusion of the eye. Younger patients can tolerate a markedly elevated pressure for a longer period before suffering detectable visual field loss. Patients who have known preexistent glaucomatous damage are less likely to tolerate a markedly elevated pressure, and early surgical intervention may be necessary to prevent further optic nerve damage. Microvascular disease also affects the optic nerve tolerance to elevated IOP.

Multiple aqueous suppressants should be employed. In this case a topical beta-blocker, an alpha-2-adrenergic agonist, and both a topical and a systemic carbonic anhydrase inhibitor were employed. Miotics should be avoided to prevent posterior synechiae formation. Prostaglandin analogs are typically not used in the inflamed eye. Hyperosmotic agents should be reserved for the markedly elevated pressure and are a short-term measure. Glycerin should be avoided in the diabetic patient, but isosorbide or mannitol are acceptable emergency measures to lower the pressure.

Frequent topical corticosteroids are necessary to control the inflammation. Although suppression of the immune response might delay resorption of the lens particles, their use is essential in an eye with this degree of inflammation. Periocular or systemic corticosteroids might also be considered. Cycloplegics/mydriatics relax the ciliary body and prevent posterior synechiae.

SURGICAL MANAGEMENT

When maximal medical management is unsuccessful in controlling the IOP and inflammation quickly and adequately, the lens material should be removed surgically. Retention of 25% or more of the lens material is a definite indication for prompt surgical removal. Often the retained cortex can be removed from an anterior approach. A pars plana vitrectomy may be necessary when the fragment is posterior to the capsular bag or the need for a more thorough vitrectomy is anticipated.

If the posteriorly dislocated lens fragment occurs during surgery, retrieval should be attempted only if it is readily accessible. Complications such as giant retinal tears have occurred when anterior segment surgeons have attempted to remove lens fragments that have fallen into the vitreous. Implantation of an intraocular lens during the original cataract surgery is generally indicated if adequate support remains.

In situations where the surgery is delayed, the lens material can be trapped within the capsule or inflammatory membranes necessitating the need for microvitrectomy instrumentation. Also a higher incidence of chronic glaucoma has been reported when the subsequent vitrectomy was performed more than 3 weeks following surgery. Surgical removal of the lens material is typically sufficient to control the IOP elevation. Additional glaucoma filtration surgery is seldom necessary.

REHABILITATION AND FOLLOW-UP

Close follow-up is necessary when a patient presents with an acutely elevated pressure from lens particle glaucoma. Typically the patient that does not respond immediately to medical management should undergo definitive surgery. Often the removal of the lens fragment is curative.

In the case presented, the patient was initially placed on intensive medical therapy for glaucoma and uveitis that included timolol, brimonidine, dorzolamide, prednisolone, and systemic acetazolamide. Despite this regimen, the patient's IOP remained higher than 40 mm Hg. Three days after presentation the patient underwent plars plana vitrectomy with removal of the

lens fragment. His IOP improved to 14 mm Hg on the first postoperative day.

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Case 16

FIBRIN DEPOSITION ON INTRAOCULAR LENSES

Christopher N. Ta, M.D.

HISTORY

A 59-year-old Caucasian woman presented to the eye clinic 5 days after intraocular surgery in the right eye, with a chief complaint of photophobia. Her past ocular history was significant for combined cataract extraction with posterior chamber lens implantation and trabeculectomy with mitomycin-C in the right eye 5 days prior to presentation and in the left eye 1 month prior to presentation. Her past medical history was significant only for hypertension. Her ocular medications were prednisolone acetate 1% every 2 hours and ofloxacin 4 times a day in both eyes.

On exam, her visual acuity was 20/60 OD and 20/200 OS. Slit-lamp examination of the right eye revealed a mild conjunctival injection with a low bleb. The cornea was clear. The anterior chamber had moderate cells and flare with no hypopyon. There was a meshwork of fibrin deposition on the intraocular lens (IOL) (Fig. 16–1). Examination of the left eye revealed a low bleb, clear cornea, and rare cells in the anterior chamber. The IOL was in good position. Dilated fundus exam was unremarkable in both eyes except for moderate and severe glaucomatous cupping of the optic nerve of the right and left eye, respectively. The poor vision in the left eye was secondary to advanced glaucoma.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Fibrinous reaction in the anterior chamber typically presents between days 2 and 8 after intraocular surgery. The patient may complain of decreased vision, red eye, pain, and photophobia. On examination, there is a cellular anterior chamber reaction without the presence of a hypopyon. The fibrin can present as strands on the IOL, in the pupillary plane, or on the iris itself. In a more severe inflammatory reaction, there can also be a fibrinous membrane covering the pupil.

2. Endophthalmitis is always in the differential diagnosis, particularly if a hypopyon is present. However, patients with endophthalmitis usually have more severe symptoms, such as pain and poor vision. On exam, the conjunctiva is injected with chemosis and there usually is a severe cellular reaction in the anterior chamber. Not uncommonly, there will be a hypopyon present. There may also be cells in the anterior vitreous.

3. The pathophysiology of fibrin deposition on the IOL is immune-mediated. From the surgical trauma, there is increased blood–aqueous permeability. The breakdown in the blood–aqueous barrier allows fibrinogen from blood plasma, a precursor of fibrin, to leak out of blood vessels and into the anterior chamber. In the presence of inflammatory mediators, such as prostaglandins, along with thrombin and activated coagulation factors, fibrinogen is converted to fibrin.

4. The incidence of fibrinous uveitis is less than 3% after normal uncomplicated cataract extraction and IOL implantation, but can be as high as 45%, depending on the patient population and study design. Certain conditions that are associated with an increase in vascular permeability predispose to fibrin formation. These include diabetes, hypertension, pseudoexfoliation syndrome, and a previous history of uveitis. Local factors that may increase the likelihood of developing a

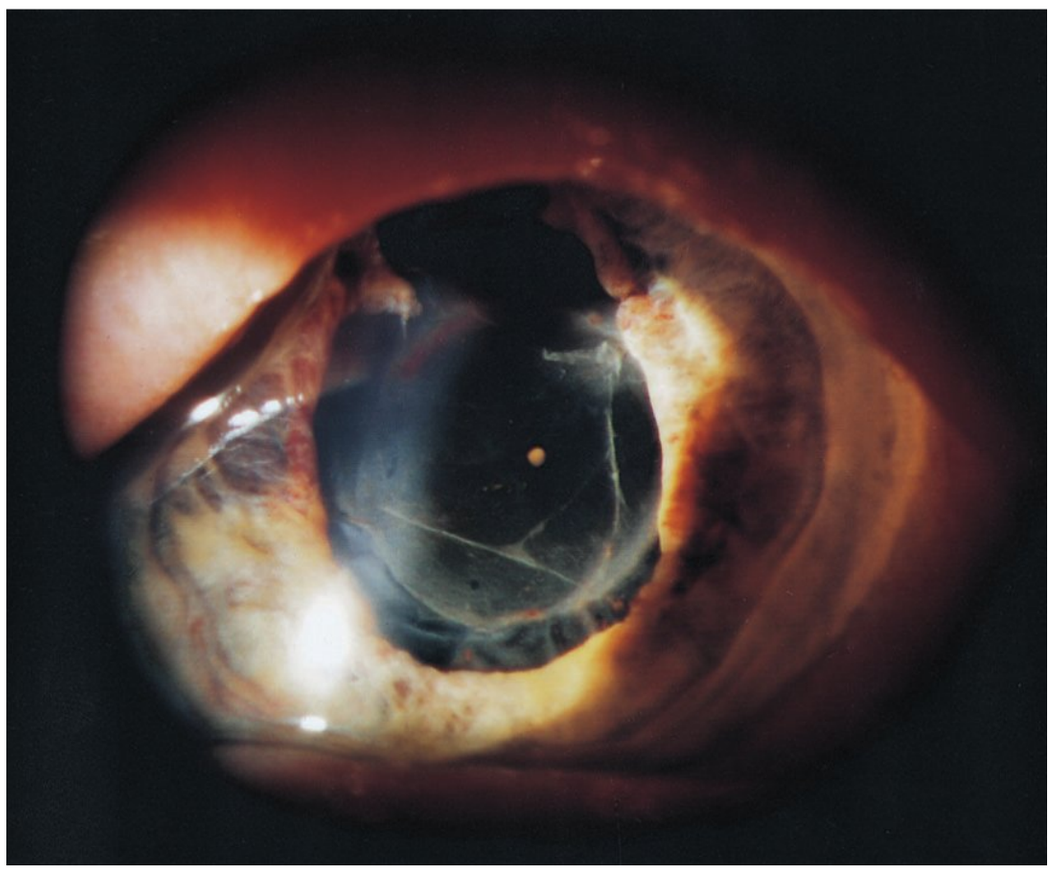

FIGURE 16–1 Fibrin deposition on the IOL 5 days postoperatively.

fibrinous reaction are surgical manipulation of the iris and incomplete removal of the lens cortex and epithelial cells. Previous history of intraocular surgery, even if done in the fellow eye, particularly if performed recently, is also a risk factor for developing fibrinous uveitis.

5. Fibrin deposition indicates a severe inflammatory reaction. Complications of fibrin uveitis are posterior synechiae, loss of iris function, membrane formation on the IOL, dislocation of the IOL, and secondary glaucoma. The risk for developing cystoid macular edema is increased with intraocular inflammation, particularly if the posterior capsule is compromised. Posterior capsular opacification is generally due to lens epithelial migration and proliferation, but the presence of fibrin and inflammation may trigger this process.

6. Pathologically, fibrin appears as fine proteinaceous fibers in a meshwork. There may be associated macrophages and giant cells.

TEST INTERPRETATION

The diagnosis is made by history and slit-lamp examination. The patients usually present 2 to 5 days postoperatively complaining of blurry vision, pain, and photophobia. However, they may be asymptomatic as well. Patients at risk for developing fibrinous uveitis include those with diabetes, hypertension, pseudoexfoliation syndrome, previous ocular surgery, history of uveitis, and intraoperative iris manipulation. Children have a higher risk than adults for developing fibrin deposition.

On exam, the visual acuity can vary considerably. Slit-lamp examination reveals the presence of cells and flare in the anterior chamber without a hypopyon. More importantly, there is the presence of fibrin in the anterior chamber, on the IOL, in the pupillary plane, and occasionally on the iris. The intraocular pressure (IOP) may be high due to secondary glaucoma, such as pupillary block or clogging of the trabecular meshwork from inflammatory cells. However, the IOP can also be low due to inflammation of the ciliary body. A dilated fundus exam typically reveals a hazy view of the retina. There are usually no cells in the vitreous and the retina appears normal.

Postoperative fibrinous uveitis can be difficult to differentiate from postoperative endophthalmitis. The time of onset and symptoms are similar between the two diagnoses, except that the patient with endopthalmitis may have more severe symptoms. On exam, the presence of ciliary injection, chemosis, a severe anterior chamber reaction and hypopyon, as well as cells in the vitreous are more likely to represent endophthalmitis. An anterior chamber and vitreous aspirate for culture should be considered when endophthalmitis is suspected.

DIAGNOSIS

Right eye: Postoperative fibrin deposition on the IOL.

MEDICAL MANAGEMENT

The goal of treatment is to reduce inflammation and restore the blood–aqueous barrier. A topical steroid, such as prednisolone, is the mainstay of treatment. The usual dose is prednisolone acetate 1%, 1 drop 4 to 6 times a day, up to hourly, depending on the level of inflammation.

Topical nonsteroidal anti-inflammatory and anti-prostaglandin agents have also been used successfully in combination with a topical steroid. In severe cases, particularly in patients with a history of uveitis prior to surgery, systemic steroid may be required to control the inflammation.

In high risk patients, fibrin deposition may be preventable by the use of topical nonsteroidal anti-inflammatory and/or topical steroid agents preoperatively. In addition, intraoperative subconjunctival injection of steroids can be of benefit in controlling postoperative inflammation.

Recombinant tissue plasminogen activator (tPA) can have a dramatic effect in breaking down fibrin in severe cases of fibrin deposition. tPA converts plasminogen to plasmin, which lyses fibrin to fibrin-split products. tPA has been shown to be effective with an intracameral injection of doses as low as 10 μg. Complications with the use of intracameral tPA are rare but can include severe bleeding and retinal toxicity at high doses. There is also the risk of introducing microorganisms into the anterior chamber with a tPA injection. Tissue plasminogen activator does not seem to damage endothelial cells, even at high doses. Urokinase, another fibrilolytic agent, can also be used.

SURGICAL MANAGEMENT

Additional surgery in an already inflamed eye is not advisable, except when there are obvious indications for surgery, such as a dislocated IOL. In cases when the IOL is the cause of inflammation (eg, an anterior chamber lens that is rubbing against the iris) it is reasonable to remove the IOL.

REHABILITATION AND FOLLOW-UP

Medical treatment is usually successful in eliminating inflammation and fibrin deposition. However, these patients are at risk for developing infectious keratitis from topical steroid use, secondary glaucoma, and cystoid macular degeneration. Eye examinations should be done at a regular interval to follow visual acuity, IOP, and signs of infection or recurrent inflammation.

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Case 17

SUBLUXATED CRYSTALLINE LENS

David F. Chang, M.D.

HISTORY

A 35-year-old woman with Marfan syndrome presents with complaints of bilateral decreased vision and disabling glare. The patient's father had Marfan syndrome and had experienced a spontaneous lens dislocation in one eye. Visual acuity is 20/200 OU with −9.00 D correction in each eye. There is bilateral ectopia lentis. The right lens (Fig. 17–1) is subluxated superotemporally with diaphanous zonules exposed across an area of at least six clock hours. There is phacodonesis, but no vitreous is present anteriorly. The intraocular pressure (IOP) and fundus examination are normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The most common cause of a dislocated or subluxated lens is trauma. This is the usual etiology of a unilateral lens subluxation. Since the trauma may have been incidental, absence of a trauma history does not rule out this cause. Less common causes of acquired lens subluxation are pseudoexfoliation and eye rubbing associated with atopy.
2. Bilateral subluxated lenses are usually associated with a hereditary systemic disorder. The Marfan syndrome is autosomal dominant. Autosomal-recessive etiologies include homocystinuria, the Weill-Marchesani syndrome, hyperlysinemia, and sulfite oxidase deficiency. Mental retardation is usually associated with the metabolic genetic disorders. A full medical and metabolic workup is indicated with nontraumatic bilateral lens subluxation to evaluate the cause. Homocystinuria can be diagnosed by a sodium nitroprusside test of the urine. Medical and ophthalmologic examinations of family members may contribute useful information.
3. Marfan syndrome is the most common hereditary disorder associated with lens subluxation. Typical physical findings include tall stature, long, thin extremities, arachnodactyly, joint laxity, pectus excavatum, kyphoscoliosis, and decreased subcutaneous fat. Establishing the diagnosis is important both for genetic counseling and because of the cardiac implications of this syndrome. Echocardiography should be performed to rule out mitral or aortic valve abnormalities and progressive dilation of the ascending aorta, since a dissecting aortic aneurism may cause sudden death. In Marfan syndrome the lens is usually dislocated in an upward or up-and-out direction. Aside from ectopia lentis, ocular associations may include axial myopia, glaucoma, blue sclera, and retinal detachment.
4. A careful ophthalmologic exam must be performed on any patient with a subluxated lens. Although a dilated exam is necessary to determine the extent of lens decentration or subluxation, phacodonesis may be more evident in the undilated eye because of associated iridodonesis. Gonioscopy may disclose a traumatic angle recession. A careful peripheral retinal exam should be performed because patients with Marfan syndrome and homocystinuria are predisposed to retinal detachment. Glaucoma, uveitis, and cataract are also associated with some of the potential etiologies.

DIAGNOSIS

Bilateral lens subluxation associated with Marfan syndrome.

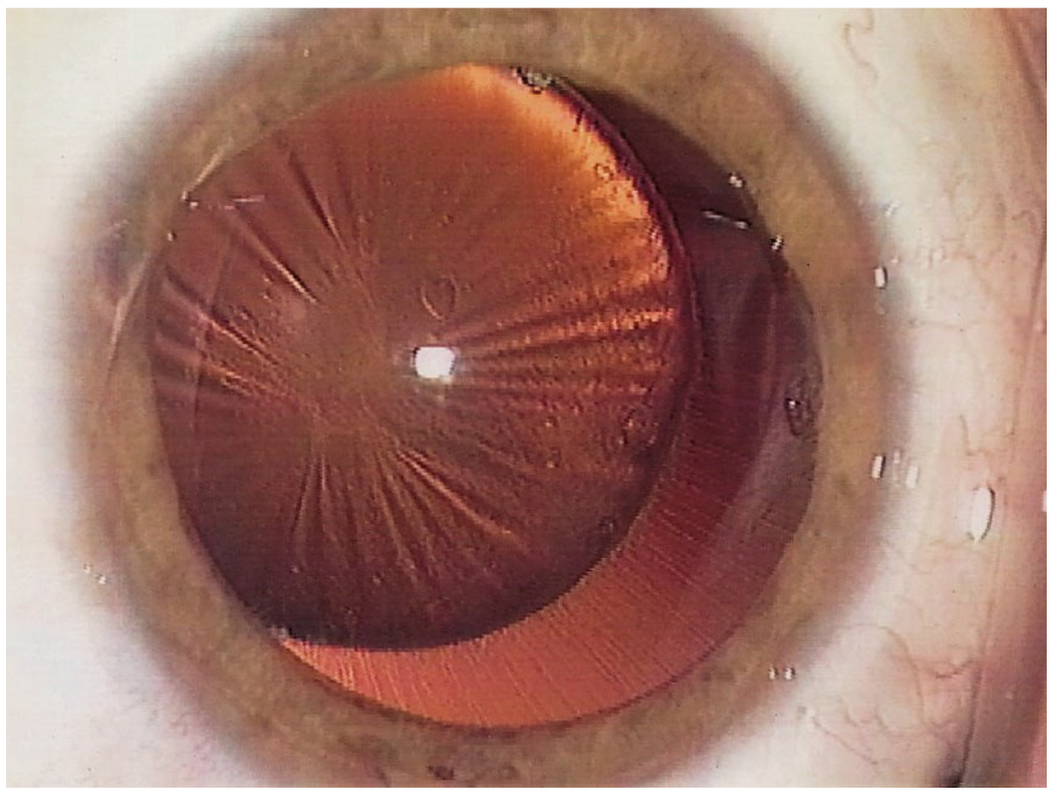

FIGURE 17–1 Upward subluxation of crystalline lens in right eye.

MEDICAL MANAGEMENT

A subluxated lens can be managed conservatively unless significant visual symptoms or complications arise. Lens-induced optical errors such as myopic shift, lenticular astigmatism, anisometropia, and prism effect can be corrected with spectacles or contact lenses. Lens subluxation in a pediatric patient may cause amblyopia, which must be aggressively treated and monitored.

If the crystalline lens is partially dislocated out of the pupillary axis, aphakic glasses or contact lenses can be utilized successfully. Cycloplegics can be used to enlarge this aphakic aperture. Alternatively, miotics can be employed to minimize monocular diplopia or optical aberrations arising from the lens edge. Neodymium: yttrium-aluminun-garnet (Nd:YAG) laser zonulysis has been used to further clear the visual axis of a partially dislocated lens. A completely dislocated crystalline lens should be well tolerated and may remain within the eye indefinitely.

A forward shift of the crystalline lens due to zonular laxity may result in pupillary block and angle-closure glaucoma. A peripheral laser iridotomy may solve this problem in the short term. More severe zonular laxity may lead to forward dislocation of the lens into the anterior chamber with resulting endothelial cell loss and corneal decompensation. The lens can be repositioned by placement of the patient in the supine position following pharmacologic mydriasis so that the lens will fall back behind the pupil—either spontaneously or with manual pressure applied against the cornea. Pharmacologic miosis is used to trap the mobile lens posteriorly. Recurrence of these complications may ultimately make a surgical lensectomy necessary.

SURGICAL MANAGEMENT

There are three basic approaches to surgical removal of a subluxated or dislocated crystalline lens. The first is an extracapsular cataract extraction with capsular fixation of a posterior chamber intraocular lens (IOL). The second is a planned intracapsular cataract extraction with an anterior chamber IOL. The third is a planned lensectomy and vitrectomy with removal of the lens capsule. In this last instance, options include placement of an anterior chamber IOL, placement of a sutured posterior chamber IOL, or leaving the patient aphakic. If an aphakic contact lens is not tolerated, a secondary IOL implantation can be performed at a later stage.

1. Extracapsular Cataract Extraction

Depending on the individual surgeon's experience, phacoemulsification may be considered if there is only a partial zonular dialysis. The advantage of this approach is the preservation of the posterior capsule, which allows posterior chamber IOL fixation and may decrease the risk of cystoid macular edema (CME), elevated IOP, and retinal detachment. However, phacoemulsification of a subluxated lens is among the most challenging of cases for an anterior segment surgeon. These eyes are predisposed to zonular dialysis, posterior capsule rupture, vitreous loss, and a dropped nucleus.

During phacoemulsification care must be taken to minimize stress on the already weakened zonules. The technique of phaco chop, which utilizes inwardly directed manual forces to reduce stress on the capsular bag, is advantageous. An endocapsular tension ring can be implanted at any point after the capsulorrhexis is completed. During surgery, this permanent polymethyl methacrylate (PMMA) ring will redistribute the instrument forces equally across the remaining zonules and may otherwise compensate

for the lack of normal centrifugal zonular tension. This may reduce the extent of subsequent capsular contraction as well. Flexible iris retractors may be useful to fixate the capsular bag during phacoemulsification. Four retractors are placed through clear corneal stab incisions to hook the capsulorrhexis edge in each quadrant.

Even if the IOL is successfully implanted, there may be problems with centration and the long-term stability of the capsular bag. Contraction of the capsulorrhexis and capsular bag may cause delayed decentration of the lens because of asymmetric centrifugal zonular tension. Posterior dislocation of the entire IOL-capsular bag complex may occur years later.

There are two surgical approaches to centering and fixating a subluxated capsular bag. The first technique uses polypropylene (Prolene) sutures as "artificial zonules" to fixate the fornix of the capsular bag to the sclera. The IOL is implanted and oriented so that its haptic axis points toward the area of greatest zonular weakness. One needle of a double-armed 10-0 polypropylene suture is introduced through the wound and passed ab interno out through the ciliary sulcus. The second needle passes through the capsulorrhexis, through the capsular fornix in the region of missing zonules, and out through the ciliary sulcus and sclera, where the knot is tied. The haptic loop is incorporated into the knot.

A second method uses the Cionni modification of the PMMA endocapsular tension ring

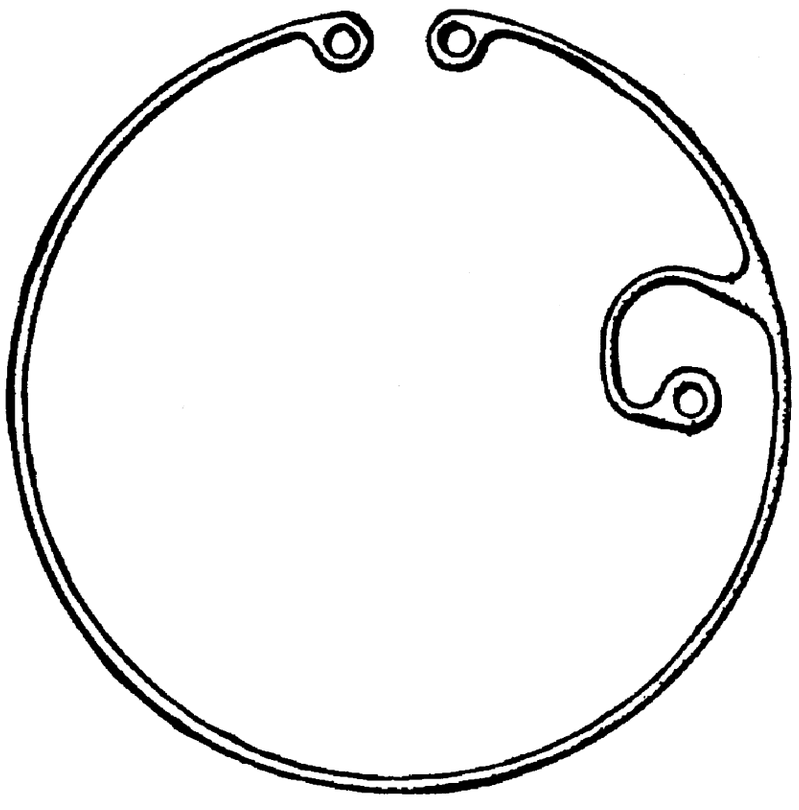

FIGURE 17–2 Cionni modification of endocapsular PMMA tension ring.

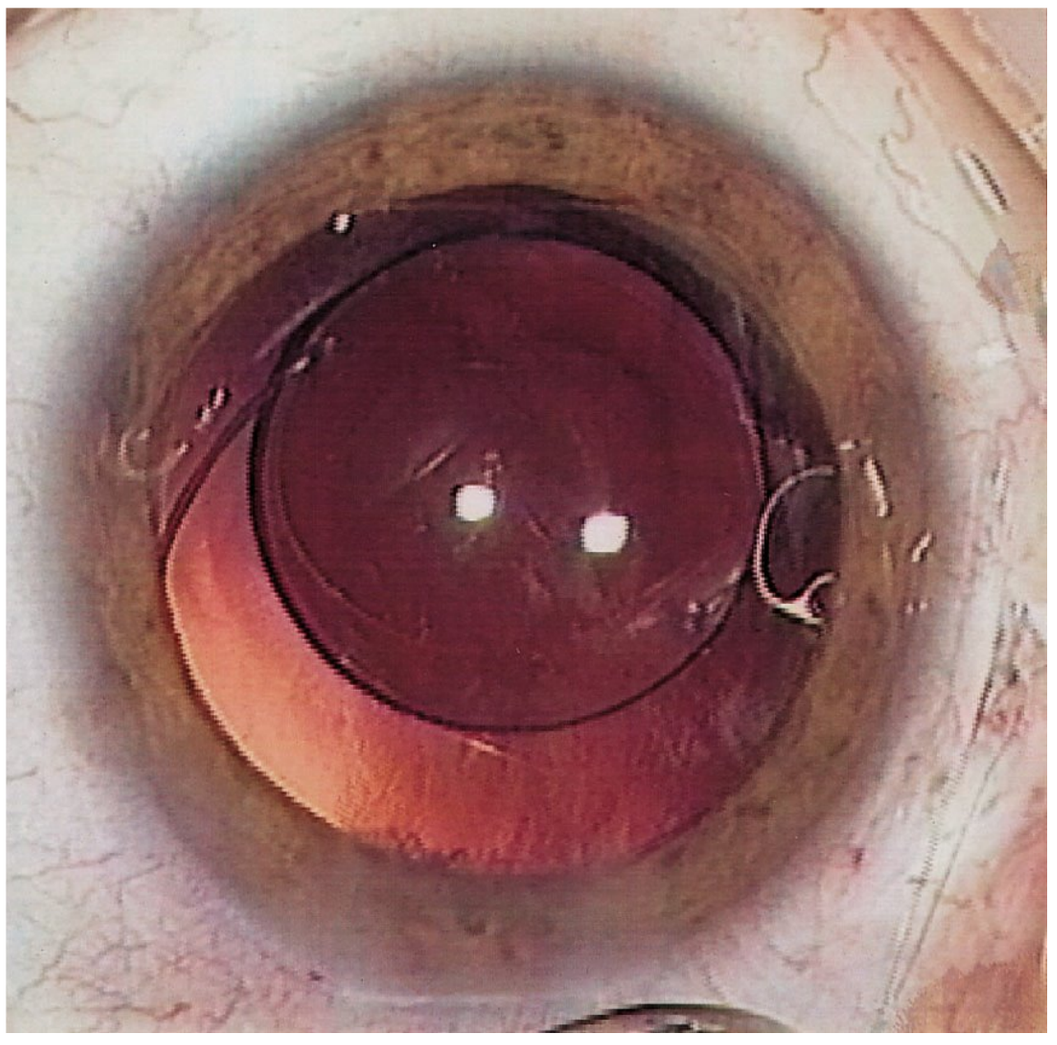

FIGURE 17–3 Capsular bag fixation of a posterior chamber IOL. The eyelet of the Cionni ring is located behind the iris and anterior to the capsulorrhexis. Polypropylene sutures passed through the ciliary sulcus fixate the eyelet to the sclera externally, securing and recentering the capsular bag.

(Fig. 17–2), which, like the conventional ring, is placed inside the capsular bag. Depending upon the design, there are one or two hooks that extend anteriorly around the capsulorrhexis margin so that an eyelet on the end of the hook is located behind the iris and just in front of the anterior capsule. The hook is positioned so that the sutured eyelet will anchor the ring to the sclera in the area of missing zonules. Prior to insertion of the Cionni endocapsular ring, the needles of a double armed 10-0 polypropylene (Prolene) suture are preplaced, passing through the eyelet, through the incision, and behind the iris, exiting through the ciliary sulcus and sclera in the meridian of the zonular dialysis. After implanting and orienting the Cionni ring, tying the knot will recenter the ring and the capsular bag prior to placement of the IOL (Fig. 17–3).

2. Intracapsular Cataract Cryoextraction

This approach can be considered if the risk of vitreous loss and a dropped nucleus are deemed to be too high because of the severity of lens

subluxation and zonular weakness. The goal would be removal of the subluxated lens and placement of an anterior chamber IOL while avoiding vitreous loss. If an intact vitreous face is preserved, implantation of a properly sized anterior chamber IOL is preferable to a sutured posterior chamber IOL. With any subluxated lens, it is important to examine the patient in the supine position preoperatively. If the lens falls too far posteriorly, extraction through a limbal approach may not be feasible.

3. Pars Plana Lensectomy and Vitrectomy

Although this procedure can be used to remove any significantly subluxated lens, there are two primary indications for this approach. One would be if the lens drops too far back while the patient is supine because of severe zonular loss or laxity. A second indication would be a significant prolapse of vitreous into the anterior chamber. Under these circumstances, the goals would include a complete removal of all lens material and a thorough vitrectomy carried out peripherally to the vitreous base. A separate limbal incision must then be made for the IOL implantation, which may be performed at the same sitting by the vitrectomy surgeon or by a separate anterior segment surgeon. IOL implantation may be deferred either because of the operative logistics or in order to allow an aphakic contact lens trial. This would be a particular consideration in young patients because of long-term concerns with noncapsule fixated IOLs.

REHABILITATION AND FOLLOW-UP

Which type of IOL to implant in a young patient lacking a posterior capsule is open to debate. Relative contraindications to an anterior chamber IOL would be coexisting glaucoma, inadequate iris support or abnormal iris/angle anatomy (eg, secondary to trauma), or an anterior segment that is expected to grow in diameter. The Marfan syndrome and trauma constitute separate risk factors for glaucoma as well. Scleral suturing of a posterior chamber IOL is more difficult and may be complicated by intraocular hemorrhage, pigment dispersion, tilting of the optic, and unintended refractive error because of its unpredictable axial position. Polypropylene knots may later erode through the conjunctiva causing discomfort and providing a track for infection. Finally, there is the long-term concern that polypropylene sutures may biodegrade over time.

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All photos courtesy of Robert J. Cionni, M.D.

Case 18

CONGENITAL CATARACT

Peter R. Egbert, M.D.

HISTORY

A pediatrician noticed white pupils in a 10-day-old girl and made the diagnosis of cataract. The mother had had an uncomplicated pregnancy with no rash or febrile illness. There was no family history of cataracts or any other eye abnormality, and her general health was good. She was referred to an ophthalmologist.

Examination showed reactive pupils with no afferent pupillary defect, normal extraocular movements, and normal external exam. The corneas and eyes were normal in size. The center of the lens was opaque white OU (Fig. 18–1). Tactile tensions were normal. The peripheral retina was normal, but the posterior pole could not be seen.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Congenital cataract is a common cause of blindness in children. Early detection is the most important factor in determining the eventual visual outcome.
2. The first important diagnostic distinction is whether leukocoria truly represents a cataract or another problem. Cataract is the most common cause of leukocoria, but other causes are retinoblastoma, retinopathy of prematurity, uveitis, Coats' disease, retinal detachment, and persistent hyperplastic primary vitreous (PHPV). PHPV occurs in microphthalmic eyes and often has an associated cataract. This entity should be suspected in any eye that is even slightly small. There is a white retrolental mass, a posterior cataract, and elongated ciliary processes. The retina may be pulled anteriorly into the retrolental mass, and in severe cases, a shallow anterior chamber with high intraocular pressure (IOP) occurs. PHPV is almost always unilateral and was therefore unlikely in this child with bilateral cataracts and normal-size eyes.
3. Approximately half of all congenital cataracts are idiopathic, and, in particular, a cause for unilateral cataract is rarely found. Nevertheless, there are many known etiologies for congenital cataract that should be kept in mind; cataracts may be inherited, infectious, related to systemic disorders, or associated with ocular syndromes. Inherited cataracts are most commonly autosomal dominant and less commonly recessive or X-linked. Examples of systemic conditions associated with congenital cataracts are galactosemia, Down syndrome, trisomy 13-15, and Lowe syndrome. Rubella is an example of intrauterine infection that causes cataracts and was often seen before rubella vaccinations were available. PHPV is the most common ocular syndrome associated with congenital cataract.
4. In congenital cataract, the opacity may involve the entire lens or it may be localized. Opacities localized to the embryonic or fetal nucleus often leave the peripheral lens cortex optically clear. The extent of the opacity is obviously important for vision.

TEST INTERPRETATION

A careful examination with dilated pupils is the best technique for diagnosing a cataract. Either the direct or indirect ophthalmoscope held close to the eye provides a good magnified view of the anterior segment. In addition, an infant can often be held up to the slit lamp for examination. The ease with which one can view the retina

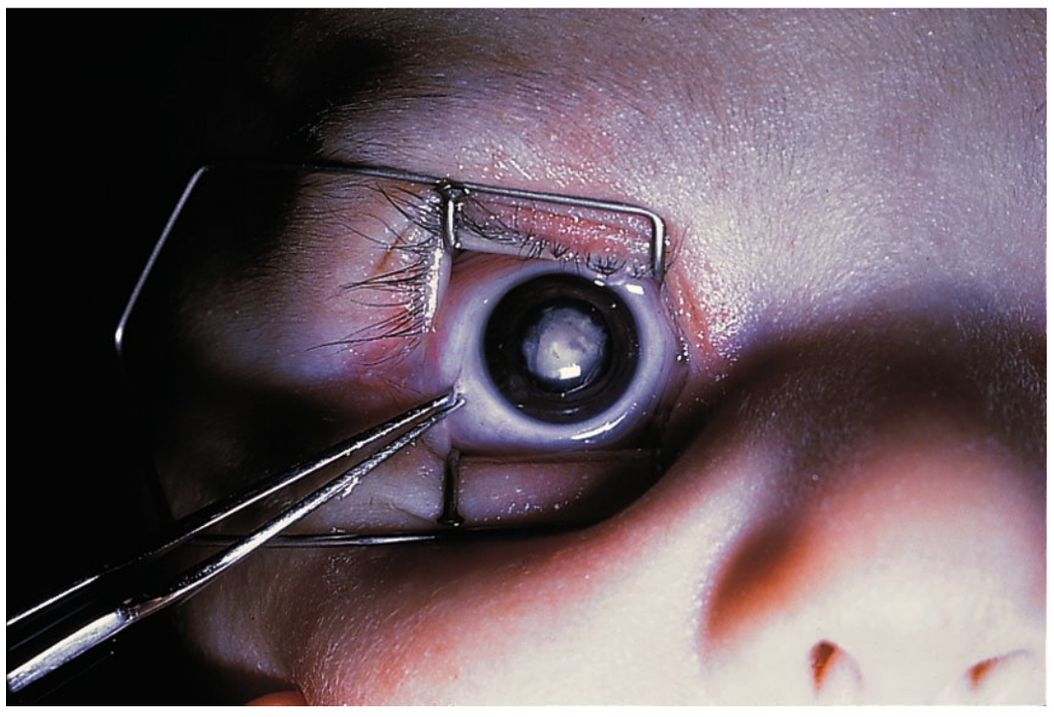

FIGURE 18–1 Central nuclear congenital cataract.

with an ophthalmoscope corresponds to the visual significance of the cataract. Many congenital cataracts are small enough that vision is unimpaired or only slightly impaired.

After diagnosing cataracts, the basic approach to a child is to determine whether the cataract is an isolated finding in an otherwise healthy child or whether the cataract is part of a systemic disorder. Unilateral cataracts in a healthy baby often need no workup except determining the family history and that the mother did not have a febrile illness or rash during pregnancy that would point to an intrauterine infection. Infants with bilateral cataracts will, in addition, usually have toxoplasmosis, other agents, rubella, cytomegalovirus, herpes simplex (TORCH) titers, and a test for reducing substances in the urine. If the child is dysmorphic, genetic counseling is appropriate; if there is failure to thrive, a more thorough search for metabolic diseases by the pediatrician may be necessary.

An ophthalmic ultrasound examination is desirable if the cataract is so dense that there is no view of the retina. This examination allows indirect visualization of the retina and vitreous so that PHPV, uveitis, and other disorders of the posterior portion of the eye are seen if present.

Sometimes it is necessary to have an examination under anesthesia. Certainly, while the child is anesthetized for cataract extraction, an examination should be performed to confirm the preoperative findings. At this time it is also important to measure intraocular pressure to rule out associated congenital glaucoma.

DIAGNOSIS

Bilateral idiopathic congenital cataract.

MEDICAL MANAGEMENT

There is no medical treatment of cataract. However, some children have central cataract that allows good vision if, and only if, the pupil is pharmacologically dilated. These children can enjoy improved vision when treated chronically with mydriatics such as atropine once a day or once every other day. Because atropinic agents can cause systemic side effects in babies, a low dose is used.

SURGICAL MANAGEMENT

If the cataract is large and dense enough to interfere with visual development, surgical removal should be performed as soon as possible. The risk of delaying surgery is amblyopia and nystagmus. The sooner surgery can be performed consistent with safe anesthesia the better—a common time is at age 2 to 6 weeks. The child in this case had surgery on the right eye at age 14 days and the left eye at age 21 days.

An important issue in surgery is whether an intraocular lens (IOL) is implanted or not. An IOL provides the best optical correction and improves the postoperative management of amblyopia. IOLs are reasonably well tolerated by children over the age of 2 who have had late maturation of congenital cataracts. But the use of IOLs in younger children is controversial. The disadvantages of IOLs include increased inflammation, intraocular scar formation, and difficulty predicting the proper lens power in an eye that is growing.

Compared to cataract surgery in adults, surgery in infants is technically more difficult. Not only is the eye much smaller and therefore harder to approach, but also the anterior capsule is tough and elastic and the posterior capsule must be removed to prevent inevitable postoperative opacification. Also, the iris has a strong propensity to adhere to the posterior capsule and vitreous, requiring pupil dilation for several weeks after surgery.

REHABILITATION AND FOLLOW-UP

Excellent optical correction together with appropriate occlusion therapy is essential in order to minimize amblyopia. This aspect of postoperative management requires patience and perseverance from both the ophthalmologist and the parents. Amblyopia will occur unless the retina receives a focused image. If amblyopia is not vigorously approached, the child will develop a severe and permanent loss of vision. Therefore, if there is no IOL the child must be fitted with contact lenses or glasses within days after the surgery. For the bilateral cataract patient, glasses are often the better alternative since they are much easier for the parents to manage (Fig. 18–2). For the unilateral patient, however, contact lenses are preferred, because unilateral correction by glasses produces intolerable distortion and image disparity between the operated and unoperated eyes. Occlusion of the better-seeing eye is carried out as needed until age 6 or 7 years.

Glaucoma can occur following congenital cataract surgery. Long-term follow-up of patients is necessary since glaucoma may become manifest many years after the surgery.

FIGURE 18–2 Postoperative optical correction with aphakic spectacles.

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Section III

GLAUCOMA

19. Ocular Hypertension
20. Open-Angle Glaucoma
21. Primary Angle-Closure Glaucoma
22. Pigmentary Glaucoma
23. Neovascular Glaucoma
24. Inflammatory Glaucoma
25. Primary Infantile Glaucoma
26. Ocular Hypotony
27. Post Trabeculectomy Wound Leak
28. Failing Filtering Bleb
29. Flat Anterior Chamber
30. Persistent Choroidal Detachment

Case 19

OCULAR HYPERTENSION

Kuldev Singh, M.D., M.P.H.

HISTORY

A 42-year-old Caucasian man was referred to the eye clinic after being told by an optometrist that his eye pressures were too high and that he might have glaucoma. Past medical history and family history were unremarkable. He was not taking any medications.

Ocular examination revealed visual acuity of 20/20 OU without correction. Pupils and motility were normal. Anterior segment biomicroscopic examination was unremarkable with a clear cornea and lens. Intraocular pressure (IOP) was 27 mm Hg OD and 28 mm Hg OS. Gonioscopy revealed wide-open angles 360 degrees with moderate pigmentation of the trabecular meshwork. Dilated funduscopic examination revealed symmetric optic nerves with mild cupping (Figs. 19–1 and 19–2). The cup-to-disc ratio was 0.2 and the neuroretinal rim intact OU. The macula, vessels, periphery, and vitreous were normal in appearance. Humphrey automated perimetry was noted to be normal in both eyes.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The finding of elevated IOP in the presence of normal-appearing optic nerves and visual fields makes idiopathic ocular hypertension (OHTN) the most likely diagnosis.

2. If there has been focal or generalized injury to ganglion cells related to this elevated IOP, the diagnosis of primary open-angle glaucoma (POAG) should be considered. As early injury in POAG is sometimes difficult to detect by nerve examination and visual field testing, the distinction between OHTN and POAG is not always easy to discern.

3. If gonioscopy revealed an obstructed trabecular meshwork, secondary causes of elevated IOP would have to be entertained. Unfortunately, these secondary causes of elevated IOP are often referred to as "glaucoma" even when the optic nerve and visual field are normal.

4. Diseases such as pigmentary dispersion syndrome and pseudoexfoliation syndrome can result in secondary IOP elevation. These diseases are associated with characteristic features that are generally visible on slit-lamp examination. Once again, patients with these conditions and elevated IOP are often referred to as having pigmentary or pseudoexfoliative glaucoma rather than OHTN.

TEST INTERPRETATION

1. Measurement of IOP is crucial in making the diagnosis. Goldmann applanation tonometry remains the gold standard. Measurement by the tonopen or pneumotonometer may be more convenient or accurate in certain settings, especially in the presence of corneal disease.

2. Slit-lamp examination to rule out causes of IOP elevation secondary to ocular conditions or syndromes is critical. Eyes with ocular conditions associated with transient or permanent elevated IOP may require therapy even in the absence of optic nerve damage. An example of this is seen in patients with rubeosis iridis who may require panretinal photocoagulation.

3. Gonioscopy should be used to rule out a narrow or closed angle, which may be associated with IOP elevation. Transient IOP elevation is fairly commonly seen with occludable

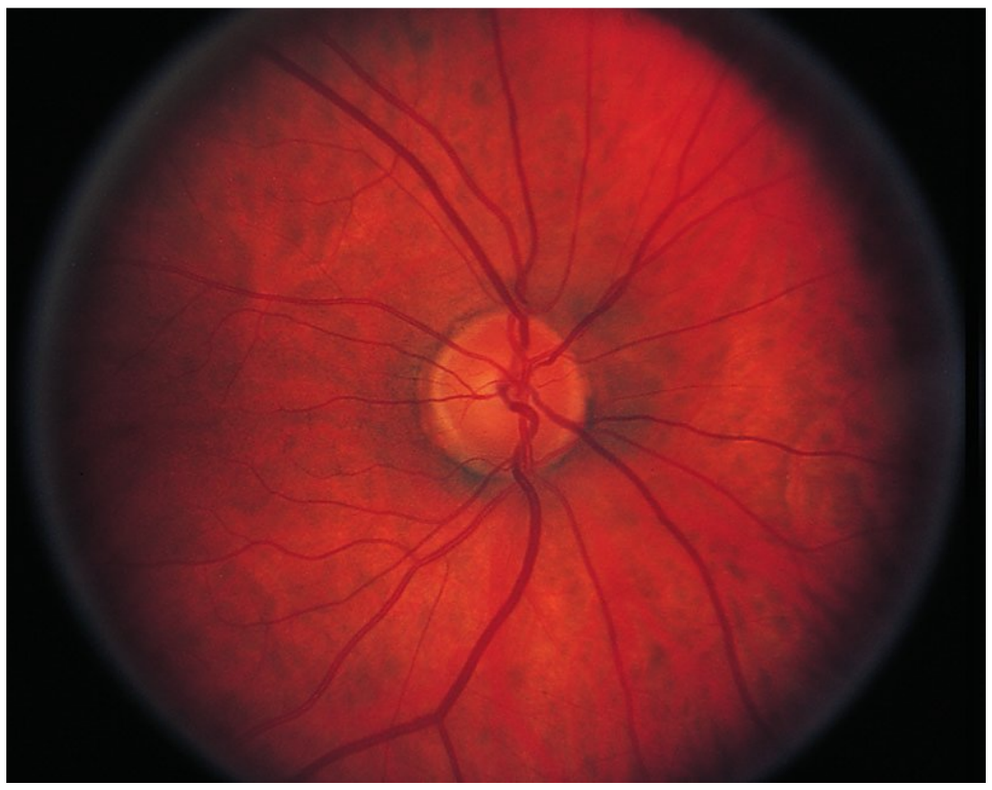

FIGURE 19–1 The right optic nerve.

angles. Laser peripheral iridotomy may not only reverse the IOP elevation but also prevent other secondary problems associated with angle closure.

4. The optic nerve is best examined under stereoscopic magnification. The fundus contact lens is the gold standard but is sometimes cumbersome and makes subsequent fundus photography difficult. The Hruby lens approaches the contact lens in stereopsis and magnification. The 78D and 90D lenses, when used with the slit lamp, exaggerate stereopsis. Nevertheless, these lenses are easy to use and, in most cases, give a good estimate of the cup-to-disc ratio and other characteristics of the optic nerve. The red-free light on the slit lamp can be used to better view the neuroretinal rim and peripapillary nerve fiber layer. Focal cupping, thinning of the rim, nerve fiber layer dropout, or significant disc asymmetry should make one consider changing the diagnosis from ocular OHTN to POAG.

Newer optic nerve imaging techniques such as scanning laser ophthalmoscopy or optical coherence tomography may provide additional information in some patients. The benefit of using these techniques in most patients remains unproven.

5. Automated perimetry has become the gold standard in visual field testing. Static threshold techniques can be highly sensitive in picking up even subtle visual field defects. Many patients are unable to undergo automated perimetry due to physical or nonphysical limitations and thus require manual perimetry. The presence of a glaucomatous visual field defect along with elevated IOP should make one entertain the diagnosis of POAG.

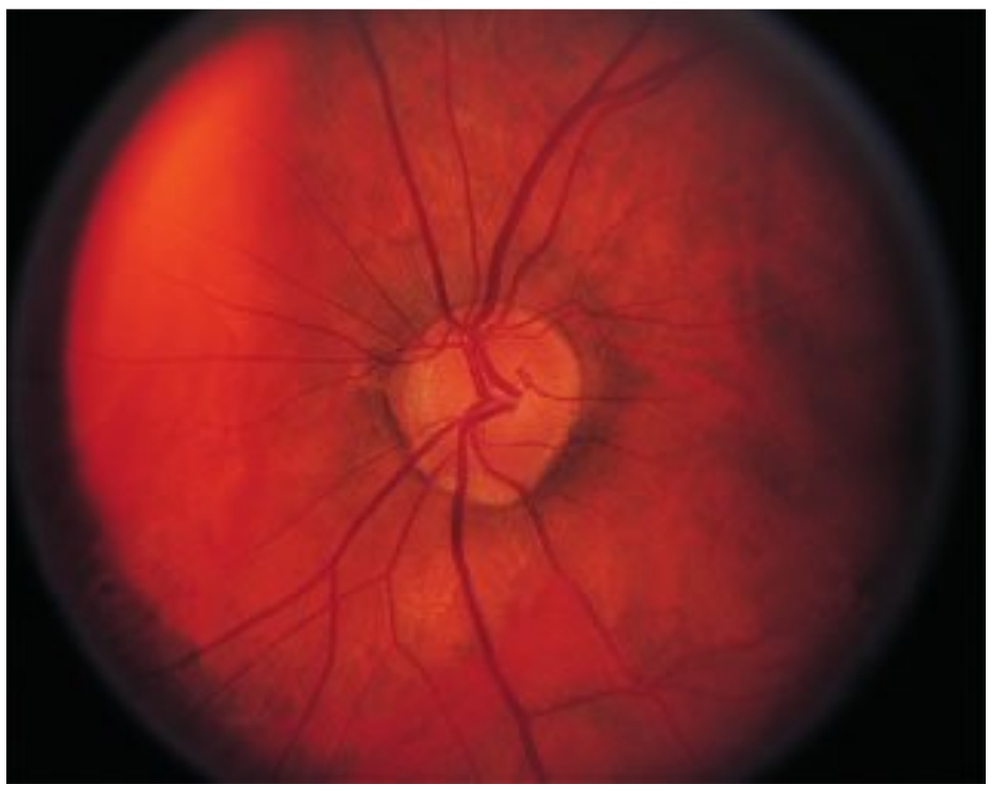

FIGURE 19–2 The left optic nerve.

DIAGNOSIS

Ocular hypertension.

MEDICAL MANAGEMENT

The decision of whether and when to begin IOP-lowering therapy in a patient with OHTN is a difficult one. If both the optic nerve and visual field are normal, you are treating a risk factor for glaucoma development (ie, IOP elevation) and not the disease itself. Once you begin treatment, you may be committing a patient to a lifetime of unnecessary therapy. On the other hand, if you don't treat, the elevated IOP may result in undetected optic nerve damage and visual field loss. Such a delay could potentially jeopardize the patient's vision, especially as he or she ages.

Each ophthalmologist generally has an IOP cutoff above which medical therapy is initiated.

Epidemiologic studies looking at this issue have failed to show a single "magic" number above which all patients should be treated. The OHTN treatment study (OHTS), which began in 1992, is looking at this issue in a randomized fashion. The findings have not been conclusive to date.

Factors that may lead one to treat patients with IOPs in the mid to high 20s include race and positive family history. Black populations have a higher prevalence of glaucomatous optic neuropathy than whites in most parts of the world, and, thus, should probably be treated earlier in the course of the disease.

The age of a patient may also be important. An 80-year-old patient with normal nerves and visual fields is less likely to suffer significant vision loss over a lifetime secondary to elevated IOP than an individual in his or her 40s.

SURGICAL MANAGEMENT

Laser trabeculoplasty and glaucoma filtration surgery are usually not to be recommended in patients with OHTN. The potential complications, especially with filtration surgery, should not be risked in eyes with healthy optic nerves.

REHABILITATION AND FOLLOW-UP

Ocular hypertensive patients, whether or not they are treated with IOP-lowering therapy, should initially be seen at least every 6 to 12 months. Yearly visual field testing and dilated optic nerve examination are recommended.

Patients who are treated with IOP-lowering therapy should be seen within 4 weeks after initiation of treatment to see if the medication is effective. After the therapy has been modified and the IOP is stable, examination every 4 to 6 months is recommended for at least 2 years. If the OHTN has been stable for many years, examination every 6 to 12 months may be adequate.

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Case 20

OPEN-ANGLE GLAUCOMA

Sally Byrd, M.D.

HISTORY

A 51-year-old African-American man presented for a routine eye exam. He had no past ocular problems and no current visual complaints. Past medical history was remarkable for mild emphysema for which he used inhalers.

Examination revealed visual acuities of 20/20 in each eye, with a refraction of −3.00 + 2.25 × 110 OD and −2.25 + 2.00 × 86 OS. The pupils reacted normally with no afferent pupillary defect. Anterior slit-lamp examination was unremarkable, and pressures by applanation tonometry were 26 mm Hg OD and 32 mm Hg OS. Gonioscopy was performed and the angles were noted to be grade IV in both eyes with a clear view of the ciliary body band for 360 degrees. There was 1+ pigment of the trabecular meshwork. On funduscopic exam, the optic nerves were noted to be as pictured in Figures 20–1A and B. There were no abnormalities of the retina or vessels. Automated visual fields were also obtained and are shown in Figures 20–2A and B.

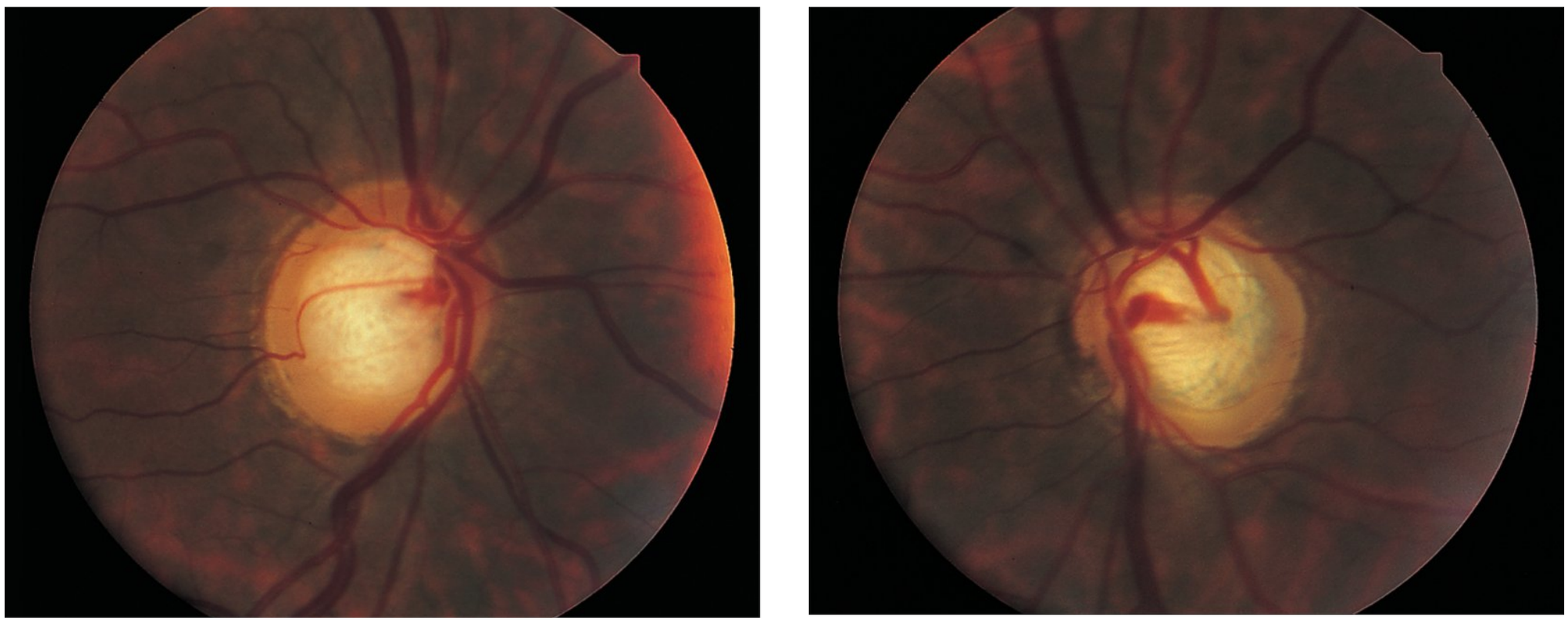
DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The findings of elevated intraocular pressure (IOP), open angles, optic nerve cupping, and arcuate visual field defects put the diagnosis of primary open-angle glaucoma (POAG) at the top of the list.
2. Secondary open-angle glaucomas, such as pigmentary and pseudoexfoliation, might also be considered, but this patient did not display the corneal endothelial pigment deposits, iris transillumination defects, or heavy trabecular meshwork pigment seen in pigmentary glaucoma, nor the fibrillar deposits, anterior iris pigment dusting, or trabecular meshwork pigment often seen with pseudoexfoliation.
3. Chronic angle closure should be ruled out by careful gonioscopy.
4. Occasionally the optic nerve atrophy that follows anterior ischemic optic neuropathy (AION) can lead to cupping which mimics that seen in glaucoma. Usually optic nerve pallor is the more distinguishing feature however, and the condition is not associated with elevated IOPs. Additionally, AION often occurs in nerves with very small tight cups, and the fellow or less involved eye should be assessed for this finding.
5. Congenital optic nerve findings such as an optic nerve pit, limited optic nerve colobomas, tilted discs, and disc drusen may lead to visual field findings that simulate glaucoma, and a careful examiner should keep these anomalies in mind.
6. Retinal lesions such as a retinal scar or branch retinal vein or artery occlusion may also mimic the findings of glaucoma on visual field examination.

TEST INTERPRETATION

A careful physical exam is crucial in making the diagnosis of POAG.

1. This patient had elevated IOPs which would support a diagnosis of glaucoma, although approximately 33 to 50% of patients with POAG will present with pressures under 21 mm Hg at the time of their initial presentation. Furthermore, approximately one-sixth of patients who have other characteristic features of POAG will have IOPs consistently lower than 21 mm Hg. These



A B

FIGURE 20–1 (A) Examination of the right disc showed generalized enlargement of the cup with increased thinning of the inferior rim. (B) The left disc also shows generalized cup enlargement with more marked thinning of the inferior neural rim.

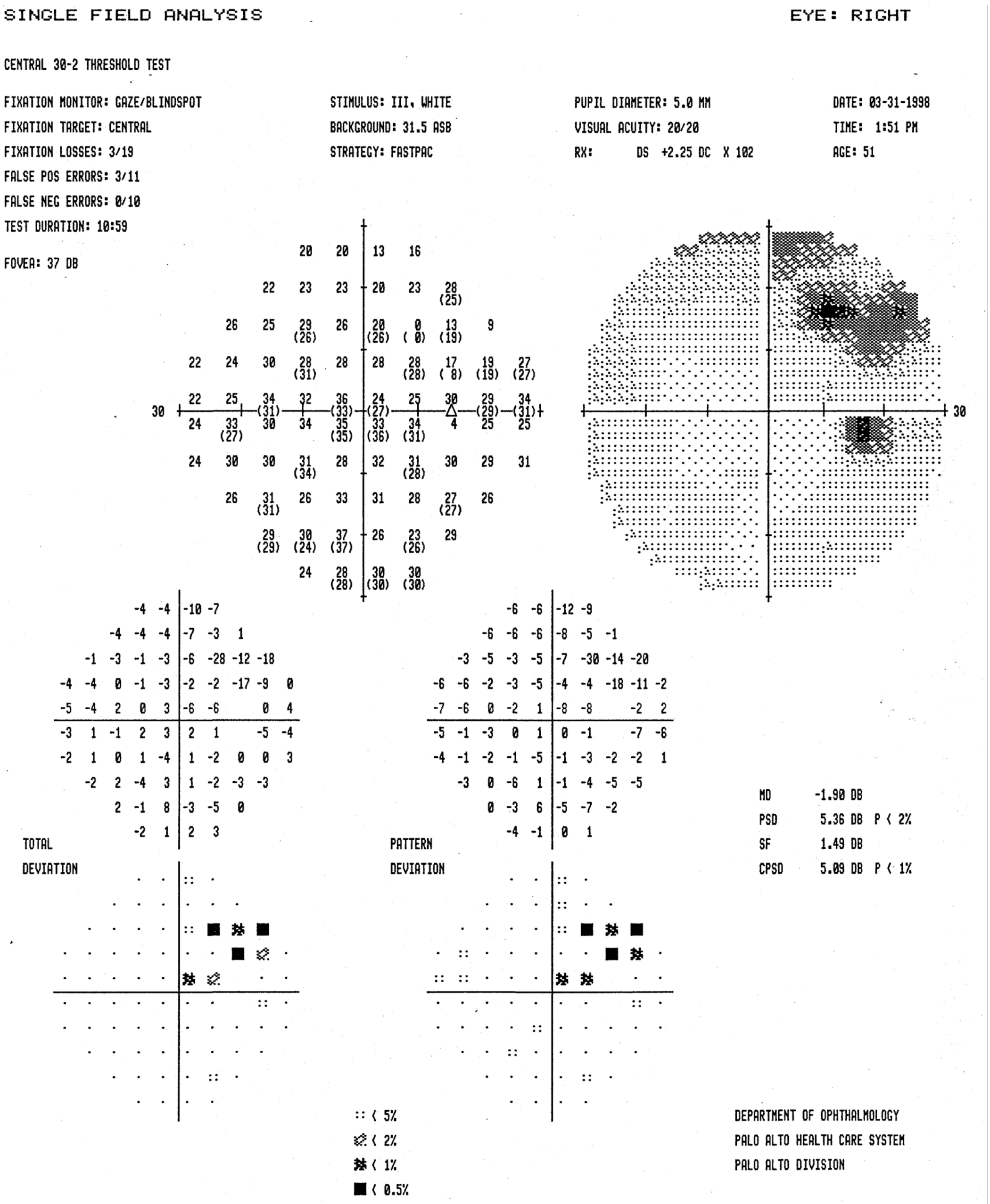
patients are often classified as having normal or low tension glaucoma.

2. Careful slit-lamp examination is important to rule out other secondary causes of glaucoma. Evaluation of the cornea may reveal pigment deposits (Krukenberg's spindle) characteristic of pigmentary glaucoma, keratic precipitates suggestive of a secondary inflammatory glaucoma, or corneal edema seen in some variations of iridocorneal endothelial (ICE) syndrome and herpes keratitis even at lower IOPs. Cell and flare in the anterior chamber would additionally support a diagnosis of inflammatory glaucoma. Examination of the iris should look to rule out peripheral transillumination defects consistent with pigmentary glaucoma; pupillary margin atrophy; gray-white flakes around the pupil; and anterior stromal pigment dusting seen with pseudoexfoliation; the rubeotic vessels of neovascular glaucoma; and the distortion, atrophy, and corectopia characteristic of the ICE syndromes.

3. Gonioscopy is of course essential to a diagnosis of POAG and necessary to rule out angle closure, as well as other secondary causes of glaucoma such as traumatic angle recession and the high iris insertion of juvenile glaucoma. Heavy trabecular meshwork pigmentation would be suggestive of pigmentary or pseudoexfoliative glaucoma.

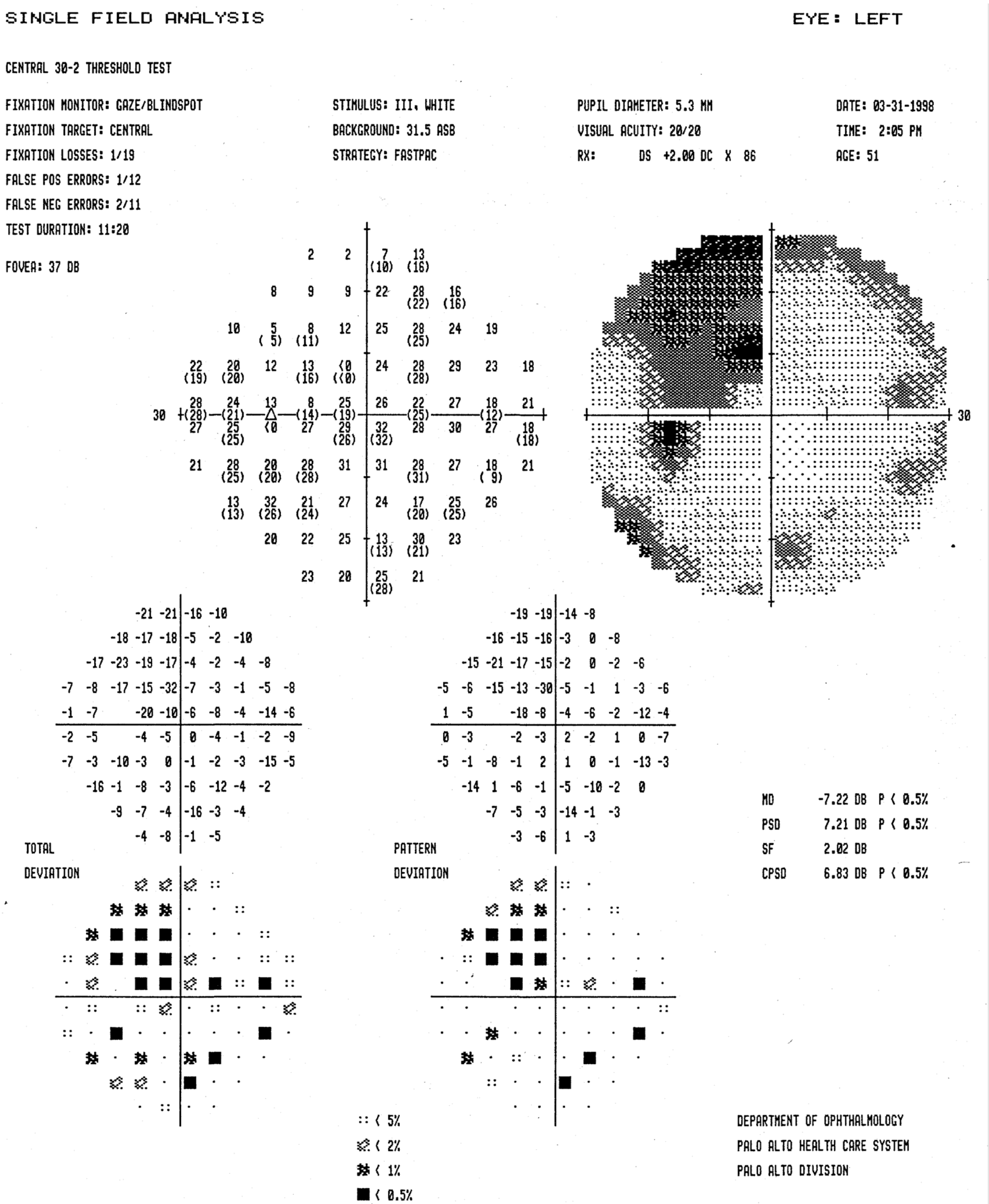
4. Examination of the optic nerve is best done under stereoscopic magnification through a dilated pupil and should document not only the overall disc size and cup-to-disc ratio, but also evidence of focal thinning or notching of the neural rim and the presence of optic disc hemorrhages. The nerve fiber layer should be assessed with a red-free light. Other disc anomalies that could also result in visual field changes, such as disc drusen, optic pits, tilted nerves, and disc pallor, should be searched for and documented when present. The retina should also be carefully examined, particularly for lesions that might explain visual field defects found to be present.

5. Visual field testing is best measured using automatic static threshold techniques or careful manual kinetic and static testing. Glaucoma classically leads to a visual field defect in a nerve fiber bundle distribution. Examples of this include arcuate or Bjerrum scotomas, nasal steps, paracentral scotomas, and temporal wedges. Glaucoma, however, may also lead to visual field constriction or diffuse depression that may be more difficult to recognize.



A

FIGURE 20–2 (A) An early superior arcuate defect is noted in the right eye.



B

FIGURE 20–2 (B) A more advanced superior arcuate defect is seen in the left eye.

DIAGNOSIS

Primary open-angle glaucoma.

MEDICAL MANAGEMENT

Management of glaucoma is primarily aimed at lowering the IOP below a target level felt to be safe (unlikely to cause further nerve damage) for a particular patient. Target pressures are generally set at a pressure at least 20% below the pretreatment level, but lower target pressures may be indicated depending on the pretreatment IOP levels and the degree of optic nerve damage already present. Medical agents for lowering IOP include β-blockers both selective and nonselective, topical and oral carbonic anhydrase inhibitors, prostaglandin analogs, adrenergic agonists, and miotics. Choice of treatment is based on a number of factors including severity of the disease, the patient's age, compliance issues, known side effects, and concomitant systemic disorders. It is often prudent to start a medication in one eye only, to better separate its effectiveness from normal fluctuations in eye pressure.

SURGICAL MANAGEMENT

Surgery is indicated when medical management fails to adequately control the IOPs and there is evidence of disease progression, or in some cases as initial therapy depending on the severity of the glaucoma and other mitigating factors.

1. Argon laser trabeculoplasty is generally performed by placing 40 to 60 50-micron spots around 180 degrees of anterior trabecular meshwork. It acts by increasing aqueous outflow and results in significant IOP lowering in about 75% of patients after initial treatment. Loss of effect in 50% of these patients within 2 to 5 years may necessitate additional treatment. Patients should be pretreated with apraclonidine or other medications to prevent acute pressure spikes and should have their pressures rechecked 1 to 2 hours after the procedure.

2. Filtering surgery, alone or combined with medical treatment, is reported as having an initial success rate in previously unoperated eyes of 75 to 95%. In eyes that have failed previous surgery however, the success rate may be as low as 36%. Antimetabolite agents such as 5-fluorouracil and mitomycin-C may greatly increase the success rates by preventing scarring, but must be used judiciously to prevent complications such as long-term hypotony and bleb leaks. Careful follow-up after filtering surgery is required to monitor and possibly treat potential complications, as well as to intervene if signs of early surgical failure are noted.

3. Implantation of various seton devices, such as the Baerveldt, Molteno, or Ahmed implants, are usually reserved for patients who have failed multiple filtering surgeries or who have extensive conjunctival scarring making successful filtering surgery unlikely.

4. Cyclodestructive procedures using cryoablation or laser are less predictable and carry a higher risk of phthisis. They are therefore usually reserved for patients who have failed multiple other procedures or who have extremely poor visual prognosis. A newer procedure using an endolaser with direct visualization of the ciliary body may be more promising.

REHABILITATION AND FOLLOW-UP

The frequency of follow-up examinations is generally based on severity of the disease, achievement of target IOP levels, evidence of disease progression, and duration of control. It is important at each visit to determine possible medication side effects and compliance problems and to assess visual acuity and IOP. Evaluation of the optic nerve and repeat visual field testing may be performed somewhat less

frequently, again depending on the factors mentioned above. Baseline stereoscopic photos of the optic nerves are important when evaluating subtle changes in the nerves over time. Indications for adjusting therapy include failure to achieve the target IOP, evidence of progressive optic nerve damage or visual field decline, and development of side effects or compliance problems with the prescribed medications.

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Case 21

PRIMARY ANGLE-CLOSURE GLAUCOMA

Peter A. Netland, M.D., Ph.D.

HISTORY

A 55-year-old woman presented with a history of several hours of discomfort and blurred vision in the left eye.

Examination showed vision of 20/20 in the right eye and 20/60 in the left eye. Intraocular pressures (IOPs) were 14 and 52 mm Hg in the right and left eyes, respectively. The pupil was sluggish and mid-dilated in the left eye. Slit-lamp examination of the left eye showed mild congestion of the episcleral and conjunctival blood vessels. There was mild corneal epithelial edema and a shallow peripheral anterior chamber (Fig. 21–1). The midperipheral iris was bowed anteriorly (Fig. 21–2). Examination of the lens showed mild nuclear sclerosis. Gonioscopy of the left eye revealed a marked convexity of iris contour and no visible anterior chamber angle structures (Fig. 21–3). Gonioscopy of the right eye demonstrated an open, narrow anterior chamber angle. The optic nerve cups were small in both eyes.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. In this patient, the IOP was elevated and gonioscopy demonstrated a closed anterior chamber angle in the left eye. The differential diagnosis should include the clinical types of angle-closure glaucoma. The most common type of primary angle-closure glaucoma in the United States is pupillary block angle-closure glaucoma. Other causes of primary angle-closure glaucoma include plateau iris configuration. In the patient described in the case history, the midperipheral iris was bowed anteriorly (iris bombé) and touched the cornea peripherally. The fellow eye had a narrow, potentially occludable anterior chamber angle. The predominant mechanism is pupillary block, although it is possible that the patient had some component of plateau iris. Reexamination and provocative testing after iridectomy would identify any plateau iris configuration.

2. Abnormalities of the lens may cause angle-closure glaucoma. In phacomorphic glaucoma, a cataractous and intumescent lens may cause closure of the anterior chamber angle. Trauma or hereditary disorders may cause anterior lens subluxation and angle-closure glaucoma. In rare cases, exfoliation syndrome or idiopathic factors may cause sufficient weakening of the zonules, anterior lens movement, and angle closure. Drug sensitivity to sulfonamides or other drugs may cause acute myopia, lens swelling, and angle-closure glaucoma. The patient described in this case did not have any findings associated with lens-induced angle-closure glaucoma.

3. The patient described an acute onset of her problem in the left eye. She denied repeated, brief episodes of these symptoms in the past, suggesting that she had not had intermittent angle closure. The time-course described by the patient, and the lack of any findings such as iris atrophy, anterior lens opacities (glaukomflecken), or peripheral anterior synechiae, indicate an acute process rather than chronic angle-closure glaucoma.

4. Other disorders may cause symptoms and signs of acute angle-closure glaucoma. In neovascular glaucoma, neovascularization

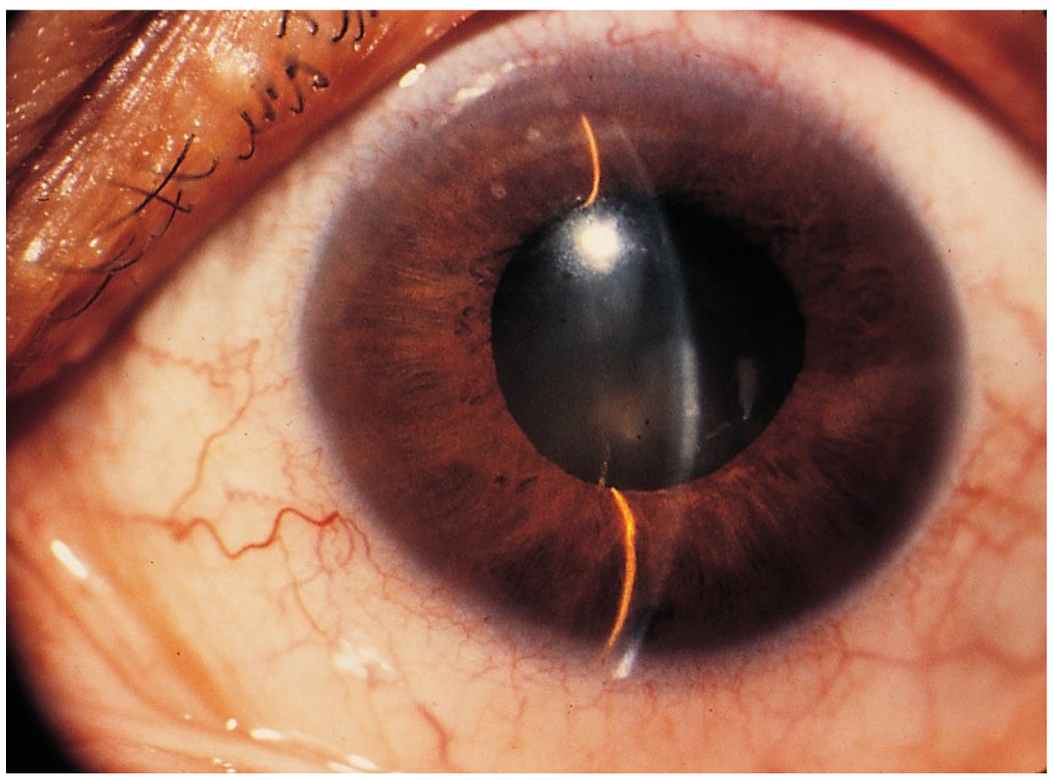

FIGURE 21–1 Slit-lamp biomicroscopy of the left eye. The conjunctiva and episclera were mildly hyperemic, and the cornea was mildly edematous. The pupil was mid-dilated and the iris had a markedly convex configuration. The IOP was 52 mm Hg.

of the iris and angle may lead to peripheral anterior synechia formation and ultimately to closure of the angle. In uveitic glaucomas, keratic precipitates may form and anterior segment inflammation may lead to angle closure due to synechia formation, except in glaucomatocyclitic crisis, in which the angle remains open. Nanophthalmos and other congenital malformations may be associated with closure of the anterior chamber angle. Malignant glaucoma, due

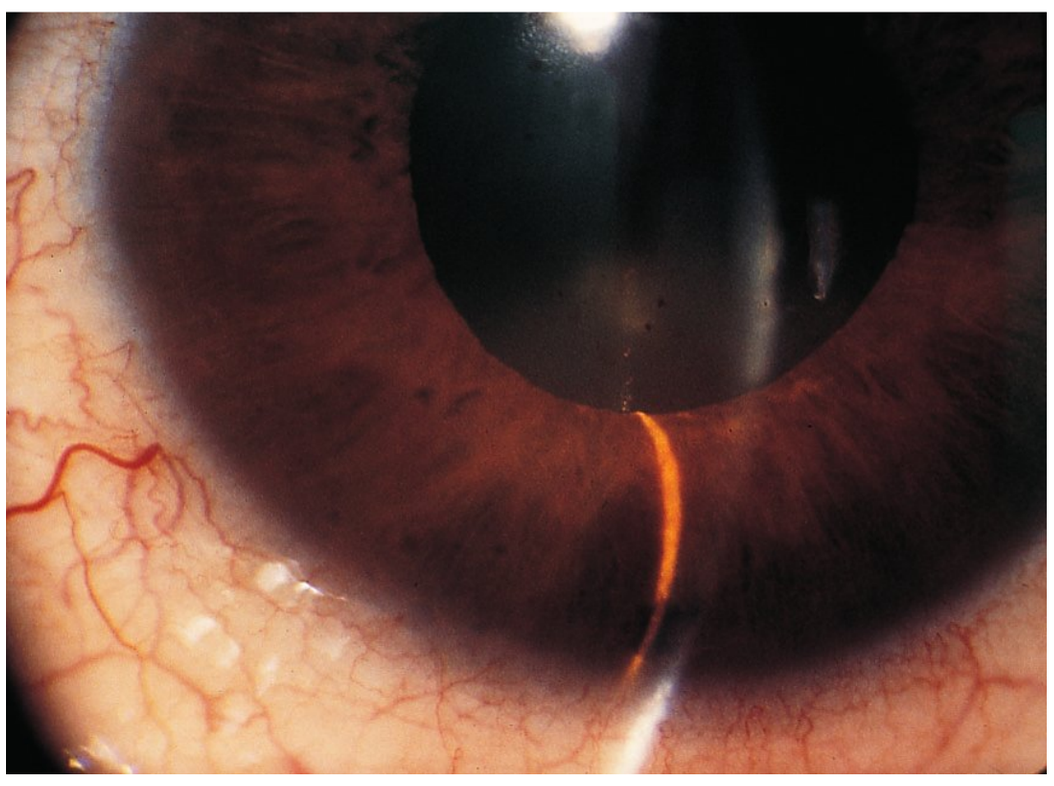

FIGURE 21–2 High-power magnification view of the anterior segment of the left eye. The slit beam clearly demonstrates the marked convexity of the iris (iris bombé). The peripheral anterior chamber is absent.

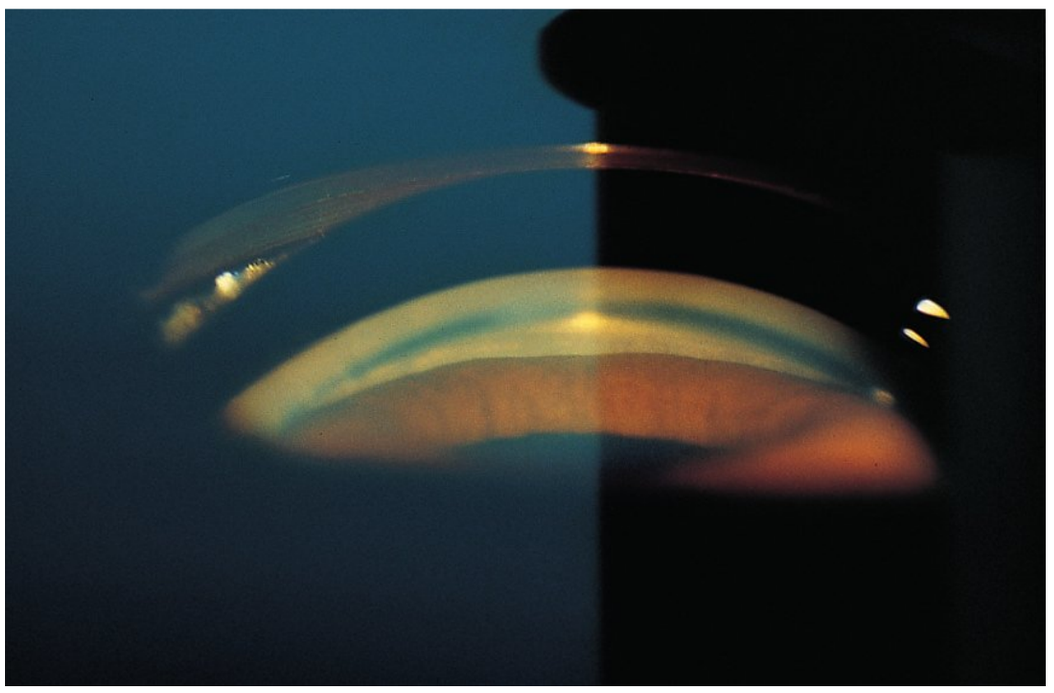

FIGURE 21–3 Gonioscopic view of the anterior chamber angle of the left eye. The midperipheral iris is bowed anteriorly and the anterior chamber angle is closed.

to posterior diversion of aqueous, is associated with a shallow axial and peripheral anterior chamber. Secondary causes of angle-closure glaucoma include posterior segment tumors, choroidal effusions, postsurgical changes, and other disorders. The patient described in this chapter did not have the history and physical findings associated with these other disorders.

TEST INTERPRETATION

In the history, the patient should be asked about blurred vision, colored halos around lights, pain, and eye redness. Previous episodes of similar symptoms and the duration of the symptoms should be documented. Inciting and associated factors, such as close work, emotional state, or ambient light level, may be identified. Patients with a family history of angle-closure glaucoma have a higher risk for angle-closure glaucoma compared with the general population. Epidemiologic studies have shown that certain factors may be associated with angle-closure glaucoma. The incidence of angle-closure glaucoma is highest between 55 and 70 years. Although angle closure may occur in eyes with any refractive error, it is most common in hyperopic eyes. The incidence of angle-closure glaucoma varies in different ethnic groups. In the Caucasian American population, angle-closure

glaucoma is about one-fifth as common as open-angle glaucoma. Compared with Caucasians, acute angle-closure glaucoma is less common in the African-American population and more common in certain Asian populations.

In the physical examination, the slit-lamp biomicroscope should be used to evaluate for signs associated with angle-closure glaucoma, including conjunctival and episcleral hyperemia, corneal edema, and central and peripheral anterior chamber depth. There may be a mild anterior chamber inflammatory reaction, and the iris may have a convex configuration. The appearance of the lens should be noted. Signs of previous episodes of angle-closure glaucoma should be documented, including iris atrophy, glaukomflecken, and peripheral anterior or posterior synechiae.

An essential part of the examination is gonioscopy, which is required to determine whether or not the patient has closure of the anterior chamber angle. In principle, high-frequency ultrasound ("ultrasound biomicroscopy") could also determine whether the angle is open or closed. Topical application of glycerin may minimize corneal edema and facilitate gonioscopy. Compression gonioscopy may be useful to determine whether the closure of the angle is appositional or synechial.

Basic elements of the eye examination should be performed, including measurement of vision and IOP. Assessment of the refractive status is helpful, because hyperopic eyes are at increased risk for developing angle-closure glaucoma. The appearance of the optic nerve should be documented when possible. The visual field should be evaluated, although this may be postponed in many cases until after the acute attack has been adequately treated. Dilation of the pupil should be deferred until after iridotomy or iridectomy.

Examination of the fellow eye usually reveals a shallow anterior chamber and a narrow angle. Although provocative testing may be helpful for certain patients considered at risk for angle-closure glaucoma, there is no need to perform provocative tests on the fellow eye in a patient who has developed angle-closure glaucoma. Approximately half of the fellow eyes in patients with acute angle-closure glaucoma will develop acute attacks within 5 years. Prophylactic iridotomy is indicated for the fellow eye, after the eye with the acute attack has been treated and is stable.

DIAGNOSIS

Right eye: Narrow anterior chamber angle, at risk for subsequent angle-closure glaucoma. Left eye: Acute primary angle-closure glaucoma.

MEDICAL MANAGEMENT

In eyes with angle-closure glaucoma, medical therapy is administered to lower the IOP rapidly and, ideally, to open the anterior chamber angle. Medical therapy usually improves the clarity of the cornea prior to definitive treatment with laser iridotomy.

Osmotic drugs may be useful in the treatment of eyes with angle-closure glaucoma. Isosorbide and glycerol are administered orally and have an onset of effect within 1 hour. Isosorbide causes less nausea and vomiting compared with glycerol. In contrast with glycerol, isosorbide is not metabolized and does not have a significant caloric content. In patients with severe nausea and vomiting, intravenous mannitol may be administered. Osmotic drugs should be used with caution or avoided in patients with renal and cardiovascular disease, or those dehydrated by vomiting.

Intravenous acetazolamide may effectively and rapidly lower the IOP in eyes with angle-closure glaucoma. Acetazolamide may be administered orally, but the maximum effect occurs at about 2 hours, which is significantly later than after intravenous administration. Carbonic anhydrase inhibitors may be administered topically, but the adsorption and effect are variable because of the inflammation and edema in the setting of acute angle-closure glaucoma.

Topical cholinergic drugs may constrict the pupil and open the anterior chamber angle in some eyes with angle-closure glaucoma. Treatment may be initiated with a drop of 2% pilocarpine administered every 5 minutes for 3 doses. In some eyes, the pupil is unresponsive because of ischemia and paralysis of the iris sphincter due

to extremely high IOP. In rare cases, paradoxical worsening of the angle-closure may occur due to forward movement of the lens and iris after treatment with cholinergic drugs.

Other topical antiglaucoma medications may be administered, including topical beta-blockers and alpha-2-agonists. These drugs are commonly used in treating angle-closure glaucoma, but their usefulness is limited by variable absorption and slow onset of action. Prostaglandin analogs are less useful in treatment of an acute attack of angle-closure glaucoma because of their slow onset of action.

Topical corticosteroids should be used to treat the marked inflammatory reaction associated with angle-closure glaucoma. Pain may be treated with analgesics, and vomiting may be treated with antiemetics. However, the focus of therapy for pain and vomiting should be on treating the underlying cause of these problems, which is the angle-closure glaucoma.

SURGICAL MANAGEMENT

Laser iridotomy is definitive therapy and the treatment of choice for angle-closure glaucoma with a component of pupillary block (Fig. 21–4). When corneal clarity permits visualization of the iris, the procedure may be performed during the attack, or the procedure may be performed after the acute attack has been treated with medical therapy when inflammation and edema have decreased. Gonioscopy determines whether the anterior chamber angle has been opened successfully after the laser iridotomy. Laser iridoplasty may be effective in opening areas of the angle that remain closed after iridotomy, even in the presence of mild to moderate corneal edema. When corneal edema resolves, laser or surgical goniosynechialysis may be performed to treat peripheral anterior synechiae that persist after the acute attack and contribute to chronically elevated IOP.

In addition to laser treatment of the eye that has developed angle-closure glaucoma, the fellow eye should be treated with a prophylactic iridotomy if the anterior chamber angle is narrow. Without prophylactic iridotomy, approximately half of the fellow eyes in acute angle-closure glaucoma patients will develop acute attacks within 5 years.

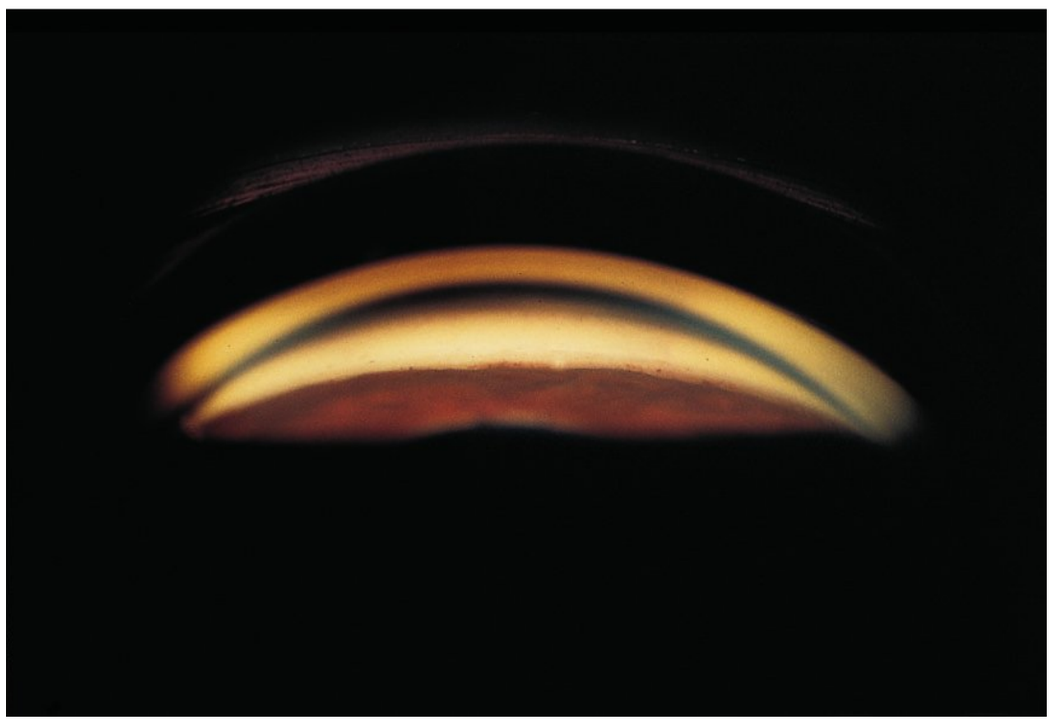

FIGURE 21–4 Gonioscopic view of the anterior chamber angle of the left eye after laser iridotomy. The iris is mildly convex but has a more flat appearance compared with the preoperative configuration. The anterior chamber angle is open.

REHABILITATION AND FOLLOW-UP

At least one IOP measurement should be performed within 30 to 120 minutes of laser surgery. A follow-up examination should be performed within a week of laser surgery. If the response to treatment is inadequate, more frequent follow-up visits will be required. An additional follow-up examination should be performed 4 to 8 weeks postoperatively. Topical corticosteroids should be tapered during the postoperative period. Pupillary dilation with postdilation IOP check and gonioscopy determine whether the angle remains open after provocation. Provocative testing with inadequate iridectomy may cause pupillary block angle-closure glaucoma. Angle closure with a patent iridectomy may be due to plateau iris configuration.

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Case 22

PIGMENTARY GLAUCOMA

Scott A. Cory, M.D.
James C. Robinson, M.D.

HISTORY

A 32-year-old man presents for routine eye examination. He currently has no complaints and denies any significant past ocular or medical history.

Examination revealed an uncorrected visual acuity of 20/20 in each eye and no afferent pupillary defect in either eye. Intraocular pressures by applanation were 28 and 26 mm Hg. Slit-lamp examination disclosed vertically oriented pigment deposition on each corneal endothelium and numerous spokelike iris transillumination defects in both eyes (Fig. 22–1). Gonioscopy showed fully open angles 360 degrees in each eye with dense pigmentation of the trabecular meshwork bilaterally. On funduscopic examination, the right optic nerve had a cup-to-disc ratio of approximately 0.7 with inferotemporal thinning at the neuroretinal rim. The left eye had a cup-to-disc ratio of 0.55. Retinal examination was normal. Automated visual field testing demonstrated a moderate superior arcuate defect in the right eye and an early nasal step in the left eye.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Elevated IOPs with pigment liberation originating from the iris, glaucomatous-appearing optic nerves, and visual field changes in a young male best fits the patient profile of pigmentary glaucoma. Pigmentary glaucoma is generally a disease of the young and affects men approximately twice as often as women. Most experts agree that patients with pigmentary dispersion syndrome or pigmentary glaucoma have abnormal mechanical interaction between the posterior iris epithelium and the lens zonules, leading to the liberation of free pigment derived from the posterior iris epithelium that ultimately blocks aqueous outflow. As aqueous humor makes its way toward the corneal epithelium, some of the pigment becomes attached to the corneal endothelium. The bulk of the pigment, however, eventually is filtered into the trabecular meshwork. Acute episodes of pigment liberation (such as with exercise) may cause an acute elevation of IOP, while the long-standing effect of pigment deposition in the trabecular meshwork leads to its sclerosis and eventual decline in function. It is often at this point when persistently elevated IOP progresses to glaucomatous optic nerve damage.

2. Although pigmentary glaucoma rarely presents a diagnostic dilemma, the differential diagnosis includes primary open-angle glaucoma with excessive pigmentation, pseudoexfoliative glaucoma, uveitis, ocular melanosis, and intraocular melanoma. A thorough and complete ocular examination is important to differentiate accurately between these various conditions.

3. Important to the diagnosis of pigmentary glaucoma is the gonioscopic examination of the trabecular meshwork. Pigmentary deposition in the trabecular meshwork due to pigmentary dispersion is often dense and evenly dispersed throughout the entire angle. In contrast, pigmentation that is pseudoexfoliative in origin is often less evenly distributed and may show dense areas of pigmentation with relatively spared areas interspersed throughout. Both pseudoexfoliative and pigmentary glaucoma may show pigmentation of Schwalbe's line known as a Sampaolesi's line. The key difference between these two diagnoses can easily be made based on careful examination of the pupillary border and anterior lens capsules. Pseudoexfoliative material is deposited on the pupillary border

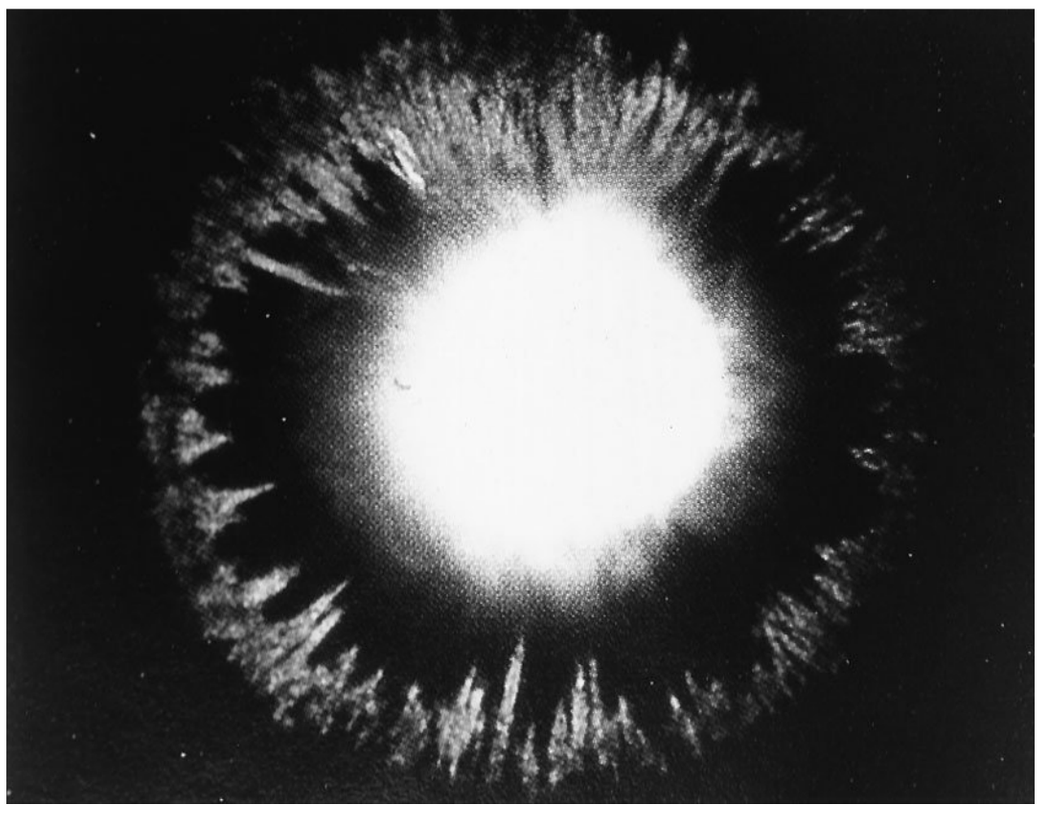

FIGURE 22–1 Extensive transillumination defects in pigmentary glaucoma.

and anterior lens capsule, which is not characteristic of pigmentary glaucoma.

TEST INTERPRETATION

The initial examination of the optic nerve is perhaps the most critical first step in establishing whether or not a patient has glaucomatous nerve damage by the traditional methods of grading, documenting, and observing the optic disc. Cup-to-disc asymmetry, superficial nerve hemorrhages, and focal or progressive rim thinning are all useful in evaluating the severity of glaucoma. Since the optic nerve can sometimes reveal glaucomatous damage or progression at levels not detectable by perimetry, a baseline set of optic nerve photos should be taken. In addition to monitoring IOPs and evaluating the optic nerve, automated perimetry has become the diagnostic mode of choice for evaluating the severity and progression of measurable field loss in all forms of glaucoma. Automated perimetry is based on projecting various levels of light or color stimuli into the patient's field of vision and estimating that field based on patient responses. Automated perimetry has allowed accurate and reproducible field analysis, which is critical for the long-term management of patients with glaucoma. Patients with pigmentary glaucoma tend to show glaucomatous field defects similar to patients with primary open-angle glaucoma. Most defects manifest as a diffuse decrease in sensitivity located in the peripheral field. With the evolution of various software packages, long-term comparisons of such field loss have become easily manageable for most office settings. At a minimum, visual field testing should be performed at least annually, and may often need to be repeated more frequently depending on the severity of a patient's particular disease course.

DIAGNOSIS

Right eye: Moderately advanced pigmentary glaucoma.

Left eye: Early pigmentary glaucoma.

MEDICAL MANAGEMENT

Management of pigmentary glaucoma should be directed at limiting the primary causal mechanism, the liberation of iris pigment. Through the use of miotics, interaction between the iris and the lens can often be eliminated or minimized, thereby normalizing the IOP. The obvious limitation of all miotic treatments is that their side effects are often poorly tolerated in the age group primarily afflicted by pigmentary glaucoma. Extended release miotic therapy may decrease the degree of myopic shift and may be better tolerated. In the event that miotic therapy is intolerable or insufficient in controlling IOP, aqueous suppressants should be instituted. Agents such as beta-blockers, carbonic anhydrase inhibitors, and alpha-adrenergic agonists are all appropriate. A desirable initial pressure reduction in IOP should be in the range of 20 to 30%. If despite this reduction there is continued visual field loss, then a multiagent regimen should be employed. When medical management fails to limit progression, or is not tolerated or is impractical, surgical alternatives should be considered.

SURGICAL MANAGEMENT

Argon laser trabeculoplasty (ALT) is often very effective in patients with a more heavily pigmented trabecular meshwork, making it ideal as

an initial treatment for patients with pigmentary glaucoma. ALT is a relatively low-risk procedure that may often provide years of effective pressure reduction. Initial treatment with ALT should be monocular and consist of a 180-degree treatment trial. If this initial treatment results in adequate pressure reduction, the other eye should be considered for treatment. Treatment of only one-half of the trabecular meshwork is often sufficient and reserves the option for future treatment. An alternative treatment that directly alters the cause of pigment liberation is that of laser peripheral iridectomy (LPI). In pigmentary glaucoma, the origin of pigment liberation is felt to be due to an abnormal interaction between the pigment epithelium of the iris and the lens zonules, also known as a reverse pupillary block. Placement of an iridectomy is believed to decrease the potential for iris/lens interaction and thus treat the primary cause of the disease process. Unfortunately, the efficacy of LPI has yet to be adequately studied. To date, trabeculectomy is the surgical procedure of choice if disease progression continues despite aggressive pharmacologic and laser therapy. Patients with pigmentary glaucoma are at no higher risk than patients with primary open-angle glaucoma for trabeculectomy.

REHABILITATION AND FOLLOW-UP

As with all forms of glaucoma, pigmentary glaucoma requires a patient-specific approach. Follow-up for pigmentary glaucoma should be based on the effectiveness of treatment, the stability of the disease process, overall severity of disease, and patient reliability.

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Case 23

NEOVASCULAR GLAUCOMA

Stephen A. Lin, M.D.

HISTORY

A 72-year-old man presents to the emergency department complaining of "a bad headache on the right side of my head." He also notes extreme redness and light sensitivity of the right eye and feels "sick to my stomach." His symptoms have developed quickly over half a day. Fearing that this may be more than "pink eye" and a tension headache, the emergency department physician requests that an ophthalmologist evaluate the patient.

Past medical history is remarkable for hypertension, diabetes, and arteriosclerosis. A review of systems is positive for nausea and one episode of vomiting. The patient had experienced an abrupt, painless, severe decline in vision approximately 3 months earlier. He was diagnosed at that time with an ischemic central retinal vein occlusion by his ophthalmologist.

Examination of the right eye reveals a visual acuity of hand motions. Slit-lamp exam shows severe corneal edema and conjunctival injection. A limited view of the anterior chamber reveals a small hyphema and cell and flare. Fine as well as irregular branching vessels are seen on the iris surface (Fig. 23–1). A gonioscopic view of the drainage angle in the right eye is obscured by corneal edema. The drainage angle is wide open in the left eye. Only a dull red reflex can be appreciated on ophthalmoscopy of the right eye. The left fundus is notable only for severe hypertensive retinopathy. The optic disc appears normal in the left eye. Intraocular pressure (IOP) is 67 mm Hg in the right eye and 19 mm Hg in the left.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

Proper diagnosis and prompt treatment are crucial in managing patients with extremely elevated IOP. Permanent vision loss can develop rapidly as a result of ischemia and optic neuropathy. Although the depicted patient has already lost significant vision from a vein occlusion, rapid initiation of treatment can alleviate pain and prevent further loss of vision. The differential diagnosis in this case centers on the key examination findings of iris neovascularization and elevated IOP. It includes neovascular glaucoma, acute angle-closure glaucoma, Fuchs' heterochromic iridocyclitis, acute iridocyclitis, and traumatic hyphema with elevated IOP.

Iris Neovascularization

Neovascularization, whether anterior or posterior, is usually associated with an underlying ischemic process involving the retina. Diabetic retinopathy and central retinal vein occlusion each account for approximately one-third of cases of iris neovascularization. Other causes of iris neovascularization include branch retinal vein occlusion, retinal artery occlusion, carotid occlusive disease, sickle cell retinopathy, uveitis, intraocular tumor, and chronic retinal detachment. It has been postulated that retinal hypoxia is associated with the release of angiogenic factors, which can diffuse anteriorly and induce neovascularization. New iris neovascularization following vitrectomy or cataract surgery complicated by a capsular break suggests that vitreous and posterior lens capsules may serve as physical barriers limiting diffusion of such factors.

Iris neovascularization usually begins with fine capillary tufts at the iris margin, which progress toward the iris root and chamber angle. Unlike iris vessels, which are uniform and radial in nature, these new vessels are irregular in caliber and direction. A fine fibrovascular membrane may be associated with these vessels and may lead to angle closure and ectropion uveae. Bleeding from

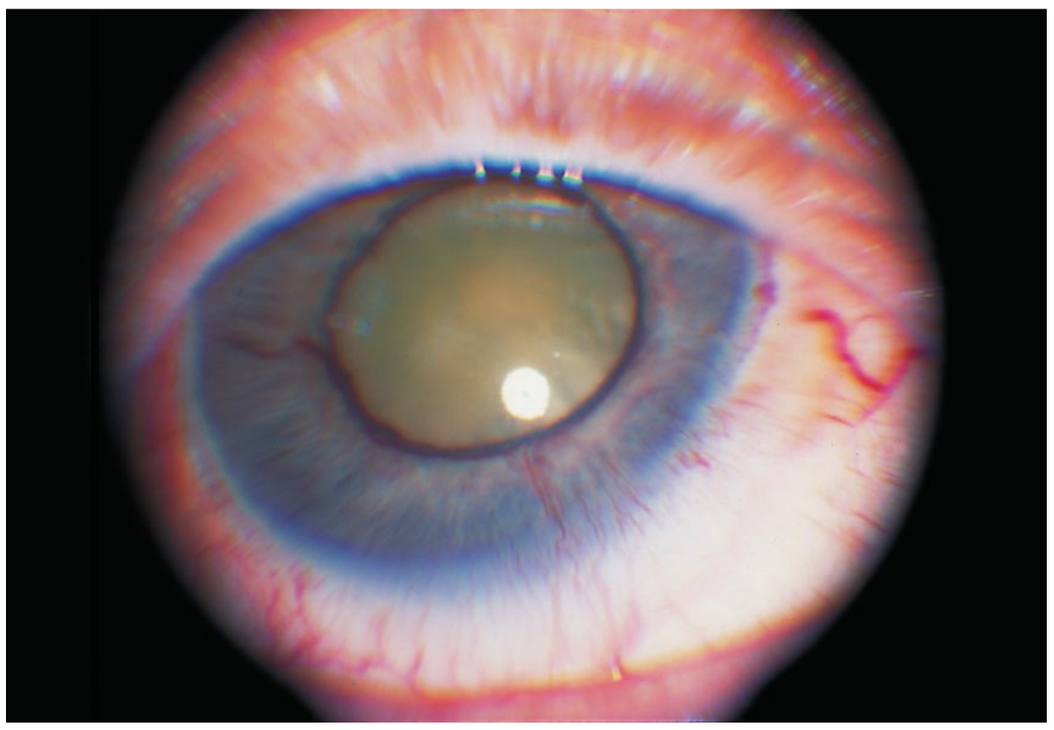

FIGURE 23–1 Fine, irregular blood vessels growing over the anterior iris surface are characteristic of iris neovascularization. Growth often begins at the pupillary margin and may extend peripherally, where involvement of the drainage angle can lead to closure and elevated IOP.

neovascular growth is not uncommon and can lead to hyphema if extensive.

Acute, Severe IOP Elevation

This condition may be associated with acute angle closure and various inflammatory conditions. Acute angle closure may be further subdivided into primary and secondary angle closure. Patients who present with primary acute angle closure often have narrow angles that are potentially occludable with the development of pupillary block. Predisposed patients are often hyperopic with shallow anterior chambers. Secondary acute angle closure may result from mechanical closure due to posterior segment tumor, choroidal detachment, or lens changes. Fibrovascular membranes associated with iris neovascularization may also produce permanent angle closure.

Various inflammatory conditions can also lead to acute IOP elevation. Acute iridocyclitis, glaucomatocyclitic crisis (Posner-Schlossman syndrome), and Fuchs' heterochromic iridocyclitis are associated with varying degrees of elevated IOP and anterior chamber cell and flare. Open angles are seen with gonioscopy. Iris vessels may be prominently dilated making it difficult to distinguish these conditions from true iris neovascularization.

Chronic, gradual elevation of IOP may be associated with a relatively quiet eye, whereas acute pressure elevation is often accompanied by corneal edema with a characteristic "steamy" appearance and conjunctival congestion. Patients complain of extreme pain and blurry vision accompanied by headache and sometimes nausea and vomiting. Corneal edema results in patient complaints of "colored halos around lights."

The history in this case is extremely important. Previous vision loss and a history of prior central vein occlusion suggest the strong likelihood of retinal ischemia and subsequent neovascularization. The finding of iris and trabecular meshwork neovascularization on examination accompanied by elevated IOP is pathognomonic for neovascular glaucoma. Gonioscopy is not always accurate in this setting as corneal edema can obscure good visualization of the trabecular meshwork. Neovascular glaucoma generally develops more rapidly following an ischemic vein occlusion than other causes of retinal ischemia and is sometimes referred to as "90-day glaucoma." The absence of a narrow angle in the fellow eye makes acute angle closure unlikely since predisposed patients generally exhibit narrow angles bilaterally. Furthermore, neovascularization and hyphema are not encountered in acute angle closure. There was no history of trauma. Iridocyclitis associated with elevated IOP is rarely associated with true iris neovascularization and hyphema. The history of prior vein occlusion makes this diagnosis a distant second to neovascular glaucoma.

Neovascular glaucoma is due to retinal ischemia. Iris neovascularization is invariably present prior to the invasion of trabecular meshwork by fibrovascular membranes and ultimately permanent angle closure. Early iris neovascularization is easily overlooked on examination unless an effort is made to carefully scan the iris surface and trabecular meshwork. Any patient with diabetes or history of vascular occlusion should be thoroughly evaluated for both posterior and anterior neovascularization. Early detection and intervention may prevent the severe complications associated with extremely high IOP.

As retinal ischemia is believed to be the underlying factor in both posterior and anterior

neovascularization, the reduction of oxygen demand by panretinal cryoablation or photocoagulation is the treatment for neovascularization. After treatment, established new vessel growth may undergo fibrosis and regress, preventing the onset of glaucoma. Because of the rapid development of neovascularization following ischemic central retinal vein occlusion, some have advocated prophylactic panretinal photocoagulation even in the absence of neovascularization.Goniophotocoagulation may reduce prominent angle neovascularization in cases with minimal or no angle closure. This may help prevent angle closure during the time interval required for panretinal ablation to take effect.

DIAGNOSIS

Neovascular glaucoma.

MEDICAL MANAGEMENT

Patients who present with acutely elevated IOP can be difficult to diagnose and treat. Corneal edema can sometimes obscure any view into the eye. All efforts should be made to lower IOP quickly. Aqueous suppressants including topical beta-blockers and alpha-2 agonists as well as topical or oral carbonic anhydrase inhibitors should be administered. Cholinergic agents and possibly prostaglandin analogs should be avoided in order to prevent possible further breakdown of the blood–aqueous barrier. Prostaglandin analogs, however, enhance uveoscleral outflow. This mechanism of outflow becomes more important if the drainage angle is closed. Hyperosmotic agents should be used with care, especially in diabetic patients. Their effectiveness, however, may be limited, as osmotic gradients are weaker in the inflamed eye. Inflammation and pain may be managed with topical prednisolone and cycloplegics.

SURGICAL MANAGEMENT

If corneal edema resolves following a reduction in IOP, a sufficient view of the posterior segment may allow for panretinal photocoagulation. Laser treatment should be administered as quickly as possible, or panretinal cryoablation may be required.

Medical management alone is frequently inadequate for controlling the IOP in patients with neovascular glaucoma. Ideally, neovascularization should be inactive prior to filtering surgery. Intraoperative bleeding is common in such cases and the prognosis for successful long-term control is limited because of fibrovascular proliferation and closure of the filtration site. Antifibrotic agents such as mitomycin-C should be used intraoperatively with adjunctive 5-fluorouracil postoperatively as indicated. The use of aqueous shunting devices (such as the Baerveldt, Molteno, and Ahmed implants) may also be effective following filtration surgery failure. These devices include a flexible silicone tube that is generally impervious to scarring and closure. An open channel is maintained for the egress of aqueous to a subconjunctival plate structure.

Neovascular glaucoma in blind eyes may be managed more conservatively with elimination of pain as the main goal. Cyclodestructive procedures with the diode or neodymium:yttrium-aluminum-garnet (Nd:YAG) laser or cryotherapy can alleviate pain associated with elevated pressure. Topical cycloplegics and steroid drops may also be of use. Retrobulbar alcohol or enucleation is usually reserved for refractory cases.

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Case 24

INFLAMMATORY GLAUCOMA

Rick S. Huo, M.D.
Anne L. Coleman, M.D., Ph.D.

HISTORY

A 38-year-old Caucasian man presented with a 2-day history of blurry vision, photophobia, tearing, and pain involving his left eye. His ocular history is notable for one episode of herpes simplex keratitis involving the left eye, which occurred 12 months ago, and which resolved after treatment with trifluridine eye drops.

Examination showed vision of 20/20 in the right eye and 20/60 in the left eye, which improved to 20/40 with pin-hole. Intraocular pressure (IOP) was 12 mm and 46 mm Hg, respectively. Slit-lamp examination of the right eye was unremarkable. The left cornea revealed fine, stellate keratic precipitates scattered in a diffuse pattern. The anterior chamber was deep centrally and peripherally, with 2+ cells and aqueous flare. Patchy atrophy of the iris pupillary spincter was noted on transillumination (Fig. 24–1). No iris nodules, heterochromia, or posterior synechiae were observed. The lens was clear. Gonioscopy demonstrated angles open to the ciliary band in both eyes with moderate pigmentation of the trabecular meshwork and prominent iris processes but no peripheral anterior synechiae. On funduscopic exam the vitreous appeared clear, and optic discs were symmetric with healthy rims.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. IOP can be elevated, stable, or reduced in response to inflammation. The main cause of IOP rise associated with uveitis, where the majority of eyes have open angles, is thought to be increased resistance to aqueous outflow. Several mechanisms have been proposed, including obstruction of the trabecular meshwork by inflammatory precipitates, swelling of the trabecular lamellae and endothelium, and alteration of aqueous dynamics by the breakdown in the blood–aqueous barrier. Less commonly, angle closure can result from pupillary block, peripheral anterior synechiae (PAS), or forward rotation of the ciliary body.

2. Large,"mutton-fat"keratic precipitates (KPs) are found in granulomatous forms of uveitis, such as sarcoidosis and sympathetic ophthalmia. Fine, fibrillar KPs in a stellate pattern, as described in this case, are associated with herpetic or Fuchs' heterochromic uveitis.

3. Iris atrophy is characteristic of herpetic inflammation. Segmental atrophy due to occlusive vasculitis of the iris stromal vessels occurs with herpes zoster, whereas patchy atrophy around the pupillary sphincter is seen in herpes simplex.

4. The risk of developing herpes simplex iridocyclitis increases with recurrent episodes of keratitis, especially stromal keratitis. Herpetic uveitis can occur, however, in the absence of noticeable keratitis. The risk of associated glaucoma in cases of herpes simplex uveitis is estimated at 28 to 40%.

5. Many conditions can produce intraocular inflammation and elevated IOP (Table 24–1). The differential diagnosis in this case includes Fuchs'heterochromic iridocyclitis (insidious onset, rarely symptomatic for ocular irritation, cataract formation, heterochromia), HLA-B27–associated uveitis (arthritic conditions, synechiae formation), and glaucomatocyclitic crisis (minimal inflammation, diagnosis of exclusion).

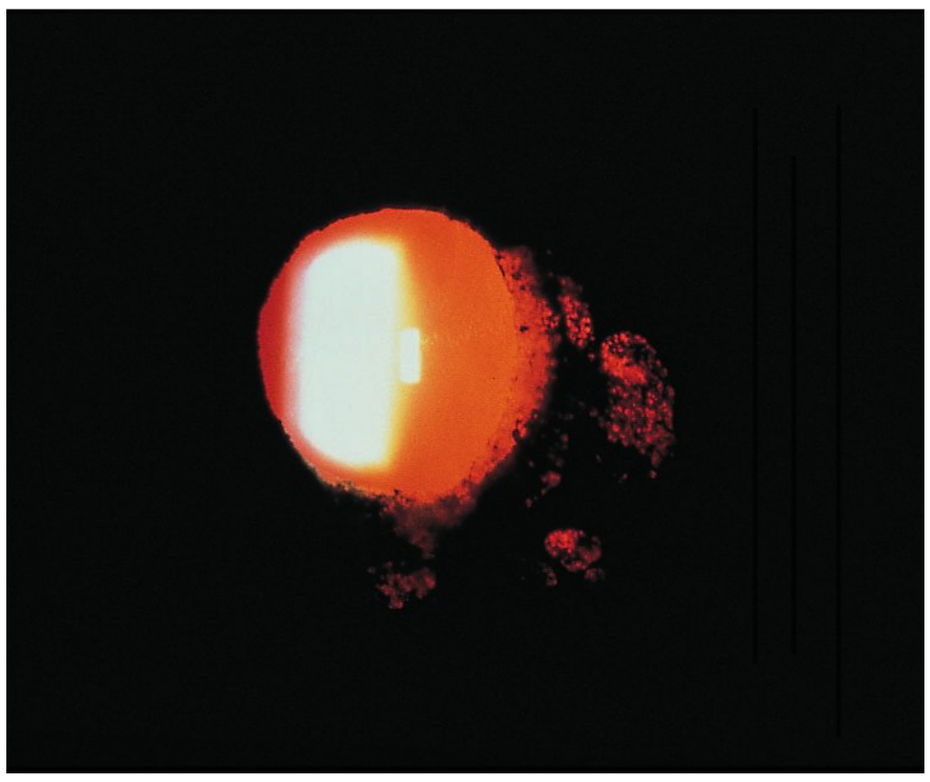

FIGURE 24–1 Transillumination of this eye makes it easy to see the patchy iris atrophy associated with herpetic uveitis. (Provided courtesy of Drs. Gary N. Holland and Thomas H. Pettit, Los Angeles, CA.)

TEST INTERPRETATION

A detailed history and review of system is essential in approaching the patient with inflammatory glaucoma. Key points include onset and duration of symptoms, unilateral or bilateral involvement, race, age, prior ocular conditions, risk factors for immune suppression or sexually transmitted diseases, and history of travel or trauma. A family history of rheumatological or ocular disease is especially important, as is a review of systems for arthritic, dermatological, or pulmonary symptoms.

Slit-lamp examination of the cornea may reveal epithelial or stromal scarring caused by herpetic or syphilitic keratitis, epithelial edema suggesting an acute rise in IOP, and KPs, which may differentiate granulomatous from nongranulomatous inflammation. The iris should be carefully evaluated for the presence of nodules (seen in sarcoidosis), heterochromia (classic for Fuchs' iridocyclitis), and posterior synechiae formation (which can cause acute angle closure from pupillary block). An anterior chamber reaction consisting of cells and aqueous flare is the hallmark of anterior uveitis. Glaucomatocyclitis crisis (Posner-Schlossman syndrome) typically presents with mild inflammation, whereas severe reactions with hypopyon formation can be seen in Behçet's disease, the HLA-B27–related uveitis, and masquerade syndromes from intraocular neoplasm.

Careful visualization of the angle, by means of gonioscopy, is critical in the evaluation of all patients with elevated IOP. The configuration of the angle should be noted, and anatomically narrow angles that may be predisposed to closure must be identified. Heavy pigmentation of the trabecular meshwork can be seen in pseudoexfoliation, pigmentary dispersion syndromes, and uveitis. In the last case, the pigment is usually heaviest in the inferior angle, overlying the pocket formed by the iris root and scleral spur. The formation of PAS is an important feature of chronic inflammation, and PAS can lead to elevated IOP and secondary angle closure. PAS can be distinguished from normal iris processes by two features: (1) PAS appear more solid or sheet-like, and (2) PAS obliterate the angle recess. Iris processes tend to be open and lacy, follow the normal curve of the angle, and reveal normal angle structures in the open spaces between processes. Neovascular vessels in the angle, which differ from normal iris vessels in that they extend anteriorly over the scleral spur to reach the trabecular meshwork, can be seen in Fuchs' iridocyclitis. In the case of an apparently closed angle, a small lens (such as the Zeiss), should be used to indent the central cornea. This

TABLE 24–1 **Inflammatory Conditions Associated with Glaucoma**

1. Anterior Uveitis
   a. HLA-B27 positive uveitis (Reiter's, ankylosing spondylitis, etc)
   b. Juvenile rheumatoid arthritis
   c. Fuchs' heterochromic iridocyclitis
   d. Lens-induced uveitis
   e. Herpetic keratouveitis (simplex and zoster)
   f. Posner-Schlossman Syndrome
2. Intermediate Uveitis (pars planitis)
3. Panuevitis
   a. Sarcoidosis
   b. Toxoplasmosis
   c. Syphilitic uveitis
   d. Behçet's syndrome
   e. Sympathetic ophthalmia
   f. Vogt-Koyanagi-Harada syndrome
4. Masquerade syndrome (intraocular neoplasm)

maneuver (indentation gonioscopy) helps differentiate between an appositionally closed angle that opens with aqueous pressure and an angle that is permanently closed by PAS.

Dilated funduscopic examination is essential in determining whether inflammation involves the posterior segment. The collection of white cellular aggregates in the vitreous ("snowballs") or inferior pars plana ("snowbank") suggests intermediate uveitis. Inflammatory changes of the retina, retinal vessels, or choroid, with concomitant iridocyclitis, suggest conditions that can cause panuveitis, such as sarcoidosis, toxoplasmosis, sympathetic opthalmia, or Vogt-Koyanagi-Harada syndrome. Detailed attention should be paid to the optic nerve to look for glaucomatous changes such as asymmetry, excavation, notching, disc hemorrhage, or nerve fiber layer defects.

Based on the history and physical exam, diagnostic laboratory testing may be helpful. Special effort should be aimed at identifying infectious etiologies that can be treated with antibiotics. Commonly ordered tests include RPR/FTA-ABS to look for syphilis, serum or aqueous titers for toxoplasmosis, and skin PPD test for tuberculosis. HLA haplotype testing is helpful for suspected HLA-B27 uveitis and Behçet's disease. ANA testing is frequently positive in juvenile rheumatoid arthritis. Herpetic keratouveitis can usually be identified by the clinical picture alone.

DIAGNOSIS

Herpes simplex anterior uveitis.

Secondary open angle glaucoma (inflammatory glaucoma).

MEDICAL MANAGEMENT

The medical management of inflammatory glaucoma should generally be directed at two main objectives: controlling inflammation and reducing IOP.

Corticosteroids constitute the mainstay of therapy for most causes of ocular inflammation. Topical administration is preferred for anterior uveitis, and commonly used agents include prednisolone 1% and dexamethasone 0.1%. Initial dosing may require frequent, every-hour treatment, which can then be tapered based on the clinical response. A newer generation of steroids, such as rimexolone and loteprednol, is reported to be less likely to cause a steroid-induced rise in IOP and may be considered for patients on chronic therapy. Nonsteroidal anti-inflammatory agents such as flurbiprofen, ketorolac, and diclofenac can also help control ocular inflammation. In severe cases or those with associated extraocular involvement, systemic therapy with immunosuppressive medications such as methotrexate or azathioprine may be necessary.

Aqueous suppressants are generally considered the drugs of choice for control of elevated IOP in inflammatory glaucoma. Topical agents in this category include beta-adrenergic antagonists, such as timolol and levobunolol, and the carbonic anhydrase inhibitors, dorzolamide and brinzolamide. Adrenergic agonists, such as apraclonidine and dipivefrin, may provide additional pressure lowering. Miotics are not usually used in the inflamed eye, as they aggravate the breakdown of the blood–aqueous barrier and potentiate the formation of posterior synechiae. Latanoprost and other prostaglandin analogs, should also be avoided if possible, as their effects on the inflammatory cascade in uveitis have not been fully studied. Recent case reports have also questioned the association of latanoprost with recurrent herpes simplex keratitis.

Uveitis caused by infectious agents, such as syphilis or toxoplasmosis, must be treated with appropriate antibiotics. Topical trifluridine is effective against herpes simplex keratitis with epithelial involvement and for prophylaxis against recurrence of epithelial disease in patients on topical steroids. Topical antivirals penetrate poorly into posterior stroma and anterior chamber, however, and oral acyclovir has been reported to be helpful against herpetic keratouveitis, both in the acute setting and for prophylactic maintenance therapy.

Cycloplegic agents, including atropine or cyclopentolate, can aid in relieving pain from ciliary muscle spasm, in preventing formation of posterior synechiae, and in stabilizing the aqueous–blood barrier.

SURGICAL MANAGEMENT

In general, glaucoma surgery should be deferred, if possible, until active inflammation has been brought under control. Surgery is indicated if, despite maximal medical therapy, the IOP remains dangerously elevated, or glaucomatous visual field defects and disc changes develop.

Laser peripheral iridotomy should be performed for acute angle closure due to pupillary block, which may be caused by posterior synechiae. The main complication is transient anterior chamber inflammation and increased IOP, which may be ameliorated by premedication with steroids and apraclonidine. If laser iridotomy is unsuccessful, a surgical iridectomy may be required.

Laser trabeculoplasty is ineffective and contraindicated in eyes with active inflammation. The risk of an acute rise in IOP is greatly increased, as is formation of peripheral anterior synechiae leading to secondary angle closure.

For inflammatory glaucoma with open angle, or chronic angle closure, a trabeculectomy can be performed to lower IOP. The use of an antimetabolite such as 5-fluorouracil or mitomycin-C significantly improves success rates. The risk of bleb failure is higher in younger patients and those with uncontrolled inflammation. Surgery to place an aqueous drainage device, such as an Ahmed valve or Molteno implant, has also been shown to be effective. Laser cyclophotocoagulation may be associated with an intense inflammatory response postoperatively and should be used with caution.

REHABILITATION AND FOLLOW-UP

Frequent follow-up is essential for patients with uveitic glaucoma, as many of these conditions have a waxing and waning course. Attention must be paid to the presence of inflammation, and steroids should be used to control inflammation despite the risk of steroid-induced pressure elevation. Problems associated with chronic intraocular inflammation, such as band keratopathy and cystoid macular edema, should be actively sought and treated.

In addition to monitoring IOP, optic nerve examination and visual field testing are required to detect the development or progression of glaucoma. In addition, the angle should be closely evaluated with gonioscopy at each visit to look for evidence of neovascularization or PAS formation, which may lead to secondary angle closure. The development of glaucomatous damage often occurs well after the initial presentation of acute inflammation, and one should remain vigilant for glaucoma even after the apparent resolution of uveitis.

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Case 25

PRIMARY INFANTILE GLAUCOMA

Alana L. Grajewski, M.D.

HISTORY

A 3-month-old female infant was referred when an ophthalmologist suggested a diagnosis of primary infantile glaucoma after the mother noted "cloudy eyes and tearing" for 3 to 4 weeks. The child was the product of a full-term uneventful pregnancy and delivery with no use of forceps. There was no known family history of glaucoma; the single sibling, 3 years of age and male, was without any ocular problems.

On examination in the office, the child was photophobic and was more comfortable in dim illumination. Both eyes had a diffuse corneal haze, the right more so than the left. Corneal diameters were borderline normal or slightly enlarged OU. Estimated corneal diameters using a paper ruler in the office were 12 mm OD and 11 mm OS (Fig. 25–1). Intraocular pressure (IOP) measurements were taken with a TonoPen while the infant nursed on a bottle. The measurements were 45 mm Hg OD (<5%) and 36 mm Hg OS (<5%).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. In this particular clinical presentation the diagnosis of primary infantile glaucoma is fairly certain. Associated ocular pathology or other ocular conditions that can present with a "cloudy cornea," cannot be excluded until an examination under anesthesia is performed. Given the clinical history and appearance on initial office examination, however, it is the most likely diagnosis.

Primary infantile glaucoma usually presents within the first 2 years of life. Generally, the younger the presentation, the more serious the disorder and the more guarded the prognosis. It is most often bilateral (75% of the cases). Unilateral and asymmetric cases are seen, such as with this particular infant. Males are slightly more commonly affected than females. Siblings of children with primary infantile glaucoma may or may not be at greater risk. The inheritance pattern is not well understood but certainly there are families with multiple siblings with glaucoma from birth. The majority of cases are sporadic in occurrence, and in general the inheritance pattern is felt to be consistent with a polygenic pattern. The most common clinical presentation includes corneal enlargement with clouding, epiphoria, and photophobia, all of which were present in this child. These symptoms are secondary to the ocular abnormalities caused by elevated IOP.

2. Other causes of corneal haze or opacity include birth trauma (forceps), sclerocornea, congenital hereditary endothelial dystrophy (CHED), posterior polymorphous dystrophy, numerous metabolic diseases, uveitis, and various forms of anterior segment dysgenesis such as Peter's anomaly. Each of these has certain unique characteristics that help distinguish it from primary infantile glaucoma.

3. The corneal enlargement associated with megalocornea and axial myopia is isolated without the other symptoms and signs of elevated IOP and corneal edema.

4. Nasolacrimal duct obstruction is the most common cause of epiphora in this age group. Photophobia, corneal haze, and corneal enlargement are not associated with this problem. A mucopurulent discharge is often present and tends to respond quickly to standard treatment.

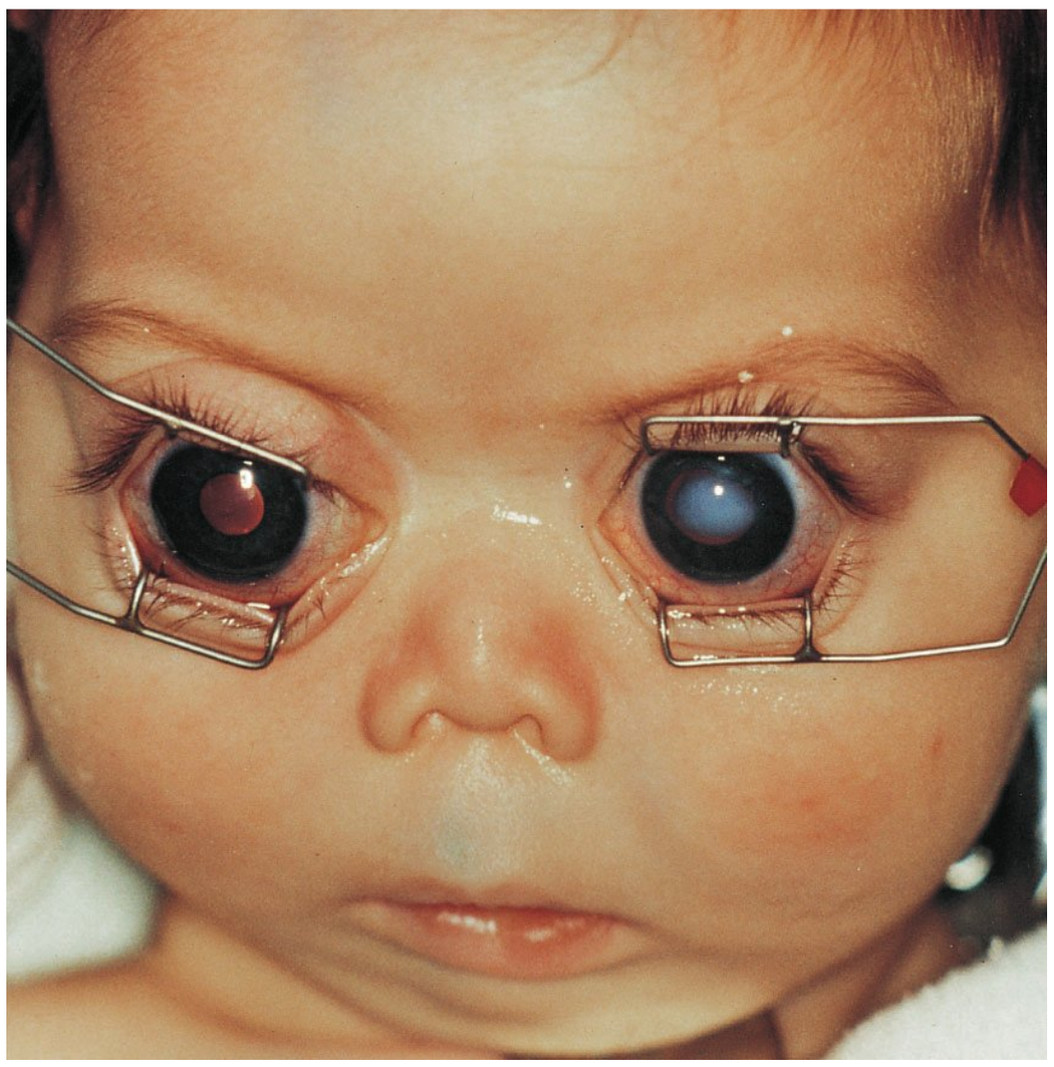

FIGURE 25–1 Examination under anesthesia. Both corneas are enlarged, the right more so than the left. The left cornea demonstrates a moderate central corneal haze; the right cornea has a more subtle epithelial edema seen best with the microscope.

5. Ocular tumors in infancy can also mimic infantile glaucoma. Some ocular tumors may be associated with a secondary elevated IOP that can produce some of the same signs and symptoms of primary infantile glaucoma. As the treatment is distinctly different it is imperative that this be considered in each child where the view to the posterior segment is obscured. Intraoperative ultrasound at the time of the initial examination under anesthesia is, in this circumstance, essential.
6. Finally, elevated IOP can also be associated with various systemic syndromes: Sturge-Weber, Rubinstein-Taybi, and Lowe's syndromes, rubella, and trisomy 13.

TEST INTERPRETATION

The testing for primary infantile glaucoma can be thought of as those examinations with or without anesthesia. An office examination is typically without anesthesia. Very young infants can often be pacified with a bottle for obtaining an initial pressure measurement in the office with either a TonoPen or a pneumatonometer. Sedated examinations, using agents such as chloral hydrate syrup without endotracheal intubation, are performed in some offices; however, it is not recommended for children less than 1 year of age or in any office not equipped to manage a pediatric airway problem emergently if the need should arise. A full examination under anesthesia is usually performed initially in the operating room and requires general anesthesia and endotracheal intubation. Brief examinations can be safely performed under anesthesia supervision without intubation using an inhalational anesthetic by mask with an oral airway. The examination under anesthesia consists of pressure measurement, corneal diameters, ultrasonography (axial length and biomicroscopy if needed), anterior segment examination, and gonioscopy. The dilated fundus examination with optic disc photos can be done if surgery is not planned.

The diagnosis of primary infantile glaucoma depends on several factors, with IOP measurement being only one. Anesthetic agents as well as facial compression from the mask can influence IOP measurement. Because of this, it is best to obtain two sets of measurements: the first under light anesthesia as soon as the child is quiet, and the second measurement once the airway is secured. Any consistent method to measure IOP is acceptable. The most commonly used are pneumatonometery, Schiotz, TonoPen, and hand-held applanation instruments. The normal IOP in infants is slightly lower than that found in adults. This is because the ciliary body does not reach the capacity for full aqueous production until several months after birth. Asymmetric IOPs are often helpful in distinguishing bilateral from unilateral or asymmetric cases.

Normal neonatal corneal diameters are 10 to 10.5 mm horizontally and increase 0.5 to 1.0 mm over the first year. Any corneal diameter $\geq$11.5 mm is almost certainly pathologic. With respect to ocular enlargement, measurement of axial length by A-scan ultrasonography is extremely useful for diagnosis and follow-up. The ocular stretching in response to elevated IOP

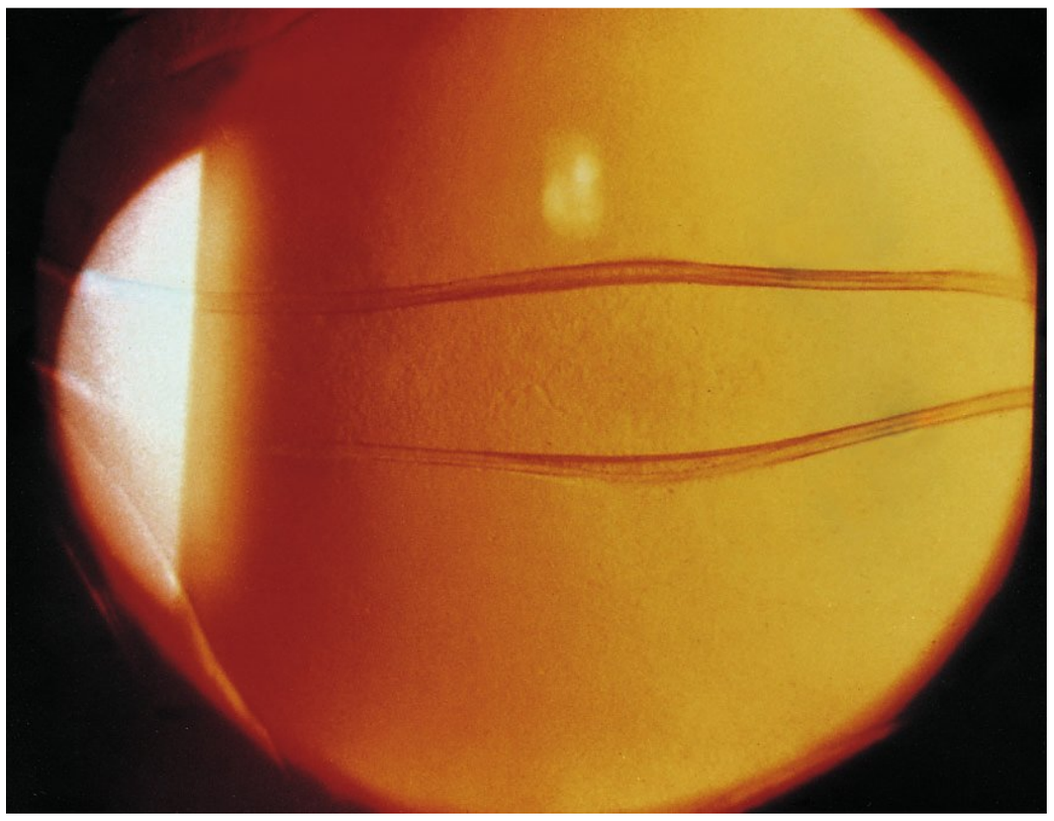

FIGURE 25–2 Horizontal break in Descemet's membrane, Haab's striae, right eye.

generally stops at 3 years of age. The remainder of the anterior segment examination can be limited by corneal edema and opacity. Nevertheless, one should record the corneal breaks in Descemet's membrane (Haab's striae) as these become useful for comparison in follow-up (Fig. 25–2). On gonioscopy, the iris appears stretched with thinning of the anterior stroma and a high flat insertion into the trabecular meshwork (Fig. 25–3). If surgery is not planned, dilated retina examination and optic disc stereo photography are performed. Stereoscopic disc photographs are clinically one of the most useful tools for long-term follow-up.

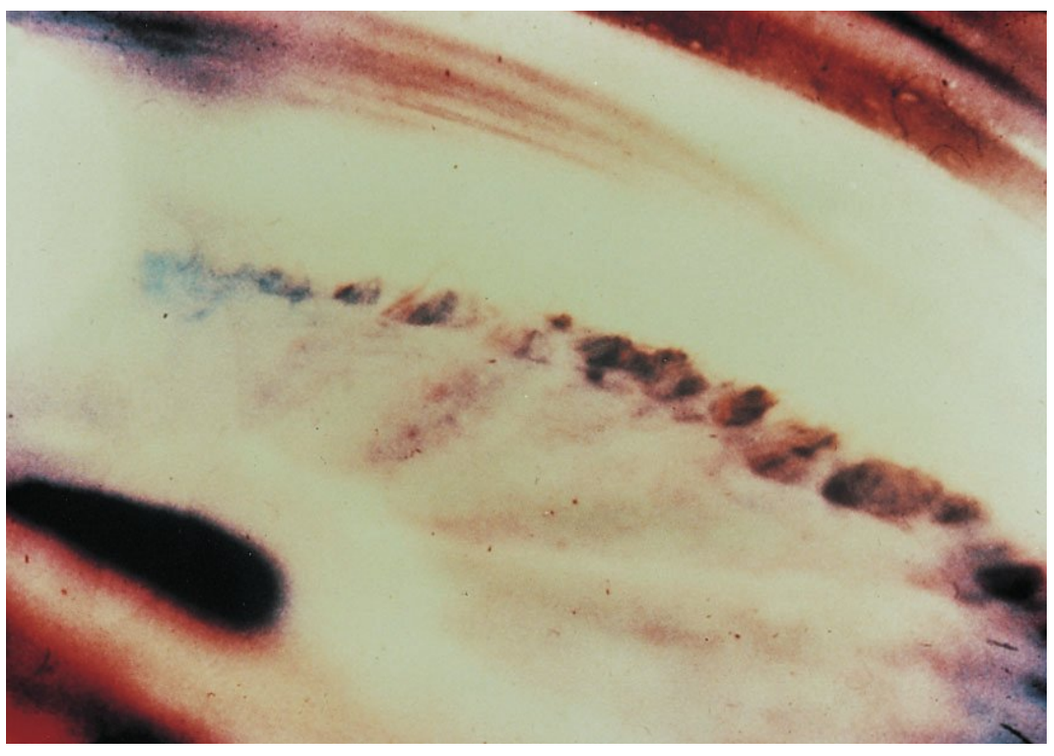

FIGURE 25–3 Gonioscopy demonstrates the high flat insertion with peripheral anterior stromal thinning typical of primary infantile glaucoma.

DIAGNOSIS

Primary infantile glaucoma.

MEDICAL MANAGEMENT

Primary infantile glaucoma is a surgical disease. Medications can be used in the preoperative period to minimize any further damage from elevated IOP as well as to allow some increase in corneal clearing, which facilitates a better examination of the anterior and posterior segments. This short-term therapy can be accurately administered in a cherry syrup suspension of injectable acetazolamide at 5 to 10 mg per kg every 6 to 8 hours. Topical carbonic anhydrase inhibitors and selective beta-blockers are also safe in reduced scheduling doses. Topical alpha-2 agonist use in small children is associated with profound sedative effects. In addition, these agents prolong the effect of anesthesia and these are contraindicated in infants.

SURGICAL MANAGEMENT

Prompt surgery is essential in most cases of infantile glaucoma. Damage from elevated IOP is more likely the longer IOP remains elevated. In an infant, such as the one in this case presentation, with the presumptive diagnosis of primary infantile glaucoma made at the time of the office examination, the child should be placed on medication (topical or oral carbonic anhydrase inhibitor) until the pediatrician and anesthesiologist give clearance for general anesthesia. In order to minimize the time until treatment as well as limit exposure to anesthesia, surgery should be planned for the same time as the initial full examination under anesthesia if the diagnosis is confirmed. For this reason the initial examination should be performed by a surgeon familiar with angle surgery for infantile glaucoma. While various surgical approaches have been reported for initial surgery, none have had the same success rate and low complication rate as traditional angle surgery: goniotomy or trabeculotomy. These procedures work equally well. The preferred approach is to treat the angle of 360 degrees with either of these

methods before moving on to other surgery. As limiting the exposure to anesthesia is desirable the 360 trabeculotomy with a prolene suture is an excellent choice. The success rate of this procedure is between 80 and 90% with initial angle surgery, thus making the need for a second procedure rare. If IOP remains uncontrolled following 360 degrees of surgical treatment of the angle, without other factors complicating the clinical picture (eg, hyphema or anterior chamber inflammation), the temporary use of topical medications can be tried. After a sufficient time from surgery and if medical therapy is not adequate, a glaucoma drainage device such as a Baerveldt shunt is placed. This style of drainage device is preferred in infants as its low contour better conforms to the globe and so it is less likely to displace the globe. There have been reports of success with trabeculectomy; however, these rarely function without the use of an antimetabolite. Mitomycin-C enhances the success rate of filtering surgery in children. Given the long-term risks of a mitomycin bleb in a child, however, traditional angle surgery and/or a drainage implant is preferred. Cyclodestructive procedures are reserved for those cases that fail filtration procedures.

REHABILITATION AND FOLLOW-UP

After completion of a full examination under anesthesia and angle surgery, the child should be placed on topical cycloplegics and steroids for 1 to 2 weeks. A second examination under anesthesia is performed at 8 to 10 weeks postoperatively. All measurements are repeated. If the IOP is acceptable, the baby is dilated for disc photography and fundus examination. Follow-up examinations under anesthesia can be performed about every 2 to 3 months, until it is certain that the IOP is stable. At that point, examinations can be every third to fourth month and then reduced to every 6 months, when the patient is stable. By the age of 3 or 4 the child can generally be examined in the office.

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Case 26

OCULAR HYPOTONY

Thomas W. Samuelson, M.D.

HISTORY

A 45-year-old woman was referred for surgical management of inflammatory glaucoma in her aphakic right eye. Her left eye had had only light perception since birth due to persistent hyperplastic primary vitreous.

The preoperative visual acuity with aphakic correction was 20/20. The intraocular pressure (IOP) was 40 mm Hg on maximum medical therapy including oral agents. There was 1+ cell and flare in the anterior chamber with scattered, fine, keratic precipitates. There was vitreous at the pupillary plane. The optic disc was markedly excavated with a cup-to-disc ratio of 0.9 and a notch inferiorly. The visual field had a superior altitudinal defect.

A trabeculectomy with mitomycin-C and subtotal vitrectomy was performed without incident. Postoperatively, the visual acuity remained 20/20. The IOP was well controlled in the range of 9 to 12 mm Hg for the first postoperative year. However, 1 year after surgery, the patient presented with a complaint of worsening vision.

The visual acuity was 20/60. An increase in hyperopic correction of +1.50 diopters improved the visual acuity to 20/20. The bleb was highly elevated, avascular, and cystic. The remainder of the examination was unchanged from baseline with the exception of moderate chorioretinal folds involving the posterior pole and macula. The IOP was 3 mm Hg.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

This patient has hypotony with maculopathy. The differential diagnosis of hypotony in this case includes several disorders.

Primary Overfiltration

This disorder is most common in the early postoperative period following trabeculectomy when the eye is still recovering from chronic pharmacologic aqueous suppression and the conjunctiva has yet to contract in the region of the filter. Hypotony related to overfiltration is a diagnosis of exclusion. Primary overfiltration implies that the basic problem relates to excessive outflow rather than to an abnormally low production of aqueous. Clinically, the bleb is generally exuberant and highly elevated. Primary overfiltration must be distinguished from secondary overfiltration that may result from a wound leak or cyclodialysis cleft. These conditions are discussed below.

Underproduction (Hyposecretion) of Aqueous

Hyposecretion of aqueous is an important cause of ocular hypotony. Hyposecretion may occur when aqueous suppressants are not discontinued following filtration surgery. Pharmacologic hyposecretion of aqueous is diagnosed by obtaining the appropriate history. Hyposecretion may also occur in response to inflammation. Clinically, there may be significant flare in the anterior chamber due to decreased clearance of proteins and altered blood–aqueous barrier. The bleb is generally lower and more vascularized in such eyes. Hyposecretion may also result from ciliary detachment or ocular ischemia; these conditions are addressed below.

Bleb Leak

A bleb leak can result in hypotony and may occur at any time following glaucoma filtration surgery. A Seidel test is mandatory in any postsurgical patient with hypotony. The entire bleb

and incision line should be painted with fluorescein; the leak is apparent where the dye is displaced. In general, a bleb leak will result in a lower bleb. However, bleb morphology may be variable in eyes with leaks and should not be relied on for the diagnosis. The diagnosis and management of bleb leaks are discussed in Case 28.

Cyclodialysis Cleft

A cyclodialysis cleft is a relatively uncommon condition that may result in profound hypotony. It is most common following cataract surgery utilizing a scleral tunnel incision. However, a cleft may also occur following glaucoma filtration surgery when the block excision is too posterior and the ciliary body is disinserted from the scleral spur. Additionally, a cleft may also occur following trauma. Hypotony results from increased outflow facility as aqueous is diverted from the anterior chamber into the suprachoroidal space. The diagnosis is made by careful gonioscopy. If the anterior chamber is too shallow to visualize the angle, viscoelastic material may be injected to deepen the anterior chamber to improve visualization.

Retinal Detachment

Retinal detachment may cause hypotony by increasing uveal scleral outflow or by decreasing aqueous production. The diagnosis is made by fundus examination or by ultrasound in the event that media opacity precludes a view of the posterior pole.

Choroidal Effusion

This is not typically a primary cause of hypotony but rather a result of hypotony. However, the presence of fluid in the suprachoroidal space may result in ciliary detachment that in turn may decrease aqueous production, which may exacerbate hypotony. The diagnosis of choroidal effusion is made by indirect biomicroscopy and identification of smooth, dome-shaped, lobular elevation of the retina. Characteristically, the anterior chamber is shallow.

Ocular Ischemia

Ocular ischemia-related hypotony results from decreased aqueous production due to underperfusion of the ciliary body. Associated findings may include rubeosis iridis, low-grade anterior chamber reaction, and scattered blot hemorrhages in the retina. Carotid artery blood flow studies or fluorescein angiography will provide the definitive diagnosis.

Occult Globe Perforation

This disorder is a rare cause of ocular hypotony. Most commonly, globe perforation occurs during retrobulbar injection or during placement of the rectus traction suture used to stabilize the globe during surgery. The diagnosis is made by fundus examination.

TEST INTERPRETATION

The slit-lamp and fundus examination generally provide the necessary information to correctly identify the etiology of ocular hypotony (Table 26–1). Once the visual acuity and IOP are measured, the bleb is examined carefully. The elevation, vascularity, and extent of the bleb should be noted (Fig. 26–1). The presence or absence of microcyst formation within the bleb should be noted. Examination of the bleb should include a Seidel test to rule out a bleb leak. A Seidel test is best accomplished by using a moistened strip of fluorescein and directly painting the bleb and incision line. A wound leak is identified by detecting a stream of bright green aqueous using cobalt blue light at the slit lamp (Fig. 26–2). It is important to realize that an intermittent leak may not be apparent if hypotony is profound and there is no flow gradient. In such cases, gentle pressure may be applied to the globe under direct visualization at the slit lamp. The increased pressure gradient may reveal an occult leak.

Slit-lamp biomicroscopy is used to document the anterior chamber (AC) depth. The AC may be shallow or normal depth. A shallow AC is a nonspecific sign and, unlike the bleb

TABLE 26–1 **Differential Diagnosis of Post-Operative Hypotony**

Diagnosis	Test Results/Exam Features*
Over Filtration	Seidel(−) Bleb High on Exam
Bleb Leak	Seidel (+) Bleb Variable–generally low
Decreased Production—Pharmacologic	History of Aqueous Suppression Therapy Seidel (−) Bleb Low
Decreased Production—Non-pharmacologic	Seidel(−) Increased Inflammation, Increased Flare Fundus Exam/Ultrasound –R/O Retinal Detachment –Ciliary Detachment –Choroidal Effusions Bleb Low
Cyclodialysis Cleft	Gonioscopy Confirms Presence of Cleft Bleb Low
Retinal Detachment	Fundus Exam/Ultrasound
Ocular Ischemia	Peripheral Retinal Hemorrhage Angle Neovascularization Carotid Studies
Globe Perforation	Fundus Exam Detects Perforation or Vitreous Hemorrhage

(*A Seidel test is mandatory on every patient with hypotony)

appearance, does not help discern the etiology of the low IOP. Finally, the presence of intraocular inflammation should be noted. This inflammation is a nonspecific sign, but pronounced AC flare may be a sign of decreased aqueous production.

The fundus examination will rule out retinal detachment, an uncommon but important cause of low IOP. Additionally, fundus examination may document the presence of choroidal effusion. Occasionally, a very anterior or annular choroidal effusion may be occult and not

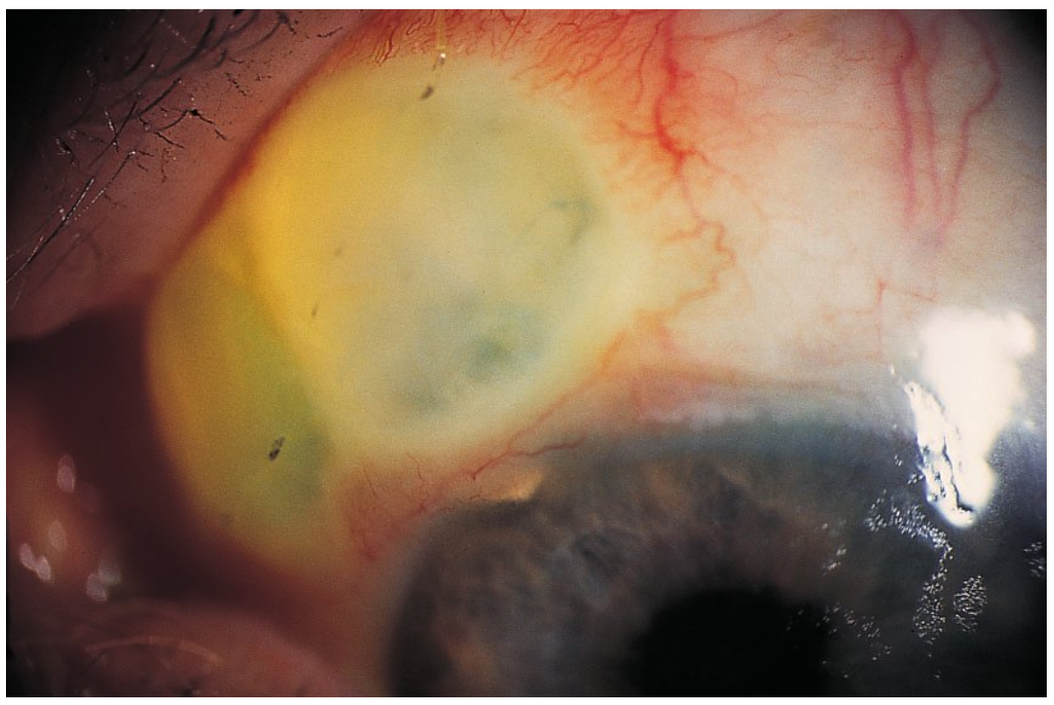

FIGURE 26–1 Typical appearance of an overfiltering bleb in a patient with hypotony.

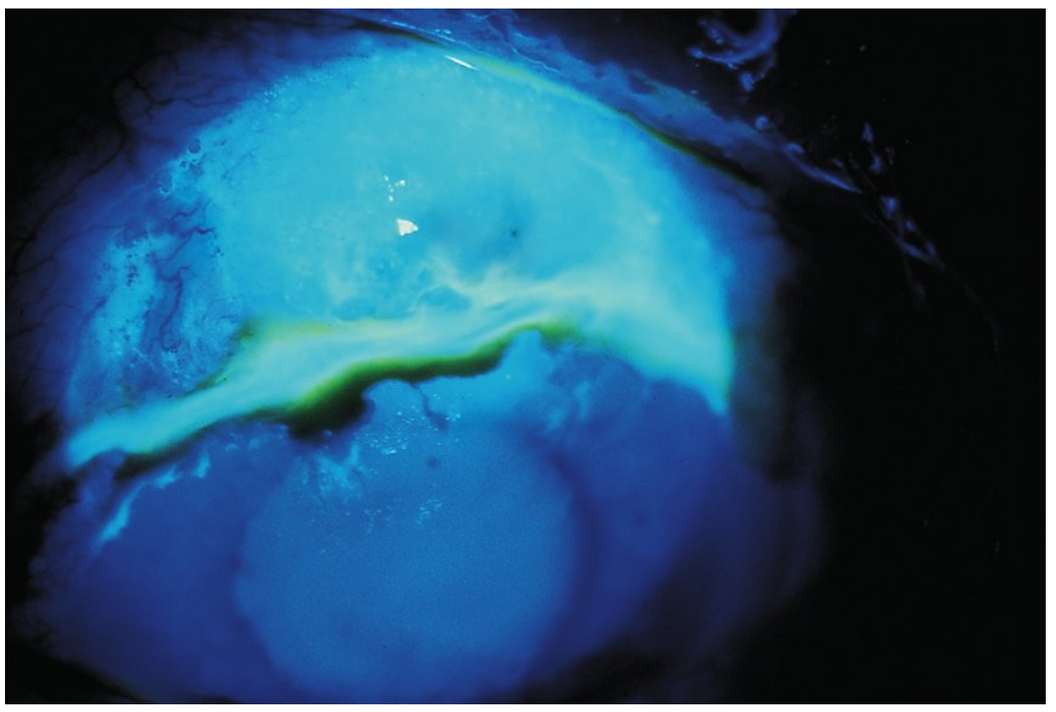

FIGURE 26–2 Positive Seidel test in a patient with hypotony.

visible on standard fundus exam with indirect biomicroscopy. Such cases may be detected by ultrasound biomicroscopy. Finally, the macula should be examined for striae, which may result from hypotony. The macular striae characteristic of hypotonous maculopathy do not typically have an exudative component. Fluorescein angiography is generally not helpful. Finally, the fundus exam may reveal a swollen or hyperemic optic disc, another nonspecific sign of hypotony.

Gonioscopy is useful to rule out a cyclodialysis cleft or excessively large sclerostomy site. Additionally, gonioscopy is necessary to rule out angle neovascularization in cases of ocular ischemia.

Refraction is useful in cases of reduced visual acuity associated with hypotony. Relative myopia may result from shallowing of the AC and forward displacement of the lens or intraocular lens. Conversely, relative hyperopia may result when profound hypotony causes contraction of the globe and decreased axial length. An axial length measurement may confirm reduced axial length relative to baseline values or compared to the fellow eye. Reduced axial length is a common finding in patients with hypotonous maculopathy (Fig. 26–3). In general, choroidal effusions are more common in elderly patients with rigid sclera while globe contraction is more common in younger patients with less rigid sclera.

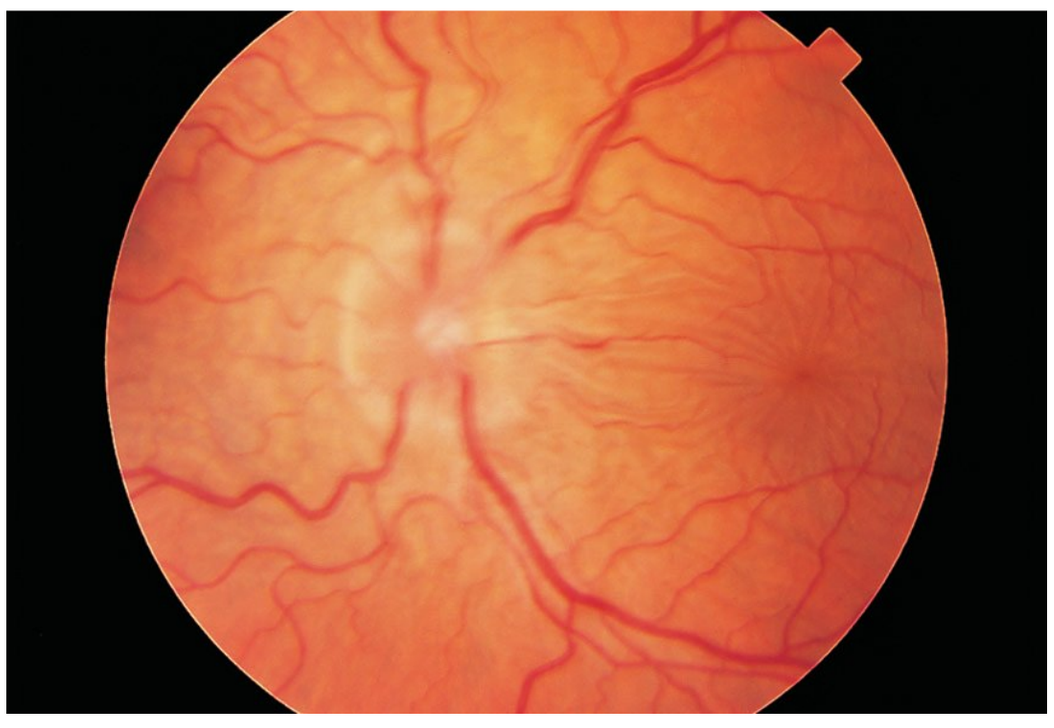

FIGURE 26–3 Typical fundus appearance of a hypotonus eye with disc swelling and chorioretinal folds.

The patient in this case discussion had hypotony associated with a large, avascular, Seidel-negative bleb. Slit-lamp examination found the eye to be quiet and noninflamed. Gonioscopy excluded a cyclodialysis cleft. The axial length was 0.75 mm shorter and refraction 1.5 diopters more hyperopic than baseline readings. Maculopathy was detected by fundus exam. There was no retinal or choroidal detachment. Finally, a careful patient history confirmed that the patient was not taking any topical or systemic medications that could suppress aqueous production.

DIAGNOSIS

Hypotony due to primary overfiltration.

MEDICAL MANAGEMENT

For mild hypotony early in the postoperative period, pharmacologic treatment may stabilize the eye until the overfiltration spontaneously resolves. Cycloplegic agents may help deepen the AC and stabilize the blood–aqueous barrier. While aqueous suppressants are often administered to treat bleb leaks, they are not helpful in cases of hypotony related to overfiltration. Topical corticosteroids may quiet the eye and maximize aqueous production. However, they may also make the bleb thinner and less vascular, preventing bleb contraction. As such, the benefit of topical corticosteroids on aqueous production must be weighed against the potential negative effect on an overfiltering bleb.

SURGICAL MANAGEMENT

When hypotony is profound and persistent, surgical intervention may be necessary. Several procedures have been advocated to treat overfiltration including compression shells or sutures, inflammation-inciting measures such as trichloroacetic acid, autologous blood patch (Fig. 26–4), and bleb remodeling with Nd:YAG laser. As a rule, mild cases may respond to these measures.

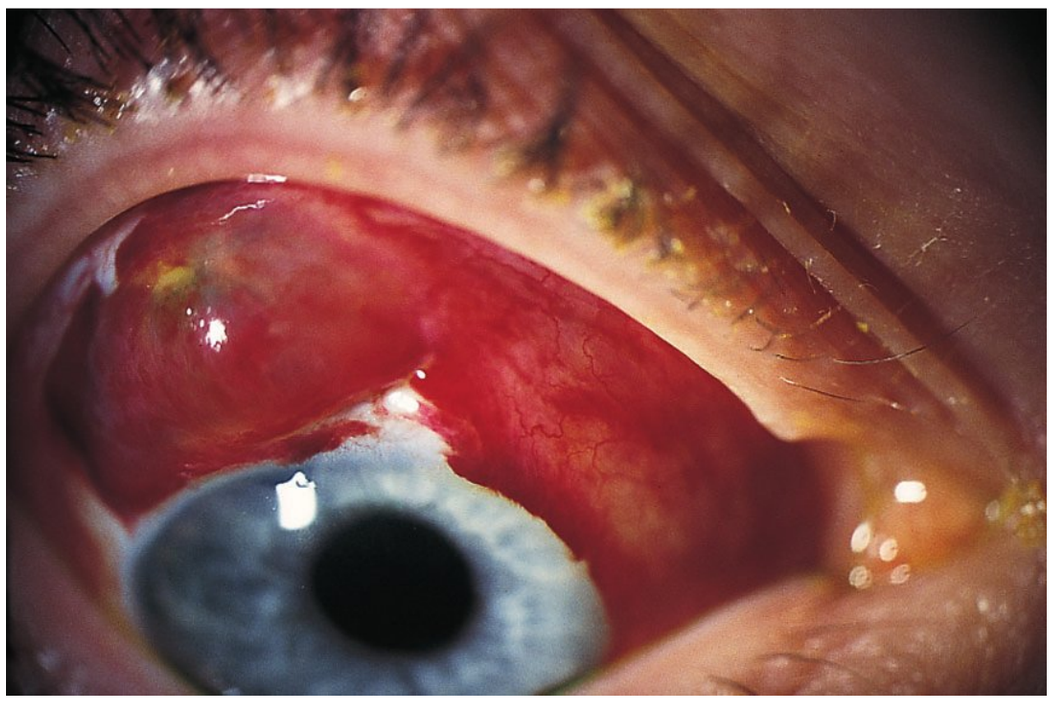

FIGURE 26–4 Mild cases of overfiltration hypotony may be successfully managed with an autologous blood patch.

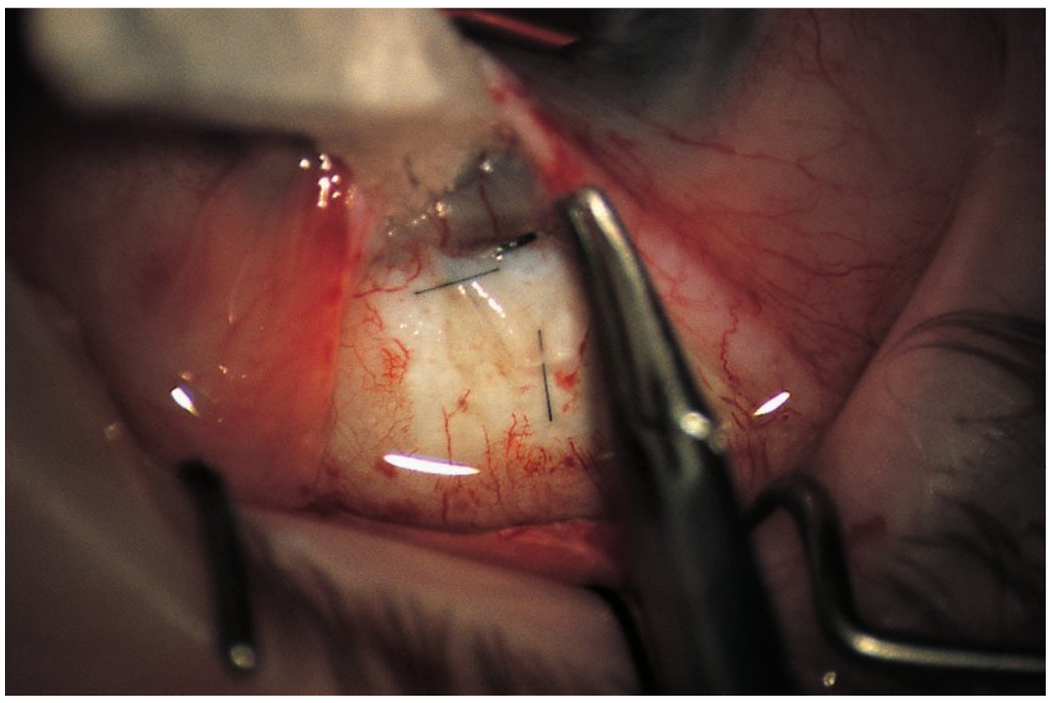

FIGURE 26–5 Resuturing the scleral flap is often effective in treating hypotony related to overfiltration when more conservative measures fail.

However, more profound and protracted hypotony often requires surgical revision such as resuturing of the scleral flap or bleb revision.

REHABILITATION AND FOLLOW-UP

Cycloplegic agents and conservative observation failed to reverse the hypotony. An autologous blood patch also failed. The patient was then taken to the operating room where two additional sutures were placed in the scleral flap (Fig. 26–5). The bleb was not excised. The patient responded well with increased IOP into the 20s. The axial length, refraction, and visual acuity returned to normal. One month postrevision, suture lysis was performed resulting in IOP of 13 mm Hg. Six years later, the IOP has remained in the low teens with no recurrent hypotony.

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Case 27

POST TRABECULECTOMY WOUND LEAK

Sherif M. El-Harazi, M.D., M.P.H.
Robert M. Feldman, M.D.

HISTORY

A 59-year-old woman, with advanced primary open-angle glaucoma, underwent a limbus-based trabeculectomy with intraoperative application of 5 FU in the right eye. The scleral flap was closed with two 10-0 nylon sutures. Tenon's capsule was closed with running locking 8-0 vicryl sutures, and the conjunctiva was closed with running nonlocking 8-0 vicryl sutures.

Five months postoperatively, the patient presented for examination because of a dramatic decrease in vision in the right eye. On examination, best-corrected visual acuity was 20/100 in the right eye and 20/30 in the left eye. The anterior chamber in the right eye was very shallow, and the intraocular pressure (IOP) was 2 mm Hg (Fig. 27–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

The causes of postoperative shallow anterior chamber and low IOP can be divided into two major groups depending on the timing of the complication.

Early Postoperative (less than 4 weeks)

Early postoperative shallowing of the anterior chamber associated with low IOP may be due to overfiltration, reduced aqueous production, wound leak, or choroidal effusion or hemorrhage.

1. Bleb over*fi*ltration. Excessive outflow with an exuberant bleb is more common following full-thickness surgery than after trabeculectomy. Relative lack of resistance to aqueous flow is the presumed cause of this complication. The incidence of early postoperative shallowing and hypotony might be reduced by tighter scleral flap suture, and sequential suture release by argon laser suture lysis (ALSL), or releasable suture techniques. Overfiltration is initially managed by external tamponade. However, surgical correction to tighten the scleral flap may be required. Usually this problem will correct itself within 2 weeks of surgery if there are no intervening complications.
2. Reduced aqueous production. Causes of postoperative aqueous hyposecretion include postoperative use of topical aqueous suppressants or systemic carbonic anhydrase inhibitors, excessive postoperative use of topical phenylephrine, and detachment of the ciliary body. Cyclodialysis clefts may lead to hypotony initially by increased outflow, which may continue or be superimposed by choroidal effusions and decreased aqueous production.
3. Wound leak. A wound leak is one of the most common causes of early shallowing of the anterior chamber with hypotony. A Seidel test is necessary to localize the leak (Fig. 27–2). Causes include conjunctival buttonholes, wound dehiscence, or a traumatized thin filtering bleb.

The management of wound leak depends on the character and location of the filtering bleb. Initial treatment may be a pressure patch with aqueous suppression and withholding of topical corticosteroids until resolved. Use of a Simmons shell or an oversized bandage contact lens may be useful. Definitive therapy is surgical closure.

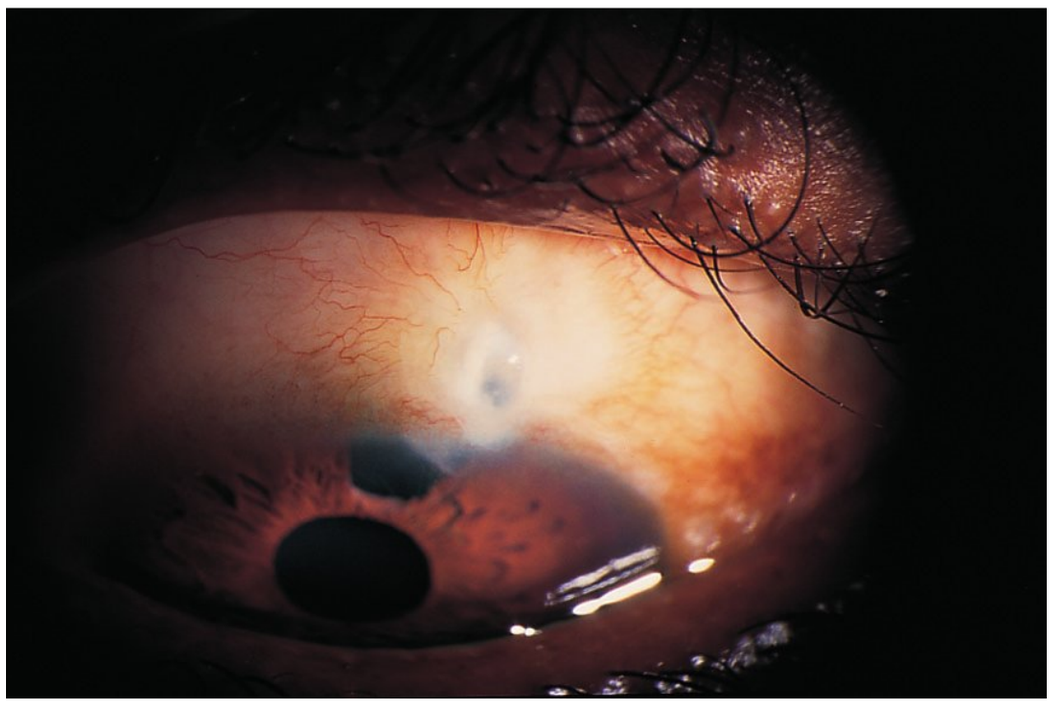

FIGURE 27–1 Slit-lamp photograph of the right eye demonstrating a low filtering bleb.

4. Choroidal effusion. Choroidal effusion is a common complication following filtering surgery and usually associated with hypotony. The effusion is usually transient, and the management is mainly topical or systemic corticosteroids combined with cycloplegics. Systemic corticosteroids should be reserved for cases of "kissing" choroidals. Surgical drainage is indicated if there is persistent shallowing of the anterior chamber, corneal decompensation, or synechial formation. These will generally resolve with conservative treatment by 2 weeks, after which drainage and reformation of the anterior chamber should be considered.

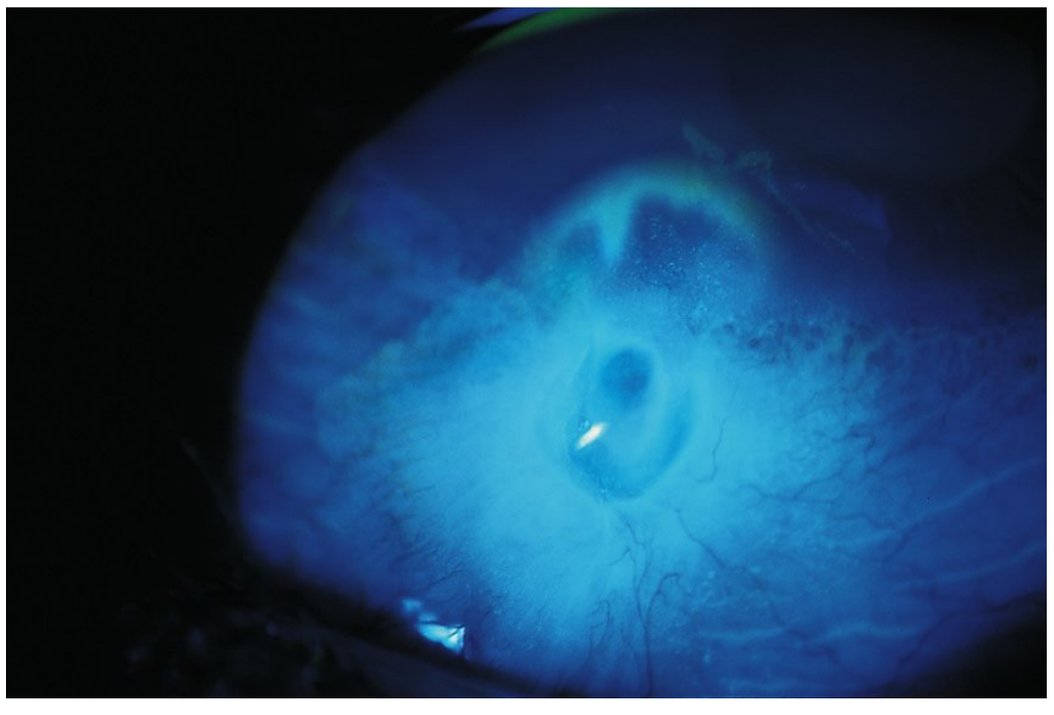

FIGURE 27–2 Cobalt blue filter slit-lamp photograph of the right eye. Leaking aqueous can be seen after the application of fluorescein dye.

Late Postoperative (greater than 4 weeks)

The most common causes of late postoperative anterior chamber shallowing with low IOP are chronic hypotony and late bleb leaks.

1. Chronic hypotony. Chronic hypotony (IOP less than 5 mm Hg) might be a manifestation of overfiltering bleb, aqueous hyposecretion, cyclodialysis cleft, undetected retinal detachment, or bleb leaks. Postoperative chronic hypotony is more common after full-thickness procedures with antifibrotics as compared to trabeculectomy alone. The most common sequela is hypotony maculopathy and this is more common with young age and in myopia. The clinical manifestations of hypotony include choroidal and retinal folds, optic disc swelling, and engorgement and tortuosity of the retinal vasculature.

   The management of chronic hypotony is mainly directed toward eliminating the underlying cause. The main goal is to decrease excessive aqueous outflow and eliminate ciliochoroidal effusion. However, aqueous suppression might lead to hypotony in a filtered eye and should be discontinued. Stopping beta-blockers in the other eye is advisable as a crossover effect exists. Also, large-overfiltering blebs should be reduced in size by placement of compression sutures, cryotherapy, argon laser, Nd:YAG, or injection of autologous blood. Bleb window cryopexy is a useful procedure to reduce symptomatic, large, overhanging blebs. If the previous measures fail, more invasive surgical bleb revision might be required.

2. Late bleb leak. Late bleb leak is a well-documented complication of filtering surgery, which might develop months or years after the initial surgery. The condition is more common with cystic, thin-walled, avascular blebs. In contrast to early leaks, the condition carries a high risk of developing blebitis, endophthalmitis, or chronic hypotony maculopathy. Hypotony maculopathy might result in permanent reduction of central vision, and endophthalmitis might lead to loss of the eye.

TABLE 27–1 **Grading System for Anterior Chamber Depth**

Grade 1.	Peripheral iris–cornea touch
Grade 2.	Iris sphincter–cornea touch
Grade 3.	Lens–cornea, or vitreous–cornea touch

TEST INTERPRETATION

The clinical examination included characterization of bleb appearance and assessment of the leak. Under cobalt blue slit-lamp illumination, a moistened sterile fluorescein strip was applied to the bleb surface. A leak was defined as a spontaneous focal-point source of aqueous leakage from an area of interrupted conjunctival tissue. Anterior chamber depth was also assessed (Table 27–1).

DIAGNOSIS

Late bleb leak.

MEDICAL MANAGEMENT

Antimetabolites have improved the outcome of glaucoma filtering surgery. However, the improved pressure-lowering effect has increased postoperative complications including bleb leaks, hypotony, and hypotony-induced maculopathy. Although many treatment options have been proposed, successful closure of bleb leaks following trabeculectomy remains difficult and the best method of repair is controversial. The multiplicity of treatments is a testimony that none of them is adequately effective. If left untreated, flat anterior chamber, cataract, corneal decompensation, synechiae, choroidal effusions, or macular edema may develop.

Management of bleb leaks is challenging. Typically, initial treatment is aqueous suppression and observation. Suppression of aqueous production slows the flow through the leak, allowing epithelial proliferation and healing across with closure of the defect. This is often inadequate as a long-term solution, as these leaks may spontaneously resolve and reappear elsewhere within the ischemic bleb. Other techniques include the following.

Autologous blood injections. Autologous blood "patches" have been used for years to treat spinal fluid leaks after spinal tap. A blood patch has been used to treat persistent pulmonary air leaks. Autologous blood can be injected into the bleb or into the surrounding subconjunctival tissue. The procedure can be performed with topical anesthesia at the slit lamp. The underlying hypothesis is that fibrin and erythrocytes obstruct fluid flow through the overfiltering bleb initially. Also, the whole blood might provide fibroplastic transformation to replace inactivated Tenon capsule fibroblasts. Complications of the procedure include bleb perforation, very high IOPs, and infection. This is often ineffective, and multiple injections might be necessary.

Argon laser. The mechanism by which argon laser closes filtering bleb leaks is not readily explained. Possibilities include a mechanical effect caused by the shrinking of the conjunctiva, which thinned the conjunctival–corneal interface, or which forced the two ends of a conjunctival tear together. The mechanical effect may be aided by the coagulation of epithelial cells from the conjunctiva and cornea to form a seal over the break. Thermal irritation of the laser may cause an increase in the number of inflammatory products deposited at the site of the leak and thus promote healing. Unfortunately, fenestration and pitting of the conjunctiva, corneal stromal opacities, and need for retreatment may occur.

Continuous-wave Nd:YAG laser. This laser is not readily available to most surgeons and is expensive. Disadvantages: iatrogenic bleb leaks; pupillary retraction toward the bleb; the pigmentation precipitated by the laser can affect future laser treatment and pupil flattening or peaking. The mechanism by which Nd:YAG laser remodels filtering blebs is not readily explained. It is presumed that the laser selectively affects the inner surface of the bleb and the uveal tissues without damaging overlying conjunctiva, causing inflammation and thus promoting healing

of the bleb. The long-term results have been disappointing.

SURGICAL MANAGEMENT

Various surgical approaches to repair leaking blebs have been described. These include excision of the bleb and replacement with advancement of adjacent conjunctiva, scleral patch grafts, free conjunctival grafts, Tenon's capsule pedicle plugs, and rotational conjunctival-Tenon's flap grafts. A technique of free conjunctival patching over a deep localized bleb has been reported to have excellent results.

REHABILITATION AND FOLLOW-UP

Once the leak is closed, the patients are to be followed closely for recurrent leaks if an ischemic bleb remains. If definitive surgical intervention was successful, the blebs are no longer ischemic and the risk of recurrence is low.

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Case 28

FAILING FILTERING BLEB

Sherif M. El-Harazi, M.D., M.P.H.
Robert M. Feldman, M.D.

HISTORY

A 53-year-old African American woman, with advanced primary open-angle glaucoma, underwent a limbus-based trabeculectomy with intraoperative application of 5-FU in the right eye. The scleral flap was closed with two 10-0 nylon sutures. Tenon's capsule was closed with running locking 8-0 vicryl sutures, and the conjunctiva was closed with running nonlocking 8-0 vicryl sutures.

Fourteen months postoperatively, the patient presented for examination because of decreased visual acuity and slight pain in the right eye. On examination, best-corrected visual acuity was 20/80 in the right eye and 20/25 in the left eye. The anterior chamber in the right eye was deep; the filtering bleb, however, was almost flat (Fig. 28–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

The causes of postoperative rise of intraocular pressure (IOP) associated with deep anterior chamber can be divided into two major groups depending on the appearance of the filtering bleb. Risk factors for filtration failure include youths, black race, uveitis, prior failed filtering procedure, neovascular glaucoma, and aphakia. Older patients show fewer tendencies toward scar formation than do younger adults. Some iatrogenic surgical techniques might lead to increased fibrosis and failure including excessive cautery, excessive bleeding, or excessive intraocular manipulation.

Elevated IOP Associated with High Bleb

The presence of temporary elevated IOP with a high bleb and deep anterior chamber is either due to high-bleb phase or encapsulated filtering bleb (Tenon's capsule cyst).

High-bleb phase. The elevation of the IOP is due to swelling of the sclera or collagenous lining of the wall of the bleb. This will limit the aqueous outflow with resultant IOP spike. The condition is usually temporary and should not be assumed to be a sign of filtration failure. The condition is usually self-limited with decrease in the IOP within a few weeks. Treatment options include ocular massage, aqueous suppressants, or laser suture lysis.

Encapsulated *fi*ltering bleb (Tenon's cyst). Encapsulated filtration bleb is the most common cause of filtration failure during the first 6 weeks after surgery. The reported incidence after trabeculectomy ranges from 10 to 14%. Clinically, the encapsulated bleb appears as an elevated, dome-shaped structure at the site of the filtration bleb. Histopathologically, the cyst consists of dense subconjunctival connective tissue, few cells, and no cellular lining. The aqueous humor becomes entrapped within a cyst-like cavity of hypertrophied Tenon's capsule.

Many encapsulated blebs will eventually resolve spontaneously without intervention. Digital compression can be applied to encourage filtration, and topical anti-inflammatory agents might be used to inhibit further fibrosis. If conservative treatment fails to reduce IOP, surgical intervention might be indicated. One surgical technique is bleb needling, in which a 25- to 30-gauge needle is passed beneath the conjunctiva and used to puncture and incise the fibrous tissue. A more invasive technique is excisional revision, in which the conjunctiva is dissected over the dome of the cyst, and the encapsulated wall is completely excised.

Elevated IOP Associated with Low Bleb

The presence of elevated IOP with low bleb and deep anterior chamber is either due to tight

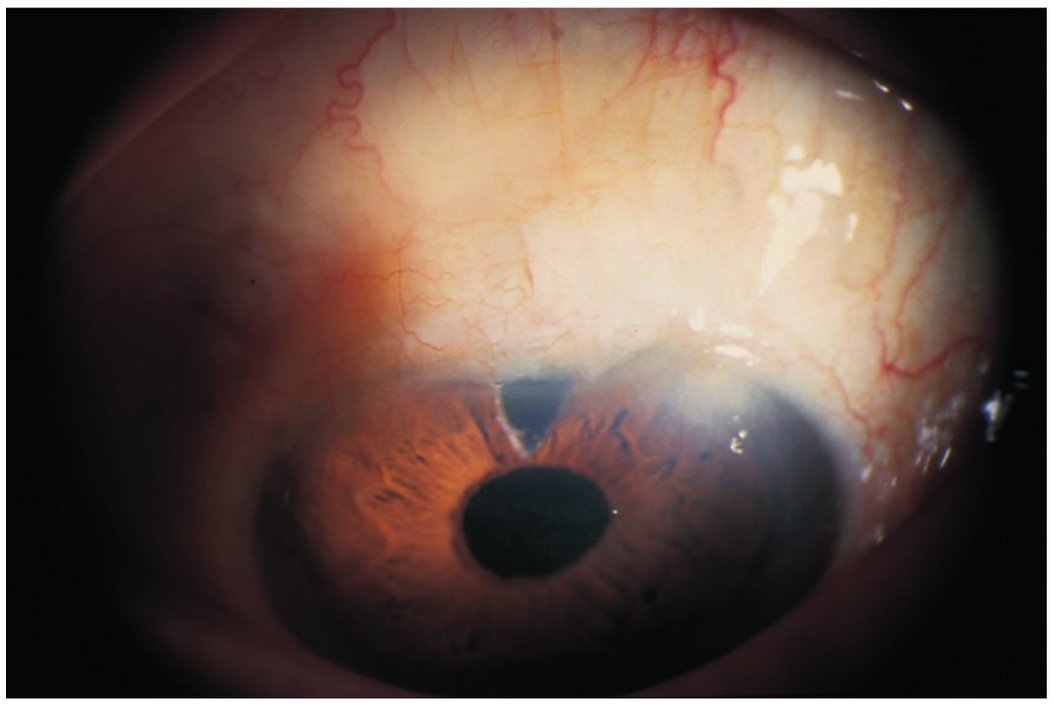

FIGURE 28–1 Slit-lamp photograph demonstrating a flat filtering bleb.

scleral flap sutures or to occlusion of the sclerostomy site, which might lead to filtration failure.

Tight scleral *flap* sutures. The elevation of IOP associated with low bleb in the early postoperative period might be related to tight scleral flap sutures. The tightness of the sutures can be controlled intraoperatively by the use of slipknots. The condition can easily and safely be managed in the office using the argon laser. A Hoskins or Rich suture lysis lens should be used under topical anesthesia. The procedure should be followed by gentle digital ocular massage to facilitate the egress of aqueous. One suture at a time should be cut and the procedure should not be done during the first 2 to 3 postoperative days to avoid overfiltration and hypotony. The advantage of releasing scleral flap sutures is the rapid egress of aqueous allowing the formation of filtering bleb; in addition, the suture ends remain buried under the conjunctiva. Unfortunately, the procedure might be associated with hypotony due to excessive flow, conjunctival burns, or buttonholes.

The presence of high IOP associated with flat bleb even after digital massage might be a sign of impending failure.

Occlusion of the sclerostomy site. In the early postoperative period, the internal sclerostomy site might become obstructed (tissue incarceration) causing elevation of IOP. Possible causes of obstruction include incompletely excised Descemet's membrane, iris, ciliary body, lens capsule, vitreous, or coagulated blood. Late in the postoperative period, progressive growth of the fibroblasts might lead to membrane proliferation over the internal ostium.

TEST INTERPRETATION

The clinical examination included characterization of bleb appearance and assessment of the anterior chamber depth. Bleb appearance is the single most important postoperative feature. The failing bleb is typically low to flat and heavily vascularized. Gonioscopic examination is an integral part of assessing the patency of the internal ostium. It allows direct visualization of the internal outflow pathway. A goniolens with a diameter smaller than the cornea (eg, Zeiss gonioprism) should be used to avoid accidental conjunctival or bleb injury.

DIAGNOSIS

Late filtration failure.

MEDICAL MANAGEMENT

- When faced with high pressure and deep anterior chamber, the possibility of internal obstruction of the fistula should be evaluated by gonioscopy.
- If the internal ostium is free from obstruction, gentle digital pressure to the globe or to the edge of the scleral flap might be sufficient to relieve the blockage.
- If the internal ostium is obstructed, argon laser retraction of pigmented tissue, or Nd:YAG photodisruption of nonpigmented membranes might be sufficient to relieve the obstruction.
- If the internal obstruction is believed to be due to fibrin blockage of the filtration site, tissue plasminogen activator (TPA) might be injected into the anterior chamber to speed lysis.
- If the internal obstruction cannot be eliminated, it might be necessary to resume antiglaucoma medication.

SURGICAL MANAGEMENT

Reoperation might be necessary if the medical management measures fail.

REHABILITATION AND FOLLOW-UP

Once the IOP is controlled, patients are to be followed closely for any signs of recurrent failure. Antiglaucoma medication might be necessary to maintain low IOP, unless definitive surgical intervention was successful.

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Case 29

FLAT ANTERIOR CHAMBER

Martha Motuz Leen, M.D.

HISTORY

A 53-year-old woman with a history of bilateral chronic angle-closure glaucoma presented with a shallow anterior chamber in the right eye 1 day after a mitomycin trabeculectomy.

Examination revealed a visual acuity of 20/400 in the right eye and 20/40 in the left eye. Intraocular pressures (IOPs) were 24 mm Hg in the right eye and 12 mm Hg in the left eye. Slit-lamp examination of the right eye showed a moderately elevated filtration bleb that was negative for Seidel testing. The anterior chamber was shallow with iridocorneal contact extending from the periphery to within 1 mm of the pupillary margin. Central shallowing was also present with a posterior chamber intraocular lens located 0.5 mm posterior to the corneal endothelium. Anterior chamber cells were graded 3+. A surgical iridectomy was confirmed to be patent since ciliary processes were easily visible. Slit-lamp examination of the left eye showed a filtration bleb, deep anterior chamber, patent surgical iridectomy, and pseudophakia.

Fundus examination demonstrated a poor view with an excellent red reflex in the right eye and moderate glaucomatous cupping with an otherwise unremarkable retina in the left eye. B-scan ultrasonography of the right eye revealed a flat retina and absence of choroidal effusions.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Shallowing or *fl*attening of the anterior chamber after filtration surgery is common, especially in the early postoperative setting. It is useful to identify those clinical features that are typical of each of the potential causes of shallowing (Table 29–1). For instance, if the IOP is low, overfiltration or choroidal effusions are suspected. If the IOP is normal or high, pupillary block, choroidal hemorrhage, and aqueous misdirection are considerations. It is also useful to classify whether shallowing of the anterior chamber involves the periphery only or both central and peripheral areas (Figs. 29–1A and B). Using bleb height as a criterion for differentiating diagnoses is not as helpful, since the bleb may be either high or low with each of these entities. In addition to these features, the response to a surgical confirmatory intervention, an iridectomy, can point to the correct diagnosis.

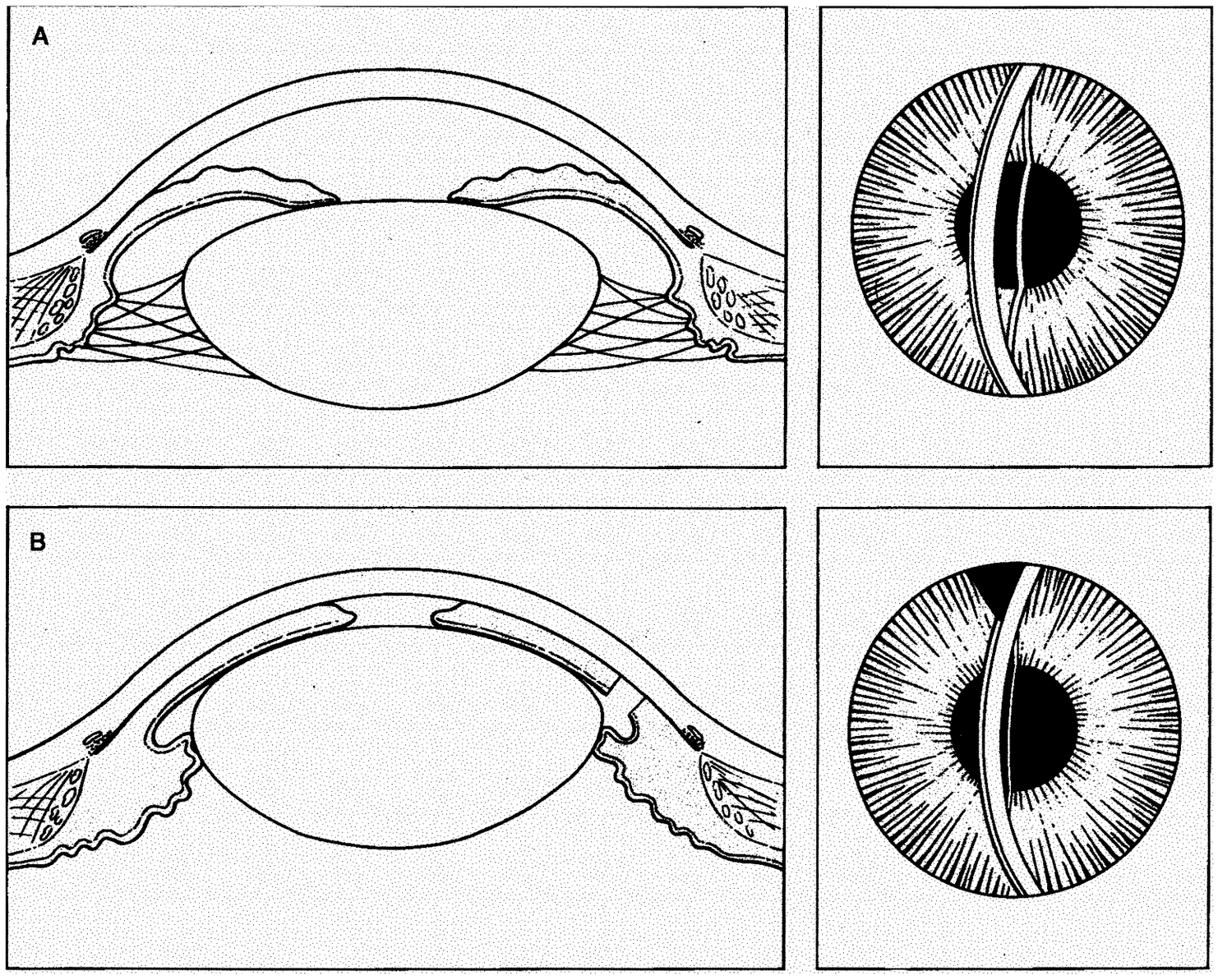
2. Over*fi*ltration is the most common cause of shallow anterior chamber after filtration surgery. In the early postoperative period, overfiltration may occur through a large bleb or loose scleral flap with little resistance to outflow, a conjunctival buttonhole, a conjunctival wound leak, or a cyclodialysis cleft. In the later postoperative period, overfiltration may occur by transudation or leak from a bleb that is avascular and very thin, especially if antimetabolites were used. Chronic overfiltration itself without hypotony is not expected to shallow the anterior chamber as the hydrostatic pressure in the anterior chamber and vitreous cavity equalize. However, when overfiltration is associated with a low IOP, the ciliary body and choroid tend to become diffusely edematous. This results in an anterior rotation of the ciliary body, leading to shallowing of the anterior chamber centrally and peripherally in phakic and pseudophakic eyes. A patent iridectomy is identified. Choroidal effusions are not present on fundus examination, but overfiltration is often a precursor for their development.

3. A choroidal effusion is an accumulation of serous fluid in the suprachoroidal space, most commonly in eyes that are severely

TABLE 29–1 **Causes of Shallow Anterior Chamber**

Diagnosis	Anterior Chamber Shallowing	IOP	Relief with Iridectomy	Common Features
Overfiltration	central and peripheral	low	no	bleb leak often present
Choroidal effusion	central and peripheral	low	no	light-brown choroidals
Pupillary block	peripheral only	normal or high	yes	iris bombé
Choroidal hemorrhage	central and peripheral	normal or high	no	dark-brown choroidals; acute pain
Aqueous misdirection	central and peripheral	normal or high	no	history of chronic angle closure glaucoma

hypotonous in the early postoperative period. Although the suprachoroidal space may be considered one continous area, firm connections of the choroid to the sclera at the vortex veins and optic nerve head lead to a lobulated appearance of choroidal effusions. This results in an anterior rotation of the ciliary body with shallowing of the anterior chamber both centrally and peripherally in phakic and pseudophakic eyes. The presence of this fluid contributes to a vicious cycle of reduced aqueous production and possibly enhanced



FIGURES 29–1 Differentiation of (A) peripheral shallowing from (B) peripheral with central shallowing. In (A), the anterior chamber is more shallow peripherally than centrally due to iris bombé, as seen with pupillary block. In (B), the anterior chamber is more uniformly shallow despite a patent iridectomy due to anterior rotation of the ciliary body, as seen with overfiltration, choroidal effusion, choroidal hemorrhage, and aqueous misdirection. (Reprinted with permission from Skuta GL. The angle closure glaucomas. In: Kaufman PL, Mittag TW, assoc eds. Glaucoma. Vol. 7. In: Podos SM, Yanoff M, eds. *Textbook of Ophthalmology*. Philadelphia, PA: Mosby-Year Book; 1994:8,23.)

uveoscleral outflow, in turn aggravating hypotony and the tendency for more choroidal effusion. Overfiltration is often identified as the initial cause of hypotony. A patent iridectomy is present. Smooth light-brown or tan choroidal elevations are seen on funduscopy. In some cases, choroidal effusions are very low and can't easily be discerned without ultrasonography. In severe cases, surgical drainage of straw-colored suprachoroidal fluid reverses the cycle.

4. Pupillary block occurs when there is apposition of the iris to the lens in phakic or pseudophakic eyes, or to the anterior vitreous face in aphakic eyes. The aqueous is unable to flow anteriorly and accumulates just beneath the iris causing a convex bowing of the iris (iris bombé). Peripheral anterior chamber shallowing results in appositional closure of the angle. It is important to recognize that the central chamber tends not to be as shallow. The IOP may be normal initially and then progressively elevated. A patent iridectomy is not present. Although creation of an iridectomy is a routine part of most glaucoma filtration surgery, a complete opening may not always be present, with underlying iris pigment epithelium still intact or iris incarceration into the sclerotomy. The iridectomy may also become obstructed with ciliary processes, blood, or vitreous, or become bound down by synechiae in an inflamed eye. If the surgical wound was dissected too posteriorly, ciliary body tissue rather than iris may have been excised. The anterior chamber will readily deepen after an iridotomy is created. If there is any doubt about its patency, another iris opening should be created.

5. A choroidal hemorrhage is an accumulation of blood that occurs in the suprachoroidal space in either the early or the late postoperative period, usually acutely and in association with severe pain. The ciliary body rotates anteriorly, shallowing the anterior chamber peripherally and centrally in phakic and pseudophakic eyes. Since the choroidal circulation is not subject to autoregulation, hypertensive patients with fragile vessels may be unable to accommodate the increased choroidal blood flow when the IOP is lowered, increasing the risk of choroidal hemorrhage. Aphakic eyes may also be at higher risk. Unlike choroidal effusions, the IOP tends to be normal or high. A patent iridectomy is present. Smooth dark-brown or red choroidal elevations are seen on funduscopy, sometimes requiring ultrasonography for confirmation when small in size. In severe cases, surgical drainage of red or dark-brown suprachoroidal fluid is required.

6. Aqueous misdirection occurs when aqueous is unable to flow anteriorly past a relative block at the junction of the ciliary processes, lens equator (when present), and anterior vitreous face. Subsequently, aqueous is diverted posteriorly within or adjacent to the vitreous body (Fig. 29–2). As the aqueous accumulates the vitreous is displaced forward, causing anterior ciliary body rotation and

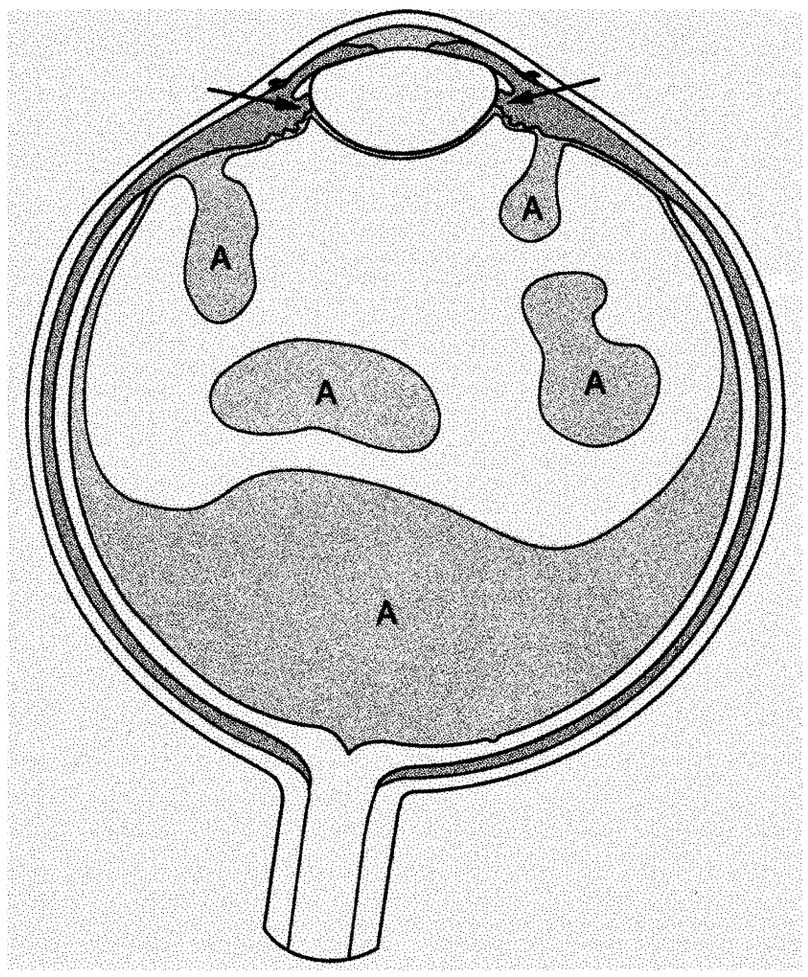


FIGURE 29–2 Aqueous misdirection in a phakic eye. Apposition of anteriorly rotated ciliary processes, lens, and anterior hyaloid (arrows) predisposes to posterior misdirection of aqueous (A) into the vitreous cavity. The lens and iris become progressively displaced anteriorly, closing the angle, and increasing the IOP. (Reprinted with permission from Skuta GL. The angle closure glaucomas. In: Kaufman PL, Mittag TW, assoc eds. Glaucoma. Vol. 7. In: Podos SM, Yanoff M, eds. *Textbook of Ophthalmology,* Philadelphia, PA: Mosby-Year Book; 1994:8,21.)

shallowing of the anterior chamber peripherally and centrally. This can lead to a vicious cycle as the aqueous volume continues to increase in the space behind the vitreous, the permeability of the compressed vitreous body decreases further, and the apposition of the anterior hyaloid face with the ciliary processes and lens equator worsens. The IOP may be normal initially and become progressively elevated as the cycle continues. The presence of a patent iridectomy must be confirmed, and choroidal elevations are generally not present. Aqueous misdirection can occur in the early postoperative period or later when cycloplegics are discontinued. It most commonly occurs after surgery on phakic eyes with chronic angle-closure glaucoma. Terms that have been used synonymously with aqueous misdirection include ciliary block and malignant glaucoma.

A wide spectrum of presentations is possible with each of these diagnoses, and more than one can occasionally occur as a sequence of events. For example, an eye with chronic angle-closure glaucoma may have developed a wound leak resulting in hypotony with initial choroidal edema, then progressing to a small anterior choroidal effusion. As the ciliary body rotates forward and the anterior chamber shallows, greater apposition occurs between the anterior hyaloid, ciliary processes, and lens equator. This leads to misdirection of aqueous posteriorly with progressive shallowing of the anterior chamber and elevation of the IOP. Therefore, presence of a choroidal effusion does not entirely eliminate the possibility of aqueous misdirection. In this example, drainage of the choroidal effusion alone might result in reversal of aqueous misdirection.

TEST INTERPRETATION

Slit-lamp examination of anterior chamber depth may reveal shallowing in the periphery only with an iris bombé configuration, features that would be suggestive of a pupillary block mechanism. If the anterior chamber is shallow both centrally and peripherally, choroidal thickening, choroidal effusion, choroidal hemorrhage, or aqueous misdirection would be more likely.

The bleb is inspected and checked for pinpoint leaks and for slow transudation, especially if the tissue is very thin. A Seidel test can be performed to identify an area of leakage or transudation by painting a bleb or incision site with a fluorescein strip and viewing the area with a cobalt blue light. Although a pinpoint leak can usually be seen immediately, delineation of an area of bleb transudation may require several seconds of observation. If present, overfiltration with choroidal thickening, or choroidal effusion, is suspected.

Determination should be made if an iridectomy exists and is patent. Even with a previously patent iridectomy, it may become blocked with iris, vitreous, blood or become bound down to the underlying lens. If a patent iridectomy is confirmed, pupillary block can be ruled out, but not the other entities. If ciliary processes are seen through a patent iridectomy and appear to be anteriorly rotated, or in apposition against the vitreous, aqueous misdirection is suspected. If there is any question of the patency of the iridectomy, it should be opened or a new iridotomy created with laser. If shallowing readily reverses as a result, a diagnosis of pupillary block is made.

If the iridectomy is patent, the pupil should be dilated. When choroidals are larger, they are easily identified on fundus examination, appearing smooth and dome-shaped and varying from one to four in number. The convex choroidals may occasionally be extensive enough that they meet in the mid vitreous, often referred to as "kissing" choroidals. Choroidal effusions tend to have a tan or light-brown appearance, whereas choroidal hemorrhages tend to have a dark-brown or red appearance. If choroidals are not seen, careful evaluation of the vitreous may suggest optically empty pockets indicative of fluid accumulation typical of aqueous misdirection.

A small pupil may prohibit adequate visualization of the posterior pole. In such cases, conventional B-scan ultrasonography is useful to identify choroidal elevation or choroidal thickening. Utrasound can also help differentiate between a choroidal effusion that is echolucent, or choroidal hemorrhage that is echogenic.

Ultrasound can be used to inspect the vitreous for pockets of fluid that may be seen with aqueous misdirection. Sometimes, a choroidal that is very anterior can be too subtle to identify despite funduscopy with a large pupil or conventional B-scan ultrasonography. In this instance, high-frequency ultrasound biomicroscopy can prove useful to better visualize the anterior choroidal, as well as to identify the ciliary block that is characteristic of aqueous misdirection.

DIAGNOSIS

In the case study described, a patent peripheral iridectomy is present with central as well as peripheral shallowing and there is no iris bombé. These features exclude pupillary block as a mechanism. There is no bleb leak or wound leak and the eye is not hypotonous, making overfiltration less likely. Funduscopy and ultrasound demonstrate no choroidals, excluding choroidal effusion or choroidal hemorrhage. The ciliary processes are noted to be easily visible through the iridectomy. The diagnosis is aqueous misdirection in the right eye. A risk factor that is consistent with this entity is the history of chronic angle-closure glaucoma.

MEDICAL MANAGEMENT

The first line of therapy for aqueous misdirection is medical management. A cycloplegic-mydriatic combination of atropine 1% and phenylephrine 2.5% is instilled 4 times a day to maximally rotate the ciliary body and lens posteriorly, attempting to break the ciliary block. A topical aqueous suppressant as well as an oral carbonic anhydrase inhibitor are used to reduce aqueous production and slow down fluid collection in the vitreous body. An oral or intravenous osmotic agent is useful to actually reduce the volume of aqueous in the vitreous cavity in an effort to break the cycle of fluid accumulation. Miotics are to be avoided since instillation results in an anterior rotation of the ciliary body, exacerbating the ciliary block. Prompt recognition and treatment of aqueous misdirection can abort the process earlier in its course.

SURGICAL MANAGEMENT

If the aqueous misdirection is not corrected medically and the condition continues to worsen, then vitreous disruption by laser treatment or surgery may be attempted. Neodymium: YAG laser disruption of anterior hyaloid face and posterior capsule through the pupil, when accessible in pseudophakic and aphakic eyes, or through an iridectomy, can be performed to allow trapped pockets of fluid to move anteriorly with more ease. Argon laser shrinkage of the ciliary processes through a peripheral iridectomy can also be attempted to break the appostion between the ciliary processes and lens or vitreous.

If there is lenticular–cornea contact and the IOP is not yet elevated, intracameral viscoelastic injection may have a therapeutic effect by deepening the anterior chamber, rotating the ciliary body posteriorly, and temporarily reversing the vicious cycle of misdirected aqueous. Even a small amount of viscoelastic injection can rapidly raise the IOP and should therefore be performed with careful monitoring.

If laser modalities are ineffective, then a core pars plana vitrectomy with reformation of the anterior chamber is recommended. Surgical disruption of the vitreous helps to reestablish anterior flow of trapped aqueous as well as to prevent the recurrence of the cycle by eliminating the potential for intact vitreous gel to act as a diaphragm across the globe. In pseudophakic and aphakic eyes, the vitrectomy is extended anteriorly to remove anterior hyaloid, lens zonules, or capsule in the vicinity of the iridectomy. In phakic eyes, anterior removal is more challenging since the integrity of the lens must be maintained. For this reason, recurrence of aqueous misdirection after vitrectomy in phakic eyes may be more common due to less complete removal of anterior hyaloid. It is useful to place a sclerotomy within reach of the iridectomy to facilitate removal of the vitreous in its vicinity.

REHABILITATION AND FOLLOW-UP

Cycloplegia, such as with atropine 1% daily, may need to be maintained indefinitely. In

cases where the aqueous misdirection is broken pharmacologically or with laser treatment, recurrence can occur when cycloplegia is discontinued, even months later. Instillation of miotics can trigger a recurrence by rotating the ciliary body and lens anteriorly, starting the cycle of misdirection. If a vitrectomy was required for reversal of aqueous misdirection, cycloplegia can often be stopped, though caution should be exercised in phakic eyes, which may be at higher risk of recurrence. In the fellow eye, prophylactic laser iridotomy, avoidance of miotics, and anticipation of possible aqueous misdirection with any future surgery are recommended protective measures.

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Case 30

PERSISTENT CHOROIDAL DETACHMENT

Donald L. Budenz, M.D.

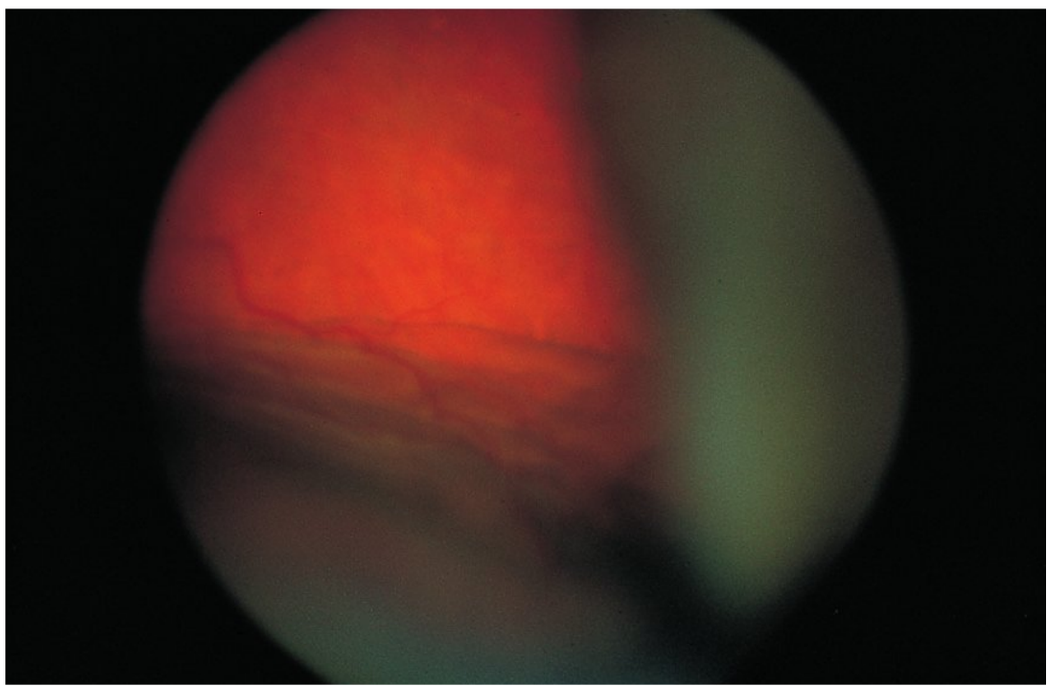
HISTORY

An 80-year-old woman with a 20-year history of glaucoma presented for consultation 8 months following combined cataract extraction, intraocular lens implant, and trabeculectomy with mitomycin-C in the right eye. She complained of a "shadow" since her surgery, which was blocking her temporal vision. This was so debilitating that she almost ran over a small boy with her car.

The visual acuity was 20/30 in the affected eye and the intraocular pressure (IOP) was 7 mm Hg. A large, ischemic filtering bleb was present with a negative Seidel test. The cornea was clear, the anterior chamber deep and quiet, and the cup-to-disc ratio was 0.8. The peripheral fundus was not visible due to a small and fibrotic pupil. A B-scan ultrasound was performed, which showed 360-degree ciliochoroidal detachments with serous fluid inside the detachments. There was a large nasal choroidal detachment that measured 8 mm (Fig. 30–1). There was no retinal detachment overlying the choroidal detachment.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Most patients with persistent choroidal effusions are asymptomatic. They present with a low or low-normal IOP as the only presenting sign. Vision may be reduced if the pressure is very low, causing corneal, retinal, or choroidal folds. Also, if the effusions are large, they may block the visual axis, causing profound visual loss.
2. The differential diagnosis of low IOP after filtering surgery includes overfiltration, filtering bleb leak, retinal detachment, cyclodialysis cleft, iridocyclitis, and choroidal effusion. Overfiltration is a diagnosis of exclusion and typically presents with a large and/or ischemic filtering bleb, which has no leak by Seidel testing. The posterior pole may have choroidal effusions, which are due to the low pressure from overfiltration. Late bleb leaks may also cause low IOP and choroidal detachments and are diagnosed by demonstrating a positive Seidel test. Occasionally, a provocative Seidel test, using gentle pressure on the globe, may reveal an occult leak. Serous retinal detachments are a rare postoperative complication of filtering surgery but should always be excluded as a possible cause of hypotony in any patient. Retinal detachment may be diagnosed on fundus examination and/or ultrasound (Fig. 30–2). A cyclodialysis cleft may result from surgical trauma and this should be ruled out on gonioscopy. This may be occult and difficult to diagnose without the aid of high resolution ultrasound (ultrasound biomicroscopy). Iridocyclitis may cause hypotony and typically presents in uveitics or following tapering of topical steroid medications.
3. Suprachoroidal hemorrhage (Fig. 30–3) may cause choroidal detachment, but the IOP is generally high and the patient usually has considerable pain associated with this.
4. Choroidal effusions have a bullous appearance, similar to retinal detachment and choroidal hemorrhage. Unlike those conditions, the bullous detachments of serous choroidal effusions have the normal orange



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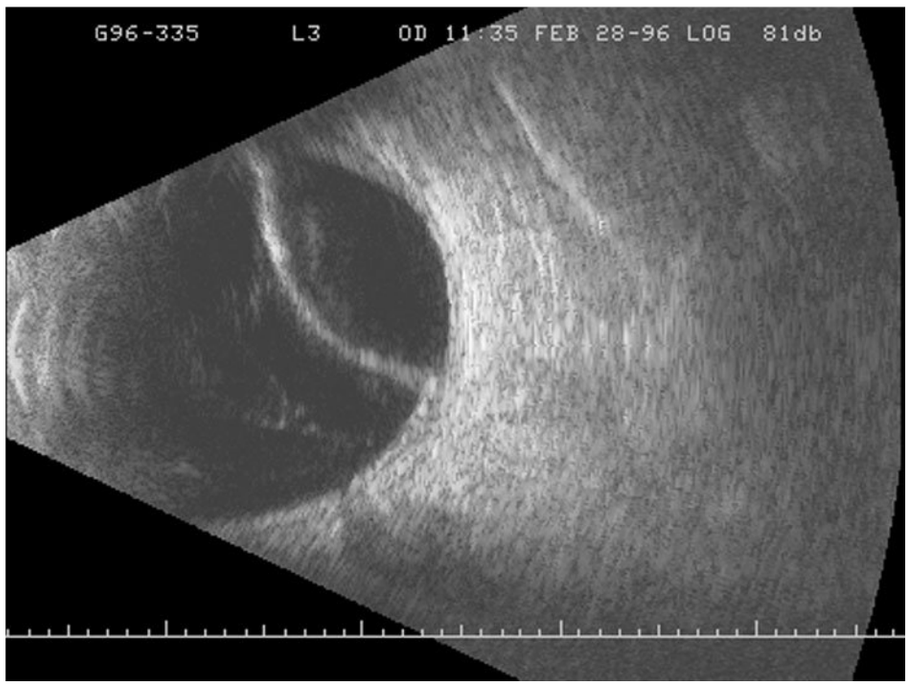

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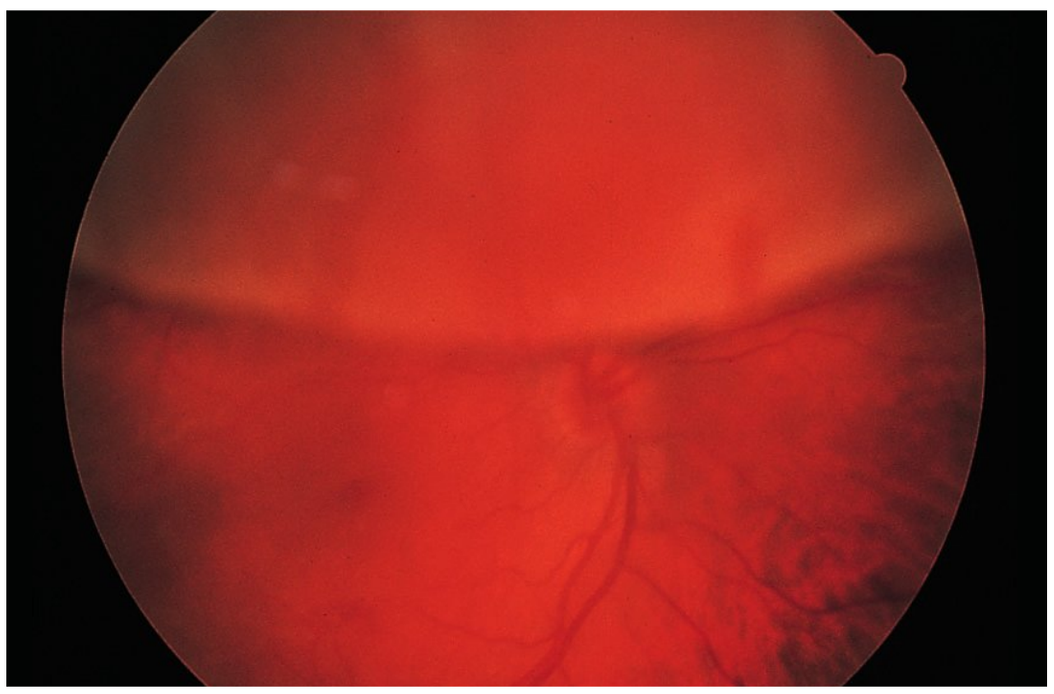
FIGURE 30–1 Serous choroidal effusions. (A) The typical appearance of serous choroidal effusion. Smooth, orange, bullous detachments are seen. (B) The typical B-scan echographic appearance of serous choroidal detachments. The wall is generally thicker and smoother than that seen in a retinal detachment. The inside of the detachment is echographically clear due to the serous nature of the interior, unlike hemorrhagic choroidal detachment. (Figure 30–1A courtesy of Albert M. Maguire, M.D., Philadelphia, PA. Figure 30–1B courtesy of Sarah Keene, Philadelphia, PA.)

fundus appearance, rather than being translucent (retinal detachment) or dark red/brown (suprachoroidal hemorrhage). Both serous and hemorrhagic choroidal detachments typically have four bullous lobes, one in each quadrant. This is because the choroid is firmly attached to the exit site of the four vortex veins, as well as being attached to the optic nerve posteriorly and scleral spur anteriorly. Transillumination with a muscle light may help distinguish serous from hemorrhagic choroidal detachments; hemorrhagic detachments will block the transillumination better than serous detachments. When in doubt, standard B-scan echography is the definitive way to differentiate these three entities (see Test Interpretation below).



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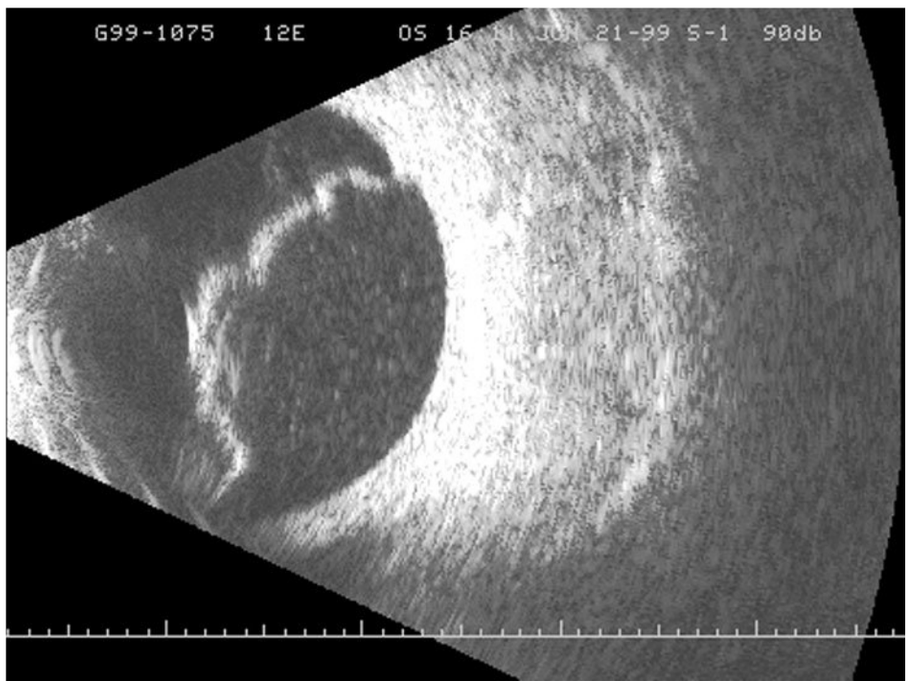

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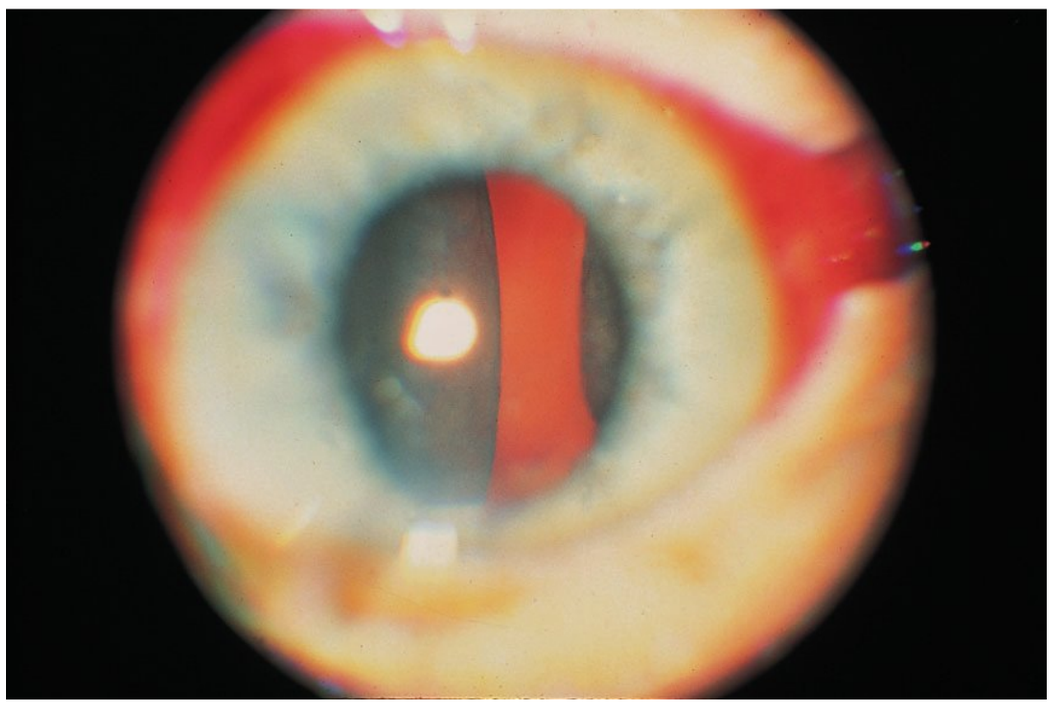
FIGURE 30–2 Retinal detachment. (A) The clinical appearance of a retinal detachment. The surface is bullous but more translucent and lacks the typical orange color of the retinal pigment epithelium usually seen in a choroidal effusion. (B) B-scan ultrasound of a retinal detachment. The wall is generally thinner and the surface is less regular than that seen in choroidal detachment. (Figure 30–2A courtesy of Albert M. Maguire, M.D., Philadelphia, PA. Figure 30–2B courtesy of Randall Hughes, Miami, FL.)



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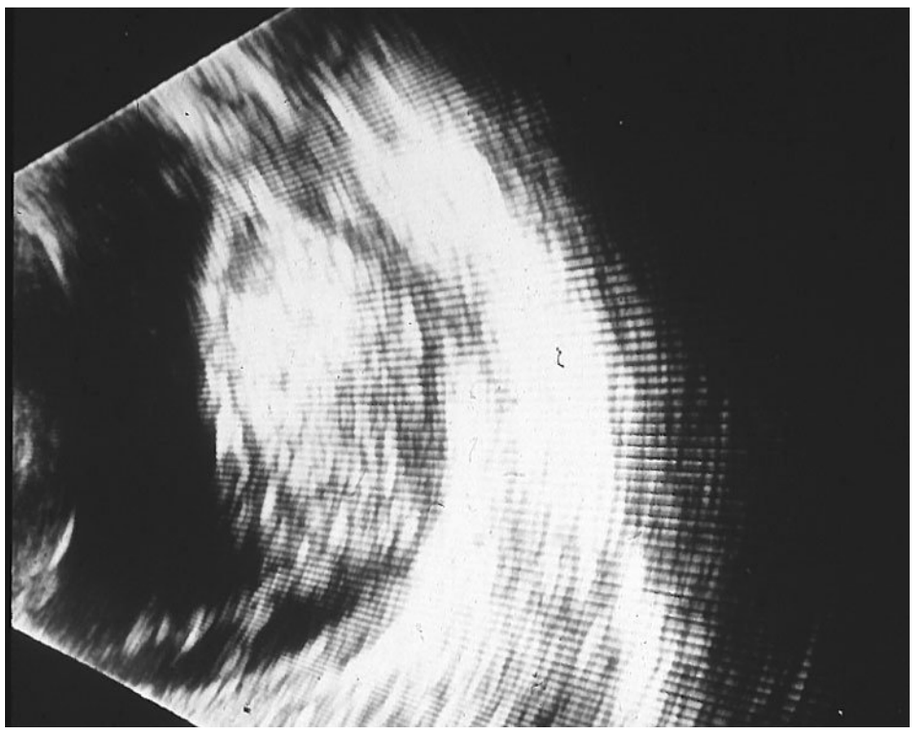

B

FIGURE 30–3 Hemorrhagic choroidal detachment. (A) Photograph of a hemorrhagic choroidal detachment. The color, ranging from dark-red to brown, is diagnostic of this entity. (B) The B-scan ultrasound shows the echographically dense cavity of suprachoroidal blood, easily distinguished from a serous detachment of the retina or choroid. (Figure 30–3A courtesy of Albert M. Maguire, M.D., Philadelphia, PA. Figure 30–3B courtesy of Sarah Keene, Philadelphia, PA.)

5. Annular ciliochoroidal detachment is an underdiagnosed condition in which the anterior-most choroid becomes separated from the sclera. The fundus typically appears normal and diagnosis is made by ultrasound biomicroscopy or conventional resolution ultrasound performed through a water bath. These patients may have a closed anterior chamber angle on gonioscopy due to forward rotation of the ciliary body. In this circumstance, the IOP may be normal or elevated.

6. Choroidal effusions are common after glaucoma filtration surgery due to surgically induced hypotony. Low IOP results in the leakage of protein-rich serum from the choroidal vasculature into the suprachoroidal space. The ciliary body often becomes detached and intraocular inflammation may result. These factors may decrease aqueous production, contributing to hypotony. Alternatively, choroidal effusion may promote increased uveoscleral aqueous outflow, contributing to hypotony. The condition can be viewed as a pathologic cycle, whereby profound hypotony leads to ciliochoroidal effusion, which in turn causes hypotony.

TEST INTERPRETATION

In serous choroidal effusion, B-scan ultrasound reveals an echographically clear space between the detached choroid and the sclera, distinguishing this from choroidal hemorrhage. Additionally, the choroid is thicker than the retina, which helps distinguish choroidal effusion from retinal detachment. The clinical and echographic appearance of choroidal effusion, retinal detachment, and choroidal hemorrhage are shown in Figures 30–1, 30–2, and 30–3.

DIAGNOSIS

Right eye: Persistent serous choroidal detachment.

MEDICAL MANAGEMENT

Observation usually results in complete resolution of ciliochoroidal effusions without sequelae. Elevation of IOP may hasten the spontaneous drainage of the serous fluid by driving proteins out through the sclera. The water component of the fluid may drain via the sclera as well, or perhaps gets reabsorbed into the choroidal capillary system. Discontinuation of systemic carbonic

anhydrase inhibitors and topical aqueous suppressants in the affected eye may aid in this resolution. Discontinuation of topical beta-blocker in the contralateral eye is also recommended, since this may contribute to reduced aqueous production in the affected eye.

The benefit of topical steroid and cycloplegic therapy has not been well established but there is little to argue against trying this treatment. We do not use systemic steroids, as advocated by some, because their effectiveness has not been established and the potential risk of systemic side-effects outweighs the potential benefit. Oral carbonic anhydrase inhibitors have been used with varied success. We believe these drugs more likely potentiate the problem, although dramatic resolution of choroidal effusions has been reported following initiation of oral acetazolomide.

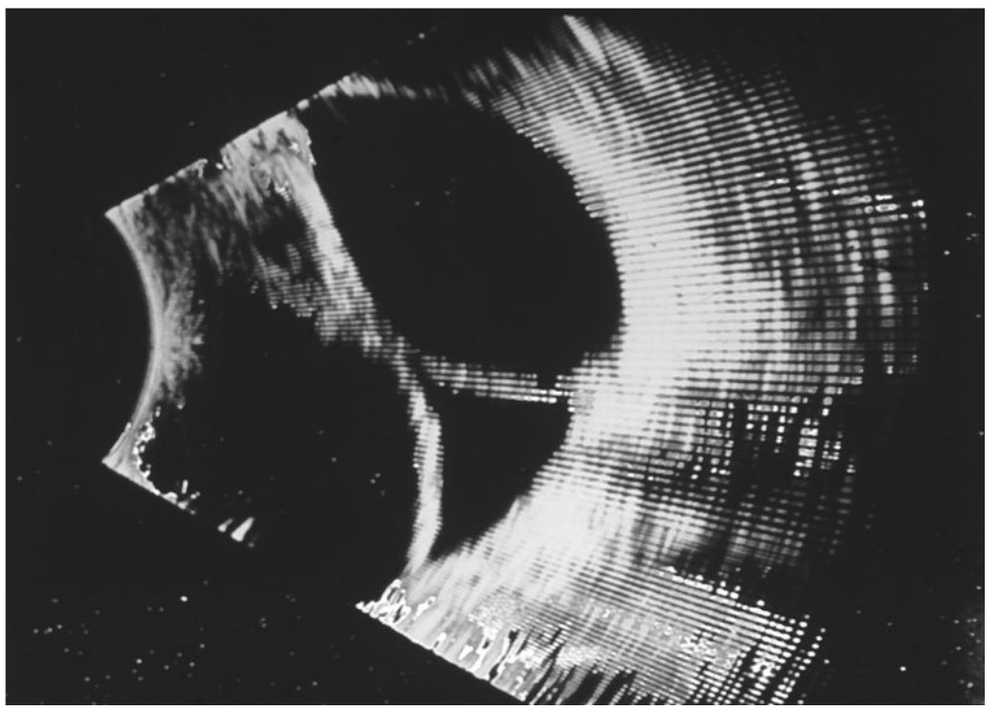

FIGURE 30–4 Kissing choroidal detachments. In severe cases, the serous detachments of the choroid may be so elevated that the contralateral retinal surfaces become apposed centrally. These have been termed "kissing" choroidals. While visually debilitating, kissing choroidal detachments have the same excellent prognosis as nonkissing detachments. The B-scan echographic appearance is shown in this figure.

SURGICAL MANAGEMENT

The indications for drainage of serous choroidal effusions include lenticulocorneal touch, nonresolving effusions blocking the visual axis, hypotony causing corneal or retinal folds, failing filtering bleb due to poor aqueous production, overlying serous retinal detachment, or serous choroidal detachment accompanying a bleb leak. The presence of "kissing" choroidal detachments (Fig. 30–4) is not necessarily an indication for immediate intervention as there seem to be no particular sequelae that accompany apposition of the retinal surfaces. However, insofar as these are accompanied by profound visual loss due to blocking of the visual axis, we prefer to drain them if they do not resolve in short order. The anxiety related to the visual loss associated with choroidal detachments that block the visual axis is substantial and drainage of choroidal effusions is a simple and effective procedure with very few potential complications.

The technique for drainage of choroidal effusions is illustrated in Figure 30–5. A paracentesis is made through the temporal peripheral cornea and the anterior chamber is reformed with balanced salt solution (BSS) or a viscoelastic if it is shallow. An anterior chamber maintainer, which is attached to a BSS infusion line, is inserted. This obviates the need to constantly reform the anterior chamber as the choroidal space is drained. A radial conjunctival incision is made in the inferotemporal or inferonasal quadrant, extending 3 to 4 mm posterior to the corneoscleral limbus. Inferior locations are chosen to permit

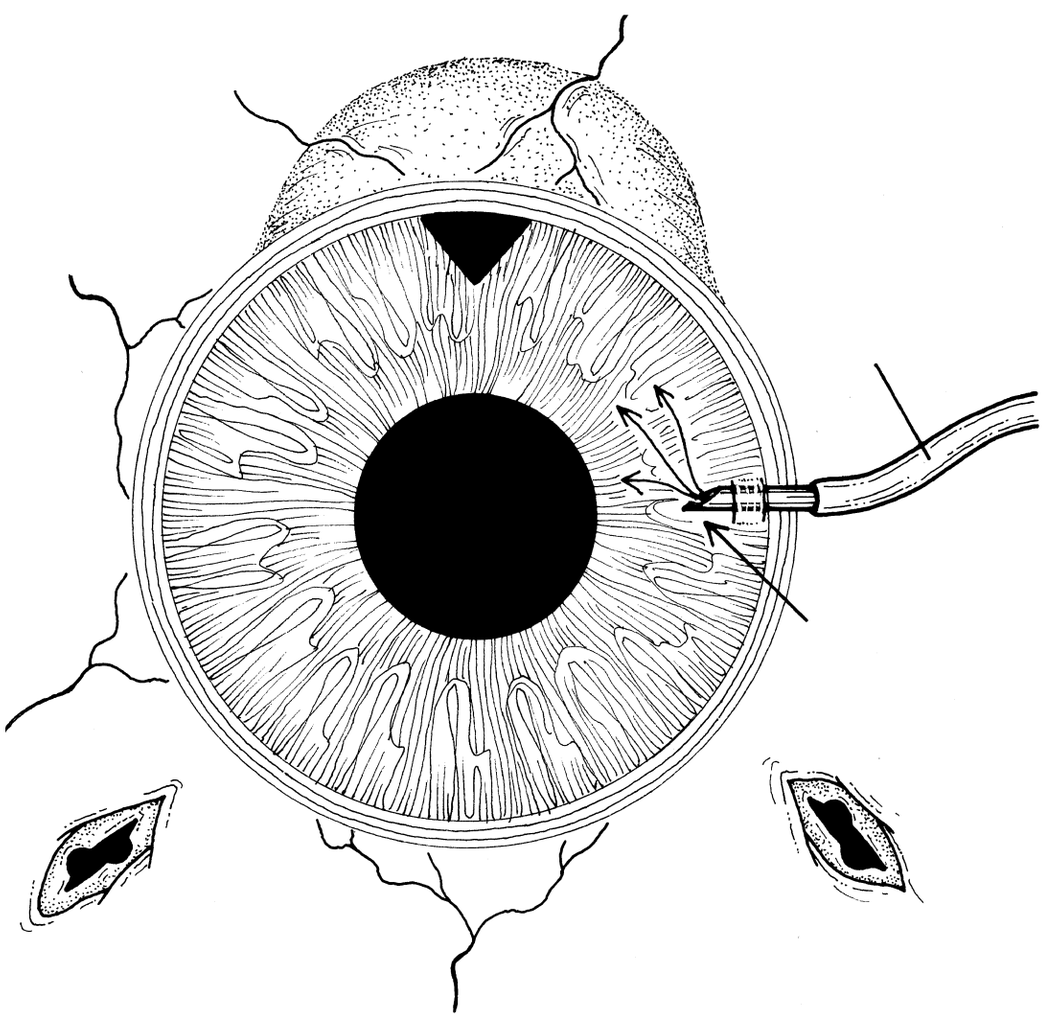

FIGURE 30–5 Drainage of choroidal effusions. See text for description of technique.

continued drainage of fluid from superior choroidal detachments via gravity postoperatively. A 2- to 3-mm radial sclerostomy is then fashioned using a supersharp blade until the suprachoroidal space is entered. The location of this incision need only be just posterior to the limbus since the choroid is detached up to the scleral spur. While making the sclerostomy incision, it is helpful for the surgeon and assistant to retract each side of the incision as the cut-down is made to aid in visualization. The critical point comes when the incision reaches the level of the suprachoroidal space and straw-colored serous fluid gushes out. The incision is opened to an adequate length to allow a sclerostomy punch to fit into it on either side. A single punch is then performed on each side of the incision to allow continued drainage of the choroidal fluid postoperatively. Also, leaving the sclera open may prevent reformation of choroidal effusions if the postoperative IOP remains low, since the pressure in the suprachroidal space will be equivalent to atmospheric pressure. The conjunctival incision is then closed with an absorbable suture and the same procedure performed in the contralateral inferior quadrant. The anterior maintainer is removed and a suture is oftentimes needed to close the paracentesis track. If a filtering bleb leak or cyclodialysis is present, these may be addressed at this time. Subconjunctival injections of antibiotics and steroids are employed.

REHABILITATION AND FOLLOW-UP

The patient is examined 1 day postoperatively and placed on a brief course of a topical steroid, antibiotic, and cycloplegic agent (if phakic). Persistent effusion and/or drainage may be noted, but complete resolution of the serous effusion is usually prompt. Visual recovery is generally dramatic if the choroidal effusion involved the visual axis.

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Section IV

RETINA

31. Nonproliferative Diabetic Retinopathy
32. Diabetic Macular Edema
33. Proliferative Diabetic Retinopathy
34. Retinal Arterial Occlusion
35. Central Retinal Vein Occlusion
36. Branch Retinal Vein Occlusion
37. Atrophic Age-Related Macular Degeneration
38. Exudative Age-Related Macular Degeneration
39. Myopic Degeneration
40. Idiopathic Central Serous Chorioretinopathy
41. Epiretinal Membrane
42. Macular Hole
43. Vitreous Hemorrhage
44. Retinitis Pigmentosa

Case 31

NONPROLIFERATIVE DIABETIC RETINOPATHY

William E. Smiddy, M.D.

HISTORY

This 53-year-old man with a 10-year history of adult-onset diabetes mellitus presented with a 2-month history of blurred vision OU. Medical history is positive for hypertension, peripheral neuropathy, and a history of hepatitis C. Best corrected visual acuity was 20/20 OU. Slit-lamp examination was unremarkable. The intraocular pressure was 11 mm Hg in the right eye and 12 mm Hg in the left eye. Funduscopic examination on the right showed a normal disc, no macular edema, macular lipid, or neovascularization. Intraretinal hemorrhages in two quadrants and a mild degree in the other two quadrants were present in both eyes. There was a cotton-wool spot superior to the right macula (Fig. 31–1). Fluorescein angiography demonstrated microaneurysms with mild perifoveal capillary dropout, but no neovascularization (Fig. 31–2).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Diabetics have a 78% prevalence of diabetic retinopathy after a 10-year duration of systemic disease. The 14-year follow-up study of the Wisconsin Eye Survey of Diabetic Retinopathy (WESDR) demonstrated a 96% incidence of developing new retinopathy, an 86% progression rate, and 26% incidence of diabetic macular edema.
2. It is common that diabetic patients present with blurred vision that they attribute to refractive problems rather than complications from diabetic retinopathy. This may delay the correct diagnosis and treatment.
3. Microaneurysms and intraretinal hemorrhages may be clinical findings in other retinal vascular conditions such as branch retinal vein occlusion, radiation retinopathy, perifoveal retinal telangiectasis, and Eales' disease. Usually the medical history yields evidence of the diabetic condition, but screening for diabetes should be performed in patients with the ophthalmoscopic features of diabetic retinopathy. The more generalized distribution in diabetes usually distinguishes nonproliferative diabetic retinopathy (NPDR) from cases of branch retinal vein occlusion, which have a segmental distribution.

TEST INTERPRETATION

The most important aspect of evaluating diabetic retinopathy is the clinical examination. The most important examination tool is magnified observation of the macula and posterior pole—accomplished most effectively with a fundus contact lens.

Fundus photography may increase the sensitivity of assessing NPDR severity and differentiate it from early proliferative diabetic retinopathy. Formal grading of the level of retinopathy was determined from photographs in the Early Treatment Diabetic Retinopathy Study (ETDRS). While detailed grading may not be clinically necessary, photographic slides may guide follow-up schedules or treatment. Fluorescein angiography may define surprisingly large areas of ischemia which, when perifoveal, may explain decreased vision. Eyes with large areas of nonperfusion may augur a poorer prognosis. Early neovascular complexes are easily recognized by fluorescein leakage.

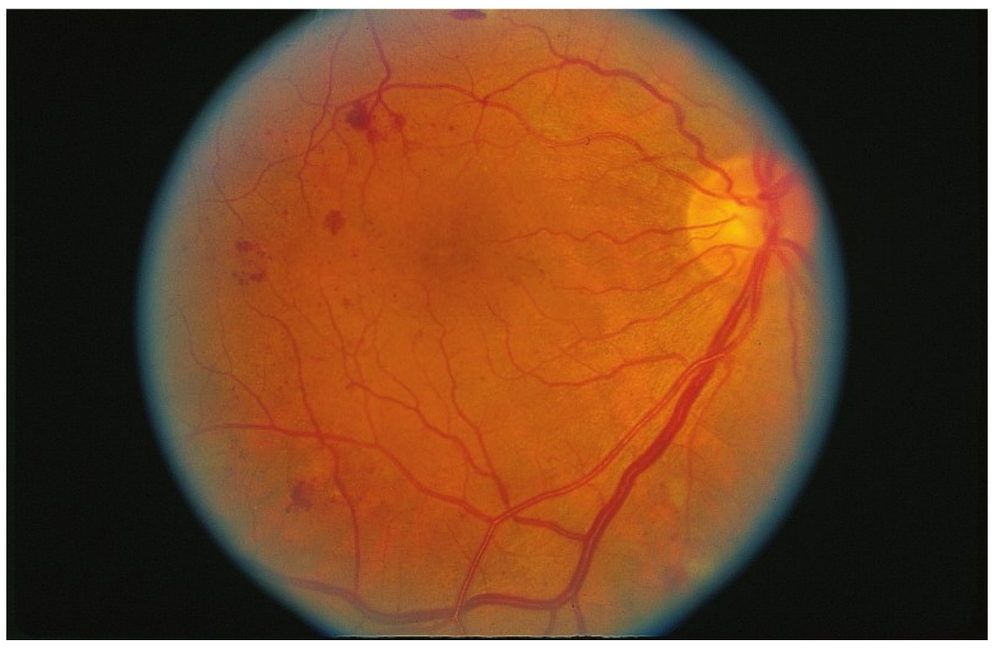

FIGURE 31–1 Shows normal funduscopic appearance of the right eye with a normal disc. There is no macular edema or macular lipid. Temporal through the macula can be seen a moderate number of intraretinal hemorrhages with microaneurysms.

Electrophysiologic studies are not part of a standard evaluation, but have been shown to demonstrate early and characteristic changes with increased degrees of ischemia.

DIAGNOSIS

Moderately severe NPDR, OU.

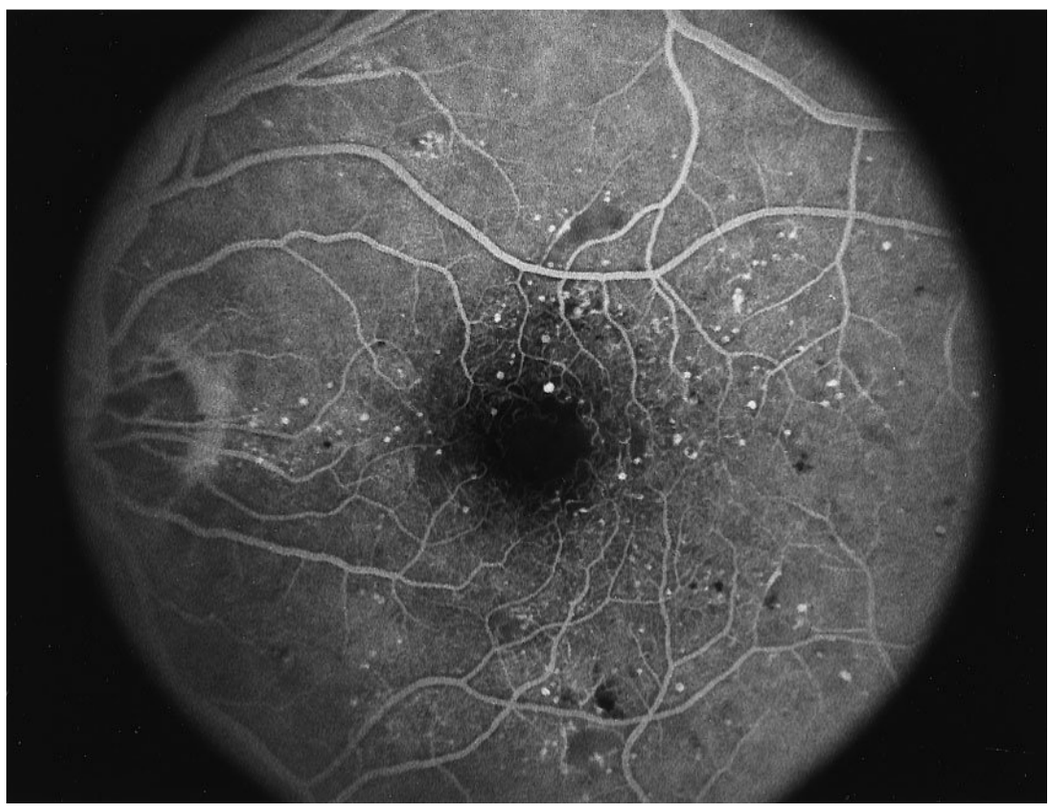

FIGURE 31–2 Angiographic appearance of the left eye showing somewhat more microaneurysms than were apparent from clinical examination. Notice the foveal vascular zone with a somewhat irregular distribution. Notice small areas of capillary nonperfusion one disc diameter inferior and superior to the foveal vascular zone and also temporal to the macula.

MEDICAL MANAGEMENT

Numerous studies including the Diabetes Complications Control Trial, the United Kingdom Prospective Diabetes Study, the ETDRS, and the WESDR have identified baseline clinical characteristics associated with a more rapid or higher rate of progression of retinopathy. These consistently include severity of baseline retinopathy, duration of disease, and degree of glycemic control. Many studies have shown that accompanying systemic features such as hypertension and hypercholesterolemia may also increase the risk of progression. Perhaps more importantly, many of these studies have also shown that control of blood glucose and hypertension may lower these risks. Thus, the importance of seeking and reinforcing optimal control of medical conditions should be emphasized to the patient.

The ETDRS has demonstrated efficacy in instituting laser treatment even before proliferative diabetic retinopathy develops. Type II diabetics show a larger treatment benefit compared to Type I patients. The threshold for considering scatter laser treatment is the presence of severe NPDR. This patient's right eye approaches that threshold. The "4-2-1" rule has been developed to assist the clinician in making this determination by simplifying the definition of severe NPDR into a clinically useful algorithm. The definition of severe NPDR includes four quadrants of microaneurysms and intraretinal hemorrhages equal to or greater than standard photograph 2A (Fig. 31–3), two quadrants of venous beading equal to or exceeding the degree present in standard photograph 6A (Fig. 31–4), and one quadrant of intraretinal microvascular abnormalities (IRMAs) equal to or exceeding the degree present in standard photograph 8A (Fig. 31–5). When two or three of these features are present, "very severe NPDR" is defined, which carries a 50% risk of developing high-risk characteristics (severe proliferative diabetic retinopathy and its incumbent risk of visual loss) within 1 year. This risk is diminished by approximately 50% with laser treatment.

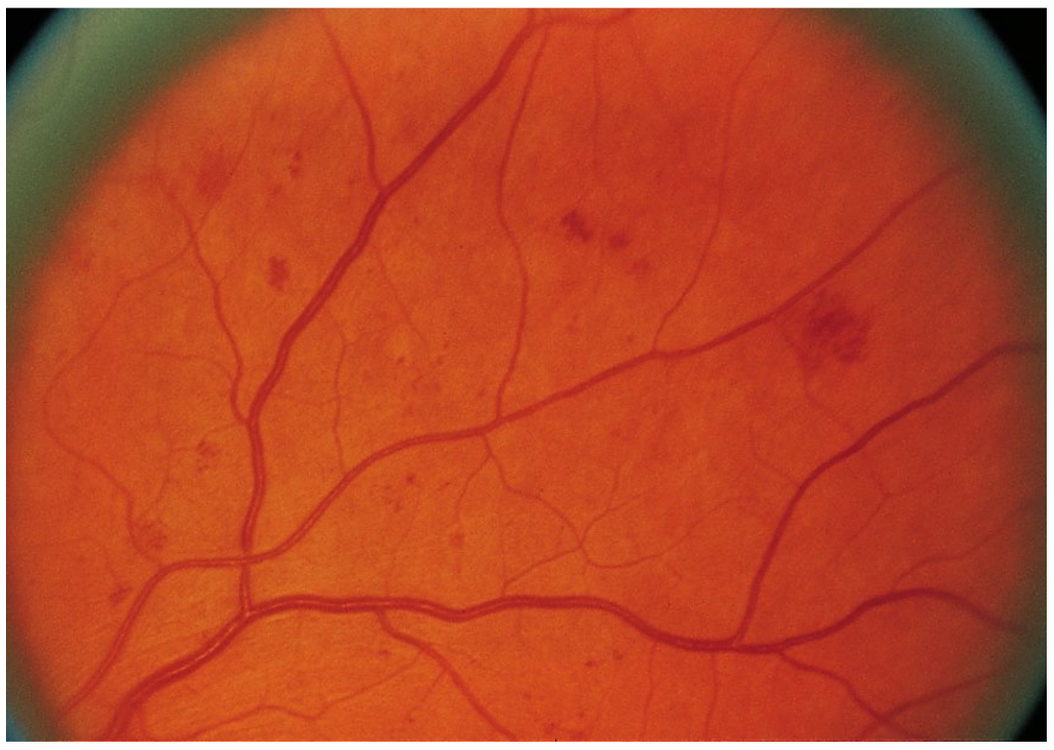

FIGURE 31–3 ETDRS standard photograph 2A, the standard for microaneurysms.

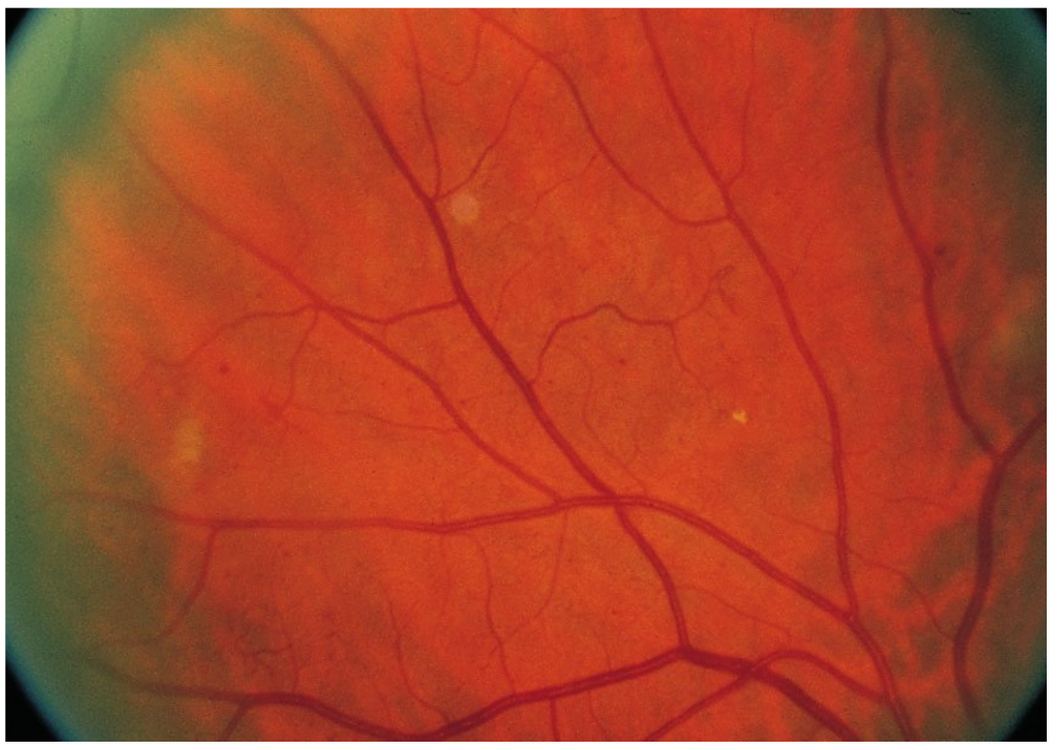

FIGURE 31–5 ETDRS standard photograph 8A, the standard for IRMAs.

REHABILITATION AND FOLLOW-UP

Patients with diabetic retinopathy require careful follow-up examinations with a frequency dependent upon the severity of the retinopathy. An annual examination is recommended for patients with minimal or absent NPDR. An examination is recommended every 6 to 12 months for patients with mild to moderate nonproliferative disease if there is no macular edema, but every 4 to 6 months if there is nonclinically significant edema present, and every 2 to 4 months if clinically significant macular edema (see Case 32, Diabetic Macular Edema) is present. Patients with severe or very severe NPDR should be reexamined every 2 to 4 months.

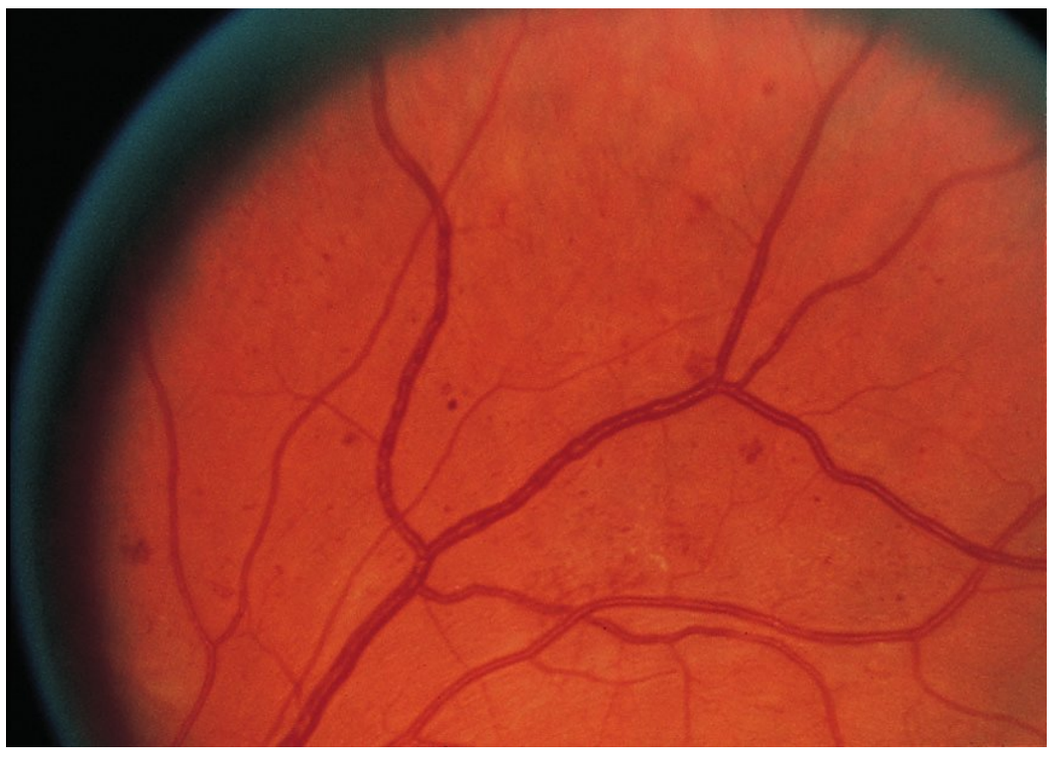

FIGURE 31–4 ETDRS standard photograph 6A, the standard for venous beading.

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Case 32

DIABETIC MACULAR EDEMA

William E. Smiddy, M.D.

HISTORY

This 58-year-old man with a 20-year history of insulin-dependent diabetes, recent onset hypertension, and chronic hypercholesterolemia sought consultation because of blurred vision of several weeks' duration.

Examination disclosed best corrected visual acuity of 20/30 in each eye. There was no afferent pupillary defect. Slit-lamp examination showed only trace nuclear lens opacity. Tensions were 20 in each eye.

Funduscopic examination showed moderate microaneurysms scattered about all quadrants of both eyes. In the right eye, there was clinically significant diabetic macular edema with a circinate lipid ring surrounding the center of the macula (Fig. 32–1). No neovascular changes were seen. In the left eye, in addition to the microaneurysms and macular edema with lipid, there was early neovascularization at the disc (NVD) (Fig. 32–2). Fluorescein angiography demonstrated macular leakage OU, and in the left eye confirmed the NVD (Fig. 32–3).

The patient underwent bilateral macular edema laser treatment. He was scheduled for follow-up examination in 1 month to reevaluate the early NVD.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The patient meets the criteria for clinically significant macular edema in each eye. The Early Treatment Diabetic Retinopathy Study (ETDRS) defines clinically significant diabetic macular edema as macular thickening within 500 microns of the center, as lipid within 500 microns of the center associated with macular thickening that may or may not be within 500 microns of the center, or as macular thickening of one disc area any portion of which is within one disc diameter of the center of the fovea. Results were statistically significant only for patients meeting one of these criteria.

2. Visual acuity is not part of the diagnosis of clinically significant macular edema and is of less importance compared to the clinical examination in deciding whether or not to recommend laser treatment. Low levels of visual acuity may lead to further testing to establish that macular edema is the primary cause of visual loss. When the visual acuity is less than 20/400 (20/400 was the lower level of eligibility in the ETDRS), treatment is often deferred. On the other end of the visual spectrum, when the visual acuity is in the 20/20 range usually treatment is recommended if there is clinically significant diabetic macular edema, but in selected cases treatment may be deferred provided close follow-up examination may be obtained.

3. This patient presented with possible early proliferative disease in the left eye. It is generally believed that panretinal photocoagulation (PRP) may exacerbate macular edema. This was a leading cause of what was termed "early persistent visual loss" following PRP in the Diabetic Retinopathy Study (DRS). Accordingly, as with this patient, it is recommended that macular edema be treated first with prompt attention to PRP following laser treatment. For patients with high-risk characteristics as defined by the DRS (which this patient did not yet have), PRP and macular edema treatments are usually offered simultaneously, or within a couple of weeks of each other. In patients with early

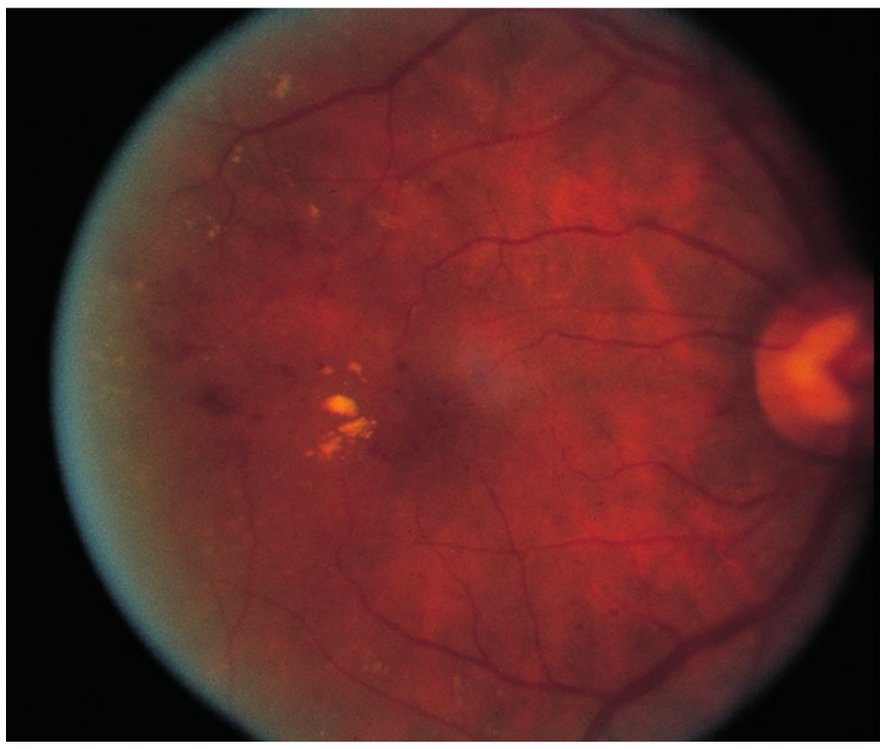

FIGURE 32–1 Funduscopic appearance of right eye demonstrating the diabetic macular edema temporal to fovea. This approaches the center and accounts for visual loss.

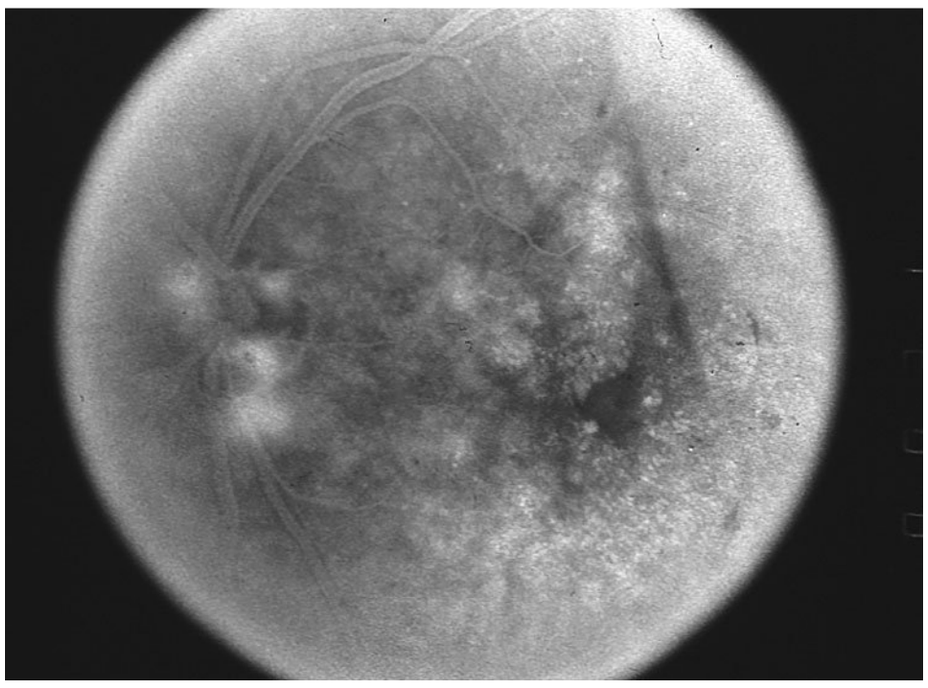

FIGURE 32–3 Fluorescein angiogram shows macular edema leakage, but also confirms the neovascularization at the disc (NVD) as evidenced by late leakage.

proliferative disease, generally PRP is considered about 6 weeks after the treatment of macular edema. For patients with severe nonproliferative disease, PRP is considered, but this is often deferred while carefully following the patient clinically for at least 3 months.

4. Optimal control of systemic conditions is important in optimizing the natural course and even the response to treatment. Patients with hypercholesterolemia or systemic hypertension tend to respond less well to laser treatment. Accordingly, medical consultation for optimal treatment of the systemic condition is recommended before reevaluating for macular edema treatment.
5. In a patient with diabetes and at least moderate retinopathy and macular thickening, the diagnosis is hardly questionable. However, hypertensive retinopathy or cystoid macular edema following cataract surgery, or radiation retinopathy, are two entities that may mimic what appeared in this patient.

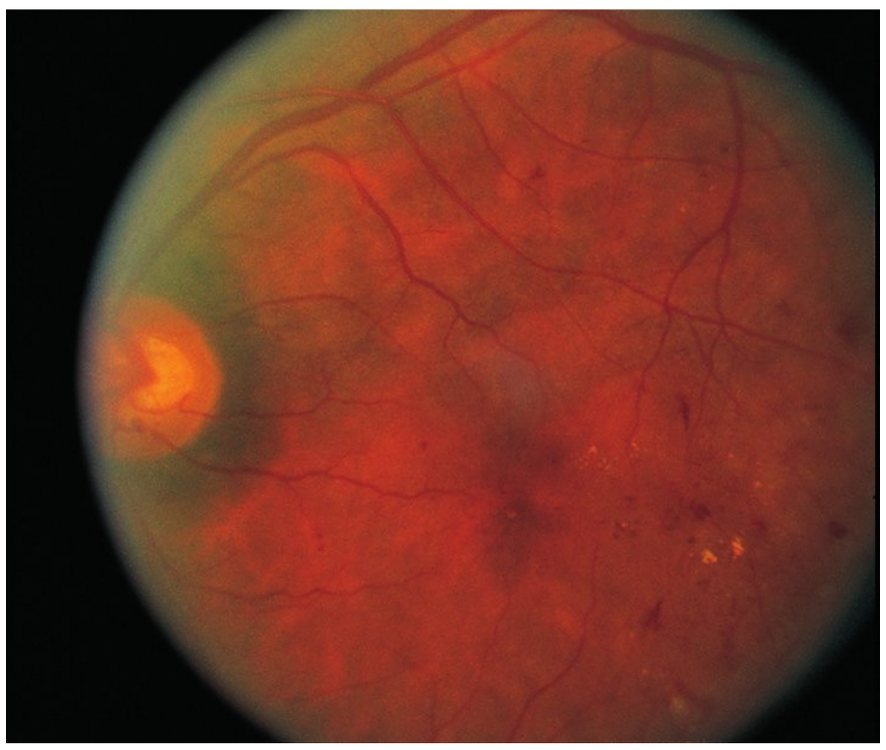

FIGURE 32–2 Appearance of left eye is similar to right with lipid and macular thickening temporal to macula. Early neovascularization at the disc (NVD) is present at the inferior part of the disc.

TEST INTERPRETATION

The clinical examination forms the basis for diagnosis and is the primary factor in deciding if treatment is recommended for patients with diabetic macular edema. Fluorescein angiography may be useful by defining degrees of nonperfusion (and therefore assigning the cause of visual loss to an entity other than macular edema) and in localizing areas of maximal microaneurysm leakage, which may be helpful in guiding treatment. In some cases, stereoscopic fundus photography may also be of value in confirming the presence or absence of macular thickening.

DIAGNOSIS

Clinically significant diabetic macular edema, OU.
Early proliferative diabetic retinopathy, OS.

MEDICAL MANAGEMENT

Medical therapies are necessary to maximize treatment of hypercholesterolemia or systemic hypertension. Optimal control of blood sugar is a long-term goal to be pursued but is rarely valuable in effecting short-term improvements in retinopathy.

SURGICAL MANAGEMENT

Laser treatment is the cornerstone of treatment for diabetic macular edema. The ETDRS showed that the risk of moderate visual loss (as defined by loss of three lines of visual acuity) can be reduced by a factor of 50% through treatment. The 3-year risk of moderate visual loss is 24% in patients with clinically significant diabetic macular edema and this is reduced to 12% with treatment. The treatment effect is more marked compared to untreated controls for patients with center involvement as opposed to those fulfilling the diabetic macular edema definition without center involvement of the macular edema. It should be pointed out that the ETDRS evaluated patients only with less severe retinopathy; severe nonproliferative and proliferative retinopathy coexisting with macular edema were not evaluated in the ETDRS. Still, the results are usually extrapolated to these groups of patients.

The treatment technique involves the use of 50- or 100-micron spot size burns with 0.1- to 0.2-second duration. Generally, the argon laser treatment is used, but other studies have shown that krypton and diode lasers are also effective. The burn-intensity endpoint is some whitening of the retina, but not as intense as for PRP. The ETDRS technique involved direct treatment of microaneurysms but allowed for a grid treatment of the thickened area. Many utilize a modified grid treatment whereby the initial treatment is aimed at obvious microaneurysms, with a filling in of the thickened area, which yields, effectively, a grid treatment.

PRP was shown by the ETDRS not to be effective in reducing visual loss due to macular edema.

Rare patients will present with macular edema that appears to be due to traction induced by a taut, thickened posterior hyaloid. Such cases are difficult to identify preoperatively but may respond to surgical removal of the thickened posterior hyaloid.

REHABILITATION AND FOLLOW-UP

Generally, after patients are treated for diabetic macular edema they are followed up in 6 to 12 weeks. If there are areas that were obviously missed with initial treatment, then they are re-treated within this time frame. Usually, repeat treatment for persistent edema in treated areas is considered 3 to 6 months following initial treatment. Care is taken not to overtreat in patients who have had multiple treatments, since it may not be possible to eliminate the macular thickening despite successive laser treatments. In addition, after a point the laser treatments may become visually counterproductive.

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Case 33

PROLIFERATIVE DIABETIC RETINOPATHY

William E. Smiddy, M.D.

HISTORY

This 50-year-old man with a 5-year history of Type II diabetes mellitus presented for a second opinion from an ophthalmologist regarding the possibility of diabetic retinopathy. The patient was asymptomatic upon initial presentation.

His examination showed vision of 20/20 in each eye. Pressures were 12 and 13 mm Hg in the right and left eye, respectively. Slit-lamp examination was unremarkable. The lens was perfectly clear. On funduscopic examination of the right eye there was a mild degree of hard exudates scattered about the posterior pole, but there was no definite macular thickening. Questionable neovascularization elsewhere was seen at the distal portion of both temporal arcades. Most prominent, however, was definite neovascularization at the disc that was in excess of one disc area in extent (Fig. 33–1). In the left eye there were intraretinal hemorrhages with microaneurysms in all four quadrants, but this exceeded the standard photograph 2A for hemorrhages in only two quadrants (Fig. 33–2).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. In the setting of a patient with diabetes mellitus with bilateral retinopathy, it is quite clear that the diagnosis is diabetic retinopathy. Of principal importance is understanding the staging of each eye so that proper treatment recommendations may be determined. The classification of diabetic retinopathy has been simplified to "nonproliferative" diabetic retinopathy and "proliferative" diabetic retinopathy. This classification system is based on the findings of numerous multicentered studies of natural history and responses to treatment. The right eye has proliferative diabetic retinopathy whereas the left eye has nonproliferative diabetic retinopathy.

   Proliferative diabetic retinopathy is typically subdivided into early proliferative diabetic retinopathy or high-risk diabetic retinopathy. The Diabetic Retinopathy Study identified four high-risk features and defined high-risk characteristics as eyes that contain three or four of these features (Table 33–1 and Fig. 33–3).

2. Other causes of retinal neovascularization should also be considered in the differential diagnosis, but given this medical history they are extremely unlikely. Neovascularization due to branch retinal vein occlusion usually does not produce neovascularization directly at the disc, so would most commonly be in the differential diagnosis of neovascularization elsewhere. However, the appearance of collateral vessels at the disc (as sometimes occurs after branch retinal vein occlusion) may mimic neovascular vessels at the disc. These are more characteristically of larger caliber ("loopy") and are nonprogressive. Unlike neovascularization, collateral vessels pose no threat of vitreous hemorrhage. Other causes of neovascularization typically share the ischemic state and may be seen in uveitis, in various forms of occult vasculitis, Eales' disease, and radiation retinopathy.

3. Other causes of nonproliferative retinopathy mimicking the findings in this patient's left eye include radiation retinopathy and hypertensive retinopathy.

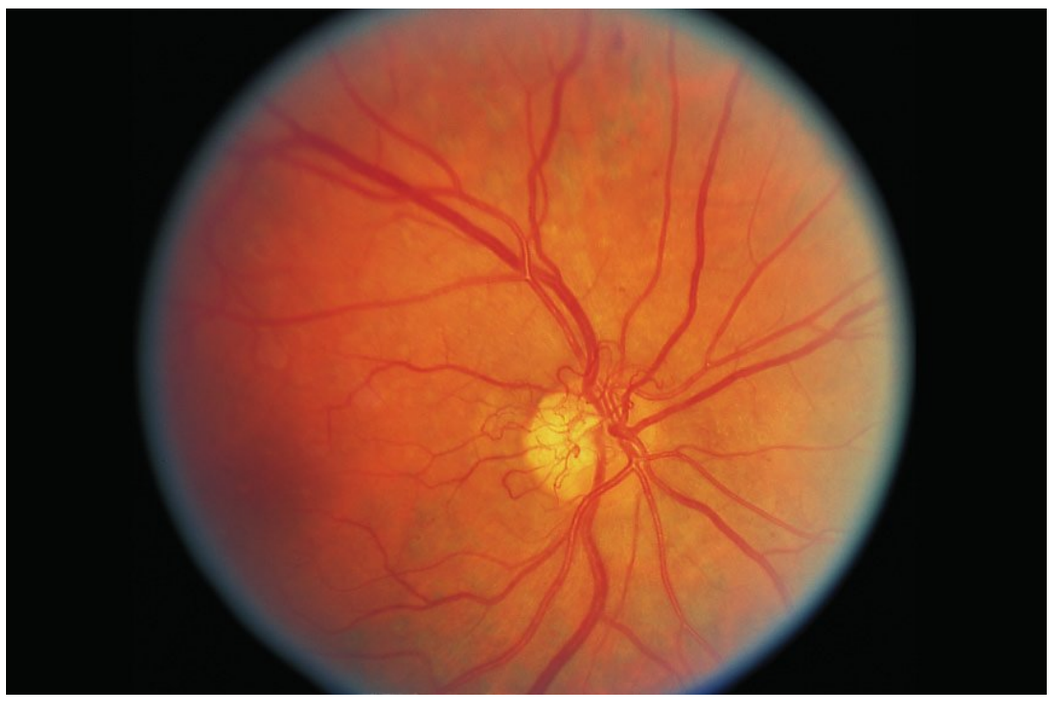

FIGURE 33–1 Examination of the right disc showed neovascularization involving over one disc area, extending beyond the temporal and superior margins of the disc. Stereoscopic view showed this clearly to be elevated over the retinal surface. No vitreous hemorrhage was present.

4. Diabetic retinopathy, particularly proliferative phases, may occur asymptomatically. It is for this reason that many patients commonly go undiagnosed until more severe complications have ensued (i.e., vitreous hemorrhage or tractional retinal detachment). Thus, a careful, complete, dilated funduscopic examination with some form of high magnification funduscopy should be performed on a regular basis.

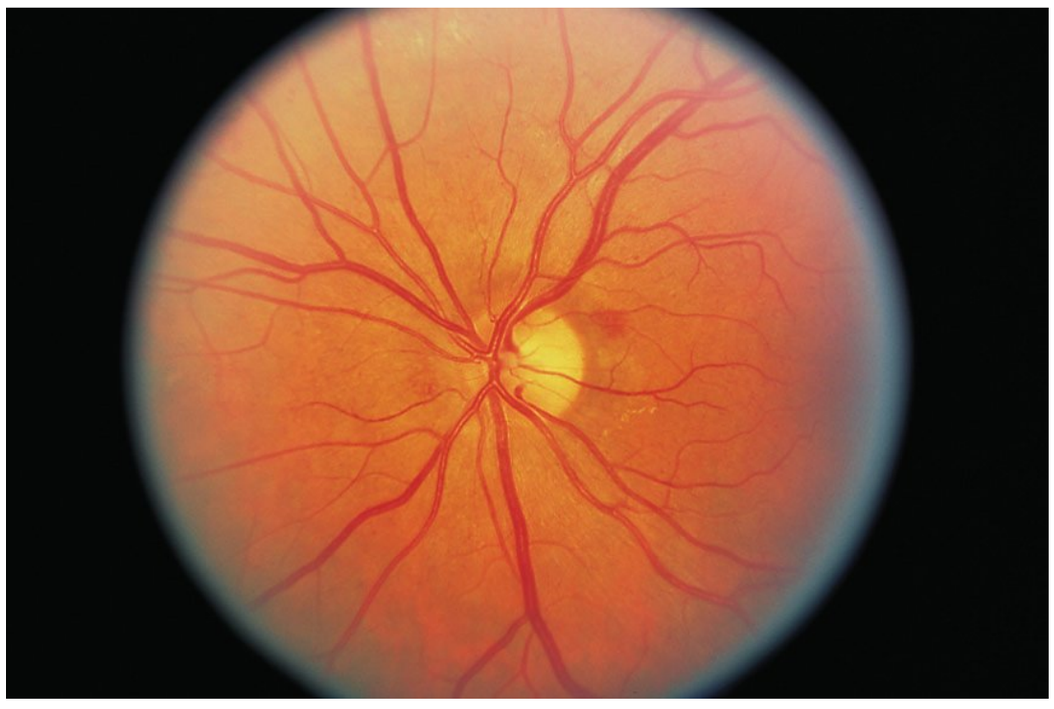

FIGURE 33–2 The left eye showed a moderate number of microaneurysms and intraretinal hemorrhages with occasional hard exudates. No intraretinal microvascular abnormalities or venous beading were noted. A moderate degree of hemorrhage was noted only in two quadrants.

TABLE 33–1 **Risk Factors for Severe Visual Loss in Diabetic Retinopathy Study**

1. Any neovascularization.
2. Neovascularization at the disc (as compared to neovascularization elsewhere).
3. Severe neovascularization:
   a. Neovascularization at the disc exceeding Diabetic Retinopathy Study standard photograph 10A (Fig. 33–3);
   b. Neovascularization elsewhere exceeding one-half disc area in extent.
4. Vitreous hemorrhage.

TEST INTERPRETATION

Usually the staging of retinopathy, either proliferative or nonproliferative, is achieved by clinical examination. While the direct ophthalmoscope may be suitable for the purposes of staging the condition, slit-lamp biomicroscopy with a precorneal lens is more accurate. The use of the 60- or 90-diopter lens gives an inverted, indirect image; however, it typically sacrifices some degree of stereopsis and, accordingly, some sensitivity. The contact lens evaluation allows optimal stereoscopic evaluation but may be limited by media opacities in many patients.

Fluorescein angiography is usually not a diagnostic modality. However, in questionable vascular lesions the fluorescein angiogram may demonstrate leakage from neovascular vessels,

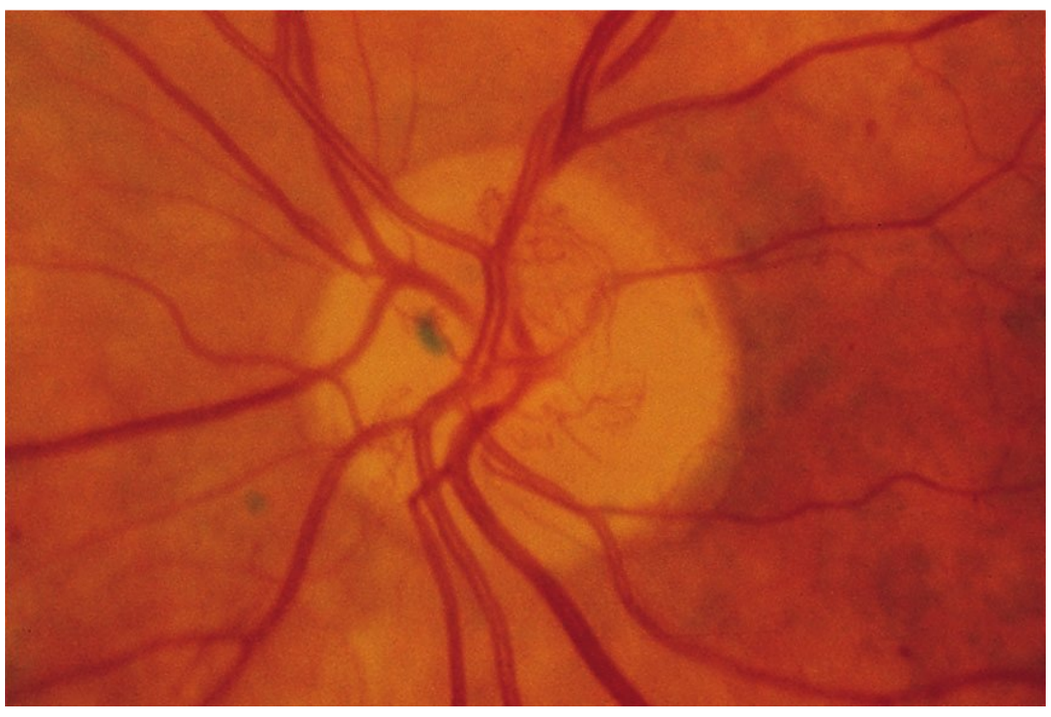

FIGURE 33–3 Standard photograph 10A from the Diabetic Retinopathy Study showing neovascularization involving one-third to one-half of the disc area.

whereas other vascular malformations such as intraretinal microvascular abnormalities may not show leakage. A clinically useful tool is to obtain high quality stereoscopic fundus photographs in all fields. Examination of these photographs is the most sensitive means of evaluating the fine details of the fundus vasculature. Strictly speaking, neovascularization is typically seen as fine vessel outgrowth from the venous side of the circulation, which most characteristically leads to slightly elevated vascular frond. This is in contrast to the intraretinal microvascular abnormalities that are within the retina and, therefore, flat.

DIAGNOSIS

Right eye: Proliferative diabetic retinopathy with high-risk characteristics.

Left eye: Moderately severe nonproliferative diabetic retinopathy.

MEDICAL MANAGEMENT

The Diabetic Retinopathy Study defined a poor prognosis for patients with neovascularization and especially for those with high-risk characteristics as defined by eyes containing three or four of the characteristics outlined in Table 33–1 (Diabetic Retinopathy Study Research Group, 1979). The mainstay of treatment for proliferative diabetic retinopathy is laser photocoagulation. Laser photocoagulation is typically performed under topical anesthesia with the use of a panfundus contact lens and is usually minimally uncomfortable. A significant proportion of patients will require retrobulbar anesthesia because of pain incurred with laser treatment. Usually laser photocoagulation is delivered in two or more sessions, to avoid either severe pain or choroidal detachment from excessive photocoagulation. Usually a relatively short burn duration (0.1 second or less) is used to minimize patient discomfort. Spot size ranging from 200 to in excess of 500 microns is usually utilized. A total of approximately 1500 laser spots is used but probably more important is the area of retina lesioned by the laser. That is, fewer spots are necessary when larger spot sizes are used. Usually a 1- to 2-week interval between laser sessions is recommended, but this is accelerated with more severe neovascularization.

Complications of panretinal photocoagulation (PRP) range from an almost universal finding of some degree of pain in the immediate post-treatment period that usually responds to over-the-counter analgesics to more severe, sight-threatening problems. Vitreous hemorrhage may occur following laser photocoagulation; it is unclear whether that is coincidence or whether it is due to laser-induced remodeling of the neovascular complexes during initial stages of regression. Most patients will recognize diminished illumination in an eye undergoing PRP, most distinctly noticed as a decrease in night vision. Although peripheral visual field loss has been documented, it is not usually clinically significant. Exacerbation of preexisting (even nonclinically significant) diabetic macular edema may follow PRP. For this reason, treatment of diabetic macular edema is recommended either before or at least during treatment with PRP. The Diabetic Retinopathy Study documented a 20% incidence of early persistent visual loss (2 lines) following PRP, mostly due to this phenomenon.

The Early Treatment Diabetic Retinopathy Study and, to a degree, the Diabetic Retinopathy Study, define potential efficacy for patients even before proliferative retinopathy ensues. These studies are described in Case 32.

The results of the Diabetic Retinopathy Study showed that for patients with high-risk characteristics, the rate of severe vision loss (5/200) decreased from 27 to 10% after 2 years. Long-term follow-up studies have documented the relative long-term stability of eyes following an initially successful response to PRP. While a treatment benefit was seen in the Diabetic Retinopathy Study for early proliferative cases, the magnitude of the response was not sufficient to support a strong treatment recommendation. Nevertheless, consideration could be given to laser treatment in these cases.

SURGICAL MANAGEMENT

The indications and surgical treatment of patients with severe complications of diabetic retinopathy is beyond the scope of this chapter. Patients with vitreous hemorrhage or fibrovascular proliferation leading to traction that threatens the macula (with or without detachment) are considered for vitrectomy. Typically, earlier vitrectomy is considered for patients with vitreous hemorrhage and Type I diabetes. Patients with Type II diabetes are commonly observed for spontaneous improvement of vitreous hemorrhage. The results of vitrectomy are best for patients with vitreous hemorrhage and worse for patients with severe degrees of traction or retinal detachment.

REHABILITATION AND FOLLOW-UP

After completion of a course of PRP, the patient should be observed within a few weeks. If the retinopathy progresses, consideration must be given to vitrectomy. If the retinopathy regresses completely then a conservative observational follow-up regimen may be pursued, contingent upon the stability of the retinopathy and visual acuity. Follow-up laser photocoagulation is considered when there are multiple recurrent vitreous hemorrhages or when the regression of the neovascularization is incomplete, particularly when the morphology of the neovascularization is feathery, with fine caliber vessels.

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Case 34

RETINAL ARTERIAL OCCLUSION

Medhat M. Mady, M.D.
William E. Smiddy, M.D.

HISTORY

A 69-year-old woman presented 4 weeks after sudden visual loss in the right eye. Medical history included a 6-year history of systemic hypertension and a 1-year history of diabetes mellitus. Examination showed visual acuity of 20/30 and 20/25 in the right and left eyes, respectively. There was no afferent pupillary defect. Intraocular pressures were 16 mm Hg in each eye. Slit-lamp examination was remarkable only for early nuclear sclerosis of the lens in both eyes. On funduscopic examination of the right eye, the inferotemporal retinal artery appeared sclerotic and attenuated with a glistening yellow cholesterol embolus (Hollenhorst plaque) at its proximal part (Fig. 34–1). There was an area of superficial retinal whitening, most prominent in the posterior pole along the distribution of the obstructed artery. Funduscopic examination of the left eye was normal.

Fluorescein angiography demonstrated a corresponding filling defect in the inferior branch retinal artery distribution (Fig. 34–2).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The hallmarks of arterial occlusion are sudden, dense loss of vision corresponding to a zone of retinal whitening and arterial attenuation. The retinal whitening is due to edema but is transient; after a few days it resolves and the diagnosis may be more difficult. The characteristic cherry-red spot of central retinal artery occlusion (CRAO) is due to the retinal pigment epithelium (RPE) and choroidal coloration remaining visible through the central, thin foveola—made more prominent because the thicker, surrounding macular tissues are translucent due to the acute ischemic edema (Fig. 34–3).

2. Approximately 57% of retinal arterial occlusions involve the central retinal artery, 39% involve the branch retinal artery, and 5% involve the cilioretinal artery.

3. Branch retinal artery occlusion (BRAO) results from embolic or thrombotic occlusion of the affected vessel. The temporal retinal arteries are involved in 90% of cases. Three main varieties of emboli include cholesterol emboli arising in the carotid arteries, platelet-fibrin emboli associated with large vessel arteriosclerosis, and calcific emboli arising from diseased cardiac valves. Generally, these cannot be easily differentiated clinically. Rare causes of emboli include cardiac myxoma, fat emboli from long bone fractures, septic emboli from infective endocarditis, and migraine (in patients less than 30 years of age).

4. CRAO is often caused by atherosclerosis-related thrombosis occurring at the level of the lamina cribrosa. Other causes include emboli, spasm, and dissecting aneurysm. Emboli are seen in the retinal arterial system in about 20% of eyes with CRAO. Patients with atherosclerotic CRAO are at increased risk of early death from systemic vascular disease.

5. Systemic workup of patients with arterial occlusions is usually deferred to the internist but might include a complete physical examination, carotid evaluation (e.g., Doppler flow studies or angiography) as indicated, electrocardiogram, and echocardiography. Systemic hypertension (70%) and diabetes (25%) are also commonly associated with retinal arterial occlusions.

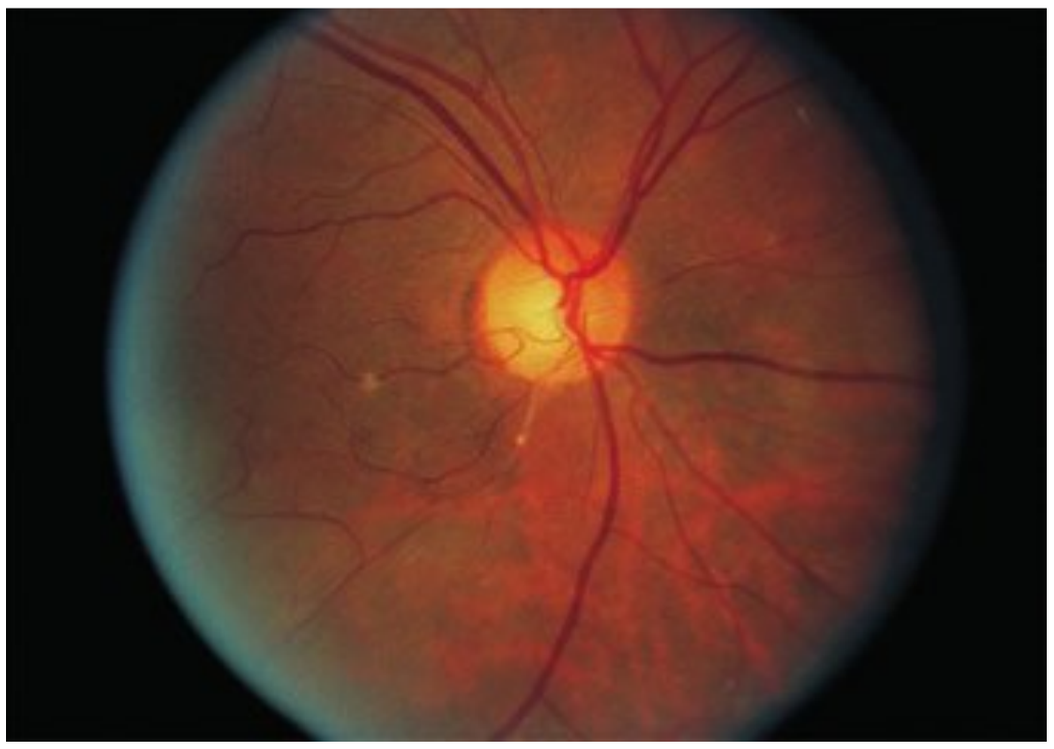

FIGURE 34–1 Photograph of the right fundus showing inferotemporal branch artery occlusion with prominent Hollenhorst's plaques.

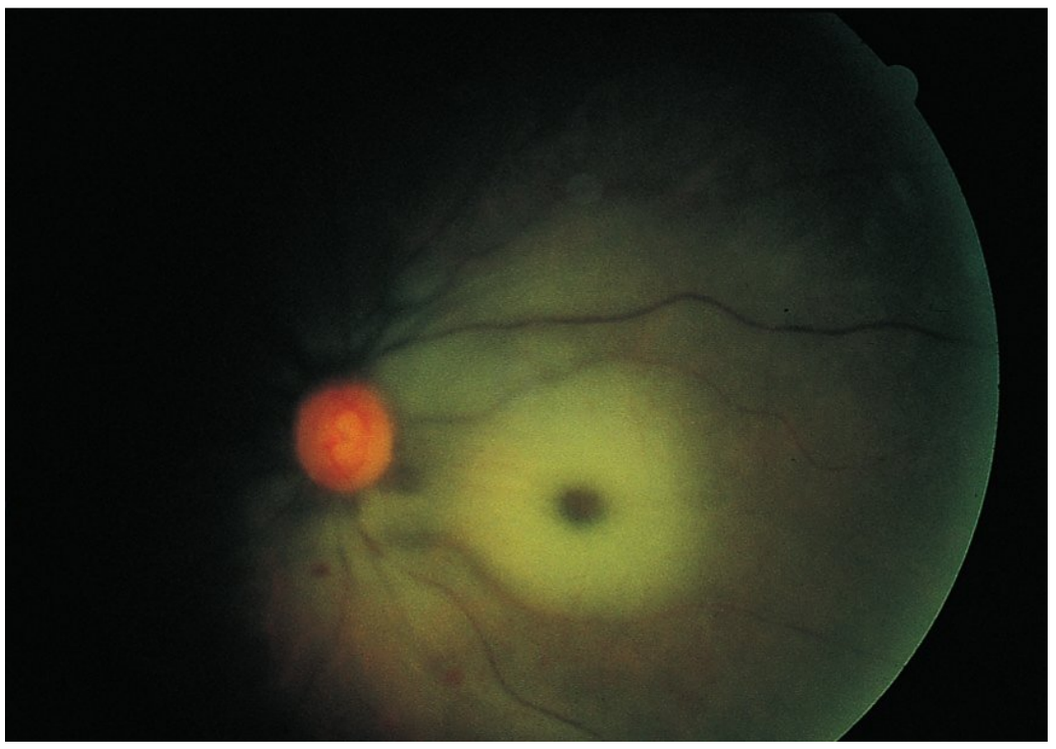

FIGURE 34–3 Funduscopic appearance of a different patient 3 days after sudden visual loss. Retinal edema indicative of central retinal artery occlusion (CRAO) is apparent, with classic foveal "cherry red spot" in evidence.

TEST INTERPRETATION

Diagnosis of most cases of acute retinal artery occlusion (CRAO or BRAO) may be achieved by clinical examination of the fundus with the indirect ophthalmoscope or slit-lamp biomicroscopy. Acute occlusions are more obvious due to the characteristic edema.

Intravenous fluorescein angiography may be useful in showing the details of the abnormal circulation of central or branch artery occlusion. The principal abnormality is delayed appearance of the dye in the arterial circulation. Cilioretinal artery sparing may be demonstrable. Late staining of the optic nerve head may also occur. The filling of the retinal arteries is often abnormal, with the fluorescein partially filling an artery. Venous filling is usually slowed, and occasionally the dye will not progress beyond laminar flow. Leakage of the dye from the vessel wall is not normally seen except at the site where an embolus lodges within a retinal artery. Delayed choroidal filling occurs in about 10% of CRAO cases and suggests ophthalmic artery occlusion. The occlusion frequently recanalizes within a few weeks of obstruction and, accordingly, the angiogram may show only subtle changes in more chronic cases.

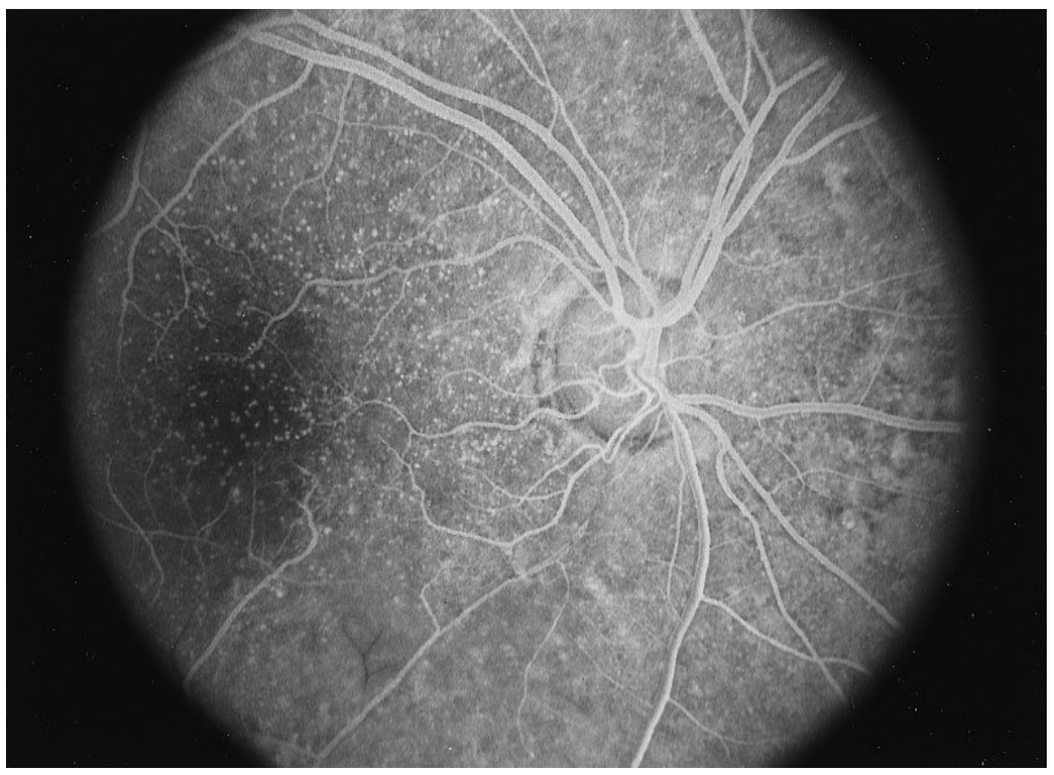

FIGURE 34–2 Fluorescein angiogram of the same eye showing limited filling of the inferotemporal retinal artery and its branches. Numerous drusen are also apparent, scattered about the posterior pole.

Visual field testing may also be helpful in making a diagnosis in nonacute cases of BRAO. The characteristic finding is a sectoral, or even hemifield, abnormality that has a distinct border respecting the horizontal midline.

Electroretinography is not usually necessary, but characteristically reflects inner retinal ischemia by a decrease in B-wave amplitude.

DIAGNOSIS

BRAO, right eye.

MEDICAL MANAGEMENT

The visual prognosis in BRAO is much better than for CRAO; 80% of eyes with BRAO eventually improve to 20/40 or better. Possibly the most important aspect of medical management is diagnosing systemic conditions.

No specific ocular therapy has been proven to improve the visual prognosis. Systemic vascular disease may contribute to the arterial occlusion and may predispose the patient to avoidable risk of future stroke or heart attack. Indeed, in one study, CRAO patients had twice the mortality rate (56% 9-year survival) of age-matched controls. In acute cases, digital pressure on the globe for 15 seconds, followed by a sudden release, may dislodge or advance an embolus. Lowering the intraocular pressure with intravenous acetazolamide, or anterior chamber paracentesis if less than 24 hours old, may also dislodge or advance an embolus. Augsburger and Magargal noted at least a three-line improvement in vision in 35% of eyes at 1 month after the acute event, when paracentesis was performed early. Inhalation of a mixture of 5% carbon dioxide and 95% oxygen (carbogen) or retrobulbar or systemically administered calcium channel blockers to promote vasodilation have been advocated, but the results are generally disappointing.

Retinal neovascularization may develop after BRAO, particularly in patients with diabetes mellitus. Iris neovascularization secondary to BRAO is extremely rare but develops in up to 20% of eyes with CRAO within 12 weeks, especially when also associated with central vein occlusion. Full-scatter panretinal photocoagulation is effective in eradicating the new iris vessels in about two-thirds of cases. Ipsilateral carotid artery stenosis may also be present and be a cause of rubeosis iridis.

There is no good evidence that anticoagulation enhances prognosis in an isolated retinal arterial occlusion.

Studies using fibrinolytic agents have been reported but have found limited use, presumably due to the need for prompt treatment, specialized catheterization techniques, or limited visual recovery.

SURGICAL MANAGEMENT

Techniques involving pars plana vitrectomy with sheathotomy at the site of the branch vein occlusion have been developed. While preliminary reports are encouraging, this approach is still under evaluation and is not commonly recommended at this time.

REHABILITATION AND FOLLOW-UP

The most important reason for follow-up examination is to monitor for subsequent neovascularization. Reinforcement of regimens prescribed by the patient's internist should be provided.

Rehabilitation efforts are not specific to arterial occlusive disease, and low vision aids as indicated may be sought. Prism glasses for patients with dense hemifield defects have been described but are of limited general benefit.

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Case 35

CENTRAL RETINAL VEIN OCCLUSION

William E. Smiddy, M.D.

HISTORY

A 76-year-old man presented with a 3-month history of decreased vision in the right eye. His only medication was 650 mg of aspirin for several years. He did not have hypertension. He had had cataract surgery in both eyes approximately 1 year before presentation. Yttrium-aluminum-garnet (YAG) laser capsulotomy had been performed in the left eye 2 months previously.

The vision had gradually diminished during the first week after onset, then stabilized. Examination disclosed best corrected visual acuity of 8/200 on the right and 20/20 on the left. There was a right afferent pupillary defect. Slit-lamp examination showed no signs of iris neovascularization, well-positioned posterior chamber lens implants, and a clear and intact capsule on the right and an open capsule on the left. Intraocular pressures were 12 mm Hg and 14 mm Hg, respectively.

Funduscopic examination on the right showed intraretinal hemorrhage distributed throughout each quadrant (Fig. 35–1). There was some associated disc edema. Macular edema was evident in most of the posterior pole. On the left the cup-to-disc ratio was 0.3. There was a posterior vitreous separation as evidenced by the presence of a Weiss ring. There were some hard drusen without exudative changes. The vessels were minimally attenuated.

Fluorescein angiography showed transmission defects from the intraretinal hemorrhage. Because the hemorrhage was only relatively moderate, substantial amounts of the retinal vasculature were visible and showed areas of nonperfusion and, in later frames, macular edema.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

Acute visual loss typically suggests a vascular event. As in this case, acute visual loss may be followed by continued deterioration. Other abnormalities based on these historical features such as optic neuropathies must be considered but are usually distinguished by clinical examination features.

1. The pattern of intraretinal hemorrhages in this case markedly narrowed the differential diagnosis. Extensive intraretinal hemorrhages in all quadrants is a characteristic finding of central retinal vein occlusion (CRVO), and only in cases with less extensive hemorrhage does diagnostic confusion exist. The distribution of intraretinal hemorrhages in all quadrants distinguishes a CRVO from branch or hemiretinal vein occlusion. Diabetic retinopathy or advanced radiation retinopathy with diffuse intraretinal hemorrhage may mimic this entity.
2. Confluent, extensive intraretinal hemorrhage may mimic subhyaloid or subretinal hemorrhage. Subretinal hemorrhage almost always is consolidated, typically in the posterior pole. Subretinal hemorrhage may be clearly distinguished by observing the overlying retinal vasculature (clinically or angiographically).
3. The most common systemic disease associated with CRVO is hypertension. A majority of patients have hypertension, cardiovascular disease, or diabetes. CRVOs are unilateral in at least 95% of cases. Patients with bilateral CRVO more commonly have other

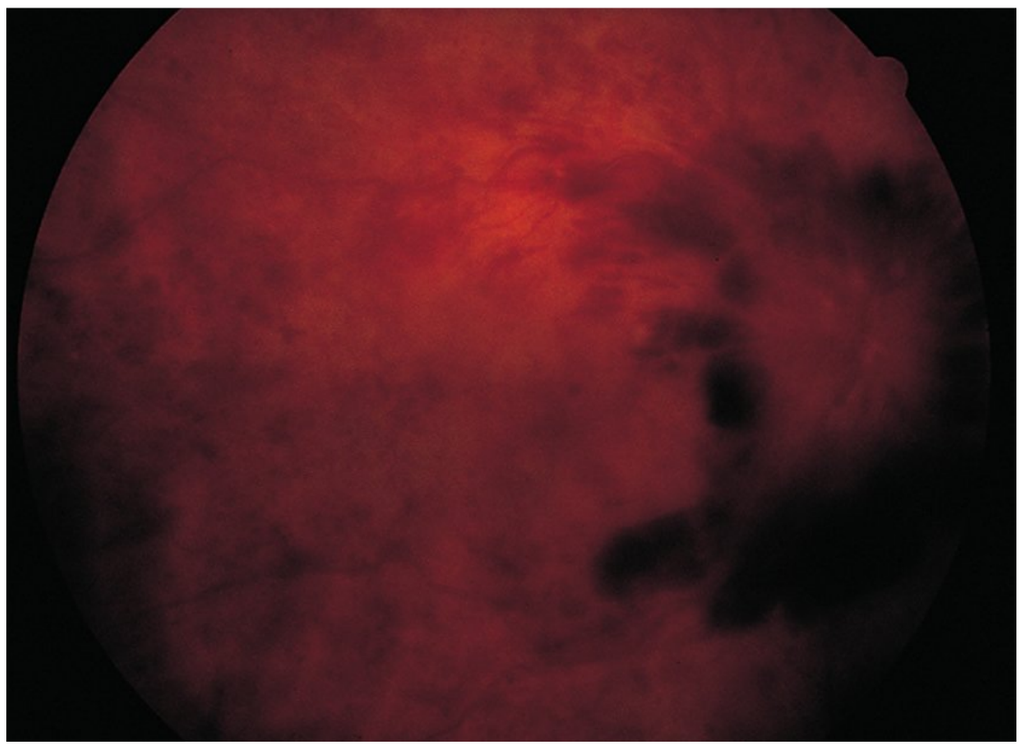

FIGURE 35–1 This patient 3 months after the onset of decreased vision. There are still substantial intraretinal hemorrhages, more particularly advanced around the disc. Fluorescein angiography did not show substantial areas of nonperfusion, however. Visual acuity was 8/200 and intraocular pressure was 12. There was no rubeosis iridis.

systemic medical conditions such as hyperviscosity syndromes (eg, multiple myeloma, macroglobulinemia, coagulation defects, or polycythemia vera). Systemic defects are found frequently enough in bilateral cases that systemic evaluation is recommended. Systemic evaluation in unilateral cases is usually limited to referral to a general medical doctor for a complete physical examination. Patients with isolated unilateral CRVOs have such a low incidence of these systemic diseases that the medical workup is left to the discretion of the patient's ophthalmologist and internist.

TEST INTERPRETATION

The ophthalmoscopic appearance is typically characteristic and diagnostic. Fluorescein angiography may demonstrate retinal nonperfusion, which may provide prognostic information for the development of neovascular glaucoma. Lower visual acuity usually implies a higher risk group.

The electroretinogram may yield valuable information. The B wave arises in the inner nuclear layer of the retina (probably the Mueller cells), and the A wave arises in the photoreceptors. A decreased B/A wave amplitude measuring less than 1.0 indicates ischemia and an increased risk of neovascular glaucoma. Cases with B/A ratios greater than 1.0 indicate that the ischemic injury has not disproportionally affected the portion of the retina subserved by the retinal versus choroidal circulation. Accordingly, such patients usually do not develop neovascular glaucoma.

DIAGNOSIS

CRVO, OD.

MEDICAL MANAGEMENT

The determining factor in the management of patients with CRVO is the presence of severe ischemia. CRVOs are generally divided into ischemic (complete, nonperfused) versus nonischemic (incomplete, well-perfused, or partial) vein occlusions. Approximately 30% of eyes with CRVO are nonperfused, and approximately half of these cases will develop neovascular glaucoma. Typically, the visual acuity is more profoundly diminished in such patients. In this patient, there was some evidence of ischemia. This prompted closely spaced follow-up examinations to monitor for the development of rubeosis iridis.

Aspirin or other anticoagulants have been shown to decrease the risk of subsequent thrombotic events in systemic thrombotic conditions. This is the rationale behind aspirin therapy (80 mg daily) after CRVO. Interestingly, this patient was taking aspirin at the time of the vascular event; similarly, other patients have been observed to develop CRVO while taking warfarin (Coumadin) or other anticoagulants. Thus, anticoagulants do not completely prevent vaso-occlusive disease, and since some side effects may occur, their use should be considered carefully for CRVO.

For patients developing rubeosis due to the nonperfused state, panretinal photocoagulation has been shown to be more effective than no treatment in controlling or preventing neovascular glaucoma. In cases with associated

vitreous hemorrhage or other media opacities that prevent laser treatment, cryopexy may offer a similar treatment benefit. Supportive treatment to lower the intraocular pressure is recommended as indicated.

Macular edema is another sight-threatening complication of central vein occlusion. The Central Vein Occlusion Study (CVOS) examined the efficacy of grid photocoagulation in patients with macular edema and found that although macular edema could be reduced, the visual outcomes were the same in control versus treated groups. Accordingly, grid laser photocoagulation is not generally recommended for patients with macular edema due to CRVO.

Laser treatment has been used and advocated to create a chorioretinal anastomosis. Limited success has been reported, but its role is not well established. Pilot studies of intravenous or intravitreal fibrinolytic agents have been reported but, also, do not have proven efficacy.

SURGICAL MANAGEMENT

A role for surgical management is currently established only for control of intraocular pressure in eyes with some visual potential. Glaucoma surgery is commonly done in conjunction with laser or retinal cryopexy. The most effective means of controlling the pressure in cases with neovascular glaucoma is placement of a shunt device (such as the Baerveldt or other implant).

REHABILITATION AND FOLLOW-UP

The CVOS found that the development of rubeotic glaucoma is maximal 3 to 6 months after the onset of the CRVO. Thus, the recommended interval for follow-up examinations is monthly for 6 months after diagnosis. After 1 year the incidence of rubeosis is extremely low unless a previously perfused case converts to a nonperfused case. This transition is usually heralded by a decrease in visual acuity.

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Case 36

BRANCH RETINAL VEIN OCCLUSION

William E. Smiddy, M.D.

HISTORY

This 60-year-old ophthalmologist had a 2-week history of decreased vision in the left eye. He noted a central scotoma that was worse in the morning, but slightly improved throughout the day. He had a 2-year history of hypertension and did not have diabetes.

The visual acuity was 20/20 in the right eye and 20/30+ in the left eye. Visual fields were full to finger counting confrontation. The intraocular pressures were 15 mm Hg in each eye. Funduscopic examination was normal in the right eye. In the left eye there was an anomalous arterial venous crossing along the superotemporal arcade with dot-and-blot hemorrhages extending from the midportion of the superotemporal arcade posteriorly into the macula (Fig. 36–1). There was minimal macular edema.

Because of the relatively good vision, observation was recommended. His visual acuity spontaneously improved to 20/25 and remained stable until approximately 6 months later when a mild vitreous hemorrhage occurred; it cleared spontaneously, but recurred 6 months later, decreasing the visual acuity to 20/50 in the left eye. Funduscopic examination showed sheathing of the superotemporal retinal vessels with still some intraretinal hemorrhage, but the view was partially obscured by a mild vitreous hemorrhage (Fig. 36–2). A twig of presumed retinal neovascularization was noted superotemporally. A segmental panretinal photocoagulation pattern (375 applications) was delivered with the argon blue-green laser (Fig. 36–3). The vitreous hemorrhage resolved and the visual acuity stabilized at 20/25 for the following 12 years (Fig. 36–4). Mild epiretinal membrane formation was noted, but was not judged to be clinically significant.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

This patient presented initially with intraretinal hemorrhages and macular edema that did not threaten the fovea. Subsequently, neovascularization and vitreous hemorrhage developed. Each of these clinical findings has a distinct differential diagnosis.

1. The most common cause of intraretinal hemorrhage is diabetic retinopathy. Characteristically, this is associated with microaneurysms in a distribution that involves many if not all quadrants. More severe diabetic retinopathy is accompanied by intraretinal microvascular abnormalities (IRMAs), lipid exudates, venous beading and other signs of ischemia including neovascularization. Less common causes of intraretinal hemorrhage include radiation retinopathy and various forms of uveitis. Central retinal vein occlusion is characterized by intraretinal hemorrhages in all quadrants. In this case, the intraretinal hemorrhages were present segmentally, in the distribution of a branch retinal vein.
2. Retinal neovascularization is a response to ischemia. This too is most commonly associated with diabetic retinopathy and may be difficult to distinguish from patients with branch retinal vein occlusions (BRVOs). However, other features of diabetic retinopathy are usually more prominent in a more generalized distribution in contrast to the segmental distribution seen with BRVOs. A vitreous hemorrhage may accompany any disease process with retinal neovascularization. Other causes of retinal neovascularization and/or vitreous hemorrhage include the sickle cell retinopathies and various forms of uveitis.

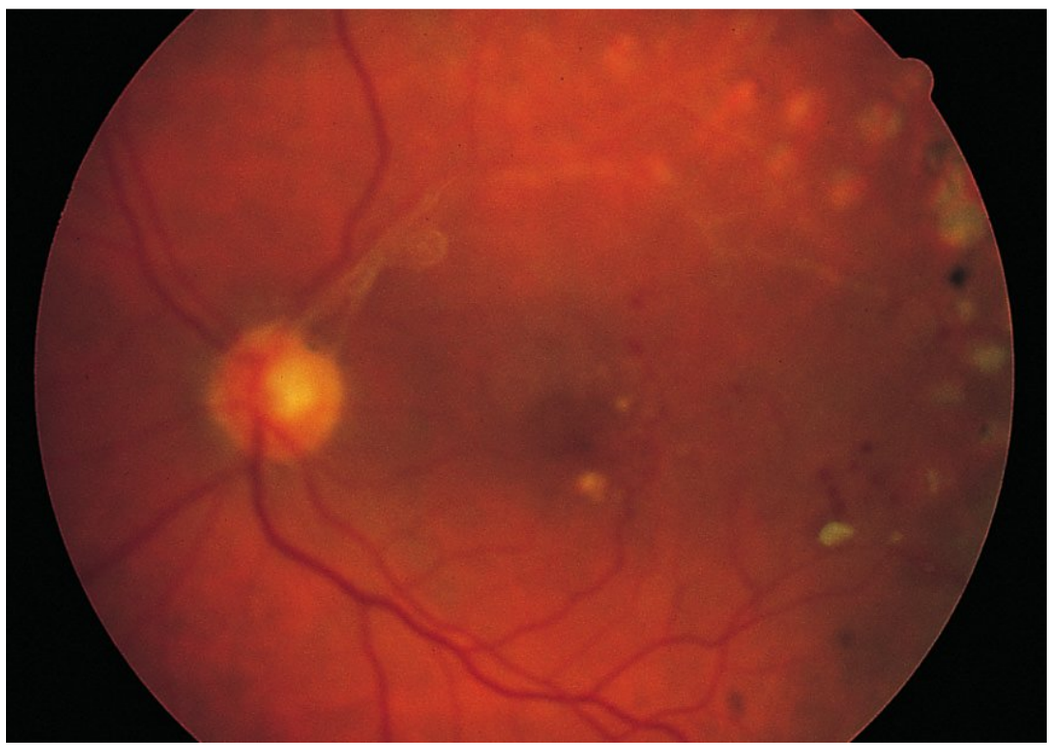

FIGURE 36–1 Funduscopic appearance of the left eye at initial presentation. While there is not any significant macular edema, there are mild intraretinal hemorrhages with blunting of the venules in the superior quadrant of the macula. Dilation of the superotemporal vein is seen distal to an arterial venous crossing approximately 1 disc diameter from the optic nerve head. No neovascularization is noted at this point.

3. With chronicity there is frequently collateralization of the flow, commonly prominent at the nerve head. These collaterals may mimic retinal neovascular vessels. The fluorescein angiogram may be valuable in differentiating between the two entities.

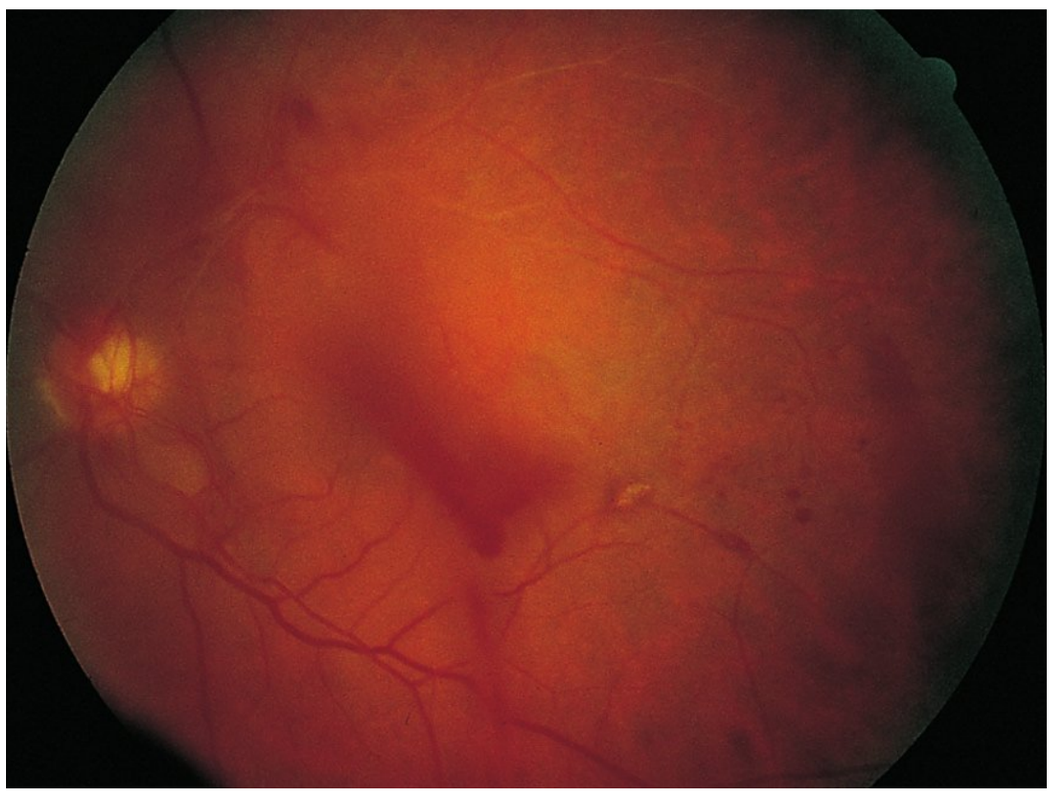

FIGURE 36–2 Clinical appearance upon representation just over 1 year later. In addition to some intraretinal hemorrhages and an indistinct but similar vascular appearance, a vitreous hemorrhage is noted, which interferes with visualization of the fundus.

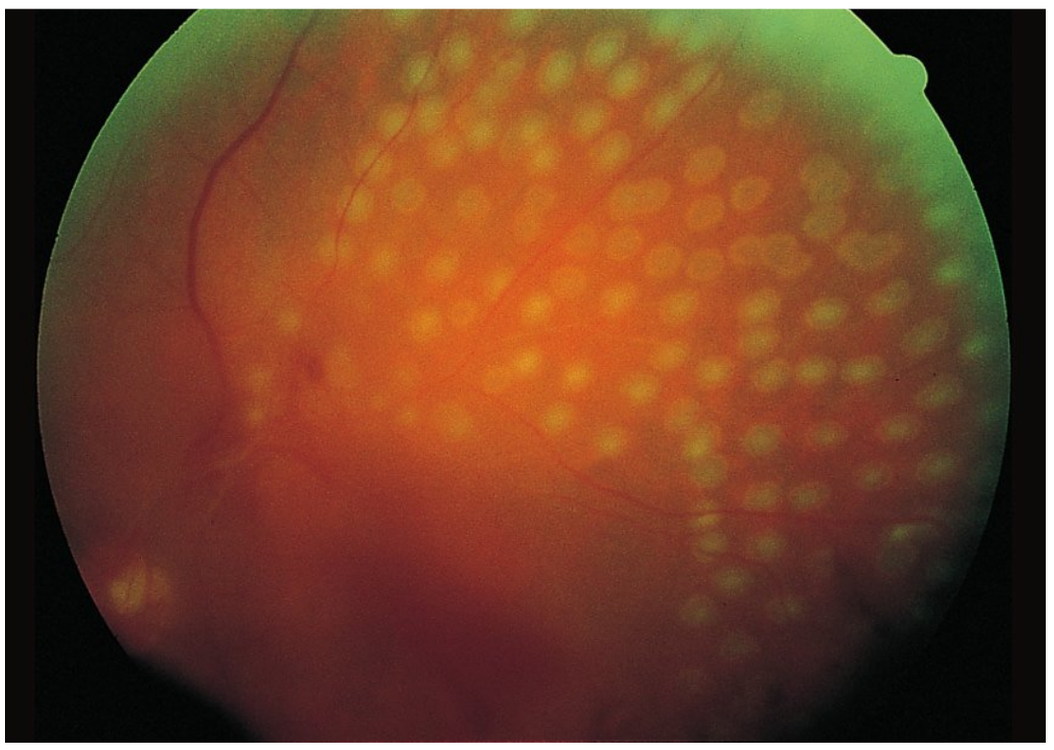

FIGURE 36–3 Appearance shortly after panretinal photocoagulation is delivered to the superotemporal quadrant. The laser spots are placed approximately two burn widths apart; 375 spots with 100-micron spots at 0.1-second burn duration were utilized.

TEST INTERPRETATION

Clinical examination is the most important diagnostic test. Ancillary tests include fundus photography and fluorescein angiography. Fundus photography may allow easier detection of diabetic

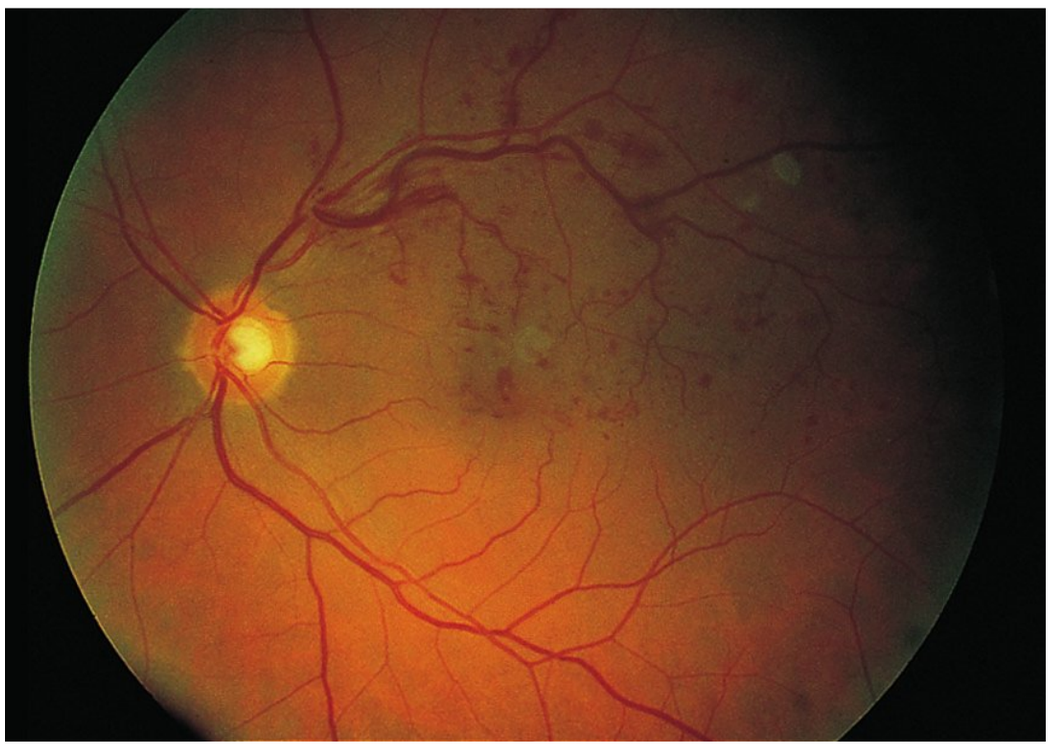

FIGURE 36–4 Regressed fibrovascular tissue extends from the optic nerve head along the superotemporal arcade but does not impinge on the macula. There is variable pigmentation from previous laser spots superotemporally. Mild venous dilation and occasional intraretinal hemorrhages are noted. No macular edema is noted. Minimal distortion of the central macula has been induced by the epiretinal membrane. This photograph was taken 4 years after photocoagulation. The vision was 20/25 at this point.

retinopathy and, consequently, earlier detection of neovascularization.

Fluorescein angiography is valuable in assessing the retinal perfusion status. Although this does not direct treatment, it may influence the frequency of follow-up examinations. If there are more than five or six disc areas of nonperfusion then such a patient is at a 40% risk of developing retinal neovascularization. Such patients should be followed more frequently because of this increased risk. The fluorescein angiogram may depict a characteristic pattern of retinal vascular leakage. While this may confirm the presence of the macular edema, it does not necessarily diagnose the cause. On clinical examination macular edema may be mimicked by zones of nonperfusion or ischemia, causing diagnostic uncertainty. The angiogram usually clarifies this. Fluorescein angiography may be valuable in confirming suspected areas of retinal neovascularization in selected cases. Specifically, it distinguishes neovascularization (which is characterized by dye leakage) from collateral vessels (which do not leak dye).

DIAGNOSIS

BRVO with secondary neovascularization and vitreous hemorrhage, OS.

MEDICAL MANAGEMENT

Systemic hypertension is a risk factor for the development of a vein occlusion, but it does not appear to be an independent risk factor for the severity of the course once a vein occlusion occurs. However, the ophthalmologist should encourage maximal control of hypertension in all patients. Other risk factors that are less firmly established include patients with diabetes, other cardiovascular disease, glaucoma, increased body mass at age 20, hyperopia, higher serum cholesterol, lower high-density liquid protein levels, and alcohol consumption.

The mainstay of medical management is laser photocoagulation. The Branch Vein Occlusion Study (BVOS) studied laser photocoagulation in patients with complications due to BRVO. The most common complication of BRVO is macular edema. This patient did not demonstrate visually significant macular edema. Macular edema is commonly self-limited with a fair degree of spontaneous resolution. However, the BVOS established that when the visual acuity is 20/40 or worse for at least 3 months, then a focal grid photocoagulation pattern is recommended in the area of edema; 63% of treated eyes gained two lines or more of vision compared to 36% of untreated control eyes after 3 years of follow-up.

The BVOS recommended that scatter laser photocoagulation be performed in the quadrant of the vein occlusion when neovascularization ensues. The exact pathogenesis of retinal vein occlusion is uncertain. However, it is observed that the occlusion of the vein typically occurs at the crossing point of an artery, where the artery and vein share a common adventitial sheath. Furthermore, the artery usually passes anterior to the vein, in contrast to a random distribution in unaffected eyes. It has been observed that the neovascularization commonly occurs in front of the vein, rather than from the arteries. It was found that the incidence of vitreous hemorrhages decreased from approximately 60% in controls to 30% of laser-treated patients with neovascularization.

An additional question was whether prophylactic laser treatment in patients with fluorescein angiographically-defined retinal capillary nonperfusion (larger than 5 disc diameters in width) decreased the incidence of visual loss due to retinal neovascularization. The results showed that only approximately 40% of such patients developed neovascularization, and only 60% of that subgroup experienced periodic vitreous hemorrhage. Therefore, laser photocoagulation was not recommended since treating at this stage would unnecessarily treat about 60% of people who would not develop retinal neovascularization. Rather, a 4-month follow-up examination was recommended.

Anticoagulant treatment has not been shown to be beneficial in the prevention or management of BRVO. However, as with the treatment of other nonocular vaso-occlusive disorders, aspirin therapy is often prescribed.

Recommended parameters for laser photocoagulation include 100-micron spot size, 0.1-second duration, and a green or argon-green laser photocoagulation to produce a medium to white burn for macular edema. A larger spot size (200 to 500 microns) and a more intense white burn are recommended for scatter photocoagulation for neovascularization.

SURGICAL MANAGEMENT

The role of vitrectomy in eyes with BRVO is limited to nonclearing vitreous hemorrhage or tractional and/or rhegmatogenous macular detachment from fibrovascular proliferation. In some cases, an epiretinal membrane may occur. Usually an epiretinal membrane induces minimal visual loss, but if the vision decreases below about 20/60, vitrectomy with membrane peeling may be considered. Surgical decompression of the common adventitial sheath at the block site should still be considered experimental.

REHABILITATION AND FOLLOW-UP

Patients presenting with BRVO and vision better than 20/40 should be followed every 3 to 6 months initially. Once visual acuity has stabilized after 1 year of observation, the follow-up interval can be safely extended.

Patients whose initial visual acuity is 20/40 or worse are recommended for observation at 6- to 12-week intervals. If visual acuity has not improved spontaneously after 3 to 6 months, grid photocoagulation should be considered. Fluorescein angiography may be used in cases with suspected macular nonperfusion, which may mimic macular edema or predispose to neovascularization. Broad areas of capillary nonperfusion (>5 disc diameters) should prompt more frequent follow-up examinations to monitor for neovascularization.

At the first detection of retinal neovascularization, a segmental scatter pattern of photocoagulation is recommended. Once there are stabilization and clearance of the hemorrhage, follow-up intervals ranging from 3 to 6 months initially and somewhat longer thereafter with stabilization should be recommended.

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Case 37

ATROPHIC AGE-RELATED MACULAR DEGENERATION

William E. Smiddy, M.D.

HISTORY

This 81-year-old woman presented for evaluation of macular pigmentary changes. The patient had noted a gradual loss of vision over several years, worse on the right side than on the left, but was not aware of a substantial loss of vision in the right eye. Visual acuity was 20/400 on the right and 20/25 on the left. Amsler grid testing revealed slight metamorphopsia in the right eye, but none on the left. Pupil examination was normal. Slit-lamp examination showed mild lens opacities, slightly worse on the right than on the left. Intraocular pressures were 19 mm Hg and 18 mm Hg, respectively. Funduscopic examination showed cup-to-disc ratios of 0.3 without glaucomatous atrophy. The macular examination was notable for marked retinal pigment epithelial (RPE) depigmentation with pigment clumping, slightly worse in the right macula compared with the left (Fig. 37–1A and B). There was no subretinal fluid, lipid, blood, or exudate.

Because of the severe loss of visual acuity in the right eye, a fluorescein angiogram was obtained to exclude the presence of occult choroidal neovascularization. Window and transmission defects in the RPE were seen, but no exudation was in evidence (Fig. 37–2A and B).

Observational follow-up was recommended, but the patient was instructed to use the Amsler grid to detect early central visual symptoms.

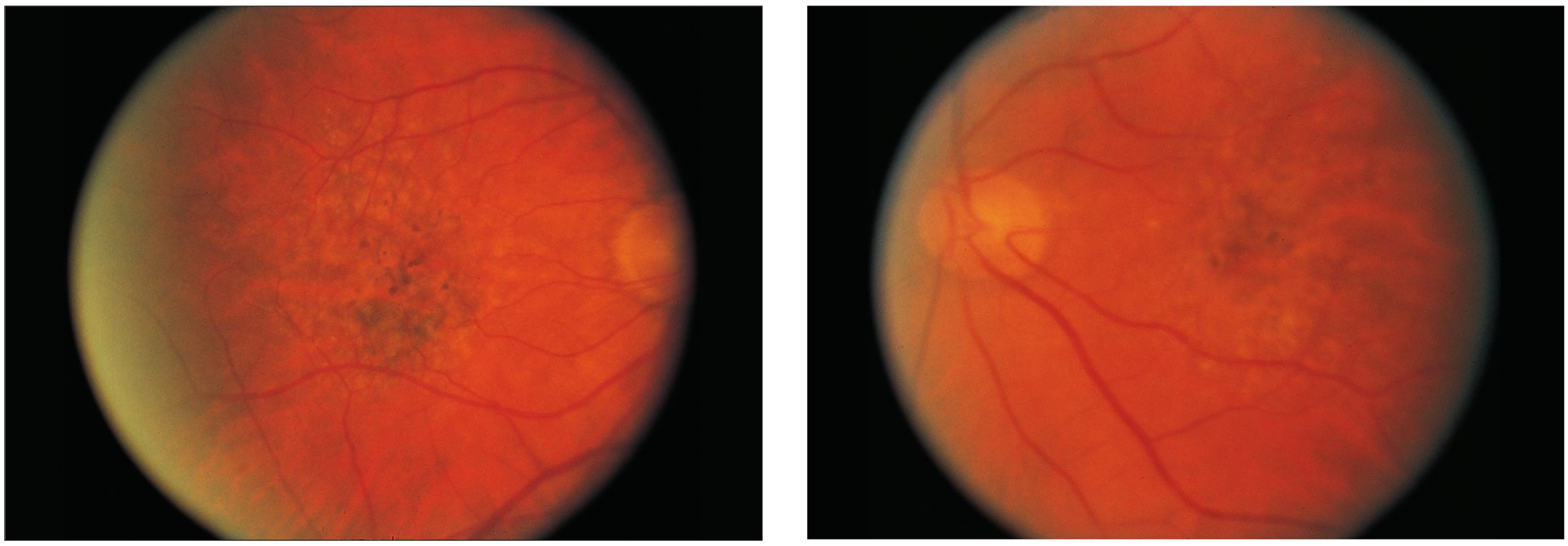
DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Correlating the degree of visual loss to the ophthalmoscopically evident degree of RPE depigmentary change in patients with bilateral drusen may be inaccurate. Confluent, geographic atrophy of the RPE involving the fovea is conspicuously and consistently associated with substantial visual loss (20/200 or worse). A disparity in the visual acuity with substantial visual loss out of proportion to the degree of pigmentation raises the possibility of occult exudative disease or coexisting diagnoses. Common coexisting disease processes include nuclear sclerotic cataract, vascular occlusive disease, amblyopia, or optic neuropathies. The normal clinical history, pupillary responses, and the normal-appearing optic nerve head seem to rule these out.

2. Fluorescein angiography was obtained in this case to rule out choroidal neovascularization. Usually with neovascularization there is subretinal fluid or subretinal or intraretinal hemorrhage. These were lacking in this case, but the visual acuity was much worse in the right compared to the left eye.

3. Surprisingly, the patient was unaware of the severity of the visual loss in the right eye compared to the left. This is not uncommon in patients with unilateral visual loss in general, and in macular degeneration in particular. The possibility of unrecognized visual loss is an important historical feature to consider in making many different diagnoses, but may be especially important in patients with macular degeneration since the likelihood of treatable exudative disease is related to duration of symptoms. Acute visual loss is more characteristic of exudative disease and should prompt a high degree of clinical suspicion.

4. Pattern dystrophies, inflammatory-induced changes, trauma-induced RPE changes, or



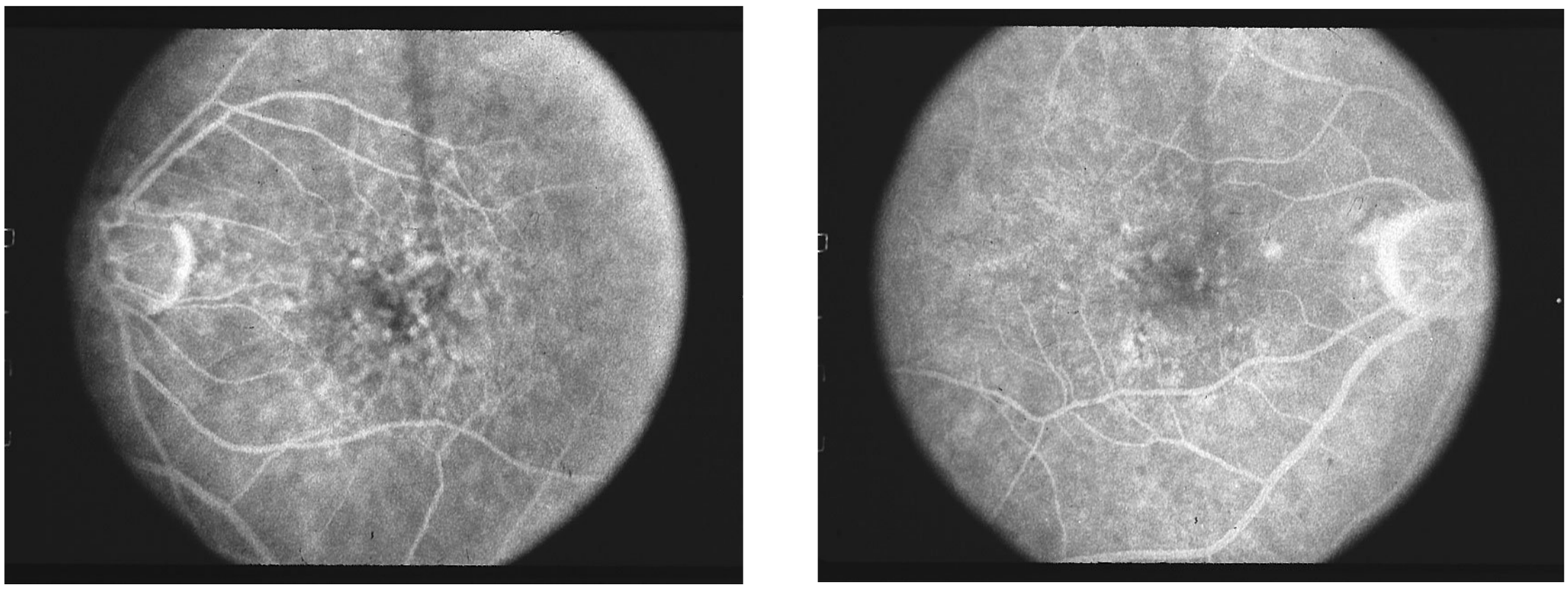
A B

FIGURE 37–1 (A) Funduscopic appearance of patient presenting with 20/400 vision in the right eye. No subretinal fluid was detected, but moderate to marked amount retinal pigment epithelial (RPE) depigmentary changes were in evidence. (B) Funduscopic appearance of the left eye of same patient. Visual acuity was 20/25.

other degenerations such as Stargardt's or cone dystrophy may mimic atrophic age-related macular degeneration (AMD). The pattern of symmetry, or clinical history of onset of visual loss, as well as angiographic features usually allow a distinction between atrophic AMD and these other entities.

TEST INTERPRETATION

Fluorescein angiography is required for determining whether or not exudative disease is present and whether or not it is amenable to laser treatment. Fluorescein angiography may enhance the assessment of the extent of RPE pigmentary changes in atrophic disease, since the contrast



A B

FIGURE 37–2 (A) Fluorescein angiogram of right eye shows widespread retinal pigment epithelial (RPE) depigmentary changes as evidenced by window defects. Centrally, there is some transmission defect due to some pigment clumping. There is no evidence of exudation or choroidal neovascularization. (B) Fluorescein angiographic appearance of left eye. There is a mild to moderate amount of RPE window defects with fewer transmission defects as compared to the right eye.

between depigmented RPE and relatively normal RPE may be less obvious ophthalmoscopically, especially in lightly pigmented patients. Fluorescein was the first dye utilized in angiography and remains the most useful in the majority of cases. Indocyanine green angiography may yield additional information, especially in cases of exudative macular degeneration involving occult neovascularization.

Other testing that might be pertinent in such patients includes tests to rule out other causes of potential visual loss such as a visual field test, color vision, and potential acuity meter testing. Potential acuity meter testing may yield falsely better result in patients with exudative disease.

Another test that is sensitive, but not specific, is the Amsler grid testing. This is a semiquantitative way of ascertaining whether the quality of vision is decreased in a manner consistent with an alteration in the RPE or subretinal space. Although it is only a minority of cases that the Amsler grid test detects transition to exudative disease, it remains a useful tool if applied as a means of monitoring a patient at risk of developing exudative maculopathy.

DIAGNOSIS

Atrophic AMD, OU.

MEDICAL MANAGEMENT

At the current time, patients with AMD are being barraged with a multiplicity of treatment modalities, ranging from vitamin supplements (such as lutein, zinc, or magnesium) to a variety of herbal medications. The rationale for the former is related to the theory that free radical oxidation of RPE constituents, principally its basement membrane, may be the means by which senescence occurs or is hastened. Thus, replacing key components may make the RPE basement membrane more resistant, thereby averting further degeneration. There is an ongoing longitudinal clinical trial for at least one of the vitamin supplements. Studies of dietary supplements of vitamins and carotenoids have yielded mixed results. The rationale for many other alternative medications available is based on anecdotal experience as controlled clinical trials are lacking. The results of a prospective trial evaluating thalidomide to prevent exudative complications are pending.

There has been some concern that excessive UV light may accelerate the oxidative process that may be accelerating macular degeneration. For this reason, UV blocking intraocular lenses and spectacle lenses have been proposed, but the benefit of shielding from UV radiation is unproven.

SURGICAL MANAGEMENT

No rationale is available for intraocular surgery for patients with atrophic macular degeneration. Laser treatment, however, has been reported by some to hasten the resolution of macular drusen. The rationale for laser treatment is to stimulate limited RPE proliferation to "rejuvenate" the function by replacing senescent RPE cells. Preliminary results suggesting the possibility that drusen reduction decreases vascularization have not been corroborated. Indeed, at least one large trial has found that laser treatment increases the risk of choroidal neovascularization associated with the laser, but its clinical significance is minimal.

REHABILITATION AND FOLLOW-UP

Low vision aids are the primary rehabilitative tools for patients with substantial visual loss. These usually restore a marginal degree of visual function but may be helpful for specific tasks. The key component in the patient with limited macular function is identifying the most convenient and effective means of providing magnification and delivering light to the subject material. Frequently, patients find that focused light is helpful, whereas bright overhead lights tend to be too diffuse to be of benefit. For distance vision, a variety of telescopic aids are available, but magnification comes at the expense of

constricting the visual field. High technology aids utilizing microprocessors hold promise but are not practical as yet. Patients considering low-vision evaluation must be counseled candidly as to the limits of potential benefits. Still, low-vision aids offer at least a modest degree of satisfaction to a majority of patients.

Patients with atrophic macular degeneration are routinely counseled to use the Amsler grid test for optimal diagnosis of transition to exudative disease. In addition, they are encouraged to evaluate each eye's perception independently for deviation of straight lines such as those in doorways, light poles, and building edges.

Examination every 3 to 12 months is generally recommended by most investigators. The follow-up interval for patients with atrophic macular degeneration is usually shorter for patients with one or more of the risk factors for progression to exudative complications. Identified risk factors include larger size of drusen (>63 microns), increased number of drusen (75), focal RPE hyperpigmentation, and systemic hypertension. The risk is also increased for patients with exudative disease in the fellow eye (approximately 5% annual incidence of progression to exudative disease). Regardless of scheduled follow-up, it is emphasized to the patient that any changes in visual symptoms, especially increased metamorphopsia, should prompt immediate reevaluation.

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Case 38

EXUDATIVE AGE-RELATED MACULAR DEGENERATION

William E. Smiddy, M.D.

HISTORY

This 88-year-old woman presented with a 1-week history of seeing a spot in the left eye. There was a 10-year history of atrophic macular degeneration noted.

Examination showed vision of 20/25 in each eye. Amsler grid testing demonstrated diffuse central metamorphopsia. There was no definite afferent pupillary defect. Slit-lamp examination showed the patient to be aphakic. Intraocular pressures were 14 in each eye. Funduscopic examination on the right showed drusen with retinal pigment epithelial (RPE) changes in the macula. On the left, there was about a 1 disc diameter subretinal hemorrhage centered temporal to center of the fovea (Fig. 38–1). The nasal edge of the hemorrhage came within ½ disc diameter of the center of the macula.

Because of the fairly dense subretinal hemorrhage, fluorescein angiography was deferred. The patient brought a fluorescein angiogram obtained with another consultant approximately 1 week before presentation, with inconclusive results. The patient returned for a follow-up examination 2 weeks later. There was still moderate subretinal hemorrhage and fluorescein angiography was deferred. When the patient returned about 3 weeks later the visual acuity was still 20/25 and the hemorrhage had cleared substantially (Fig. 38–2). Fluorescein angiography (Fig. 38–3) and indocyanine green (ICG) examination (Fig. 38–4) showed a choroidal neovascular membrane that appeared to be confined to an extrafoveal location. The patient underwent treatment of choroidal neovascular membrane using the argon blue-green laser (Fig. 38–5).

Visual acuity 3 months following treatment remained 20/25 with no sign of recurrence.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Subretinal hemorrhage is typically a consequence of subretinal choroidal neovascularization. However, in rare instances severe intraretinal hemorrhages from retinal vascular disease, trauma, or a retinal tear may also lead to subretinal hemorrhage.
2. Subretinal hemorrhages may extend substantially, even after initial onset. Usually with choroidal neovascularization there is relatively localized hemorrhage; less commonly, a massive subretinal hemorrhage may affect the entire macula or be even more extensive.
3. The differential diagnosis of subretinal hemorrhage is, for the most part, the differential diagnosis of subretinal choroidal neovascularization. The most common cause of choroidal neovascularization is age-related macular degeneration. The hallmark of macular degeneration is the RPE change with drusen. These should be demonstrable either within the same eye or in the fellow eye. The presumed ocular histoplasmosis syndrome is another common cause of choroidal neovascularization but is usually accompanied by other stigmata such as atrophic "punched out" choroidal scars ("histo spots"). A third cause of subretinal neovascularization and hemorrhage is myopic degeneration with widespread RPE depigmentary changes or staphyloma formation. A fourth category is so-called idiopathic neovascularization. Other causes are much rarer.
4. The clinician should define the presence of choroidal neovascularization. This is often

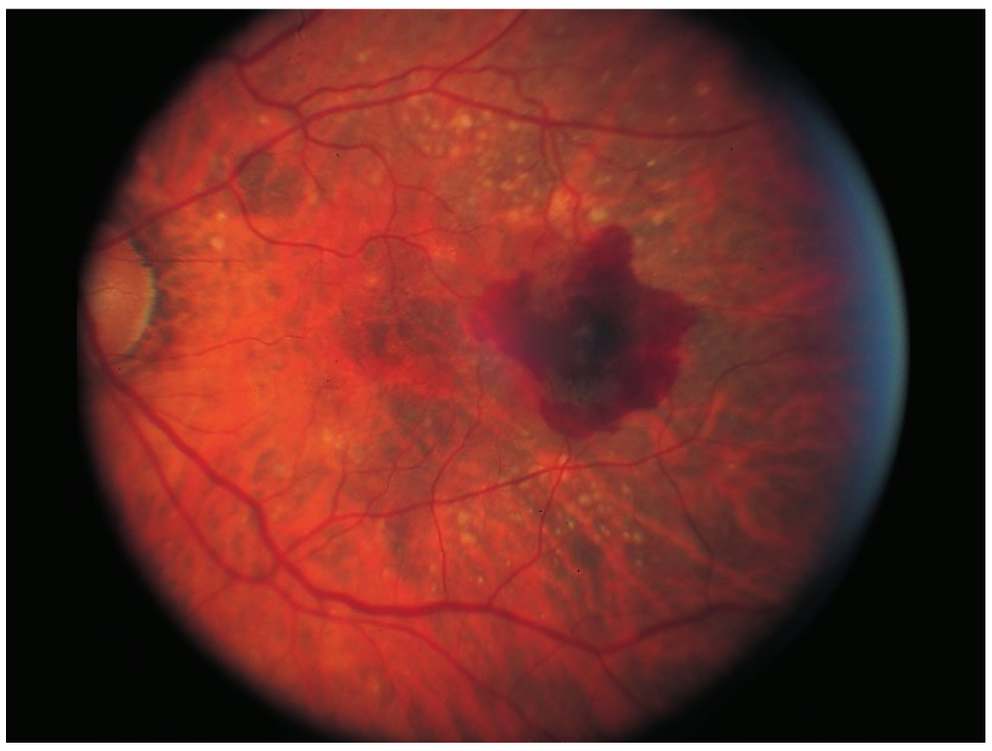

FIGURE 38–1 Funduscopic appearance of patient presenting with a 1-disc diameter region of subretinal blood OS. The lesion is centered temporal to the fovea and does not appear to underlie its center.

impossible when the neovascular membrane is at least partially obscured by subretinal hemorrhage. In such cases it may not be possible to treat because of blocked transmittance of the incident laser light. Incomplete treatment may be worse than no treatment in that choroidal neovascularization may grow more rapidly after incomplete treatment.

5. The location of the choroidal neovascularization or blood is directly related to the visual acuity, prognosis, and amenability to laser treatment. Extrafoveal membranes characteristically affect the vision minimally and are most amenable to treatment, whereas subfoveal membranes typically have a more profound effect on the vision and respond less well to treatment.

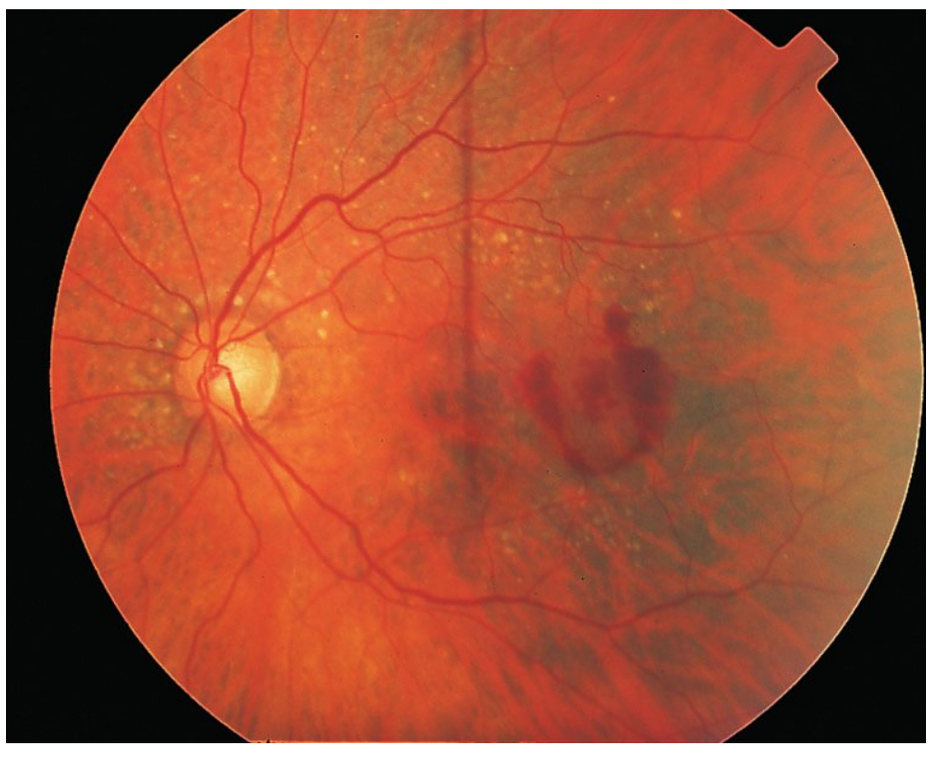

FIGURE 38–2 Funduscopic appearance 5 weeks after presentation with partial resolution of the subretinal blood OS. Features of choroidal neovascularization can now be seen sandwiched between two thin zones of persistence of subretinal blood.

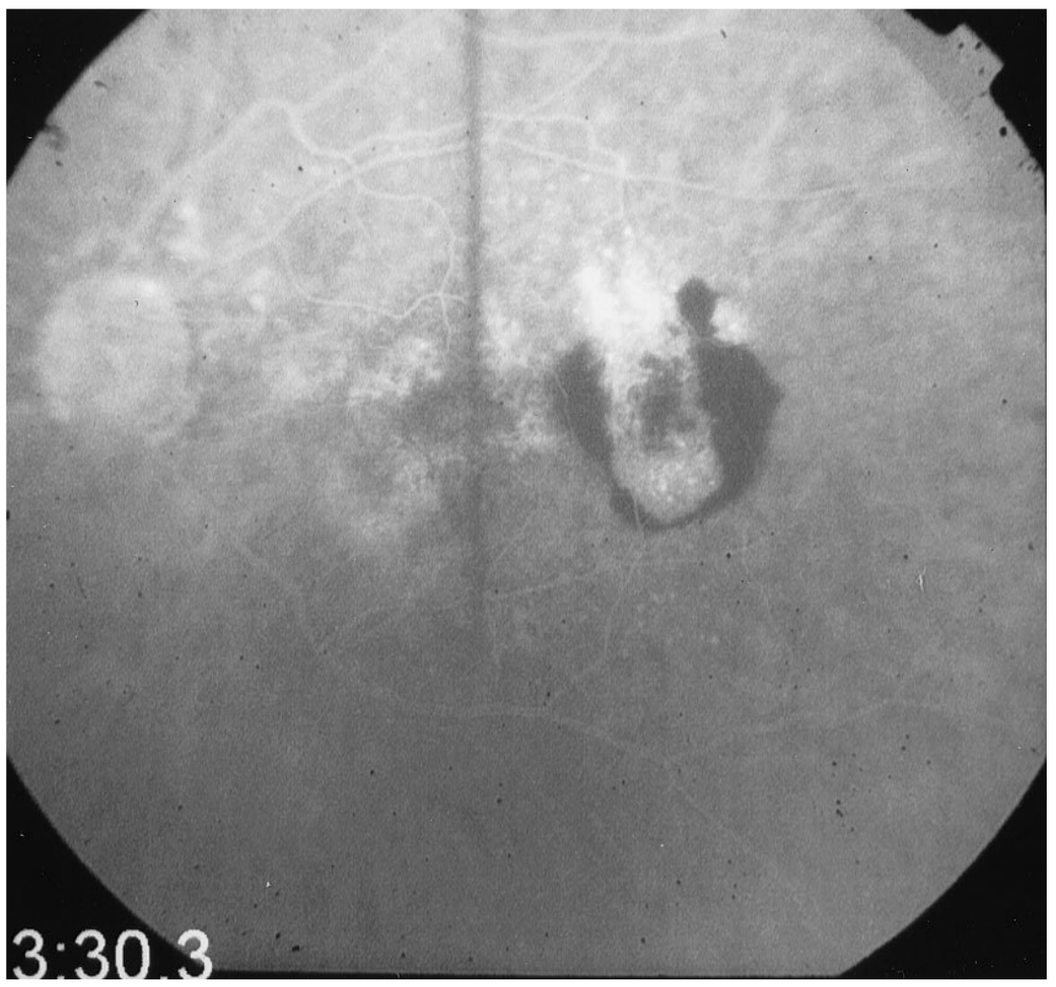

FIGURE 38–3 Fluorescein angiographic appearance of the patient 5 weeks after presentation shows choroidal neovascularization OS, but with blocked transmittance from the overlying subretinal hemorrhage nasally and temporally.

TEST INTERPRETATION

Fluorescein angiography is the gold standard for defining characteristics and location of choroidal neovascularization. An extrafoveal membrane is located greater than 200 microns from the center of the fovea. A juxtafoveal membrane is located within this zone, but not underlying the center. A subfoveal membrane involves the foveal center. A classic choroidal neovascular membrane demonstrates filling in the early frames, with leakage of the membrane in the later frames. Such features are used to define either "classic" or "nonclassic" portions of the membrane. The terms poorly defined or occult choroidal neovascularization describe membranes that are more extensive than the area of apparent dye leakage. These augur a worse prognosis with treatment.

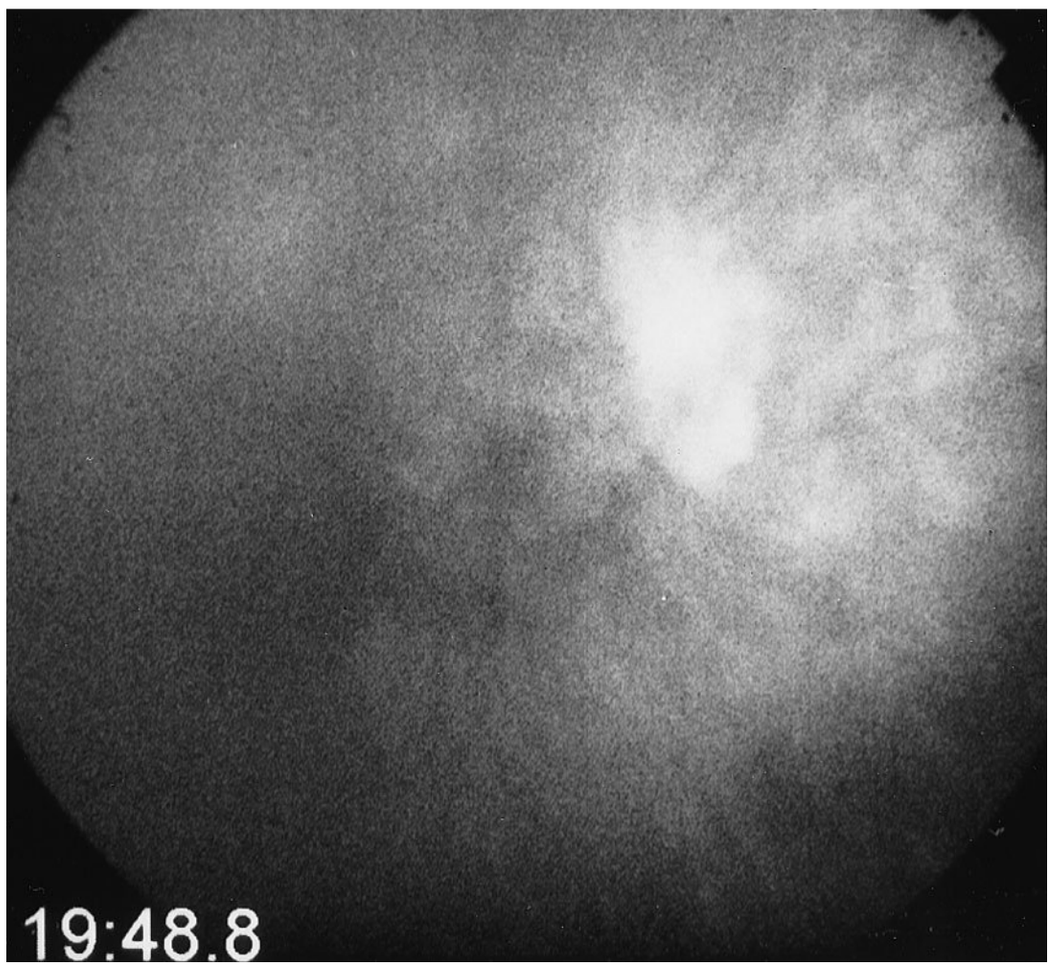

FIGURE 38–4 Indocyanine green (ICG) angiographic appearance of same patient at the same time showing the limited extent of the choroidal neovascular membrane. Some late transmittance extending more broadly involving the entire central retina may represent early, occult choroidal neovascularization, but this finding is not a diagnostic feature.

The quality of fluorescein angiography may be limited by the presence of subretinal blood. Whenever more than an approximately 50-micron thickness layer is encountered, incident light and radiant fluorescence are relatively blocked, obscuring the fluorescein angiographic filling features of the choroidal neovascular membrane.

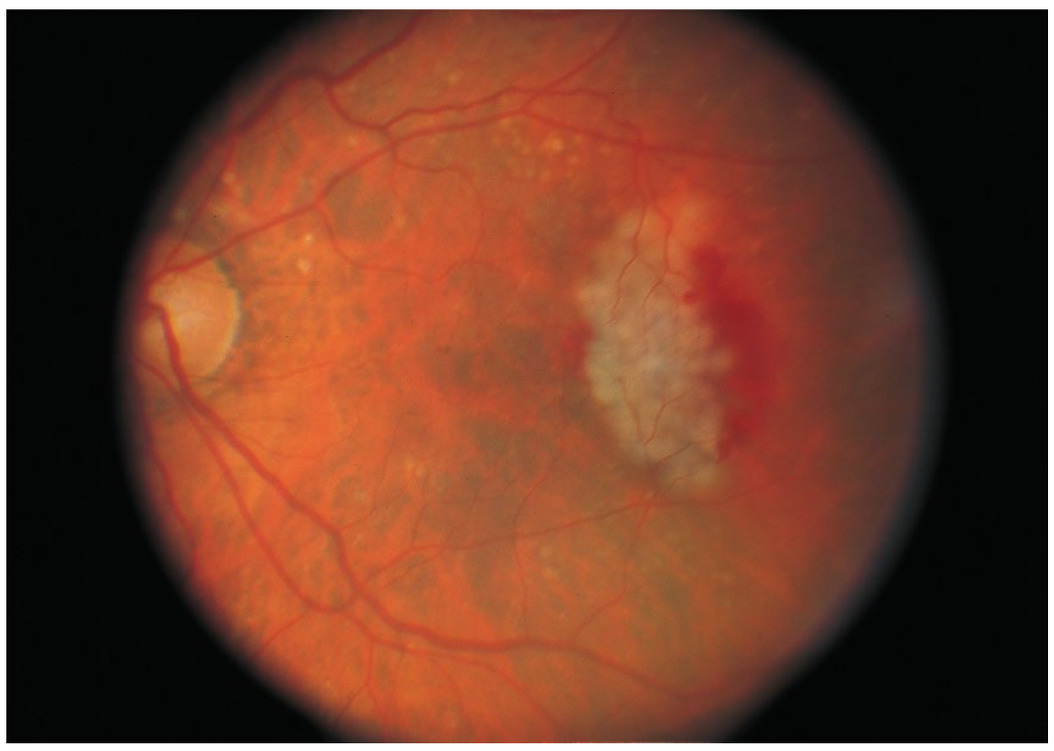

FIGURE 38–5 Appearance immediately after confluent argon blue-green laser treatment to the lesion.

Neovascular membranes may be imaged by ICG angiography. ICG offers the advantage that the wavelength of ICG dye can traverse at least thin layers of blood. However, the image is not as discrete compared to fluorescein angiography. Similar to the fluorescein angiogram, choroidal neovascularization is evident by extravasation of dye corresponding to the region of the neovascularization. In addition, other plaque-like areas of fluorescence may correspond to occult choroidal neovascularization.

The fluorescein angiogram allows differentiation of a detachment of the neurosensory retina or pigment epithelium from choroidal neovascularization. These diagnostic distinctions are important since treatment is based on the diagnosis.

DIAGNOSIS

Subretinal neovascularization with subretinal hemorrhage secondary to age-related macular degeneration, OS.

MEDICAL MANAGEMENT

The first established treatment of choroidal neovascularization was laser photocoagulation. The Macular Photocoagulation Study (MPS) showed that laser treatment lowers the risk of severe visual loss for classic extrafoveal neovascular membranes from 62% for untreated eyes to 48% at 5 years for treated eyes. The treatment benefits are greatest in the first 2 post-treatment years and for patients with an initial visual acuity of 20/100 or better.

The differences are lower with longer follow-up due to a recurrence rate after treatment of about 50%. For juxtafoveal choroidal neovascular membranes, the benefits were greatest for normotensive patients and eyes with classic-only neovascularization.

Eyes with subfoveal membranes had poorer prognoses in both groups. An algorithm for treatment has been proposed such that smaller lesions (less than 2 disc area) with worse levels of vision (less than 20/200) are usually recommended for treatment, whereas eyes with

larger lesions or better initial visual acuity are more likely to be observed without treatment.

The treatment technique involves the use of the argon laser for extrafoveal lesions and, commonly, a red or yellow laser wavelength for subfoveal or juxtafoveal lesions. Overlapping burns are placed with 200- to 500-micron spot sizes to cover the entire membrane. A 0.2- to 0.5-second burn duration is commonly employed. Treatment is first applied on the foveal side, subsequently around the edges, and finally in the middle of the membrane to yield a confluent, chalky-white burn. The endpoint is slightly less intense for red laser burns compared to green laser burns. The advantage of the red laser is its retinal transmittance rather than its absorption, yielding more selective destruction of the neovascular membrane. Treatment complications can include a Bruch's membrane rupture, which may be associated with additional subretinal bleeding or additional neovascularization. Recurrences even in the groups with the best prognosis (ie, extrafoveal cases) were found to occur in 57% of eyes over a 4-year follow-up in the Macular Photocoagulation Study. Treatment of retinal pigment epithelial lesions has not shown benefit.

A new treatment with encouraging results has been photodynamic treatment. A dye that has an affinity for choroidal neovascular vessels is injected intravenously. Shortly after injection, a laser with a wavelength matched to the absorptive characteristics of the dye is applied at low energy and long duration to a zone including the area of suspected choroidal neovascularization. This so-called cold laser has been found to reduce the risk of visual loss in patients with mostly classic and all occult choroidal neovascularization. Recurrences are common in patients undergoing this treatment modality and repeat treatment is usually necessary.

Radiotherapy has not conclusively demonstrated a treatment benefit. Transpupillary thermal treatment using long duration, low power diode laser burns is currently under investigation.

SURGICAL MANAGEMENT

Patients with breakthrough vitreous bleeding from choroidal neovascularization may be suitable candidates for vitrectomy for removal of nonclearing hemorrhages. While this may restore use of peripheral retina, it does not restore function in the zone of subretinal hemorrhage or neovascularization.

Surgical evacuation of subretinal hemorrhage has shown limited positive results. Adjuncts such as using tissue plasminogen activator may facilitate the blood removal, but long-term visual outcome results are still questionable. Initial surgical approaches involve the use of large retinotomies for the removal of choroidal neovascularization and severe hemorrhage. Visual results were very poor in these cases, however.

Excision of subretinal membranes is considered principally for patients with subfoveal neovascularization due to the poor natural history of such cases and the minimal treatment benefit demonstrated for laser treatment compared to other localities. The subfoveal surgery results for age-related macular degeneration have been disappointing, whereas excision of membranes due to presumed ocular histoplasmosis syndrome or idiopathic cases is more encouraging. Histopathologic studies of excised membranes have indicated that in macular degeneration more frequently the membranes are present in a sub-RPE location, whereas in other diagnoses the membrane may be subretinal (anterior to RPE). Accordingly, excision of membranes that preserve the RPE are associated with better visual prognoses. Refinement of surgical instruments and techniques has allowed the use of very small retinotomies for removal of membranes. However, the removal of the RPE and the recurrence of choroidal neovascularization have limited the surgery in most patients.

A newer surgical technique is macular translocation. A detachment of the posterior retina is induced, a scleral buckling effect is created by imbrication and, with fluid-gas exchange, the reattached retina is translocated away from the choroidal membrane. A limitation of this technique, however, has been that the retina can only be moved approximately 500 microns. Hence, only eyes with relatively small and acute choroidal neovascular membranes are candidates for macular translocation.

REHABILITATION AND FOLLOW-UP

Macular degeneration is the most common cause of significant, irreversible visual loss in the elderly population. Low-vision rehabilitation, including magnifiers and focused lights, should be considered in these cases. However, before embarking on the purchase of such equipment, the patient must be counseled as to the limitations and expense involved.

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Case 39

MYOPIC DEGENERATION

William E. Smiddy, M.D.

HISTORY

A 38-year-old urologist presented with a 1-year history of visual loss in the right eye. He had been told that he had a choroidal neovascular membrane in that eye that was not amenable to any treatment. At the time of presentation, he had a 1-month history of distortion with a paracentral scotoma in his left eye. The patient was noted to be a high myope with a spherical equivalent refraction of −10 diopters.

Examination disclosed vision of 20/200 in the right eye and 20/20 in the left eye. The slit-lamp examination was unremarkable. The funduscopic examination showed a tilted (myopic) disc and a pigmented choroidal neovascular membrane surrounded by pigment epithelial atrophy (Fig. 39–1). In the left eye there was a similar tilted myopic disc with a prominent lacquer crack extending across the superior aspect of the fovea with some hemorrhage on the nasal side of the fovea (Fig. 39–2). The fluorescein angiogram confirmed the large subfoveal choroidal neovascular membrane in the right eye (Fig. 39–3). However, it also showed small, extrafoveal choroidal neovascular membranes superior to the left fovea as well as inferonasal to it.

No treatment was recommended for the right eye. Argon blue-green laser treatment was recommended and performed for the choroidal neovascular membrane in the left eye. The patient maintained 20/20 vision in the left eye without recurrent neovascularization for 6 years.

He then returned with a 1-month history of decreased central vision in the left eye. He characterized the loss of vision as finding everything to be cloudy. The visual acuity was 20/200 in the right eye and 20/30 in the left eye. The slit-lamp examination was unremarkable. The funduscopic examination of the right eye showed a somewhat enlarged area of retinal pigment epithelium atrophy approximately 3 times the size of the original (untreated) choroidal neovascular membrane. There were signs of chronic leakage. In the left eye there was a nearly 1-disc-area region of retinal pigment epithelial (RPE) atrophy corresponding to the previous laser treatment scar. However, along the inferior and temporal (foveal side) of this there was evidence of recurrent choroidal neovascularization (Fig. 39–4).

Laser treatment was performed utilizing the krypton laser in the left eye. The patient returned to Peru for further follow-up examination locally.

The patient had a history of glaucoma for which he was using Propine drops OU initially. Upon presentation, his glaucoma regimen had been changed to a beta-blocker OU. The intraocular pressures were 14 mm Hg in the right eye and 13 mm Hg in the left eye on second presentation and 9 mm Hg in the right eye and 12 mm Hg in the left eye upon initial presentation. Also, retinal lattice degeneration was noted in the periphery of both eyes although no atrophic holes were seen in association with this.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The patient was a high myope (−1D). Myopic degeneration characteristically occurs only in patients with high myopia (6 diopter refractive error).
2. The characteristic appearance of a highly myopic patient includes an oblique, tilted optic nerve head. As in this case, a variable amount of peripapillary RPE atrophy may frustrate a major parameter that a physician may use to chart the course of the coexisting glaucoma.
3. The patient also had retinal lattice degeneration, without atrophic holes. Prophylactic

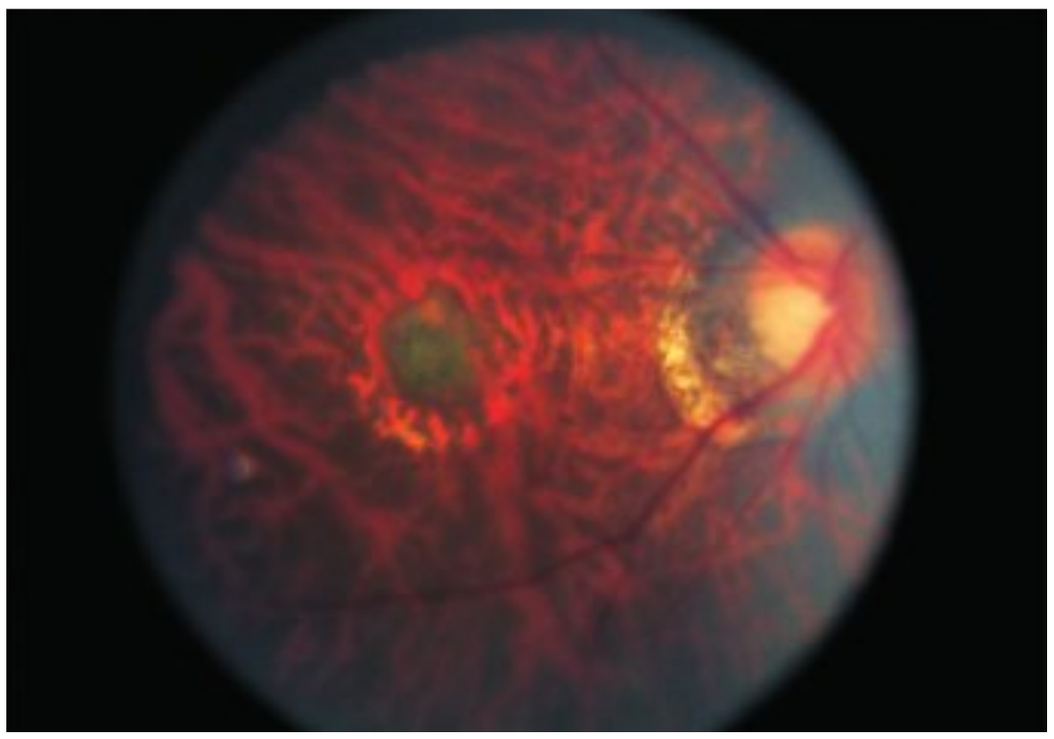

FIGURE 39–1 Funduscopic appearance of right eye at presentation. A rim of retinal pigment epithelial atrophy surrounds a central area of choroidal neovascularization. The optic nerve head is tiled with some peripapillary atrophy. The vision was 20/200.

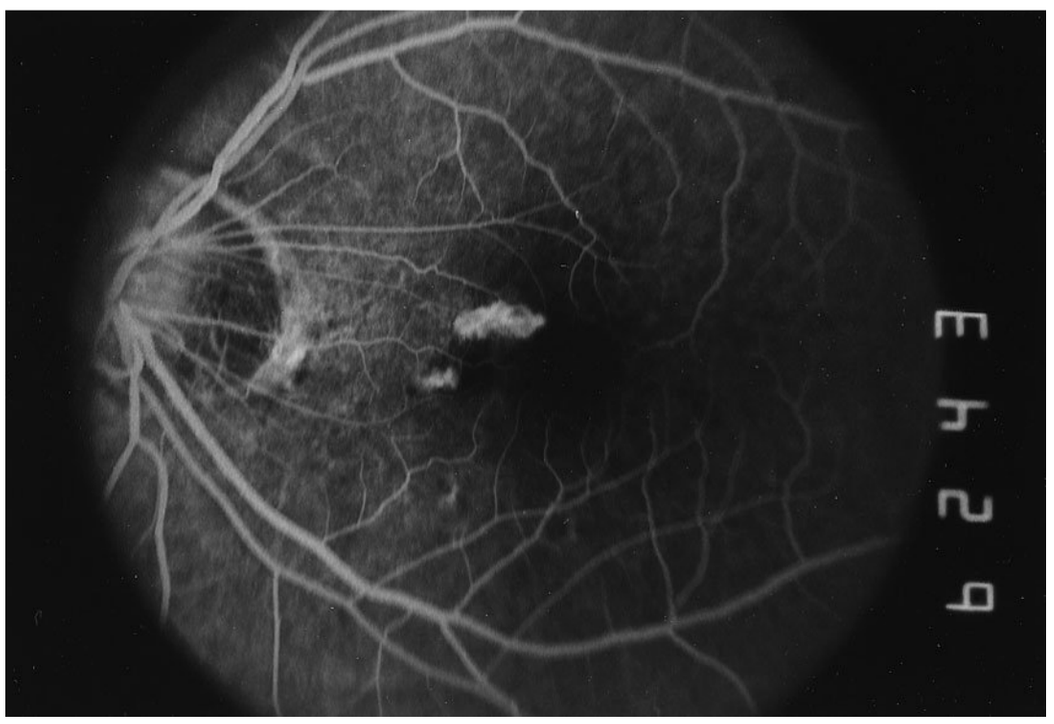

FIGURE 39–3 Fluorescein angiographic appearance of the left eye at initial presentation. It shows a choroidal neovascular membrane just above the fovea as well as a smaller one inferonasal to fovea.

treatment of such lesions is probably not indicated at this stage. If the fellow eye (especially if highly myopic) developed a retinal detachment then the patient would be at a higher risk for developing a retinal detachment in the fellow eye and prophylactic laser or retinocryopexy treatment should be considered, but many would still not recommend treatment.

4. The fluorescein angiogram and clinical features show characteristic features of choroidal neovascularization. There are several conditions that may be the cause of choroidal neovascularization. Most common is age-related macular degeneration, unlikely in this young patient. Other causes of choroidal neovascularization include presumed ocular histoplasmosis syndrome (POHS), which is usually accompanied by atrophic chorioretinal scars ("histo spots") which are distributed throughout the retina, typically most prominently in the mid periphery. These were not present in this case. Any chorioretinal scar,

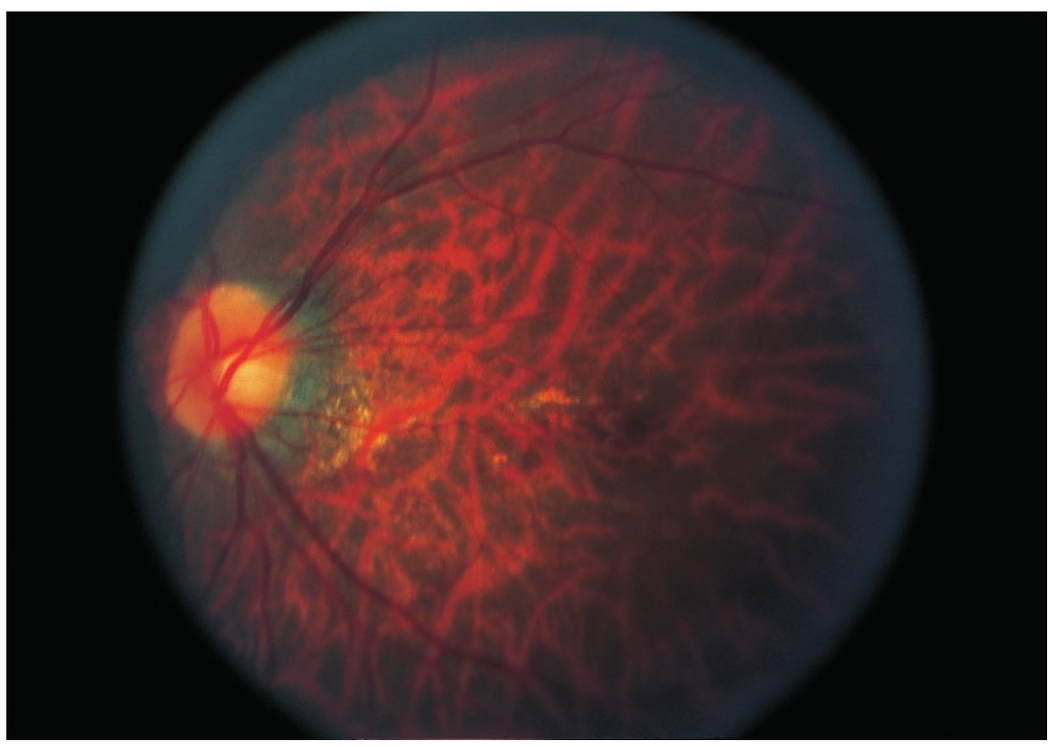

FIGURE 39–2 Funduscopic appearance of left eye. A lacquer crack is evident coursing across the superior macula. Along the nasal aspect of this is slight subretinal fluid consistent with a choroidal neovascular membrane.

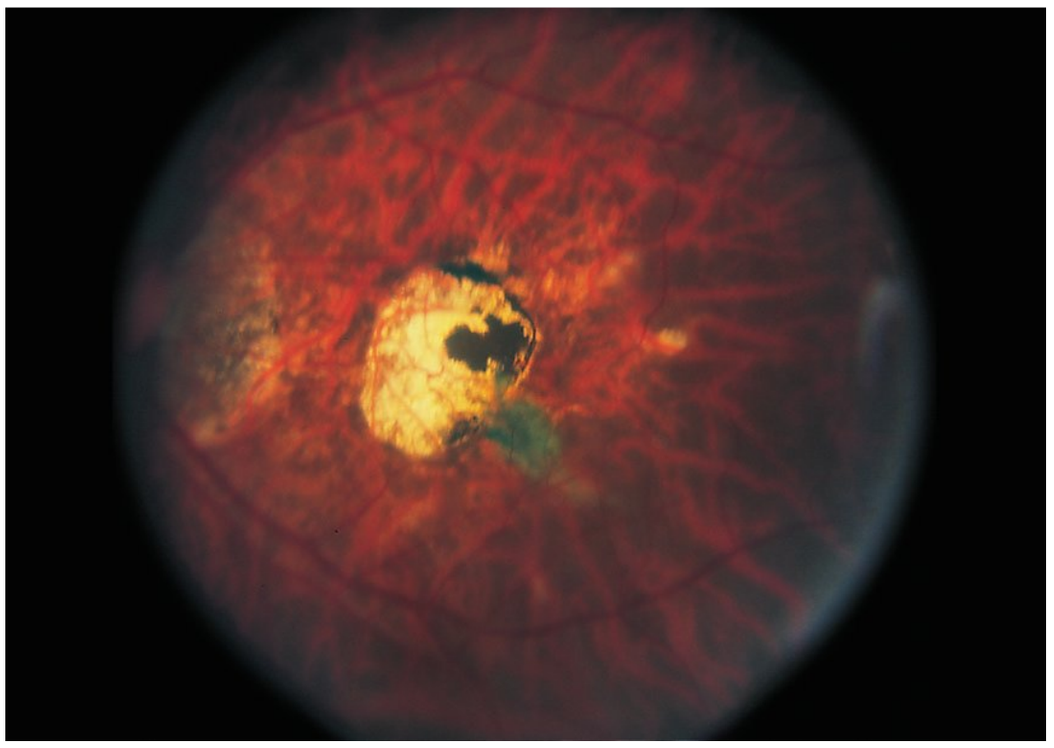

FIGURE 39–4 Fluorescein angiographic appearance 6 years after treatment confirms a juxtafoveal recurrence of the choroidal neovascularization inferior and temporal to the original scar.

whether it is from previous inflammatory or from infectious chorioretinitis, may ultimately give rise to choroidal neovascularization.

5. A trauma-induced choroidal rupture may also be the site of choroidal neovascularization and should be considered in the differential diagnosis.

TEST INTERPRETATION

Aside from clinical examination, the fluorescein angiogram forms the mainstay for diagnosis and delineation of a choroidal neovascular membrane. The indocyanine green may also contribute information regarding the nature and location of more poorly defined choroidal neovascularization. Combined A- and B-scan ultrasonography may demonstrate the increased axial length or a staphyloma that commonly accompanies patients with myopic degeneration.

DIAGNOSIS

Subretinal choroidal neovascularization and recurrence secondary to myopic degeneration, OU.

MEDICAL MANAGEMENT

In uncontrolled trials and isolated case reports, corticosteroids have reportedly produced variable regression of choroidal neovascularization. Laser photocoagulation is the treatment for selected neovascular membranes. Choroidal neovascularization is seen in about 5% of patients with axial length 26.5 mm, is bilateral in 12% of those cases, and is often represented as a Fuchs' spot—a subfoveal dark spot generally accepted to represent a late, self-limited stage of neovascularization.

There may be two types of neovascularization, with elderly patients having a more progressive form of vessel growth and younger patients frequently having a more focal, self-limited form that causes less visual loss. Lacquer cracks (characteristic breaks in Bruch's membrane) appear to represent the point of entry for choroidal neovascularization, as they have been found to be more frequent in cases with neovascular membranes.

Frequently, the patient will present with focal, well-defined choroidal neovascularization surrounded by RPE atrophy. Such cases (as in this patient's right eye) are characteristically not accompanied by significant subretinal fluid. In contrast with age-related macular degeneration, the progression of such neovascularization is frequently limited and, accordingly, most cases with choroidal neovascularization due to myopic degeneration are not recommended for laser treatment.

Principles regarding treatment of choroidal neovascularization are inferred from results of macular photocoagulation studies. Characteristically, argon green or argon blue-green photocoagulation is used for extrafoveal lesions; subfoveal lesions, if treated at all, are characteristically treated with krypton red photocoagulation. The rationale is that the red wavelengths typically penetrate the retinal tissues with less "runoff" damage to adjacent and overlying retina. While this has been generally established for age-related macular degeneration, it has not been vigorously established to be clinically significant for patients with myopic degeneration.

New developments utilizing photodynamic treatment (PDT) of choroidal neovascularization hold promise for the potential of using lower power levels of laser photocoagulation over a broader zone to coagulate and induce involution of choroidal neovascularization without destroying unaffected adjacent and supra-adjacent tissues. The subgroup of patients with subfoveal myopic degeneration has been shown to have a better prognosis with PDT compared to untreated controls.

SURGICAL MANAGEMENT

Surgical options to consider include vitrectomy with excision of the subretinal choroidal neovascular membrane, or macular translocation. Published experience has been very limited in such cases. The relatively self-limited nature of the growth of the choroidal neovascular membranes may not justify these treatments. Patients with relatively fewer

associated RPE atrophic changes are more frequently considered for surgery than those with evidence of more widespread RPE disease.

REHABILITATION AND FOLLOW-UP

Patients with nonexudative myopic degeneration may commonly suffer visual symptoms just as severe as those with exudative complications. Specifically, a loss of central vision from a moderate-to-severe degree is extremely common. Patients are typically recommended for follow-up examinations once or twice annually; however, patients should monitor their central visual acuity with an Amsler grid. New distortion or central metamorphopsia should prompt ophthalmological consultation.

The decision to treat is based on the location and associated degree of chorioretinal scarring; lesions rarely change in a way that reverses an initial nontreatment recommendation.

Patients should be followed after treatment for recurrent choroidal neovascularization (which occurs in about a third of cases) more frequently initially, and less frequently when the treatment appears to have induced stabilization. An evaluation should be performed 2 to 3 weeks following initial treatment, 2 to 3 weeks later, and 8 to 12 weeks following treatment. Thereafter, 3- to 6-month examination intervals are commonly recommended.

Rehabilitation efforts include the use of low-vision aids. Typically, with the loss of macular function, the need for magnifiers and focal delivery of light are the general strategies. These may take the form of high plus lenses in a spectacle, magnifying loupes, telescopic magnification lenses, or closed circuit video instruments. There is some promise in the possible use of implantable microchip technology, but as yet this is not clinically feasible.

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Case 40

IDIOPATHIC CENTRAL SEROUS CHORIORETINOPATHY

Arezo Amirikia, M.D.

HISTORY

A 40-year-old man, a corporate lawyer, presented with a 2-week history of blurred and distorted vision in his right eye. Past medical history was unremarkable. Past ocular history was significant for hyperopia (+2.50 sphere).

Vision was 20/60 in the right eye and 20/20 in the left. Vision in the right eye improved to 20/25 with an additional +1.75 sphere. Amsler grid testing of the right eye demonstrated central metamorphopsia. Intraocular pressures and slit-lamp examination of both eyes were unremarkable. Dilated funduscopic examination of the right eye was notable for a round neurosensory detachment involving the fovea (Fig. 40–1). There was no associated hemorrhage or exudate and the media was clear. Examination of the left eye was notable for mild stippling of the retinal pigment epithelium (RPE) within the macula. Fluorescein angiogram of the right eye revealed an area of early pinpoint leakage within the macula with increasing fluorescence superiorly into a "smokestack" configuration (Fig. 40–2).

At 3 months following presentation, despite visual improvement to 20/20, the patient complained of persistent distortion in the affected eye. Examination revealed complete resolution of the neurosensory detachment in the right eye with minimal RPE alterations.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The differential diagnosis of a serous retinal detachment involving the macula includes a variety of systemic and ocular conditions (Table 40–1). The history is helpful in eliminating several of these conditions including malignant hypertension, toxemia of pregnancy, disseminated intravascular coagulopathy, and sympathetic ophthalmia.

A congenital optic pit may present with a serous detachment that is contiguous with the margin of the optic disc. Vogt-Koyanagi-Harada's disease could present as a serous retinal detachment, but typically presents with multiple serous detachments in both eyes with vitreous cells and multiple areas of leakage on fluorescein angiography. Patients with this condition may have systemic symptoms including poliosis, vitiligo, and tinnitus and rapidly respond to oral corticosteroids. Choroidal tumors with an overlying serous retinal detachment would be visible on clinical examination. Posterior scleritis and uveal effusion syndrome demonstrate thickening of the sclera on B-scan ultrasonography. Subretinal neovascularization secondary to age-related macular degeneration should be a consideration, especially in an older individual. These eyes typically present with bilateral drusen, and the affected eye may have a serous macular detachment in association with hemorrhage and exudate. Fluorescein angiography may demonstrate choroidal neovascularization.

2. The presence of a unilateral serous macular detachment, the absence of other ocular findings, and the "smokestack" phenomenon on fluorescein angiography are most consistent with the diagnosis of idiopathic central serous chorioretinopathy (ICSC).

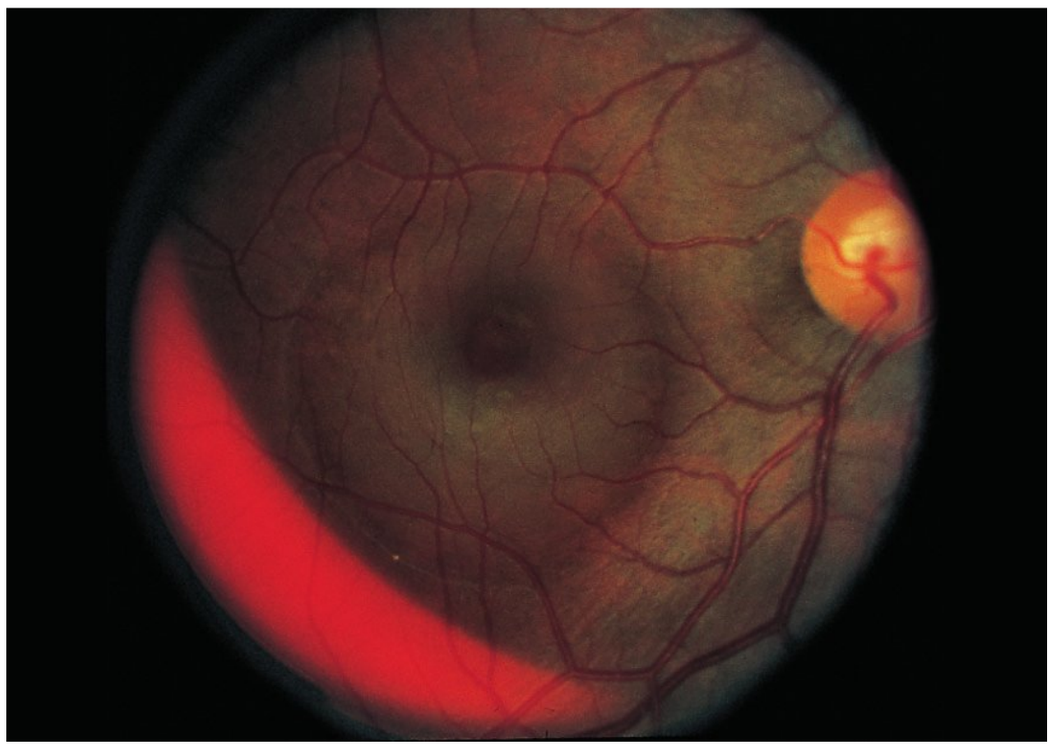


FIGURE 40–1 Fundus photograph of the right eye notable for a round neurosensory detachment involving the macula.

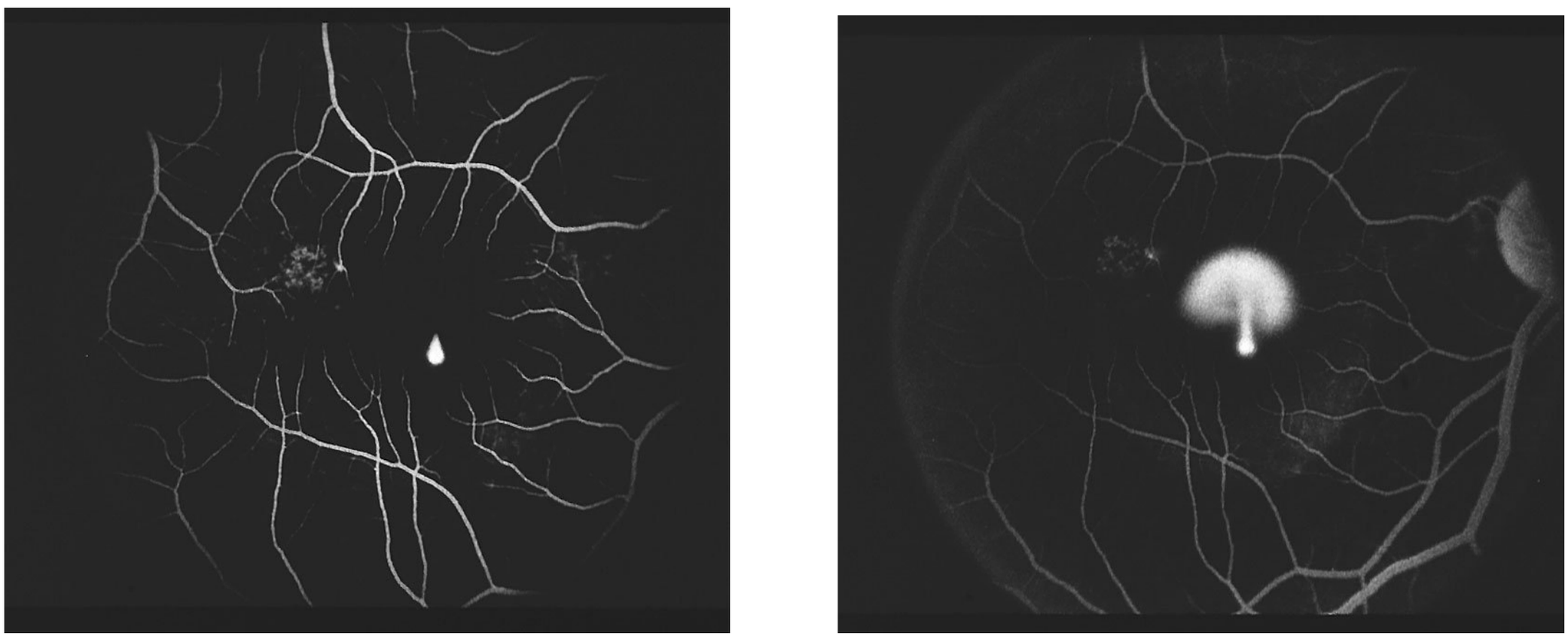
3. In addition to central metamorphopsia, micropsia is a common symptom reported by patients with a serous neurosensory macular detachment.

TABLE 40–1 **Etiology of Serous Retinal Detachment Involving the Macula**

Central Serous Chorioretinopathy
Cushing's Syndrome
Idiopathic
Pregnancy
Systemic Lupus Erythematosus
Choroidal Tumors
Choroidal Hemangioma
Choroidal Melanoma
Choroidal Osteoma
Leukemia
Metastatic Carcinoma
Congenital Optic Pit with Neurosensory Detachment
Crohn's Disease
Malignant Hypertension
Posterior Scleritis
Subretinal Neovascularization
Age-Related Macular Degeneration
Presumed Ocular Histoplasmosis Syndrome
Sympathetic Ophthalmia
Uveal Effusion Syndrome
Vitreomacular Traction Syndrome
Vogt-Koyanagi-Harada's Disease

TEST INTERPRETATION

The diagnosis of ICSC requires a combination of history, clinical examination, and fluorescein angiography. The history can eliminate other systemic conditions that may result in central serous chorioretinopathy similar to ICSC including pregnancy, organ transplantation, Cushing's syndrome, and systemic lupus erythematosus. Patients with ICSC are more commonly male with a type-A personality pattern. Patients present with



A B

FIGURE 40–2 Fluorescein angiogram of the right eye reveals an area of early hyperfluorescence (A) with a classic "smokestack" configuration in the late frames (B).

a several-week history of blurred vision with metamorphopsia or micropsia.

Examination may reveal variable vision and a hyperopic shift. Slit-lamp biomicroscopy typically demonstrates a round or oval neurosensory detachment or less commonly a pigment epithelial detachment. RPE stippling may be present in the involved or fellow eye implying a previous episode. Atypical presentations include bullous retinal detachment, cystoid macular edema, atrophic RPE tracks, "bull's eye" RPE window defects, or subretinal fibrosis.

Fluorescein angiography may be necessary to confirm the diagnosis of ICSC and to exclude such entities as subretinal neovascularization secondary to a variety of conditions. Fluorescein angiography in eyes with ICSC may demonstrate one of four patterns: (1) "smokestack" phenomenon (10 to 20%); (2) pinpoint leakage (70 to 80%) that becomes more intense throughout transit; (3) diffuse leak across a pigment epithelial detachment beneath an overlying neurosensory detachment; or (4) a complete absence of leakage suggesting an involutional phase.

DIAGNOSIS

Right eye: ICSC.

MEDICAL MANAGEMENT

ICSC is typically a self-limited disease not requiring treatment. Many medical therapies have been tried including beta-blockers, corticosteroids, and acetazolamide. To date no form of medical therapy for ICSC has proven effective in clinical studies. Patients with ICSC already on corticosteroid therapy for a variety of systemic conditions may undergo spontaneous recovery with reduction in steroid dosage. Similarly, instituting or increasing systemic corticosteroids may exacerbate the clinical features and symptoms.

Laser photocoagulation with argon or krypton wavelengths has been utilized for eyes with ICSC. Two approaches to treatment have been advocated: laser photocoagulation to the area of leakage (direct treatment) or laser photocoagulation to an area of RPE away from the leak (indirect treatment). For direct treatment, a few light argon or krypton laser photocoagulation spots should be applied to the area of leakage as seen on fluorescein angiography. Heavy treatment is unnecessary and should be avoided to prevent subretinal neovascularization, large scotoma, and heavy scarring. Direct laser photocoagulation hastens the absorption of subretinal fluid and may reduce the frequency of recurrences but does not improve the visual outcome.

Treatment should be considered for patients with more time-dependent occupational visual needs (eg, airline pilots). Patients with bilateral disease, multiple recurrences, or visual deficit from a previous episode of ICSC also should be considered for early treatment. Eyes that develop evidence of chronicity including perifoveal RPE atrophy or cystic macular degeneration may benefit from laser photocoagulation. In general treatment should be individualized and one should wait 4 or more months after the first episode for spontaneous resolution.

SURGICAL MANAGEMENT

There are no surgical treatment options for ICSC.

REHABILITATION AND FOLLOW-UP

For the majority of patients with ICSC, a conservative follow-up course should be pursued every 4 to 8 weeks until the neurosensory detachment resolves, and every 6 to 12 months thereafter. Treatment may be considered at follow-up examination when spontaneous resolution has been delayed and chronic changes have developed including perifoveal RPE atrophy and cystic macular degeneration.

Spontaneous resolution occurs within 3 months in 60 to 80% of patients and after longer than 6 months in 20%. Despite good visual acuity, 50% of patients complain of permanent subjective deterioration in the affected

eye as compared to the uninvolved eye. Patients should be aware that this condition may recur in 18 to 50% of patients and that the condition may occur in the contralateral eye in about 20% of patients. When occurring in patients 60 years of age or older, it may be associated with an increased risk of choroidal neovascularization.

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Case 41

EPIRETINAL MEMBRANE

William E. Smiddy, M.D.

HISTORY

A 54-year-old man presented with a 4-month history of progressively decreasing vision in the left eye. The onset had occurred 3 weeks after treatment of a symptomatic nasal peripheral retinal break (Fig. 41–1). The decreased vision involved marked metamorphopsia. He had metamorphopsia with vision to 20/300. Funduscopic examination in the left eye showed a confluent, L-shaped area of epiretinal membrane formation that covered the macula and extended inferotemporally (Fig. 41–2). Whiter intraretinal areas (representing axoplasmic stasis) were distributed around the edges of the more obvious epiretinal membrane. There was mild macular edema and moderately severe vascular distortion.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. There are relatively few entities to consider in the differential diagnosis of an appearance such as this one. Cystoid macular edema may give the appearance of a more diffuse preretinal membrane, probably because of the altered reflection created by a stippling of the internal retinal surface induced by the edema. A diagnostic subset of an epiretinal membrane is the vitreomacular traction syndrome-preretinal tissue formation that follows a zone of incomplete posterior vitreous separation.

2. The classification of epiretinal membranes is generally based on morphology or etiology. Morphology runs a full spectrum from mild cellophane-like changes (cellophane maculopathy) or surface wrinkling retinopathy to a more severe distortion of the macular components (macular pucker). All of these terms describe epiretinal membranes. The etiologic groups are idiopathic or secondary epiretinal membranes. Posterior vitreous separation may be a stimulating factor for the formation of idiopathic membrane. As a general rule, the clinical appearance of idiopathic and secondary epiretinal membranes are the same; it is the history and other associative features that may allow one to distinguish between these diagnoses. Entities that cause secondary epiretinal membrane include a retinal break formation (as in this patient) with or without retinal detachment, inflammatory disorders, retinal vascular disorders, trauma, or previous surgery.

3. The classic symptomatology includes a subacute onset of decreased vision most commonly characterized by metamorphopsia. The visual loss may be biphasic; not infrequently, the first phase of visual loss may be more generalized and attributable to debris in a separated vitreous. Usually the epiretinal membrane has formed maximally by 3 to 6 months and its appearance or effect on vision changes little thereafter. Associated features include the distortion of the macular vessels, which may in turn cause a vascular leakage and cystoid edema (Fig. 41–3), obstructed axoplasmic flow, and, in the most severe cases, a low-lying tractional retinal detachment. Cases secondary to previous retinal detachment may have a pigmented component to the epiretinal membrane, but the vast majority of idiopathic and secondary cases are translucent.

TEST INTERPRETATION

The only test that is utilized with substantial frequency to evaluate epiretinal membrane is the fluorescein angiogram. As illustrated in Figure 41–3 (not the patient in this case),

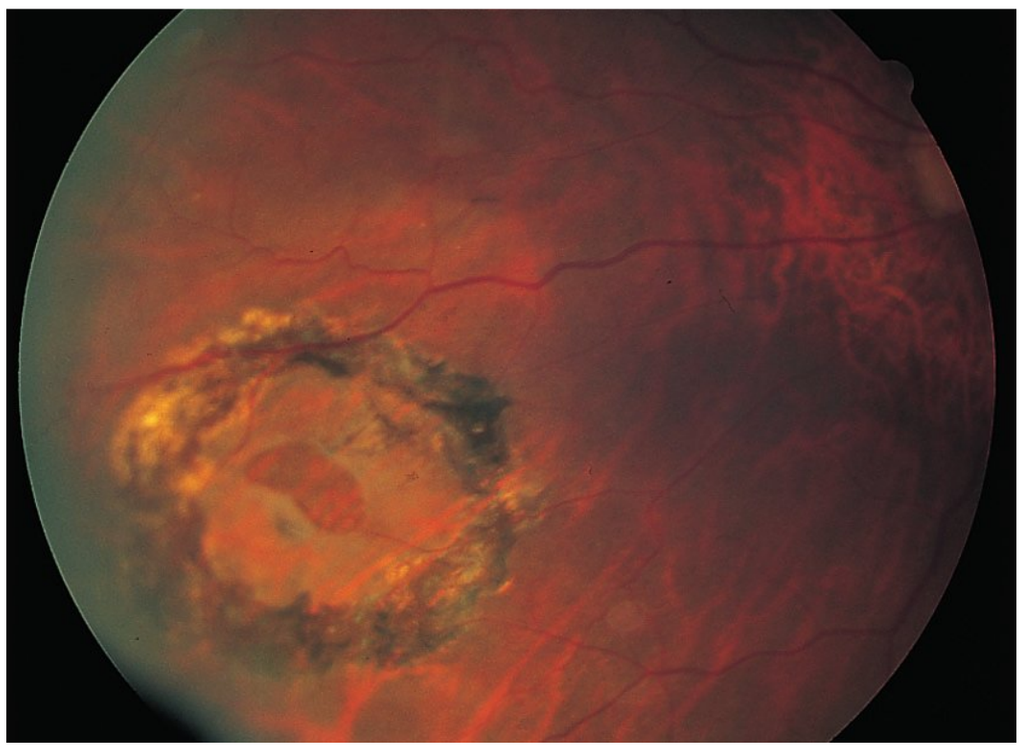

FIGURE 41–1 Clinical appearance on presentation, 4 months following laser treatment of peripheral retinal break inferotemporally in the left eye. There is a confluent chorioretinal scar surrounding the horseshoe-shaped break in the nasal periphery.

mild diffuse retinal vascular leakage is seen throughout the distribution of the epiretinal membrane. This is in contrast to cases of diabetic macular edema in which the leakage is typically more focal either in areas of leaking microaneurysm or cases of cystoid macular

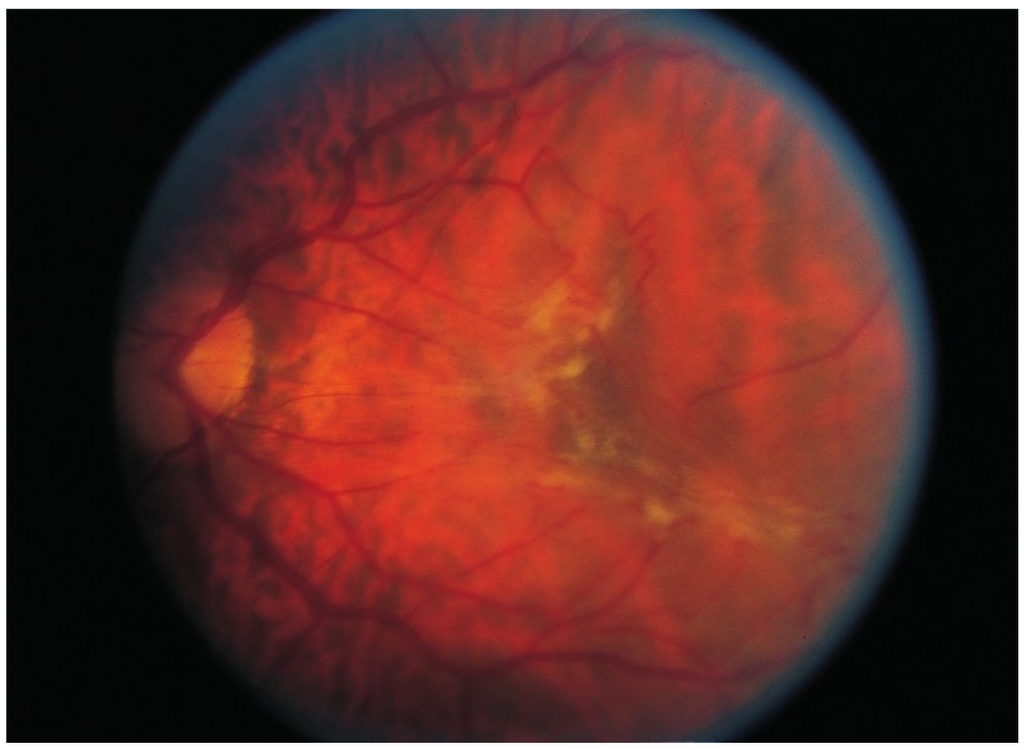

FIGURE 41–2 Clinical appearance immediately before epiretinal membrane peeling. The L-shaped epiretinal membrane can be seen above the fovea and inferotemporal to it. The lack of sharp focus on the retinal surface indicates some macular edema. There is vascular distortion that is most apparent at the superior and inferior edges of the epiretinal membrane. Rimming the inferior and superior margins are areas of more focal whitening that represent areas of axoplasmic stasis.

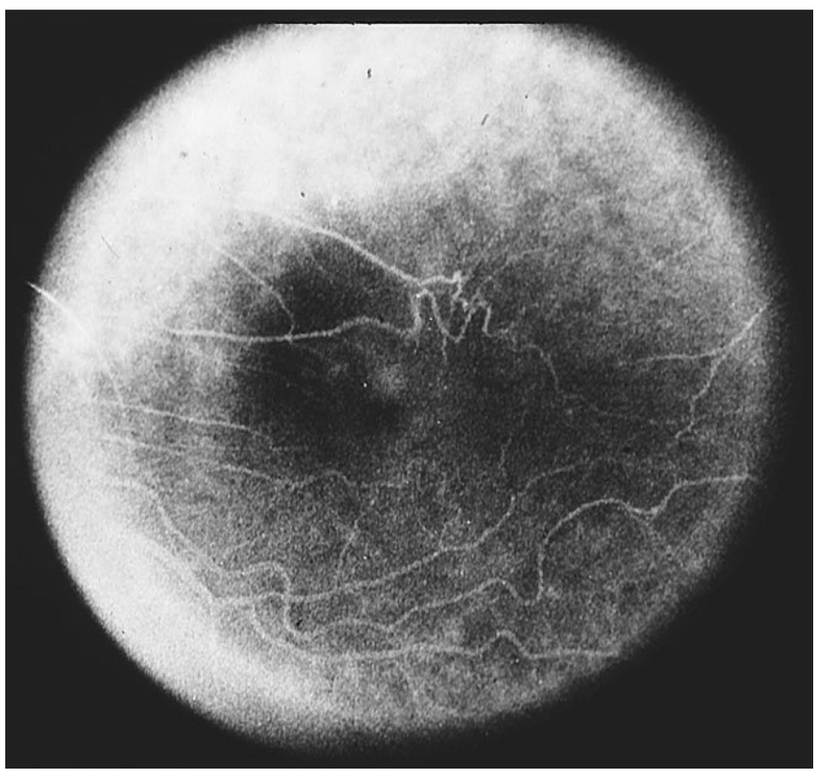

FIGURE 41–3 A different patient who presented with an epiretinal membrane shows a typical fluorescein angiographic appearance with more prominent vascular distortion superotemporal to the fovea. There are several areas of focal leakage in association with these distorted vessels. Most prominent is an area of focal leakage superior to the fovea.

edema in which the leakage is centered on the fovea. The vascular distortion may be more apparent on fluorescein angiography than on clinical examination. Ultrasound may show a high posterior vitreous separation that may be of some value in distinguishing this from an impending or full-thickness macular hole in which the posterior vitreous separation may not yet have occurred.

DIAGNOSIS

Epiretinal membrane secondary to previous peripheral retinal break, left eye.

MEDICAL MANAGEMENT

Medical management may involve treatment of an underlying inflammatory disorder. For epiretinal membranes secondary to peripheral retinal breaks or even idiopathic membranes, however, there is no known medical treatment. Observational follow-up examination is recommended when the visual acuity loss and symptoms are minimal. Epiretinal membranes normally form over a few months, but usually do not cause

any additional visual loss after their formation. Thus, a patient may be reassured that visual acuity, once stable, will likely not decline further.

SURGICAL MANAGEMENT

Once the visual acuity reaches the 20/50 or 20/60 range or worse, or in selected cases in which the visual acuity is better but the metamorphopsia is more severe and out of proportion to the visual acuity, surgical treatment may be considered. Surgical treatment includes vitrectomy, which is typically facilitated by a preexisting posterior vitreous detachment. Next the epiretinal membrane is engaged with a vitreoretinal pick. If there is not an edge under which the pick can be safely placed, a sharp instrument such as a barbed MVR blade is used to cut down and construct an edge in the macula. Typically, the thickest part of the epiretinal membrane is sought in such cases. Naturally, the center of the fovea should be avoided whenever possible in developing such an edge. The membrane is then carefully raised from the retinal surface, ideally releasing any adhesions from the macula first. Once approximately half of the circumference of the membrane has been released, intraocular forceps are used to complete the removal of the membrane in one large piece. Often the internal limiting membrane is removed along with this, which seems not to be visually consequential. When the epiretinal membrane is thinner, it may be necessary to remove it in three or four pieces.

The patient in this case underwent a vitrectomy with removal of the epiretinal membrane. By 3 months postoperative, the visual acuity had improved to 20/30 (Fig. 41–4). His symptomatology had markedly improved. The appearance of the macula shows no evidence of epiretinal membrane formation.

REHABILITATION AND FOLLOW-UP

Postoperative treatment typically involves topical corticosteroid and antibiotic drops. The visual acuity improves most rapidly during the 6 weeks following surgery and is usually maximally improved by 3 to 6 months postoperatively. There may be small degrees of improvement even after this. The surgical complication rate is acceptably low with less than 5% of patients developing any complication (the most common complication is retinal detachment). Phakic patients have an extremely high rate of progressive nuclear sclerosis, as do all eyes after vitrectomy, but cataract surgery may be performed in an uncomplicated fashion. Most series of epiretinal membrane report visual acuity improvement of approximately 50% in 80% of cases. The recurrence of epiretinal membranes is very rare, with less than 3% developing a clinically significant recurrence.

The most important prognostic factor associated with best overall final vision is good preoperative vision.

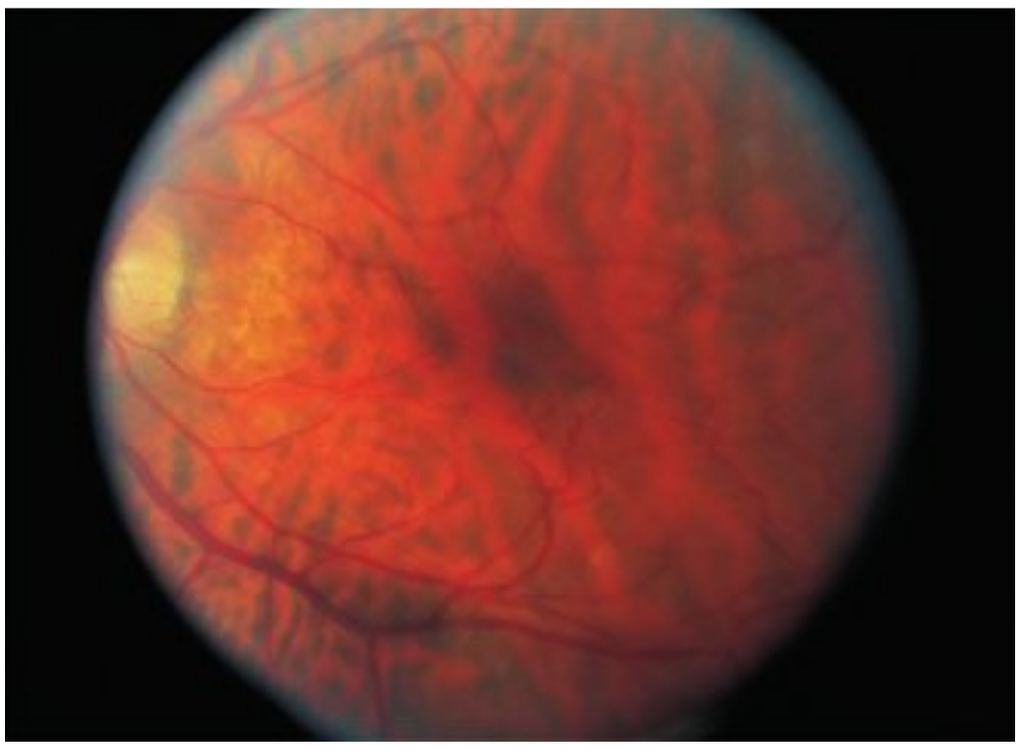

FIGURE 41–4 Clinical appearance 6 weeks following the removal of the epiretinal membrane. Vision is improved to 20/30 and the distortion and surface opacities are markedly improved.

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Case 42

MACULAR HOLE

William E. Smiddy, M.D.

HISTORY

This 50-year-old woman presented with a 2-year history of decreased vision in the right eye and a 3-month history of gradual blurred vision in the left eye. She described the vision in the left eye as giving a "butterfly" outline with a black border in the central vision. Her vision was 20/400 on the right and 20/30 on the left. Slit-lamp examination was unremarkable. There was a one-third disc diameter, fully developed macular hole with a small rim of subretinal fluid and an arrowhead-shaped operculum suspended in front of the macular hole (Fig. 42–1). In the left eye, there was a tiny, yellowish ring in the inner fovea with a small operculum sitting just anterior to it; this was interpreted as an inner lamellar hole (Fig. 42–2). A fluorescein angiogram showed a sharply defined area of hyperfluorescence underlying the center of the fovea (Fig. 42–3). An ultrasound showed an operculum in the left eye, but there was no definite posterior vitreous detachment.

Over the following 4 months, she developed progressive loss of vision in the left eye to the level of 20/80 with increased distortion of her central vision. An unequivocal full-thickness macular hole was noted (Fig. 42–4). Surgery was recommended for the full-thickness macular hole in the left eye.

A vitrectomy with fluid–gas exchange was performed. The patient maintained strict face-down positioning for 2 weeks postoperatively. At the 3-month postoperative visit, the vision was 20/60. The edges were no longer visible and the subretinal fluid cuff had resorbed. She developed progressive nuclear sclerosis over the 21 months after the macular hole surgery and underwent uncomplicated cataract surgery in the left eye. Within 1 month, the vision had returned to 20/40, and by 6 years following the original surgery her vision was 20/20 in the left eye (Fig. 42–5). The hole remained closed with no sign of recurrence.

In the right eye, the vision remained 20/400 with no change in the morphology of the full-thickness macular hole.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The ophthalmoscopic appearance of a full-thickness macular hole is often diagnostic. The morphology of the hole showed it to be circular with a subretinal fluid cuff and with an overlying operculum. Very few other conditions mimic a full-thickness macular hole with such distinct features. The limited local posterior vitreous detachment and stable-sized macular hole constitute a stage 3 macular hole in accordance with the Gass classification.
2. The diagnosis of the left eye at initial presentation was less clear. Certainly, the abnormalities in the macula accounted for the visual symptoms; the question was whether a full-thickness macular hole existed. The presence of a macular hole in the right eye increased the possibility that a macular hole syndrome was developing in the left eye. An impending, or stage 1, macular hole characteristically causes an ophthalmoscopically apparent macular abnormality, but usually only slightly decreased vision. Many cases like these may represent an occult stage 1b macular hole—one in which a tiny initial hole is at least temporarily sealed by a local gliotic response that may be directed by the adjacent posterior hyaloid surface. Probably these progress to full-thickness, more apparent macular holes over a several-week to several-month time frame, as illustrated in this patient.
3. There are many conditions that may simulate a full-thickness macular hole. Most common is an epiretinal membrane with a

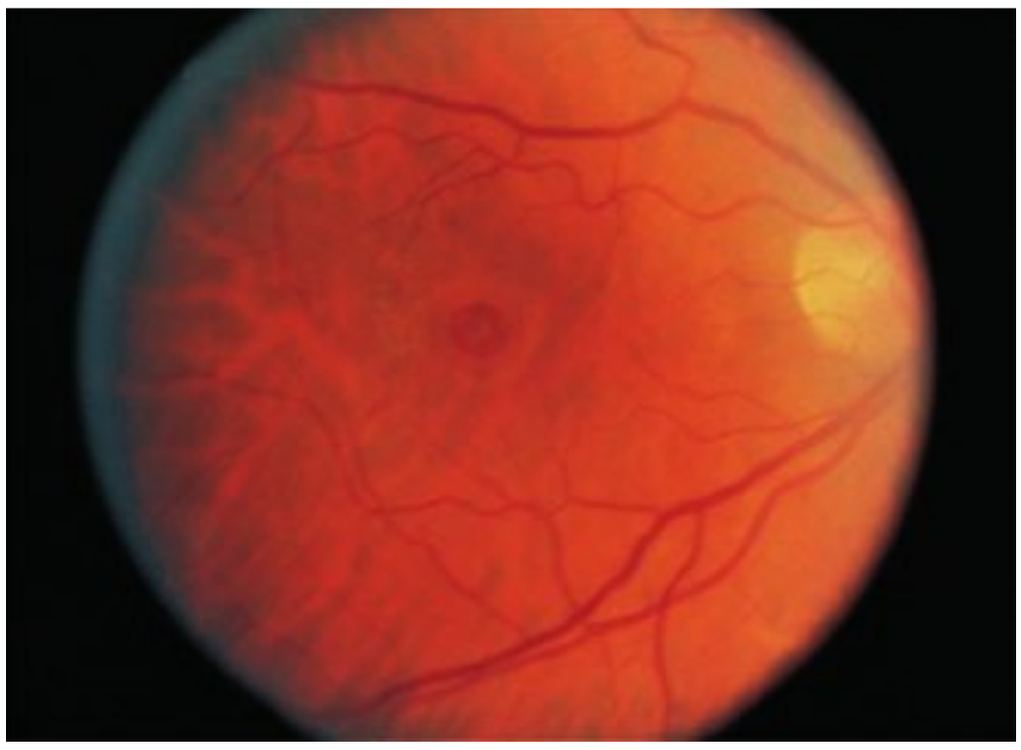

FIGURE 42–1 Initial appearance of right eye. Vision is 20/400. A circular full-thickness macular hole is in evidence with a cuff of surrounding subretinal fluid. This appearance remained unchanged over 7 years of follow-up.

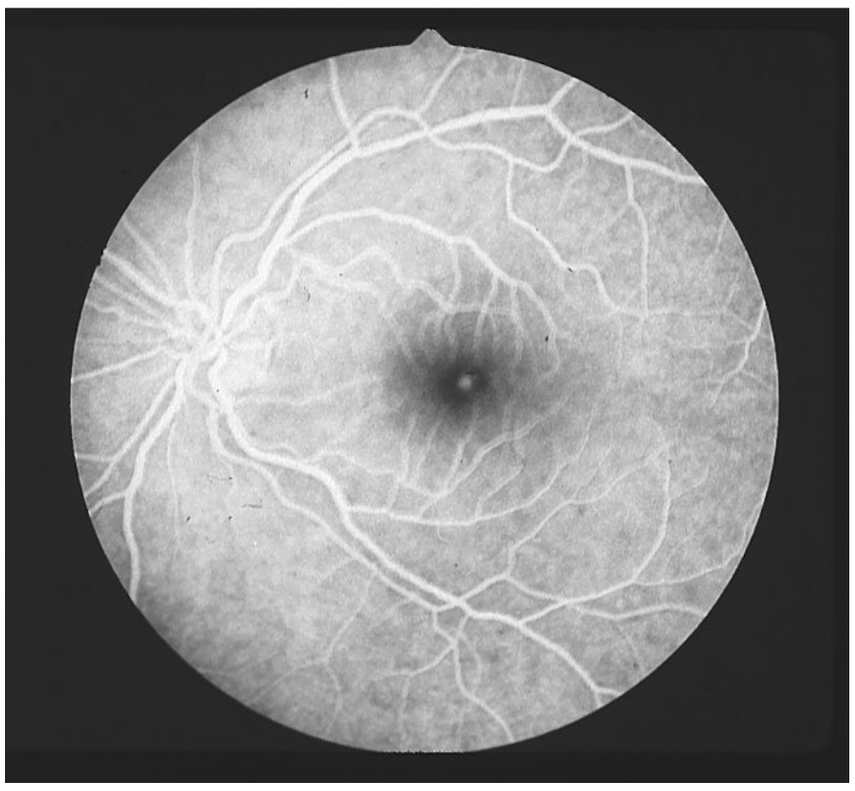

FIGURE 42–3 Fluorescein angiogram shows characteristic hyperfluorescence of an impending or full-thickness macular hole confined to the very central part of the fovea in the left eye at presentation.

pseudo-hole configuration. A hole in the epiretinal membrane overlying the center of the fovea allows an unobstructed view of the thin underlying fovea, yielding the pseudo-hole appearance. Features that suggest the diagnosis of a pseudo-hole rather than a full-thickness hole include lack of a discrete subretinal fluid cuff, lack of discrete edges of the hole, lack of circular contour of the hole, and the presence of a posterior vitreous detachment, especially when the "hole" is small. Furthermore, excellent visual acuity despite what appears to be a more completed hole suggests a pseudo-hole.

Other less common configurations may also simulate a full-thickness macular hole including atrophic or neovascular age-related macular degeneration, cystoid macular edema with central coalescence of microcysts, vitreo-macular traction syndrome with traction on the central fovea, and macular detachment from conditions such as central serous or an

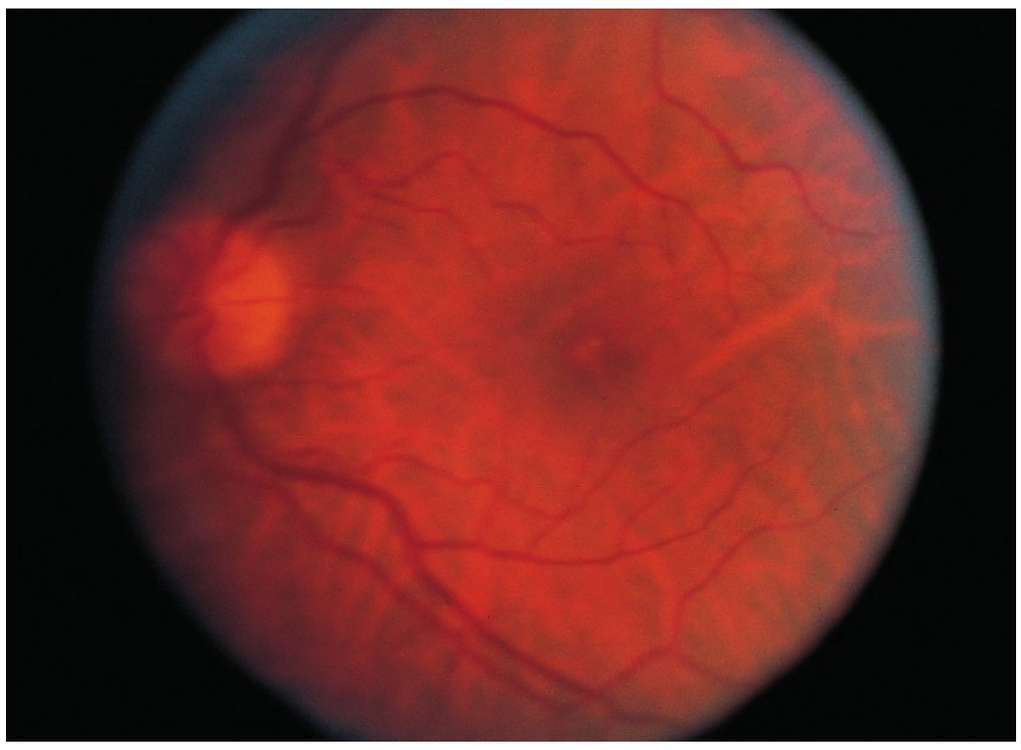

FIGURE 42–2 Initial presentation of the left eye with apparent impending macular hole. A deep yellowish ring is in evidence. A full-thickness macular hole is not apparent. The vision is 20/30 at this point.

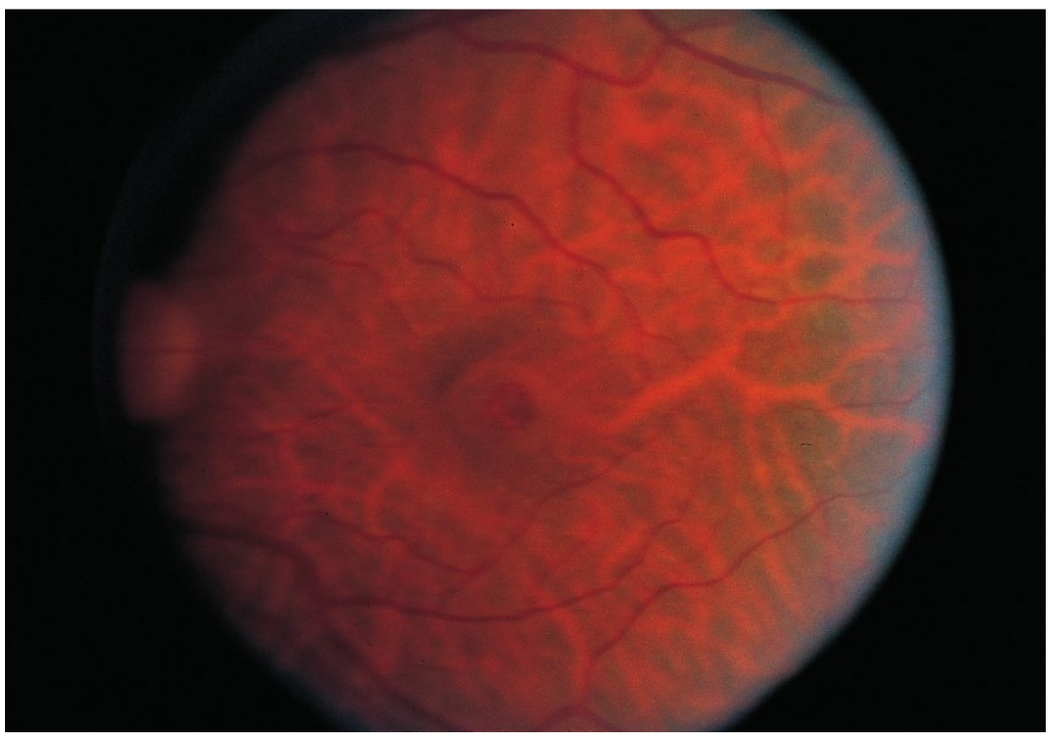

FIGURE 42–4 Appearance 4 months after initial presentation of left eye. Visual acuity is now 20/80 and a full-thickness macular hole is more apparent.

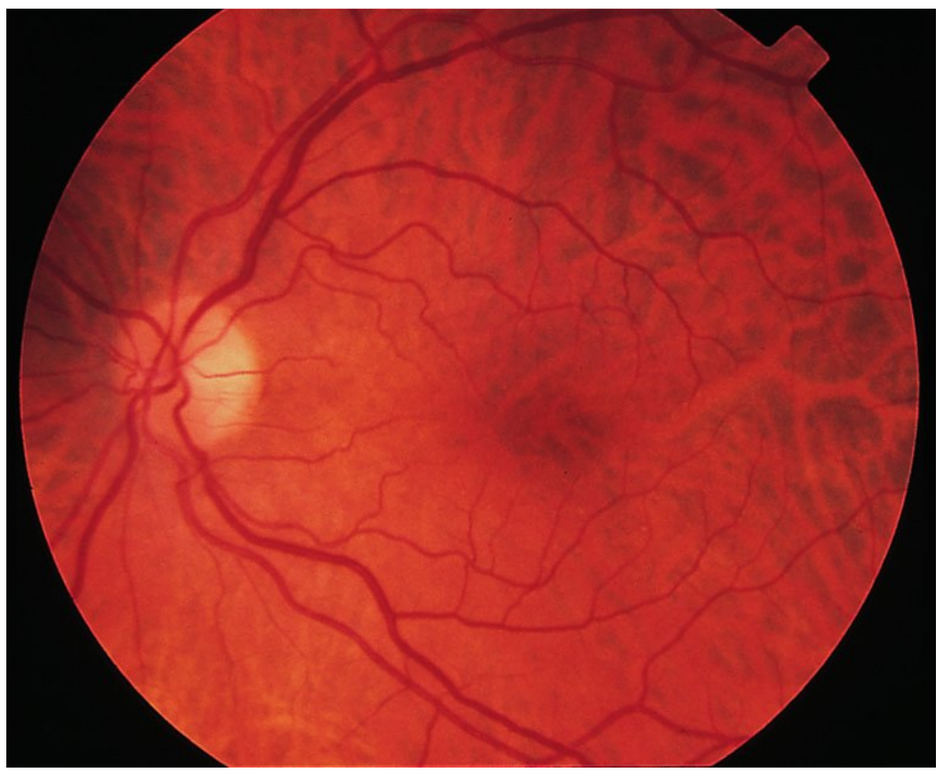

FIGURE 42–5 Follow-up fundus photograph 6 years after successful macular hole surgery. The vision is 20/20. There is no evidence of a full-thickness macular hole and only minimal RPE pigmentary changes underlie the fovea.

optic nerve pit. In these cases the central fovea appears to represent a hole by contrast to a hydrated or elevated perifoveal retina, or normally pigmented RPE surrounding a central atrophic spot.

4. It is even more difficult to differentiate an impending macular hole from many of these same conditions when they simulate an impending macular hole. Furthermore, with the concept of an occult stage 1b macular hole (according to the revised Gass classification), it is very probable that many cases previously called impending macular holes may be full-thickness macular holes that have undergone a degree of self-sealing. The glial plug that seals the hole may be still attached to the overlying cortical vitreous, which may ultimately open once a higher posterior vitreous separation occurs. Alternatively, remodeling of the gliotic plug may allow a dehiscence of the plug from the edges of the occult hole.

TEST INTERPRETATION

The most definitive way to determine whether or not a patient has a macular hole is the combination of the history and the physical findings. The most sensitive observational step involves the use of a fundus contact lens at the slit lamp, which offers optimal stereoscopic and magnification capabilities. Utilizing a suspended precorneal lens may yield a deceiving conclusion by the inherent loss of stereopsis or magnification. An important clinical finding is the visual acuity. It is extremely rare for patients to have true full-thickness macular holes when the vision is 20/40 or better. Most commonly, with a fully developed macular hole the vision will be 20/100 or worse. Earlier stage macular holes (with correspondingly smaller holes) may be associated with intermediate levels of visual acuity.

Other tests lack either sensitivity or specificity. Fluorescein angiography classically shows a circular window defect underlying the center of the fovea in full-thickness holes and even in early stage 1 holes. This may be due to a repositioning of pigment-containing foveal components more peripherally, but is not a specific or even a universal feature. Echography may directly detect the macular hole, or a cortical vitreous separation, and the operculum is sometimes visible, but this too is not as sensitive or specific as is desirable. Ocular coherent tomography (OCT) gives excellent resolution of the contour of the retinal surface and can demonstrate the discontinuity of the retina in the foveal area; it may become an important diagnostic tool.

DIAGNOSIS

1. Full-thickness (stage 3) macular hole, OD.
2. Stage 1 macular hole OS, with progression to full-thickness macular hole.

MEDICAL MANAGEMENT

There are no medical treatments for impending or full-thickness macular holes. Discontinuous and confluent laser photocoagulation have yielded disappointing results and, accordingly, have not gained widespread use. The introduction of an expansile vitreous gas bubble (by analogy with pneumatic retinopexy for rhegmatogenous retinal detachment) has been reported with some success with early stages of macular holes (stages 1 and 2), but has not gained widespread usage.

SURGICAL MANAGEMENT

Vitrectomy with varying degrees of manipulation of the macular hole is the mainstay of treatment for full-thickness macular holes. Indications for surgery typically are limited to patients with definite full-thickness macular holes for less than 1 to 2 years. Patients with bilateral vision loss are more likely to be considered for surgery beyond 2 years.

The surgical steps involve removal of the cortical vitreous when present utilizing a silicone-tipped suction system. Historically, a variety of adjuvants have been tested with at least initial success. These are typically added over the surface of the macular hole after doing a fluid–gas exchange. The rationale is to stimulate gliosis to close the hole. More recently, however, it has been found that the surgical success rates without using adjuvant are equivalent. In some cases this may be because of a technique that has been developed whereby the internal limiting membrane is dissected from the surface surrounding the macular hole.

Long-acting internal gas tamponade with prone positioning is generally held to offer the optimal rate of macular hole closure, but some investigators have found that this may not be as important as previously considered.

Serious potential surgical complications include retinal detachment in approximately 2% of cases, elevated intraocular pressure in up to 30% (almost always temporary and responsive to topical agents), cystoid macular edema, choroidal neovascularization, endophthalmitis, visual field loss, and choroidal hemorrhage. One almost-universal side effect is progressive nuclear sclerotic lens opacity. This patient demonstrated this and underwent uncomplicated and successful cataract surgery in the left eye 9 months after the macular hole surgery.

An initially sealed macular hole reopens months later in 5% of cases, but additional surgery usually yields results approximating the initial success.

REHABILITATION AND FOLLOW-UP

Currently, anatomic success rates in excess of 90% are standard. The visual acuity typically improves by 50% or to about 20/40 in a majority of cases. A recently discovered finding is that the visual acuity continues to improve—in many cases for a few years after the initial surgery. The visual acuity improved to 20/20 6 years postoperatively after initial improvement to the 20/40 range in this patient. This continued visual acuity improvement seems to be independent of the effect of having the cataract removed.

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This case was contributed by Dr. Harry W. Flynn Jr., Miami, FL.

Case 43

VITREOUS HEMORRHAGE

William E. Smiddy, M.D.
Ghassan J. Cordahi, M.D.

HISTORY

This 90-year-old woman presented with a 3-month history of sudden decreased vision in the left eye. Her visual acuity was 20/40 OD and 2/200 OS. Intraocular pressures were 12 in each eye. Slit-lamp examination showed a well-positioned posterior chamber lens implant on the right. There was vitreous adherent to the wound superiorly. In the left eye, she had 2+ nuclear sclerosis. There was a very dense vitreous hemorrhage in the left eye precluding a view posteriorly.

Past ocular history was pertinent for vision of 20/50 on the right and 20/200 on the left 3 years previously due to atrophic age-related macular degeneration OD and a previously treated, subfoveal choroidal neovascular membrane OS. Medical history was negative for diabetes or hypertension.

B-scan/A-scan ultrasonography showed vitreous hemorrhage with posterior vitreous detachment OS (Fig. 43–1). There was no retinal tear or detachment, and a disciform scar could not be resolved in the left macula.

The patient was observed without treatment for 3 months. On follow-up, the visual acuity improved to 20/400 and a subfoveal laser scar with contiguous subretinal hemorrhage extending inferiorly to the mid periphery was visible.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Spontaneous vitreous hemorrhage in an elderly patient, especially with the history of exudative age-related macular degeneration, suggests the possibility of breakthrough bleeding into the vitreous cavity from a subretinal hemorrhagic process. Extension of subretinal hemorrhage before breakthrough bleeding occurs may compound sight-causing tissue damage from the underlying neovascularization process.

2. The most common causes of vitreous hemorrhage in nondiabetic patients are posterior vitreous detachment (PVD), retinal tear (with or without avulsed retinal vessel syndrome), and retinal detachment. Other less common or historically obvious causes include blunt trauma, Terson's syndrome, choroidal melanoma, penetrating trauma, and macroaneurysms.

3. Prompt diagnosis and treatment may prevent further or permanent visual loss. Vitreous hemorrhage at the time of PVD is associated with a higher risk of retinal tear (23 to 45%) than PVD without hemorrhage (3 to 12%). Untreated proliferative retinopathies should also be considered in all cases.

4. Vitreous hemorrhage often occurs in proliferative retinopathies. The most common cause of vitreous hemorrhage in a patient with diabetes mellitus is proliferative diabetic retinopathy. Other proliferative etiologies include branch retinal vein occlusion, sickle cell retinopathy, or choroidal neovascularization. Often, the possibility of these entities is apparent from the previous history or from examination of the fellow eye.

5. It may be difficult to differentiate vitreous blood, especially when chronic, from vitreous opacities due to inflammatory disorders. Conditions such as toxoplasmosis, pars planitis, or other forms of intermediate and posterior uveitis may present with vitreous opacities. In such cases, careful examination for granulomatous signs in the anterior segment may betray the diagnosis. Pars planitis

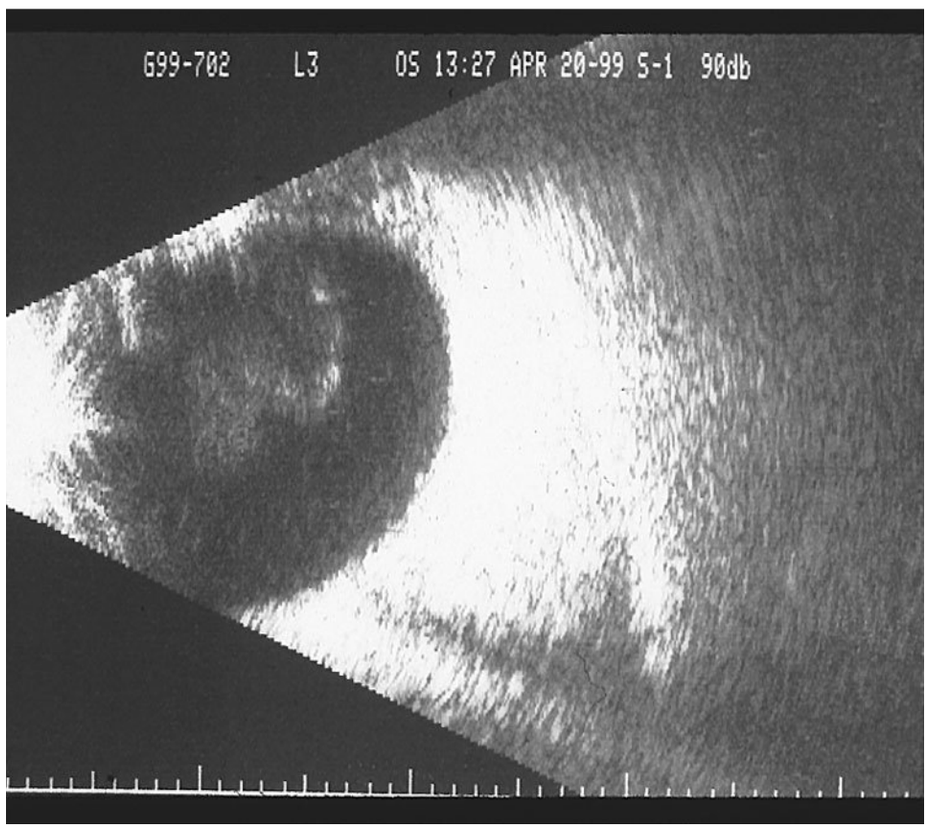

FIGURE 43–1 Ultrasonographic appearance showing vitreous opacities and posterior vitreous detachment. No retinal detachment is in evidence. This slice through the macula does not show macular elevation.

may lead to neovascularization and vitreous hemorrhage directly. Clues may sometimes be obtained from careful examination of the fellow eye and careful delineation of the previous history.

TEST INTERPRETATION

One key element of the clinical examination is the presence or absence of an afferent pupillary defect. More extensive disease, such as retinal detachment or extensive subretinal hemorrhage with breakthrough bleeding, often manifests with an afferent pupillary defect. Indirect ophthalmoscopy with scleral depression may allow a view of the peripheral retina despite substantial degrees of blood in the mid vitreous. Seeing the peripheral retina intact at or near the ora serrata for 360 degrees lends some confidence in ruling out associated retinal detachment.

The most important ancillary test to rule out progressive causes for vitreous hemorrhage is echography. It is generally possible to rule out retinal detachment with echography. In some selected cases, a peripheral retinal tear may be detectable by ultrasound. Proliferative retinopathies may frequently be able to be diagnosed by echography as the vitreoretinal attachment of the retinal neovascularization may be evident.

If it is uncertain whether the vitreous opacities may represent inflammatory cells rather than red blood cells, laboratory testing (such as toxoplasmosis titers, TB skin testing, syphilis serologies) or even diagnostic vitrectomy may be indicated.

DIAGNOSIS

Vitreous hemorrhage due to breakthrough bleeding associated with choroidal neovascularization, OS.

MEDICAL MANAGEMENT

There are no known medical treatments to hasten the clearance of vitreous hemorrhage. Having the patient sleep in a slightly inclined position does not hasten the clearance of the hemorrhage, but it may allow the blood to settle inferiorly and facilitate examination of the patient. The temporary, partial visual improvement is reassuring to the patient. Discontinuing anticoagulants is generally not helpful, unless evaluation discloses overcoagulation.

Laser treatment when possible is the mainstay of treatment for most proliferative retinopathies.

SURGICAL MANAGEMENT

Vitrectomy for cases of nonclearing vitreous hemorrhage in eyes with acceptable visual potential is the mainstay of surgical treatment. The appropriate timing and indication for surgery are controversial. In patients with known proliferative retinopathies, such as diabetic retinopathy, surgical intervention is dependent upon a variety of factors, including the chronicity of the hemorrhage, the presumed severity of the existing proliferation, and the degree of previous laser photocoagulation applied. Generally, Type I diabetics undergo earlier vitrectomy compared to Type II diabetics, with vitrectomy usually being recommended for patients with nonclearing vitreous hemorrhage of 2 to 6 months' duration.

Patients with vitreous hemorrhage not associated with proliferative retinopathies, retinal detachment, or retinal tears are generally observed. If there are no signs of spontaneous clearing within 3 to 6 months, vitrectomy can be recommended. However, it is important to attempt to assess the visual potential in such cases. In patients with macular degeneration, the visual potential is understandably limited. A special case is vitreous hemorrhage due to penetrating trauma or a globe rupture. Usually further vitreous surgery, which may include vitrectomy, scleral buckling, and other maneuvers, is recommended within 2 weeks of onset to preempt irreversible cicatricial changes.

REHABILITATION AND FOLLOW-UP

In this patient, the visual acuity was improving 2 months after presentation. The visual potential was 20/200, and there was good vision in the fellow eye. Surgical intervention therefore was deferred. However, even in patients in which the vitreous hemorrhage is noted to be due to breakthrough bleeding from macular degeneration, vitrectomy can be considered. The most common setting in which vitrectomy is offered despite limited visual potential would be in a patient with bilateral visual loss. Furthermore, it is important to counsel patients preoperatively as to appropriate expectations.

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Case 44

RETINITIS PIGMENTOSA

Byron L. Lam, M.D.
Lourdes A. Casuso, M.D.

HISTORY

A 24-year-old woman with progressive decreased peripheral vision and visual difficulties at night was evaluated. Since the age of 10, the patient has had trouble reading with dim light and performing outdoor activities after dusk. A year ago, the patient stopped driving at night because she no longer felt safe. For many years, the patient has been "clumsy" and often walked into surrounding objects, which she could not see well. The patient was otherwise healthy. Family history was negative for ocular problems, and there was no consanguinity.

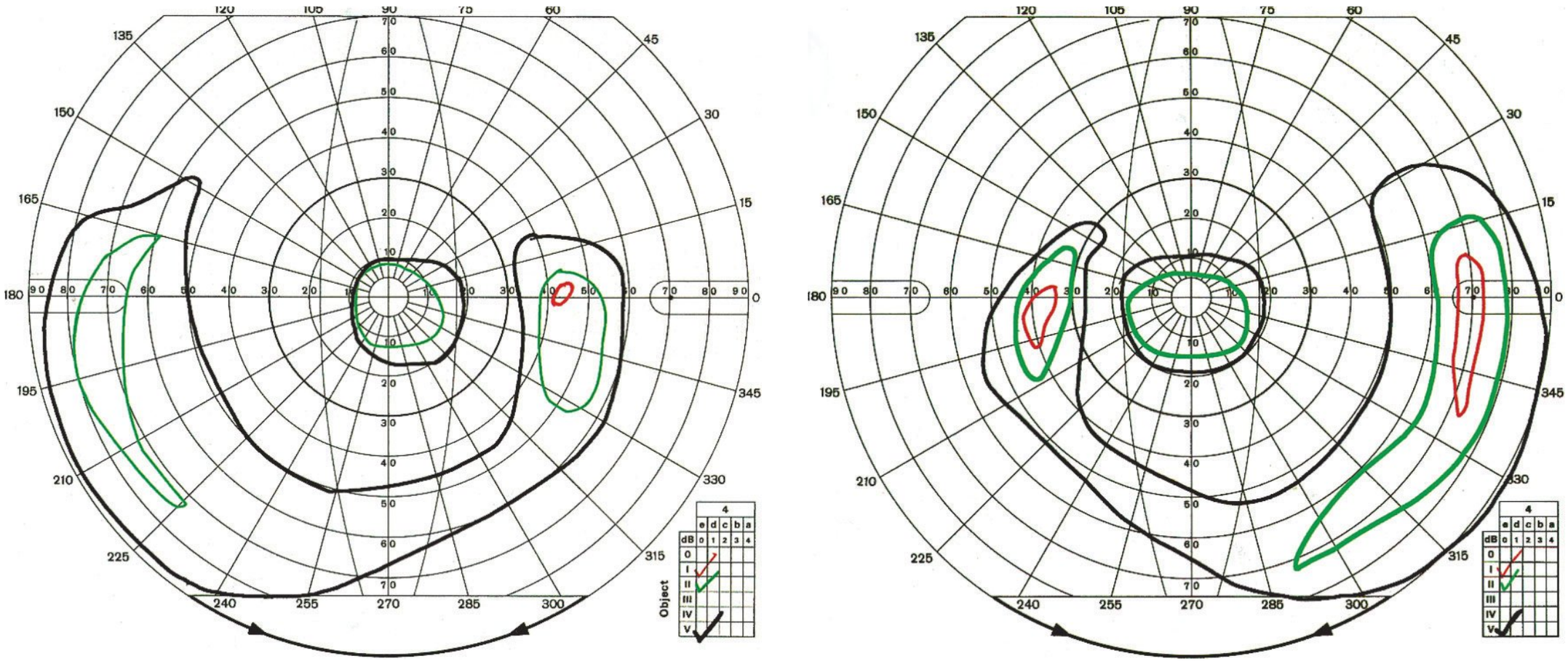
Best-corrected visual acuity was 20/25 in each eye with no relative afferent pupillary defect. Goldmann visual fields revealed large midperipheral ring-shaped scotomas (Fig. 44–1). Funduscopic examination showed atrophy of the midperipheral and peripheral retina with areas of pigment clumping ("bone spicules," Fig. 44–2). Attenuation of the retinal vasculature in the area of retinal atrophy was evident. Full-field electroretinography showed nondetectable rod and cone responses.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. In a young patient with progressive night visual difficulties or nyctalopia and decreased peripheral vision, a diagnosis of hereditary retinal degeneration should be considered. As a group, the rod–cone dystrophies are the most common clinical type of hereditary retinal degeneration. The prevalence is approximately 1 per 3000 to 4000 persons in the general population. Rod–cone dystrophies, traditionally known as retinitis pigmentosa (RP), refer to a large genotypically diverse and phenotypically diverse group of retinal dystrophies characterized by the early onset of rod photoreceptor dysfunction. Nyctalopia and progressive loss of peripheral vision are common early symptoms. Visual acuity and macular function, in contrast, are usually relatively spared until late in the disease.

Symptoms typically start insidiously between the second and fifth decades of life and continue to progress gradually. Retinal findings include retinal atrophy with vascular attenuation and pigmentary clumping (bone spicules). The ophthalmoscopic signs include diffuse or patchy areas of retinal degeneration in the midperipheral regions of the retina, optic nerve atrophy, atrophic macular lesions, cystoid macular edema, and vitreous syneresis with mild vitritis. Posterior subcapsular cataracts are also common findings in RP. Approximately 50% of RP patients have no family history of RP and are designated as having isolated RP. The hereditary pattern in patients with isolated RP is presumably autosomal recessive. The remaining 50% of RP patients have autosomal dominant (20 to 25%), X-linked (10 to 15%), and recessive (15%) pedigrees.

2. Aside from RP, other conditions that may produce progressive nyctalopia in healthy individuals with no other associated systemic symptoms include choroideremia, gyrate atrophy, and vitamin-A deficiency. Choroideremia is an X-linked recessive chorioretinal dystrophy characterized by a progressive degeneration of the choroid and the retinal pigment epithelium. Choroideremia results from defects in the human Rab escort protein-1 (REP-1) gene, which encodes for a component of rab geranylgeranyl transferase, an enzyme involved in cellular transport. Affected males usually start to have onset of

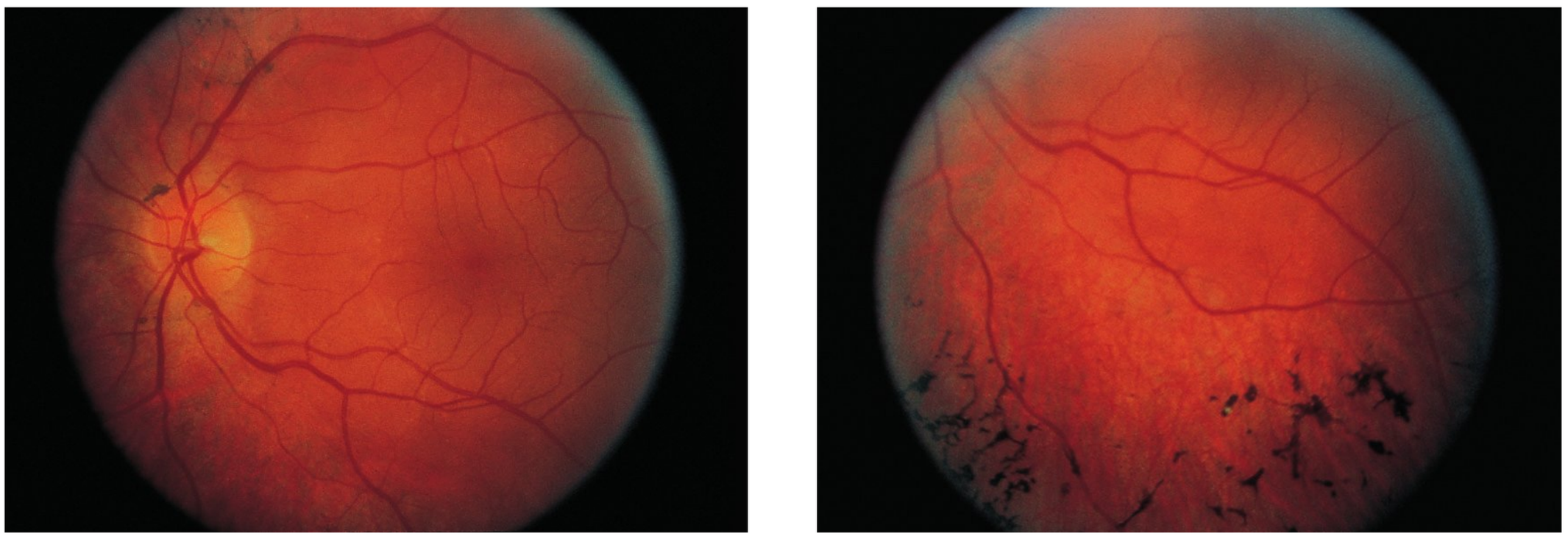


A B

FIGURE 44–1 (A, B) Goldmann visual fields showed midperipheral ring-shaped scotomas in each eye.

poor night vision and decreased peripheral vision starting in the first two decades of life. Female carriers are asymptomatic but have a diffuse or localized "moth-eaten" appearance of the retinal pigment epithelium.

Gyrate atrophy is an autosomal recessive chorioretinal dystrophy due to a generalized deficiency of the mitochondrial matrix enzyme ornithine aminotransferase. Many patients are first diagnosed with the disease when poor night vision becomes noticeable between the ages of 20 to 40 years. Multiple discrete scallop-shaped areas of chorioretinal atrophy occur initially in the peripheral and midperipheral regions of the fundus. Over time, the lesions coalesce and progress



A B

FIGURE 44–2 (A, B) Funduscopic findings were similar for both eyes. A view of the left fundus showing retinal atrophy midperipherally near the vascular arcades. The retinal atrophy is more apparent in a view of the inferior quadrant of the retina. Prominent choroidal vasculature appearance and retinal vascular attenuation is evident in the area of the retinal atrophy, and areas of pigmentary clumping ("bone spicules") are visible.

toward the macula with corresponding progressive impairment of peripheral vision and night vision.

Worldwide, dietary vitamin-A deficiency is the most common cause of progressive nyctalopia. The prevalence is higher in less developed countries, and nyctalopia is often the earliest symptom. With progression, dryness of the conjunctiva and cornea as well as metaplastic keratinization of areas of the conjunctiva occur.

3. Several retinal degenerative disorders associated with pigmentary retinal atrophy have been traditionally listed under the broad category of RP. The disorders include Usher syndrome, Refsum syndrome, Bardet-Biedl syndrome, Bassen-Kornsweig syndrome, and neuronal ceroid lipofuscinosis (Batten disease). However, these conditions are associated with other systemic findings and are not likely in our healthy adult patient. Of interest, toxic retinopathies such as thioridazine-induced retinopathy may also produce an RP-like clinical picture.

TEST INTERPRETATION

Goldmann visual field testing often reveals midperipheral ring-shaped scotoma in patients with early RP. As the disease progresses, the scotoma expands and the visual field becomes more constricted.

Full-field electroretinography (ERG) is an extremely valuable tool in diagnosing RP because ERG responses are affected early in the disease. Patients with early stages of RP have reduced and prolonged dark-adapted rod ERG responses and near normal or slightly reduced light-adapted cone responses. Patients in early stages of RP are often asymptomatic, and the retinal atrophy may or may not be clinically apparent. With further progression of the disease, the rod and cone ERG responses diminish and become nondetectable. Therefore, the ERG responses of most RP patients are either very small or nondetectable. In fact, it is not unusual for ERG responses to be nondetectable on initial evaluation in some RP patients.

Genetic testing has become an increasingly useful tool in determining the specific hereditary pattern and the fundamental biochemical defect in RP patients. The genotypes of RP are numerous and extremely diverse. For example, mutations of rhodopsin account for only 25% of all autosomal dominant RP, and yet at least 90 different codon mutations in rhodopsin have thus far been identified to be associated with RP.

Despite many advances in the past decade, genotypes can be identified only in a limited number of RP patients, most of whom have autosomal dominant and X-linked recessive forms. Identification of the genetic mutations associated with RP suggest that at least three biochemical mechanisms may be affected: (1) the renewal and shedding of photoreceptor outer segments; (2) the visual transduction cascade; and (3) the retinol (vitamin A) metabolism. The first group includes defects in the rhodopsin and peripherin/RDS genes, which often result in dominant phenotypes. The second group includes defects in the cGMP phosphodiesterase genes and cGMP-gated cation channel gene, which often result in recessive phenotypes. The third group includes defects in the retinal pigment epithelium protein RPE65, which result in recessive phenotypes. In addition, defects in the RP GTPase regulator (RPGR) gene accounts for 20 to 30% of X-linked RP, but the biochemical role of RPGR is not yet well understood.

Lastly, fluorescein angiography is helpful in identifying cystoid macular edema, which may occur rarely in RP patients. Characteristic late macular hyperfluorescence is seen.

DIAGNOSIS

Isolated rod–cone dystrophy or retinitis pigmentosa, moderately advanced.

MEDICAL MANAGEMENT

Currently, RP is not curable, and only a few treatments have been shown to have modest effect under scientific scrutiny. In one prospective study, it has been shown that oral vitamin-A palmitate

(15,000 I.U.) daily may help to delay the progression of RP while oral vitamin E daily may hasten progression. Of interest, oral acetazolamide has been found to be more effective than topical agents such as dorzolamide in treating cystoid macular edema in RP. Reducing retinal exposure to damaging solar ultraviolet light with sunglasses is recommended in RP patients. For those RP patients with reduced visual acuity, low-vision aids may be helpful.

Counseling of patients and their families regarding visual prognosis and disease susceptibility should be provided if desired. However, the clinical expression of a known genotype may have some interindividual variability even for affected individuals of the same family.

SURGICAL MANAGEMENT

There is no proven role for surgical management of this problem.

REHABILITATION AND FOLLOW-UP

Periodic yearly liver function tests may be helpful in RP patients placed on vitamin-A therapy. However, the risk of toxicity from the recommended dosage is low, and whether repeated liver function testing is necessary in all patients is uncertain. If cataract or cystoid macular edema develops, treatment should be considered. Multiple laser posterior capsulotomies after cataract extraction are often necessary in RP patients because postoperative fibrotic reaction of the posterior capsule is common. If the ERG was recordable initially, it may be repeated if quantification of the progression of the disease is desired by the patient. Likewise, Goldmann perimetry may be repeated to follow progression and to determine the patient's degree of disability.

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Section V

UVEITIS

45. Choroiditis
46. Retinitis
47. White Dot Syndromes

Case 45

CHOROIDITIS

Cathleen M. McCabe, M.D.

HISTORY

A 24-year-old Hispanic woman complained of constant pain in the right eye for 3 weeks, blurred vision, redness, and tearing for 1 week, and a 1-month history of headache and neck stiffness. Computed tomography of the brain was normal. A lumbar puncture showed a mild pleocytosis. She noted flulike symptoms 2 days before presentation. She denied any history of trauma.

On examination, visual acuity was 20/20 in both eyes. Intraocular pressure was 18 mm Hg in the right eye and 16 mm Hg in the left eye. Slit-lamp examination revealed moderate anterior chamber cell and flare in the right eye with granulomatous keratic precipitates on the corneal endothelium. A mild anterior chamber inflammatory reaction was noted in the left eye. Vitreous cells were present in the right eye. Funduscopic examination of the right eye showed optic disc edema with focal areas of serous retinal detachment and folding of the retina within the macular region. The left eye was unremarkable. B-scan ultrasonography of the right eye showed diffuse choroidal thickening with low reflectivity and a shallow serous macular detachment. Treatment with topical prednisolone acetate and cycloplegics was initiated.

The patient returned 1 week later with persistent pain and markedly decreased visual acuity in the right eye to 3/200 vision. Although the anterior chamber reaction had decreased slightly in the right eye, the left eye had increased cell and flare with a few keratic precipitates. The funduscopic examination showed increased optic disc edema, subretinal fluid and retinal folds, and focal yellow-white lesions at the level of the retinal pigment epithelium in the macula (Fig. 45–1). Although the vision was 20/25 in the left eye, a new focal area of subretinal fluid in the nasal macula was noted. Fluorescein angiography of the right eye demonstrated multiple areas of pinpoint hyperfluorescence in the juxtapapillary region and macula that leaked in the later frames (Fig. 45–2). The area of thickening in the left eye adjacent to the optic disc had a similar appearance on fluorescein angiography.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. One of the first steps in evaluating patients with intraocular inflammation is defining the location and extent of tissue involvement. Causes of panuveitis include Behçet's disease, syphilis, sarcoidosis, Vogt-Koyanagi-Harada syndrome (VKH), and infectious endophthalmitis. Additionally, it is important to determine the primary tissue layer involved (eg, retina or choroid) and whether the lesions are unifocal or multifocal. Causes of multifocal choroiditis, as in the presented case, include autoimmune disorders (sympathetic ophthalmia, VKH, and sarcoidosis), infectious diseases (histoplasmosis), or other inflammatory causes (birdshot choriodopathy and serpiginous choroidopathy).
2. Second, it is important to determine the onset of symptoms. Acute causes of uveitis include postsurgical infection, trauma, toxoplasmosis, the white dot syndromes (acute posterior placoid pigment epitheliopathy and multiple evanescent white dot syndrome), VKH, acute retinal necrosis, and most causes of anterior uveitis.
3. Most causes of posterior uveitis are bilateral in presentation. Cases that remain unilateral upon follow-up examination may include sarcoidosis, trauma, parasitic disease (such as toxoplasmosis), retained intraocular foreign bodies, and postsurgical uveitis. Bilateral involvement may indicate a systemic cause of inflammation, such as autoimmune

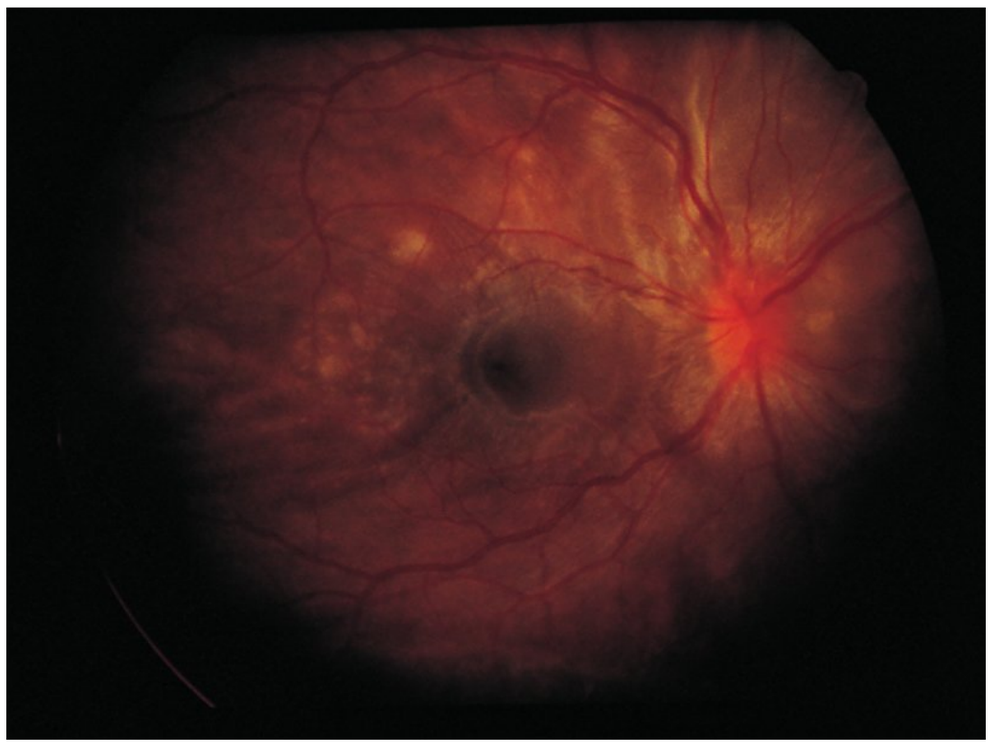

FIGURE 45–1 Funduscopic appearance of patient's right eye showing focal yellow-white lesions at the level of the retinal pigment epithelium (RPE) superior and temporal to the macula. Note the optic nerve had swelling.

disorders and infectious etiologies. Additionally, some cases may present with unilateral inflammation, with bilaterality of the condition revealed only on subsequent follow-up examination, as was the case with the patient presented here.

4. Careful examination of the anterior chamber reaction with identification of granulomatous versus nongranulomatous type of inflammation is helpful in narrowing the differential diagnosis. Causes of granulomatous inflammation include sarcoidosis, VKH, sympathetic ophthalmia, toxoplasmosis, ocular Lyme borreliosis, tuberculosis, and syphilis.

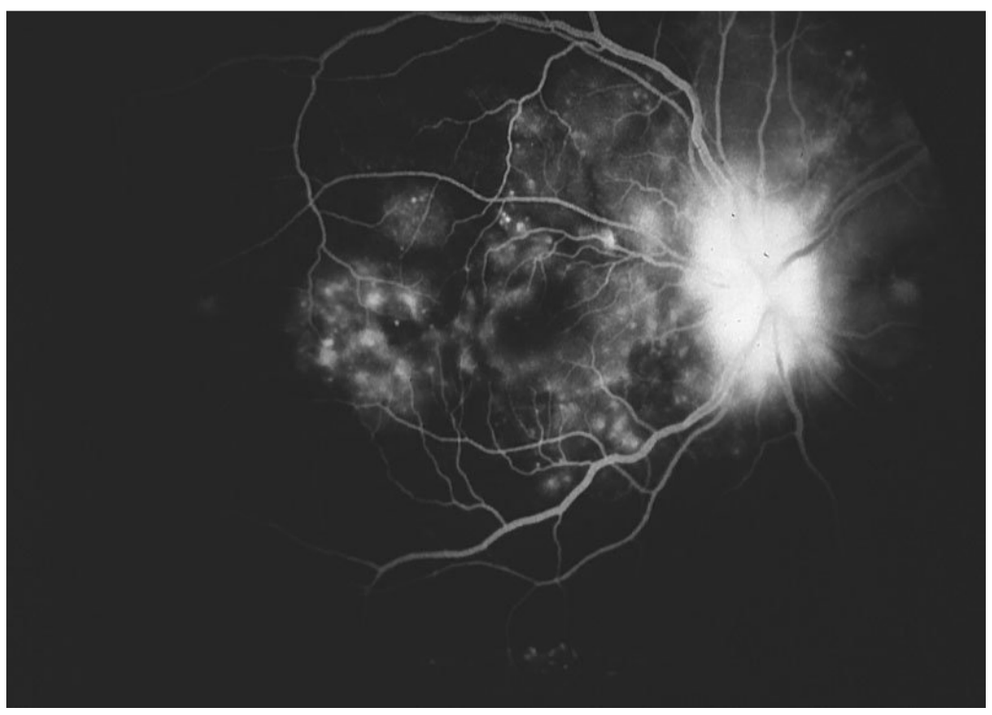

FIGURE 45–2 Fluorescein angiography of the same eye at the same time showing prominent disc edema, but also endpoint hyperfluorescence corresponding to retinal pigment epithelium (RPE) lesions.

5. Neurologic signs and symptoms warrant further investigation to rule out meningeal infection or central nervous system (CNS) disorder. A computed tomographic (CT) scan with and without contrast or magnetic resonance imaging (MRI) of the brain may be diagnostic. Lumbar puncture with cerebrospinal fluid (CSF) sent for cell count and differential, protein, glucose, VDRL (Venereal Disease Research Laboratories), bacterial stains, and culture can aid in establishing the diagnosis. Primary intraocular B-cell lymphoma can also present as chronic uveitis with associated neurologic abnormalities. Appropriate blood tests to evaluate for malignancy or systemic infection may include a CBC with differential, ANA, RPR, FTA-ABS, Lyme titer, ACE, and PPD with anergy panel and a chest x-ray when the diagnosis is uncertain.

6. Several associated signs and symptoms along with patient demographics are important in the diagnosis of posterior uveitis and may eliminate the need for extensive laboratory and ancillary testing. Patients with VKH syndrome are typically pigmented (Hispanic, Asian, Native American, and African American), female, age 20 to 40 years, with associated systemic manifestations including auditory symptoms (tinnitus, hearing loss) or cutaneous findings (vitiligo, alopecia, poliosis). Neurologic symptoms (nausea, headache, vertigo, stiff neck) or signs (CSF pleocytosis) are frequent findings. Criteria for the diagnosis of VKH were set forth by the American Uveitis Society in 1978 (Table 45–1).

7. The clinical course of the disease is important in confirming the diagnosis. VKH generally follows three phases. The initial prodromal stage mimics a viral illness with neurologic signs and symptoms and is followed by the uveitic stage with bilateral posterior uveitis, peripapillary retinal elevation or disc edema, and thickening of the posterior choroid. Finally, chronic changes are seen including a "sunset glow" fundus (yellow-orange retinal

TABLE 45–1 **Vogt-Koyanagi-Harada Syndrome: Criteria for Diagnosis**

1. No history of ocular trauma or surgery.
2. At least 3 of the following:
   a. Bilateral chronic iridocyclitis;
   b. Posterior uveitis, including exudative retinal detachment, forme fruste of retinal detachment, disc hyperemia or edema, and "sunset-glow" fundus;
   c. Neurologic signs (tinnitus, stiff neck, central nervous system problems, or cerebral spinal fluid pleocytosis);
   d. Cutaneous findings (alopecia, vitiligo, poliosis).

(Reprinted from Am J Ophthalmol, 90, Snyder DA, Tessler HH, Vogt-Koyanagi-Harada syndrome; 69–75, 1980, with permission from Elsevier Science.)

pigment epithelial color change), Dalen-Fuchs' nodules (yellow-white choroidal granulomatous inflammatory infiltrates), poliosis, vitiligo, and retinal pigment epithelial mottling.

8. VKH and sympathetic ophthalmia share many characteristics, including fluorescein angiographic appearance, clinical characteristics, and a strong association with HLA-DR4. Therefore, a careful history to elicit even a remote history of penetrating ocular trauma is important.

TEST INTERPRETATION

Evaluation of the patient begins with a careful history, in this case with special emphasis on prior ocular surgery or trauma, systemic infections or inflammatory diseases, neurologic or auditory symptoms, and skin or hair depigmentation. Patient demographics are important clues to the diagnosis of intraocular inflammation, as many causes of intraocular inflammation affect characteristic patient populations. Next, a complete ocular examination must be performed to evaluate the location and type (granulomatous versus nongranulomatous) of inflammation, the distribution and appearance of choroidal inflammatory lesions, and any associated posterior pole pathology, including disc edema and/or serous retinal detachment.

Fluorescein angiography is an important adjunct in the diagnosis of posterior uveitis, as entities with similar clinical appearance may have very different fluorescein angiographic characteristics. Fluorescein angiography in the acute phase of VKH typically shows numerous pinpoint areas of hyperfluorescence at the level of the retinal pigment epithelium overlying areas of choroiditis. Optic disc edema is present in approximately 70% of patients. During the chronic phase, multiple retinal pigment epithelial window defects are seen. A similar angiographic appearance is seen in patients with sympathetic ophthalmia. Patients with lymphoma or a form of "white dot syndrome," such as acute posterior multifocal placoid pigment epitheliopathy (APMPPE) and multiple evanescent white dot syndrome (MEWDS), may have a similar clinical appearance but have distinct fluorescein angiographic characteristics.

B-scan ultrasonography can be helpful in evaluating patients with posterior uveitis in order to rule out posterior scleritis (scleral thickening present), uveal effusion syndrome (may have scleral thickening and may often involve the peripheral choroid), or infiltrative lesions. Echographic features of VKH include diffuse, low-to-medium reflective choroidal thickening, mild vitreous opacities, and serous retinal detachment located in the posterior pole.

DIAGNOSIS

Vogt-Koyanagi-Harada syndrome.

MEDICAL MANAGEMENT

Prompt treatment with systemic corticosteroids (80 to 200 mg per day orally), a cycloplegic agent, and topical prednisolone acetate 1% (frequency tailored to control anterior segment inflammation) may result in rapid resolution of symptoms of redness, pain, and photophobia. The sooner treatment is initiated, the more rapid the resolution of symptoms. H2-blockers, such as oral ranitidine 150 mg twice daily, should be administered to protect against gastric ulcer formation

while patients receive high-dose systemic steroid treatment. In particularly severe cases, initial treatment with intravenous steroids may be considered. Oral prednisone should be tapered very slowly (over 4 to 6 months) with careful observation as nearly half of recurrences occur within this time period. If symptoms do not resolve with prednisone, other systemic immunosuppressants such as cyclosporine, cyclophosphamide, chlorambucil, and azathioprine can be used.

SURGICAL MANAGEMENT

Surgical intervention does not play a direct role in the management of most causes of posterior uveitis that are a result of a systemic inflammatory disease. Exudative retinal detachments usually resolve with resolution of intraocular inflammation. Complications associated with chronic intraocular inflammation, such as cataract formation, angle-closure glaucoma, or choroidal neovascularization, may require future surgical intervention.

REHABILITATION AND FOLLOW-UP

The patient should be followed frequently in the initial stages of the disease in order to adjust treatment with corticosteroids for adequate control of inflammation and prevention of sequelae such as posterior synechiae and angle closure. Early aggressive treatment with systemic corticosteroids can be followed by a gradual taper with less frequent ocular examination once a decrease in inflammation and exudative detachment is noted. When steroids alone are unable to control intraocular inflammation, or the patient is intolerant of the side effects of steroids or relapses while on high-dose steroid treatment, other immunosuppressive agents can be used. Once complete resolution of inflammation and serous detachment is achieved, a slow taper over 6 months decreases the risk of acute reactivation of disease. Patients should be monitored on a regular basis for evidence of cataract, choroidal neovascularization, or angle-closure glaucoma.

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Case 46

RETINITIS

Scott Anagnoste, M.D.

HISTORY

A 32-year-old female with a 10-year history of acquired immune deficiency syndrome (AIDS) complained of new onset of multiple black spots in the visual field of the right eye and black spots in the visual field of the left eye for 2 weeks. She had a CD4 count of 64 and was on highly active antiretroviral therapy (HAART).

Examination revealed a best corrected visual acuity of 20/30 in the right eye and 20/40 in the left eye. The intraocular pressure was 10 in each eye. The anterior segment was unremarkable with no anterior chamber cell or flare. Funduscopic examination of the right eye showed creamy, yellowish-white retinitis with prominent, associated hemorrhage within the lesion (Fig. 46–1). There was active vitritis and vascular sheathing superior to the disk extending along the superotemporal arcade. The left eye had a peripheral area of retinitis temporally (Fig. 46–2).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Any complaint of floaters in a patient with a positive test for human immunodeficiency virus (HIV) and a relatively low CD4 count should prompt a complete funduscopic examination. A high index of suspicion for cytomegalovirus (CMV) retinitis exists since 20 to 30% of HIV-positive patients will develop this opportunistic infection in their lifetimes. The rate of CMV infection is markedly higher in those patients with CD4 counts below 100. Prior to the development of HAART, CMV retinitis was commonly seen within 1 year after diagnosis with AIDS; since the advent of HAART therapy CMV retinitis is being diagnosed much later in the course of the disease.

2. Although CMV retinitis is the most common chorioretinal inflammatory condition in HIV-positive patients, several conditions may have ophthalmoscopically similar appearances. Acute retinal necrosis syndrome (ARNS), which is most commonly caused by the herpes zoster virus, presents with a similar retinitis. However, ARNS is much less common, often associated with prior herpes zoster dermatitis, and progresses rapidly, usually sparing the vasculature. Generally, ARNS tends to progress in a circumferential fashion whereas CMV progresses along the arcades.

3. Toxoplasmosis may also present with a similar appearance in HIV-positive individuals. Whereas the vast majority of toxoplasmosis seen in an immunocompetent population is unilateral and consists of small areas of retinitis often adjacent to areas of chorioretinal scarring, HIV-positive patients rarely have preexisting chorioretinal scars, develop larger lesions, and may present bilaterally in up to 40% of cases. This is because retinitis due to toxoplasmosis most commonly represents reactivation of congenital infection in immunocompetent individuals, whereas a significant proportion of immunocompromised patients have acquired new infection.

4. In patients with AIDS, syphilis may also present as a retinitis, with a vitritis and underlying large pale placoid subretinal lesions. These lesions are usually focal but may be bilateral. In addition to the opportunistic infections that cause retinitis, both Pneumocystis carinii and Cryptococcus neoformans can present with multifocal choroiditis. Neither condition typically causes a prominent retinitis.

5. Because the symptoms of CMV retinitis may initially be mild and often occur in the context of significant concurrent illness, many patients present relatively late in the course of infection. For this reason, ophthalmoscopic screening is recommended every 3 to 6 months in HIV-positive patients with a

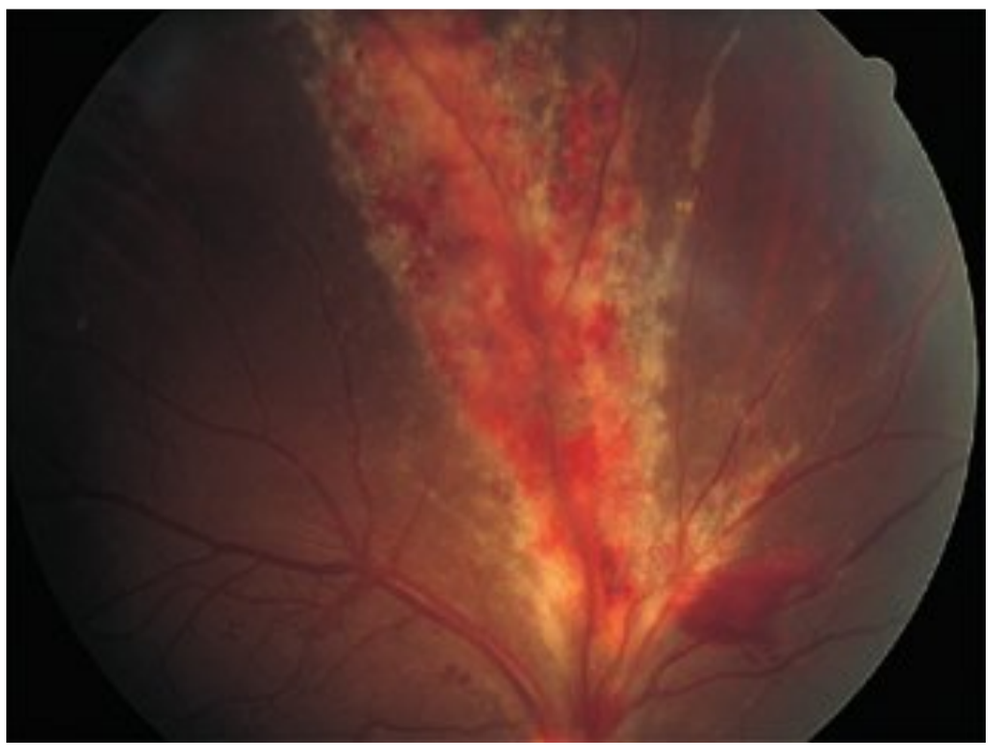

FIGURE 46–1 Fundus photograph of right eye at presentation shows confluent wedge of retinitis with prominent hemorrhage extending from the superior nerve head margin anteriorly into the mid periphery.

CD4 count below 100. Direct ophthalmoscopy provides only a small field of view and may be further limited in the presence of media opacities, so complete ophthalmic examination with indirect ophthalmoscopy is advised.

TEST INTERPRETATION

The diagnosis of CMV retinitis is based primarily on the ophthalmoscopic appearance. Both serologic testing and viral culture are of limited value because a large proportion of unaffected individuals show evidence of previous exposure to CMV, and many HIV-positive patients are chronic carriers of the virus in their throat, urine, and blood. A marker for CMV viral load may become available shortly and would be of use in following these patients.

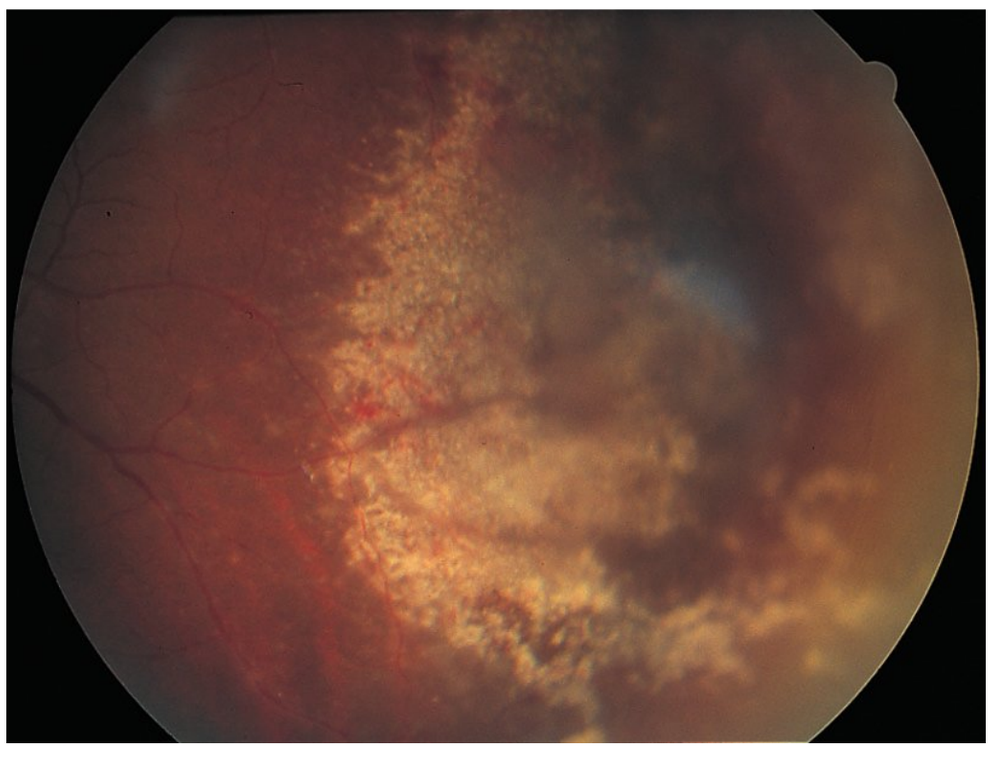

FIGURE 46–2 The left eye had a large area of retinitis without hemorrhage in temporal mid periphery.

DIAGNOSIS

CMV retinitis, OU, in a patient with AIDS.

MEDICAL MANAGEMENT

The initial management of CMV is usually medical with either intravenous ganciclovir or foscarnet. After 2 weeks of high-dose induction of ganciclovir (5 mg/kg once daily) or foscarnet (60 mg/kg 3 times daily), patients who respond well to treatment may be switched to lower-dose daily intravenous therapy or oral therapy. Cidofovir (5 mg/kg) has been approved by the FDA for treatment of CMV. Because of its long half-life, it can be administered intravenously once per week for induction and then every 2 weeks for maintenance. Patients with progression despite induction or those with disease that imminently threatens the macula may benefit from intravitreal injection of ganciclovir (2000 mcg) or foscarnet (1.2 mg). Since ganciclovir has myelotoxic side effects and foscarnet can result in renal toxicity, those patients who cannot tolerate systemic administration of these drugs or who progress despite it may benefit from intravitreal insertion of a ganciclovir implant that delivers adequate concentrations of the drug for 4 to 8 months.

SURGICAL MANAGEMENT

Ganciclovir implants offer a therapeutic alternative for patients with unilateral disease, especially if complications with systemic therapy are encountered.

Retinal detachment is a frequent complication of CMV retinitis, between 40 and 50% within the first year. Some small peripheral detachments

may be contained by laser demarcation. However, because most of the retinal detachments seen are the result of multiple areas of necrosis and often extend to the posterior pole, pars plana vitrectomy with silicone oil tamponade is usually the procedure of choice. Often, a ganciclovir implant is inserted at the time of the procedure. Overall, approximately 90% of CMV-related retinal detachments achieve anatomic success with this approach.

REHABILITATION AND FOLLOW-UP

With improvements in the care of HIV-positive patients, median survival after CMV infection has increased significantly. Therefore, issues such as cataract formation and long-term visual outcomes have become more important. Even after an initial flare-up of CMV retinitis is controlled medically or surgically, close follow-up with photographic documentation is essential.

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Case 47

WHITE DOT SYNDROMES

Nauman A. Chaudhry, M.D.

HISTORY

A 38-year-old woman presented with a 1-week history of seeing a veil over her left eye. She also complained of seeing floaters along with a dull, aching pain in the same eye. Earlier that week, she had had repeated episodes of nausea, vomiting, and diarrhea. Her past ocular history was unremarkable. Visual acuity was 20/20 in the right eye and 20/200 in the left eye. There was a 1+ afferent pupillary defect in the left eye. Anterior segment examination of the right eye was normal but the left eye showed 2+ cells in the anterior chamber and 1+ cells in the anterior vitreous. Funduscopic examination of the right eye was unremarkable. The left eye had multiple, ill-defined, small, round, white spots in the peripheral macula and juxtapapillary areas (Fig. 47–1). Multiple yellow dots were also seen in the foveolar area. Fluorescein angiogram showed wreathlike areas of hyperfluorescence that were consistent in location with the white lesions seen on clinical examination (Fig. 47–2). Indocyanine green angiography (ICG) demonstrated multiple hypofluorescent spots in the posterior pole and hypofluorescence around the optic nerve (Fig. 47–3). Humphrey visual field testing showed an enlarged blind spot in the left eye. Electroretinography showed a profound decrease in both the a-wave and early receptor potential amplitudes.

Seven weeks following the initial presentation, visual acuity improved to 20/20 in the left eye with resolution of photopsias. Repeat fluorescein angiogram, visual fields, and electroretinogram were all within normal limits. One year later, visual acuity was stable at 20/20 in both eyes without any recurrence.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The history, ocular examination, and clinical course are most consistent with the diagnosis of multiple evanescent white dot syndrome (MEWDS). MEWDS is an acute unilateral condition that affects young adult females. There is no racial or regional predisposition. Patients often have a history of a recent viral illness and complain of blurry vision and photopsias. Objective findings include decreased vision (20/20 to 20/300), afferent pupillary defects, and an enlarged blind spot on visual field testing. Dyschromatopsia has also been described. Funduscopic examination usually shows multiple white dots seen in the deep retina or retinal pigment epithelium (RPE) concentrated in the perimacular area, along with yellow-orange dots in the fovea. Vitreous veils, venous sheathing, and mild blurring of the disc margin may also be seen. The condition is self-limiting, and typically does not recur.

2. Other disease entities that should be considered in the differential diagnosis include acute posterior multifocal placoid pigment epitheliopathy (APMPPE), serpiginous choroiditis, pseudo-presumed ocular histoplasmosis syndrome (multifocal choroiditis and panuveitis syndrome, punctate inner choroiditis), birdshot choroiditis, and diffuse unilateral subacute neuroretinitis (DUSN).

3. APMPPE typically occurs in young adults with an antecedent viral-like illness. Vitreous cells may be present and funduscopic examination shows multiple, large, placoid, well-defined, yellow-white lesions randomly scattered in the posterior pole. The lesions

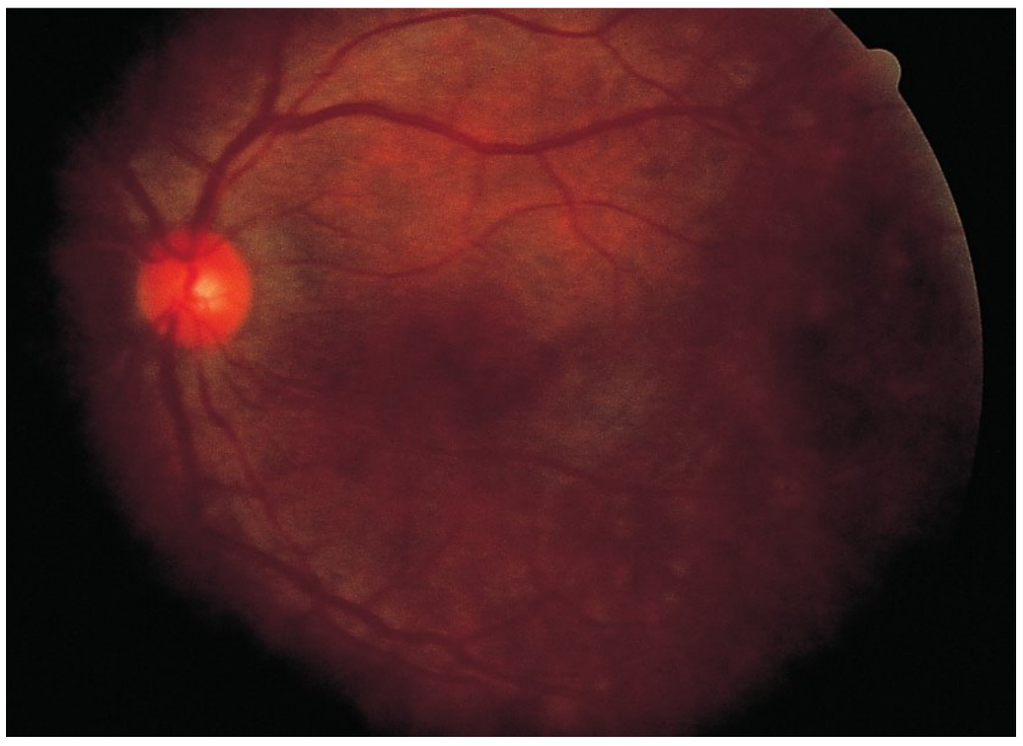

FIGURE 47–1 Color fundus photograph of the left eye. Note the multiple, ill-defined, white dots in the perimacular area.

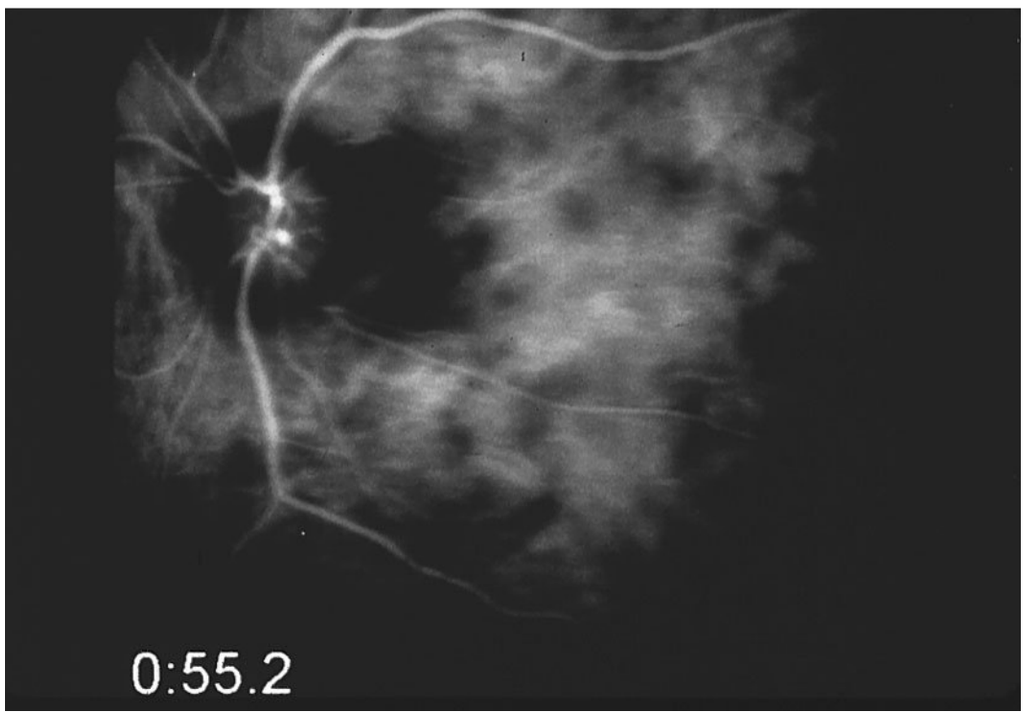

FIGURE 47–3 Indocyanine green (ICG) of the left eye (late phase) showing the hypofluorescent spots in the macula and hypofluorescence around the optic nerve.

are larger than seen in the present case. Additionally, fluorescein angiogram typically shows early hypofluorescence of the lesions followed by hyperfluorescence. The disease is self-limiting.

4. Serpiginous choroiditis (geographic or helicoid choroiditis) affects healthy young and middle-aged adults who present with acute loss of vision. It is a bilateral disease but the second eye may not be affected for many years. Vitritis may be seen and funduscopic examination reveals yellow-white, well circumscribed, placoid, often geographic-shaped or jigsaw puzzle–shaped lesions in the juxtapapillary region and posterior fundus. Solitary lesions may involve the peripheral fundus. Active lesions resolve with the development of atrophic chorioretinal scars. Fluorescein angiogram of the acute lesions demonstrates early hypofluorescence with late staining. Inactive lesions show late staining at the margins. Recurrences are common and usually occur adjacent to old lesions. Visual prognosis is guarded.

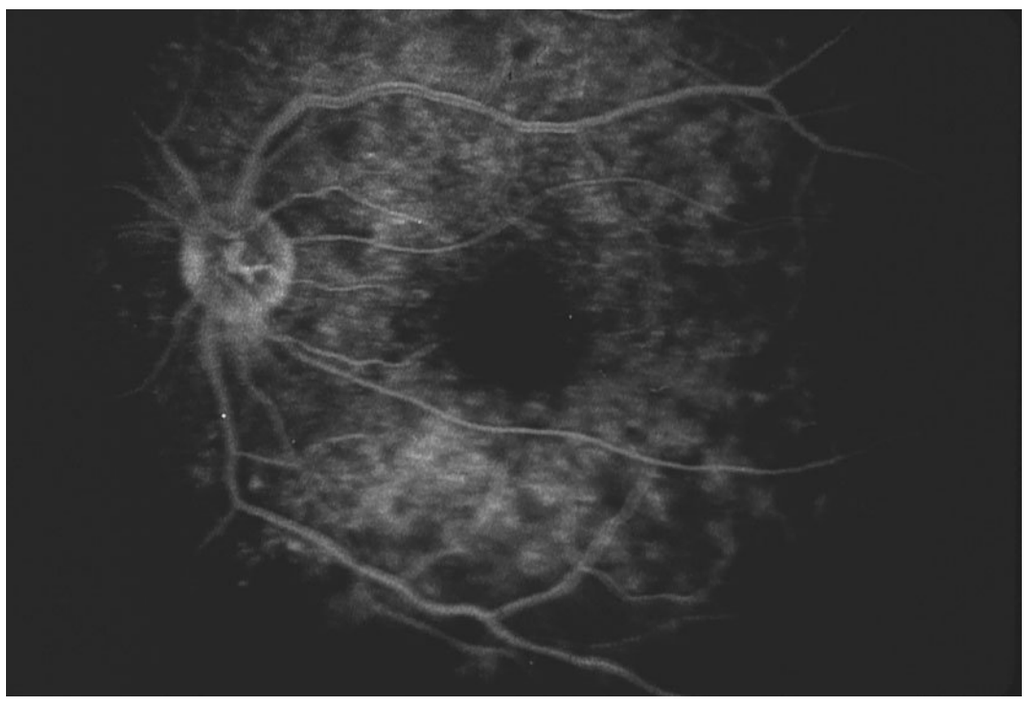

FIGURE 47–2 Fluorescein angiogram of the left eye (early phase) showing the wreathlike pattern of hyperfluorescence corresponding to the white dots on clinical examination.

5. Pseudo-presumed ocular histoplasmosis syndrome (multifocal choroiditis and panuveitis syndrome, punctate inner choroiditis) typically occurs in healthy young adult females. It is usually bilateral, but there may be delay in second-eye involvement. Vitreous cells are often absent when lesions are confined to the macula (punctate inner choroiditis), but are usually present in patients with multiple peripheral lesions (multifocal choroiditis and panuveitis). Multifocal small, round, discrete white lesions occur at the level of the RPE and inner choroid. Visual field testing may show an enlarged blind spot. Fluorescein angiogram of the active lesions shows early hypofluorescence with late staining. Electroretinogram (ERG) is often abnormal in patients with widespread lesions. In more advanced cases, the lesions show RPE changes. In cases of multiple

peripheral lesions, narrowing of retinal vessels, optic nerve pallor, and, occasionally, massive subretinal fibrosis are noted. Visual prognosis is guarded.

6. Birdshot chorioretinitis (vitiliginous choroiditis) is a bilateral disease that affects older (50+) healthy women. Patients initially complain of floaters with or without visual loss. In early stages, vitritis is almost always present with multifocal, ill-defined, oval or linear, yellow lesions, most numerous around the nasal two-thirds of the optic disc. There may also be optic disc edema and cystoid macular edema. These earlier lesions may show little or no change on fluorescein angiogram. It is usually a chronic, slowly progressive disease that may result in loss of central vision with narrowing of the retinal vessels, optic disc pallor, and focal and diffuse RPE atrophy. ERG is abnormal with marked reduction of b-wave.

7. DUSN is described in healthy children and young adults, with males affected more frequently (2:1 or 3:1). It is a unilateral disease and presents with acute or insidious loss of vision. Vitritis is usually present and funduscopic examination typically shows clusters of white, round, variable-sized outer retinal lesions, usually involving less than one quadrant of the fundus. In chronic cases, multiple atrophic chorioretinal scars and irregular areas of RPE disturbance may be present in extramacular areas along with variable degrees of retinal vessel narrowing and pallor of the optic disc. A motile subretinal nematode may be seen near the active outer retinal lesions. The ERG is subnormal, with the b-wave being affected more than the a-wave. During fluorescein angiography, acute lesions show early hypofluorescence with late staining along with staining of the optic disc. Visual prognosis is good if the worm is destroyed within several weeks after onset of visual loss.

TEST INTERPRETATION

Diagnosis of MEWDS can be made on the basis of clinical findings but several ancillary tests are of help in difficult cases. Fluorescein angiography demonstrates early wreath-like hyperfluorescence of the lesions with late staining. Staining of the optic nerve head is also seen in some patients. ICG shows multiple hypofluorescent spots in the posterior pole and hypofluorescence around the optic nerve. Visual field testing classically shows an enlarged blind spot. Electrophysiologic studies demonstrate a profound decrease in both the a-wave and early receptor potential amplitudes in the acute phase of the illness representing widespread photoreceptor dysfunction. However, during the recovery phase these amplitudes return to normal.

DIAGNOSIS

Multiple evanescent white dot syndrome, left eye.

MEDICAL MANAGEMENT

Topical steroids are indicated for the control of anterior segment inflammation. Otherwise, MEWDS is a self-limiting disease and no specific treatment is necessary.

SURGICAL MANAGEMENT

No surgical treatment is indicated.

REHABILITATION AND FOLLOW-UP

MEWDS is a self-limiting disease with excellent visual prognosis. The white dots usually fade in 1 to 2 weeks while the yellow-orange foveal dots persist for many weeks. Visual acuity and field defects improve in 6 to 12 weeks in 75% of cases. Recurrences have been reported but are extremely uncommon. Choroidal neovascularization is an extremely rare complication. Before or following MEWDS, some patients develop evidence of multifocal choroiditis, acute macular neuropathy, acute zonal occult outer retinopathy, or acute idiopathic blind spot enlargement.

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This case was contributed by Michael Yen, M.D. and Philip Rosenfeld, M.D., Miami, FL. Some of the written material was adapted from the unpublished lecture notes on "Inflammatory White Spot Syndromes" of J. Donald Gass, M.D.

Section VI

TUMORS

48. Vascular Tumor

49. Choroidal Melanoma

Case 48

VASCULAR TUMOR

Antonio V. Aragon II, M.D.
William E. Smiddy, M.D.

HISTORY

A 20-year-old man presented for evaluation of a peripheral retinal lesion of the left eye. The patient was asymptomatic. The patient's father and two siblings had a diagnosis of von Hippel-Lindau disease.

Examination revealed visual acuity of 20/20 bilaterally. External examination was unremarkable. There was no afferent pupillary defect. Visual field and motility examinations were unremarkable. Slit-lamp examination was normal. Funduscopic examination of the left eye revealed several dilated, tortuous arterioles and venules emanating from the optic disc and traveling nasally (Fig. 48–1). These vessels led to a collection of reddish-pink nodules, which emanated from the surface of the retina. There was a small associated area of subretinal fluid with adjacent exudate (Fig. 48–2). Funduscopic examination of the right eye was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. With the family history of von Hippel-Lindau disease and the classic appearance of the lesions, the diagnosis of retinal angiomatosis is readily made in this patient. These benign retinal hemangiomas were first described by von Hippel in 1895 and are sometimes referred to as von Hippel tumors. The appearance of retinal angiomas may vary greatly. Retinal angiomas found in the periphery are associated with a dilated feeding arteriole and draining venule, whereas those found in the peripapillary region often do not have the accompanying vessels. These associated vessels may present as twin vessels, separated by no more than a venule width. The presentation is also size dependent. Early lesions may be so small that they are clinically imperceptible. As the angiomas grow they may be first noted as small yellow or red nodules with dilated vessels. Later, the typical reddish-orange mass with dilated feeding vessels is observed. Angiomas arising from the inner retina have an endophytic appearance while those arising from the outer retina result in an exophytic appearance.

2. Retinal angiomas tend to manifest themselves in one of two different forms. Exudative form is characterized by progressive leakage from the angioma. This results in accumulation of subretinal fluid and exudate. Loss of vision in these cases may result from exudative retinal detachments or from accumulation of exudative material in the central macula from a peripheral angioma. The endophytic, or vitreoretinal, form is characterized by reactive fibrosis of the overlying vitreous, epiretinal membranes, and retinal traction. Vision loss occurs secondary to tractional or combined tractional-rhegmatogenous retinal detachments or epiretinal membranes. Interestingly, these epiretinal membranes may develop centrally, even in peripheral angiomas.

3. In this case, the family history and the classic funduscopic appearance of the retinal lesions quickly narrow the differential diagnosis. Other entities may mimic retinal angioma. Twin retinal vessels may be seen in cavernous hemangiomas of the retina or racemose hemangiomas. In these cases it is the lesions at the terminal portion of the twin vessels that allow for differentiation. Retinoblastoma and astrocytic hamartoma arise from the retina, but these lesions are typically yellowish-white as opposed to the reddish-orange appearance of an angioma. An arteriolar macroaneurysm may simulate an early angioma; however, the patient's age and the associated hypertensive changes of the retinal vasculature should differentiate between

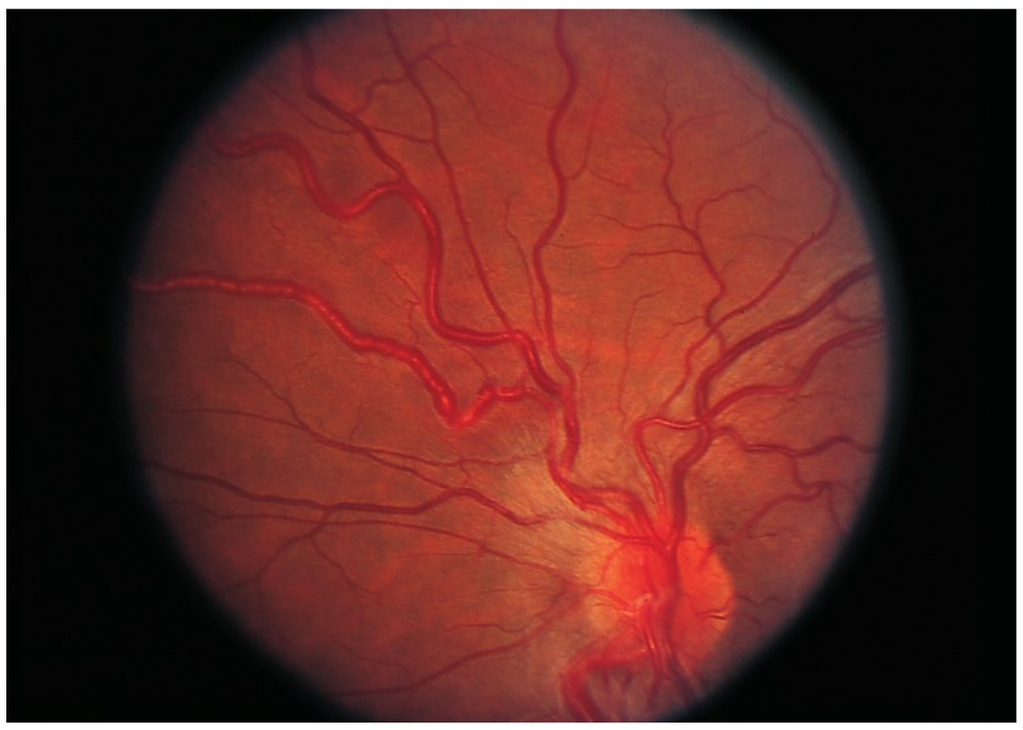

FIGURE 48–1 Examination of the posterior pole of the left eye demonstrates the multiple tortuous, dilated vessels arising from the optic disc and radiating toward the nasal periphery. Note that the affected vessels include arterioles and venules.

the two entities. A retinal granuloma, particularly papillary lesions due to a nematode, foreign body, or inflammatory disease, may be indistinguishable from an angioma. Associated findings and ancillary tests should help to provide the correct diagnosis. A peripheral sea fan with associated hemorrhage may have the gross appearance of an angioma, but close inspection and medical history lead to the correct diagnosis. It is important in cases with exudative retinal detachment to consider retinoblastoma, Coats' disease, and familial exudative vitreoretinopathy. Choroidal melanoma must also be considered in the differential diagnosis. Particular attention needs to be given to papillary or peripapillary lesions, as retinal angiomas may appear as a wide variety of lesions.

4. Special attention should be paid to distinguishing between a von Hippel lesion and a vasoproliferative retinal tumor, or acquired capillary hemangioma. The appearance of the masses can be quite similar, but the vasoproliferative tumor does not exhibit the dilated vessels associated with a retinal angioma. These lesions may occur in the setting of an existing retinal disease and have preponderance for the inferotemporal quadrant.
5. Multiple angiomas, whether they be unilateral or bilateral, tend to imply the presence of von Hippel-Lindau disease. A family history of von Hippel-Lindau disease or conditions consistent with von Hippel-Lindau disease should be taken in all patients with retinal angiomas.
6. Unlike peripheral retinal hemangiomas, peripapillary and capillary hemangiomas are usually not associated with the von Hippel-Lindau syndrome.

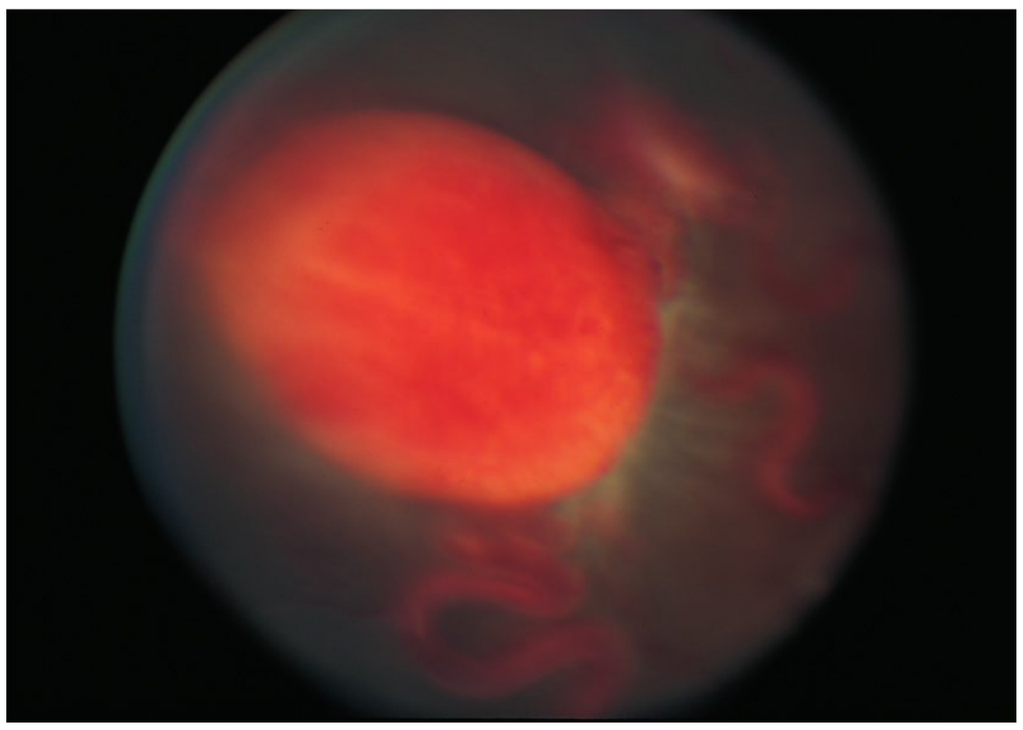

FIGURE 48–2 Peripheral examination revealed a collection of reddish-orange tumors. Each had an associated dilated feeding arteriole and draining venule. There also was a small associated area of adjacent subretinal fluid and exudate.

TEST INTERPRETATION

The diagnosis of a retinal angioma is a clinical one. Slit-lamp biomicroscopy with the use of a hand-held aspheric lens may provide a diagnostic view of posterior lesions. Indirect ophthalmoscopy provides the optimal view of more peripheral lesions. However, in certain difficult cases, ancillary tests can assist in making the diagnosis.

Fluorescein angiography may be helpful in differentiating some angiomas, particularly exophytic masses. Angiography typically reveals the dilated retinal arteriole in the early arterial phase. This is followed by hyperfluorescence of the tumor itself due to filling of the individual capillaries. The venous phase generally reveals the prominently dilated venule as well as continued

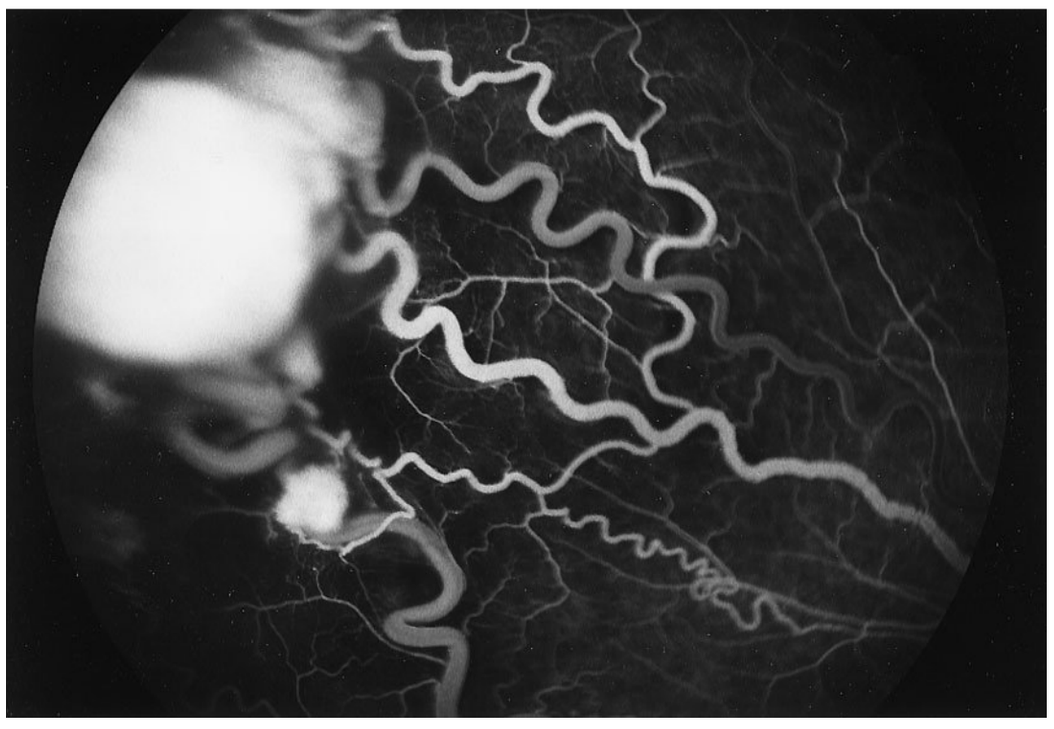

FIGURE 48–3 Laminar venous phase fluorescein angiogram reveals filling of dilated arterioles and hyperfluorescence of the angiomas. Laminar filling of the venules is also seen.

hyperfluorescence of the angioma (Fig. 48–3). Late phase angiography will exhibit continued hyperfluorescence of the angioma as well as possible leakage of fluorescein.

Fluorescein angioscopy can be of great utility in detecting early angiomas. These lesions may be very small or subtle due to the reddish coloration of the lesion blending into the background on indirect ophthalmoscopy. Use of angioscopy by performing indirect ophthalmoscopy with the use of an excitation light during fluorescein injection can assist in locating very small angiomas.

Ultrasound examination can assist in identifying and quantitating the size of some retinal angiomas. It is best used in angiomas larger than 2 mm, but may detect smaller lesions. B-scan ultrasonography will typically reveal a high-density echo at the inner border of the mass with a uniform acoustic signal throughout the mass. Associated retinal detachment and subretinal fluid may be demonstrated; however, no choroidal component will be noted. A-scan ultrasonography will demonstrate a high spike at the internal border of lesion and a high internal reflectivity.

Computed tomography (CT) and magnetic resonance imaging (MRI) are generally reserved for cases with larger tumors and those with exudative retinal detachments. CT may reveal an enhancing intraocular mass. MRI reveals low signal intensity from a retinal angioma. This results in an isointense to hyperintense signal on T1-weighted images and an isointense to hypointense signal on T2-weighted images with respect to the vitreous. The lesion will demonstrate moderate enhancement with gadolinium administration. Unfortunately, the MRI appearance is not diagnostic, as melanomas as well as retinoblastomas may have a similar appearance. Patients should undergo neuroimaging, however, to exclude intracranial findings of von Hippel disease.

DIAGNOSIS

1. Multiple retinal angiomas OS.
2. von Hippel-Lindau disease.

SURGICAL MANAGEMENT

In the management of retinal angiomas one must first decide whether to treat or to observe. Most lesions causing vision loss or impending vision loss should be treated. The treatment of asymptomatic angiomas is controversial. Some angiomas remain stable while others progressively enlarge and result in vision loss. Smaller lesions are more easily treated, with less risk of complications, than larger lesions (those greater than 2.5 disc diameters).

Treatment modalities will vary, depending primarily on the size of the lesion. Laser can be particularly effective against smaller lesions. Success has been shown in treatment with either feeder vessel or direct treatment. Some advocate a stepwise approach, which includes feeder vessel treatment to induce closure of the vessels followed by direct treatment of the angioma. Slightly larger and more peripheral tumors can be successfully treated with double or triple freeze–thaw cryotherapy. Plaque radiotherapy using apex dose of 1000 to 5000 centigray may be used with large angiomas. External beam radiotherapy is employed in the setting of a mass associated with an abundant amount of subretinal fluid and exudate. Pars plana vitrectomy may relieve vitreoretinal traction, remove epiretinal membranes, and treat the angiomas directly.

The response to treatment can take a number of months, and in some cases a paradoxical response with increasing subretinal fluid, exudate, and vitreoretinal traction may occur. These responses tend to occur in larger lesions. This is part of the rationale for treatment of early lesions. Importantly, the epiretinal membranes may resolve spontaneously after treatment of the angioma. Therefore, it is suggested to wait 4 to 6 months before considering surgical correction.

REHABILITATION AND FOLLOW-UP

Von Hippel-Lindau disease should be considered in any patient with retinal angiomatosis. Von Hippel-Lindau is an autosomal dominant condition affecting organ systems throughout the entire body (Table 48–1). It is considered to be one of the phakomatoses. Its incidence has been estimated to be 1 in 35,000 to 1 in 40,000. The von Hippel-Lindau gene codes for a tumor suppressor protein and has been mapped to chromosome 3p25-26. Classically, the diagnosis has been made in patients exhibiting two or more findings consistent with von Hippel-Lindau if there is no family history or in patients with one finding and an affected first-degree relative. Genetic screening is also available to assist in early diagnosis.

Retinal angiomas develop in a majority of patients with von Hippel-Lindau disease. They tend to be the initial findings, usually in the patient's early to mid twenties. However, retinal examinations need to begin as soon as possible because angiomas have been seen in children under the age of 10. Due to the continued high risk of development of angiomas these patients deserve periodic examination, including indirect ophthalmoscopy. Annual to biannual examinations for affected individuals and first-degree relatives are recommended.

The systemic features of this disease are potentially debilitating or fatal and therefore patients and first-degree relatives must undergo periodic systemic screenings. These screenings include imaging of the central nervous system and the thoracic and abdominal cavities. Twenty-four-hour urine collection and analysis for pheochromocytoma is warranted. The ophthalmologist must work in concert with colleagues in other fields of medicine to ensure that patients with or at risk for von Hippel-Lindau disease receive the appropriate initial workup and subsequent follow-up.

TABLE 48–1 **Clinical Manifestations of von Hippel-Lindau Disease**

Eye	Retinal angiomas
Central Nervous System	Cerebellar hemangioblastoma Medullary hemangioblastoma Spinal cord hemangioblastoma Syringobulbia Syringomyelia
Renal	Renal cell carcinoma Hemangioblastoma Cysts
Adrenal Glands and Sympathetic Chain	Pheochromocytoma Paraganglioma
Pancreas	Hemangioblastoma Cysts
Epididymis	Cysts

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Case 49

CHOROIDAL MELANOMA

Arezo Amirikia, M.D.
Timothy G. Murray, M.D.

HISTORY

A 65-year-old man presented with a 2-week history of blurred vision involving the nasal field of vision in the right eye. Past medical history was notable for hypertension, hypercholesterolemia, gout, and arthritis. Past ocular history was unremarkable.

Examination revealed a visual acuity of 20/40 in the right eye and 20/20 in the left eye. Intraocular pressures were 15 in both eyes. There was a 1+ right afferent pupillary defect. Slit-lamp examination was notable for mild nuclear sclerotic alterations in both eyes. Dilated funduscopic examination of the right eye revealed an inferotemporal pigmented mass involving the macula with height of 6.1 mm and base of 13.5 mm × 12.0 mm confirmed by echography (Fig. 49–1). There was orange pigmentation on the surface of the mass and an overlying retinal detachment with shifting fluid. Examination of the left eye was unremarkable. A fluorescein angiogram of the right eye demonstrated a lesion with intrinsic vascularity and late staining (Fig. 49–2). Echography revealed a dome-shaped lesion with low reflectivity, high vascularity, and no evidence of extrascleral extension (Fig. 49–3). The patient underwent a medical workup to rule out the presence of metastasis including liver function tests and a chest x-ray that was unremarkable.

The impression at this time was that the patient had a medium-sized posterior uveal melanoma. The alternative treatment options were discussed and the patient underwent radioactive plaque therapy with iodine-125.

The patient was followed with serial evaluation every 4 to 6 months, including annual liver function testing and chest x-ray. Six years following radioactive plaque therapy, visual acuity in the right eye was 20/400. Slit-lamp examination revealed progressive nuclear sclerosis of the lens. The mass had decreased in size post-treatment to a height of 2.0 mm and base of 12.5 mm × 11.0 mm (Fig. 49–4). There was significant pigmentary alteration involving the original extent of the lesion with resolution of the overlying neurosensory detachment. The remainder of the retina revealed minimal nonproliferative radiation-related vasculopathy (Fig. 49–5).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The differential diagnosis of a pigmented choroidal lesion seen on presentation includes choroidal nevus, congenital hypertrophy of the retinal pigment epithelium (CHRPE), peripheral disciform lesion, ruptured macroaneurysm, melanocytoma of the optic nerve, and choroidal detachment. Choroidal nevi by definition are typically asymptomatic, less than 1.0 mm in height, and rarely demonstrate growth. CHRPE lesions are flat, heavily pigmented lesions with sharp borders and a surrounding hypopigmented halo. Peripheral disciform lesions and ruptured macroaneurysms can often be differentiated with fluorescein angiography. Melanocytomas of the optic nerve are typically jet black in color—a color rarely seen in choroidal melanomas. Choroidal detachment typically occurs in the setting of intraocular surgery, hypotony, or uveitis and is often accompanied by pain.
2. The differential diagnosis of a nonpigmented choroidal lesion includes metastatic carcinoma, choroidal hemangioma, choroidal osteoma, and posterior scleritis.

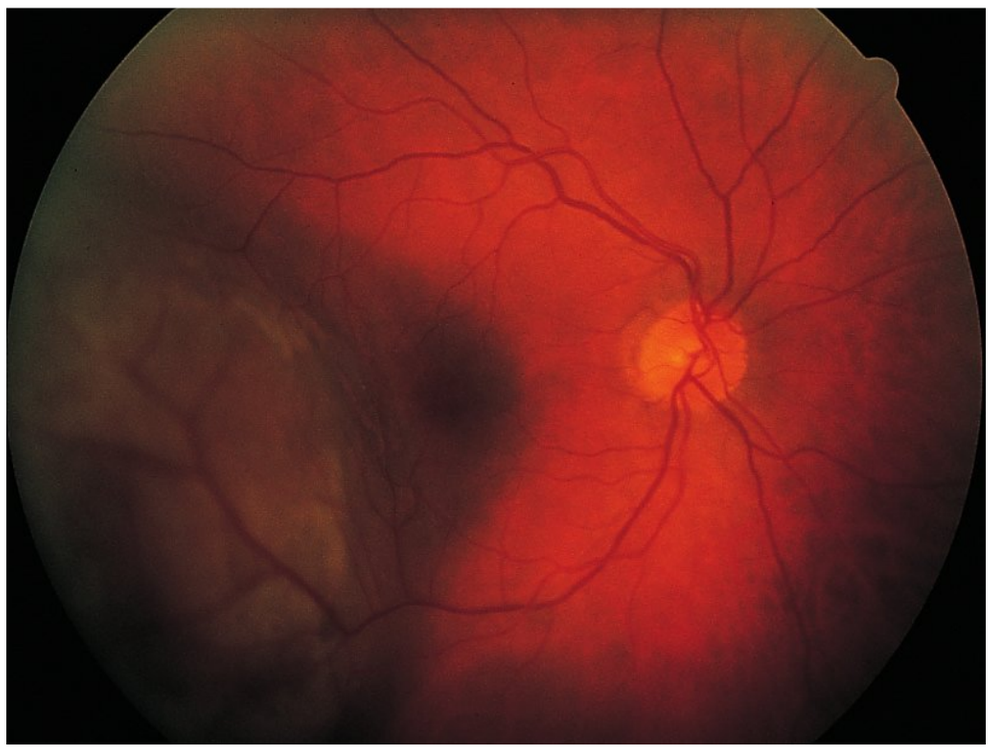


FIGURE 49–1 Color photograph of the right eye demonstrating a pigmented lesion involving the inferotemporal macula with overlying orange pigmentation and exudative retinal detachment.

Metastatic lesions are more frequently bilateral and multifocal and on ultrasound demonstrate higher internal reflectivity than choroidal melanomas. Choroidal hemangiomas demonstrate high internal reflectivity on ultrasound with widespread, diffuse leakage on fluorescein angiography. Choroidal osteomas typically occur in young women and are typically peripapillary in location. Ultrasound and computed tomography are of benefit diagnostically by demonstrating calcification within these lesions. Posterior scleritis with choroidal elevation is commonly associated with pain and often demonstrates thickening of the posterior sclera and the T-sign on B-scan ultrasonography, representing fluid in Tenon's capsule.

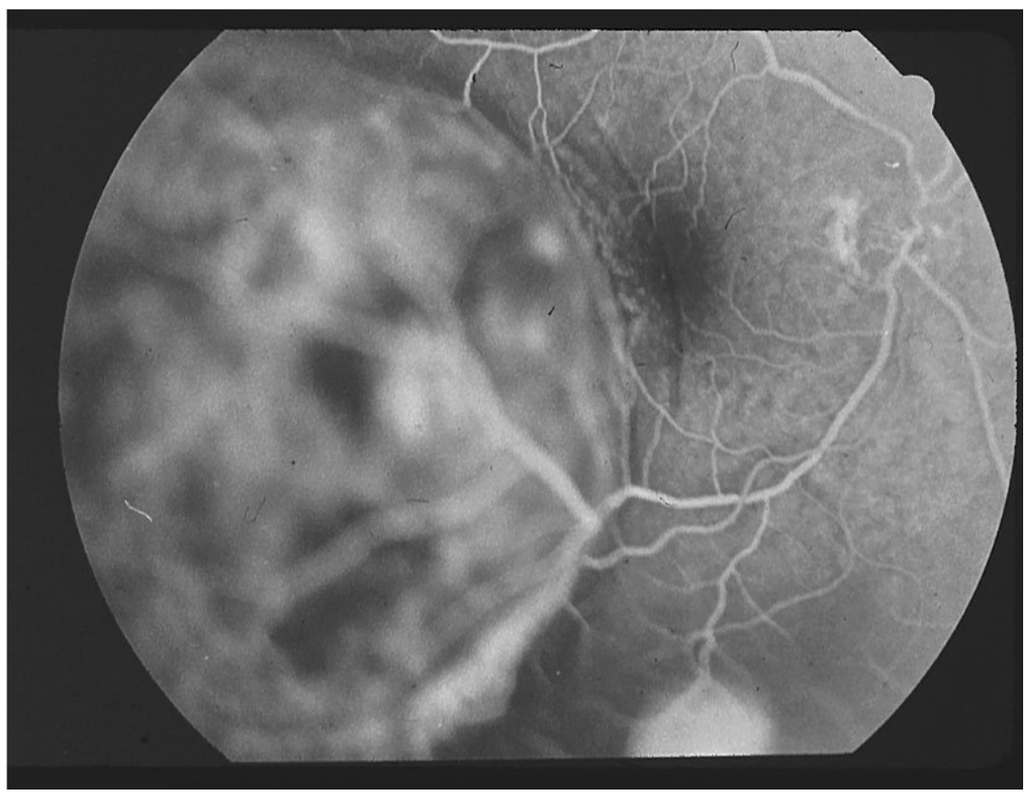


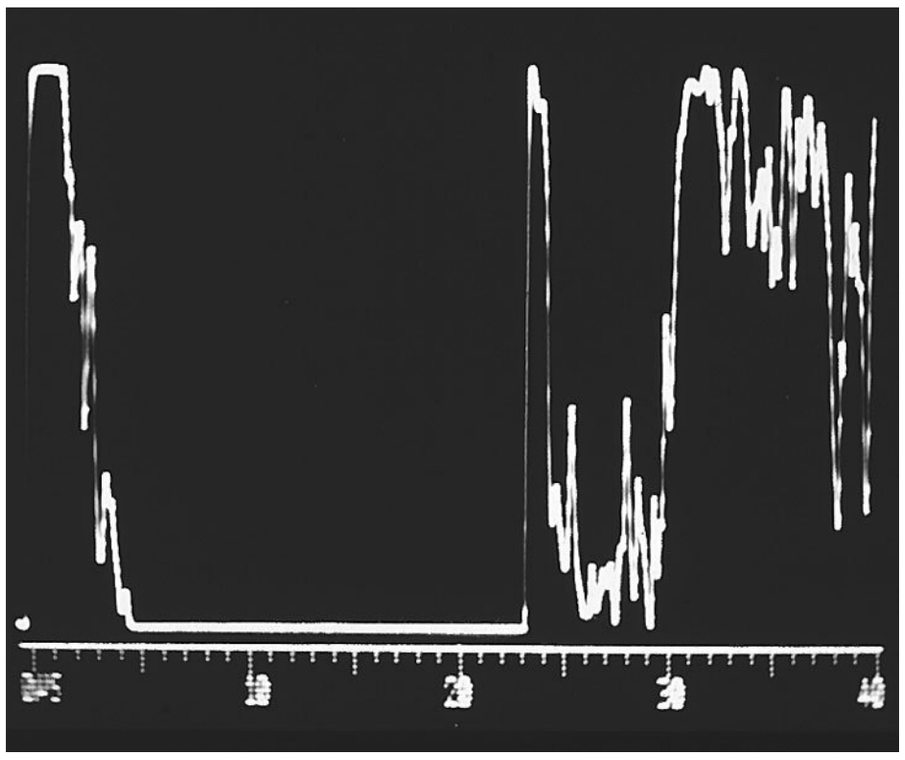
FIGURE 49–2 Transit phase fluorescein angiogram of the right eye demonstrating the normal retinal vessels overlying the tumor in addition to the intrinsic vasculature of the tumor (double circulation).

3. The etiology of an exudative retinal detachment with shifting fluid may or may not be evident on funduscopic examination. The cause of retinal detachment in this case presentation is readily visible as an associated pigmented lesion. Exudative retinal detachments may develop in association with choroidal tumors, intraocular inflammation including posterior scleritis, choroidal neovascularization, systemic conditions including hypertension and toxemia of pregnancy, and extensive retinal photocoagulation or cryopexy.

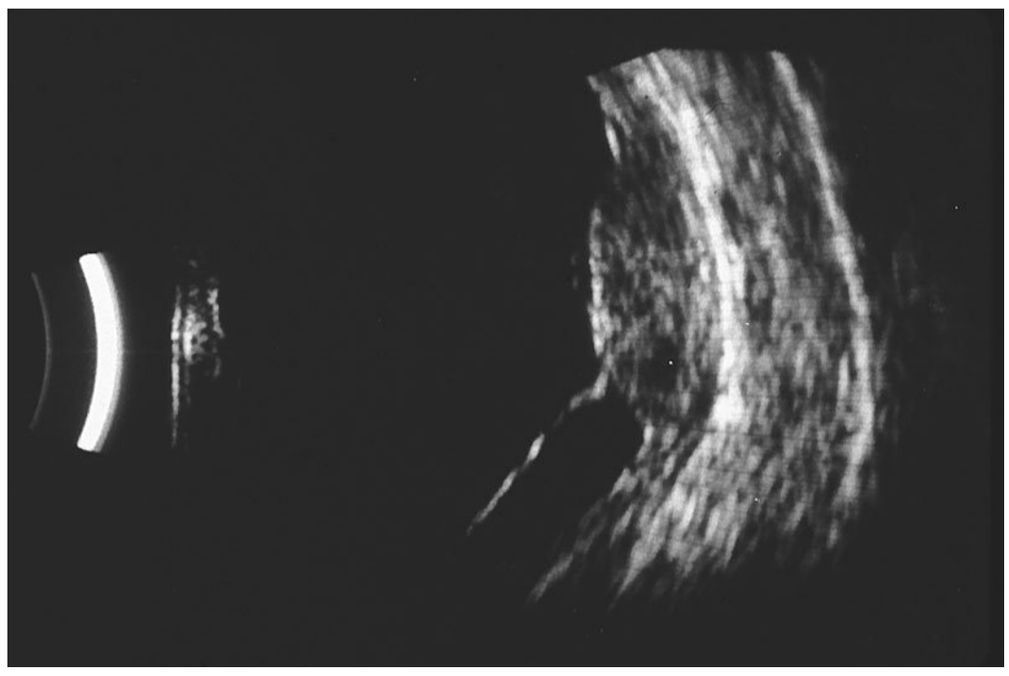
TEST INTERPRETATION

The diagnosis and staging of choroidal melanoma require clinical examination with ancillary testing. The history is typically not very useful in differentiating choroidal melanomas from other simulating lesions. The most common presenting symptoms include blurred vision, photopsias, and visual field defects. Clinical examination including slit-lamp biomicroscopy and indirect ophthalmoscopy are the most important tools in evaluating choroidal melanomas. Lesions may range from amelanotic to deeply pigmented with a dome- or collar-button configuration. The tumor may affect adjacent structures that may be evident as sentinel vessels (dilated episcleral vessels), cataract, vitreous hemorrhage, orange pigmentation (lipofuscin), drusen, choroidal neovascularization, exudative retinal detachment, and secondary glaucoma. Melanomas are typically categorized by size as small, medium, or large (Table 49–1). This classification is important in determining the available treatment options and in predicting survival outcomes.

Fundus photography is useful to document, evaluate, and monitor suspicious small pigmented lesions for growth, and to follow



A



B

FIGURE 49–3 (A) An A-scan ultrasound of the mass in the right eye revealed low internal reflectivity. (B) A B-scan ultrasound of the mass in the right eye revealed a mass with overlying exudative retinal detachment without extrascleral extension.

eyes with medium-sized melanomas following radioactive plaque therapy.

Fluorescein angiography is of limited use in diagnosing choroidal melanomas, but may be extremely useful in the evaluation of simulating lesions such as ruptured macroaneurysms and disciform lesions. A choroidal melanoma may demonstrate intrinsic vasculature,"hot spots,"vascular leakage, and late staining within the tumor.

Combined A- and B-scan ultrasonography is the most important ancillary test in the evaluation of patients with choroidal masses. It is useful for diagnosis, sizing, and evaluation of tumor response to treatment, and for differentiating choroidal melanomas from other lesions. A-scan ultrasonography typically reveals low to medium reflectivity and variable vascularity. It can also provide information on the presence or absence of scleral infiltration and extraocular extension. B-scan echography often demonstrates the three classic features of choroidal melanoma: shadowing, choroidal excavation, and an acoustically hollow zone within the tumor. Moreover, B-scan ultrasonography provides basal and apical dimensions and lesion configuration that can be used to document and monitor tumor growth.

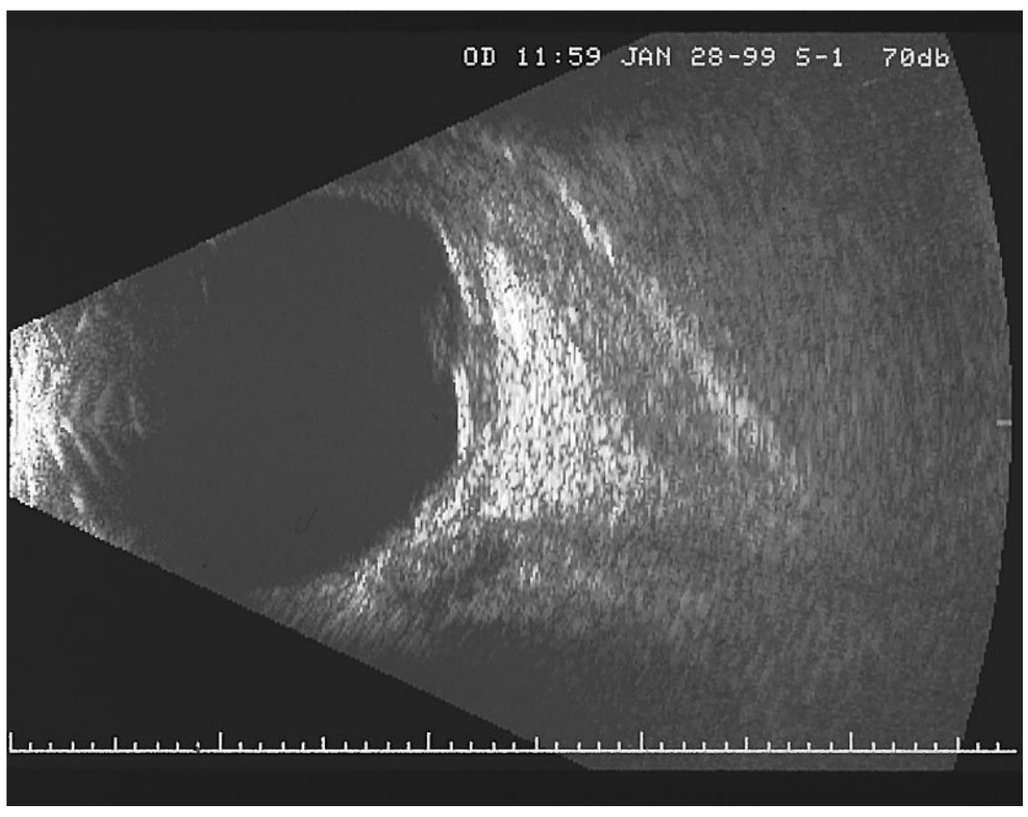


FIGURE 49–4 A B-scan ultrasound at 6 years' follow-up revealed a significant decrease in tumor height with resolution of the overlying retinal detachment.

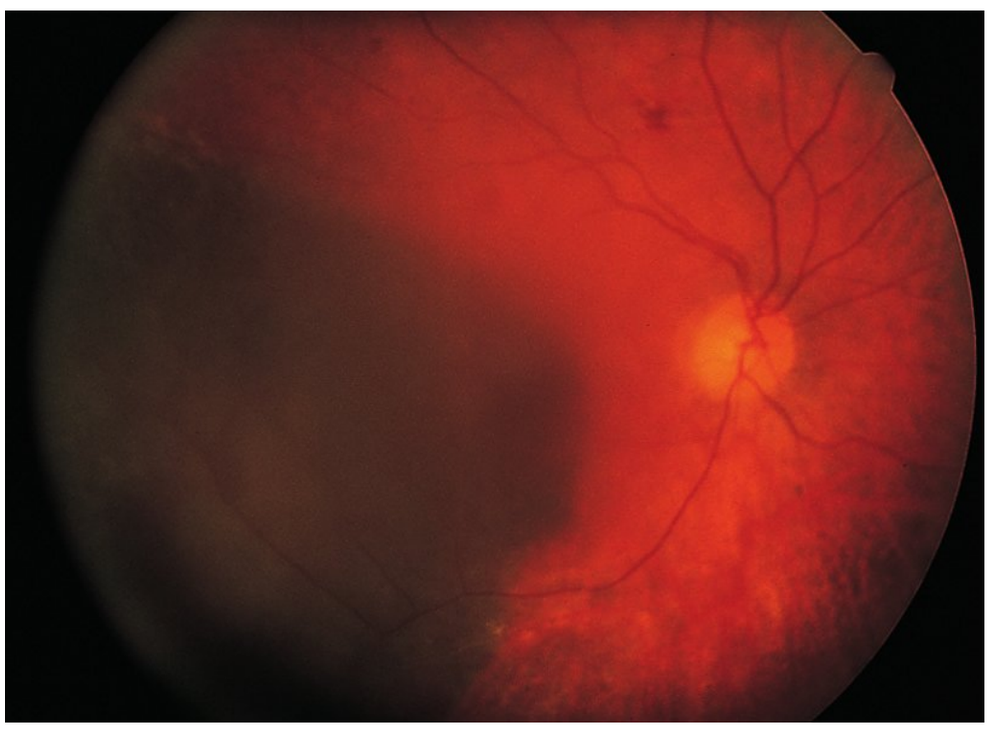


FIGURE 49–5 A photograph of the right eye post-treatment demonstrating substantial pigmentary alterations involving the original extent of the tumor and nonproliferative radiation-related vasculopathy of the retina.

TABLE 49–1 **COMS Classification of Choroidal Melanoma***

Small	
Apical height	1.0–3.0 mm
Basal diameter	5.0–16.0 mm
Medium	
Apical height	2.5–10.0 mm
Basal diameter	≤16.0 mm
Large	
Apical height	>10 mm (8 mm for peripapillary tumors)
Basal diameter	>16 mm

*As measured by ultrasound testing

DIAGNOSIS

Right eye: Medium-sized choroidal melanoma with secondary exudative retinal detachment.

MEDICAL MANAGEMENT

Tumor characteristics, status of the contralateral eye, results of metastatic workup, and the age and general health of the patient are important in determining the optimal management options for patients with malignant melanoma of the choroid. Treatment options include radiotherapy, enucleation, observation, photocoagulation, and local resection.

Laser photocoagulation has been used with short-term success for small, growing melanomas posterior to the equator and less than 3 mm in height and 10 mm in diameter. There are no medical treatment options available for medium-sized choroidal melanomas.

SURGICAL MANAGEMENT

The Collaborative Ocular Melanoma Study (COMS) is a prospective randomized multicenter clinical trial designed to evaluate alternative methods of management for choroidal melanoma. Treatment options vary with the size of the melanoma. The Medium Tumor Trial compared enucleation versus radioactive plaque therapy with iodine-125. The Large Tumor Trial compared enucleation alone to enucleation with pre-enucleation external beam radiation therapy (PERT). The Large Tumor Trial found no survival difference attributable to PERT of large choroidal melanomas.

Enucleation remains the treatment of choice for large choroidal melanomas. The Medium Tumor Trial found no survival difference between enucleation as compared to iodine-125 brachytherapy.

Radioactive plaque therapy is currently utilized as an alternative to enucleation for medium-sized tumors. The surgical procedure involves examination of the eye to confirm the presence of the tumor in the eye. A conjunctival peritomy is performed and the tumor is localized utilizing transillumination techniques. Proper plaque placement may require muscle disinsertion. The plaque is positioned over the involved sclera and three 5-0 nylon sutures are used to secure the plaque to the sclera in a temporary fashion. Ultrasound is next utilized to confirm proper positioning of the plaque. Next the eye is copiously irrigated with antibiotics and the conjunctiva is closed with 7-0 plain sutures. The eye is next patched with a lead shield and the plaque remains in place on average 3 to 7 days, depending on the size of the tumor and the rate of radiation delivery by the plaque (as calculated by the radiation oncologist). Postoperatively, patients may develop transient diplopia and radiation-related complications including radiation retinopathy and cataract.

REHABILITATION AND FOLLOW-UP

Follow-up examinations are performed every 4 months during the first 3 years and every 6 months thereafter. Clinical examination, fundus photography, and ultrasonography are performed in all patients for documentation of tumor regression and for the detection of local recurrences or complications. Ultrasonography during the first 6 months following radioactive plaque therapy may demonstrate an increase in height post-treatment secondary to intratumor

edema. Annual liver function testing and chest x-ray are recommended to detect metastatic disease. Estimated 5-year melanoma-specific mortality rates are 35% for large melanomas, 10% for medium melanomas, and less than 2% for small melanomas after treatment. Complications of globe-conserving radiotherapy include radiation-vasculopathy and optic neuropathy which occur at rates of approximately 30 to 50% at 5 years and are clearly increased for tumors adjacent to the optic nerve or fovea.

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Section VII

POSTERIOR SEGMENT COMPLICATIONS

50. Dislocated Posterior Chamber Intraocular Lens
51. Cystoid Macular Edema
52. Endophthalmitis
53. Suprachoroidal Hemorrhage

Case 50

DISLOCATED POSTERIOR CHAMBER INTRAOCULAR LENS

Mozart de O. Mello Jr., M.D.
William E. Smiddy, M.D.

HISTORY

A 64-year-old woman presented with sudden decreased vision in the left eye 2 days after an uncomplicated extracapsular cataract extraction surgery with posterior chamber intraocular lens (PCIOL) insertion. During the procedure a central posterior capsular rupture was noted, but the IOL was placed anterior to the remaining anterior capsule into the ciliary sulcus.

Her vision was 20/30 in the left eye with an aphakic correction. Slit-lamp examination showed a 2+ microbullous corneal edema superiorly and moderate cells in the anterior chamber. The pupil was round, but there was vitreous incarceration in the wound. The pupillary space was clear. Residual capsule was not noted. Funduscopic examination disclosed a freely mobile PCIOL within the vitreous cavity inferiorly. The retina was attached.

Surgery was recommended and performed with repositioning of the dislocated PCIOL into the ciliary sulcus using a scleral suturing technique to fixate the haptics. The scleral fixation sutures were placed through two partial-thickness superotemporal and inferonasal scleral flaps to cover the suture knots.

The IOL was in good position 1 month postoperatively with vision at 20/60. The vision returned to 20/20 within 6 months and remained so 6 years after the surgical repair. The IOL remained centered and well positioned, with no sign of complication.

In the right eye, the vision was 20/400 due to nuclear sclerosis.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. This patient developed the PCIOL dislocation following a complicated cataract extraction (posterior capsular rupture), the most common scenario for dislocated IOLs. The specific details of the cause of the dislocation are frequently not evident, although suboptimal posterior capsule support following posterior capsular rupture during cataract extraction is known to be a common element. When dislocation occurs a few days or weeks after surgery, the cause is less apparent and may be the result of spontaneous IOL haptic rotation out of a zone of posterior capsule remnant, asymmetric haptic placement, or zonular dehiscence. Dislocation months or years after placement is rare and may be due to traumatic or spontaneous loss of zonular support, as in eyes with pseudoexfoliation syndrome.

2. Visual symptoms such as decreased vision, glare, monocular diplopia or pain, and associated ocular complications (inflammation, increased intraocular pressure, cystoid macular edema, and coexisting retinal detachment) are the main indications for surgery. A mobile IOL in the absence of other complications is surprisingly well tolerated but may be removed if symptomatic.

3. The optimal timing for intervention for intraoperative IOL dislocation is probably during the initial cataract extraction. The logistics are easier for the patient, but may be impracticable for the surgeon. If this is not feasible, surgery within 2 weeks for acute dislocation

allows initial inflammation to subside or time to determine the visual or refractive severity of the dislocation. Most cases do not manifest dislocation intraoperatively, however. Thus, for other cases surgery is usually performed within a couple of weeks unless other complications coexist or intervene.

4. A pars plana approach is generally preferred because it allows optimal treatment of complications, but a limbal approach may be suitable for decentered and subluxated IOLs that are readily accessible and not enveloped by prolapsed vitreous. Regardless of the approach used, all accessible vitreous should be removed to avoid subsequent inflammatory and tractional complications.

TEST INTERPRETATION

Clinical examination at the slit lamp and with indirect ophthalmoscopy using a +20D lens is the standard diagnostic method.

Echography may be helpful to rule out associated complications when the anterior and posterior segments cannot be visualized due to opaque ocular media (hyphema, inflammation, or vitreous hemorrhage). A posteriorly dislocated PCIOL appears as a large foreign body–like structure within the vitreous cavity. Gonioscopy may be helpful to evaluate how much of the peripheral lens capsule remains and to assess for unrecognized vitreous incarceration in the cataract wound.

Since IOL exchange may become necessary, IOL power calculations should be available if lens exchange is performed.

DIAGNOSIS

Dislocated posterior chamber IOL, OS.

MEDICAL MANAGEMENT

Topical miotics may satisfactorily reduce glare, eliminate monocular diplopia, and improve visual function in selected patients with decentration of the lens optic. Supportive treatment with topical anti-inflammatory or ocular hypotensive agents is the mainstay of medical treatment.

Observation only is pursued for PCIOLs with simple decentration, if other superseding medical or ocular problems prohibit further surgery, if aphakic contact lens correction is satisfactory, or if the patient chooses not to pursue further surgery.

SURGICAL MANAGEMENT

The surgical management options available for dislocated PCIOLs include IOL repositioning with or without sutures, or IOL removal with or without exchange. Vitrectomy affords the most options for control of complications, but in selected cases a limbal approach allows effective achievement of necessary objectives. The timing may be modified by associated complications, but surgery is usually pursued within 2 weeks of acute symptomatic dislocation.

Nonsutured repositioning of dislocated PCIOL in the ciliary sulcus is the least traumatic surgical alternative. It is the preferred approach in eyes with at least six clock hours of residual peripheral capsular support. More extensive capsular support is necessary, however, when the inferior capsule is absent or if the residual capsule is questionable in extent.

Repositioning with transscleral suture (9-0 polypropylene) fixation is elected in eyes without adequate capsular support (Fig. 50–1). In some cases it is unnecessary to suture both haptics. Components common to all scleral suture fixation techniques include: (1) retrieving of the IOL; (2) introducing a suture loop through the ciliary sulcus; (3) passing the suture loop around the IOL haptic; (4) securing the suture to the sclera; and (5) covering or burying the scleral suture knot. Many techniques have been described to achieve these goals, and the method chosen may be based on surgeon preference and experience, IOL design, and associated circumstances. Transscleral suturing techniques are vulnerable to a variety of complications such as suture knot erosion, endophthalmitis, hemorrhage, IOL torsion or malposition, and recurrent dislocation due to suture breakage.

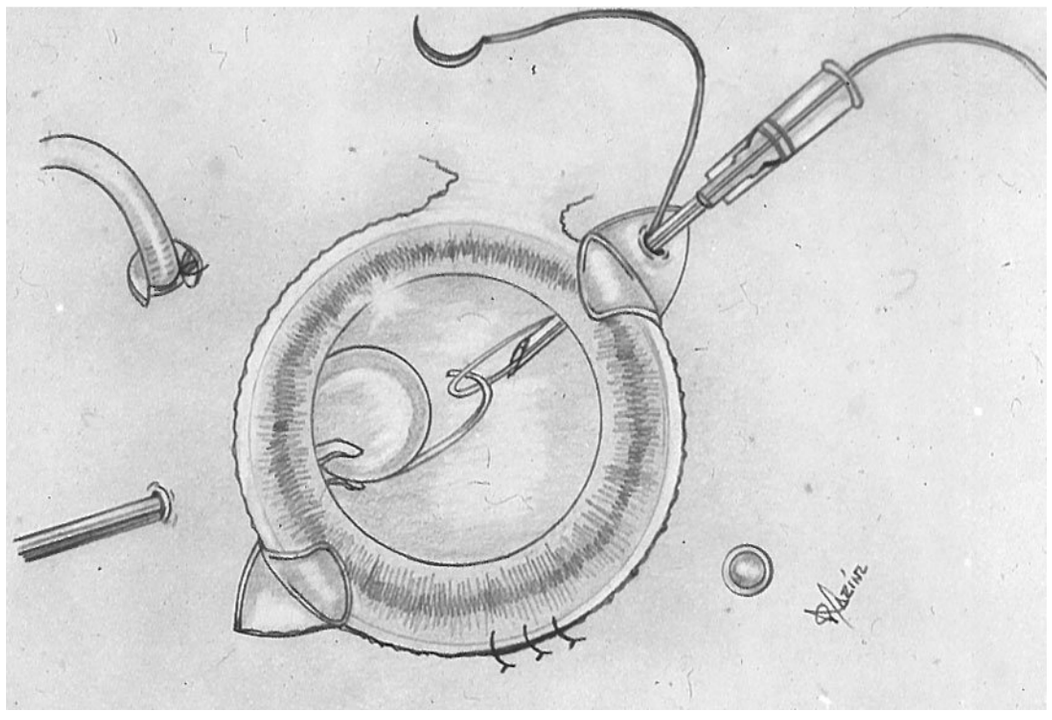

FIGURE 50–1 A schematic representation (surgeon's view) depicts preferred technique for scleral suture fixation of dislocated posterior chamber lens implant. After doing a core vitrectomy, the eye wall is mobilized and ultimately grasped with the forceps through the left-hand sclerotomy site. Care is taken to grasp the optic rather than the haptic. A 25-gauge needle pre-threaded with a 9-0 Prolene suture is introduced 1 mm posterior to the limbus through the bed of a partial-thickness scleral flap at the 7-o'clock meridian. The IOL haptic is then guided through the resultant loop with the left hand. The needle is passed through the bed of the flap, securing the inferior haptic. A similar maneuver is performed for the superior haptic.

IOL removal with or without exchange is usually performed for small optics implants, damaged haptics, for highly flexible haptics unsuitable for suture support, when available instrumentation is lacking, and in eyes with coexisting complex retinal detachment. Avoiding IOL removal or exchange avoids endothelial trauma and postsurgical astigmatism from reopening a limbal wound. IOL removal rates have decreased, probably because of improved repositioning techniques.

Special considerations are necessary with silicone plate IOLs. After successful placement into the capsular bag, YAG capsulotomy may allow posterior prolapse of the IOL. Also, insertion without complete posterior capsular support may result in dislocation (Fig. 50–2). Silicone plate IOLs can usually be repositioned into the ciliary sulcus anterior to the residual anterior capsule (Fig. 50–3). However, removal may be necessary.

The most frequent surgical complications in eyes with dislocated PCIOL include cystoid macular edema (usually low grade), elevated intraocular pressure, and retinal detachment (RD). Although the incidence of RD is relatively low (2%), careful intraoperative and postoperative examinations of the retinal periphery to look for retinal tears or detachment is necessary.

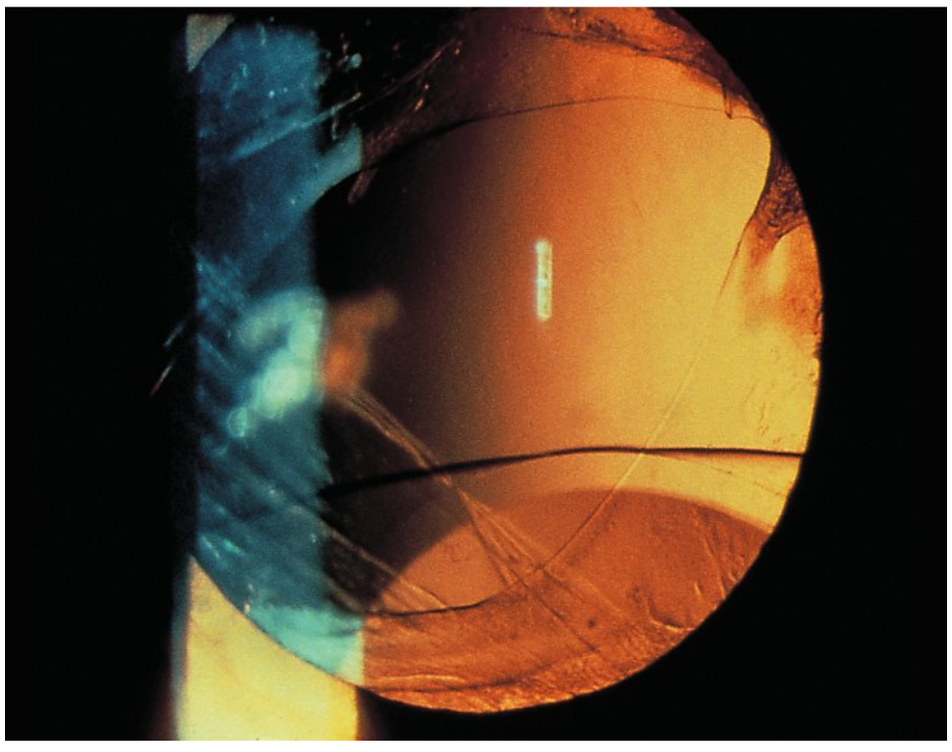

FIGURE 50–2 Clinical appearance of patient 2 weeks following YAG capsulotomy. A dislocated silicone plate IOL is visible behind the capsular remnants.

REHABILITATION AND FOLLOW-UP

Although visual acuity outcomes after surgical management of dislocated PCIOLs are usually good, the final visual acuity depends on preoperative macular function, complications

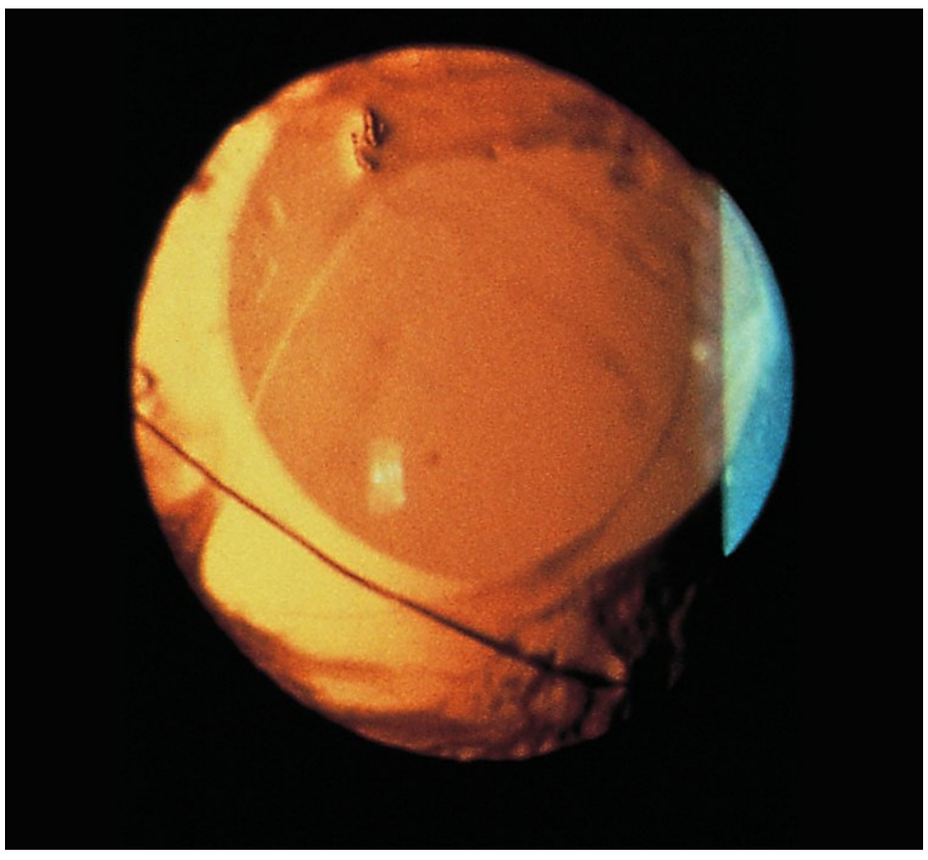

FIGURE 50–3 Postoperative appearance shows the silicone plate haptic IOL well positioned in the ciliary sulcus (anterior to the anterior capsular remnants).

from the original cataract surgery, and dislocation surgical management. In a majority of cases visual acuity is 20/40 or better. In this patient, after initial visual improvement to 20/60, the final visual acuity reached 20/20 6 years postoperatively. The relatively low rates of retinal detachment and cystoid macular edema limit the vision in only a minority of cases.

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Case 51

CYSTOID MACULAR EDEMA

Scott R. Anagnoste, M.D.

HISTORY

A 66-year-old woman presented 8 weeks after cataract surgery complaining of decreased visual acuity in the right eye. She had undergone phacoemulsification via a clear cornea incision using topical anesthesia with insertion of a foldable acrylic intraocular lens in the ciliary sulcus because of a central posterior capsular rupture. The patient reported that after the operation her visual acuity had been excellent but had declined substantially over the next 2 weeks. The patient reported no other significant medical or ophthalmic history. She denied diabetes mellitus or hypertension.

Examination revealed a best corrected visual acuity of 20/80 in the right eye. The pupillary exam and confrontation visual fields were normal. The cornea was of normal thickness and clear with a well-healed corneal incision temporally. The iris was normal and the anterior chamber was deep and quiet. The intraocular lens was well centered and appeared stable in position. Examination of the posterior pole revealed a posterior vitreous detachment. The optic nerve head was normal with a cup-to-disk ratio of 0.2. The retinal vessels were normal. The macula was thickened with cystic spaces apparent in the fovea upon examination with a Goldman contact lens. The peripheral retina was normal.

Fluorescein angiography demonstrated late leakage of dye from perifoveal vessels with a symmetric, petaloid pooling pattern (Fig. 51-1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Thickening of the macula is a clinical finding that defines macular edema. Various forms of macular edema may be a component of several disease processes. The visualization of cystic spaces within the fovea is diagnostic of cystoid macular edema (CME), but often requires examination with a Hruby or fundus contact lens to detect it. CME represents accumulation of intraretinal fluid (thought to be from retinal vascular leakage) in the inner nuclear and outer plexiform layers.

2. While postoperative inflammation is the most common cause of CME, numerous conditions may present with CME. These include other surgical procedures (eg, trabeculectomy, scleral buckling, strabismus surgery, and vitrectomy), almost any cause of intraocular inflammation (eg, uveitis, choroiditis, or retinitis), retinal vascular disease, retinal degeneration, epiretinal membranes, and drugs (eg, topical epinephrine, dipivefrin, betaxolol, latanoprost, or oral niacin or tamoxifen).

3. The incidence of pseudophakic CME varies according to the definition used. Typically, clinically significant CME, defined as CME with a characteristic ophthalmoscopic appearance and visual acuity worse than 20/40, occurs in 2 to10% of extracapsular cataract surgery. The incidence is reported to be slightly lower after phacoemulsification. Angiographic CME, which is defined as the presence of fluorescein leakage in a petaloid pattern in the fovea without significant visual loss, is much more common, occurring in 20 to 30% of uncomplicated cataract extractions. Posterior capsular rupture, vitreous loss, and retained nuclear or cortical material increase the incidence of CME.

4. The finding of vitreous incarceration into the limbal wound, iridovitreal synechiae, or iridocapsular synechiae may represent a

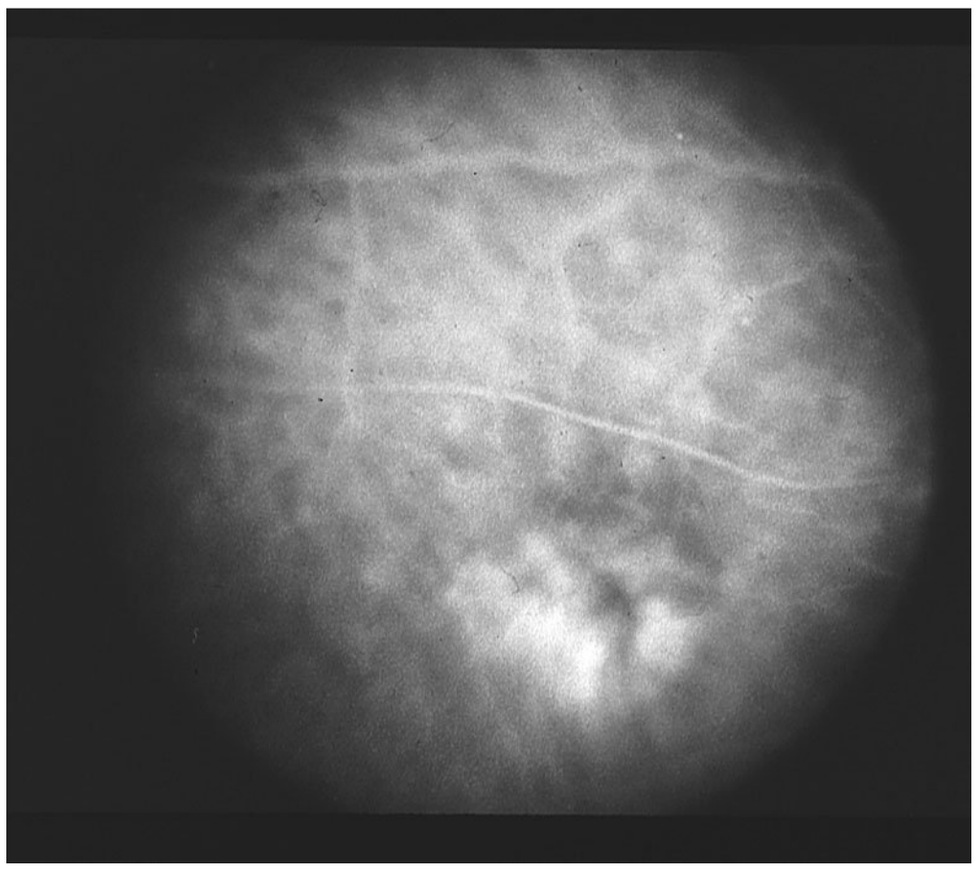

FIGURE 51–1 Fluorescein angiogram frame from the midvenous phase shows pooling of extravasated dye in the macula.

mechanical stimulus for inflammation (possibly via iris irritation) and may respond to surgical lysis.

5. The exact cause of CME is unclear. It is believed that inflammatory mediators cause breakdown of the blood–retinal barrier leading to fluid accumulation in the retina. These mediators may be released as a result of ultraviolet light exposure during and after cataract surgery, traction on vitreomacular adhesions leading to localized inflammation of the Mueller's cells, or more generalized intraocular inflammation. Most research has focused on components of the arachidonic acid pathway, but no specific mediator has yet been identified.

6. The macular edema of CME is ophthalmoscopically distinct in appearance from that of diabetic macular edema but overlap may exist. In the setting of postoperative visual loss in a diabetic patient, especially one with a history of diabetic retinopathy, the distinction between exacerbation of diabetic macular edema and CME may be difficult to make and often necessitates fluorescein angiography. Similarly, patients with age-related macular degeneration may require angiographic studies to determine the etiology of visual loss following cataract surgery.

TEST INTERPRETATION

Fluorescein angiography is the most useful adjunct to the clinical examination in the diagnosis of CME. The characteristic angiographic appearance consists of parafoveal capillary leakage with a petaloid pattern of intraretinal pooling of dye. The optic disk may demonstrate staining or leakage (especially in severe cases). Angiographic evidence of CME is much more common than clinically significant disease.

Optical coherence tomography and retinal thickness analysis have been used for research on CME and have been reported as a tool to follow the course of CME in a quantitative fashion. The use of this technique has been limited by the clinical value of such information and by the substantial equipment and labor costs involved.

DIAGNOSIS

Postoperative (pseudophakic) cystoid macular edema, OD.

MEDICAL MANAGEMENT

The medical management of CME consists of both prophylaxis and treatment. Many clinicians advocate the use of preoperative nonsteroidal anti-inflammatory agents (NSAIDs) or steroids to block the arachidonic acid pathway. Typically, flurbiprofen or suprofen are applied topically prior to the procedure, but this has not been shown to be consistently effective.

The treatment of CME is controversial and often unsuccessful. The majority of patients will resolve spontaneously even without treatment; many others will at least improve partially. However, a substantial minority of patients may have persistent, clinically significant CME. Initial treatment usually consists of topical corticosteroid such as 1% prednisolone four to eight times per day, or NSAID, such as 0.1% diclofenac four times per day, for 4 to 6 weeks. If there is no significant improvement, periocular steroid injections or oral carbonic anhydrase inhibitors may be tried.

SURGICAL MANAGEMENT

Surgical management of CME is usually reserved for cases in which the anterior segment manifests iris or vitreous traction or adhesion. Classically, vitreous prolapse to a limbal wound with peaking of the pupil is recognized as a surgically treatable cause of CME. Iridovitreal or iridocapsular synechiae may be causative and may respond to surgical lysis. Finally, relief of iris capture or tucking from an IOL may be curative. In selected cases Nd:YAG laser lysis of thin vitreous stands extending to the wound or sweeping via a paracentesis site at the slit lamp has been used with success in small trials.

REHABILITATION AND FOLLOW-UP

After initiation of medical treatment for CME, the patient should be observed within 4 to 6 weeks. If no improvement is noted, further treatment may be warranted. A significant number of patients may develop recurrent CME after cessation of a successful medical regimen; therefore, even patients who experience improvement or resolution of their symptoms should be followed carefully.

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Case 52

ENDOPHTHALMITIS

Magdalena F. Shuler, M.D., Ph.D.
William E. Smiddy, M.D.

HISTORY

This 82-year-old woman had a 4-day history of decreasing vision associated with increasing redness and mild pain, OD. She had undergone cataract surgery 6 days previously. Examination disclosed visual acuity of hand motion OD, moderate conjunctival and scleral injection, marked posterior synechiae, a 1 mm hypopyon with a marked fibrin response, and a posterior chamber intraocular lens (IOL)(Fig. 52–1). There was no view to the posterior pole due to the inflammatory opacities.

The patient underwent a vitreous tap and injection of intravitreal vancomycin, ceftazidime, and dexamethasone, followed by hourly treatment with topical fortified vancomycin, ceftazidime, corticosteroids, and topical atropine four times a day. The vitreal cultures grew Streptococcus species. As the clinical signs of inflammation improved, the topical medications were gradually tapered. One month after her presentation, her vision had improved to 20/70, with moderate but slowly resolving vitreous opacities.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

Painful loss of vision with prominent inflammation in the immediate postoperative period should be considered to be due to infectious endophthalmitis until proven otherwise.

1. An infectious corneal ulcer may present with conjunctival injection, hypopyon, and anterior chamber fibrin reaction. Important historical information includes contact lens use, corneal trauma, and recent history of intraocular surgery.
2. The classification of endophthalmitis is based on the clinical setting and time of onset. Endophthalmitis, an inflammatory reaction of the intraocular fluids or tissues, is classified as one of the following types: postoperative endophthalmitis (acute or chronic), post-traumatic endophthalmitis, endogenous endophthalmitis, or sterile uveitis. Postoperative endophthalmitis might occur after any procedure including cataract surgery, glaucoma filtering procedure, secondary IOL insertion, penetrating keratoplasty, pars plana vitrectomy, and eye muscle surgery. Acute postoperative endophthalmitis is defined as the presentation of endophthalmitis within 6 weeks of surgery, while chronic postoperative endophthalmitis presents greater than 6 weeks after surgery. The most common organism in acute postoperative endophthalmitis is Staphylococcus epidermidis which is usually less virulent than other causal organisms such as Staphylococcus aureus, other Streptococcus species, gram-negative rods like Pseudomonas, Proteus, and Serratia species. Post-traumatic endophthalmitis occurs after penetrating trauma, is especially common with trauma in rural areas, and is associated with poorer visual prognosis compared to other categories.
3. The classic signs and symptoms include decreased vision, afferent pupillary defect, pain, hypopyon, corneal edema, corneal infiltrate, fibrinoid anterior chamber response, and retinal periphlebitis. External signs include ciliary injection, chemosis, and lid edema. Acute postoperative endophthalmitis usually has a dramatic presentation while chronic postoperative endophthalmitis usually has a more insidious presentation. Postoperative inflammation that is unresponsive to intensive topical corticosteroids is suspicious for postoperative endophthalmitis, and an intraocular culture should be obtained.

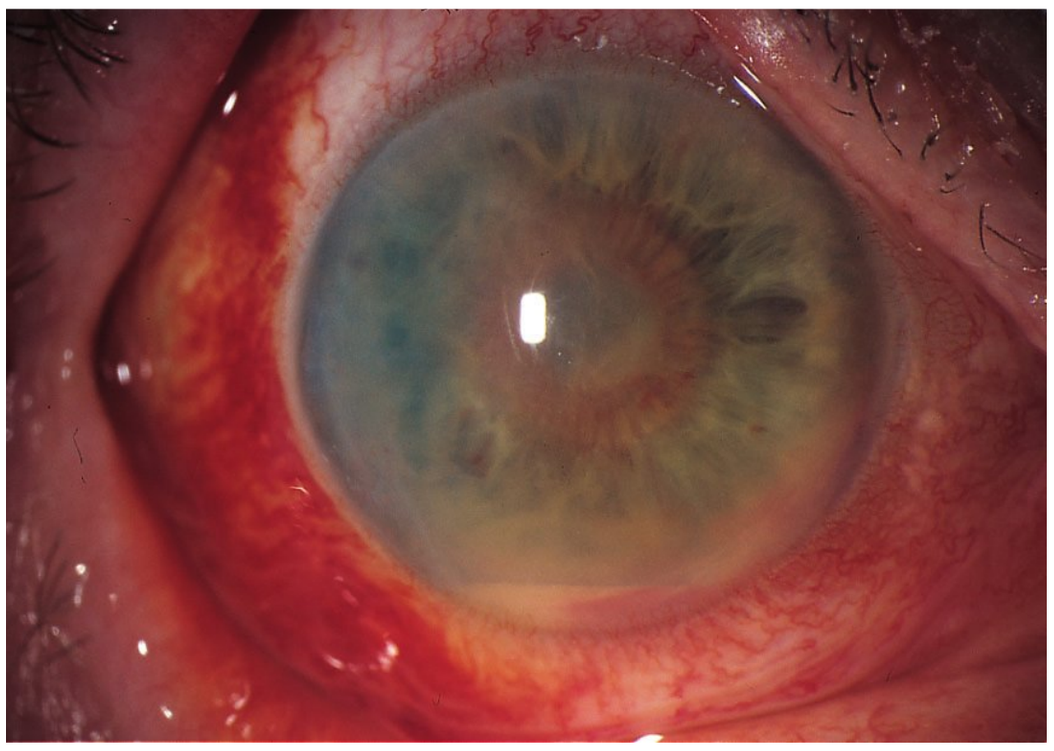

FIGURE 52–1 Slit-lamp examination showing conjunctival injection, hypopyon, fibrin, and synechiae.

TEST INTERPRETATION

Ultrasonography is useful to evaluate for choroidal or retinal detachment and to quantitate the severity of vitreous opacities in cases of suspected endophthalmitis with a limited view to the posterior pole.

Vitreous sampling, cultures, and Gram stain are critical to diagnosing and managing endophthalmitis. Empiric treatment is usually instituted initially, and the specific or later treatment is determined by culture results.

DIAGNOSIS

Acute infectious postoperative endophthalmitis, OD.

MEDICAL MANAGEMENT

Preoperative risk factors for postoperative endophthalmitis include blepharitis, conjunctivitis, canaliculitis, lacrimal duct obstruction, and diabetes. Intraoperative risk factors include inadequate lid and conjunctival disinfection, prolonged surgery, and polypropylene haptic intraocular lens. A nonrandomized, prospective trial by Speaker showed that 5% Povidone-iodine solution in the conjunctival fornices preoperatively reduced the bacterial load and decreased the incidence of culture positive endophthalmitis. The efficacy of preoperative topical antibiotics, intraoperative subconjunctival antibiotics, and postoperative topical antibiotics is unproven. Risk factors for postoperative endophthalmitis include wound leaks, wound dehiscence, inadequately buried sutures, and vitreous incarceration in the wound.

The Endophthalmitis Vitrectomy Study (EVS) Group studied the use of systemic antibiotics in patients with postoperative endophthalmitis. They found no significant difference in visual acuity or media clarity in patients whether or not they received systemic antibiotics. The findings of the EVS support the omission of systemic antibiotics and hospital admission as part of the initial treatment regimen for acute postoperative endophthalmitis.

SURGICAL MANAGEMENT

The EVS evaluated the results of vitreous tap (biopsy) versus pars plana vitrectomy (PPV) for endophthalmitis following cataract extraction or secondary IOL. Both groups received intravitreal antibiotics. The outcome measures were visual acuity and media clarity. In the EVS, the initial visual acuity was a good predictor of final visual outcome and response to vitrectomy. For patients presenting with visual acuity better than light perception (LP), final visual acuity was equal in the PPV versus vitreous biopsy groups. Patients with postoperative endophthalmitis who presented with only LP vision had a better visual outcome with immediate PPV.

Most authors recommend intravitreal antibiotics, including vancomycin (1.0 mg/0.1 mL) and either ceftazidime (2.25 mg/0.1 cc) or amikacin (0.4 mg/0.1 mL) for all patients with postoperative endophthalmitis. Topical vancomycin (50 mg/mL) and either amikacin (20 mg/mL) or ceftazidime (50 mg/mL) are also usually recommended.

Intravitreal or systemic steroid treatment was not studied in the EVS but might be useful in decreasing the damaging inflammatory effects of endophthalmitis.

The EVS studied only patients with acute postoperative endophthalmitis after cataract extraction or secondary IOL implantation. Extrapolation of results to other classes of endophthalmitis might not be valid.

REHABILITATION AND FOLLOW-UP

Postoperative treatment usually involves topical corticosteroids and antibiotic drops. Patients who do not respond to initial treatment should be considered for further surgery. Post-treatment ocular complications include retinal detachment, macular pucker, and posterior capsular opacity.

Many patients will maintain reading vision in the involved eye with rapid initiation of treatment at presentation. According to the EVS, more than half of the study patients achieved 20/40 vision.

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Case 53

SUPRACHOROIDAL HEMORRHAGE

Ingrid U. Scott, M.D., M.P.H.

HISTORY

A 78-year-old woman presented 4 days after cataract surgery in her left eye, complaining of acute onset severe pain and loss of vision in the left eye. Past medical history was notable for cardiac bypass surgery 2 years previously and systemic hypertension. Past ocular history was significant for myopia (−9.00 sphere) and primary open-angle glaucoma. Ocular medications included timolol 0.5% in both eyes twice daily, dorzolamide 2% in both eyes three times per day, and prednisolone acetate 1% in the left eye four times per day.

Vision was 20/60 on the right and hand motion on the left. Intraocular pressure was 12 mm Hg on the right and 39 mm Hg on the left. Slit-lamp examination of the right eye disclosed nuclear sclerotic lens changes. Slit-lamp examination of the left eye was notable for 2+ conjunctival injection, a temporal clear cornea incision reapproximated with interrupted nylon sutures, a shallow anterior chamber, aphakia, and a bullous appositional retinal detachment posterior to the iris plane (Fig. 53–1). An ultrasound examination demonstrated appositional ("kissing") suprachoroidal hemorrhages (Fig. 53–2). Due to the clotted nature of the suprachoroidal blood on echography, observation including serial echography was recommended. The patient's elevated intraocular pressure in the left eye was managed medically.

Ten days after presentation, echography demonstrated persistent retinal apposition with liquefaction of the suprachoroidal blood. A pars plana vitrectomy with drainage of the suprachoroidal hemorrhage and fluid–gas exchange was performed. At the 3-month follow-up visit, vision in the left eye was 20/400.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The differential diagnosis of the bullous retinal detachment seen on the presenting examination includes rhegmatogenous retinal detachment, exudative retinal detachment, serous choroidal effusion, and suprachoroidal hemorrhage. Severe pain is not consistent with a rhegmatogenous retinal detachment; exudative retinal detachments may be accompanied by pain if due to uveitis, a tumor that has undergone massive hemorrhage, or suprachoroidal hemorrhage. There was no evidence of uveitis. Acute onset severe pain, often seen in the context of suprachoroidal hemorrhage, is not typical of serous choroidal effusion.

2. The differential diagnosis of acute ocular pain accompanied by a shallow anterior chamber after cataract surgery includes malignant glaucoma, pupillary block, serous choroidal detachment, and suprachoroidal hemorrhage. Intraocular pressure is typically normal or elevated in all of these conditions, except for serous choroidal detachment, which is generally accompanied by a low intraocular pressure. The retina and choroid are flat in malignant glaucoma and pupillary block. If funduscopic evaluation is not prohibited by appositional retinal detachment, the differentiation between serous and hemorrhagic choroidal detachments may be made on the basis of the color of the choroidal elevations; serous choroidal detachments appear as light brown choroidal elevations while hemorrhagic choroidal detachments appear as dark brown or dark red choroidal elevations.

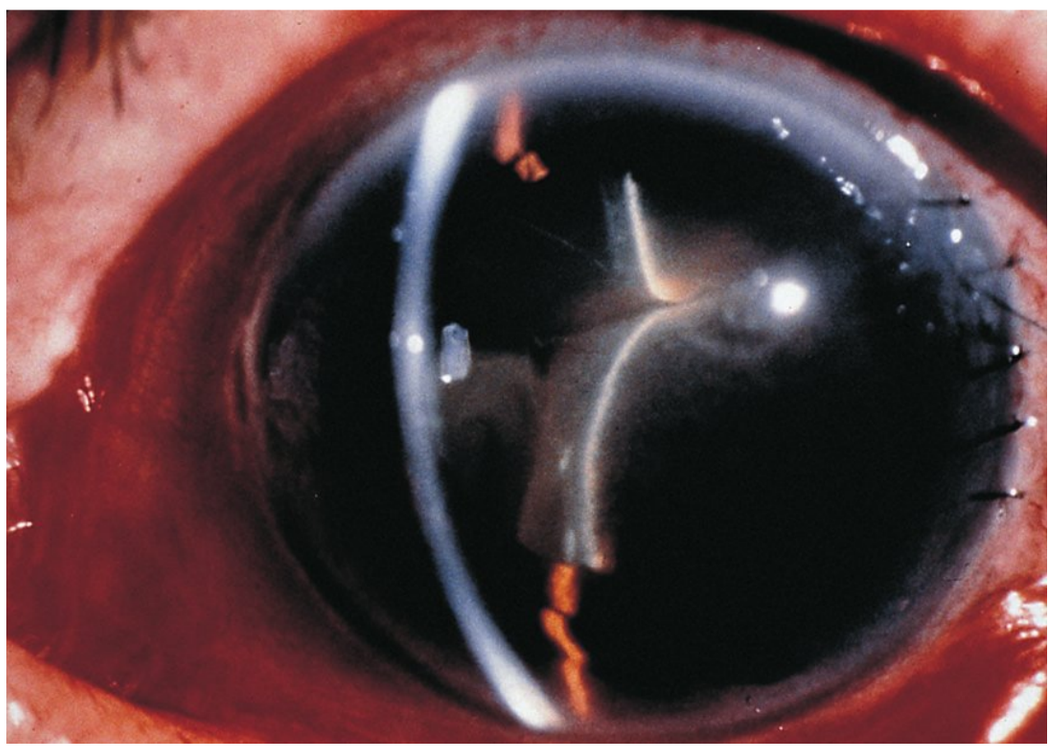

FIGURE 53–1 Initial presentation of left eye. Vision is hand motion. Note temporal clear cornea cataract incision reapproximated with nylon sutures, aphakia, and bullous appositional retinal detachment posterior to iris plane.

3. The history of acute onset severe ocular pain and vision loss in a perioperative period is most consistent with suprachoroidal hemorrhage. The patient described in this case has several risk factors for the development of suprachoroidal hemorrhage, including advanced age, atherosclerotic cardiovascular disease, hypertension, myopia, glaucoma, aphakia, and recent intraocular surgery.

4. The nylon sutures reapproximating the temporal clear cornea incision and the lack of an intraocular lens suggest that a suprachoroidal hemorrhage (perhaps limited) may have developed intraoperatively, leading the cataract surgeon to end the case and close the cataract incision as quickly as possible.

5. The first clue of an intraoperative suprachoroidal hemorrhage may be an alteration of the light reflex through the pupil or a tensing or anterior bowing of the lens–iris diaphragm. A rapid increase in the firmness of the eye to palpation is another indication of suprachoroidal hemorrhage.

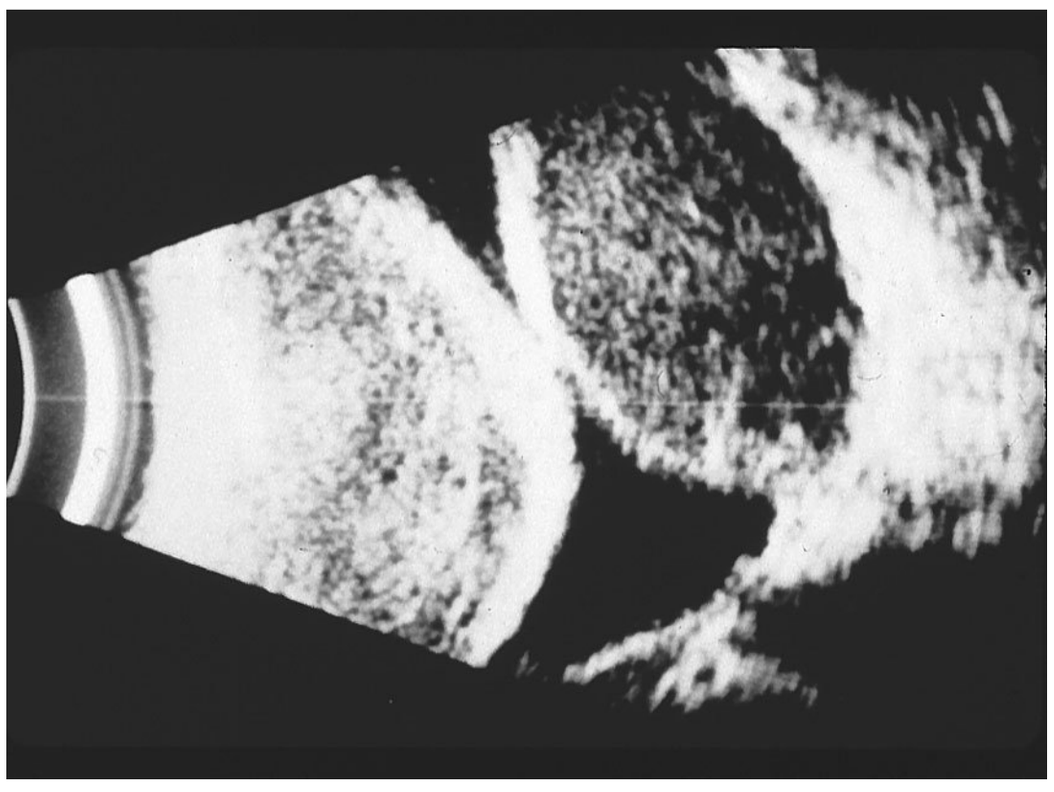

FIGURE 53–2 Echography demonstrates appositional suprachoroidal hemorrhage.

TEST INTERPRETATION

A combination of the history and physical findings is the most definitive way to diagnose a suprachoroidal hemorrhage. Patients with suprachoroidal hemorrhage generally give a classic history of sudden onset severe ocular pain, usually during or following intraocular surgery or ocular trauma. Intraocular pressure may be normal or elevated, and examination typically demonstrates a shallow or flat anterior chamber. Ophthalmoscopy demonstrates dark brown or dark red choroidal elevations.

In cases with overlying exudative appositional retinal detachment, echography may be necessary to confirm the presence of suprachoroidal hemorrhage and exclude such entities as choroidal tumor with hemorrhage or age-related macular degeneration disciform lesion with hemorrhage.

DIAGNOSIS

Appositional (“kissing”) suprachoroidal hemorrhage, right eye.

MEDICAL MANAGEMENT

Given the often guarded prognosis of eyes with suprachoroidal hemorrhage, the preferred management of this potentially devastating condition is prevention. Knowledge of risk factors permits the employment of prophylactic measures to decrease the likelihood of suprachoroidal

hemorrhage. The surgical plan may even be altered in high-risk patients. Preoperative intraocular pressure should be normalized via medical therapy or anterior chamber paracentesis. A Flieringa ring in myopic eyes may minimize intraoperative hypotony and, thus, decrease the risk of suprachoroidal hemorrhage. In "high-risk" eyes, preplacement of sutures will permit rapid wound closure. Intraoperative hypotony should be avoided, and intraoperative blood pressure and tachycardia should be controlled.

If surgical intervention is not indicated (see below for a discussion of indications for surgical management of suprachoroidal hemorrhage) or if the suprachoroidal hemorrhage has not become sufficiently liquified to permit surgical intervention, medications to control ocular hypertension and alleviate eye pain are employed. While systemic and topical steroids may stabilize blood vessel permeability (ie, help prevent further bleeding) and decrease ocular discomfort, their benefit in the management of suprachoroidal hemorrhage remains unproven.

SURGICAL MANAGEMENT

For intraoperative suprachoroidal hemorrhage, all ocular incisions should be closed immediately with strong sutures, and vitreous prolapse into the wound should be removed if possible. If the hemorrhage is massive and threatens to extrude the retina and lens-iris diaphragm, or if elevated intraocular pressure persists, a sclerotomy should be made into the suprachoroidal space in the meridian of maximal elevation approximately 9 to 10 mm posterior to the limbus. It may be necessary to refill the globe with sterile balanced salt solution or air/gas tamponade. The sclerotomy should be left open to permit continued drainage postoperatively. Although primary intraoperative suprachoroidal hemorrhage drainage is almost never complete, it is usually successful in controlling the intraocular pressure.

There are no randomized prospective controlled clinical trials addressing the optimal timing of secondary surgical intervention for intraoperative or postoperative suprachoroidal hemorrhage. Most surgeons recommend waiting 7 to 14 days to allow liquefaction of the hemorrhage, which facilitates drainage of the blood. Serial echography is useful for following the extent of suprachoroidal hemorrhage liquefaction.

Indications for surgery in eyes with suprachoroidal hemorrhage include markedly increased intraocular pressure uncontrolled with medical therapy, severe eye pain, kissing choroidals with retinal apposition, macular involvement with anterior retinal displacement and iris touch, and associated retinal detachment. Briefly, the surgical procedure consists of a 360-degree conjunctival limbal peritomy, isolation of each rectus muscle on a 2-0 cotton suture, and careful examination with indirect ophthalmoscopy to determine the areas of greatest suprachoroidal hemorrhage (if there is inadequate visualization of the fundus, this information may be obtained with echography).

In eyes with massive suprachoroidal hemorrhage, the placement of a pars plana infusion cannula may be associated with iatrogenic retinal breaks or cannula placement in the suprachoroidal space; thus, in aphakic or pseudophakic eyes a 1.5 mm infusion cannula or an infusing #23-gauge butterfly needle may be placed via the limbus; phakic eyes may require a lensectomy. A drainage sclerotomy is made radially with a 64 Beaver blade in the area of greatest hemorrhage approximately 9 or 10 mm posterior to the limbus. A limited anterior vitrectomy may be performed, with or without injection of perfluorocarbon liquid to facilitate drainage. Some surgeons advocate the use of perfluorocarbon liquid over air, as perfluorocarbon liquids force the blood anteriorly while air may cause an anterior tamponading force with posterior displacement of the hemorrhage, thereby necessitating more posterior drainage sites. Perfluorocarbon liquids may also assist in the management of coexisting retinal detachment.

After drainage of as much hemorrhage as possible, a 4 or 6 mm infusion cannula may be placed through the pars plana into the vitreous cavity and a standard pars plana vitrectomy is performed. Coexisting retinal detachment is managed with a scleral buckle and/or intraocular gas tamponade.

REHABILITATION AND FOLLOW-UP

Risk factors for poor visual outcome include concurrent or delayed retinal detachment, more than two quadrants of suprachoroidal hemorrhage, vitreous incarceration in the wound/bleb, afferent pupillary defect on presentation, poor presenting visual acuity, and retinal apposition for longer than 14 days. Patients with postoperative suprachoroidal hemorrhage generally achieve better final visual acuities than do patients who develop suprachoroidal hemorrhage intraoperatively or following trauma.

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Section VIII

TRAUMA

54. Ruptured Globe

55. Intraocular Foreign Body

Case 54

RUPTURED GLOBE

William E. Smiddy, M.D.

HISTORY

This 80-year-old woman presented the morning after falling at her nursing home. Although the exact history was unclear, periocular ecchymoses suggested direct ocular trauma on a piece of furniture. Initially the patient had not noticed pain or visual loss, but upon waking the next morning realized poor vision and sought consultation. Cataract surgery with a nuclear expression extracapsular technique had been performed 3 years previously. Before the injury, the vision had been documented as 20/30, limited by some atrophic macular degeneration changes.

Upon presentation visual acuity was hand motions and the intraocular pressure was 10 mm Hg. The cornea appeared relatively clear with a formed anterior chamber (Fig. 54–1). However, there was conjunctival chemosis temporally and superiorly (Fig. 54–2). While raising the upper lid, there was no conjunctival laceration, but a scleral dehiscence was evident, apparently at the previous cataract wound. Upon close examination of the superotemporal quadrant, the posterior chamber implant was seen in the subconjunctival space. The view posteriorly was limited by a dense vitreous hemorrhage. The pupil was not peaked, and there was no vitreous anterior to the iris.

The patient was taken to the operating room that afternoon for a vitrectomy with placement of an encircling scleral band. The intraocular lens (IOL) was removed. There was a sheet of vitreous streaming to the wound from behind the dehisced iris. There was no retinal detachment, but a focal subretinal hemorrhage limited to the superotemporal mid periphery was present.

Three months postoperatively the retina was attached posteriorly with a minimal epiretinal membrane (Fig. 54–3). Temporally, at the base of the buckle the subretinal hemorrhage had organized; this traction was self-limited, counteracted by the scleral buckling effect (Fig. 54–4). Visual acuity was 20/100 (with aphakic correction).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The most important key point is suspecting and detecting the rupture. In this case the referring physician had not been aware of the anterior rupture. A valuable clinical sign in detecting occult rupture is chemosis. In a patient with previous cataract surgery, the line of the previous suture is a common site of dehiscence and should be carefully inspected. In eyes without previous surgery, more variable patterns of corneal and scleral laceration occur (whether they be from sharp or blunt objects). Since prognosis is related to the most posterior extent and size of the rupture, there is some value in attempting to assess this extent preoperatively, but extensive diagnostic manipulations are avoided. An important clinical sign of occult scleral rupture visible best by transillumination in some cases is blood-highlighted vitreous streaming to the site.

2. Another important prognostic factor is the presence or absence of an afferent pupillary defect. This patient did not have an afferent pupillary defect and, accordingly, even though the posterior pole could not be seen, her prognosis was better because substantial retinal trauma or detachment was less likely than if the pupillary response had been abnormal.

3. Because of the circumstances and patient population involved in ocular trauma, a clear history of the events leading to the trauma is frequently not forthcoming. While a majority of trauma occurs in a relatively young male population, it may occur in substantial numbers of patients in an elderly group, as epitomized by this patient. Accordingly, a high index of suspicion must be maintained for a rupture in such cases.

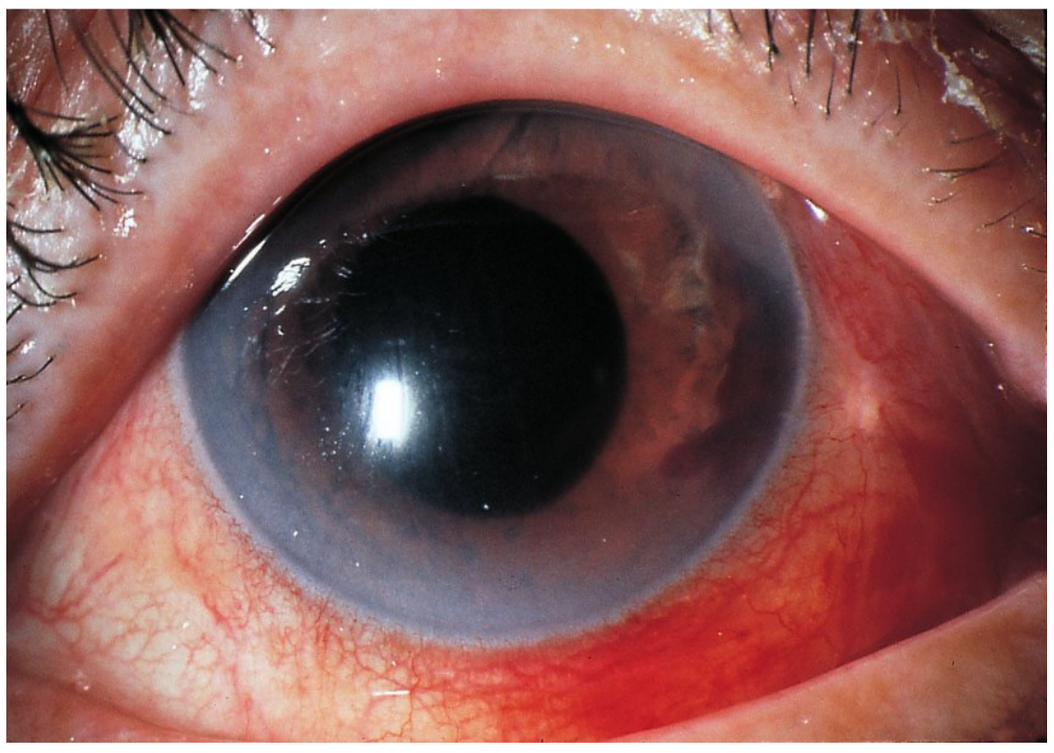

FIGURE 54–1 Clinical appearance of patient 2 days after blunt trauma. Vision was hand motions and pressure was 10. There is subconjunctival hemorrhage and temporal and superior chemosis. The anterior chamber is deep and the patient has an aphakic pupillary space where this dense vitreous hemorrhaged posteriorly.

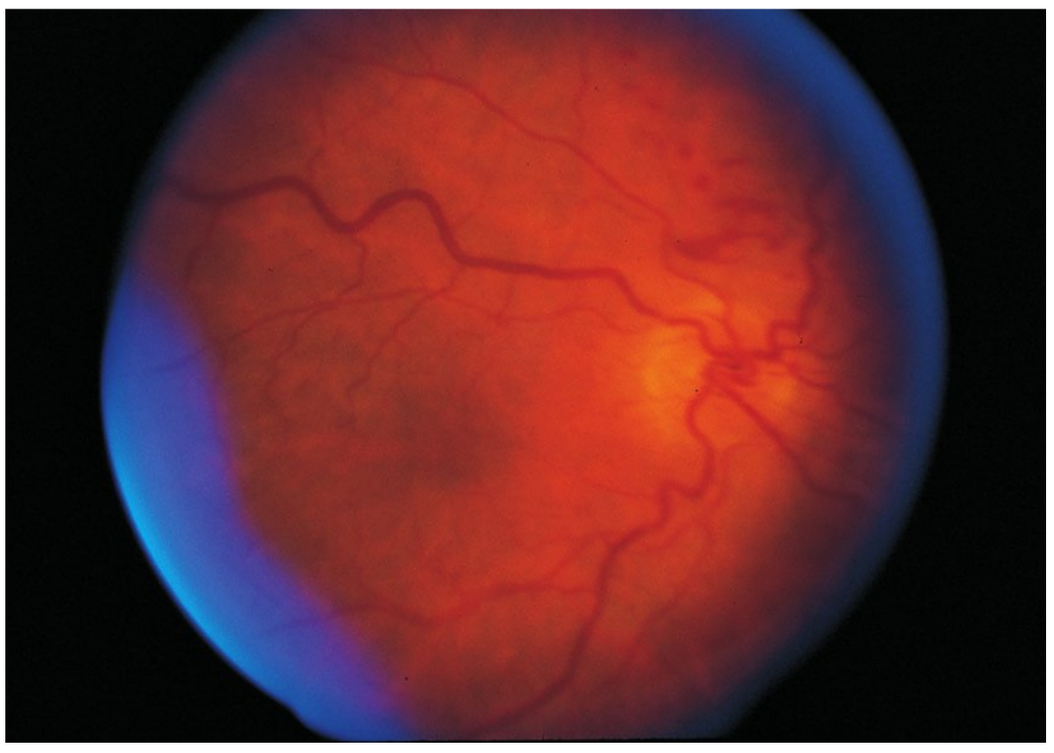

FIGURE 54–3 Three months postoperatively the view to the posterior pole is clear. There is mild residual intraretinal hemorrhage superiorly, but no sign of epiretinal membrane or retinal detachment. The vision is 20/100.

TEST INTERPRETATION

The clinical history (as available) and clinical examination typically yield the most important information determining the necessary management of the patient. Based on these clinical findings the general extent of the dehiscence can often be determined (ie, anterior to the limbus or posterior to the limbus, or large and likely posterior to the ora serrata). The integrity of the lens must also be established. Frequently, the presence of a retinal detachment cannot be directly visualized, but usually is hemorrhagic if present, since a rhegmatogenous retinal detachment usually requires at least a couple of days to develop after the retinal tear occurs.

Care must be taken not to generate additional forces on an open globe or else vitreous or other intraocular contents may be prolapsed, compounding the injury. Still, gentle, screening

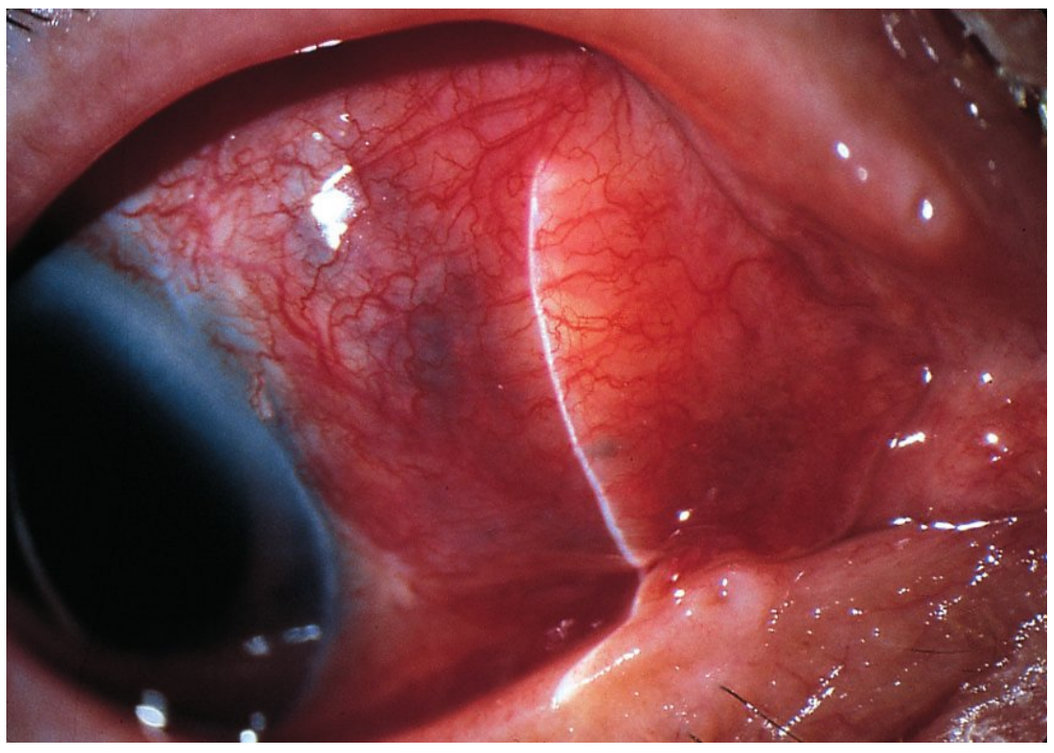

FIGURE 54–2 The chemosis is much more evident and a dehiscence of the cataract wound is in evidence. The IOL (as evidenced by the blue-colored haptic visible toward the bottom part of the slit) is in the subconjunctival space.

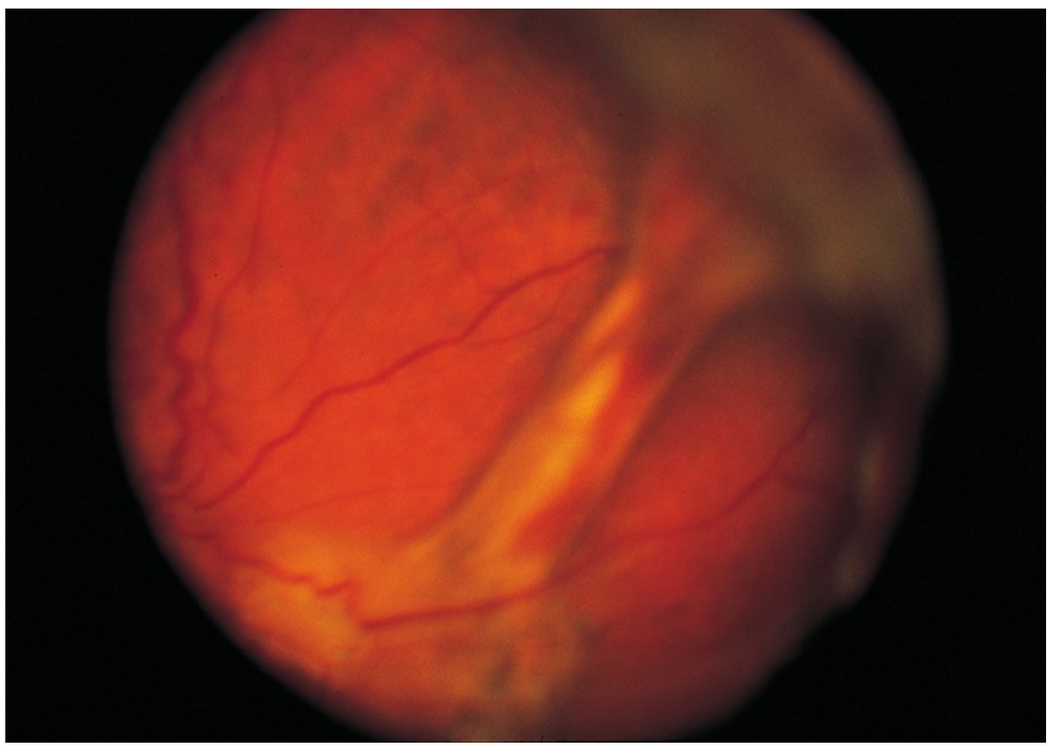

FIGURE 54–4 Superiorly and nasally there is evidence of subretinal traction leading to the posterior aspect of the scleral buckle. There is no rhegmatogenous retinal detachment and this was nonprogressive.

B-scan ultrasonography (through the lids) usually yields valuable information regarding the presence of vitreous, subretinal, or choroidal hemorrhages. Also, the posterior extent of the corneoscleral laceration may be accurately estimated.

A CT scan or MRI scan may be useful in further delineating the integrity of the globe. However, these scans are most valuable when there is suspicion of periorbital trauma, optic nerve damage, or intraocular foreign body.

DIAGNOSIS

Ruptured globe, OS.

MEDICAL MANAGEMENT

Primary medical management involves parenteral administration of broad spectrum antibiotics to lessen the chance of endophthalmitis. Endophthalmitis occurs in up to 10% of globe injuries (a higher percentage in rural, farm settings), although many culture-positive cases are not clinically significant. Usually a protective shield is placed on the eye to protect it from further trauma and pressure. The patient's vaccination history should be taken; if a tetanus shot has not been delivered within the last 5 years it should be administered. Often the first examination offers the best view to assess extent of injury; corneal edema, hemorrhage, and inflammation often deteriorate the view subsequently.

SURGICAL MANAGEMENT

The most important feature determining initial management is the patient's visual acuity. If the patient has no light perception (NLP) and the finding is commensurate with extreme ocular trauma (such as extensive, posterior, or multiple chorioretinal rupture sites with obvious major compromise of the globe integrity), primary enucleation should at least be considered. This is reserved only for the most exceptional and unequivocal cases since determination of visual function can be extremely difficult in an eye in the acute phase of severe trauma. Also, rare trauma cases have been reported in which vision returned despite initial presentation with NLP. If there is any question, primary repair with careful follow-up monitoring is recommended.

Except in cases of retained intraocular foreign body, the most common strategy is to perform a primary closure of the corneoscleral laceration, although some advocate simultaneous or early vitreoretinal repair. This is generally performed regardless of the presence of severe vitreous hemorrhage, retinal detachment, or disruption of the lens capsule. Surgical repair includes closure of the corneal portion of the rupture site. Typically 10-0 nylon should be used with shorter suture bites in the central cornea and longer suture bites more peripherally to minimize irregular astigmatism. Slightly larger polygalactin or silk sutures are recommended for the scleral wound. The suture that is placed at the limbus is critical to effect proper lateral realignment of the wound edges. After placing the limbal suture the wound is usually best closed in the cornea and then front-to-back in the sclera. Consecutively placing adjacent sutures is recommended to avoid making adjacent sutures too loose (and having to replace them). A viscoelastic substance may help to maintain the anterior chamber, to exclude iris or vitreous elements from the internal aspect of the wound, and to facilitate intraoperative visibility of anterior structures. The conjunctiva must be opened to allow exploration of the complete extent of the scleral rupture. A common location for scleral rupture is through the muscle insertion, since this is where the sclera is thinnest. In such cases, it may be necessary to disinsert the rectus muscle temporarily to close the scleral wound. Generally, the posterior extent of the laceration should be identified and closed. This may not be possible in lacerations extending extremely posteriorly, such as those approaching the optic nerve head.

Intravenous antibiotics are typically continued for at least 36 hours after initial presentation. If there is no sign of infection and clinical progress is evident, these are discontinued and

the patient is discharged and followed as an outpatient.

The patient is monitored for the following week or 10 days. If light perception is maintained, a secondary (vitreoretinal) repair is considered. At this point, the posterior vitreous is usually separated and may be removed more readily. However, it may be incarcerated or adherent at the area of the laceration site. It should be internally amputated there as effectively as possible. In cases with rupture involving the vitreous base or substantial vitreous loss, prophylactic scleral buckling is usually combined with vitrectomy and, as necessary, lensectomy. Typically, endolaser photocoagulation is applied around the edges of the laceration, since subsequent contraction may cause retinal tears and traction at this site. Primary silicone oil infusion may be considered in cases with extreme traction or numerous, large retinal breaks.

Delaying the secondary repair longer than 2 weeks after the injury may allow formation of aggressive fibrous proliferation such that subsequent surgical efforts are less likely to be effective (Fig. 54–5). This is especially important to consider in cases appearing to have vitreous hemorrhage; not infrequently other ocular injuries coexist that result in vitreous base contracture leading to retinal detachment.

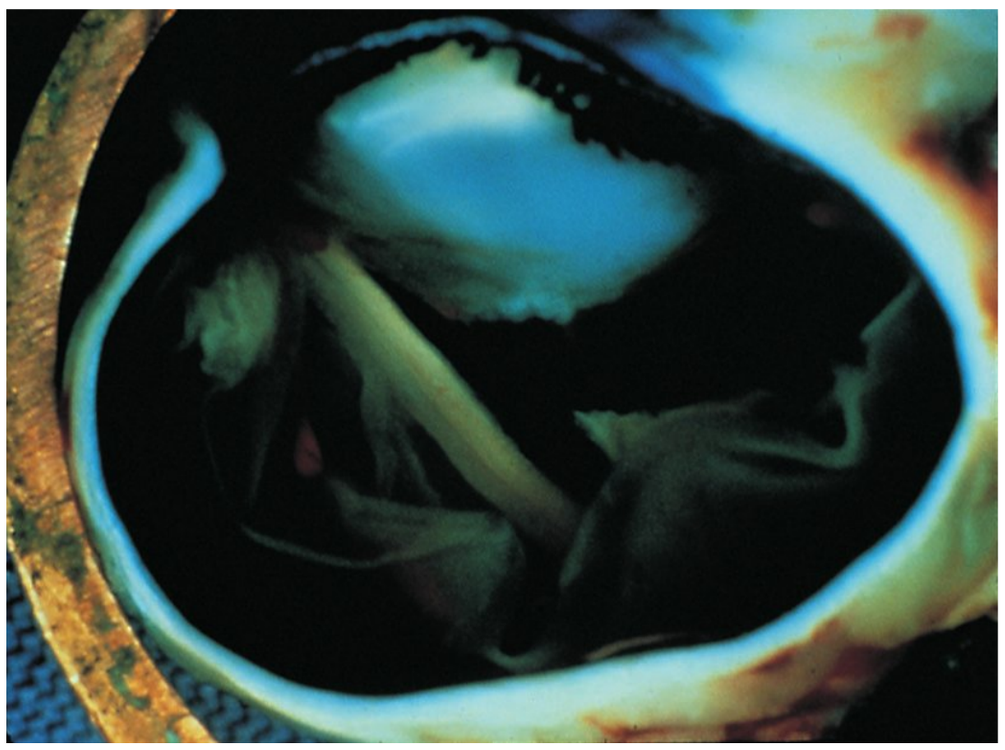

FIGURE 54–5 Gross photograph of a different patient whose eye was enucleated because of trauma. Internalized retinal detachment can be seen, but most prominent is the posterior to anterior band of organized vitreous and fibrous proliferation streaming to the more interior rupture site.

REHABILITATION AND FOLLOW-UP

As long as anatomic and visual stabilization is observed, follow-up intervals are lengthened following surgical repair. Usually the cicatricial response determining anatomic success is completed by 6 weeks following surgery. Occasionally additional surgery such as removal of an epiretinal membrane or implantation of an IOL is considered approximately 3 months following surgery for visual rehabilitation. Rigid contact lenses may be effective to neutralize aphakia and may obviate the need for a secondary IOL. However, a large fraction of patients are unable to tolerate aphakic contact lenses.

Shatter-proof safety glasses are strongly recommended, even if the other eye is emmetropic, to lessen the risk of a similar process occurring in the other eye.

Vocational rehabilitation may be necessary in patients with limited vision in this one eye, since unilateral visual loss may disqualify the patient from certain occupations. These efforts must be coordinated with social workers and vocational rehabilitation specialists.

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Case 55

INTRAOCULAR FOREIGN BODY

William E. Smiddy, M.D.

HISTORY

This 32-year-old man was working aboard a docked marine biology research ship repairing a metal banister. While striking the metal rail with a metal hammer, he experienced a minor pain in his left eye. Over the ensuing 2 hours, he noticed a subtle but definite decrease in vision. On presentation his visual acuity was 20/30. Slit-lamp examination showed a deep anterior chamber with minimal cell and flare. There was a defect in the temporal iris approximately 1 mm from the limbus. Corresponding to this site was a slit-like corneal defect that was not leaking aqueous fluid by Seidel testing. Posterior to the iris, there was a sectoral, white opacity in the peripheral lens (Fig. 55–1). A view to the posterior pole showed a small intraocular foreign body (IOFB) embedded in the retinal mid periphery. There was a collar of retinal edema surrounding it, but no hemorrhage (Fig. 55–2).

The patient was taken to the operating room where, under a local anesthesia, vitrectomy with lensectomy and intraocular lens (IOL) implantation was combined with magnetic extraction of the IOFB. A low, encircling scleral buckle was also placed. The power of the lens was estimated from measurements of the fellow eye. Laser photocoagulation was applied surrounding the retinal defect after removal of the foreign body, since there was mild bleeding at the site of removal from the retina. There was not a previous posterior vitreous detachment, but one was introduced intraoperatively with the vitrectomy instrument using controlled aspiration. Postoperatively, the retina remained attached and the patient regained vision of 20/20, which has been maintained throughout 8 years of follow-up examinations.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The history in a patient sustaining an IOFB is commonly less remarkable than one might expect. If the patient was aware of the foreign body entry incident at all, it was usually perceived to be something like a piece of dust going onto the eye. Normally, a few hours pass before pain or decreased vision from inflammatory components causes the patient to seek consultation.
2. The most commonly encountered IOFBs are metallic and magnetic. These classically occur during an activity that involves metal being hammered upon metal in the absence of protective eyewear.
3. The time-honored teaching that the heat generated by the launching of the small metallic IOFB sterilizes the foreign body and eliminates the risk of endophthalmitis is not true; studies have documented a 7% incidence of endophthalmitis with IOFBs. Also, a more rapidly progressive and aggressive organism, Bacillus cereus, has been described in such cases. Catastrophic visual results, especially with delayed treatment, may result in irreversible blindness.
4. It is easier to make the diagnosis when the history is clear-cut and clear media allow direct visualization of the IOFB in the anterior or posterior segment. When the media are not clear, but the history is suspicious, other imaging studies may be necessary.
5. It may be necessary for the clinician to make some deductions regarding location based on the nature of the injury and the angle of entry site. Usually the track of a posterior segment foreign body can be seen in the

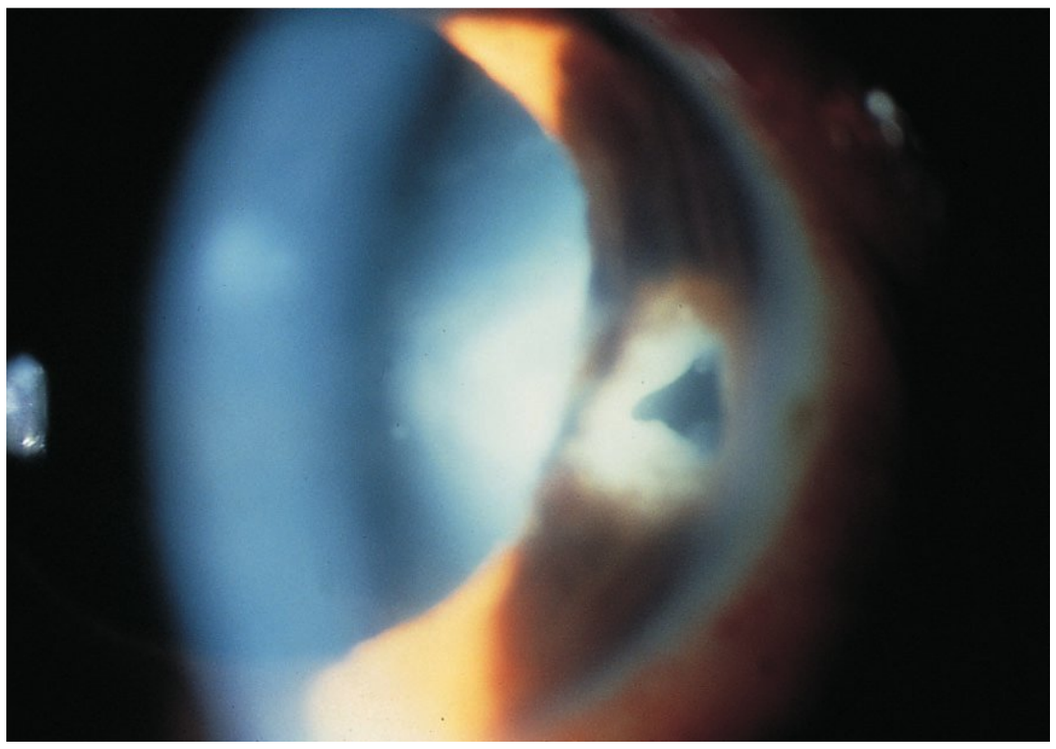

FIGURE 55–1 External appearance approximately 6 hours after a metallic intraocular foreign body (IOFB) traversed the temporal peripheral cornea, iris, and lens.

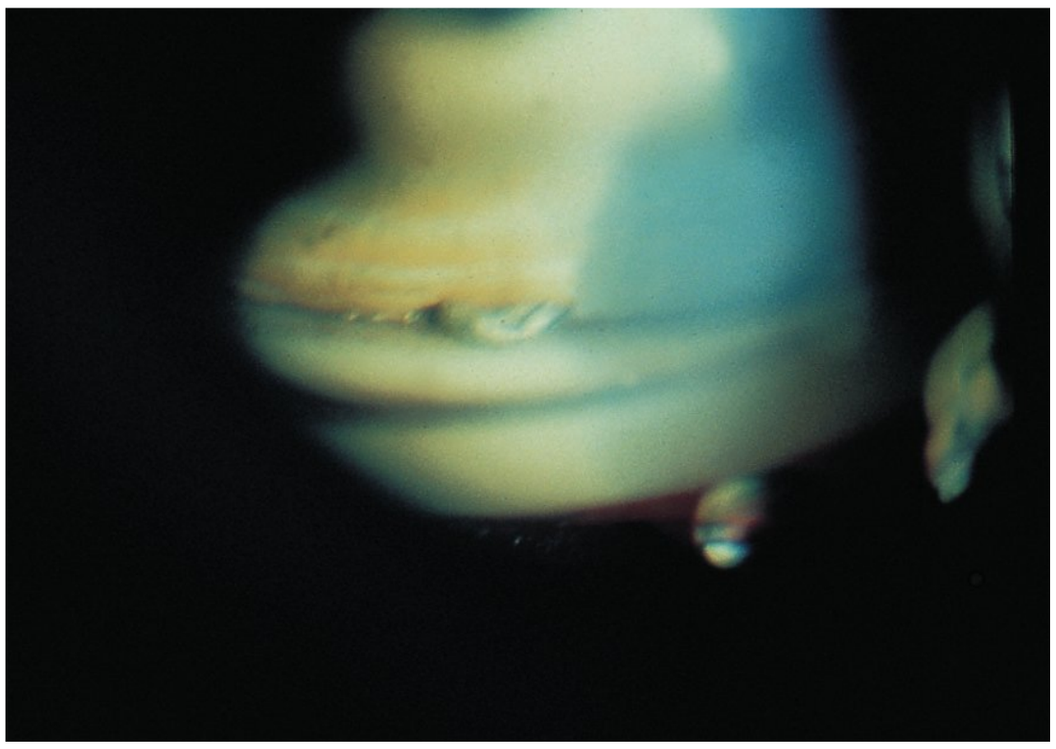

FIGURE 55–3 Gonioscopic appearance of a metallic foreign body resting in the inferior anterior chamber angle. An oblique corneal entry site led to the suspicion of the foreign body being in the anterior segment.

cornea, iris, and lens, or there is a superficial track visible in the conjunctiva and sclera. In the latter cases, the foreign body may come to rest at the ora serrata and indirect ophthalmoscopy with careful scleral indentation may allow or even be necessary for the visualization of the foreign body. In cases in which there is an apparent oblique entry to the cornea, the possibility of an IOFB retained in the anterior chamber angle must be considered. This would be readily apparent with gonioscopic evaluation (Fig. 55–3).

6. Self-sealing, small entry wounds usually allow sufficient globe integrity to permit surgical repair without the need for general anesthesia. However, if the wound is large or leaking, general anesthesia must be considered to lessen the risk of expulsing intraocular contents in the event of a retrobulbar hemorrhage during the block.

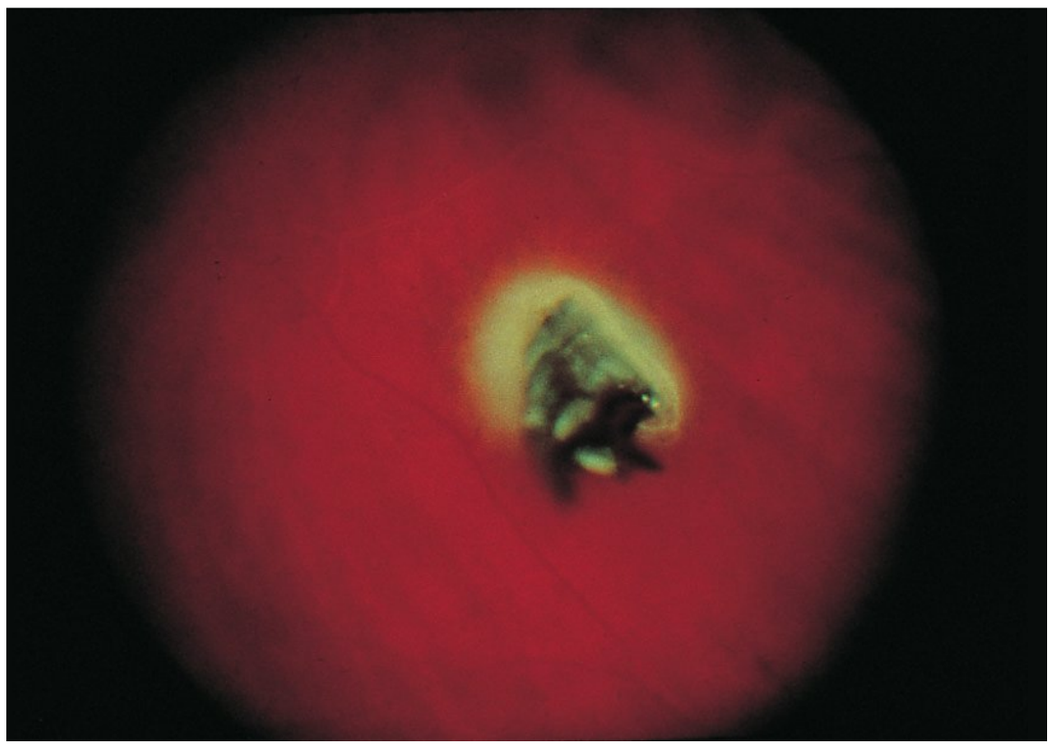

FIGURE 55–2 The intraocular foreign body (IOFB) is embedded in the midperipheral retina temporally. It appears to be metallic and is likely magnetic. There is a collarette of retinal edema at the impact site.

TEST INTERPRETATION

When direct visualization is possible, no further diagnostic testing is indicated. Although the history may suggest the possibility that multiple IOFBs exist, this is usually apparent from the nature of the injury. In eyes with opaque media or suspected occult location of the foreign body, a screening test is the plain film x-ray. Frequently a combination of anterior–posterior and lateral views allows localization to the eye or orbit. Of critical importance is detecting whether the foreign body is intraocular or extraocular. Nonmetallic IOFBs may not appear on plain film. Frequently, glass foreign bodies do appear, since drinking glasses or bottles usually have a high lead content.

The second test that usually allows detection of an IOFB is the combined A- and B-scan ultrasound (Fig. 55–4). This is feasible for foreign bodies of all compositions and is most effective when done with probe contact on the cornea.

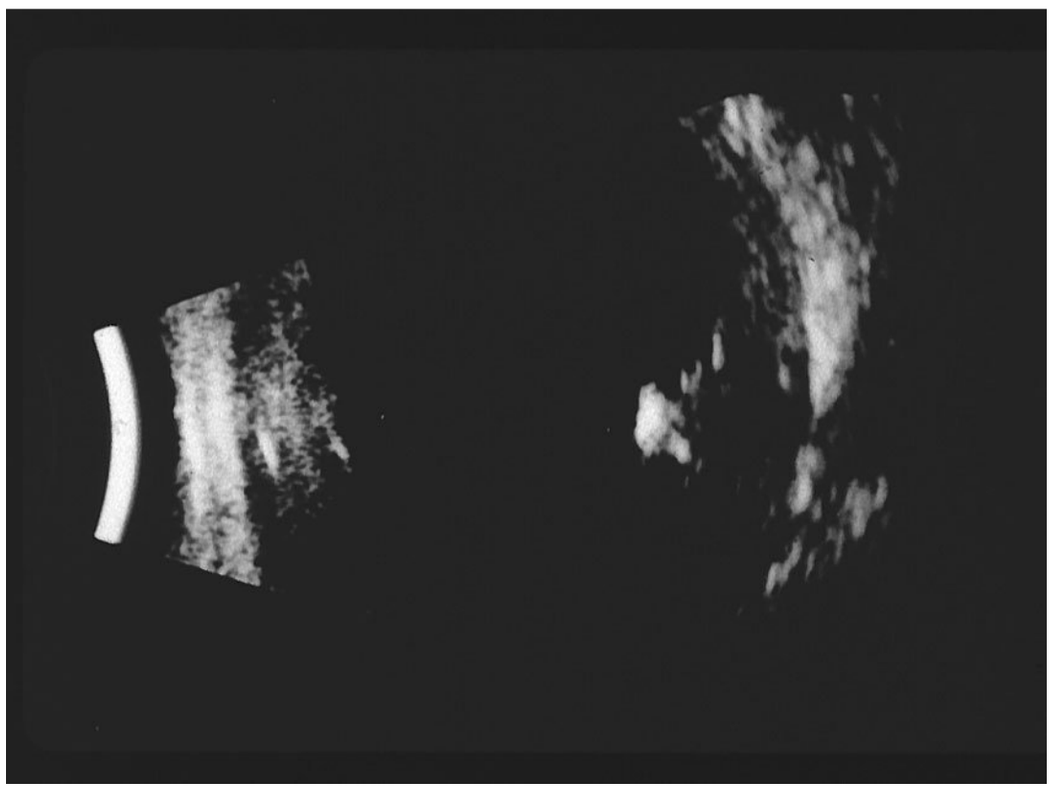

FIGURE 55–4 Echogram of a different patient with an IOFB that is suspended approximately 2 mm anterior to the retinal surface. Other echos demonstrate vitreous blood above, suggesting the possibility that the foreign body bounced off the retina and came to rest in the posterior vitreous.

This may be contraindicated depending upon the condition of the entry site.

A third useful diagnostic test is a CT scan (Fig. 55–5). Again, for metallic and usually for glass foreign bodies, this is generally definitive. However, foreign bodies of vegetable matter will usually not manifest on radiologic evaluation. Also, the CT scan in suspected cases may localize the foreign body anteriorly, prompt-ing reexamination using maneuvers such as gonioscopy or directed, intraoperative vitreous base examination (Fig. 55–6).

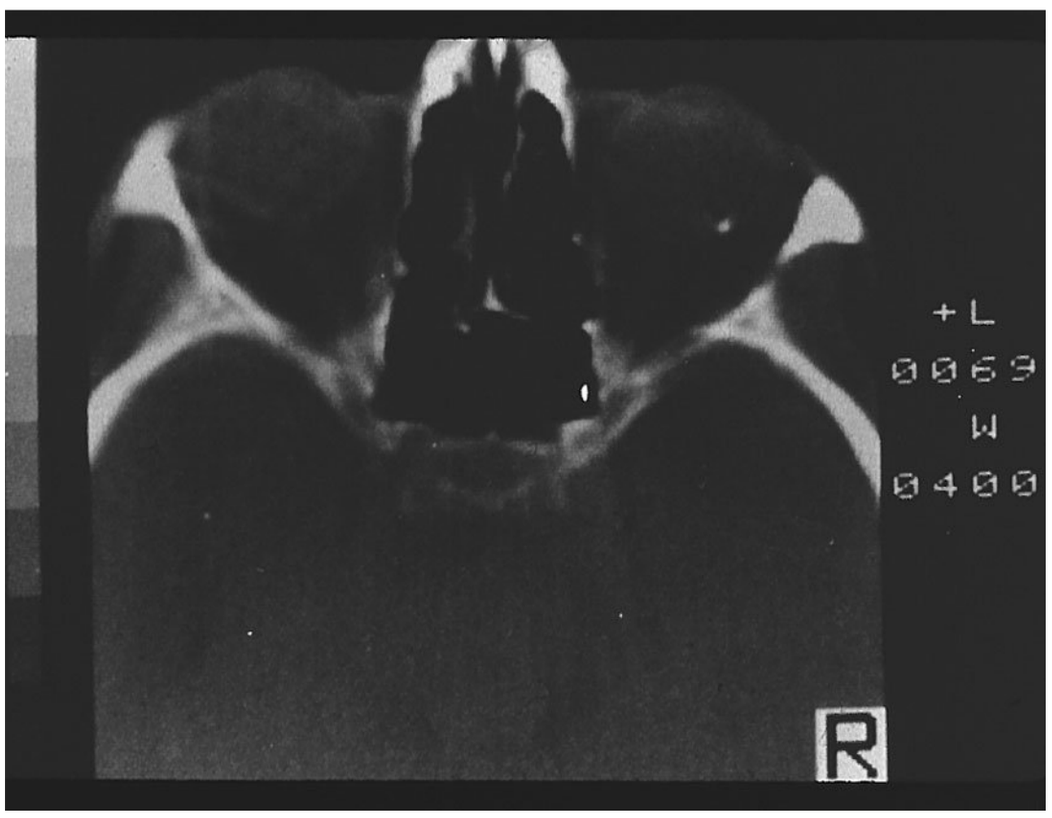

FIGURE 55–5 CT image of a patient with IOFB. The radiopacity at the posterior and temporal eye wall of the patient's right eye depicts the IOFB.

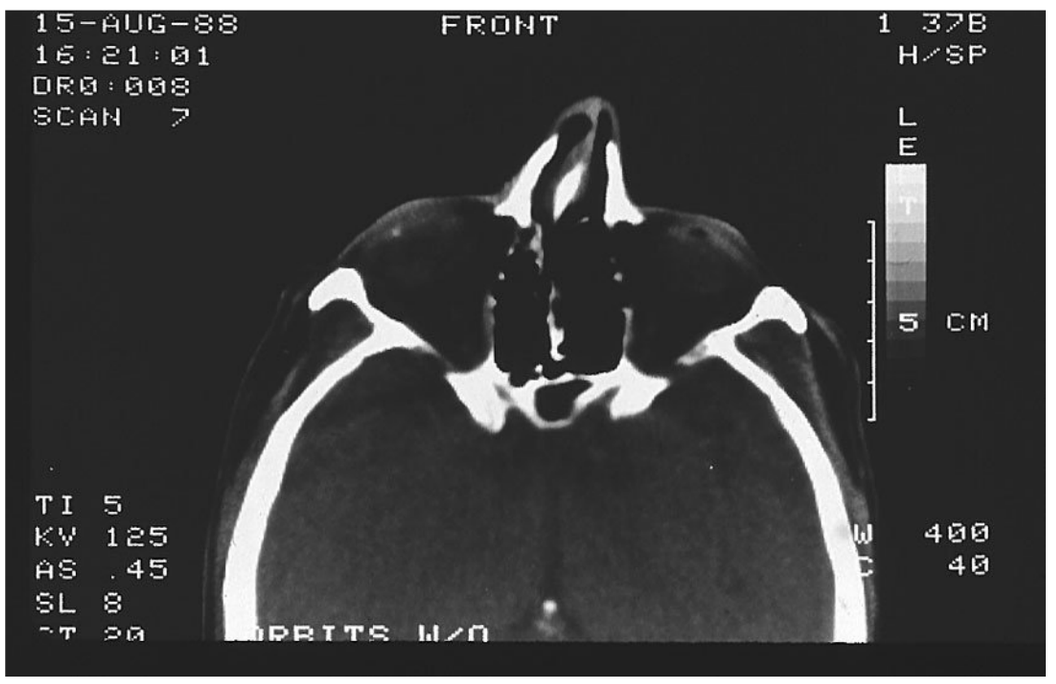

FIGURE 55–6 CT scan shows a radiopacity in an anterior location. This foreign body was not clinically visible due to its peripheral location. Intraoperatively it was ultimately detected in the vitreous base of the left eye temporally.

Magnetic resonance imaging is contraindicated when magnetic IOFBs are suspected.

DIAGNOSIS

Retained magnetic intraocular foreign body (IOFB), OS.

MEDICAL MANAGEMENT

Medical management is confined initially to an efficient and prompt diagnostic evaluation. Prompt institution of prophylactic antibiotics is probably indicated in most cases and may be tailored depending upon the nature of the IOFB. Although a metallic IOFB causes endophthalmitis with only a 7% incidence, the devastating consequences merit a broad spectrum antibiotic use. One study has shown a much higher incidence of infection in rural injuries. Accordingly, farm- or field-related injuries, which are at increased risk of harboring Bacillus cereus organisms, should receive antibiotic coverage for anaerobic organisms. Usually the patient is treated with systemic antibiotics while being readied for surgical repair; intravitreal antibiotics may be administered in especially suspicious cases. If surgery can be promptly commenced, systemic antibiotic administration may

be deferred until after surgery so that the culture would be valid. An important point to recognize is that subsequent corneal edema hinders the view to the posterior pole, rendering the initial examination the most revealing one; this should not be truncated in the interest of arranging ancillary evaluations.

Patients presenting with a chronic IOFB may be managed more electively if there is no sign of infection. Such cases are not treated with prophylactic antibiotics since the risk of endophthalmitis occurring more than a couple of days after the injury is minimal.

SURGICAL MANAGEMENT

Occasionally, IOFBs confined to the anterior segment may be managed from a limbal incision. Most IOFBs present in the posterior segment and a pars plana approach is preferable. Foreign bodies lodged under the retina may be approached with an external magnet and removed via a sclerotomy, but most are approached internally.

The first surgical objective is to reestablish the structural integrity of the eye. Often the entry site is small enough that few or no 10-0 nylon sutures are necessary. The second objective is removal of media opacities, which may include lens opacity, disrupted lens material, or hemorrhage. Accordingly, a lensectomy and vitrectomy are often necessary. Frequently, enough capsular support may be preserved to allow simultaneous or subsequent implantation of a posterior chamber IOL in the ciliary sulcus. The third objective is to identify, mobilize, and remove the foreign body. A pick, forceps, or intraocular magnet may be used to release embedded foreign bodies. Nonmetallic foreign bodies usually require intraocular forceps. A variety of forcep designs including the basket-like Wilson forceps may be useful for grasping and removing the IOL once it is mobilized. A foreign body can be removed through either a sclerotomy or the entry wound, although it may be necessary to enlarge the site. An extremely large foreign body may be brought into the anterior chamber and removed via a separate limbal incision. Commonly, the foreign body is mobilized, brought anteriorly with the magnet, and transferred to forceps for extraction, since it often disengages from the magnet if withdrawn through the sclerotomy.

The final surgical objectives involve closure of retinal holes and prophylaxis against future retinal breaks. As a general rule, a low encircling scleral buckling band is considered if the foreign body traverses the vitreous base. Cases with IOFBs that traverse the lens without passing through vitreous base usually do not require scleral buckling. Endolaser photocoagulation at the impact site may not be necessary since the inflammatory reaction initiated by the impact may create an adequate adhesion; however, one row of light laser surrounding the site with fluid–gas exchange (air only) is usually performed.

Certain glass IOFBs may be safely retained since they are inert and do not carry the risk of hemosiderosis as do metallic IOFBs. This option is especially attractive for glass IOFBs that are deeply embedded, especially if perforating the posterior sclera.

The timing of surgery for cases of suspected retained IOFBs is of critical importance. IOFB removal within 6 to 12 hours is generally recommended when possible because of the substantial risk of aggressive endophthalmitis.

REHABILITATION AND FOLLOW-UP

The patient is monitored postoperatively with intravenous antibiotics and topical corticosteroid, antibiotics, and/or cycloplegic agents, as indicated. If there is no sign of endophthalmitis within 24 to 48 hours and good clinical progress is in evidence, systemic antibiotics are discontinued.

Patients are observed at approximately 1- to 2-week intervals in the first month following surgery and less frequently thereafter. The patient is monitored for recurrent retinal detachment and/or epiretinal membrane formation that is of visual significance. If the patient has been rendered aphakic, then a second IOL

implantation or aphakic contact lens fitting efforts are considered.

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Section IX

NEURO-OPHTHALMOLOGY

56. Optic Neuritis
57. Optic Disc Edema with Macular Star (Neuroretinitis)
58. Anterior Ischemic Optic Neuropathy —Nonarteritic
59. Anterior Ischemic Optic Neuropathy —Arteritic
60. Progressive Optic Neuropathy—Tumor
61. Papilledema—Pseudotumor Cerebri
62. Visual Field Defect—Junctional Scotoma
63. Visual Field Defect—Pituitary Lesion
64. Visual Field Defect—Homonymous Hemianopia
65. Transient Monocular Visual Loss
66. Third Nerve Palsy—Ischemic
67. Third Nerve Palsy—Aneurysm
68. Fourth Nerve Palsy—Congenital
69. Sixth Nerve Palsy
70. Internuclear Ophthalmoplegia
71. Diplopia—Ocular Myasthenia Gravis
72. Thyroid Ophthalmopathy
73. Anisocoria—Tonic Pupil
74. Anisocoria—Horner's Syndrome
75. Anisocoria—Eye Drops

Case 56

OPTIC NEURITIS

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 35-year-old woman noted the acute onset of blurred vision in her right eye 12 days ago. She complained of moderately severe retro-orbital pain on the right that was made worse by eye movements. The vision had deteriorated over the first 3 or 4 days but had since stabilized. She noted that when she attempted to perform aerobic exercises, her vision became worse. She denied any precipitating factors for her visual loss or any history of neurologic symptoms, except for rare diffuse headaches for many years. She has been otherwise healthy and denies any family history of visual impairment.

Examination revealed the visual acuity to be 20/80 on the right and 20/20 on the left. The patient identified three of ten Hardy-Rand-Rittler pseudoisochromatic plates on the right and ten of ten plates on the left. Visual field examination revealed a superior arcuate field defect on the right. The pupils were 5 mm bilaterally and reacted well to light and near, but there was a significant relative afferent pupillary defect (RAPD) on the right. Examination of the efferent system was normal. Slit-lamp examination was normal. The right optic disc was moderately swollen and hyperemic without hemorrhages or exudates (Fig. 56–1). There were no vitreous cells. The left fundus was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The differential diagnosis in this case includes demyelinating, infectious, inflammatory, ischemic, infiltrative, compressive, and heredofamilial (eg, Leber's disease) optic neuropathy. The patient's young age, lack of atherosclerotic risk factors, retro-orbital pain, and lack of pallid disc swelling make ischemic optic neuropathy less likely. The acute, painful onset makes a compressive or infiltrative lesion unlikely. Leber's hereditary optic neuropathy is usually painless, is not common in women, is associated with a dense central scotoma, and patients often have a family history of optic neuropathy. The most likely diagnosis is optic neuritis (ON), a general term for an optic neuropathy resulting from idiopathic, inflammatory, infectious, or demyelinating etiology. As the optic nerve is swollen, the term papillitis or anterior ON is used (if the optic nerve is normal, then it is called retrobulbar ON).

2. Idiopathic or demyelinating ON usually presents with a "typical" profile as outlined in Table 56–1.

3. The deterioration of vision with exercise or heat exposure (eg, a hot shower) is referred to as Uhthoff's symptom. Although this symptom is characteristically seen with demyelinating optic neuropathy, it is not specific, and may occur with other optic neuropathies (eg, Leber's hereditary optic neuropathy).

4. The disc swelling that occurs in approximately 35% of typical ON patients is usually of mild to moderate degree, associated with minimal or no hemorrhages, associated with no more than trace vitreous cells, and not associated with retinal exudates or a macular star. Thus, consider an alternate diagnosis to "typical" demyelinating ON if severe disc edema, marked hemorrhages, cotton wool spots, lipid maculopathy, more than trace vitreous cells, pallid disc edema, or retinal arteriolar narrowing are present.

5. The Optic Neuritis Treatment Trial (ONTT), a randomized, controlled trial that enrolled 457 patients with ON at 15 centers in the United States between the years 1988 and

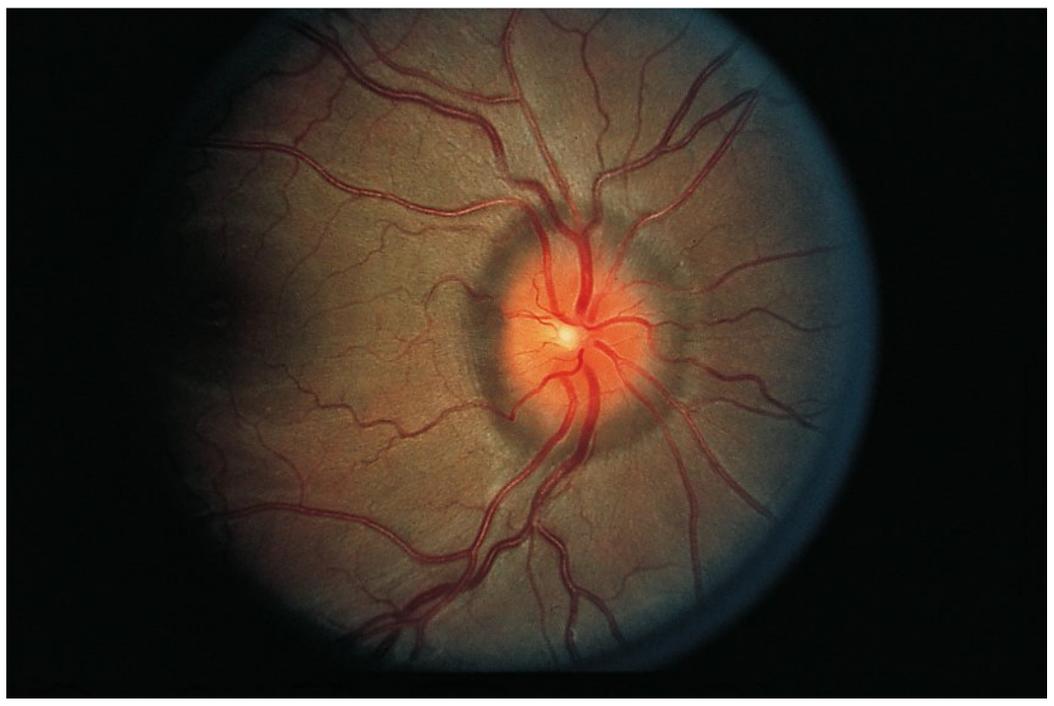

FIGURE 56–1 Fundus photograph of the right eye reveals a moderately swollen and hyperemic optic disc without hemorrhages or exudates.

1991, has generated significant useful data concerning the treatment and natural history of ON.

TEST INTERPRETATION

The ONTT determined that chest radiograph, laboratory studies (eg, syphilis serology, ANA titers, serum chemistries, and complete blood count), and lumbar puncture are not necessary for typical ON but should be considered in atypical cases. See Table 56–2. Serologic testing for Lyme disease should be considered in patients with ON, especially with a history of the typical rash of erythema migrans, who live in or have visited Lyme endemic areas.

Magnetic resonance imaging (MRI) of the brain is of limited value in disclosing an alternate diagnosis in patients with typical ON. In the ONTT, an alternate etiology for visual loss was noted in only two patients: one with a pituitary tumor and one with an ophthalmic artery aneurysm. MRI is, however, a valuable predictor of the future development of multiple sclerosis (MS). In the ONTT, the 5-year overall cumulative probability for the development of clinically definite MS was 30%, but this probability was 51% for patients that had three or more lesions suggesting demyelination on MRI.

TABLE 56–1 **Features of Typical Optic Neuritis (ON)**

Acute, usually unilateral loss of visual acuity and/or visual field
A relative afferent pupillary defect in unilateral or bilateral but asymmetric cases
Periocular pain (90%), especially with eye movement
Normal (65%) or swollen (35%) optic nerve head
Young adult (<40 years)
Eventual visual improvement 88% improve at least one line by day 15 95% improve by at least one line by day 30 Visual improvement may continue for months

(Adapted from Lee AG and Brazis PW. *Clinical Pathways in Neuro-Ophthalmology: An Evidence-Based Approach.* New York, NY: Thieme; 1998:25, with permission.)

TABLE 56–2 **Features of Atypical Optic Neuritis (ON)**

Bilateral simultaneous onset of ON in an adult patient
Lack of pain
Ocular findings suggestive of an inflammatory process: Anterior uveitis Posterior chamber inflammation more than a trace Macular exudate or star figure Retinal infiltrate or retinal inflammation
Severe disc swelling
Lack of improvement of visual functioning or worsening of visual function after 30 days
Lack of at least one line of visual acuity improvement within the first 3 weeks after onset of symptoms
Age greater than 50 years
Diagnosis or evidence of other systemic condition (eg, inflammatory or infectious diseases, including AIDS) other than MS that might cause optic neuropathy
Exquisitely steroid sensitive or steroid dependent optic neuropathy

(Adapted from Lee AG and Brazis PW. *Clinical Pathways in Neuro-Ophthalmology: An Evidence-Based Approach.* New York, NY: Thieme; 1998:26, with permission.)

In patients with clinical features of atypical ON (Table 56–2), further studies are indicated. These include MRI, blood studies (eg, syphilis serology, Lyme titers, ANA, Bartonella henselae titers, ACE, ANCA), or lumbar puncture to investigate for other infectious, inflammatory, and infiltrative processes.

DIAGNOSIS

Typical optic neuritis (idiopathic or demyelinating) —papillitis.

MEDICAL MANAGEMENT

The ONTT randomly assigned patients to one of three treatment arms: (1) IV methylprednisolone sodium succinate (250 mg every 6 hours for 3 days) followed by oral prednisone (1 mg/kg per day for 11 days); (2) oral prednisone (1 mg/kg per day for 14 days); (3) oral placebo for 14 days followed by a short oral taper.

Treatment with high-dose IV steroids followed by oral steroids accelerated visual recovery but provided no long-term benefit to vision. Treatment with "standard-dose" oral prednisone alone did not improve the visual outcome and was associated with an increased rate of new attacks of optic neuritis. Treatment with the IV followed by oral steroid regimen reduced the rate of development of clinically definite MS during the first 2 years, particularly in patients with 3 or more lesions consistent with demyelination on MRI at time of study entry. By 3 years, however this treatment effect had subsided.

Based on the ONTT results, it is recommended that treatment with oral prednisone in standard doses be avoided in ON. Treatment with IV methylprednisolone should be considered in patients with an abnormal MRI (may possibly reduce the subsequent risk of development of MS) or a particular need (eg, monocular patient or occupational requirement) to recover visual function more rapidly.

SURGICAL MANAGEMENT

No surgical management is indicated.

REHABILITATION AND FOLLOW-UP

In the ONTT, 88% of patients improved at least one Snellen line by day 15 after study entry and 96% improved at least one Snellen line by 30 days. For most patients recovery of visual acuity was nearly complete by 30 days after study entry. Among the patients with incomplete recovery by 30 days, most showed slow gradual improvement for up to 1 year. The only predictor of poor visual outcome in patients enrolled in the ONTT was poor visual acuity at time of study entry. Even so, of 160 patients starting with visual acuity 20/200 or worse, all had at least some improvement and only 8 (5%) had visual acuities that were still 20/200 or worse at 6 months.

As noted above, there is significant risk of developing MS in patients with isolated ON. This risk is greater in patients with an abnormal MRI (three or more lesions), with a history of nonspecific neurologic symptoms, with a history of previous ON, or with increased cerebrospinal fluid IgG. Factors that decrease the subsequent risk of MS include a normal MRI, bilateral simultaneous ON, childhood onset, or marked disc edema.

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Case 57

OPTIC DISC EDEMA WITH MACULAR STAR (NEURORETINITIS)

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 22-year-old woman noted the onset of blurred vision in her right eye 3 weeks ago. She noted minimal right periorbital pain. She denied any history of previous medical, ophthalmologic, or neurologic illnesses, but she did complain of recent occasional headaches of mild and diffuse nature and noted that the visual blurring seemed to have started a week or so after a nonspecific "flulike" illness. She has three cats at home.

Examination revealed visual acuity to be 20/60 on the right and 20/15 on the left. She identified four of ten Hardy-Rand-Rittler pseudoisochromatic plates on the right and ten of ten on the left. Visual field examination revealed a cecocentral scotoma on the right and was normal on the left. Pupils were 5 mm bilaterally and equally reactive to light and near, but there was a right relative afferent pupillary defect. Motility examination was normal. The right fundus exam revealed significant optic disc edema with peripapillary and macular exudates, the latter in a star configuration (Fig. 57–1). There were 1+ vitreous cells on the right. The left fundus examination was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The differential of optic nerve edema with a macular star includes infectious or idiopathic neuroretinitis (idiopathic optic disc edema with a macular star, or ODEMS), vascular disease (anterior ischemic optic neuropathy, branch or central retinal artery occlusion, hypertensive or diabetic retinopathy, polyarteritis nodosa, and Eales' disease), papilledema, optic nerve head tumor or infiltrate, diffuse unilateral subacute neuroretinitis (DUSN), and acute neuroretinopathy associated with progressive hemifacial atrophy (Parry-Romberg syndrome). The unilateral nature of the condition in this patient argues against papilledema, hypertensive or diabetic retinopathy, or polyarteritis nodosa as an etiology of her disease. Her young age, presence of vitreous cells, and lack of vascular risk factors are strongly against anterior ischemic optic neuropathy. The most likely diagnosis is idiopathic or infectious ODEMS (neuroretinitis).
2. ODEMS usually occurs in children or young adults, with the average age of onset between 20 and 40 years. Men and women are equally affected. Most cases are unilateral but bilateral involvement has been noted in up to a third of patients. The condition may be painless, but retrobulbar pain, pain on eye movement, or associated headache may occur. A nonspecific "viral" illness precedes or accompanies the visual loss in approximately half of the cases. Visual acuity ranges from 20/20 to light perception, dyschromatopsia is often present, and perimetry reveals optic neuropathy defects (eg, arcuate, altitudinal, central).
3. Optic disc edema is the earliest sign of ODEMS and may be severe. This edema is associated with leakage of disc capillaries, with the fluid spreading from the disc through the outer plexiform layer of the retina. The serous component of the fluid accumulation in Henle's layer is resorbed,

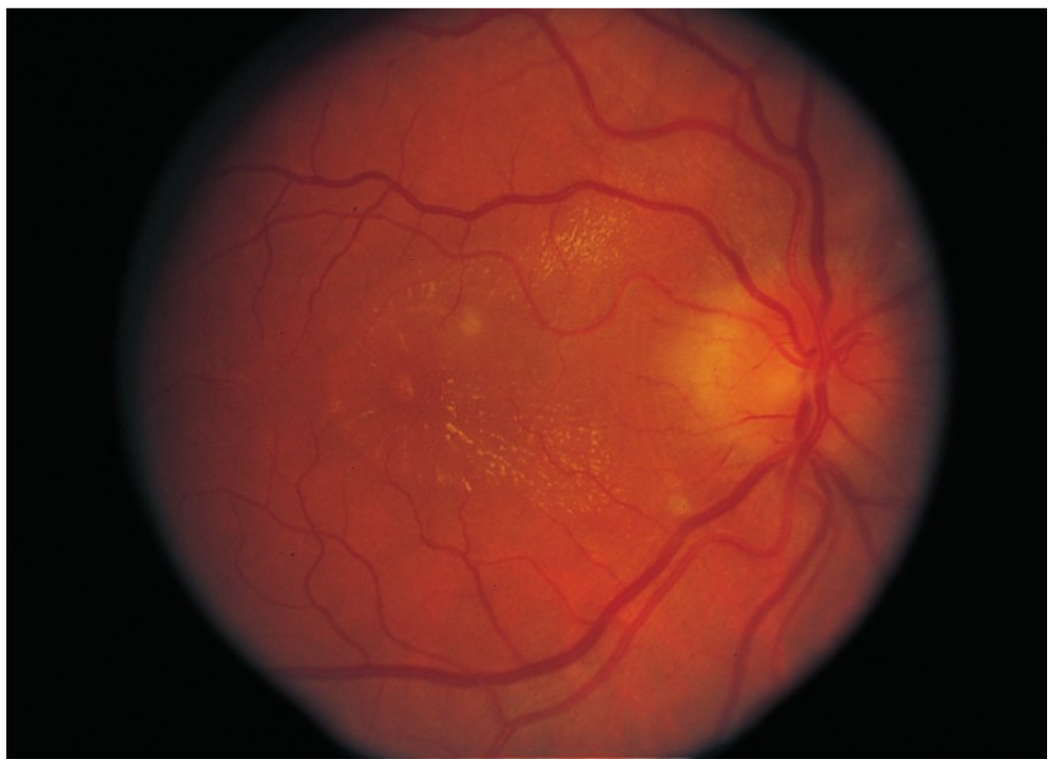

FIGURE 57–1 Fundus photograph of the right eye reveals significant optic disc edema with peripapillary and macular exudates, the latter in a star configuration. There were 1+ vitreous cells in the right eye.

and the lipid precipitate forms a macular star. The macular star may even occur after the disc swelling is starting to resolve. Vitreous cells are commonly observed.

4. Most cases of ODEMS are idiopathic and thought to be the result of a nonspecific viral infection or some immune-mediated process. Although ODEMS has been described with multiple infectious processes, the most important associations have included syphilis, cat-scratch disease, Lyme disease, and toxoplasmosis.

TEST INTERPRETATION

It is important to look for funduscopic changes of toxoplasmosis as a clue to this etiology as a cause for ODEMS. Syphilis serology, Bartonella henselae (the infectious agent of cat-scratch disease; positive in this case) titers, toxoplasmosis titers, and Lyme serology should be considered.

DIAGNOSIS

ODEMS or neuroretinitis secondary to cat-scratch disease.

MEDICAL MANAGEMENT

ODEMS is usually a benign disorder that resolves spontaneously over a period of months without treatment. Steroids have been used in some cases with unclear effect. If a specific infectious agent is discovered, appropriate antibiotics should be instituted.

SURGICAL MANAGEMENT

No surgical management is indicated.

REHABILITATION AND FOLLOW-UP

The prognosis for visual recovery is usually good, but significant residual visual disability may occasionally occur. Optic atrophy and macular retinal pigment epithelial changes may be residuals. Recurrences of ODEMS in the same or fellow eye have been described in idiopathic as well as infectious cases, especially in patients with toxoplasmosis.

Although optic neuritis is a risk factor for the development of multiple sclerosis, ODEMS is not. Because a macular exudate may not develop in cases of ODEMS until 2 weeks after presentation, patients who demonstrate acute papillitis with a normal macula should be reevaluated within 2 weeks for the development of a macular star. The finding of ODEMS makes the subsequent development of multiple sclerosis extremely unlikely.

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Case 58

ANTERIOR ISCHEMIC OPTIC NEUROPATHY—NONARTERITIC

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 65-year-old woman states that on awakening from sleep 3 days ago she noted severe visual loss in the left eye. She denied any headache, eye pain, jaw claudications, episodes of transient visual loss, or any other neurologic or ophthalmologic complaints. She related a past history of hypertension, increased cholesterol, and diabetes mellitus.

Examination revealed visual acuity to be 20/20 on the right and 20/200 on the left. She identified ten of ten Hardy-Rand-Rittler pseudoisochromatic plates on the right but only two of ten plates on the left. Visual fields were normal on the right but revealed a dense inferior altitudinal defect on the left. Pupils were 3 mm bilaterally, reacted well to light on the right and poorly to light on the left, and there was a left relative afferent pupillary defect. Extraocular motility was normal. Fundus examination was normal on the right with the cup-to-disc ratio of 0.1 (Fig. 58–1). The left optic disc was diffusely swollen and pale and there were peripapillary hemorrhages (Fig. 58–2). The retinal arterioles were attenuated somewhat on the left.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The patient has a left optic neuropathy that may be ischemic, compressive, infectious, inflammatory, or infiltrative. The older age of the patient, lack of pain, and presence of pallid disc edema argue strongly against optic neuritis. The acute onset makes a compressive lesion unlikely. The acute onset, lack of pain, altitudinal visual field defect, pallid disc swelling, and vascular risk factors are all compatible with anterior ischemic optic neuropathy (AION).

2. AION is characterized clinically by the acute onset of usually painless (pain may occur in up to 8 to 30% in some series) unilateral visual loss in a middle age or older patient (usually greater than age 50 years); an ipsilateral relative afferent pupillary defect; and edema of the optic nerve head with or without peripapillary hemorrhages. Later the optic disc often develops sector or diffuse pallor.

3. A small cup-to-disc ratio (less than 0.2) is an important predisposing structural factor for the development of AION ("disc at risk"). If a patient with AION has a large cup-to-disc ratio, giant cell arteritis should be strongly considered. The most important risk factors for nonarteritic AION are hypertension, hypotension, and diabetes mellitus.

4. Giant cell arteritis should be considered in all patients presenting with AION. This patient had no symptoms suggestive of this disease but a sedimentation rate or C-reactive protein should be performed in all patients with this presentation.

5. Findings atypical for nonarteritic AION are outlined in Table 58–1. If any of these findings are present, other etiologies for the optic neuropathy must be considered.

6. Visual loss with AION often is noted on awakening from sleep in the morning, perhaps due to nocturnal hypotension contributing to optic nerve ischemia. The visual loss in AION is usually acute but some worsening of vision may occur for 2 to 4 weeks after onset. Other important predisposing factors to

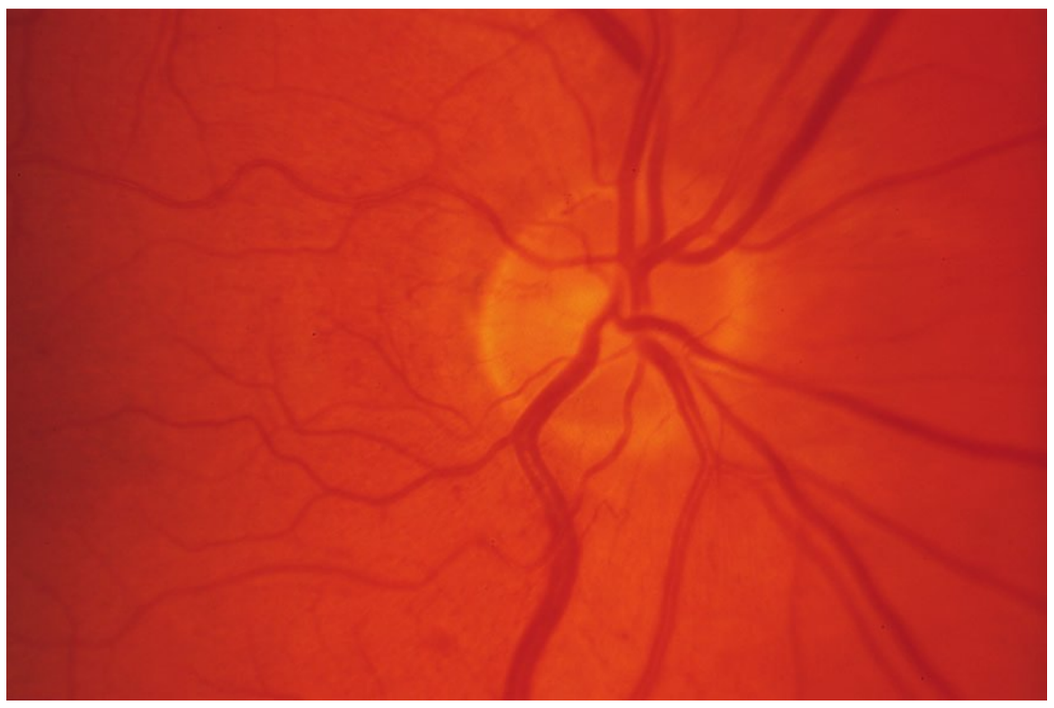

FIGURE 58–1 Fundus photograph of the right optic nerve shows a cup-to-disc ratio of 0.1 (the "disc at risk").

AION include hypotension or anemia due to surgery, severe hypotension or blood loss, and collagen vascular diseases.

TEST INTERPRETATION

A sedimentation rate or C-reactive protein should be obtained to investigate the possibility of giant cell arteritis. If the sedimentation rate or C-reactive protein is elevated, if there are other clinical symptoms of giant cell arteritis (eg, headache, jaw claudications), or if there are atypical features for nonarteritic AION (eg, a large cup-to-disc ratio), temporal artery biopsy should be performed. Otherwise, laboratory studies are mainly aimed at control of vascular risk factors (eg, diabetes, increased cholesterol, smoking). Carotid doppler flow studies and cardiac investigations are not warranted in typical AION because it is not usually an embolic disease.

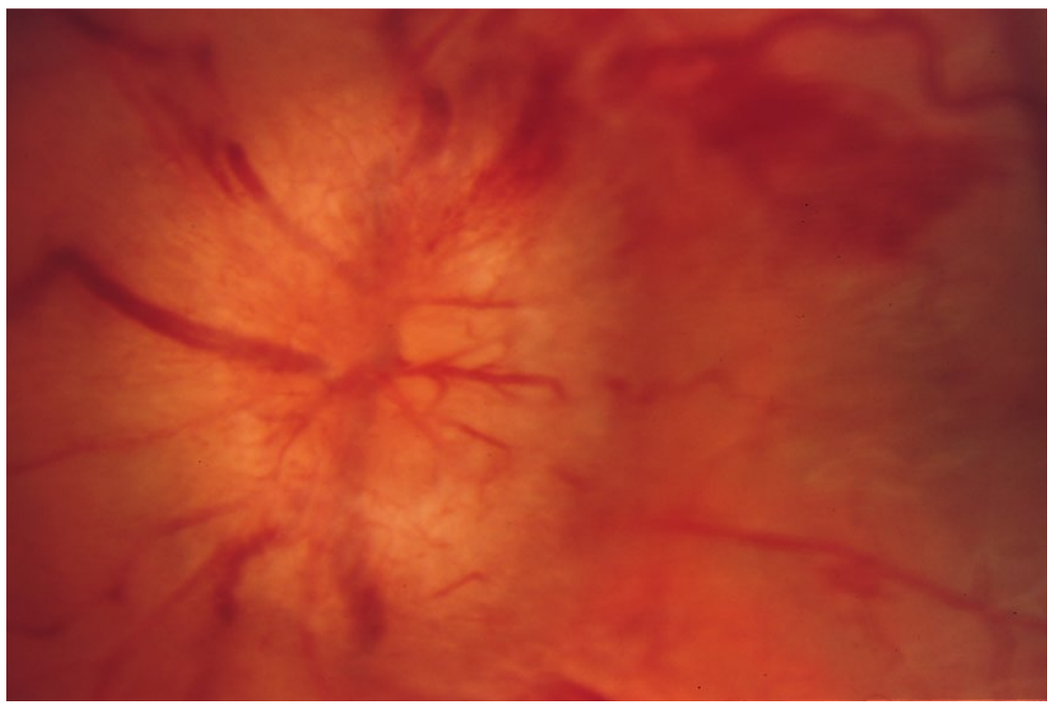

FIGURE 58–2 Fundus photograph reveals a left optic disc that is diffusely swollen and pale with surrounding peripapillary hemorrhages. The retinal arterioles were attenuated somewhat on the left.

TABLE 58–1 **Clinical Features Atypical for Nonarteritic Anterior-Ischemic Optic Neuropathy**

Age younger than 40 years
Bilateral simultaneous onset
Visual field defect not consistent with an optic neuropathy (eg, bitemporal hemianopia)
Lack of optic disc edema in acute phase
Lack of relative afferent pupillary defect in unilateral cases
Large cup-to-disc ratio in the fellow eye
Lack of vasculopathic risk factors
Presence of premonitory symptoms of transient visual loss
Progression of visual loss beyond 2–4 weeks
Recurrent episodes in the same eye
Anterior or posterior segment inflammation (eg, vitreous cells)

(Adapted from Lee AG and Brazis PW. *Clinical Pathways in Neuro-Ophthalmology: An Evidence-Based Approach*. New York, NY: Thieme; 1998:53 with permission.

DIAGNOSIS

Nonarteritic AION, OS.

MEDICAL MANAGEMENT

Vascular risk factors must be controlled. There is no proven therapy for nonarteritic AION. Aspirin therapy may reduce the risk of AION in the fellow eye and may decrease the risk of stroke and myocardial infarction.

SURGICAL MANAGEMENT

Initial reports of visual improvement following optic nerve sheath fenestration for nonarteritic

AION were encouraging but anecdotal. A well-designed, masked, prospective, randomized study at 25 clinical centers (Ischemic Optic Neuropathy Decompression Trial Research Group or IONDT) showed that optic nerve sheath fenestration is not effective and may be harmful in nonarteritic AION.

REHABILITATION AND FOLLOW-UP

The risk of AION in the fellow eye is approximately 12% in the patient's lifetime. Aspirin and control of stroke risk factors may decrease this risk but is unproven. According to the IONDT study, 42.7% of patients will experience spontaneous (three or more lines of Snellen acuity) improvement from baseline at 6 months.

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Case 59

ANTERIOR ISCHEMIC OPTIC NEUROPATHY—ARTERITIC

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 68-year-old woman complained of severe visual loss in the left eye. She states that over a period of hours the vision became markedly blurry. Over the last 2 weeks she had noted two or three episodes of painless, transient visual loss lasting minutes in the left eye. She denied any periocular or orbital pain, but stated that over the last several months she had noted diffuse, dull headaches with occasional superimposed "ice pick–like" pains affecting her left or right temples. She had a past history of hypertension. She reported jaw claudication, and polymyalgia rheumatica-like symptoms.

Examination revealed visual acuity to be 20/20 on the right and 20/400 on the left. She could identify ten of ten Hardy-Rand-Rittler pseudoisochromatic plates on the right but identified zero of ten on the left and could not name colors grossly on the left. The right visual field was normal and the left visual acuity was diffusely impaired, more inferiorly than superiorly. The pupils were 5 mm bilaterally; the right pupil reacted well to light but the left pupil was trace reactive. There was a left relative afferent pupillary defect. Motility was normal. Fundus exam was normal on the right. The cup-to-disc ratio on the right was 0.5. The left optic disc was swollen and pale and there were several peripapillary hemorrhages (Fig. 59–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The acute onset of visual loss in an elderly individual with evidence of pale optic disc swelling strongly suggests a diagnosis of anterior ischemic optic neuropathy (AION). The major question to be addressed is whether this is nonarteritic AION or arteritic AION (secondary to giant cell arteritis).

2. Features that are suggestive of arteritic AION instead of nonarteritic AION are listed in Table 59–1. In this patient, the episodes of transient visual loss preceding the onset of AION, the recent onset of headache, the jaw pain, the cup-to-disc ratio greater than 0.2, and the chalky white disc swelling are all strongly suggestive of a diagnosis of arteritic rather than nonarteritic AION.

3. Arteritic AION occurs in patients older than 50 years of age and presents with acute, often severe, visual loss that may be unilateral or bilateral (bilateral visual loss more common with arteritic AION than nonarteritic AION). Constitutional symptoms are common and may include headache, scalp or temporal artery tenderness, weight loss, jaw claudications, anorexia, fever, diaphoresis, and polymyalgia rheumatica.

4. Approximately 20% of patients with giant cell arteritis present with only ophthalmic changes ("occult" giant cell arteritis).

5. Causes of visual loss in giant cell arteritis include AION, posterior ischemic optic neuropathy, central retinal artery occlusion, branch retinal artery occlusion, the ocular ischemic syndrome, choroidal ischemia, and, rarely, occipital lobe ischemia. Giant cell arteritis must be strongly considered in a patient over the age of 50 who presents with a central retinal artery occlusion with no visible emboli.

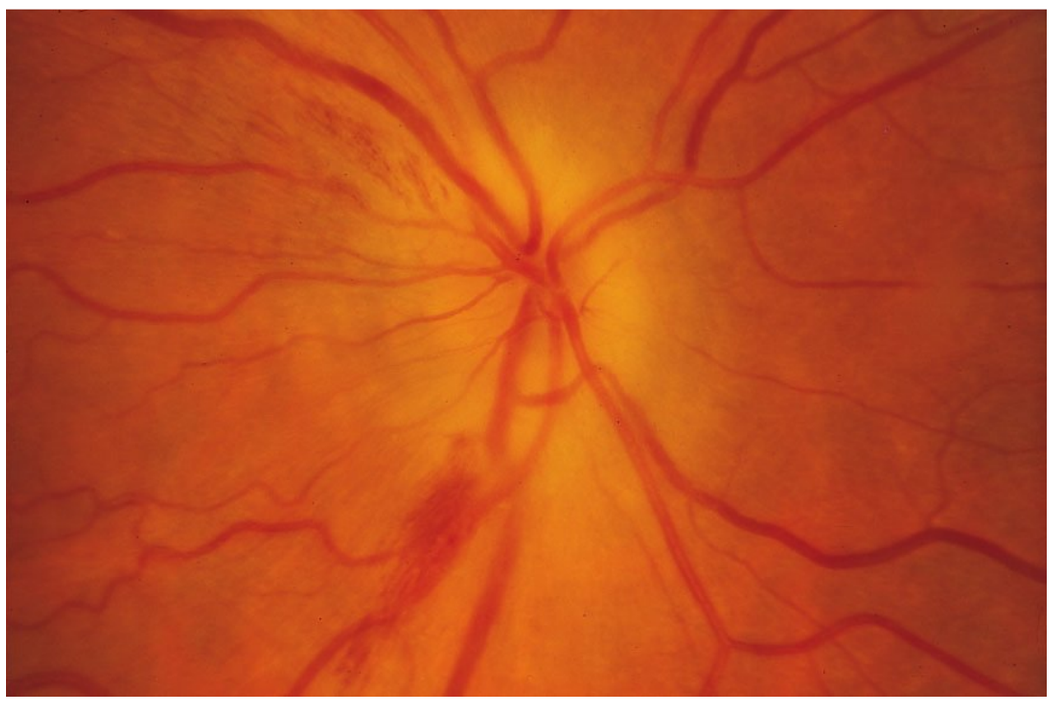

FIGURE 59–1 Fundus photograph reveals that the left optic disc is swollen and pale and there were several peripapillary hemorrhages.

TEST INTERPRETATION

An elevated sedimentation rate occurs in approximately 90% of patients with giant cell arteritis, but a normal sedimentation rate does not rule out giant cell arteritis. Another acute phase reactant, C-reactive protein (CRP), may be more sensitive than the sedimentation rate. Temporal artery biopsy should be performed in all patients who are suspected of having giant cell arteritis. Bilateral temporal artery biopsies may have a higher yield than unilateral biopsy.

TABLE 59–1 **Features Suggestive of Arteritic AION Instead of Nonarteritic AION**

Elderly patient with constitutional symptoms (especially scalp tenderness or jaw claudications)
Polymyalgia rheumatica
Elevated sedimentation rate (ESR) or C-reactive protein
Ocular findings
Posterior ischemic optic neuropathy
Cup-to-disc ratio greater than 0.2 in fellow eye
Early massive (no light perception to count fingers) or bilateral simultaneous visual loss
Markedly pallid optic disc edema (chalk white)
Fluorescein angiogram or clinical findings of simultaneous choroidal nonperfusion and AION
AION associated with choroidal nonfilling
Simultaneous nonembolic central retinal artery occlusion or cilioretinal artery occlusion and AION
Simultaneous choroidal or retinal infarction and AION

(Adapted from Lee AG and Brazis PW. Clinical Pathways in Neuro-Ophthalmology: An Evidence-Based Approach. New York: Thieme; 1998:70 with permission.)

DIAGNOSIS

Arteritic AION. The sedimentation rate in this patient was 70 mm/hr and temporal artery biopsy was positive for giant cell arteritis.

MEDICAL MANAGEMENT

When a diagnosis of giant cell arteritis is considered, the patient must be started immediately on corticosteroids in order to prevent further visual loss. Treatment should not be delayed until after temporal artery biopsy as corticosteroids do not alter the histopathological findings acutely. Most authors recommend an initial dose of oral prednisone of 1.0 mg/kg to 1.5 mg/kg per day. Some authors favor intravenous steroids in patients with severe visual loss of less than 48 hours duration due to giant cell arteritis, especially if there is bilateral involvement, if the patient is monocular, or if the patient has lost vision during oral steroid therapy. Every other day steroid therapy does not seem to sufficiently control disease activity. Most patients can be tapered off steroids within 1 year, but some patients may require prolonged or even indefinite therapy.

SURGICAL MANAGEMENT

No surgical management is indicated.

REHABILITATION AND FOLLOW-UP

Untreated, there is a high risk of further visual loss in the involved or fellow eye in patients with giant cell arteritis. Patients must be carefully monitored for visual impairment, constitutional symptoms, and ill effects of the steroid therapy, with some guidance provided by serial

sedimentation rate studies. Consultation with an internist or rheumatologist is recommended.

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Case 60

PROGRESSIVE OPTIC NEUROPATHY—TUMOR

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 64-year-old woman complained of painless progressive visual loss in her right eye. Three years previously she had noted visual blurring in her right eye and visual acuity had been found to be 20/40 on the right and 20/20 on the left. Her visual difficulty had been attributed to nuclear sclerotic cataract and observation was recommended. One year later, her vision continued to deteriorate to 20/60 on the right and 20/20 on the left and right cataract surgery was performed. She felt that her vision was no better after the surgery and the vision was still getting worse on the right. She denied any headache or eye pain.

Examination revealed visual acuity to be 20/100 on the right and 20/20 on the left. She was able to identify two of ten Hardy-Rand-Rittler pseudoisochromatic plates on the right and nine often on the left. Visual field exam revealed a diffuse depression of the visual fields on the right with normal fields on the left. The pupils were 5 mm bilaterally, poorly reactive to light on the right and briskly reactive on the left, and there was a right relative afferent pupillary defect. Motility was normal. Hertel measurements at a base of 95 were 22 mm on the right and 19 mm on the left. Slit-lamp exam revealed a posterior intraocular lens on the right and a mild nuclear sclerotic cataract on the left. Fundus exam revealed a pale, atrophic nerve on the right (Fig. 60–1). The left optic disc was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The patient's history of painless progressive visual loss is not consistent with optic neuritis or ischemic optic neuropathy. Compressive or infiltrative optic neuropathies cause painless, progressive, gradual loss of visual function (visual acuity, visual field, and color vision), a relative afferent pupillary defect (in unilateral or asymmetric cases), and optic disc edema or atrophy (the disc may be normal initially). Mild proptosis in this case raises the possibility of an orbital process causing her progressive optic neuropathy.

2. Compressive optic neuropathy that is due to orbital or intracanalicular lesions may result in ipsilateral optic disc edema followed by atrophy and may also be associated with the development of abnormal blood vessels on the disc head called optociliary shunt vessels. These vessels probably represent collateral circulation between the retinal and choroidal venous circulation that allows blood to bypass the compression at the level of the optic nerve.

3. The presence of an unexplained relative afferent pupillary defect or unexplained optic atrophy should prompt appropriate neuroimaging studies. Lesions causing compressive optic neuropathy include benign and malignant tumors (eg, meningioma, glioma, craniopharyngioma, lymphoma, metastasis), orbital fracture, inflammatory or infectious diseases (eg, mucocele), primary bone diseases (eg, osteopetrosis, fibrous dysplasia), vascular masses (eg, orbital hemorrhage, aneurysms, orbital venous anomalies), thyroid ophthalmopathy, and iatrogenic causes (eg, intracranial catheters, postoperative changes).

TEST INTERPRETATION

Perimetry and color vision testing are helpful in differentiating visual loss due to optic neuropathy from media problems. All patients should

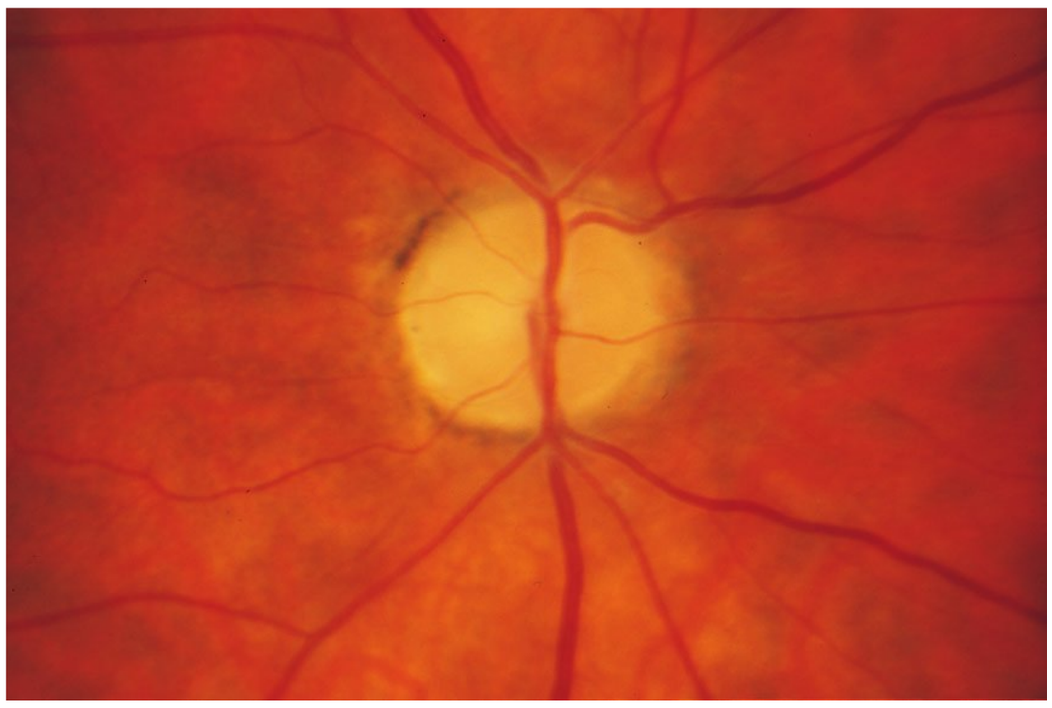

FIGURE 60–1 Fundus photograph revealing a pale, atrophic optic nerve on the right.

have neuroimaging studies, preferably magnetic resonance imaging (MRI), of the brain and orbit with and without gadolinium contrast material to investigate the cause of the optic nerve compression.

DIAGNOSIS

Compressive optic neuropathy on the right. MRI revealed an optic nerve sheath menigioma on the right (Fig. 60–2).

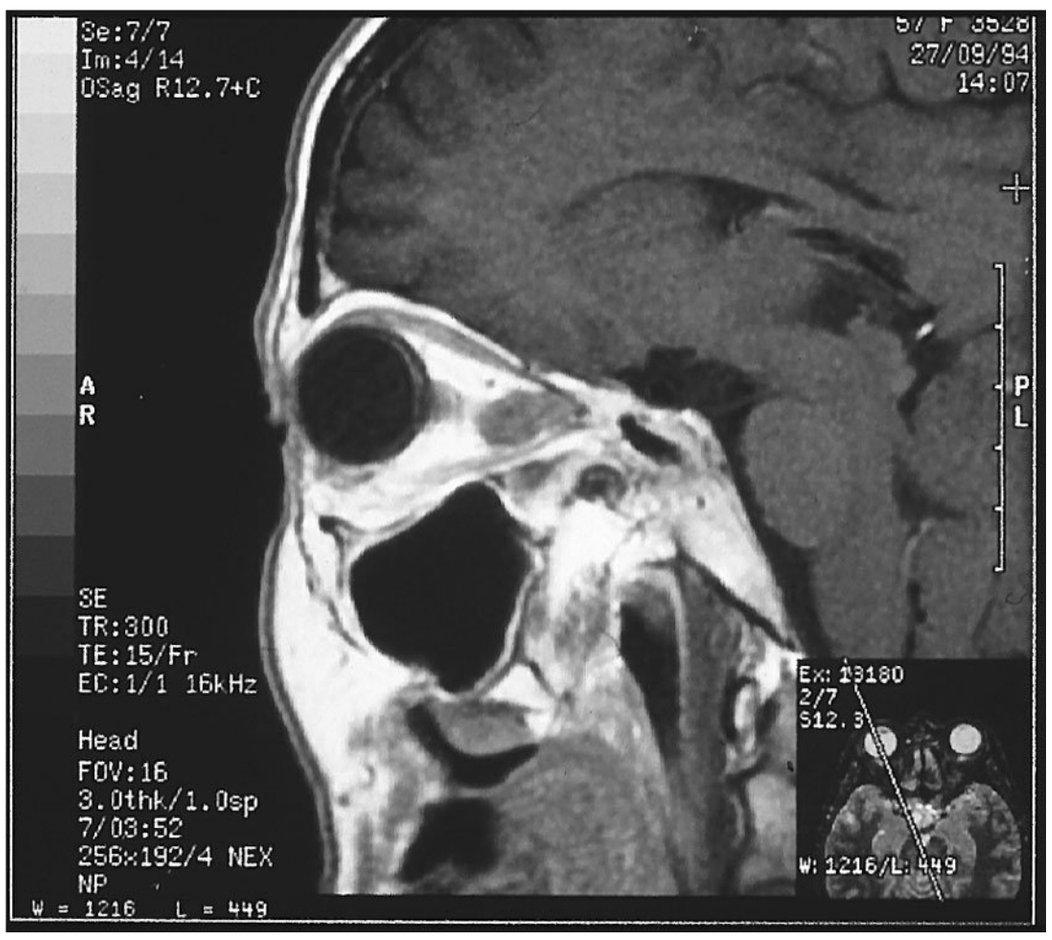

FIGURE 60–2 MRI (sagittal image) revealed an optic nerve sheath meningioma on the right.

MEDICAL MANAGEMENT

The management of lesions causing optic nerve compression depends upon the nature of the lesion. For optic nerve sheath meningiomas, close observation may be all that is necessary. If progressive visual deterioration occurs, radiation therapy may be appropriate.

SURGICAL MANAGEMENT

Surgical intervention for primary sheath meningiomas is usually considered if there is progressive intracranial extension of the lesion through the optic canal. Parachiasmal meningiomas causing optic nerve compression are often initially treated surgically with total resection if feasible or subtotal excision if the tumor surrounds vital structures. Postoperative radiation therapy for a nonresectable tumor should be considered, although some authors reserve postoperative radiation for cases in which there is clinical progression.

REHABILITATION AND FOLLOW-UP

Patients with tumors such as meningiomas require clinical reevaluation (eg, every 6 months) including visual fields and repeat MRIs (eg, every 6 months for 2 years, and then yearly if no growth is indicated clinically or by imaging). More malignant processes require more frequent follow-up and more aggressive treatment measures.

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Case 61

PAPILLEDEMA—PSEUDOTUMOR CEREBRI

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 22-year-old woman had an 8-month history of headache. The headaches occurred almost daily, were diffuse, and were rarely associated with nausea. Over the last 2 months she had noted a "pulsating sound" in her head that was most noticeable when changing posture, especially when going from a lying to a standing posture. Over the last 2 weeks she had noted episodes lasting seconds at a time of transient visual loss in the left or right eye. She denied any other neurologic complaints or diplopia.

Examination revealed an obese woman weighing 250 pounds. Blood pressure was 135/85. Visual acuity was 20/20 bilaterally, color vision was normal, and visual fields were normal except for enlarged blind spots bilaterally. Pupils were 5 mm bilaterally, reacted well to light, and there was no relative afferent pupillary defect. Motility was normal. Fundus examination revealed bilateral severe optic disc swelling (Fig. 61–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Although bilateral disc swelling can be seen in bilateral optic neuropathies, the patient has no visual loss, color impairment, or visual field defects suggestive of an optic neuropathy. Bilateral disc edema with normal visual function may be seen with hypertension but her blood pressure was normal and there were no other signs of hypertensive retinopathy. Thus, the patient's disc swelling is likely due to increased intracranial pressure, ie, papilledema.
2. Patients with papilledema must be assessed for space-occupying lesions of the brain, such as hydrocephalus, masses (eg, tumor, hemorrhage, abscess), encephalitis/meningitis, and subarachnoid hemorrhage. If neuroimaging studies are normal or cerebrospinal fluid contents are normal, and lumbar puncture opening pressures are elevated, the patient, by definition, has pseudotumor cerebri (PTC).
3. Pseudotumor cerebri is often idiopathic but may occur in association with certain systemic conditions (eg, drugs, pregnancy, and intracranial or extracranial venous obstruction). Obstruction or impairment of intracranial venous drainage may result in cerebral edema with increased intracranial pressure and papilledema. Tumors that occlude the posterior portion of the superior sagittal sinus or other cerebral venous sinuses may cause increased intracranial pressure as may septic or aseptic thrombosis or ligation of the cavernous sinus, lateral sinus, sigmoid sinus, or superior sagittal sinus. Venous sinus thrombosis may be the mechanism of PTC reported with systemic lupus erythematosus, protein S deficiency, antithrombin III deficiency, the antiphospholipid antibody syndrome, and other blood dyscrasias. In fact, elevated intracranial venous pressure is thought by some authors to be the "universal mechanism" of PTC of varying etiologies.
4. Many systemic diseases, drugs, vitamin deficiencies and excesses, pregnancy, and hereditary conditions have been associated with PTC. The drugs most firmly associated with PTC include hypervitaminosis A, steroid withdrawal, anabolic steroids,

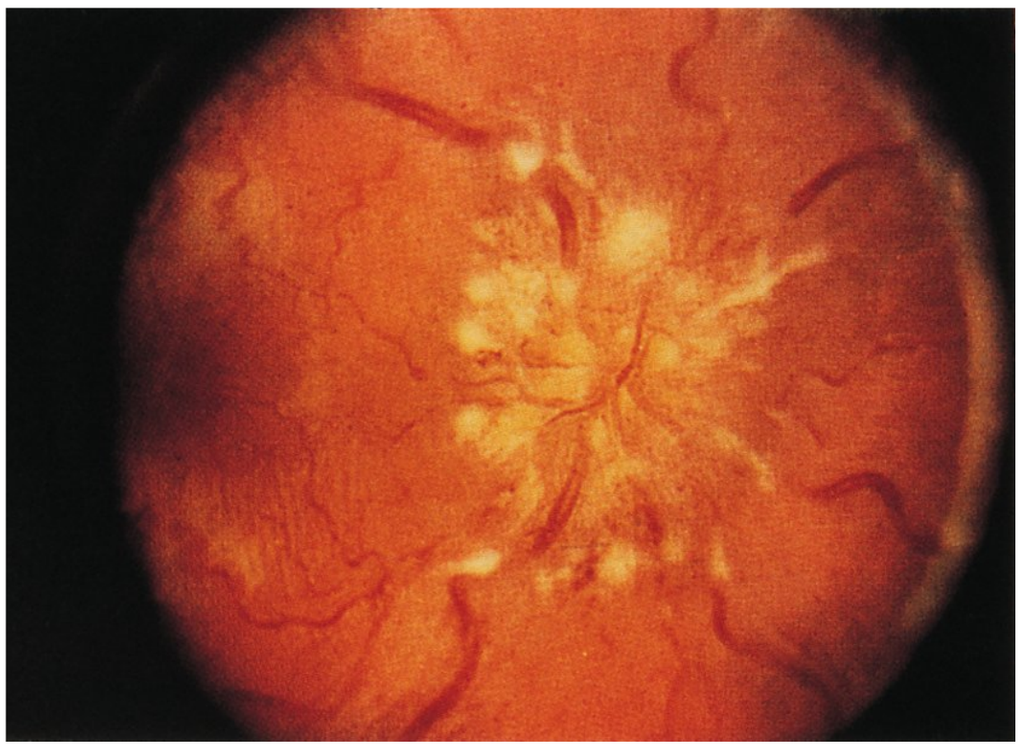

FIGURE 61–1 Fundus examination revealed marked bilateral disc swelling with diffuse exudates, hemorrhages, and dilated vessels.

lithium, naldixic acid, the insecticide chlordecone (Kepone), isoretinoin, ketaprofen (Orudis) or indomethacin in Bartter's syndrome, thyroid replacement in hypothyroid children, danazol, all-trans-retinoic acid (ATRA) or tretinoin, cyclosporine, exogenous growth hormone, and tetracycline. The systemic diseases most closely linked to PTC include Behçet's syndrome, renal failure, Addison's disease, hypoparathyroidism, systemic lupus erythematosus, and sarcoidosis.

5. Idiopathic PTC is typically a disease of obese women in the childbearing years. The occurrence of PTC in a man, the elderly, or thin patients should raise the possibility of venous occlusive disease or a secondary cause. The diagnostic criteria for PTC are listed in Table 61–1. The most common symptoms of PTC include headache, transient obscurations of vision, pulsatile tinnitus, and diplopia. The headaches in patients with PTC may be constant or intermittent. Transient visual obscurations last seconds, may be unilateral or bilateral, may be related to changes in posture, do not correlate with the degree of intracranial hypertension or the extent of disc swelling, and are not considered to be harbingers of permanent visual loss. Intracranial noises are common with PTC and are perhaps due to transmission of intensified vascular pulsations via cerebrospinal fluid under high pressure to the walls of the venous sinuses.

6. Visual field and, eventually, visual acuity loss are the major causes of morbidity in PTC. Complete blindness and optic atrophy may occur. Often the patient is unaware of peripheral visual field dysfunction and Snellen acuity testing is a poor indicator of early visual deficit in PTC. The papilledema causes optic nerve fiber attrition, which results in field constriction and nerve fiber bundle defects. Blind spot enlargement is commonly encountered but is more a reflection of the disc swelling itself, rather than optic nerve damage, and is improved with refraction.

TABLE 61–1 **Criteria for the Diagnosis of Idiopathic Pseudotumor Cerebri (PTC)**

1. Increased intracranial pressure must be documented in an alert and oriented patient without localizing neurologic findings (except for cranial nerve VI palsy). It should be noted that spinal fluid pressures between 200 and 250 mm H_2O may occur normally in obese patients and that when elevated spinal fluid pressure is suspected, confirmation requires values greater than 250 mm H_2O.
2. The cerebrospinal fluid should have normal contents (including protein and glucose) with no cytologic abnormalities. Occasionally the cerebrospinal fluid protein level may be low.
3. Neuroimaging (preferably MR imaging with and without contrast, and possibly MR venography) should be normal with no evidence of hydrocephalus, mass lesion, meningeal enhancement, or venous occlusive disease. Neuroimaging may show enlarged optic nerve sheaths, empty sellae, and reversal of the optic nerve head in some patients with pseudotumor cerebri.
4. No secondary cause should be present.

TEST INTERPRETATION

In all patients with bilateral optic disc swelling, blood pressure should be checked to evaluate for possible malignant hypertension. Neuroimaging

is required in all patients. CT imaging is the study of choice in the acute setting in evaluating the patient with possible acute vascular processes (eg, subarachnoid, epidural, subdural, or intracerebral hemorrhage, acute infarction) or after head trauma. Otherwise, MR imaging, with and without contrast, is the imaging modality of choice. In selected cases, MR angiography or MR venography could be obtained at the same time to evaluate the patient for arterial disease or venous obstruction, respectively. If neuroimaging shows no structural lesion or hydrocephalus, then lumbar puncture is warranted. Studies should include an accurate opening pressure, to evaluate for intracranial hypertension, as well as cell count and differential, glucose, protein, cytology, and appropriate cultures.

DIAGNOSIS

Papilledema. The MRI and MR venogram were normal in this patient. Spinal tap revealed an opening pressure of 350 mm of H2O secondary to idiopathic pseudotumor cerebri.

MEDICAL MANAGEMENT

Some patients require no treatment as long as symptoms are minimal and visual function is normal, but all require serial monitoring of visual function, especially visual fields, to observe closely for signs of visual impairment. Weight reduction, including surgically induced weight reduction in morbidly obese patients, may improve the papilledema and reduce intracranial pressure. Medical treatments for PTC include carbonic anhydrase inhibitors, loop diuretics, corticosteroids, and repeat lumbar punctures. Acetazolamide in doses of 2 to 4 grams per day has proven effective in most patients with PTC. Acetazolamide should probably not be used during pregnancy except in unusual circumstances, especially during the first 20 weeks, because of potential teratogenic effects; caloric restriction and the use of other diuretics are also relatively contraindicated during pregnancy. Other carbonic anhydrase inhibitors, such as methazolamide (Neptazane), can be used in acetazolamide-intolerant patients but their efficacy has not been proven. Furosemide (Lasix) inhibits cerebrospinal fluid production and may have an additive effect with acetazolamide, but the use of this agent alone has not been systematically studied. Corticosteroids may be efficacious in the short run, but the complications of this medication, especially in the chronic treatment of an already obese individual, have resulted in most clinicians suggesting that their use be avoided.

Repeated lumbar punctures have never been systematically studied for the treatment of PTC. As these procedures are uncomfortable, are of questionable benefit, and are potentially associated with complications (eg, infection, intraspinal epidermoid tumors), they should not be performed as a primary therapy. Finally, if acetazolamide does not control the headache associated with PTC, symptomatic headache treatments are warranted.

SURGICAL MANAGEMENT

When medical therapy fails for headache or visual dysfunction, surgical therapies for PTC should be considered.

The two main procedures performed include lumboperitoneal shunt (LPS) and optic nerve sheath fenestration (ONSF). Various authorities have vehemently advocated one or the other procedure. There has been no prospective study comparing the efficacy of the two procedures. Both ONSF and LPS may improve vision and prevent deterioration of vision in patients with PTC. Both procedures have their advantages and disadvantages and either may fail with time. Patients who fail LPS may benefit from ONSF and vice versa. Until a prospective, randomized study comparing ONSF with LPS for PTC is performed, the question of which surgical procedure is best for the treatment of PTC remains unanswered.

REHABILITATION AND FOLLOW-UP

Patients must return monthly for 6 to 12 months with careful evaluation of visual fields, stereo-optic disc photos, visual acuity, color vision, and relative afferent pupillary defect (RAPD) testing. The time between visits can be lengthened depending upon the stability of the ophthalmologic findings. Regression of symptoms and papilledema are the endpoint. However, patients must continue to be closely followed, even after successful surgery, because of the possibility of late recurrences, failed shunts, etc.

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Case 62

VISUAL FIELD DEFECT—JUNCTIONAL SCOTOMA

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 55-year-old man complained of progressive painless visual impairment in his right eye over a period of 1½ years. He denied any visual difficulty in his left eye and denied any other history of neurologic or ophthalmologic impairment.

Examination revealed visual acuity of 20/80 on the right and 20/20 on the left. He could identify four of ten Hardy-Rand-Rittler pseudoisochromatic plates on the right and ten of ten on the left. Pupils were 4 mm bilaterally and both reacted well to light and near but there was a right relative afferent pupillary defect. Visual fields revealed diffuse impairment on the right (Fig. 62–1) and a superotemporal field defect on the left (Fig. 62–2). Motility was normal. Slit-lamp examination was normal. The right optic disc was diffusely pale. The left optic disc, vessels, and macula were normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The visual acuity, color vision, and field impairment on the right, with a relative afferent pupillary defect and optic atrophy, all suggest a right optic neuropathy. The progressive, painless visual loss raises the possibility of a compressive or infiltrative optic nerve lesion.
2. Lesions at the junction of the optic nerve and chiasm may produce specific types of visual field defects that allow topographical localization. Selective compression of the crossed or uncrossed visual fibers at the junction may result in a unilateral temporal or nasal hemianopic defect, respectively (junctional scotoma of Traquair). In addition, involvement of the inferonasal fibers of the anterior knee (Wilbrand's knee) results in a superotemporal visual field defect contralateral to the lesion (junctional scotoma).
3. The patient therefore has a lesion of the optic nerve at the junction of the right nerve with the chiasm causing an ipsilateral optic neuropathy and a contralateral superior temporal defect (junctional scotoma).
4. Recently, the existence of Wilbrand's knee has come into question. It has been hypothesized that Wilbrand's knee may be an artifact of enucleation caused by atrophy of the optic nerve and not a normal anatomic finding. Nevertheless, whether Wilbrand's knee exists anatomically, the localizing value of junctional visual field loss to the junction of the optic nerve and chiasm remains undiminished since chiasmal compression alone may result in a contralateral superotemporal visual field defect.
5. Junctional field loss is usually due to a mass lesion, with a differential diagnosis including pituitary tumors, suprasellar meningiomas, supraclinoid aneurysms, craniopharyngiomas, and gliomas. Chiasmal neuritis (eg, due to multiple sclerosis), pachymeningitis, and trauma are rare etiologies of the junctional syndrome.

TEST INTERPRETATION

Patients with junctional scotoma of Traquair or junctional scotoma should be considered to have a compressive lesion at the junction of the optic nerve and chiasm until proven otherwise. Neuroimaging studies (preferably MRI) should be directed to this location. Patients with junctional scotomas (as the described patient) may be unaware of a small superotemporal visual field defect. Therefore, in any patient with presumed unilateral visual loss, careful testing should be performed in the contralateral asymptomatic eye.

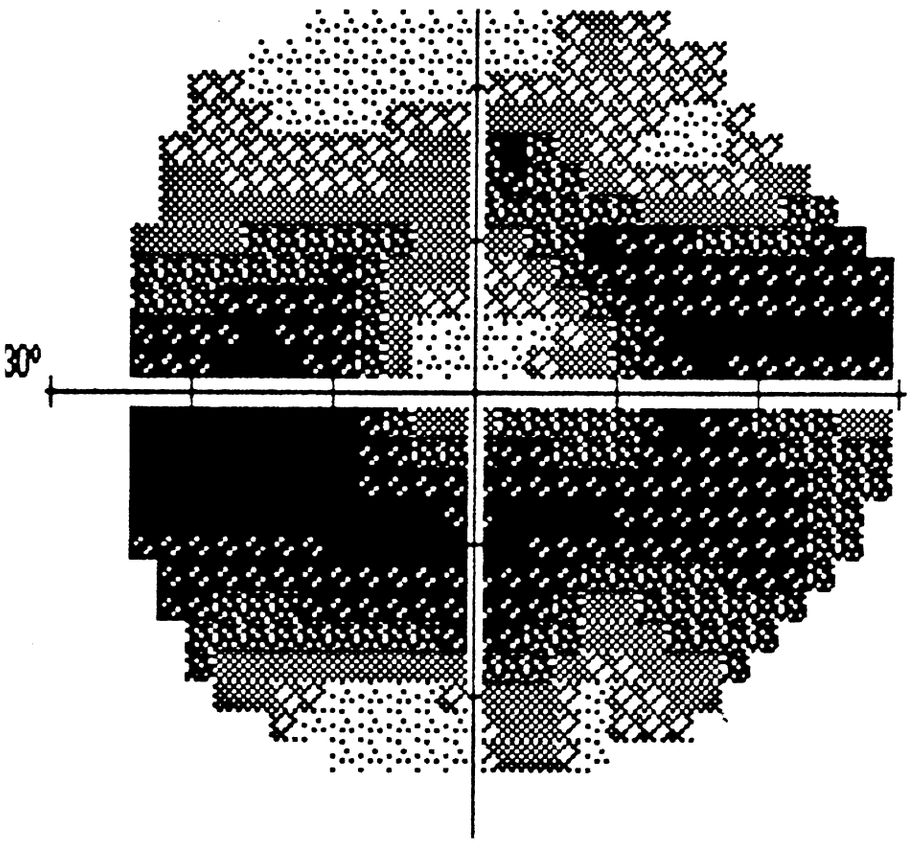

FIGURE 62–1 Static perimetry showing diffuse visual field impairment on the right.

DIAGNOSIS

Right optic neuropathy with junctional scotoma secondary to compressive lesion of the junction of the right optic nerve with the chiasm (pituitary adenoma) (Fig. 62–3).

MEDICAL MANAGEMENT

There is usually no role for medical management of this problem. Prolactin secreting pituitary tumors are sometimes treated with dopomine agonists.

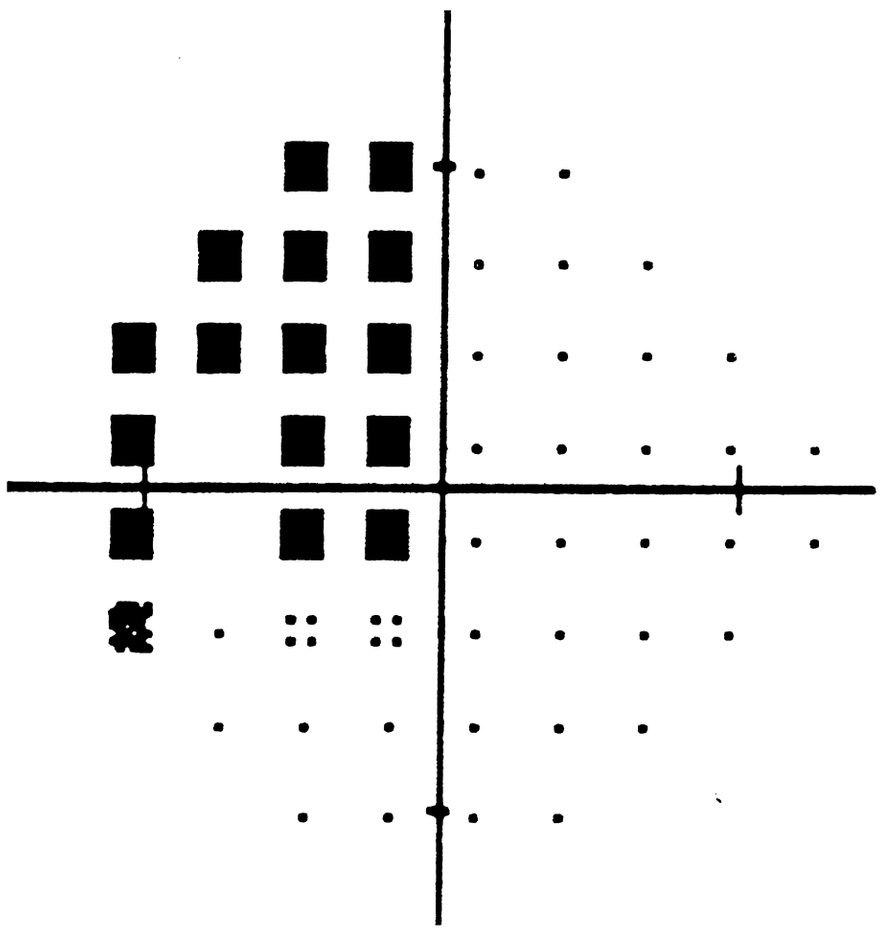

FIGURE 62–2 In the left eye, perimetry revealed a superotemporal field defect respecting the vertical meridian.

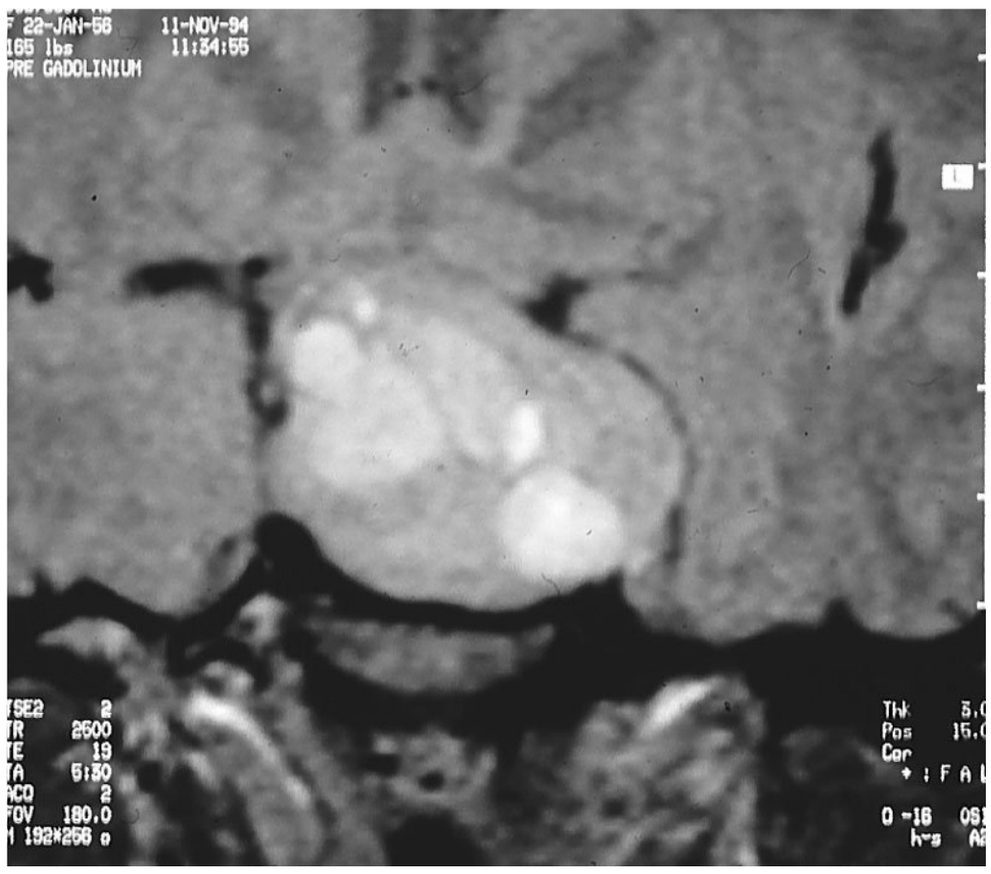

FIGURE 62–3 MRI (axial view) revealed a mass (pituitary adenoma) at the junction of the right optic nerve with the chiasm.

SURGICAL MANAGEMENT

The treatment is surgical removal, if possible, of the underlying structural lesion responsible for the visual field defect. In this case, the patient underwent decompressive surgery.

REHABILITATION AND FOLLOW-UP

Follow-up of this patient's ophthalmologic examination, including visual field testing, was performed every 4 months for 1 year, and every 6 months thereafter, with periodic MRIs to monitor for tumor growth.

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Case 63

VISUAL FIELD DEFECT—PITUITARY LESION

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 45-year-old woman complained of blurred vision bilaterally and a poor driving performance with multiple accidents due to "poor vision." The visual difficulty had been present for the last year and was slowly deteriorating. She also complained of occasional frontal headaches over the last 6 months. She denied any past history of neurologic or ophthalmologic illnesses and took no medicines except acetaminophen for her headaches.

Examination revealed visual acuity to be 20/25 on the right and 20/20 on the left. She identified ten of ten Hardy-Rand-Rittler pseudoisochromatic color plates bilaterally. The pupils were 4 mm bilaterally, were equally reactive to light and near, and there was no relative afferent pupillary defect. Motility was normal. Slit-lamp examination and fundus exam were normal. Visual field testing showed bitemporal hemianopic defects (Figs. 63–1A and B).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The visual field exam reveals a bitemporal field defect indicating a lesion of the optic chiasm. Bitemporal hemianopias may be peripheral, paracentral, or central and are most often due to a compressive lesion of the optic chiasm.

2. Clinically, three optic chiasm syndromes may be recognized: (1) the anterior chiasm or junctional syndrome, in which a unilateral optic nerve defect is associated with a superior defect in the other eye; (2) the body of the chiasm syndrome, in which patients demonstrate bitemporal field abnormalities. Visual acuity is often normal and the optic discs may be normal or pale; (3) the posterior chiasm syndrome, in which visual field testing reveals bitemporal paracentral scotomas. Visual acuity and the optic discs are normal.

3. Superior bitemporal field defects may also occur with tilted discs, but in these cases the field defects do not respect the vertical meridian.

4. The most common cause of bitemporal visual field impairment is a parasellar mass, most often pituitary adenomas, meningiomas, or craniopharyngiomas. Other mass lesions include dysgerminomas, chiasmal gliomas, metastases, and suprasellar aneurysms. Nonmass lesions that may cause a chiasmal syndrome include demyelinating disease (multiple sclerosis), ischemia, meningitis or encephalitis, syphilis, inflammatory diseases (eg, collagen vascular disease, sarcoidosis), radiation necrosis, trauma, and some toxins (eg, Placidyl).

5. Pituitary masses may occasionally cause an optic neuropathy without evidence for chiasmal damage, especially if the chiasm is postfixed, or may cause an optic tract syndrome if the chiasm is prefixed.

TEST INTERPRETATION

Visual field testing characteristically reveals a bitemporal visual field impairment with chiasmal compression due to pituitary lesions. Because a mass lesion is likely, MRI with and without gadolinium with attention to the sellar region is warranted. If a pituitary adenoma is found, endocrinologic evaluation is warranted.

DIAGNOSIS

Bitemporal visual field defect secondary to pituitary macroadenoma (Fig. 63–2).

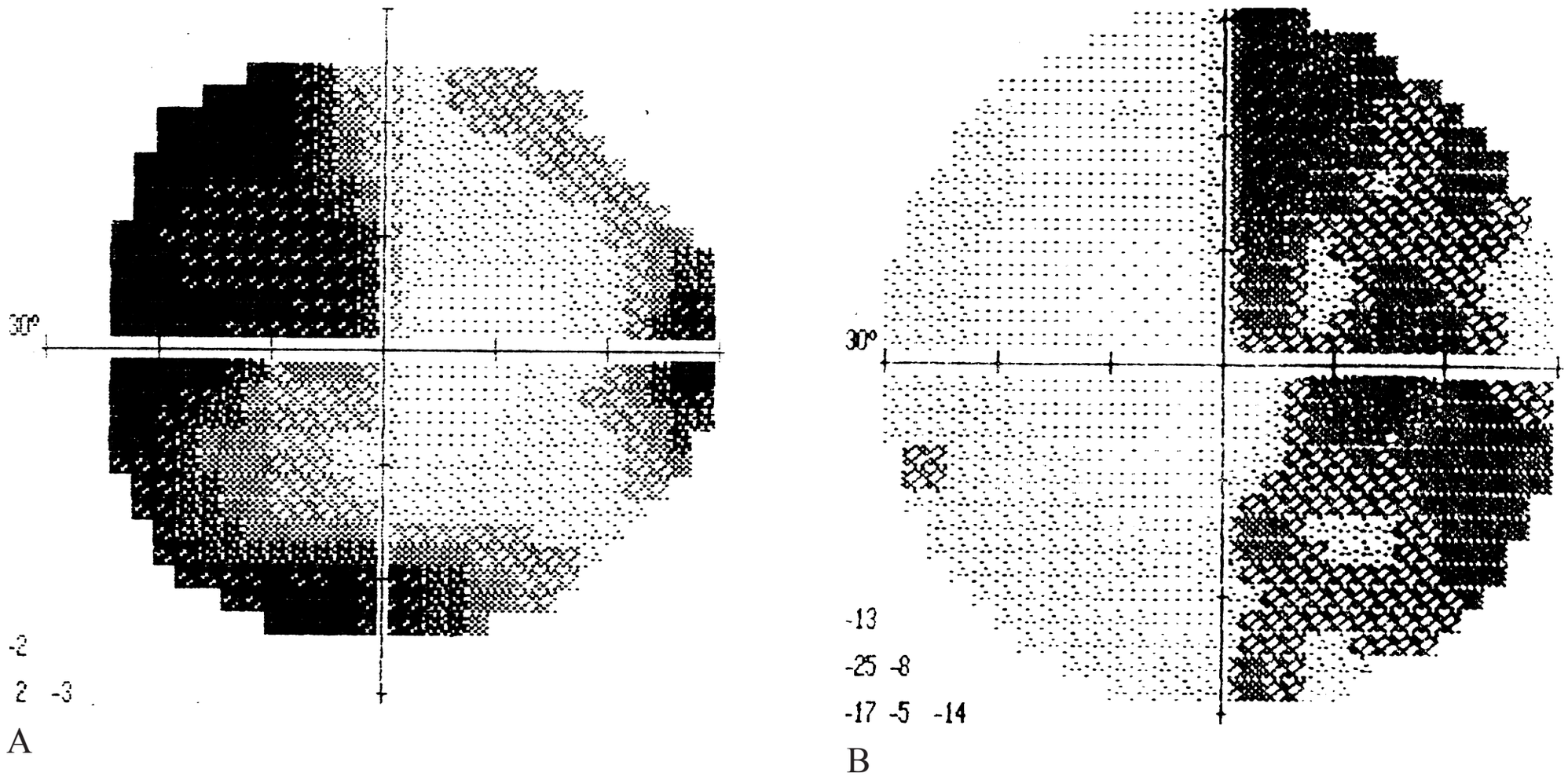

FIGURE 63–1 Static perimetry revealed bitemporal hemianopic defects in the left eye (A) and right eye (B).

MEDICAL MANAGEMENT

Prolactinomas may respond to therapy with medications, such as bromocriptine.

SURGICAL MANAGEMENT

Pituitary adenomas or other masses causing chiasmal compression usually are treated surgically.

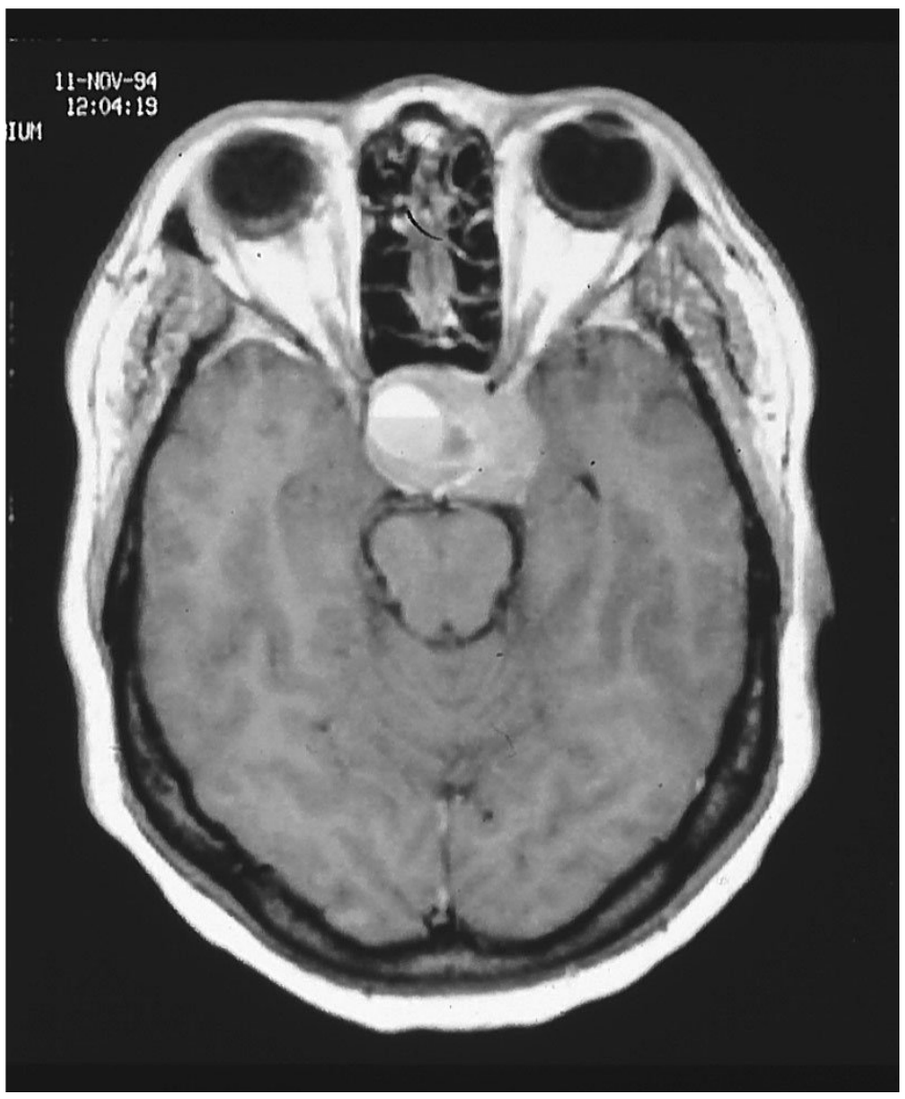

FIGURE 63–2 MRI revealed a large pituitary macroadenoma.

Postoperatively, hormonal replacement may be required.

REHABILITATION AND FOLLOW-UP

Postoperatively, visual field and ophthalmologic examination should be performed as soon as the patient is able to tolerate the procedure. Visual fields and serial ophthalmologic examination should then be performed (eg, in 3 months, then at 6-month intervals for 2 years, yearly for 5 years, and every 2 years thereafter) to monitor for recurrence. MRI studies should be repeated at regular intervals (eg, 6 months, 1 year, and then yearly for several years).

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Case 64

VISUAL FIELD DEFECT—HOMONYMOUS HEMIANOPIA

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 57-year-old male underwent coronary bypass surgery 6 weeks prior to evaluation. His recovery was apparently uneventful and within several weeks he returned to his usual duties. However, since surgery he noted that he would often "lose his place" or "miss lines" when reading. He had also noted that he bumped his left front fender on several occasions when attempting to park his car in the garage. He had a past history of hypertension, diabetes, and increased cholesterol. He had no other neurologic symptoms.

Examination revealed visual acuity to be 20/20 in both eyes. He identified nine of ten Hardy-Rand-Rittler pseudoisochromatic plates bilaterally, but often had difficulty with the figures in the left part of the diagrams. The pupils were 4 mm bilaterally, reacted well to light and near, and there was no relative afferent pupillary defect. Motility was normal. Slit-lamp exam revealed mild bilateral nuclear sclerotic cataracts. Fundus exam revealed mild hypertensive changes (A-V nicking, arteriolar sclerosis) with normal discs. There were no hemorrhages or exudates. The general neurologic examination was otherwise normal. Visual field testing showed a left homonymous hemianopia (Fig. 64–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The visual field exam reveals a complete left homonymous hemianopia indicating a retrochiasmal lesion of the visual pathways. In general, visual field defects with lesions affecting the optic tract or lateral geniculate body tend to be incongruous, while more posteriorly located lesions of the optic radiations or occipital lobe result in congruous field defects. In general, tumors produce sloping field defects while vascular lesions produce sharp field defects.

2. Complete homonymous hemianopias are nonlocalizing and may occur with any lesion of the retrochiasmal visual pathways.

3. Optic tract lesions usually cause macular-splitting, incongruous homonymous hemianopia, usually without impaired visual acuity unless the lesion extends to involve the optic chiasm or nerve. Optic tract lesions are associated with a relative afferent pupillary defect in the eye with the temporal field loss (contralateral to the side of the lesion) because within the tract there are more crossed than uncrossed fibers. Chronic optic tract lesions may eventually cause bilateral optic atrophy with a characteristic "band" or "bow-tie" pallor in the contralateral eye and a more generalized pallor in the ipsilateral optic nerve, with loss of nerve fiber layer in the superior and inferior arcuate regions corresponding to the bulk of temporal fibers subserving the nasal visual fields (hemianopic optic atrophy). Etiologies for tract lesions include space-occupying lesions, especially tumors, aneurysms, arteriovenous malformations, demyelinating disease, and trauma.

4. Lateral geniculate body lesions may also cause a complete macular-splitting homonymous hemianopia. Partial lesions result in an incongruous homonymous field defect. Hemianopic optic atrophy may develop and no relative afferent pupillary defect is evident.

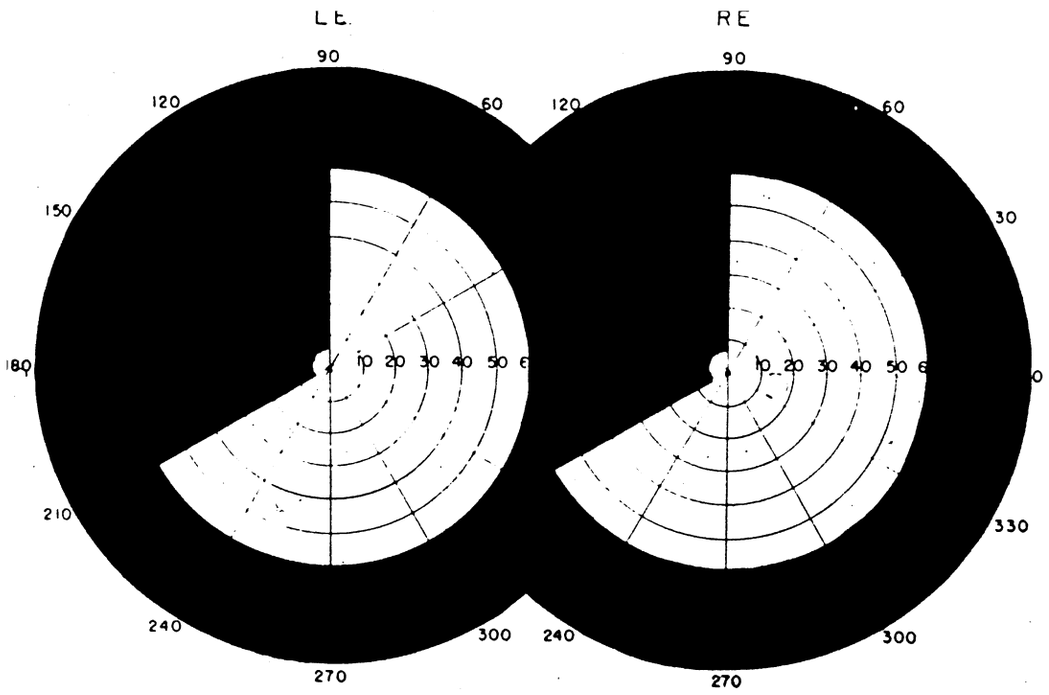

FIGURE 64–1 Visual field testing revealed a dense, congruous left homonymous hemianopia indicating a retrochiasmal lesion of the visual pathways.

Although lesions of the lateral geniculate body often cause incongruous field defects, two somewhat specific patterns of congruous homonymous field defects with abruptly sloping borders, associated with sectorial optic atrophy, have been attributed to focal lesions of the lateral geniculate body caused by infarction in the territory of specific arteries. Occlusion of the anterior choroidal artery may cause a homonymous defect in the upper and lower quadrants with sparing of a horizontal sector (quadruple sectoranopia). Interruption of the posterior lateral choroidal artery, which perfuses the central portion of the lateral geniculate, causes a horizontal homonymous sector defect (wedge shaped). Etiologies for lateral geniculate damage include infarction, arteriovenous malformation, trauma, tumor, inflammatory disorders, demyelinating disease, and toxic exposure (eg, methanol).

5. Lesions of the proximal portion of the optic radiations may result in a complete homonymous hemianopia with macular splitting. Superior homonymous quadrantic defects ("pie-in-the-sky" field defects) may result from a lesion in the temporal (Meyer's) loop of the optic radiations or in the inferior bank of the calcarine fissure. Although visual field defects may occur in isolation with temporal lobe lesions, other signs of neurologic impairment are often evident. Involvement of the optic radiations in the depth of the parietal lobe gives rise to a congruous homonymous hemianopia, denser inferiorly ("pie on the floor"). Such defects are usually more congruous than those produced by lesions of the temporal lobe and since the entire optic radiation passes through the parietal lobe, large lesions may produce complete homonymous hemianopia with macular splitting. Patients may often be unaware of their visual field defects. Visual field defects may occur in relative isolation, but often parietal lobe lesions betray themselves by other signs of neurologic dysfunction.

6. Homonymous quadrantic visual field defects may occur with unilateral occipital lesions. Superior quadrantic defects may be seen with inferior calcarine lesions and inferior quadrantic defects may occur with superior calcarine lesions. Medial occipital lesions cause highly congruous homonymous field defects. When both the upper and the lower calcarine cortices are affected, a complete homonymous hemianopia, usually with macular sparing, develops. Sparing of the central 5 degrees of vision (macular sparing) is common with occipital lesions, probably due to a large macular representation in the occipital pole. The central 10 to 15 degrees of vision fill a majority of the total surface area of the occipital cortex (as much as 50 to 60%). Patients with purely occipital lesions may be unaware of their deficit. The most common cause of unilateral occipital disease is infarction in the distribution of the posterior cerebral artery. Other etiologies include venous infarction, hemorrhage, arteriovenous malformations, tumors, abscess, and trauma.

TEST INTERPRETATION

The congruous nature of the visual field abnormality, the absence of a relative afferent pupillary defect, and the absence of other neurologic

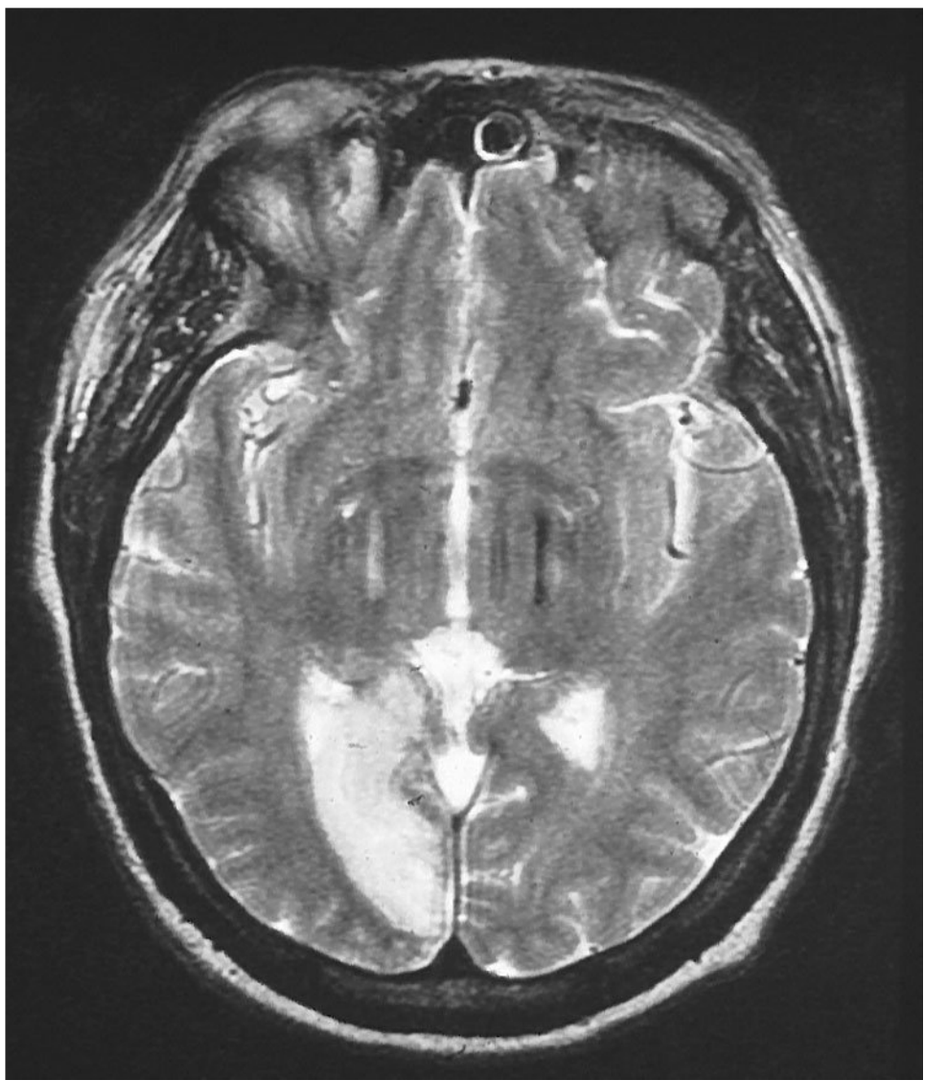

FIGURE 64–2 Magnetic resonance imaging study showed a right occipital infarct.

findings suggest an optic radiation or occipital localization for the patient's visual field impairment. In all patients with a retrochiasmal visual field defect, neuroimaging is warranted. In the acute setting CT scanning is appropriate, but in most other settings, MRI is indicated.

DIAGNOSIS

Right occipital lobe infarction causing a dense, congruous left homonymous hemianopia (Fig. 64–2).

MEDICAL AND SURGICAL MANAGEMENT

Management depends upon the underlying cause of the retrochiasmal visual field impairment. In this case, there is little to offer except control of stroke risk factors and probably aspirin for stroke prophylaxis.

REHABILITATION AND FOLLOW-UP

Patients should have repeat visual fields and ophthalmologic examination approximately 6 months after the onset of the defect to see if there is any improvement.

Reading problems are common in patients with homonymous field defects. Patients with right hemianopias cannot see which letters or words follow those they have already read and patients with left hemianopias often lose their place when reading, often beginning again on an unrelated line. Use of a ruler to guide the patient's vision is often useful and some patients with hemianopias can improve their reading by turning the material 90 degrees and reading vertically in their intact hemifields. Hemianopic patients may also be trained to perform large saccades into the blind field and to search their entire field in various patterns resulting in some visual improvement.

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Case 65

TRANSIENT MONOCULAR VISUAL LOSS

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 65-year-old woman noted three episodes of transient visual loss (TVL) in her right eye over the last 3 weeks. She noted no precipitants for the episodes but the vision would "gray-out" in the right eye for a period of 5 or 6 minutes. She denied any associated headaches, jaw claudication, persistent visual loss, or any transient neurologic dysfunction. She had a past medical history of hypertension and increased cholesterol, both being controlled by medications.

Examination revealed visual acuity 20/25 on the right and 20/20 on the left. She identified nine of ten Hardy-Rand-Rittler pseudoisochromatic plates bilaterally. Pupils were 4 mm bilaterally and both reacted well to light and near. There was no relative afferent pupillary defect. Visual fields were normal. Motility exam was normal. Slit-lamp exam revealed mild bilateral nuclear sclerotic cataracts. Fundus exam revealed an intravascular embolic debris in the right eye (Fig. 65–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The most important questions that need to be addressed in the assessment of the patient with TVL include:

a. Is the visual loss monocular or binocular? Monocular TVL implies disease of the eye, retina, optic nerve, orbit, circulation to the eye (heart, aorta, carotid artery, ophthalmic artery, central retinal artery, etc.), or migraine. Binocular TVL implies bilateral eye disease, disease affecting the circulation to both eyes (eg, bilateral carotid stenosis), increased intracranial pressure with papilledema, or, most often, disease of the vertebrobasilar circulation (especially vertebrobasilar transient ischemic attacks [TIAs]) or migraine.

b. What is the temporal profile of the transient loss of vision? For example, TVL in one eye lasting seconds is characteristic of transient obscurations of vision due to optic nerve ischemia or papilledema, while monocular TVL lasting 2 to 30 minutes is characteristic of TVL associated with ischemia of the retina.

c. What are the precipitants of the visual loss? For example, patients with an intraorbital mass may develop TVL only in certain eye positions due to the mass compressing the ipsilateral optic nerve or optic nerve circulation (gaze-evoked amaurosis). Monocular or binocular TVL due to carotid disease may occur following exposure to bright light.

d. Are any optic nerve or retinal vessel abnormalities evident on fundus examination? For example, fundus exam may well reveal papilledema in a patient with transient obscurations of vision, retinal emboli in a patient with carotid or cardiac disease, and disc anomalies in a patient with monocular TVL.

2. Episodes of TVL lasting less than 60 seconds may occur in patients with papilledema. These transient obscurations of vision may occur in one or both eyes (individually or simultaneously) and typically last only a few seconds. Rarely, they may last for hours. The episodes may be precipitated by changes in position and are

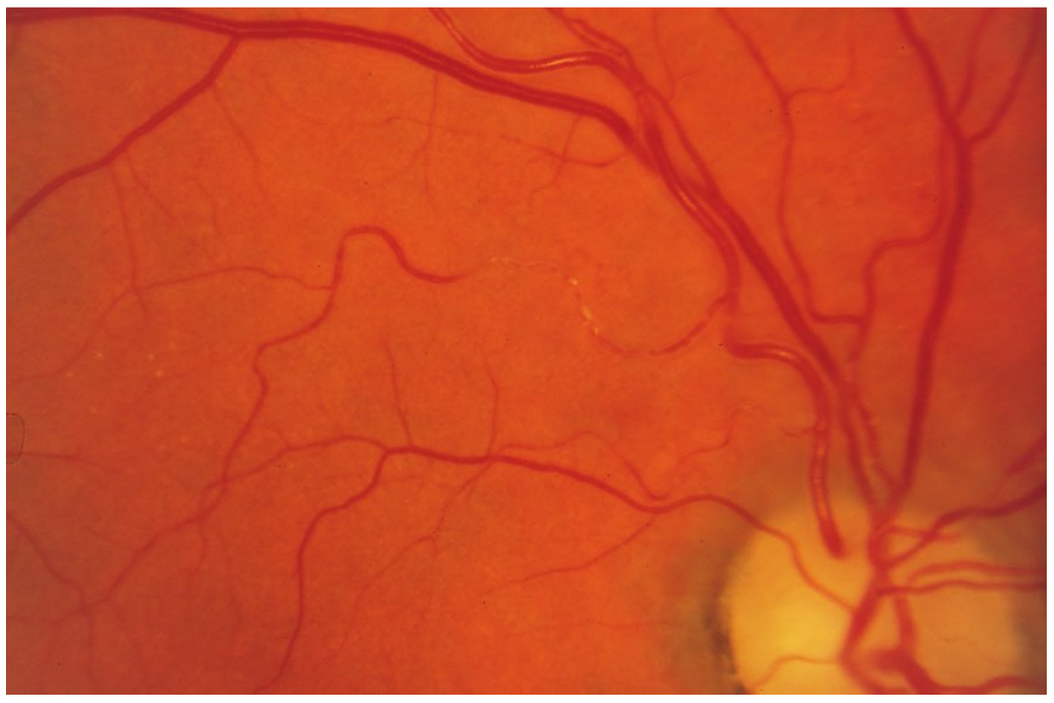

FIGURE 65–1 Fundus photograph of right eye showing retinal emboli.

thought to be related to the effects of increased intracranial pressure on the flow of blood to the eye, perhaps where the central retinal artery penetrates the optic nerve sheath to enter the substance of the nerve. Similar monocular episodes of TVL lasting seconds may occur in patients with optic nerve sheath meningiomas and are probably unrelated to increased intracranial pressure. Transient obscurations of vision may also occur in an eye with congenital abnormalities of the optic disc, such as peripapillary staphyloma (see below) or optic disc drusen. Finally, carotid atherosclerotic disease may rarely cause very brief episodes of TVL, but more often attacks of TVL with carotid disease last 2 to 15 minutes.

3. Monocular TVL lasting 5 to 60 minutes (usually 2 to 30 minutes) is strongly suggestive of thromboembolic disease. These episodes are most often due to emboli, involving the retinal arterial system, which may arise from aorta or carotid artery atherosclerotic disease or a cardiogenic source. Patients often describe a veil or shade descending or ascending over a portion or the whole of their visual field. Other patients complain of patchy visual loss ("Swiss cheese" pattern) or peripheral constriction with central visual sparing. Patients with TVL from thromboembolic disease may demonstrate emboli lodged within the retinal vessels. In general, emboli may be composed of clotted blood, fibrin, platelets, atheromatous tissue, white cells, calcium, infectious organisms (septic emboli), air, fat, tumor cells, amniotic fluid, or foreign materials (eg, talc, artificial valve material, catheters, silicone, cornstarch, mercury, corticosteroids). The most common types of emboli seen in patients with atherosclerotic disease of the aorta/carotid arteries or cardiac disease include the following:

a. *Cholesterol emboli* (Hollenhorst plaques) are bright, glistening, yellow or copper-colored fragments, most often seen in peripheral arterioles in the temporal fundus. These emboli most often arise from atheromatous plaques in the aorta or carotid bifurcation.

b. *Platelet-fibrin emboli* are dull, white, gray, often elongated, and subject to fragmentation and distal movement. These emboli most often lodge at bifurcations of retinal vessels and arise from the walls of atherosclerotic arteries or from the heart, especially from heart valves. They may also be seen in patients with coagulopathies.

c. *Calcific emboli* tend to be large, ovoid or rectangular, and chalky-white. These emboli often occur over or adjacent to the optic disc and usually arise from cardiac (aortic or mitral) valves, less often from the aorta or carotid artery. Unlike cholesterol emboli, which often disappear in a few days, calcific emboli may remain permanently visible.

4. TVL may also occur from ocular hypoperfusion rather than embolization. In some patients, monocular TVL may occur when the patient is exposed to bright light. These patients usually have severe ipsilateral carotid occlusive disease. Venous stasis retinopathy (hypotensive retinopathy), associated with severe carotid or ophthalmic artery occlusive disease, may also be associated with TVL. This syndrome is characterized by visual loss and ischemic retinal infarction often accompanied by signs of ciliary artery obstruction, pallor of the disc, and hypotony.

5. Giant cell arteritis may produce attacks of TVL lasting minutes to hours indistinguishable from those produced by atheromatous disease. TVL probably results from intermittent inflammatory occlusion of the ophthalmic, posterior ciliary, or central retinal arteries. TVL may also occur in association with increased antiphospholipid antibodies, hyperviscosity and hypercoagulable states, polycythemia vera, systemic lupus erythematosus, and arteriovenous malformations that divert blood flow from or reduce blood flow in the ophthalmic artery (ophthalmic steal syndrome).
6. Vasospasm, especially associated with migraine, may also produce TVL without any of the visual phenomena typically seen during a migraine attack. Vasospasm of the retinal vessels has been documented by ophthalmoscopy during some attacks of monocular TVL.
7. TVL lasting 15 to 20 minutes (occasionally up to 7 hours) may occur during episodes of spontaneous anterior chamber hemorrhage (hyphema). In these patients TVL may be associated with erythropsia (seeing red) and color desaturation. Such hemorrhages are most likely to occur in patients who have undergone cataract extraction and are particularly apt to occur after placement of an iris fixation lens implant. Intermittent angle-closure glaucoma may also cause brief episodes of monocular TVL that are usually, but not always, associated with ipsilateral eye pain and occasionally simultaneous dilation of the pupil. Finally, TVL may also be associated with the congenital anomalies peripapillary staphyloma and morning glory syndrome. Episodes of TVL with these anomalies may last 15 to 20 seconds (obscurations of vision) or up to 20 minutes, the latter mimicking TVL with thromboembolic disease. The episodes of TVL in patients with peripapillary staphyloma may be associated with intermittent dilation of the retinal veins and may be orthostatic.
8. Episodes of monocular TVL lasting hours are rare. However, such spells may occur with thromboembolic disease, as a postprandial phenomenon associated with critical carotid stenosis, and with migraine.
9. In the patient described, the episodes of monocular TVL lasted minutes and on examination there was evidence of plaque in the retinal arterioles. Thus thromboembolic disease is the most likely etiology of the episodes.

TEST INTERPRETATION

All patients with monocular TVL lasting minutes should have a complete ophthalmoscopic examination to investigate for such conditions as intermittent angle-closure glaucoma, morning glory syndrome, and peripapillary staphyloma. Spontaneous anterior chamber hemorrhage (hyphema) should also be considered, especially in patients with associated erythropsia and in patients who have undergone cataract extraction.

Patients with monocular TVL lasting minutes associated with visible retinal emboli need to be evaluated for carotid and aortic vascular disease and cardiac valvular disease. Stroke risk factors (smoking, hypertension, diabetes mellitus, hyperlipidemia, etc.) should be evaluated and controlled. Studies to evaluate the carotid arteries might include carotid Doppler and ultrasound, MR angiography, and conventional angiography. Cardiac investigations might include transthoracic and transesophageal echocardiography and cardiac MR imaging.

In patients older than 55 years with a history of monocular TVL lasting minutes without visible retinal emboli, giant cell arteritis should be considered and an erythrocyte sedimentation rate should be performed. If this is significantly elevated or the patient has other symptoms of giant cell arteritis, such as recent headaches, jaw claudication, or polymyalgia rheumatic-like symptoms, the patient should undergo temporal artery biopsy. If the sedimentation rate is negative and there are no clinical symptoms suggestive of giant cell arteritis, then evaluation for carotid or cardiac thromboembolic disease is warranted.

Patients with evidence of monocular TVL due to ocular hypoperfusion (venous stasis retinopathy and the ocular ischemic syndrome) may have decreased retinal artery pressure documented by ophthalmodynamometry. The patient should be investigated for carotid stenosis.

If no thromboembolic source for the episodes of TVL is documented, then further studies could be performed. These include MR imaging of the brain with MR angiography to investigate for possible vascular malformation, and laboratory studies, including sedimentation rate, complete blood count, antiphospholipid antibodies, antinuclear antibodies, collagen vascular disease profile, and studies to investigate the presence of dysproteinemia. Young patients (less than 45 years old) with monocular TVL are unlikely to have significant carotid disease. A cardiac embolic source as well as a vasculitis or coagulopathy must be sought.

DIAGNOSIS

Retinal emboli secondary to right carotid stenosis causing transient monocular visual loss.

MEDICAL MANAGEMENT

In the patient with less than 30% carotid stenosis, a cardiac or aortic embolic source should be sought and, if none is found, the treatment is aspirin or other anti-platelet therapy plus control of stroke risk factors.

SURGICAL MANAGEMENT

In patients with monocular TVL and ipsilateral carotid stenosis of 70 to 99%, carotid endarterectomy may be indicated if the patient is a suitable surgical candidate and if the perioperative morbidity and mortality rate of the surgeon is in the 2% or less range. Carotid endarterectomy in this group reduces the 2-year ipsilateral stroke rate from 26 to 9% and decreases the major or fatal ipsilateral stroke rate from 13.1 to 2.5%. In a patient with 30 to 69% stenosis, it remains to be seen whether endarterectomy would be beneficial. In patients with emboli from a cardiac valvular source, especially patients with cardiac dysrhythmias such as atrial fibrillation, anticoagulation may be warranted if the patient is an appropriate medical candidate.

REHABILITATION AND FOLLOW-UP

Medical supervision of stroke risk factors is warranted. Periodic reevaluation of the carotid artery for re-stenosis is warranted by noninvasive studies (eg, carotid Doppler or MR angiography).

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Case 66

THIRD NERVE PALSY—ISCHEMIC

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 70-year-old man had a 4-week history of binocular diplopia. The diplopia developed and worsened over a 5-day period, but it then "stabilized" and in fact had "improved" since his right eye "drooped." In the first 2 weeks he had also noticed severe retro-orbital pain on the right but this pain became minimal. He had a history of bilateral cataract extraction but his vision had otherwise been "stable." He had a past history of hypertension and diabetes. He smoked one pack of cigarettes daily. He denied any facial numbness, recent headache, jaw claudications, or other neurologic deficits.

Examination revealed visual acuity of 20/30 on the right and 20/25 on the left. Pupils were 3 mm bilaterally and both reacted well to light and near. There was no relative afferent pupillary defect. Visual fields were normal. He had complete ptosis of his right lid (Fig. 66–1) with markedly impaired levator function. He could not adduct (Fig. 66–2), elevate, or depress (Fig. 66–3) the right eye but he could fully abduct the eye. Attempts at depression of the right eye resulted in mild incyclodeviation of the eye. Motility was normal in the left eye. There was no proptosis, facial sensation was normal, and general neurologic exam was otherwise normal. Slit-lamp exam revealed bilateral intraocular lenses. Fundus exam revealed mild bilateral diabetic background retinopathy without disc pathology.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The severe ptosis and marked impairment of elevation, adduction, and depression in the right eye are compatible with a pupil-sparing, complete motor third nerve palsy (TNP). Full abduction and the incyclodeviation on downward gaze suggest that sixth nerve and fourth nerve function, respectively, are spared.

2. TNPs are divided into nonisolated and isolated TNP. The isolated TNP were defined as TNP without associated neurologic findings (eg, other cranial neuropathies). The types of TNPs are outlined in Table 66–1.

3. Isolated TNP with a normal pupillary sphincter and completely palsied extraocular muscles is almost never due to an intracranial aneurysm. This type of TNP is most commonly caused by ischemia, especially diabetes mellitus. In patients with isolated atraumatic TNP, diabetes mellitus is the most common etiology accounting for 46% of all the cases with pupil sparing documented in 68 to 86% of the cases. The probable explanation for pupillary sparing in diabetic TNP is the lack of damage to the periphery of the nerve where the majority of pupillomotor fibers are thought to pass. This type of TNP involvement may rarely occur with pituitary adenoma or other compressive lesions.

TEST INTERPRETATION

Patients who develop an isolated TNP with completely palsied extraocular muscles but with pupillary sparing do not need angiography. An MRI need not be performed initially, as the yield for detecting a compressive lesion is very low. Neuroimaging should be performed in patients with no vasculopathic risk factors or in patients who do not improve by 12 weeks of follow-up. Patients who are seen within 1 week of onset of this type of TNP should be observed at 24- to

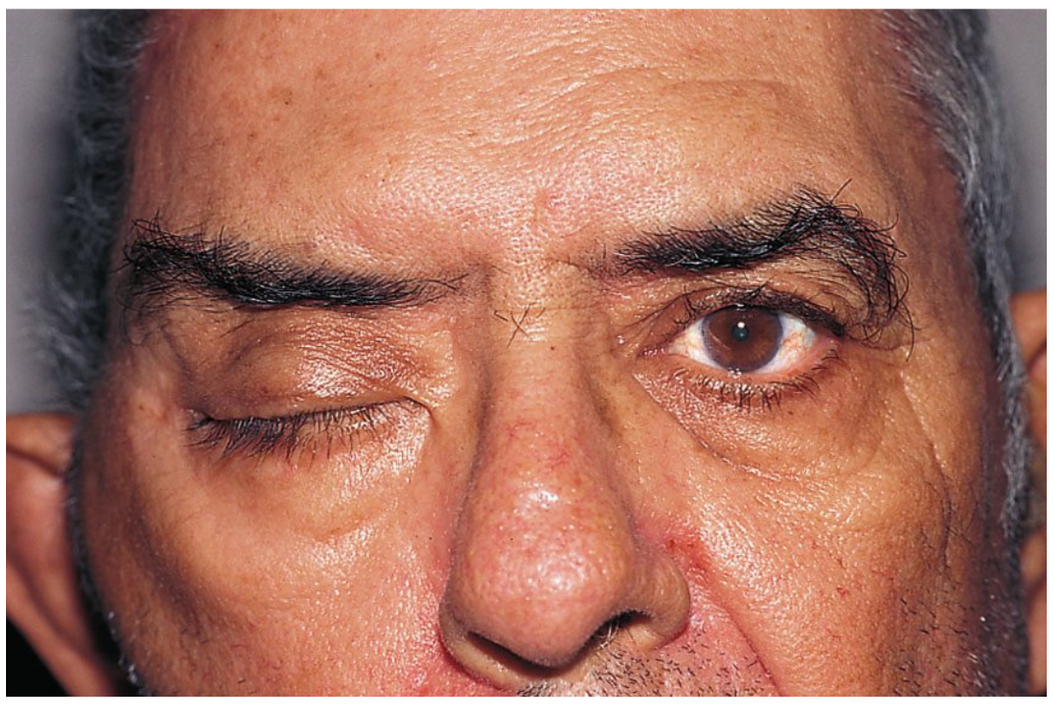

FIGURE 66–1 External photography reveals a complete ptosis of the right upper eyelid with markedly impaired levator function.

48-hour intervals during the first week because some patients with aneurysms may develop delayed pupil involvement. Patients who develop pupil involvement should be reevaluated for the possibility of a compressive lesion, such as an aneurysm.

Patients over the age of 55 years, especially those with other symptoms suggestive of giant cell arteritis (eg, headache, jaw or tongue claudication, polymyalgia rheumatica symptoms), should have a sedimentation rate. Temporal artery biopsy should be considered if the sedimentation rate is elevated or other systemic symptoms are present.

Myasthenia gravis may rarely mimic this type of TNP, so a Tensilon test should be considered, primarily in patients with fluctuating or

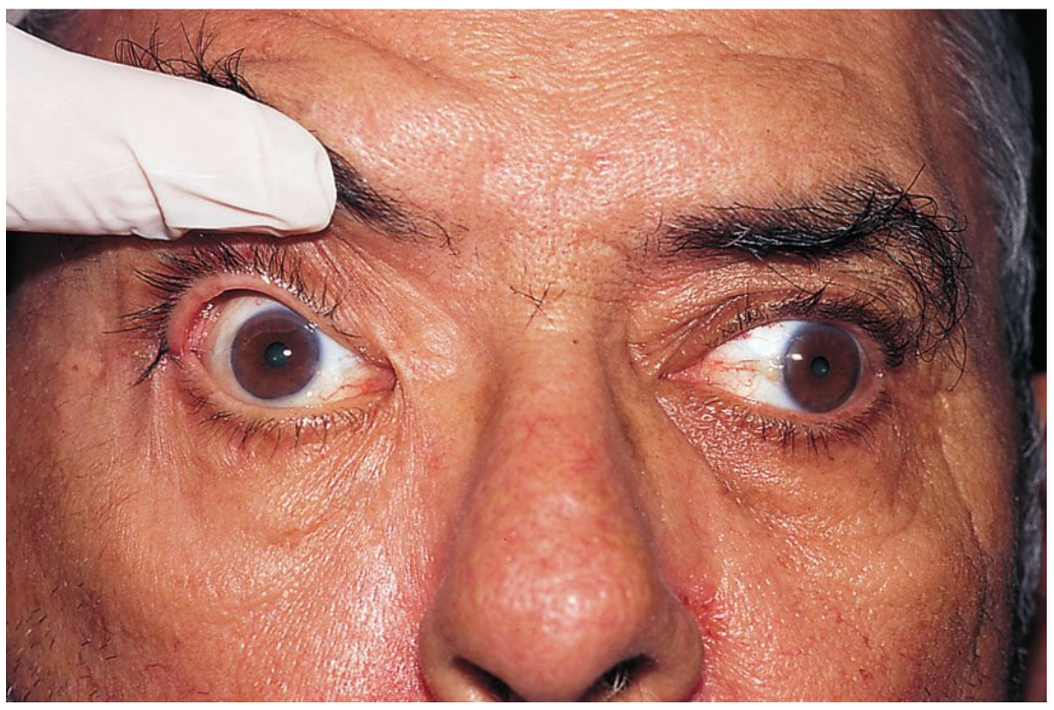

FIGURE 66–2 The patient could not adduct the right eye.

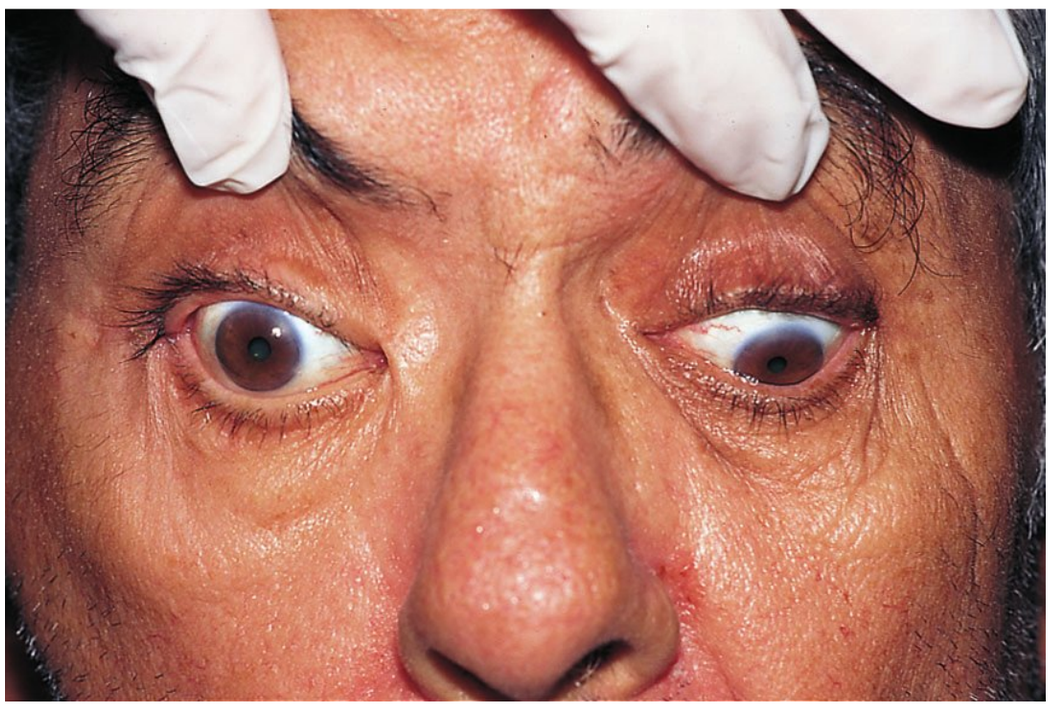

FIGURE 66–3 The patient could not depress the right eye.

TABLE 66–1 **Definitions of the Five Types of Third Nerve Palsy (TNP)**

Type 1:	Nonisolated TNP–TNP is considered nonisolated in the presence of the following features: Other neurologic or neuro-ophthalmologic signs (eg, other cranial nerve palsies, brainstem signs, orbital signs) Evidence to suggest myasthenia gravis such as fatiguability of the motility defect
Type 2:	Traumatic isolated TNP–Isolated unilateral TNPs, which have a clearly established temporal relationship to significant previous head trauma and do not progress, are considered traumatic in origin
Type 3:	Congenital isolated TNP–TNP that a patient is born with or is noted to have within the first 3 months of life
Type 4:	Acquired, nontraumatic isolated TNP **Type 4A:** TNP with a normal pupillary sphincter with completely palsied extraocular muscles **Type 4B:** TNP with normal pupillary sphincter and incomplete palsied extraocular muscles **Type 4C:** TNP with subnormal pupillary sphincter dysfunction and partial or complete extraocular muscle palsies
Type 5:	TNP with signs of aberrant regeneration

(Adapted from Lee AG and Brazis PW. *Clinical Pathways in Neuro-Ophthalmology: An Evidence-Based Approach.* New York, NY: Thieme; 1998, with permission.)

fatiguing ptosis or ophthalmoplegia. If the complete, pupil-spared TNP improves following a period of observation, no neuroimaging is required.

DIAGNOSIS

Ischemic isolated TNP.

MEDICAL MANAGEMENT

Vasculopathic risk factors, especially diabetes mellitus, hypertension, and increased cholesterol, should be sought and controlled.

SURGICAL MANAGEMENT

Strabismus surgery or lid surgery may be helpful in selected patients with unresolved ophthalmoplegia, diplopia, or ptosis.

REHABILITATION AND FOLLOW-UP

The patient should be followed at 1- to 2-month intervals to see if the TNP improves. Complete resolution for ischemic TNP is expected to occur in 3 to 6 months. If no improvement is evident by 3 months after onset, neuroimaging for a compressive lesion is warranted.

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Case 67

THIRD NERVE PALSY—ANEURYSM

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 45-year-old man noted the acute onset of binocular diplopia 8 days prior to evaluation. He noted the acute onset of left-sided frontal-periorbital pain and then noted the onset of diplopia with a left-sided lid droop. He was previously well with no history of significant illnesses.

Examination revealed visual acuity of 20/20 bilaterally. He identified ten of ten Hardy-Rand-Rittler pseudoisochromatic plates bilaterally. Pupils were 3 mm on the right and 5 mm on the left, the left pupil reacted poorly to light, and there was no relative afferent pupillary defect. Visual fields were full to confrontation. The patient had a mild left hypotropia and a moderate exotropia. Duction testing was normal on the right but revealed partial paresis of elevation, adduction, and depression in the left eye. There were 3 mm of ptosis on the left with mildly impaired levator function. Facial sensitivity and strength were normal with normal corneal reflexes bilaterally. Slit-lamp exam and fundus exam were normal. General neurologic examination was otherwise normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The patient has evidence of an isolated, partial third nerve palsy (TNP) on the left with pupillary involvement.
2. Isolated TNP may occur with lesions localized anywhere along the coarse of the third nerve from the fascicle in the mesencephalon to the orbit.
3. Patients with a "relative pupil-sparing" TNP should have magnetic resonance imaging (MRI) and MR angiography (MRA), and possible cerebral angiography, to rule out the possibility of a compressive lesion, especially a cerebral aneurysm.
4. Because 10 to 20% of patients with ischemic TNP have pupillary dysfunction, there will be a certain percentage of normal angiograms in patients with partial TNP. In a series of 26 consecutive patients with diabetes-associated TNP, internal ophthalmoplegia occurred in 10 of 26 patients (38%), and the degree of anisocoria was 1 mm or less in most patients. None of these cases had a fully dilated, nonreactive pupil. It was concluded that anisocoria rather than pupil reactivity to light should be the defining criterion for pupil involvement.
5. Patients with an incomplete motor TNP with no pupillary involvement require an MRI and MRA to rule out a mass lesion. If the MRI is normal, cerebral angiography could be considered to investigate the presence of an aneurysm, dural-cavernous sinus fistula, or high-grade carotid stenosis. MRA may eventually take the place of arteriography; however, at this time, cerebral angiography is the "gold standard" for the diagnosis of cerebral aneurysms. Although MRA may be able to detect up to 95% of cerebral aneurysms that will bleed, it cannot completely exclude aneurysm as the etiology of a pupil-involved TNP.
6. Complete TNP with pupil involvement occurring in isolation is often due to compressive lesions or meningeal infiltration; thus, an MRI and MRA are initially warranted. If these studies are negative, a cerebral angiogram is often necessary to investigate aneurysm or dural-cavernous sinus fistula. If meningeal signs are present, spinal fluid evaluation is warranted. A fully dilated and nonreactive pupil occurs in up to 71% of

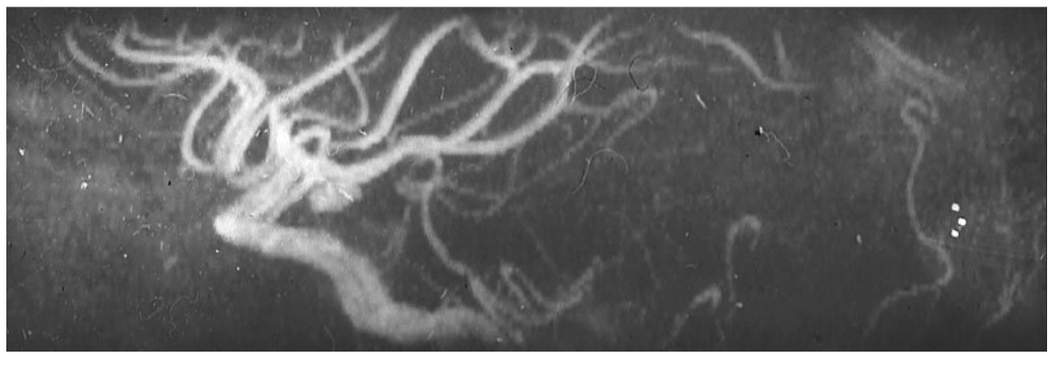

FIGURE 67–1 Cerebral aneurysm of the posterior communicating artery causing a partial third nerve palsy.

patients with aneurysmal compression and TNP. Aneurysms impair the pupil in 96% of TNP and the remaining 4% in which the pupil is spared have only partial TNP.

TEST INTERPRETATION

In this patient, MRI and MRA are warranted, especially to consider a cerebral aneurysm. Cerebral angiography should also be considered.

DIAGNOSIS

Partial TNP due to cerebral aneurysm of the posterior communicating artery (Fig. 67–1).

MEDICAL MANAGEMENT

There is no role for medical management of this problem.

SURGICAL MANAGEMENT

Surgery or endovascular therapy to repair the aneurysm is necessary to prevent aneurysmal rupture, which carries a high morbidity and mortality.

REHABILITATION AND FOLLOW-UP

Patching the eye to relieve the diplopia is often required.

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Case 68

FOURTH NERVE PALSY—CONGENITAL

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 10-year-old boy noted the acute onset of vertical binocular diplopia for 2 weeks. He stated that one image was "below and to the side of the other" and denied any subjective torsion of the images. He denied any clear precipitants for the diplopia and denied any associated headaches, facial numbness, ptosis, or any other complaints. He had no significant past medical history.

Exam revealed visual acuity to be 20/20 bilaterally with normal color vision. Pupils were 5 mm bilaterally and equally reactive to light and near and there was no relative afferent pupillary defect. The patient tended to tilt his head to the left (Fig. 68–1). There was a 4 prism diopter (PD) right hypertropia at distance, 8 PD on left gaze, 1 PD on right gaze, 2 PD on upward gaze, and 7 PD on downward gaze. Head tilt to the right caused an 8 PD right hypertropia and head tilt to the left was associated with a 2 PD right hypertropia. Double Maddox rod testing revealed 4 degrees of right excyclodeviation. Vertical fusional amplitudes were 10 PD. Ductions, versions, saccades, and pursuit eye movements were intact. There were no ptosis, facial paresis, or abnormalities of facial sensation. Slit-lamp exam and fundus exam were normal but indirect ophthalmoscopy revealed some degree of excyclotropia in the right eye.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The right hypertropia, worse on gaze to the left and right head tilt, is compatible with a right superior oblique paresis, most often due to a fourth cranial nerve palsy. Other entities to be considered include myasthenia gravis and thyroid eye disease.

2. Fourth nerve palsies (FNPs) may cause the following:

a. Noncomitant hypertropia demonstrated with the three-step maneuver. The hypertropia increases on head tilt toward paralyzed side (positive Bielschowsky's test). Hypotropia may occur in the normal eye if the affected eye is fixating; if the unaffected eye is fixating, hypertropia occurs in the involved eye. This hypertropia is usually most prominent in the field of gaze of the involved superior oblique muscle, especially in cases of acute or recent onset. The hypertropia may also be most prominent in the field of gaze of the ipsilateral overacting inferior oblique muscle in subacute or chronic cases or may be evident in the entire paretic field (spread of comitance).

b. Underaction of the ipsilateral superior oblique muscle, overaction of the ipsilateral inferior oblique muscle, or overaction of the contralateral superior oblique muscle. Pseudo-overaction of the superior oblique in the uninvolved eye occurs with spread of comitance and secondary contracture of the superior rectus muscle in the involved eye with the hypertropia involving the entire lower field of gaze. In a patient with a superior oblique muscle paralysis who habitually fixates with the paretic eye and in whom overaction of the ipsilateral inferior oblique muscle has developed, less than the normal amount of innervation will be required when the patient looks up and to the contralateral side. Since the innervation flowing to the opposite superior rectus is "determined" by the overacting ipsilateral inferior oblique (Hering's law), the opposite superior rectus muscle will

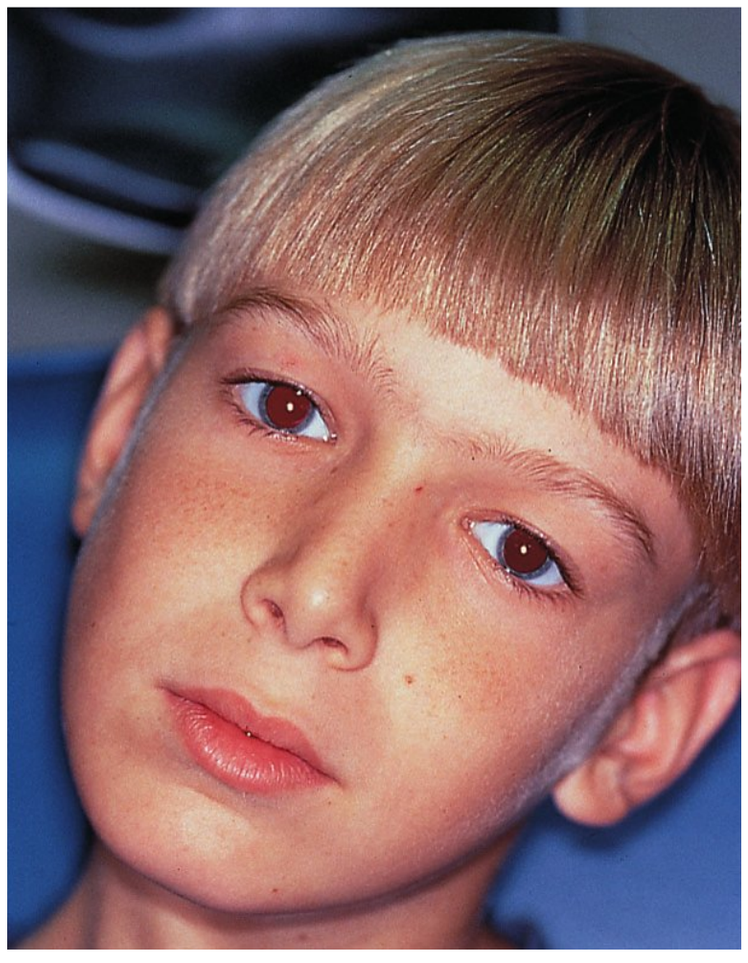

FIGURE 68–1 External photograph demonstrates anomalous tilt of the patient's head to the left.

seem paretic (inhibitional palsy of the contralateral antagonist). In these cases, the head tilt test will correctly determine which of the two eyes is paretic.

c. Excyclotropia, which is usually evident on fundus exam and double Maddox rod testing. This cyclotropia is usually symptomatic only in acquired (vs congenital) cases.

d. A head tilt. This is present in approximately 70% of patients with FNP and is usually away from the involved side but may be paradoxical (toward the involved side) in about 3% of patients.

3. It is important to differentiate patients with decompensation of a congenital FNP from patients with an acquired FNP. In patients with congenital FNP:

a. Old photos may show a long-standing head tilt.

b. Patients usually are noted to have cyclotropia on examination but do not complain of cyclotropia (subjective image tilting) as do some patients with acquired FNP.

c. Large vertical fusional amplitudes (greater than 6 to 8 prism diopters) in primary gaze are characteristic of congenital cases.

d. Facial asymmetry (hypoplasia on side of head turn) suggests a congenital FNP.

4. Bilateral FNPs are suggested by:

a. A right hypertropia in left gaze and left hypertropia in right gaze.

b. A positive Bielschowsky test on tilt to either shoulder ("double Bielschowsky test").

c. Large excyclotropia (greater than 10 degrees).

d. V-pattern esotropia (15 prism diopters or more difference in esotropia between upward and downward gaze). The "V" pattern is caused by a decrease of the abducting effect of the superior oblique(s) in depression and overaction of the inferior oblique muscle(s).

e. Underaction of both superior oblique muscles and/or overaction of both inferior oblique muscles.

f. In general, bilateral FNPs tend to have a smaller hypertropia in primary position than do unilateral FNPs.

TEST INTERPRETATION

The large fusional amplitudes and lack of subjective image tilting are compatible with congenital right FNP. The recent onset of symptoms is due to decompensation of a chronic phoria. Old photographs reveal a head tilt present for years.

DIAGNOSIS

Decompensation of old right FNP.

MEDICAL MANAGEMENT

Observation or the use of prisms may be all that is required.

SURGICAL MANAGEMENT

Many patients may benefit from strabismus surgery.

REHABILITATION AND FOLLOW-UP

No rehabilitation and follow-up are required if the problem is resolved.

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Case 69

SIXTH NERVE PALSY

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 56-year-old man complained of a 3-month history of binocular diplopia. The diplopia was primarily present at distance but was absent at near and was worse on gaze to the left. He had also noted some numbness and tingling in the left forehead and mild left frontotemporal headaches. He denied any recent head trauma, visual loss, or history of previous neurologic or ophthalmologic symptoms. He was a diabetic using oral agents to control his blood sugar.

Exam revealed visual acuity to be 20/20 bilaterally. He identified ten of ten Hardy-Rand-Rittler pseudoisochromatic plates bilaterally. Pupils were 4 mm bilaterally and equally reactive to light and near and there was no relative afferent pupillary defect. Visual fields were full to confrontation. He had a 4 prism diopter (PD) esotropia at distance with no esotropia at near. The esotropia was nil on gaze to the right, 8 PD on gaze to the left, and 4 PD on gaze up and down. Duction testing revealed paresis of abduction in the left eye. There was no ptosis. No facial weakness was noted but sensory testing revealed decreased sensation to soft touch over the left forehead, and the left corneal reflex was slightly depressed. Slit-lamp exam and fundus exam were normal. No papilledema was evident. The rest of the general neurologic examination was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Causes of acquired esotropia include sixth nerve palsy, orbital myositis, myasthenia gravis, thyroid eye disease, trauma, ocular neuromyotonia, cyclic esotropia, divergence insufficiency or paralysis, spasm of the near reflex, pseudo-sixth nerve palsies due to thalamic or midbrain lesions, acquired motor fusion deficiency, and the hemifield slide phenomena (seen with chiasmal lesions). In this patient, there is evidence of paresis of the left lateral rectus muscle and a left sixth nerve palsy is likely. This paresis has not occurred in isolation, as there is also evidence of left facial numbness and sensory changes in the distribution of the ophthalmic branch (V1) of the trigeminal nerve, as well as left-sided headache. Thus, purely motor syndromes, such as myasthenia gravis, are excluded. The sixth nerve is near the ophthalmic branch of the trigeminal nerve in Meckel's cave and in the cavernous sinus. A lesion in these locations must strongly be considered.

2. Vasculopathic sixth nerve palsies are common and can be observed without neuroimaging for 4 to 12 weeks. However, these palsies occur in isolation and although they are often associated with eye or retro-orbital pain, they are not associated with facial sensory loss. Even though the patient is a diabetic, ischemic sixth nerve palsy is not a likely consideration.

3. Compressive lesions in the cavernous sinus or Meckel's cave may cause a sixth nerve palsy and include tumors (eg, meningiomas, trigeminal nerve tumors, neuromas, metastases, skull base tumors, leukemia, nasopharyngeal carcinoma), cavernous sinus fistulas or thrombosis, aneurysms, and inflammatory or infectious diseases (eg, herpes zoster, mucormycosis).

TEST INTERPRETATION

Nonisolated sixth nerve palsies should undergo neuroimaging, preferably by MRI, and further evaluation, including lumbar puncture in some cases. If a patient with a sixth nerve palsy has papilledema, neuroimaging is mandatory, as a unilateral or bilateral sixth nerve palsy may be a

false localizing sign of increased intracranial pressure; if MRI is normal, spinal tap is warranted to investigate meningeal infectious, inflammatory, and neoplastic processes and pseudotumor cererbi. Isolated sixth nerve palsies in a vasculopathic patient may be observed without neuroimaging but if no improvement occurs in 3 months, neuroimaging is mandatory. Nonvasculopathic isolated sixth nerve palsies should undergo neuroimaging (MRI) to rule out a compressive lesion. Younger patients and those without vascular risk factors should undergo more extensive evaluation including complete blood count, fasting blood glucose, blood pressure evaluation, and lumbar puncture. In patients with an isolated sixth nerve palsy with variable esotropia, fatigue of eye movements, or ptosis, myasthenia gravis should be considered. Any patient with progressive or unresolved sixth nerve palsy should undergo neuroimaging.

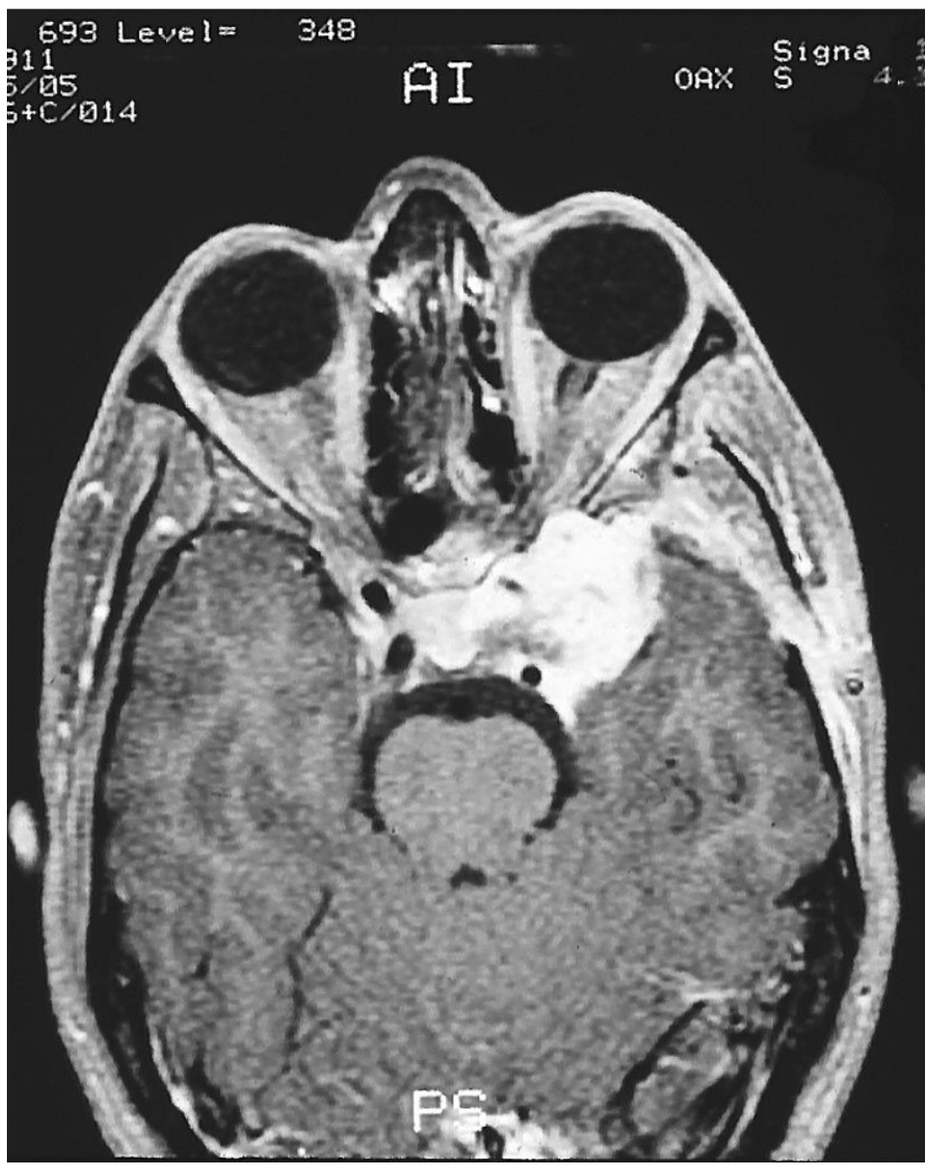

FIGURE 69–1 Magnetic resonance scan shows left-sided meningioma of the cavernous sinus causing sixth nerve palsy.

DIAGNOSIS

Left sixth nerve palsy and damage to the left ophthalmic branch of the trigeminal nerve secondary to meningioma of the cavernous sinus (Fig. 69–1).

MEDICAL MANAGEMENT

Treatment is aimed at the responsible underlying lesion and may include surgery, radiation therapy, or even simple observation. The diplopia is controlled by patching, prisms, or, if chronic and stable and depending upon the etiology, surgery. Early botulinum injection into the ipsilateral medial rectus may improve diplopia and increase the likelihood of subsequent improvement.

SURGICAL MANAGEMENT

Strabismus surgery may be necessary for residual ophthalmoplegia or diplopia.

REHABILITATION AND FOLLOW-UP

Patients must be observed for recurrence of further neurologic and ophthalmologic deficits depending upon the etiology of the sixth nerve palsy. Symptomatic diplopia treatment is warranted.

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Case 70

INTERNUCLEAR OPHTHALMOPLEGIA

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 27-year-old woman with a history of multiple sclerosis complained of "difficulty focusing" her eyes. Her previous multiple sclerosis course included a history of optic neuritis in the right eye. She did have mild gait instability, bladder disturbance, and leg numbness. Her eye difficulty started several months prior to ophthalmologic evaluation. She was taking no medications.

Ophthalmologic examination revealed visual acuity to be 20/20 bilaterally. She identified seven of ten Hardy-Rand-Rittler pseudoisochromatic plates on the right and ten of ten on the left. Visual fields showed a relative central scotoma on the right. Pupils were 5 mm bilaterally and equally reactive to light and near, but there was a mild right afferent pupillary defect. The patient had a 2 prism diopter left hypertropia that was comitant in left, right, up, and down gaze. There was mild paresis of adduction in the left eye but otherwise ductions were full. On gaze to the right, the adducting saccade in the left eye was quite slow compared to the abducting saccade in the right eye. Saccades to the left and vertically were normal. On attempting to hold her gaze to the right, monocular nystagmus was noted in the right eye in the direction of abduction. Convergence was normal. There was no ptosis. Facial sensation and movement were normal. Slit-lamp examination was normal. Fundus exam revealed mild temporal pallor in the right eye but was otherwise normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The impaired color vision, relative afferent pupillary defect, and mild optic nerve pallor on the right are the likely the residual of a previous episode of optic neuritis in this patient with known multiple sclerosis.
2. The adduction weakness in the left eye, slow saccades in adduction in the left eye, and dissociated monocular nystagmus in abduction in the right eye with preserved convergence all indicate the presence of a left internuclear ophthalmoplegia (INO). The comitant hypertropia is likely a skew deviation due to the medial longitudinal fasciculus lesion.
3. The abducens nucleus has two types of intermingled neurons: motor neurons and internuclear neurons. The axons of the internuclear neurons cross to the contralateral side in the lower pons and ascend in the medial longitudinal fasciculus (MLF) to synapse in the portion of the oculomotor nucleus that innervates the medial rectus muscle. Lesions of the MLF result in INO.
4. Clinically, INO is characterized by adduction weakness on the side of the MLF lesion and monocular nystagmus of the opposite abducting eye. Convergence is usually preserved unless the responsible lesion is high in the midbrain. Often patients with INO have no visual symptoms but some complain of diplopia (due to skew deviation with the higher eye on the side of the lesion) or oscillopsia.
5. INO is most evident during saccadic eye movements and the "adduction lag" is best brought out during optokinetic testing using a rotating tape or drum. For example, with a right INO when the drum is rotated to the right the amplitude and velocity of the adducting quick phase of the right eye is smaller and slower than that of the abducting saccades in the left eye. The pathogenesis of the

nystagmus in the abducting eye is unclear but is likely a normal adaptive process that helps overcome the adducting weakness of the fellow eye. Unilateral INO may rarely be associated with exotropia (wall-eyed monocular INO, also called WEMINO syndrome).

6. Bilateral INO results in bilateral adduction paresis or lag with the eyes generally aligned in primary gaze. Occasionally exotropia will occur, with both eyes deviated laterally (wall eyed-bilateral internuclear ophthalmoplegia, or WEBINO syndrome). These patients will often also demonstrate vertical gaze-evoked nystagmus, impaired vestibular and pursuit vertical eye movements, and impaired vertical gaze holding.

7. INO is due to pathologic processes affecting the medial pontine or midbrain parenchyma. Often there are associated brainstem symptoms and signs although occasionally unilateral or bilateral INO may occur in isolation. The nature of the responsible pathologic process is suggested by the temporal mode of onset of the INO, the general clinical circumstances, and associated signs on neurologic and neuro-ophthalmologic examination. INO is most often due to multiple sclerosis or brainstem infarction. Other etiologies include brainstem infections and masses, degenerative extrapyramidal diseases, drug intoxications, and certain nutritional and metabolic disorders (eg, Wernicke's encephalopathy and pernicious anemia). The pattern of extraocular muscle weakness with myasthenia gravis can mimic INO (pseudo-INO); myasthenic pseudo-INO is not uncommon.

TEST INTERPRETATION

In general, the investigation of a patient with INO depends upon the clinical circumstances. For example, in the patient presented, multiple sclerosis is evident. INO in isolation or with associated unexplained brainstem signs and symptoms requires neuroimaging. If there is variability of the adduction deficit, associated fluctuating ptosis, or other variable ocular motor signs suggestive of myasthenia gravis, a myasthenic pseudo-INO should be considered.

Magnetic resonance imaging (MRI) is superior to computed tomography (CT) in evaluating patients with INO. MRI may give useful diagnostic data by also giving information about supratentorial processes likely to be involved in the etiology of the INO, such as multiple sclerosis and multiple cerebral infarcts. If an infarct is detected as the cause of INO in a patient greater than 50 years of age, giant cell arteritis should be considered as an etiology, especially if other stroke risk factors are not evident.

If MRI in nontraumatic cases is normal, then rarer etiologies for the INO should be considered. If the INO is bilateral, drug intoxication should be suspected. As pernicious anemia has rarely been reported to cause INO, a B_{12} level is also indicated but of low yield. Syphilis may rarely cause INO so serology for syphilis is also suggested. If MRI reveals meningeal enhancement or if meningeal signs or symptoms are present, spinal fluid examination is warranted to investigate for infectious or carcinomatous meningitis.

DIAGNOSIS

Optic neuropathy on the right and INO on the left due to multiple sclerosis.

MEDICAL MANAGEMENT

Treatment is directed at the underlying etiology of the INO. If associated skew deviation or exotropia is symptomatic, prisms may be required to relieve diplopia.

SURGICAL MANAGEMENT

Usually no surgical treatment is required.

REHABILITATION AND FOLLOW-UP

Follow-up for resolution of the INO is important.

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Case 71

DIPLOPIA—OCULAR MYASTHENIA GRAVIS

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 57-year-old woman complained of intermittent diplopia over the last 6 months. The diplopia was often not present on awakening in the morning but tended to occur and worsen "as the day goes on." She especially had difficulty driving, often seeing "two lines instead of one" in the middle of the road. Her spouse also had noted that at times her left or right eyelid would droop. She denied significant past medical problems except for a history of pernicious anemia for which she takes monthly B_{12} shots. She denied any headache, facial numbness or pain, dysphagia, dysarthria, breathing difficulty, or extremity paresis or sensory symptoms.

Examination of the afferent visual system was normal. Pupils were 5 mm and equally reactive to light and near. No relative afferent pupillary defect was evident. She had an esotropia of 10 prism diopters (PD) in primary position that increased to 15 PD on left gaze, 18 PD on right gaze, and 12 PD on up and down gaze. When she attempted to hold her gaze to the left or the right the separation of images worsened subjectively and her esotropia increased. Although she had no obvious vertical misalignment in primary gaze, on holding her gaze upward she eventually developed a left hypertropia. Duction testing suggested paresis of both lateral rectus muscles. She had bilateral ptosis. The ptosis worsened in each eye when the opposite lid was held upward. Levator function was mildly weak bilaterally. Facial sensation was normal but she had mild paresis of eye closure bilaterally. Slit-lamp and fundus exams were normal. General neurologic examination was otherwise normal.

A Tensilon test resulted in improvement of the patient's esotropia and ptosis. Acetylcholine receptor antibodies were not present, thyroid-stimulating hormone (TSH) was normal, and computed tomographic (CT) scan of the chest was negative for thymoma.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Although the esotropia was worse on gaze to the left and gaze to the right may suggest bilateral sixth nerve palsies, the patient also has bilateral ptosis. The fatigability of the esotropia on attempted lateral gaze holding, the development of a hypertropia on prolonged upward gaze (fatigue), and the increased ptosis with elevation of the opposite eyelid (enhanced ptosis) are all strongly suggestive of myasthenia gravis (MG).

2. MG is a chronic disorder of neuromuscular transmission characterized clinically by varying degrees of weakness and fatigue of voluntary muscles. MG is caused by an acquired autoimmunity to the motor endplate and is associated with antibodies that block or cause increased degradation of acetylcholine receptors (AChR). There is abnormal weakness in some or all voluntary muscles. The weakness increases with repeated or sustained exertion and increases over the course of the day, but is improved by rest; it also may be worsened by elevation of body temperature and is often improved by cold.

3. The levator palpebrae superioris and extraocular muscles are involved initially in approximately 50 to 70% of cases, and these muscles are eventually affected in about 90% of patients. Ocular myasthenia (OM) is a form of MG confined to the extraocular, levator palpebrae superioris, and/or orbicularis oculi muscles. Approximately 50% of patients initially present with OM, but only

12 to 50% of these remain ocular. Of the 50 to 80% of patients with purely ocular symptoms and signs at onset that go on to develop generalized MG, most, but not all, develop generalized symptoms within 2 to 3 years of onset of the disorder.

4. Ptosis in MG may occur as an isolated sign or in association with extraocular muscle involvement. The ptosis may be unilateral or bilateral and, when bilateral, is usually asymmetric. The ptosis may be absent when the patient awakens, but appears later in the day, becoming more pronounced as the day progresses. Prolonged upward gaze may increase the ptosis. Enhanced or seesaw ptosis may be demonstrated (ie, a worsening of ptosis on one side when the opposite eyelid is elevated and held in a fixed position), but this sign is not specific for MG as it may rarely be seen with age-related ptosis, ocular myopathy, Lambert-Eaton myasthenic syndrome, Fisher's syndrome, and even third nerve palsy. During refixation (a vertical saccade) from down to the primary position, the upper eyelid may either slowly begin to droop or else twitch several times before settling in a stable position (Cogan's lid-twitch sign).

5. Involvement of extraocular muscles with MG usually occurs in association with ptosis; however, cases without clinical involvement of the levator muscles occur. MG should be considered in any case of ocular motor weakness without pupil involvement because MG may mimic any pattern of neurogenic paresis. Any extraocular muscle may be selectively impaired, especially the medial rectus, and weakness characteristically increases with sustained effort. Myasthenia can mimic pupil-sparing third nerve palsies, superior division third nerve palsies, abducens nerve palsies, or trochlear nerve palsies and internuclear ophthalmoplegia.

TEST INTERPRETATION

The diagnosis of OM is based on the clinical history, the physical findings, pharmacological testing, and, in selected individuals, sleep test, electromyography (EMG) investigations including study of the decremental response, conventional needle EMG, and single-fiber recordings, and determination of the serum anti-AChR antibody titers. The diagnosis of OM should be considered in any patient with ptosis and/or ocular motor weakness without pupillary involvement. Weakness and fatigue confined to the extraocular muscles or lids combined with orbicularis oculi paresis is especially suggestive of OM. Significant clinical involvement of the pupil, eye pain or headaches, proptosis, visual loss, or involvement of trigeminal sensation essentially negate this diagnosis.

A positive Tensilon (edrophonium hydrochloride) or Prostigmin (neostigmine methylsulfate) test is usually, but not always, indicative of ocular myasthenia. The improvement of extraocular muscle function should be quantified with prisms, a Hess screen, or the Lancaster red-green test. A negative Tensilon or Prostigmin test in no way rules out MG. The "sleep test" may also be incorporated to demonstrate objective improvement in myasthenic symptoms after rest. The patient is kept in a quiet, darkened room and instructed to close the eyes and rest for 30 minutes; ptosis and ocular motility are quantified before and after the rest period. This study may be positive in some Tensilon-negative myasthenics but may also be negative in Tensilon-positive patients. Another noninvasive test is the ice pack test which may be useful in the diagnosis of OM in the patient with ptosis. Ice in a surgical glove is placed over one lightly closed eye for 2 minutes or to the limit of patient tolerance. In cases of bilateral ptosis, the opposite (uncooled) eye serves as control.

AChR antibody titers are quite useful in the diagnosis of MG. In one large and representative study, the percentage of positive tests in different clinical forms of MG were as follows: remission, 24%; ocular, 50%; mild generalized, 80%; moderately severe or acutely severe, 100%; chronic severe, 89%. Overall, AChR antibodies are positive in 80 to 95% of patients with generalized MG and 34 to 56% of patients with OM. Testing for AChR binding, blocking, and modulating antibodies increases the assay yield in patients with generalized MG and OM . In OM, the antibody titer tends to be low and the serum

antibody titer correlates poorly with the severity of MG when a group of patients is studied.

As there is an increased risk of thymoma in patients with MG, all patients with the diagnosis of MG should undergo CT or magnetic resonance imaging (MRI) of the mediastinum. Thymoma occurs in 5 to 20% of myasthenic patients overall and about one-third to one-half of patients with thymoma have myasthenia gravis. The risk of thymoma in patients with OM is probably lower. Thymoma is more common in older patients and in patients with high AChR antibody titers. Because thyroid disease may be associated with MG, all patients should also have sensitive (thyroid stimulating hormone) TSH levels measured.

DIAGNOSIS

Ocular myasthenia gravis.

MEDICAL MANAGEMENT

About 10 to 20% of patients with OM will undergo spontaneous remission, which may be temporary or permanent. While corticosteroid treatment produces a higher incidence of remission and improvement, there is no evidence that anticholinesterase agents affect the course of the disease. Generalized MG may be a life-threatening disease requiring aggressive treatment with anticholinesterase drugs, corticosteroids, other immunosuppressive agents, plasmapheresis, intravenous gamma globulin, and possible thymectomy.

For patients with OM, if the diplopia or ptosis is mild, then observation or patching one eye may be sufficient. Ptosis may be eliminated in some patients by having a crutch attachment placed on a spectacle frame for one or both eyes, although this often causes irritation of the eyes from exposure.

SURGICAL MANAGEMENT

Ptosis surgery may be performed in patients with stable disease, particularly those who are refractory to medical therapy or in whom ptosis is a predominant finding. For more severe ocular motor weakness, anticholinesterase agents, such as pyridostigmine bromide (Mestinon), are warranted although these agents often do not succeed in correcting the diplopia. Diplopia is often more refractory to treatment than is ptosis. If moderate or large doses of anticholinesterase drugs fail or cannot be tolerated and symptoms are troublesome, then corticosteroids, often at relatively low alternate-day doses, are usually effective in correcting the diplopia. Although some authors have suggested the use of azathioprine for patients who are inadequately controlled on low-dose steroids or who are experiencing steroid side effects, this agent, cyclophosphamide, cyclosporine, intravenous immunoglobulin, and plasmapheresis are not usually used in patient with purely ocular myasthenia because their benefit–risk ratios have not been adequately studied.

The presence of a thymoma in any patient with MG is an absolute indication for thymectomy and, thus, all patients with OM should be evaluated with mediastinal CT or MRI. Although thymectomy can be effective in ocular MG without thymoma and may prevent generalization of the disease, most clinicians are reluctant to recommend this procedure for purely ocular symptoms.

REHABILITATION AND FOLLOW-UP

Patients need close supervision of medications used to control symptoms. Patients with purely OM must be warned of the possibility of generalization of the disease process and should specifically be instructed to inform their physician immediately if symptoms such as dysphagia, respiratory involvement, or extremity weakness develop.

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Case 72

THYROID OPHTHALMOPATHY

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 35-year-old woman complained of a 2-month history of eye discomfort and diplopia. The eye pain was a mild to moderate "eye irritation" or "foreign body-type" feeling that was constant but fluctuated in severity. She also complained of vertical diplopia that was binocular and constant. She often patched one eye in order to read or drive. Her husband noted that over the last few weeks her eyes appeared to be "bulging." She related a past history 1 year ago of hyperthyroidism treated with radioactive iodine. She was taking thyroid supplements. She denied other medical problems.

Examination revealed visual acuity of 20/25 bilaterally. She identified ten of ten Hardy-Rand-Rittler pseudoisochromatic plates bilaterally. Pupils were 4 mm bilaterally and equally reactive to light and near and there was no relative afferent pupillary defect. Visual fields were full on static perimetry. She had a left hypertropia of 4 prism diopters (PD) in primary gaze. This increased to 8 PD in upward gaze, 10 PD in downward gaze, and was 4 to 5 PD in left and right gaze. There was also an esotropia of 5 PD in primary gaze that was relatively comitant in up, down, left, and right gaze. Duction testing revealed limitation of elevation and depression in both eyes and limitation of abduction in both eyes, worse on the left. Adduction was relatively normal. She had no ptosis but had definite lid retraction and lid lag bilaterally. Proptosis was present with Hertel measurements at a base of 95 mm that were 22 mm on the right and 24 mm on the left, respectively (Fig. 72–1). Facial sensation and movements were normal. Slit-lamp examination revealed mild punctate keratopathy bilaterally. Funduscopic examination was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The motility impairment noted could be related to myasthenia gravis, but lid lag and retraction, rather than ptosis, makes this diagnosis unlikely. Bilateral orbital pseudotumor or other infiltrative orbitopathies are also a possibility, but the pain noted is mild and superficial, rather than severe and deep, and the lid lag and retraction are not easily explained by an infiltrative process. The constellation of impaired motility, lid lag and retraction, and proptosis, especially in the light of a history of previous hyperthyroidism treated with radioactive iodine, all make thyroid orbitopathy the likely diagnosis in this patient.

2. The ophthalmopathy of thyroid disease (thyroid eye disease, thyroid orbitopathy, or Graves' disease) is an autoimmune process with a progressive but self-limited variable course extending over 1 to 3 years. It is a common cause of acquired diplopia or exophthalmos in adults. The ophthalmopathy spans a clinical spectrum from minor eye symptoms and signs to severe, disabling, vision-threatening problems. Thyroid ophthalmopathy is considered to be present if eyelid retraction occurs in association with objective evidence of thyroid dysfunction or abnormal regulation, exophthalmos, optic nerve dysfunction, or extraocular muscle involvement.

3. The median age at the time of diagnosis of Graves' ophthalmopathy is 43 years (range, 8 years to 88 years). Approximately 90% of patients have Graves' hyperthyroidism, 1% has primary hypothyroidism, 3% have

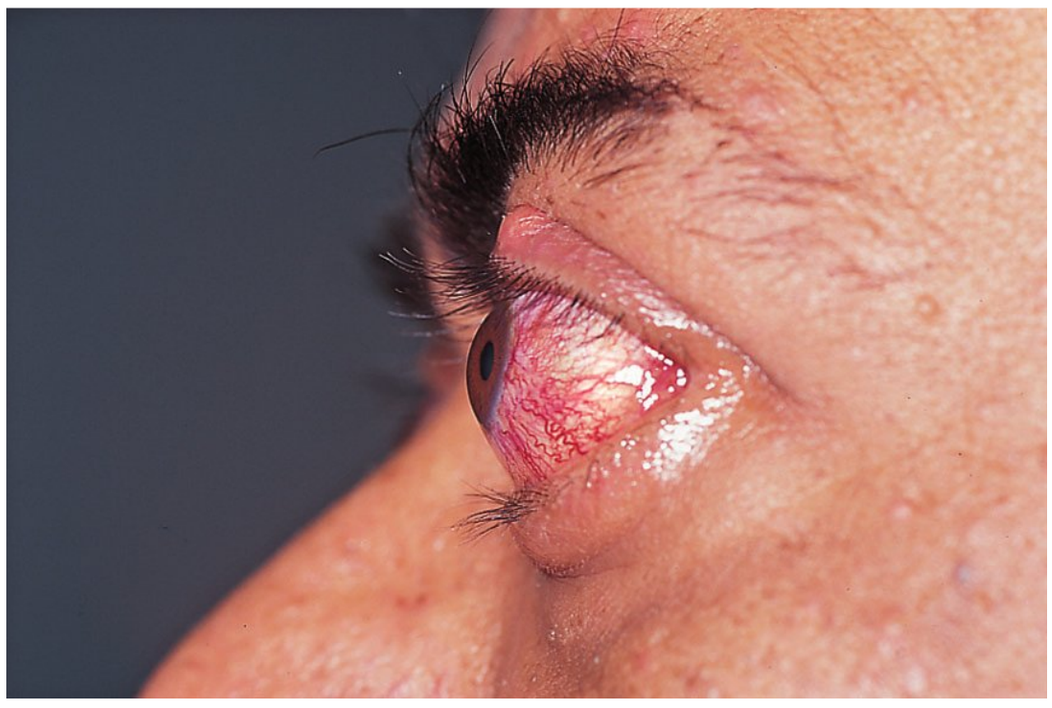

FIGURE 72–1 External appearance showing proptosis.

Hashimoto's thyroiditis, and 5% are euthyroid. Among patients with hyperthyroidism, Graves' ophthalmopathy develops in 61% within 1 year of the onset of thyrotoxicosis.

4. Eyelid retraction is the most common ophthalmic feature of autoimmune thyroid disease, present either unilaterally or bilaterally in more than 90% of patients at some point in the clinical course. Exophthalmos of one or both eyes affects approximately 60% of patients, restrictive extraocular myopathy is apparent in about 40% of patients, and optic nerve dysfunction occurs in either one or both eyes in 6% of cases. The restrictive myopathy especially affects the inferior, medial, and superior recti and rarely affects the lateral rectus muscle: therefore, exotropia in a patient with thyroid orbitopathy should raise the possibility of concomitant ocular myasthenia gravis. Only 5% of patients have a complete constellation of classic findings: eyelid retraction, exophthalmos, optic nerve dysfunction, EOM involvement, and hyperthyroidism. At the time of diagnosis of Graves' ophthalmopathy, the most frequent ocular symptom is pain or discomfort, which affects 30% of patients. Some degree of diplopia is noted by 17% of patients, lacrimation or photophobia is present in about 15% to 20%, and 7.5% of patients have blurred vision. Decreased vision attributable to optic neuropathy is present in less than 2% of patients by the time of diagnosis of Graves' disease.

5. Thyroid ophthalmopathy may be quite asymmetric between the two orbits and the disease process often undergoes spontaneous exacerbations and remissions of clinical activity. The disorder often starts with an acute, active inflammatory phase, lasting 6 to 18 months, which is mediated by lymphocytic and fibroblastic infiltration into orbital tissues.

TEST INTERPRETATION

Forced duction testing will indicate that the diplopia is due to restrictive rather than paretic disease process affecting the extraocular muscles. Thyroid function studies need to be assessed. CT scan or MRI of the orbits is useful to document extraocular muscle enlargement.

DIAGNOSIS

Thyroid orbitopathy.

MEDICAL MANAGEMENT

The treatment of thyroid eye disease begins with adequate control of the underlying endocrinopathy as many of the eye signs, except for proptosis, may improve with thyroid treatment. Patients should be instructed to stop smoking as smoking has been associated with the ophthalmopathy. Ocular discomfort is usually due to corneal and conjunctival exposure and often responds to methycellulose artificial tears during the day and ointment at night. As periorbital edema is often most prominent in the morning after a period of recumbency, elevating the head of the patient's bed and sleeping partially supine are advised. Wearing dark glasses with side protection will help photophobia.

For more severe symptoms, taping the eyelids shut at night or the use of goggles to provide a humidified chamber may be helpful. In general, patients should be observed closely throughout the period of active inflammation

without more aggressive therapeutic interventions, although suppression of inflammation with systemic corticosteroids or radiation therapy may be considered for more severe symptoms. Three exceptions that require prompt and aggressive early therapy are severe exposure keratopathy, severe proptosis or globe luxation, and optic neuropathy.

Diplopia during this period is usually due to tethering of the inferior and medial rectus muscles or less often the superior rectus or other muscles. Patients are thus usually esotropic and have vertical ocular misalignment. The diplopia of the early inflammatory phase is treated with patching or prisms as outlined concerning the symptomatic management of diplopia. Botulinum toxin injection into the tight and stiff muscles may temporarily help to correct a pathologic eye position and help regain binocular single vision. Strabismus surgery is deferred until the ocular deviation has been documented as unchanged for at least a period of 6 to 12 months and the patient is in the chronic phase of thyroid ophthalmopathy.

Systemic corticosteroids have been used successfully in the treatment of congestive thyroid orbitopathy. They may improve soft tissue involvement and compressive optic neuropathy but usually have little effect on strabismus and are not useful for chronic fibrotic thyroid ophthalmopathy. Possible indications for the use of corticosteroids include: (1) acute severe signs and symptoms of orbital inflammation of recent (less than 3 months) onset; (2) optic neuropathy, especially when used in conjunction with surgical decompression of the orbit or orbital radiation therapy; (3) prevention of progressive thyroid orbitopathy during the treatment of thyroid disease with radioactive iodine; and (4) control of signs and symptoms of thyroid orbitopathy that worsen despite previous orbital radiation and/or decompression. Corticosteroids may improve the orbitopathy in approximately 50 to 60% of patients, but the orbitopathy often worsens when the dosage of medication is reduced or discontinued. Chronic corticosteroid therapy is discouraged in thyroid ophthalmopathy patients because of the multiple ill effects of the medication. In general, corticosteroids are a valuable temporizing measure for thyroid orbitopathy but rarely provide meaningful long-term benefit or resolution of the disorder.

Radiation therapy, like corticosteroids, is most effective within the first year of onset of thyroid orbitopathy before significant fibrotic changes have occurred in orbital tissues. Possible indications for orbital radiation include (1) optic neuropathy, especially if the patient is a poor surgical candidate; and (2) symptoms of active orbital inflammation and congestion.

Optic neuropathy with thyroid ophthalmopathy is usually caused by apical compression of the optic nerve by enlarged extraocular muscles and can cause permanent visual loss. Medical treatment possibilities include high doses of oral or intravenous corticosteroids, orbital irradiation, or a combination of these procedures.

SURGICAL MANAGEMENT

In general, the major clinical problems in patients with thyroid ophthalmopathy include a congestive orbitopathy with eye irritation and inflammation, diplopia, visual loss from corneal exposure or compressive optic neuropathy, and cosmesis.

The clinical manifestations of the acute phase may be responsive, at least partially, to systemic corticosteroid treatment, other immunosuppressives, and orbital radiation therapy. Therapy during the acute period is mainly directed at local measures to protect the eyes from exposure and provide comfort while awaiting spontaneous stabilization of the disease process. The acute phase is followed by a chronic phase, characterized by hypertrophy and fibrosis of the extraocular muscles, lacrimal glands, and orbital fat. The clinical manifestations of this late phase do not regress spontaneously, are usually unresponsive to immunotherapy or radiation, and often require surgical correction for relief.

Extraocular muscle surgery in patients with thyroid ophthalmopathy should be postponed until the muscles are no longer inflamed and the deviation has remained stable for at least 6 months. Eyelid retraction in patients with thyroid ophthalmopathy may result from excessive

sympathetic activity, levator fibrosis, or contracture of the inferior rectus muscle. The lid retraction may be controlled by botulinum toxin injection into the levator palpebrae superioris muscle. Surgical procedures are available to improve eyelid retraction with options including lateral tarsorrhaphy, Müller's muscle and levator muscle lengthening, lower eyelid elevation, and blepharoplasty with orbital fat excision. Orbital decompression may improve lid retraction that is due to distortion from the proptotic globe. Strabismus surgery may relieve the compensatory component of lid retraction related to restrictive extraocular muscles but recessions of the inferior rectus muscle often worsen the eyelid retraction. Therefore, the order of surgery in a patient with thyroid ophthalmopathy requiring all three procedures should in general be orbital decompression followed by strabismus surgery followed by lid surgery. Patients who fail medical treatment of optic neuropathy in thyroid disease may require orbital decompression.

REHABILITATION AND FOLLOW-UP

The patient must understand that the treatment of thyroid ophthalmopathy usually extends over several years and that often a sequence of treatments is warranted. A team approach is necessary with input from endocrinology, ophthalmology, and other clinical specialties. The patient must have close ophthalmologic supervision to monitor for corneal epithelial breakdown that would require more aggressive treatments (eg, surgical tarsorrhaphy). Visual acuity, color vision, fields, and fundus must be observed closely for signs of optic neuropathy.

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Case 73

ANISOCORIA—TONIC PUPIL

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 45-year-old woman was evaluated because of anisocoria. She stated that while at a cocktail party 2 weeks ago a friend noted that one pupil was larger than the other and she feared that "it could be due to a brain tumor." She complained of occasional headaches over the last several years but denied any other illnesses, significant head or eye trauma, the use of any eye drops, or any visual symptoms. She went to see a neurosurgeon who performed magnetic resonance imaging (MRI) of the brain that was normal and stated that she may need a cerebral angiogram.

Examination revealed visual acuity to be 20/20 bilaterally. Color vision and visual fields were normal. The right pupil measured 6 mm in darkness while the left pupil measured 3 mm. The right pupil reacted poorly and segmentally to light (Fig. 73–1), while the left pupil reacted briskly and symmetrically to light. The right pupil slowly constricted to near and then slowly redilated on looking in the distance. The left pupil constricted briskly to near and quickly redilated at distance. Motility was normal and there was no ptosis. Slit-lamp exam revealed vermiform movements of some sections of the right iris to light. Fundus exam was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. If a large pupil is poorly reactive to light and the visual afferent system is normal, then a defect in the efferent parasympathetic innervation of the pupil is likely. The major entities causing an abnormal large pupil include third nerve palsy, iris damage, pharmacologic dilation, or tonic pupil.

2. In the absence of an extraocular motility deficit and ptosis, an isolated dilated pupil is rarely due to a third nerve palsy.

3. Careful slit-lamp biomicroscopy of the iris should be performed in all patients with anisocoria to exclude structural iris abnormalities or damage. No such damage was noted in this patient.

4. A careful history is usually all that is required in patients with inadvertent or intentional exposure to agents that may affect pupil size. The pupil size of patients with pharmacologic blockade is often quite large, on the order of 10 to 12 mm in diameter, which is much greater than the mydriasis usually noted in patients with third nerve palsy or a tonic pupil. Usually the mydriasis of pharmacologic agents affects the pupil completely in 360 degrees, as compared to the segmental paresis of the pupil in tonic pupils. A pupil dilated from a third nerve palsy or tonic pupil will constrict to pilocarpine 1%, while a pharmacologically blocked pupil will not constrict or will constrict only partially to pilocarpine 1%.

5. The anisocoria is, thus, mostly likely due to a tonic pupil. Tonic pupils may be due to local (ocular or orbital) lesions affecting the ciliary ganglion or nerve (eg, trauma), may be due to diffuse neuropathic processes, or may be idiopathic (Adie's tonic pupil syndrome). The clinical features of a tonic pupil are outlined in Table 73–1. Pharmacologic testing with low-dose pilocarpine (0.125% to 0.1%) may demonstrate cholinergic supersensitivity in the tonic pupil.

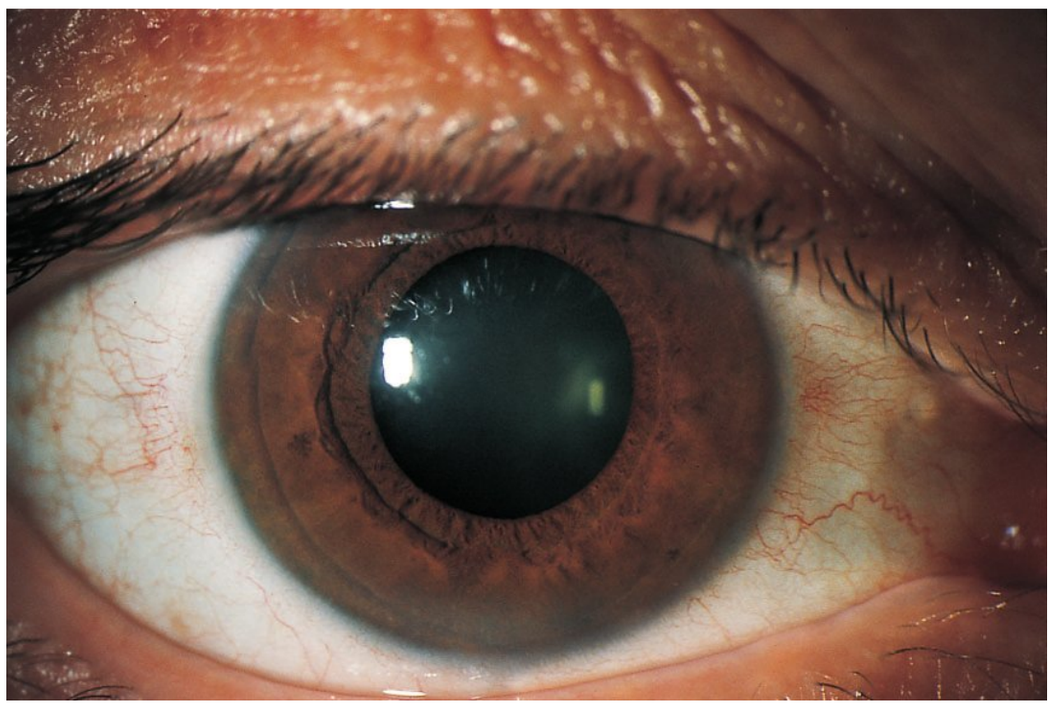

FIGURE 73–1 The right pupil measured 6 mm in darkness while the left pupil measured 3 mm. The right pupil reacted poorly and segmentally to light.

TABLE 73–1 **Clinical Features of a Tonic Pupil**

Poor pupillary light reaction
Vermiform movements of the iris to light on slit-lamp exam
Segmental palsy of the sphincter
Tonic pupillary near response with light-near dissociation
Cholinergic supersensitivity of the denervated muscles (eg, to dilute pilocarpine)
Accommodative paresis (that tends to recover)
Induced astigmatism at near
Tonicity of accommodation
Occasional ciliary cramp with near work

(Adapted from Lee AG and Brazis PW. *Clinical Pathways in Neuro-Ophthalmology: An Evidence-Based Approach*. New York: Thieme, 1998:362, with permission.)

TEST INTERPRETATION

Slit-lamp biomicroscopy revealed no iris injury but did show vermiform, segmental movements of the iris characteristic of a tonic pupil. A dilute solution of pilocarpine (0.125%) caused pupillary constriction on the affected side (this supersensitivity is often not present for the first several weeks after onset). Patients with bilateral isolated tonic pupils should have serologic testing for syphilis.

DIAGNOSIS

Isolated, idiopathic tonic pupil.

MEDICAL AND SURGICAL MANAGEMENT

There are no proven roles for medical and surgical management of this problem.

REHABILITATION AND FOLLOW-UP

No treatment, except reassurance, is usually required. Unequal bifocal reading aids or a unilateral frosted bifocal segment may be used in patients with permanent accommodative paresis. The initially mydriatic pupil may become smaller over time ("little old Adie's"). Although most Adie's tonic pupils present unilaterally, bilateral involvement may develop at a rate of 4% per year.

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Case 74

ANISOCORIA—HORNER'S SYNDROME

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 50-year-old man noted the onset of left frontotemporal and periorbital headaches for the last 3 weeks. He denied any visual complaints but noted some drooping of his left upper eyelid. He denied any diplopia, trauma to his head or neck, facial numbness or weakness or other neurologic complaints. He had a history of systemic hypertension.

Examination revealed visual acuity of 20/20 bilaterally with normal color vision. Pupils measured in bright light were 4 mm on the right and 3 mm on the left, but immediately after the lights were turned off, the pupils were noted to be 5 mm and 3 mm, respectively (Fig. 74–1). Both pupils reacted well to light and near and there was no relative afferent pupillary defect. Visual fields were normal. Motility was normal. There were 2 mm of left ptosis. Facial sensation and movement were normal. Slit-lamp examination and fundus exam were unremarkable.

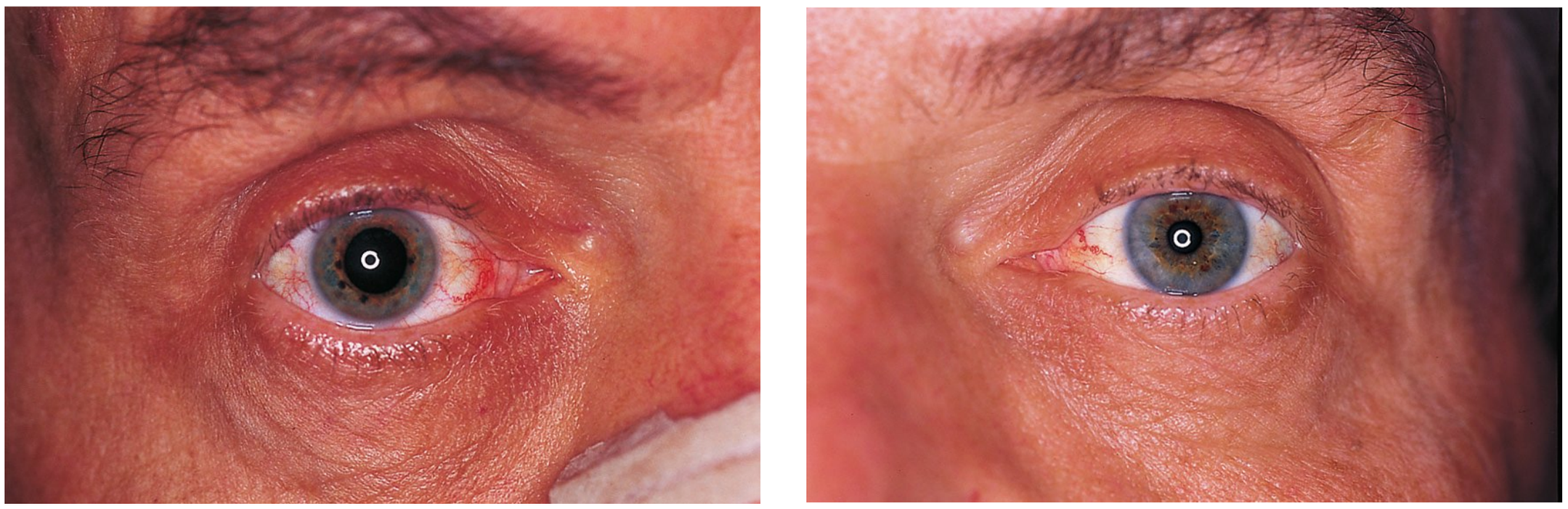
The instillation of topical cocaine 10% into both eyes revealed marked dilation of the right pupil, but poor dilation of the left pupil (noted in darkness 45 minutes after two drops instilled in both eyes). The patient returned 4 days later and hydroxyamphetamine 1% (Paradrine) was instilled in both eyes and resulted in full dilation in the right eye but poor dilation in the left eye.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. In a patient with anisocoria but normal pupil reaction, the main differential is between a Horner's syndrome (HS) and physiologic anisocoria. The left ptosis strongly favors a left Horner's syndrome but there are many cases reported of a "pseudo-Horner's syndrome" in which physiologic anisocoria is associated with some other unrelated cause of ptosis (eg, levator dehiscence). Simple or physiologic anisocoria has a prevalence as high as 21% in the general population and is associated with equal anisocoria in light and darkness.

2. Topical cocaine 10% will dilate both pupils equally with physiologic anisocoria but will not dilate or will poorly dilate the pupil in a patient with HS. Thus, cocaine testing is necessary to prove the existence of an HS. Cocaine inhibits the reuptake of norepinephrine at the neuromuscular junction. Therefore, topical cocaine will dilate a normal pupil but will not dilate a pupil with HS regardless of the location of the sympathetic damage.

3. HS may result from a lesion anywhere along the three-neuron pathway that arises as a first-order (central) neuron from the posterolateral hypothalamus, then descends in the brainstem and lateral columns of the spinal cord to exit at the cervical (C8) and thoracic (T1–T2) levels (ciliospinal center of Budge) of the spinal cord as a second-order neuron. This second-order (intermediate) preganglionic neuron exits the ventral root and arches over the apex of the lung to ascend in the cervical sympathetic chain. The second-order neurons synapse in the superior cervical ganglion and exit as a third-order neuron. The third-order postganglionic neuron travels with the carotid artery into the cavernous sinus, on to the sixth cranial nerve for a short course, and then travels with the ophthalmic division of the trigeminal nerve to join the nasociliary branch of the trigeminal nerve, pass through the ciliary ganglion, and reach the eye as long and



A B

FIGURE 74–1 (A) Right pupil and (B) left pupil showing anisocoria and mild left ptosis.

short ciliary nerves. Damage anywhere along this sympathetic pathway will result in an HS.

4. Patients with central or first-order HS usually have associated signs of hypothalamic or brainstem dysfunction. Preganglionic (intermediate) HS patients may have neck or arm pain, anhidrosis involving the face and neck, brachial plexopathy, vocal cord paralysis, or phrenic nerve palsy. A second-order HS may also occur in isolation. Important etiologies of a second-order HS include neoplasms (eg, apical lung cancer or infiltrative breast cancer), mediastinal lymphadenopathy, cervicothoracic abnormalities (eg, disc disease), neck or shoulder trauma, thoracic aneurysm, or local infections or inflammations. Postganglionic (third-order) HS may occur in isolation but may also occur with eye pain (eg, cluster headache) or palsies of the third, fourth, sixth, and ophthalmic division trigeminal nerves (eg, cavernous sinus thrombosis, infection, or neoplasm). Etiologies of third-order HS include high cervical lymphadenopathy, otitis and petrositis, trauma, and vascular abnormalities of the internal carotid artery (eg, carotid artery aneurysm or dissection). Dissection of the internal carotid artery, either spontaneous or posttraumatic, may result in a postganglionic HS. The HS in these cases may occur in isolation but is often associated with other features including ipsilateral orbital, facial, or neck pain, diplopia from cavernous sinus involvement, transient ischemic attacks (eg, transient ipsilateral visual loss), retinal artery occlusion or ischemic optic neuropathy, neck bruit or swelling, and other cranial neuropathies.

5. Hydroxyamphetamine 1% (Paradrine) releases the stored norepinephrine from postganglionic adrenergic nerve endings at the dilator muscle of the pupil. Therefore, a preganglionic HS (with intact postganglionic third-order neuron) will dilate after administration of topical hydroxyamphetamine 1% while a postganglionic HS pupil will not dilate (no norepinephrine stores). The Paradrine test cannot be performed on the same day as the cocaine test.

TEST INTERPRETATION

The response to eye drops in this patient was consistent with a postganglionic (third-order) HS and in the setting of headache, neuroimaging was performed of the brain and cervical region and magnetic resonance (MR) angiography of the carotid artery. MR angiography revealed a dissecting aneurysm affecting the high cervical carotid artery. An etiology of all cases of HS must be aggressively sought depending on response to eye drops, associated neurologic or medical symptoms, and the clinical situation. An isolated second-order HS may, for example, be the first sign of a lung neoplasm.

DIAGNOSIS

Postganglionic HS due to spontaneous dissection of the internal carotid artery.

MEDICAL MANAGEMENT

HS per se requires no treatment. The etiology of the HS must be treated. The patient in this case was treated for 3 months with coumadin and afterward was maintained on aspirin.

SURGICAL MANAGEMENT

No surgical treatment is indicated.

REHABILITATION AND FOLLOW-UP

Cases in which no etiology is evident require close observation to investigate for the development of other neurologic or medical signs or symptoms.

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Case 75

ANISOCORIA—EYE DROPS

Paul Brazis, M.D.
Andrew G. Lee, M.D.

HISTORY

A 24-year-old student nurse was referred for headaches and anisocoria. The headaches had been present for several years, but had been worse over the last few months. They occurred daily, were diffuse in nature, and were not associated with nausea or vomiting. Because of the headaches, she saw a neurologist who noted anisocoria and she was thus sent for ophthalmologic examination. She states that her vision was always "blurry," especially with her headaches. She denied diplopia or other eye problems. She was taking medications only for her headaches.

Examination revealed visual acuity to be 20/20 bilaterally. She identified ten of ten Hardy-Rand-Rittler pseudoisochromatic plates bilaterally. Visual fields were full. Pupils were 8 mm on the right (Fig. 75–1) and 4 mm on the left. The right pupil did not react to light or near, while the left pupil reacted briskly to light and near. No relative afferent pupillary defect was documented. Motility was normal and there was no ptosis. Facial sensation and strength were normal. Slit-lamp exam revealed both pupils to be smoothly round without irregularities and there was no segmental contraction of the right pupil to light. Fundus exam was normal with no disc swelling noted.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Presence of a unilateral large, nonreactive pupil raises several possibilities, including a right third nerve palsy, tonic pupil, iris damage, or pharmacologic mydriasis. The normal motility and absence of ptosis argue strongly against a third nerve palsy. The absence of pupillary irregularity and the absence of visible structural iris abnormality on slit-lamp examination argue against iris damage. There is no tonicity of the near response or segmental sphincter palsy suggestive of a tonic pupil. The most likely etiology of the anisocoria is thus pharmacologic mydriasis.
2. Nurses, physicians, and other health care workers are particularly prone to inadvertent or intentional exposure to pharmacologic mydriatics. The most common agents implicated in accidental exposure include sphincter blockers (such as belladonna alkaloids, scopolamine patches, anticholinergic inhalants, topical gentamicin, or lidocaine) or dilator stimulators (eg, ocular decongestants or adrenergic inhalants used in the intensive care setting).
3. The pupil size of patients with pharmacologic blockade is often quite large, usually greater than 8 mm and often 10 to 12 mm in diameter, which is much greater than the mydriasis seen with third nerve palsy or tonic pupil syndrome. The pupil is usually smoothly dilated over the entire 360-degree circumference and no pupillary irregularities are noted.

TEST INTERPRETATION

A pharmacologic dilated pupil will not constrict to dilute pilocarpine (vs a tonic pupil) and will constrict poorly or not at all to pilocarpine 1% (vs third nerve palsy). Over time with observation alone, the pupil will return to normal size.

DIAGNOSIS

Pharmacologic mydriasis.

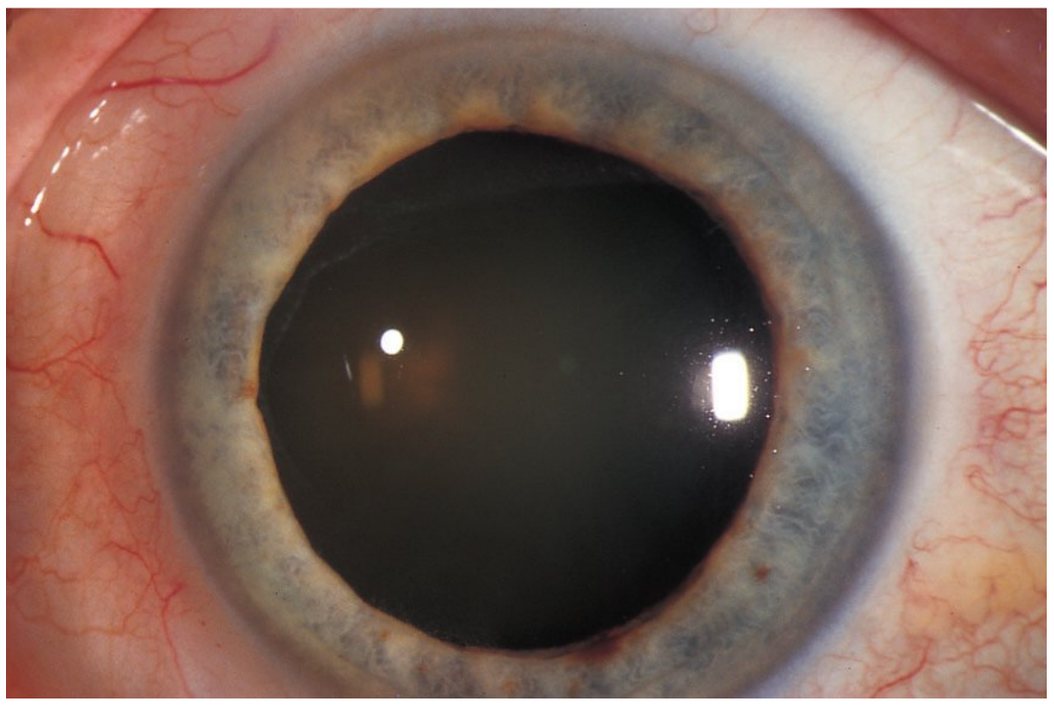

FIGURE 75–1 The pupil measured 8 mm on the right and did not react to light or near.

MEDICAL MANAGEMENT

No treatment is required except discussion concerning the findings, possible etiologic agents, and reassurance.

SURGICAL MANAGEMENT

No surgical treatment is indicated.

REHABILITATION AND FOLLOW-UP

Follow-up to ensure resolution of the symptoms is reasonable.

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Section X

PEDIATRICS

76. Leukocoria
77. The Child Who Sees Poorly Out of One Eye
78. Childhood Torticollis
79. Aniridia
80. Retinopathy of Prematurity
81. Childhood Esotropia
82. Childhood Exotropia
83. Childhood Ptosis
84. The Apparently Blind Infant
85. Optic Nerve Hypoplasia
86. Childhood Optic Pathway Glioma

Case 76

LEUKOCORIA

David K. Coats, M.D.

HISTORY

The family of a 9-month-old girl noted that her left eye has looked "funny" for the last 3 months. The girl's pediatrician detected leukocoria and referred her to an ophthalmologist for evaluation and treatment. The child is an otherwise healthy 9-month-old with a negative review of systems with the exception of the white pupil. She was born 2 weeks prematurely and had a birth weight of 6 lb., 8 oz. There is no history of systemic disease or exposure to animals, and there is no family history of childhood ocular disease.

Examination reveals a normal right eye, though only the posterior pole can be seen on retinal examination. In the left eye, a white, vascular lesion is obvious with a surrounding large serous retinal detachment (Fig. 76–1). The child fixes and follows well with her right eye, but does not fix or follow with her left eye. Strong objection to occlusion of the right eye is noted.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. When leukocoria is noted on ophthalmologic examination, an extensive differential diagnosis must be considered. Almost all of the conditions that produce leukocoria in a child are serious vision- or life-threatening problems. Leukocoria is therefore an urgent ophthalmologic problem.

2. Retinoblastoma is the most ominous cause of leukocoria. It is the most common intraocular malignancy in childhood, occurring in approximately 1 in 20,000 live births. In the United States, there are an estimated 250 to 500 new cases per year. Most are diagnosed prior to the age of 4 years, but retinoblastoma has occasionally been reported even in adults. The condition may be unilateral or bilateral, and there is no race or sex predilection. The most common presenting signs of retinoblastoma include leukocoria, strabismus, poor vision, and family history of retinoblastoma. Other less common presenting signs include vitreous hemorrhage, microphthalmus, and orbital cellulitis. Retinoblastoma is classified based upon the location and extent of the tumor according to the Reese-Ellsworth classification.

3. Coats' disease is another common cause of leukocoria. It is typically unilateral, but may be bilateral. Coats' disease is characterized by an exudative retinal detachment with associated telangiectatic retinal vessels and subretinal lipid exudation. Coats'disease can usually, but not always, be differentiated from retinoblastoma on clinical examination alone.

4. Persistent hyperplastic primary vitreous (PHPV), more appropriately called persistent fetal vasculature (PFV), can present with leukocoria that on initial clinical examination may resemble an extensive retinoblastoma. The anterior portion of the lens is clear and an associated cataract, which is at the level of the posterior capsule, can be stark white and vascular. Eyes with PHPV cataracts tend to be smaller than normal, a feature that is uncommon in eyes with retinoblastoma. The correct diagnosis can usually be made with careful ophthalmologic examination and ultrasound.

5. Numerous other conditions are included in the differential diagnosis of leukocoria, including advanced retinopathy of prematurity with cicatricial retinal detachment, toxocariasis, large chorioretinal colobomas, uveitis, severe vitritis, extensive medullated nerve fibers, and other types of cataracts.

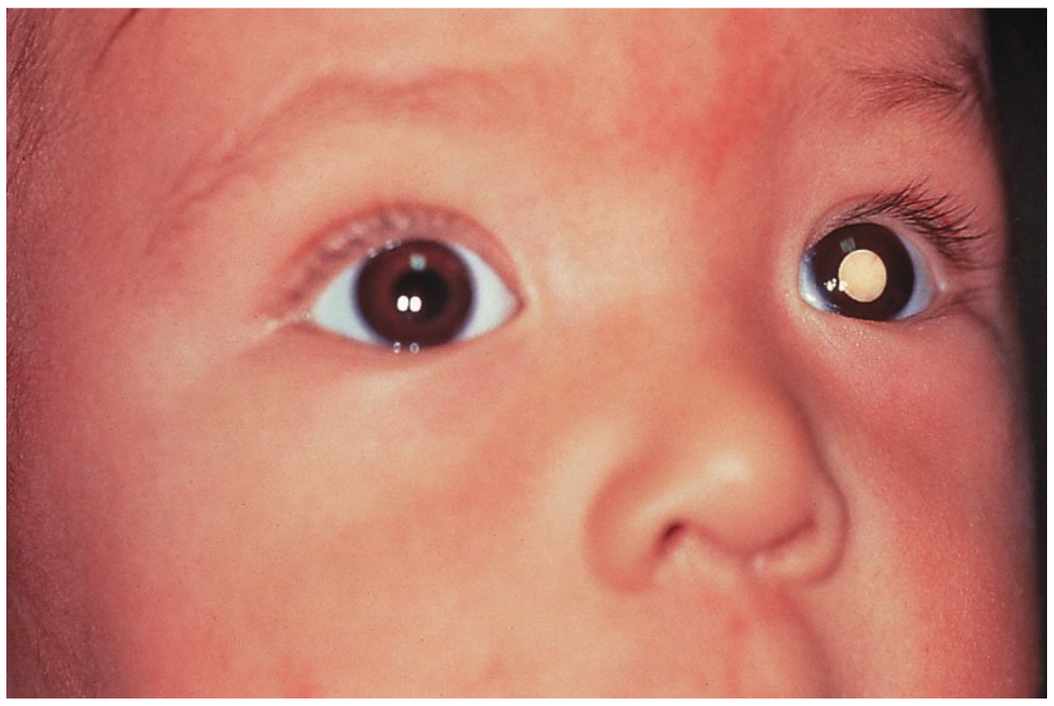


FIGURE 76–1 Clinical photograph of the patient demonstrating leukocoria of the left eye.

6. Genetics of retinoblastoma. Most patients with retinoblastoma are karyotypically normal. However, a small group of patients will have a chromosome 13q14 deletion. Features of this syndrome include mental retardation, developmental delay, and mild structural facial anomalies. Hereditary and nonhereditary cases of retinoblastoma exist. Hereditary forms can be identified with certainty only in cases of bilateral retinoblastoma or in cases of multiple affected family members. Genetic testing of retinoblastoma is of limited utility in many families because the gene is large, mutations may occur throughout the gene, and techniques for directly sequencing the gene are labor intensive and time consuming. Defects in the retinoblastoma gene can often be detected in the retinoblastoma cells of an enucleated eye and comparisons made with other somatic cells to determine if the tumor is hereditary. Examination of parents and siblings of an affected patient is important both to rule out active retinoblastoma in younger siblings and to detect evidence of regressed retinoblastoma in parents and older siblings.

TEST INTERPRETATION

The major diagnostic considerations in this child are to determine the extent of local disease involvement, to rule out disease in the contralateral eye, and to determine if extension of the tumor has occurred outside of the eye.

1. A computed tomography (CT) scan of the head and orbits was obtained (Fig. 76–2). The presence of calcium in an intraocular lesion noted on CT scan in a child less than 3 years of age is virtually diagnostic of retinoblastoma. On the other hand, patients with leukocoria who do not have calcium in the lesion most likely do not have retinoblastoma, though calcification is not always present in retinoblastomas. A CT scan is also useful in detecting retrobulbar extension, tumor in the contralateral eye, and tumor in the central nervous system due to either metastases or the presence of a pineal tumor, the so-called trilateral retinoblastoma.

2. Ultrasound testing can offer both diagnostic and therapeutic assistance. Calcium may be detected on B-scan ultrasonography, which can also demonstrate tumor extent. A-scan ultrasonography is useful in determining the height of the tumor and is valuable in monitoring treatment response if the tumor is to be treated with local measures.

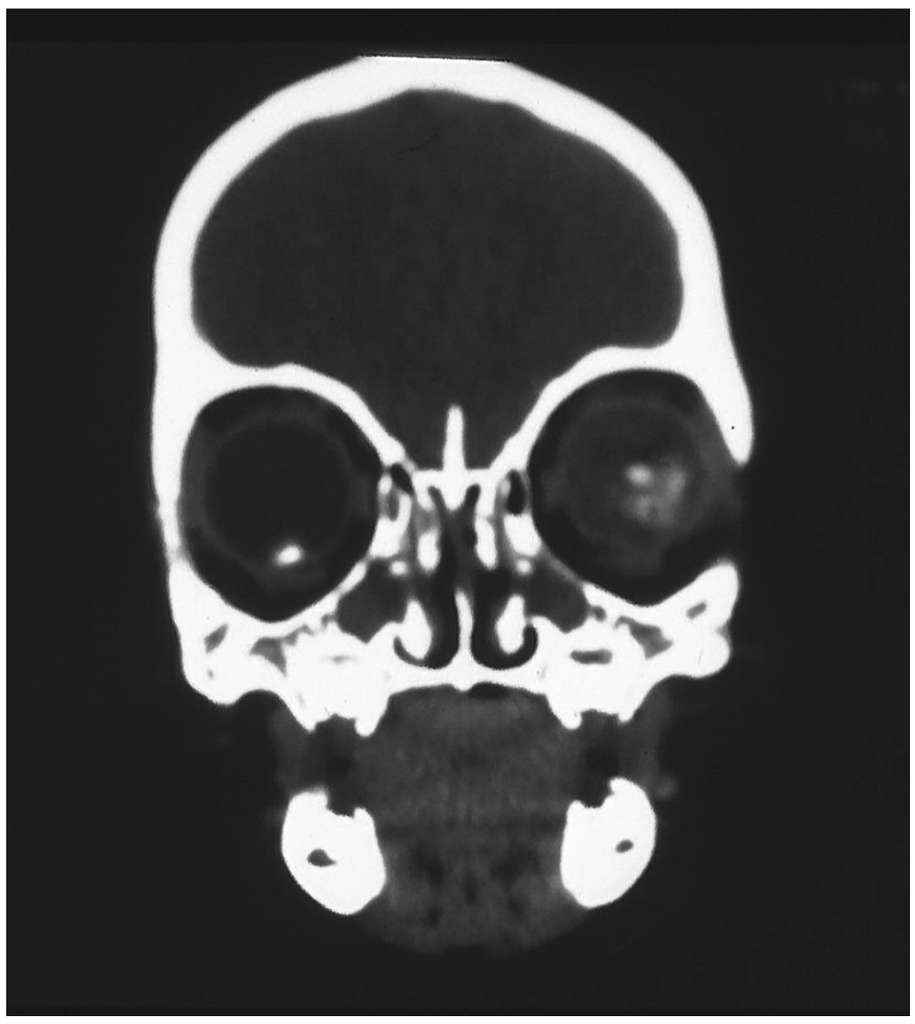


FIGURE 76–2 Computed tomography (CT) scan demonstrating a large retinoblastoma in left eye and a small, previously undiagnosed retinoblastoma in the right eye.

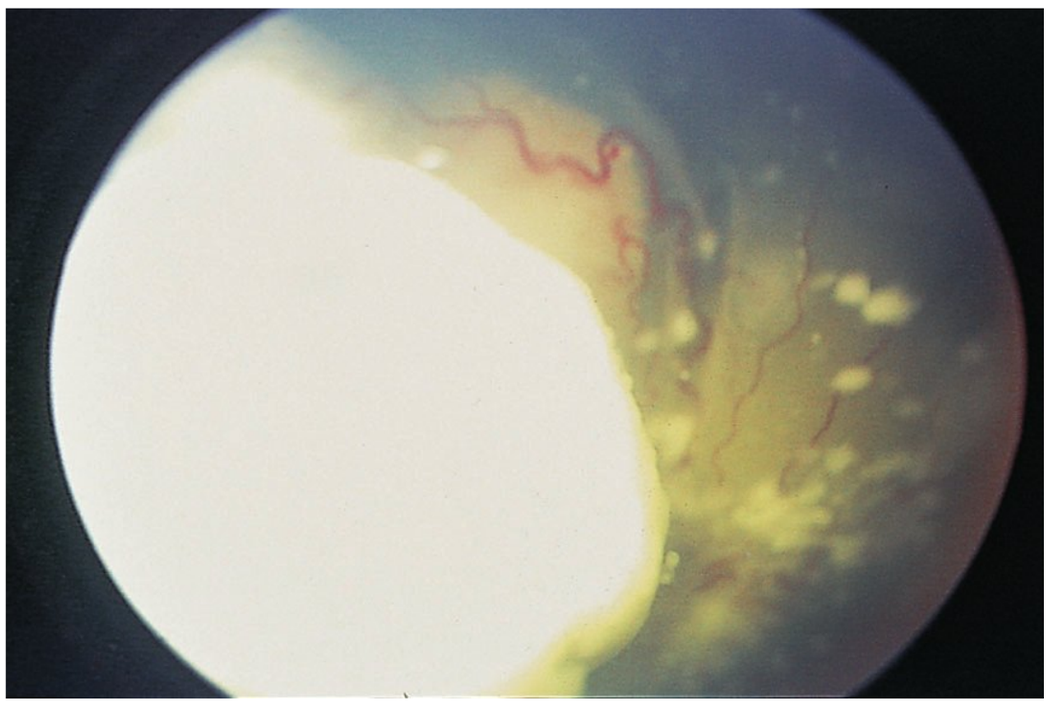


FIGURE 76–3 Large retinoblastoma with vitreous seeding of a large exudative retinal detachment.

3. Other testing. All patients affected with retinoblastoma should undergo genetic counseling and a general physical examination. Bone marrow and cerebrospinal fluid evaluation are utilized in selected cases when disease beyond the globes is suspected. The enucleated eye should be submitted for pathologic examination, and genetic testing of the tumor cells considered.
4. Examination of the eyes under anesthesia was performed and demonstrated a massive tumor with retinal detachment in the left eye (Fig. 76–3). In addition, a small tumor was noted in the inferior retina of the right eye.

DIAGNOSIS

Bilateral retinoblastoma.

MEDICAL MANAGEMENT

Chemotherapy can be used in a process known as a chemoreduction to shrink the size of the tumor. Chemoreduction is used in conjunction with local surgical measures, such as photocoagulation and cryotherapy, which are applied after the tumor has decreased in size. There are three primary indications for chemotherapy in retinoblastoma, including treatment of intraocular retinoblastoma prior to the use of local surgical treatment modalities (chemoreduction), treatment of extraretinal intraocular disease, and treatment of extraocular and metastatic disease. Typically, three to six chemotherapeutic cycles are required. External beam radiation is utilized in selected cases in an attempt to salvage an eye with retinoblastoma or to treat local orbital extension.

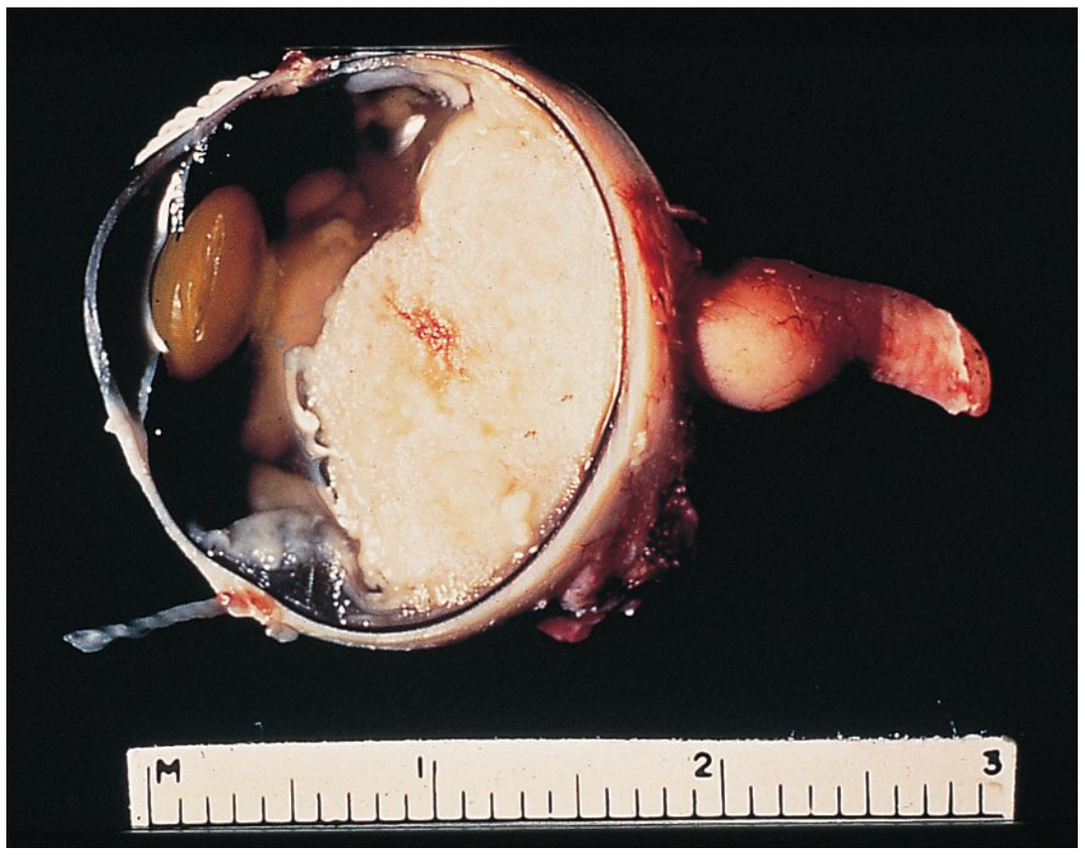
SURGICAL MANAGEMENT

Examination under anesthesia is almost always required to fully evaluate infants and young children with retinoblastoma or suspected retinoblastoma. This case highlights the importance of examination under anesthesia in that the tumor in the right eye was not detected on clinical office examination, where only the posterior pole could be readily examined.

While patients with retinoblastoma can be managed medically in many cases, enucleation of an eye with extensive tumor and no visual potential is still the treatment of choice. This patient should undergo enucleation of the left eye using meticulous technique in an attempt to obtain a long optic nerve segment since the tumor tends to spread by direct extension into the optic nerve. Figures 76–4A,B,C show the gross and microscopic appearance of a retinoblastoma. The right eye can be approached with both medical and surgical modalities. The potential surgical treatments include cryotherapy, laser therapy, and radioactive plaque treatment.

REHABILITATION AND FOLLOW-UP

Recurrence of the tumor can occur in the orbit even if the cut margin of the optic nerve was free of tumor. The physician should, therefore, examine the socket of the enucleated eye each time he or she examines the contralateral eye. Following local control of the tumor in this child's right eye, follow-up examinations under anesthesia should be conducted every 2 to 4 months until the child is 3 to 4 years of age. Frequent examinations must continue for several more years and an annual eye examination is prudent thereafter. Long-term safety issues include protecting the



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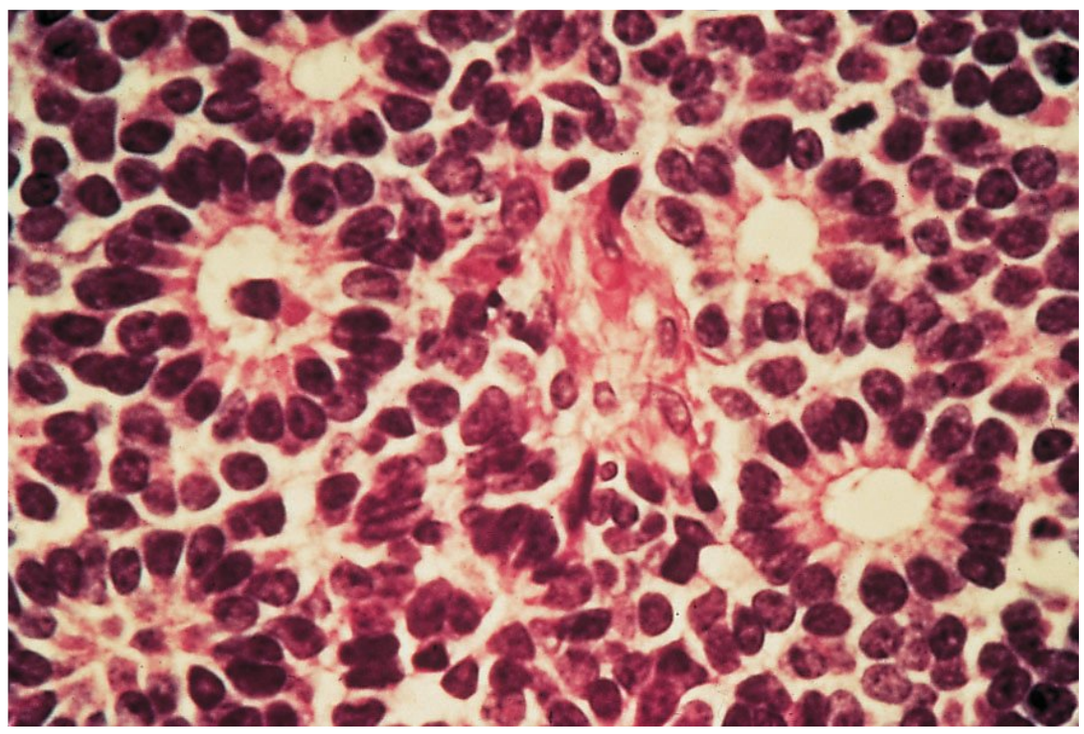

C

FIGURE 76–4 (A) Gross appearance of retinoblastoma. Note long segment of optic nerve obtained at the time of enucleation. (B) Large retinoblastoma with invasion of the optic nerve. (C) Histologic example of retinoblastoma demonstrating Flexner-Wintersteiner rosettes. (Photos courtesy of Ramon L. Font, M.D., Houston, TX.)

remaining eye with the use of polycarbonate safety glasses and providing patient education on eye safety. These measures are important in all monocular patients. Patients treated with chemotherapy and/or external beam radiation and patients with hereditary retinoblastoma have a high incidence of secondary tumors, both in the orbit and elsewhere, and should be followed long-term with these issues in mind.

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Case 77

THE CHILD WHO SEES POORLY OUT OF ONE EYE

David K. Coats, M.D.

HISTORY

A 4-year-old boy failed his preschool vision screening test. The vision screening failure was confirmed by his pediatrician and he has been sent for ophthalmologic evaluation and treatment recommendations. The child is a robust 4-year-old with no history of medical or ophthalmologic problems. The review of systems is negative and, specifically, there is no history of eye injury, strabismus, spectacle wear, squinting, or other ophthalmologic problems. The child has not previously had an ophthalmologic examination and there is no family history of amblyopia or childhood eye disease.

On examination, the technician found 20/40 vision in each eye with Allen figure testing. His stereoacuity is 60 seconds of ARC using the Titmus fly test. Motility evaluation reveals orthotropia at distance and an exophoria of 4 prism diopters at near with full ductions and versions. His cycloplegic refractive error following administration of 17% cyclopentolate is +3.00 in the right eye and +1.00 in the left eye. The ophthalmologist repeated the visual acuity testing using the E game and found a visual acuity of 20/50 in the right eye and 20/30 in the left eye.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The majority of children who fail a school vision screening test will have a normal eye examination. However, as many as 25 to 30% of screening failures will have an ophthalmologic problem that can benefit from treatment. The differential diagnosis of poor vision in one eye includes amblyopia, uncorrected refractive error, a structural eye abnormality, and poor effort. Four causes of amblyopia must be considered including refractive, deprivational, strabismic, and idiopathic amblyopia (Figs. 77–1A, B, and C). Idiopathic amblyopia is probably amblyopia that occurred from one of the other causes, but which is now undetectable by physical examination.

2. Terminology: Before proceeding with the discussion on amblyopia, a review of some important amblyopia terminology is in order.

a. *Occlusion amblyopia* is a term used to describe iatrogenic amblyopia that occurs in the normal seeing eye as a result of wearing a patch to treat amblyopia in the fellow eye. This term should not be used to describe deprivational amblyopia such as that caused by a cataract or corneal opacities.

b. *Foveal form vision deprivational amblyopia* is a term used to describe amblyopia caused by failure to produce a clear image on the fovea of the involved eye. It can be caused by media opacities and high refractive errors.

c. *Abnormal binocular interaction* is a term used to describe a situation in which the image size or shape on the two foveas is so dissimilar that the images cannot be fused. One of the images is suppressed and amblyopia may develop. This type of amblyopia most commonly occurs due to uncorrected anisometropic refractive errors and strabismus. A combination of form vision deprivation and abnormal binocular interaction can coexist in some patients.

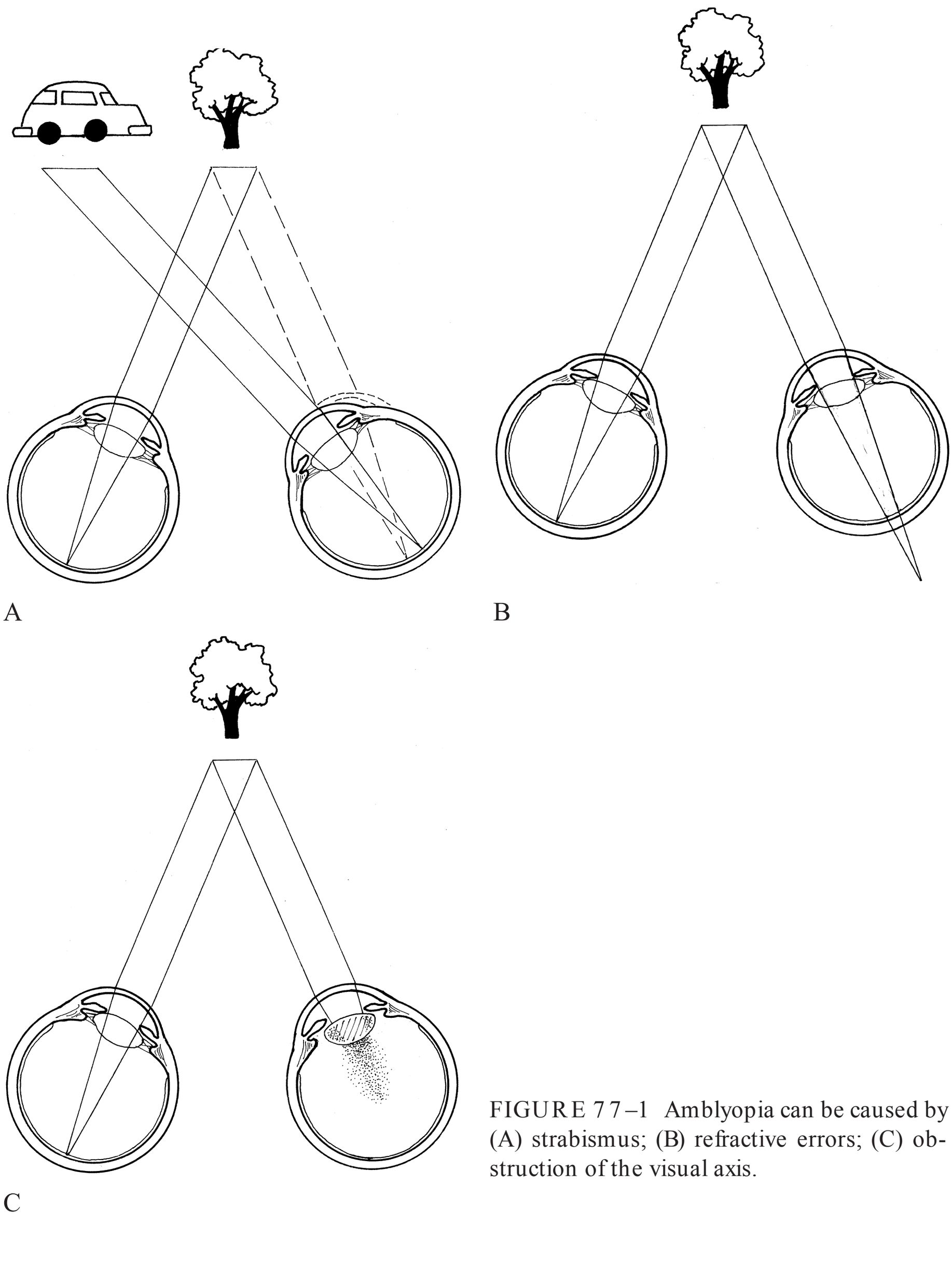


FIGURE 77–1 Amblyopia can be caused by (A) strabismus; (B) refractive errors; (C) obstruction of the visual axis.

d. *Anisometropic amblyopia* is amblyopia that develops on the basis of an unequal refractive error. In a hyperope, amblyopia usually develops in the most hyperopic eye. The condition is less common in children with myopia or astigmatism, but may occur when the refractive error is large.

e. *Ametropic amblyopia* is bilateral amblyopia due to the presence of bilateral large refractive errors. It is most common with hyperopia, but may also occur with high myopia and astigmatism.

3. Refractive amblyopia is common. It most commonly occurs in one eye, but can occur in both eyes where it is called ametropic amblyopia. Because the eyes are usually straight when this condition is present and there are no other obvious abnormalities visible to the

child's family, the condition is often not diagnosed until the child fails a vision screening examination either at school or in the pediatrician's office. Refractive amblyopia can occur with any type of refractive error but is more common with anisometropic hyperopia. Refractive amblyopia is the most readily treated form of amblyopia and can even be treated if detected late in the first decade of life. A positive family history of refractive amblyopia is common.

4. Strabismic amblyopia is also very common. It is most often seen with esotropia but can occur with any type of strabismus. It is least likely to occur with intermittent exotropia. The size of the strabismic deviation is unrelated to the presence or severity of amblyopia. Amblyopia is more likely to be detected early in children with large angle strabismus because parents are readily able to detect large angle strabismus prompting a visit to the ophthalmologist. Strabismic amblyopia typically responds well to treatment measures, but is often more difficult to treat than refractive amblyopia.

5. Deprivational amblyopia is the most serious form of amblyopia. It may occur in one or both eyes and is due to media opacities such as cataracts, corneal opacities, vitreous hemorrhage, and visual obstruction secondary to ptosis. Clearing of the visual axis with institution of amblyopia treatment measures such as occlusion are most likely to be successful if implemented within the first few months of life. Deprivational amblyopia can be recalcitrant to treatment.

TEST INTERPRETATION

Psychophysical testing, which involves the use of recognition acuity tests such as Allen figure testing and Snellen figure testing, is the most important means of detecting the presence of amblyopia and for monitoring the response to treatment. This child's examination results reveal a critically important feature of recognition acuity tests. Note that his vision was equal in the two eyes on Allen figure testing, but was reduced in the right eye on E game testing. Allen figure testing tends to overestimate visual acuity in children with amblyopia. Therefore, Allen figure testing should be supplemented with another test such as a fixation preference test, and the child should be tested with a more sophisticated test such as the E game, Landolt ring test, or Snellen acuity test as soon as the child is able to cooperate. Young children are often not able to cooperate well enough to read the 20/20 line, but should have equal vision in the two eyes.

Fixation behavior, fixation preference, and occlusion objection may be the only means of detecting amblyopia in small children. An effort should be made to assure that each eye will readily fixate on a small target and that one eye is not preferred over the other. In children with straight eyes, the eyes can be dissociated with a vertical or horizontal prism and fixation preference tested during the period of prism dissociation.

Common among all recognition tests is a feature known as the crowding phenomenon. Patients with amblyopia are frequently able to identify much smaller optotypes if the optotypes are shown in isolation than if they are shown a line in a full chart of letters. It is, therefore, imperative that a line of letters or single letters with crowding bars be utilized to minimize the chance that amblyopia will be overlooked (Fig. 77–2).

Stereoacuity should also be tested in all children who are old enough to cooperate. The presence of good to excellent stereopsis is prognostic with good stereoacuity indicating a higher likelihood of a favorable treatment response.

DIAGNOSIS

Anisometropic amblyopia in the right eye due to uncorrected hyperopia.

MEDICAL MANAGEMENT

The first task in management of this child with amblyopia is to correct his refractive error. The ophthalmologist may prescribe the full cycloplegic

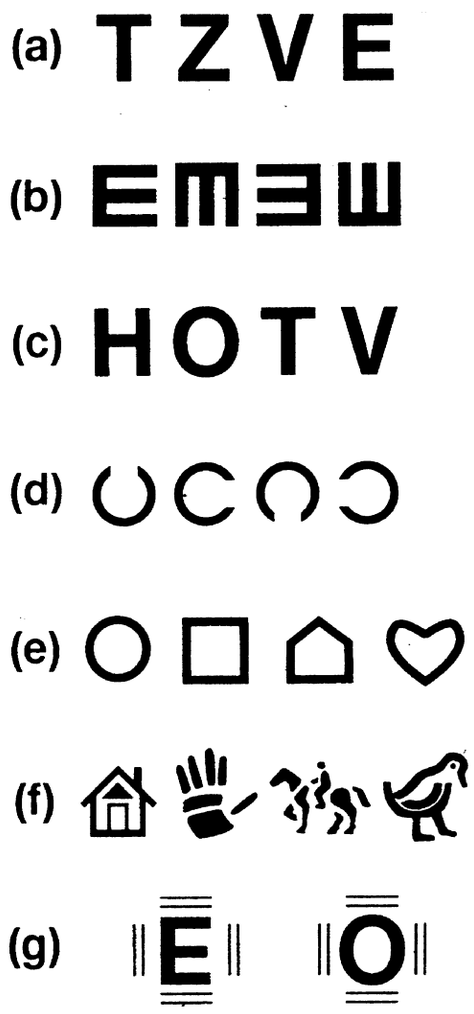
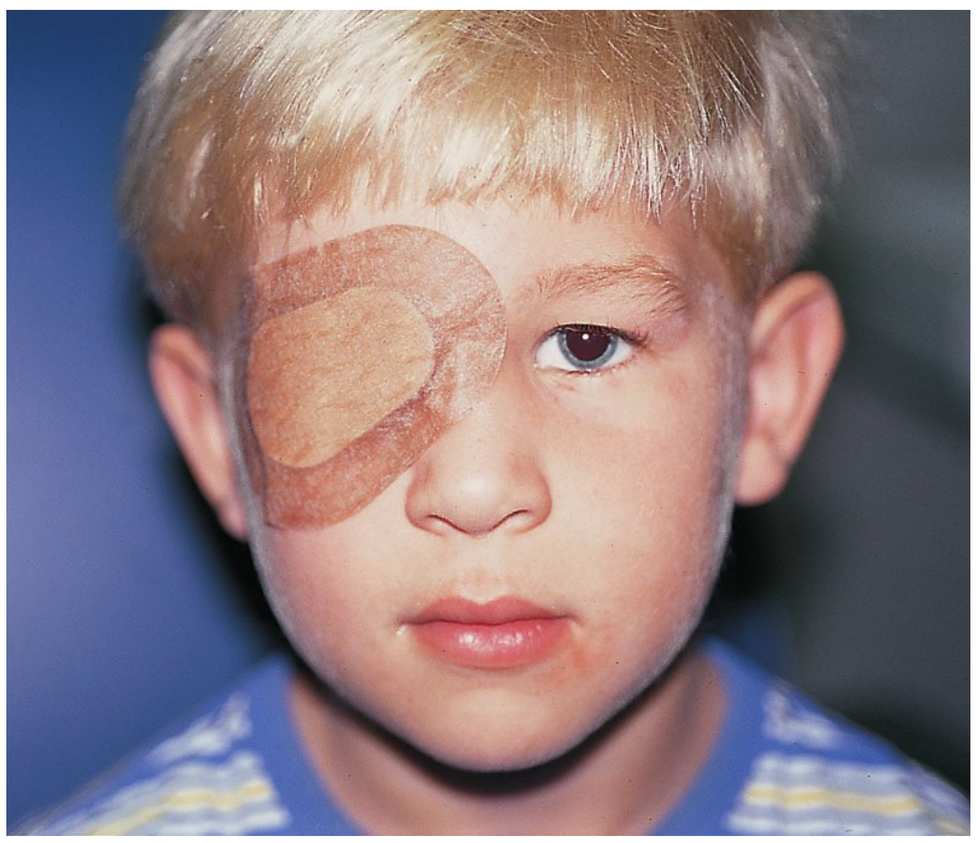


FIGURE 77–2 Typical psychophysical tests of visual function: (line a) Snellen test; (line b) E game; (line c) HOTV test; (line d) Landolt test; (line e) Lea test; (line f) Allen test; (line g) single optotypes with crowding bars.

refraction or may symmetrically reduce the hyperopic correction in each eye so that the child must continue to accommodate slightly in order to see clearly. Either of these methods is reasonable provided that reduction in the spectacle prescription is exactly the same in both eyes, so that the same amount of accommodation is required to see with either eye.

The child should be examined 4 to 8 weeks following the initiation of spectacle correction. Often, the visual acuity on follow-up examination will have responded to glasses alone and no other treatment measures are required. If vision remains reduced on retesting, other treatment measures must be instituted. Frequently, children will not adapt to the use of hyperopic spectacles, particularly when the hyperopic correction is moderate or high. In such cases, atropine drops may be prescribed once a day for several days. This will produce a pronounced and prolonged cycloplegia, thus encouraging the child to wear the glasses, which are needed to produce clear vision during the period of time the cycloplegia is in effect. The atropine effect will gradually wear off over several days, allowing the child to comfortably adjust to wearing spectacles.

Occlusion therapy with the use of an eye patch is a common means of treating amblyopia (Figs. 77–3A and B). A patch is utilized to cover the better-seeing eye, thus encouraging use of the amblyopic eye. There are no standardized patching schedules and different examiners might choose a wide variety of different patching schedules. In general, for children more than 1 year of age, occlusion of the better-seeing eye should be done for 1 week per year of age, and then a follow-up examination done. If occlusion



A

B

FIGURE 77–3 Two commonly used methods of occlusion to treat amblyopia are (A) adhesive patch; (B) spectacle-mounted patch.

amblyopia has not occurred and if amblyopia persists, the follow-up interval can be increased and the child followed on a regular basis. Part-time occlusion schedules are also acceptable and have the theoretic advantage of minimizing the development of occlusion amblyopia and reducing the frequency of required follow-up. Many ophthalmologists prefer part-time occlusion when the eyes are straight to avoid constant disruption of fusion.

Optical penalization is also a useful option in treating amblyopia. Atropine eyedrops and/or spectacles are utilized for optical penalization. If atropine is used, it can be placed in the better-seeing eye each morning. This greatly reduces the child's ability to accommodate and thus encourages utilization of the amblyopic eye. The child is given spectacles to correct the refractive error in the amblyopic eye, while the better-seeing eye is given a plano lens. Atropine is unlikely to work in cases of extremely dense amblyopia because such children are likely to still prefer vision in the normal eye. In cases where amblyopia is not severe, atropine can still be utilized even in children who have only a small or no refractive error in the normal eye. In such cases, the child may still prefer the normal eye for distance viewing, he will most likely prefer vision in the amblyopic eye at near where accommodation is more important. Spectacles correction with a blurring lens can be utilized instead of or in addition to atropine penalization and may be useful in selected patients with amblyopia. Levodopa (as levodopa/carbydopa), a precursor for the catecholamine dopamine, is a neurotransmitter/neuromodulator known to influence the visual system at both retinal and cortical levels, and has been tried in the treatment of amblyopia with limited and unsustained results.

SURGICAL MANAGEMENT

The role of surgery in the management of amblyopia is to clear the visual axis (ie, correct ptosis or remove a media opacity such as a corneal leukoma or cataract). If amblyopia is caused by strabismus, it is best to defer strabismus surgery until amblyopia has been maximally treated. Strabismus surgery itself does not improve amblyopia.

REHABILITATION AND FOLLOW-UP

Frequent ophthalmologic follow-up examinations are necessary even after amblyopia has been maximally treated. Gains from excellent amblyopia management can be lost if children are not observed carefully for recurrence. Refractive error will gradually change as the child ages and updated prescriptions will be required. Strabismic amblyopia can recur even if the eyes appear aligned, due to the presence of difficult to detect microstrabismus. Because of the potential of recurrence, maintenance patching is often needed until the age of 7 to 8 to prevent loss of amblyopia treatment gains.

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Case 78

CHILDHOOD TORTICOLLIS

David K. Coats, M.D.

HISTORY

A 5-year-old boy is brought to his ophthalmologist's office at the request of his pediatrician for evaluation of an anomalous head tilt. The child has undergone orthopedic evaluation and neck muscle abnormalities are absent. The child has had a relatively constant left head tilt since he first gained head control during the first year of life. His parents note that he strongly resists any attempts to straighten his head. During the last 2 months, they have noticed that his eyes sometimes do not appear to move together. Family history is unremarkable and the review of systems is notable only for frequent eye rubbing and blinking behavior.

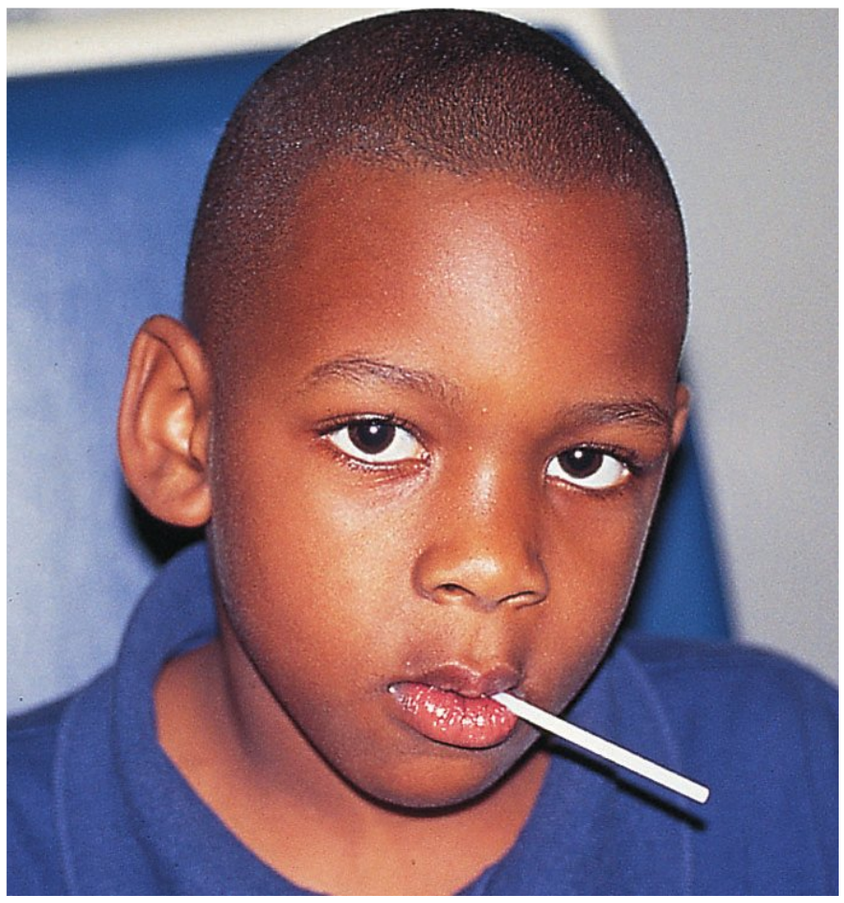
On examination, the patient has a constant 10- to 15-degree left head tilt (Figs. 78–1A and B). He fixes and follows well with either eye, there is no objection to occlusion, and he alternates fixation on prism dissociation testing. In the primary position, an intermittent right hypertropia of 12 prism diopters is measured. The deviation increases to 18 prism diopters in left gaze and decreases to 4 prism diopters in right gaze. A 15 prism diopter right hypertropia is present on right head tilt while a 5 prism diopter right hypertropia is present on left head tilt. Moderate over-elevation of the right eye is noted in adduction (Figs. 78–2A, B, C, and D). Anterior segment and pupillary examination are normal. Cycloplegic refraction is +1.75 +0.75 axis 090 in both eyes. Fundus examination is normal in both eyes, though mild excyclorotation of the left fundus is noted. (Figs. 78–3A and B).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The differential diagnosis of the child with a history of infantile torticollis is extensive but can usually be narrowed on clinical examination. Known causes of infantile torticollis include sternocleidomastoid abnormalities, superior oblique palsy, Brown syndrome, dissociated vertical deviation, nystagmus, uncorrected or improperly corrected refractive errors, homonymous hemianopia, other forms of restrictive or paralytic strabismus, and even unilateral hearing loss.

2. Superior oblique palsy is one of the most common etiologies of infantile torticollis seen in pediatric ophthalmology practice. Superior oblique palsy may be either congenital or acquired. Some believe that congenital superior oblique palsy represents an anatomic laxity of the superior oblique tendon, with the muscle itself functioning normally. Superior oblique palsy, both acquired and congenital, can be bilateral or unilateral. Unilateral superior oblique palsies are much more common. It is important to make the distinction between acquired and congenital superior oblique palsy because acquired superior oblique palsy may require neurologic evaluation including neuroimaging, while congenital superior oblique palsy does not. Two clinical features that help to identify a congenital superior oblique palsy are the presence of a long-term anomalous head tilt and/or facial asymmetry. It is theorized that a chronic head tilt results in structural musculoskeletal changes in the face due to gravity or other unknown factors resulting in permanent structural changes in the face.

3. Brown syndrome is an interesting but uncommon cause of infantile torticollis. It is typically unilateral, but may be bilateral. Like superior oblique palsy, it can occur on a



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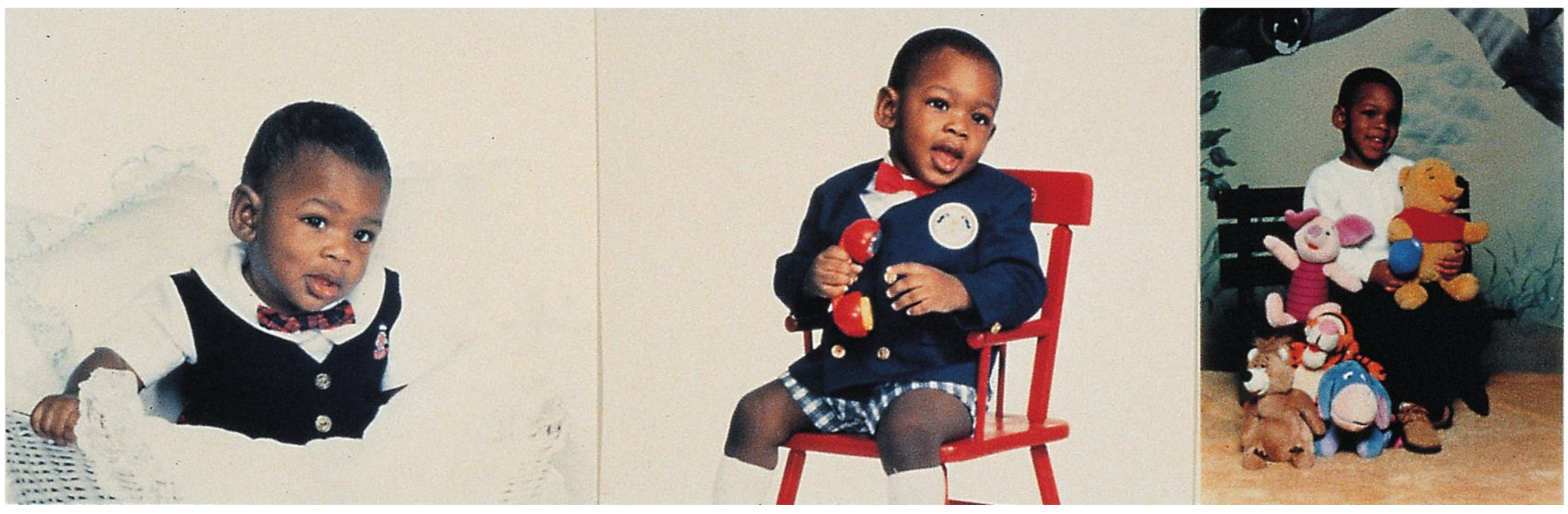
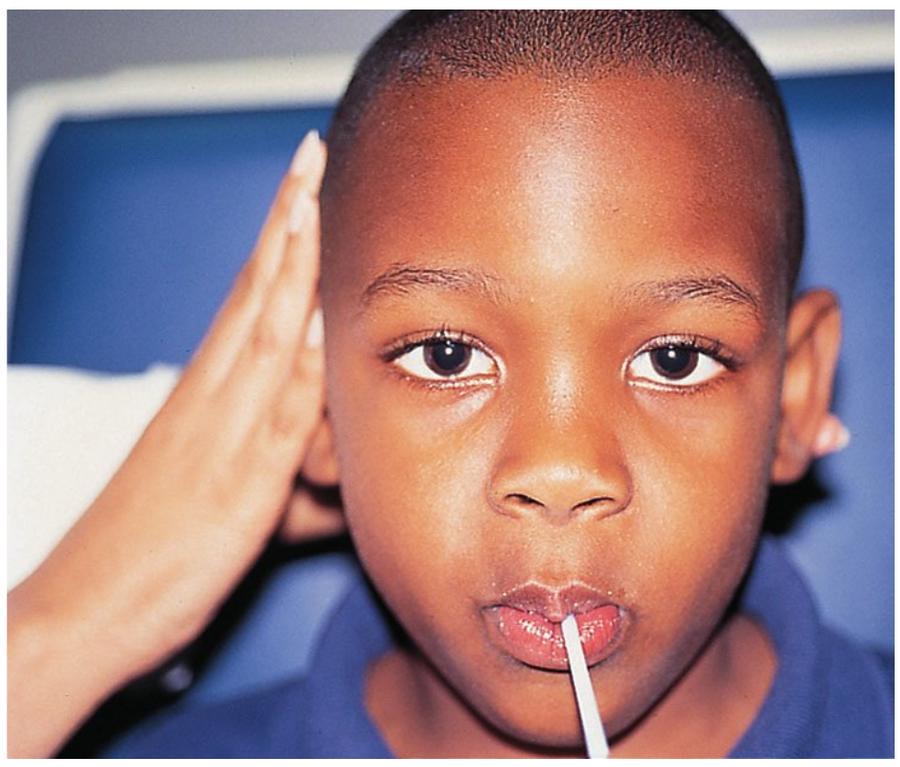


B

FIGURE 78–1 Photographs of the patient (A) at examination and (B) during childhood, demonstrating a left head tilt.

congenital or acquired basis. Brown syndrome results from an anomaly of the superior oblique tendon/trochlea complex that prevents normal elevation of the eye. In classic Brown syndrome, the involved eye elevates poorly or not at all in adduction, demonstrates improved elevation in supraduction, and shows normal or near normal elevation in abduction. A Brown syndrome can typically be differentiated from a superior oblique palsy by two main factors including inability to elevate the eye in adduction, the opposite of what occurs in superior oblique palsy. In addition, the typical child with Brown syndrome adopts a head tilt to the the opposite side, but also adopts a chin-up head posture.

4. Dissociated vertical deviation is an interesting form of strabismus characterized by elevation, abduction, and excyclotorsion of the involved eye when the eye is occluded or the patient inattentive. For largely unknown reasons, some children will adopt an anomalous head posture. The anomalous head posture may be ipsilateral or contralateral to the dissociated vertical deviation. In very small children, it can be difficult to distinguish dissociated vertical deviation from superior oblique palsy. Careful evaluation and repeated examinations, when necessary, will help to make the distinction.
5. Other less common considerations in the diagnosis of infantile torticollis include



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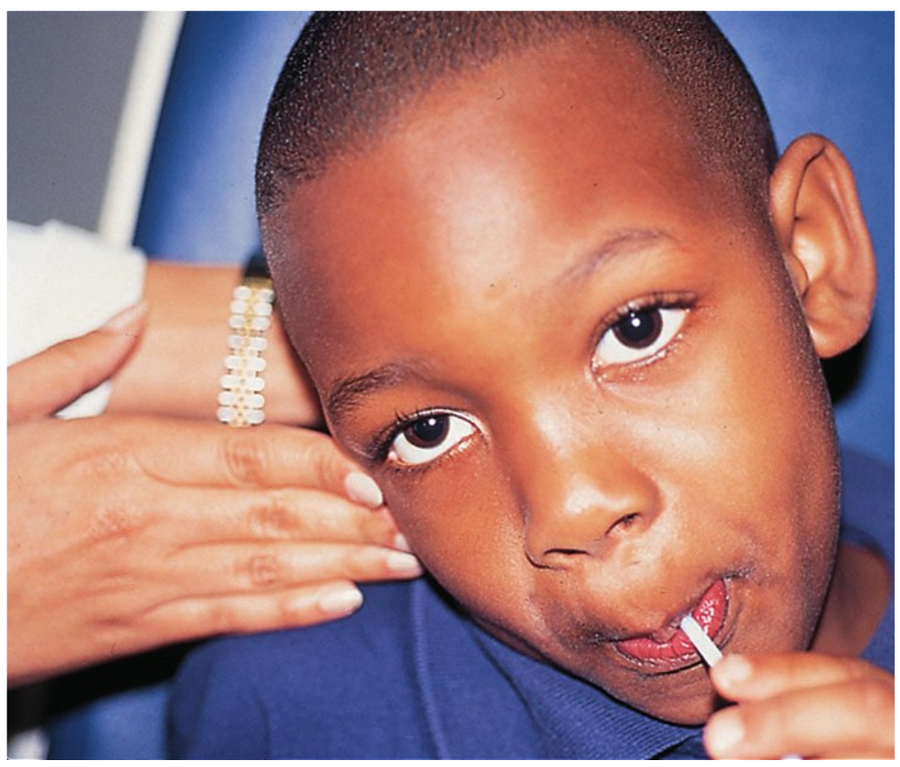

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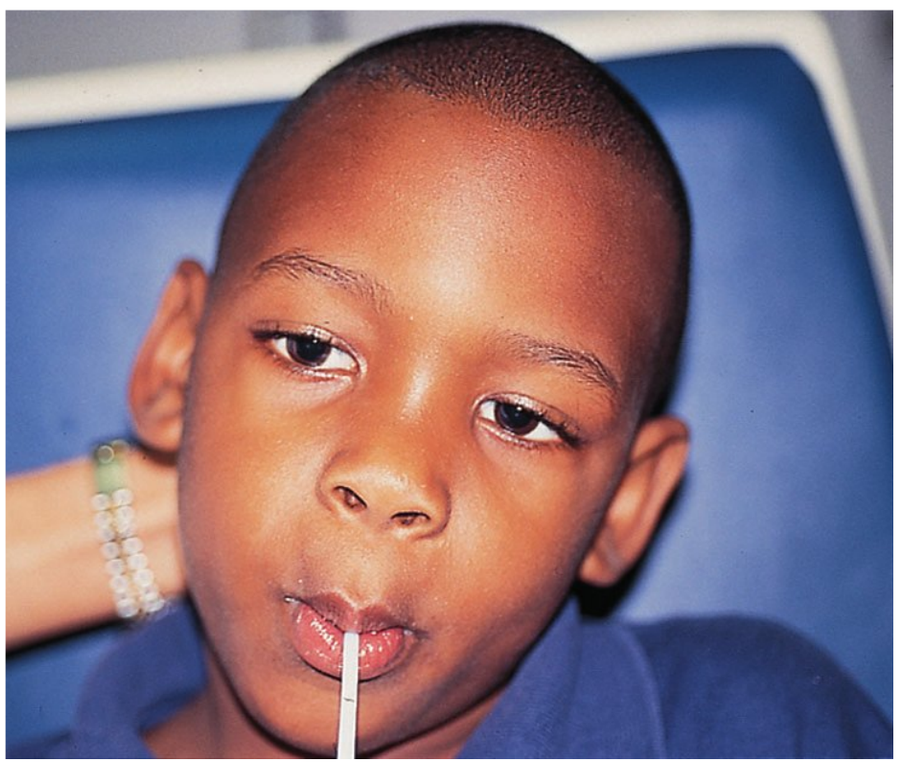


D

FIGURE 78–2 Ocular alignment in (A) the primary position and (B) left gaze and with head tilt to (C) right and (D) left. Note secondary "overaction" of the right inferior oblique muscle with left gaze and hypertropia, which increases with right head tilt. Also note mild facial asymmetry with left side of face smaller compared to the right side of the face.

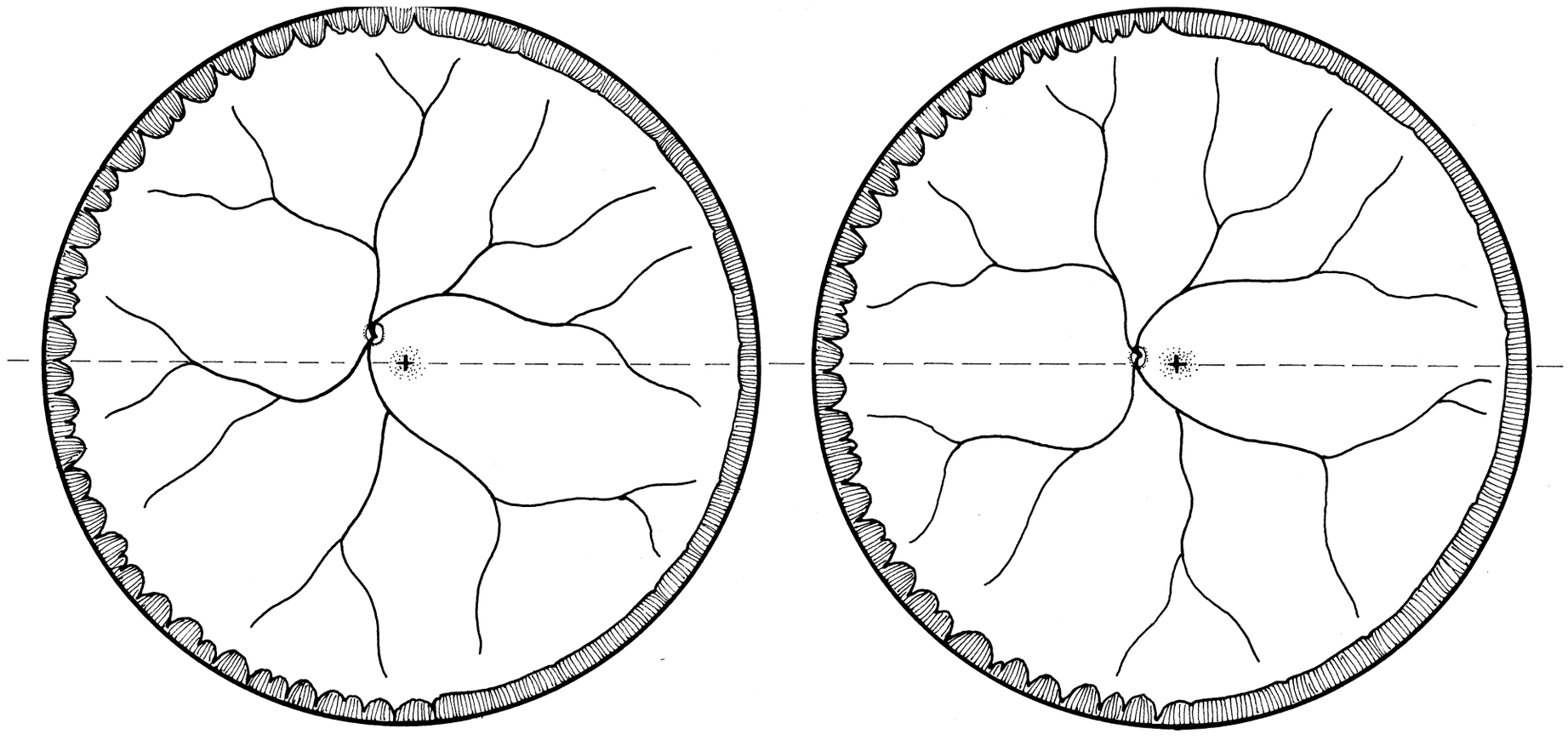
congenital fibrosis syndrome, blowout fractures, orbital tumors, myasthenia gravis, thyroid disease, unilateral hearing loss, and sternocleidomastoid abnormalities.

TEST INTERPRETATION

The child should undergo a comprehensive ocular motility evaluation including a three-step test. The three-step test involves measuring the hypertropia in the primary position, right and left gaze, and on right and left head tilt. By analyzing the ocular alignment in the various positions of gaze, the examiner is able to identify the paretic muscle. The child's alignment in the nine positions of gaze and on right and left head tilt is shown in Figure 78–4.

The family should be asked to bring in a photo album demonstrating photographs of the child in the months and years preceding the examination. (Figure 78–1B). Old photographs should be examined for the presence of a long-term, consistent head tilt. When found, this strongly supports the diagnosis of a congenital superior oblique palsy and renders neuroimaging unnecessary.

If the examiner is not able to demonstrate features of a congenital superior oblique palsy and no other explanation is obvious, the child should undergo neuroimaging of the brain and



A B

FIGURE 78–3 Left fundus drawing demonstrating excyclotorsion. (A) The disc is rotated superiorly relative to the macula because of torsion (in reality, the optic nerve is rotated upward, while the macula maintains its central position for fixation). (B) Compare disc/macula orientation of the normal fundus.

orbit. Central nervous system structural abnormalities and orbital abnormalities can result in superior oblique palsy or a motility pattern that resembles superior oblique palsy, and these conditions should be ruled out if the palsy is thought to be acquired and the etiology is unclear.

DIAGNOSIS

Right superior oblique palsy with chronic left head tilt and mild facial asymmetry.

RHT 4	RHT 12	RHT 20	Right Head Tilt 15 PD
RHT 4	RHT 12	RHT 18	Left Head Tilt 5 PD
RHT 12	RLHT 10	RHT 14	

RHT = right hypertropia

PD = prism diopters

FIGURE 78–4 Prism and cover test results in the diagnostic positions of gaze and on right and left head tilt.

MEDICAL MANAGEMENT

Patients with asymptomatic or minimally symptomatic superior oblique palsy do not need surgical intervention. Many patients with mild superior oblique palsy are able to develop sufficient vertical fusional amplitudes to maintain comfortable single vision most or all of the time without treatment. Such patients, however, may become symptomatic later in life as control of their deviation decreases and diplopia becomes manifest. Patients with small hypertropias and a mild or absent anomalous head posture may benefit from treatment with an appropriate vertical prism. In general, patients do not tolerate prism powers greater than 4 or 5 prism diopters, though there are many exceptions to this rule. Patients with a large degree of ocular torsion are unlikely to be adequately managed with prism therapy.

SURGICAL MANAGEMENT

Indications for strabismus surgery with acquired and congenital superior oblique palsy include improvement of fusion, improvement of an anomalous head posture, and resolution of

diplopia. Surgical treatment of superior oblique palsy typically involves weakening procedures of the ipsilateral inferior oblique muscle such as inferior oblique myectomy or recession. Others are treated with superior oblique strengthening procedures such as a superior oblique tuck, while still others may undergo a combination of procedures including surgery on the superior and inferior oblique muscle of the involved eye as well as rectus muscle surgery. Superior oblique strengthening procedures are typically reserved for patients with lax superior oblique tendons.

REHABILITATION AND FOLLOW-UP

Parents should be advised at the time of surgery of the potential for an over- or under- correction and the potential need for additional surgery in the future. Patients who have undergone a superior oblique tuck often develop a mild to moderate Brown syndrome with limitation of elevation in adduction following surgery. This problem typically improves or resolves with time, but may persist. In children, amblyopia may have developed prior to surgery or may develop following surgery if ocular misalignment persists or later develops. Therefore, children with superior oblique palsy should undergo periodic ophthalmologic evaluations with particular attention to fusion, stereopsis, and visual acuity testing to detect, prevent, and treat amblyopia.

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Case 79

ANIRIDIA

David K. Coats, M.D.

HISTORY

A 9-month-old boy is referred to his ophthalmologist with a history of "jiggling eyes" and large pupils, both noted during the first month of life. The child closes his eyes in bright sunlight and does not appear to see as well as his two older siblings. The boy was born at term, the mother received prenatal care, and there were no perinatal complications. The child's medical history is notable for a hypospadias repair 2 months earlier and for developmental delay. He has two healthy siblings and two healthy parents with no significant family history of ophthalmologic or medical problems.

On examination, the child appears to fix and follow, but the fixation behavior is abnormal. A low amplitude/high frequency horizontal pendular nystagmus is noted. Examination reveals peripheral corneal opacification and vascularization. The child appears to have only a very small peripheral remnant of iris and an anterior pyramidal cataract is noted in both eyes (Figs. 79–1A and B). Retinal examination is notable for the absence of an obvious umbo or foveal pigmentation (Fig. 79–2). The child's parents and two older siblings were examined and found to have normal ophthalmologic examinations.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

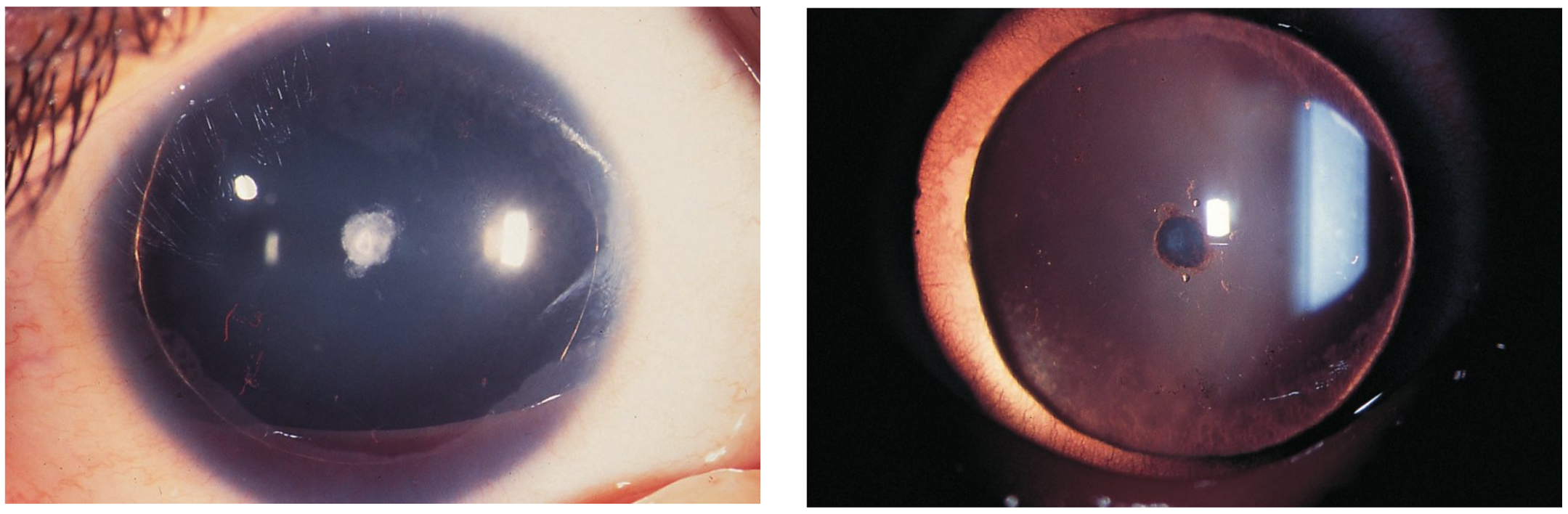
1. The syndrome of aniridia is a rare cause of infantile nystagmus. It is a panocular problem that occurs with a frequency of 1 in 50,000 to 100,000 live births. Multiple ophthalmological defects may be present including cataracts, glaucoma, corneal opacification and vascularization, ectopia lentis, foveal hypoplasia, colobomas, and nystagmus. It can occur as an autosomal dominant or sporadic condition.

2. The differential diagnosis of infantile nystagmus is quite extensive, but can be broadly divided into three categories, including sensory defect nystagmus, motor defect nystagmus (ie, idiopathic infantile nystagmus, congenital motor nystagmus), and neurological defect nystagmus. Neurological defect nystagmus is usually obvious based upon the presence of other neurologic abnormalities. Motor defect nystagmus is a diagnosis of exclusion. The majority of cases of infantile nystagmus are due to a severe bilateral afferent abnormality and are thus classified as sensory defect nystagmus.

3. Other more common causes of sensory defect nystagmus can usually be ruled out on the basis of clinical examination. The most common include albinism, optic nerve hypoplasia, achromatopsia, and other congenital retinal abnormalities.

4. The genetics of aniridia are quite interesting. The condition can occur as an autosomal dominant condition with variable penetrance or as a sporadic condition. Autosomal dominant forms of the condition are due to a defect in the PAX-6 gene. Mutations in this gene typically cause translational terminations by nonsense and frameshift mutations and by splice errors. Haploinsufficiency of the gene product has been suggested as the cause of the aniridia phenotype.

5. Other cases of aniridia occur on a sporadic basis with no family history. As many as 25 to 40% of infants with sporadic aniridia will develop a Wilms' tumor, typically during the first few years of life. Children who are at greatest risk of developing a Wilms' tumor in association with sporadic aniridia are those with concurrent congenital genitourinary abnormalities and mental retardation. The complex of Wilms' tumor, aniridia, genitourinary abnormalities, and retardation has been referred to as the WAGR syndrome.



A B

FIGURE 79–1 (A) Slit-lamp photograph demonstrating multiple anterior segment abnormalities, including corneal pannus, severely hypoplastic iris, and anterior pyramidal cataract. (B) View with retroillumination. (Photographs courtesy of Jim Shigley, Certified Ophthalmic Photographer.)

TEST INTERPRETATION

Issues that must be considered in children with aniridia are the potential for development of other ophthalmologic problems and the potential development of serious systemic problems such as Wilms' tumor. Consultation with a geneticist and a pediatrician is often indicated in the management of children with aniridia.

1. In autosomal dominant cases, multiple defects in the PAX-6 gene have been identified. The parents and siblings of affected children should be evaluated for obvious and subtle signs of aniridia. Subtle signs of aniridia in affected family members include absence of the iris collarette and eccentric pupils and on angiography, a decreased retinal foveal avascular zone and incomplete iris collarette. Deletion of a portion of the short arm of chromosome 11 (11p13 deletion) is frequently present in children with sporadic aniridia. Children with such a deletion are more likely to have the WAGR syndrome and are at high risk for Wilms' tumor. This patient has an 11p13 deletion.

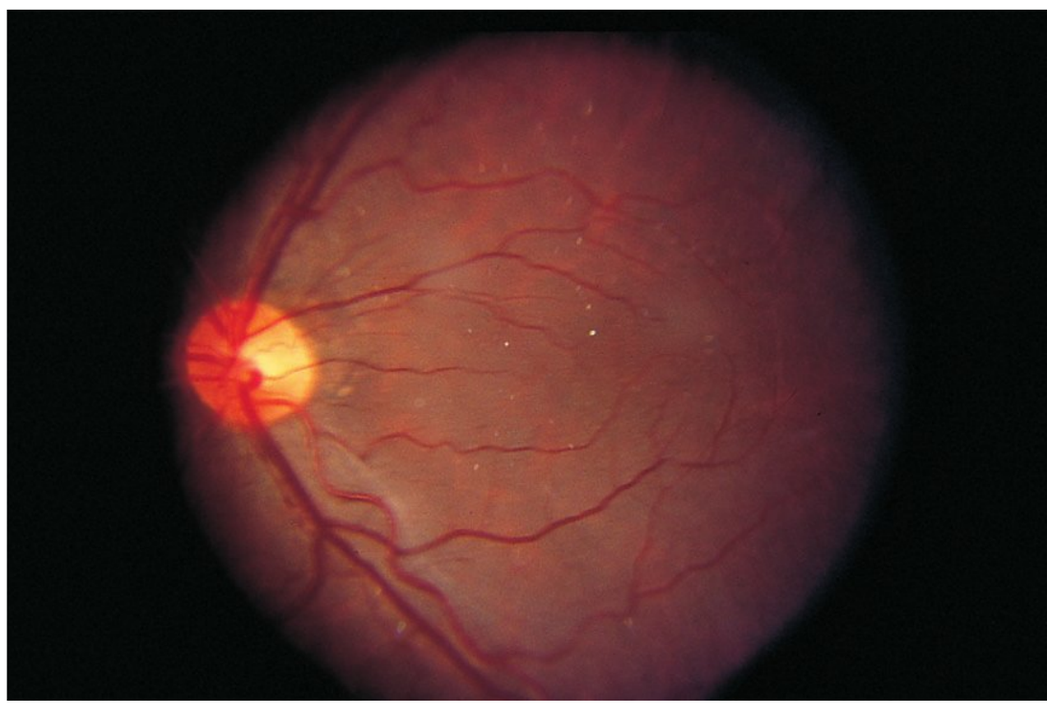


FIGURE 79–2 Fundus of patient demonstrating foveal hypoplasia. (Photograph courtesy of Jim Shigley, Certified Ophthalmic Photographer.)

2. Initial screening and periodic follow-up abdominal ultrasound evaluation and abdominal physical examination are recommended in aniridic children at risk for Wilms' tumor (Fig. 79–3). The frequency and duration of these examinations is controversial, but in general, most affected children will develop Wilms' tumor by the age of 3 years. Some have questioned the utility of periodic ultrasonography of the abdomen based upon the fact that Wilms' tumor is a very fast-growing tumor and abdominal ultrasound examinations spaced more than 1 to 2 months apart are unlikely to detect the disease at its earliest stage. Additionally, some argue that the tumor responds readily to treatment such that diagnosis at an early stage may not

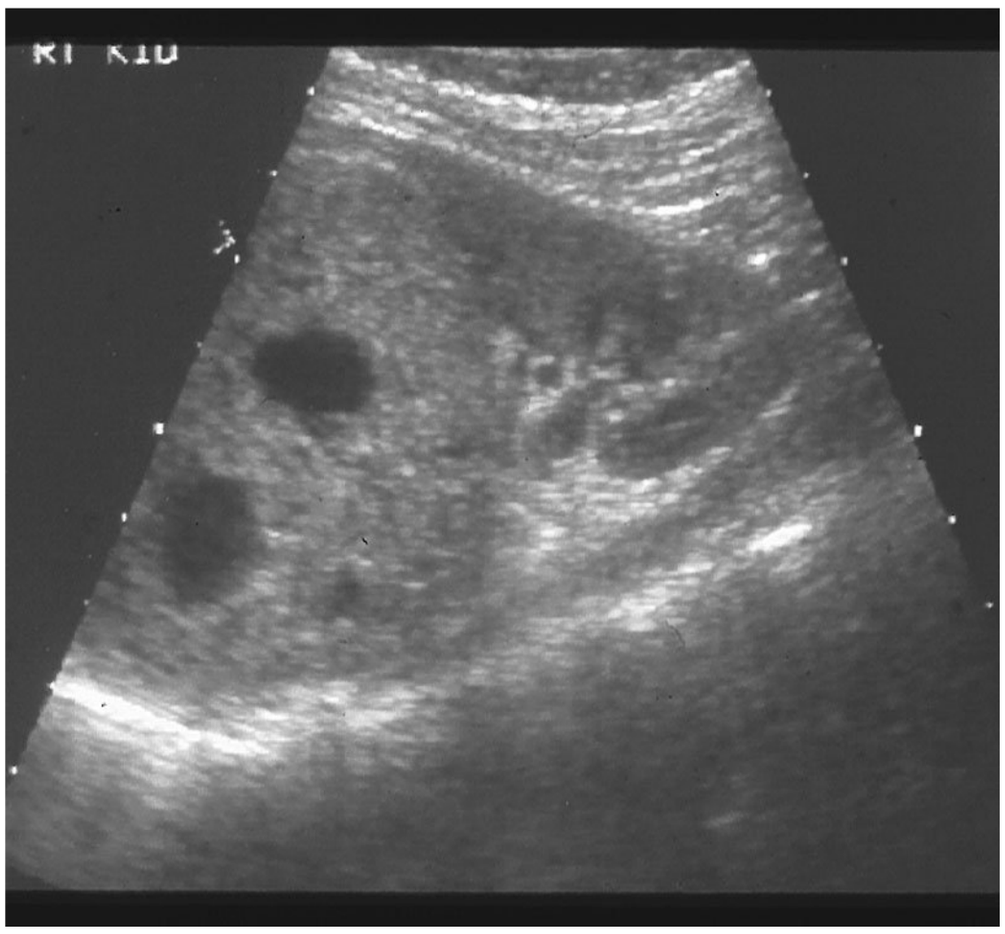


FIGURE 79–3 Abdominal ultrasound demonstrating a renal mass consistent with a Wilm's tumor. The hypoechoic (black) areas are areas of necrosis. (Photograph courtesy of Scott Dorfman, M.D., Houston, TX.)

significantly affect the long-term survival. A baseline abdominal ultrasound of this child was normal.

DIAGNOSIS

Sporadic aniridia associated with developmental delay and genitourinary abnormalities. He has three components of WAGR syndrome and is at high risk for developing Wilms' tumor. An 11p13 deletion is present.

MEDICAL MANAGEMENT

The child's symptoms of photophobia can be improved by prescription of sunglasses or shaded contact lenses. Even though the child appears to have reasonable vision at this point, progressive corneal opacification and vascularization, development of progressive cataracts, and development of glaucoma can result in future vision loss. The child should undergo a careful screening ophthalmological examination including efforts to rule out glaucoma. Abdominal ultrasounds should be obtained at regular intervals until approximately 3 years of age. If a renal abnormality is noted on abdominal ultrasound, Wilms'tumor should be suspected. Further evaluation with magnetic resonance imaging (MRI) is done if an ultrasound abnormality is found, and the child should be referred for biopsy if findings consistent with Wilms'tumor are noted on magnetic resonance imaging (MRI) scan. If Wilms' tumor is confirmed on histopathologic examination, a pediatric oncologist should be consulted.

SURGICAL MANAGEMENT

While this patient does not presently demonstrate ophthalmologic abnormalities that require surgical care, the development of progressive cataracts, glaucoma, and/or progressive corneal opacification are strong possibilities in the future. Ophthalmologic surgery on patients with aniridia is fraught with complications, and surgery should only be entertained after careful consideration of the risk/benefit ratio and after exhausting nonsurgical treatment modalities.

REHABILITATION AND FOLLOW-UP

Long-term follow-up for systemic abnormalities such as Wilms' tumor have already been discussed. The child should undergo periodic ophthalmological screening examinations to detect the presence of progressive ocular disease as described above. Early childhood educational intervention and a low-vision evaluation should be done as early in the child's life as possible. Intervention in the form of preemptive education efforts and low-vision aids can prove helpful in almost any patient with vision abnormalities in childhood.

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Case 80

RETINOPATHY OF PREMATURITY

Evelyn A. Paysse, M.D.

HISTORY

An 11-week-old, former 24-week estimated gestational age premature girl presented for consultation. She is due for another retinopathy of prematurity (ROP) screening examination. Her last examination occurred 2 weeks ago and demonstrated Stage 1 ROP in Zone 2, with no Plus Disease. Since this last examination, she has developed sepsis and respiratory compromise, requiring intravenous antibiotics and reintubation/ventilatory support. Her birth weight was 650 grams. She has anemia of prematurity and had an episode of necrotizing enterocolitis 4 weeks ago.

Examination reveals a frail-appearing infant girl who is intubated. She is receiving 50% oxygen. She blinks briskly to the light of the indirect ophthalmoscope with either eye. On fundus examination, she is found to have significant neovascular tissue in the equatorial retina for 360 degrees with severe dilation and tortuosity of the posterior pole retinal vessels (Fig. 80–1).

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Differential diagnosis: The differential diagnosis of ROP is not long. It is rarely confused with other disease entities. The differential diagnosis includes familial exudative vitreoretinopathy, Eales' disease, and Norrie's disease. Infants with these conditions are typically term infants, hence there is little chance of confusion with ROP.
2. Demographics: ROP affects roughly 40,000 neonates in the United States annually. As many as 600 children suffer severe visual impairment because of the disease each year. ROP affects males and females equally. The severity of ROP may be greater in some Caucasian populations.
3. Pathogenesis: ROP is a vasoproliferative disorder of the retina that affects premature infants. It can cause retinal detachment or cicatricial retinal folds leading to severe visual impairment or blindness. The peripheral retina in premature infants is avascular and relatively ischemic. This ischemic retina produces angiogenesis factors to stimulate blood vessel growth, which often leads to abnormal neovascularization of the retina. This is known as ROP. As the retinal neovascularization occurs, it can extend into the vitreous, producing retinal traction. If the traction is strong enough, a retinal detachment can occur. This neovasular tissue is fragile and can bleed easily into the vitreous.
4. Normal retinal vascularization: Normal retinal vascularization begins at 16 weeks postconceptional age. The blood vessels grow out from the optic disc toward the periphery. The retina attains mature retinal vascularization in the nasal retina at 8 months postconceptional age and in the temporal retina at 10 months postconceptional age.
5. ROP risk factors: The most important risk factors associated with ROP are low birth weight and low estimated gestational age and high oxygen exposure. Other possible risk factors include maternal bleeding, prolonged intravenous nutrition, hypocarbia, prolonged ventilation, multiple birth status, intraventricular hemorrhage, hypotension, anemia, sepsis, and necrotizing enterocolitis. It is very difficult to isolate individual factors, because affected neonates have multiple medical problems occurring simultaneously.
6. Classification of ROP.

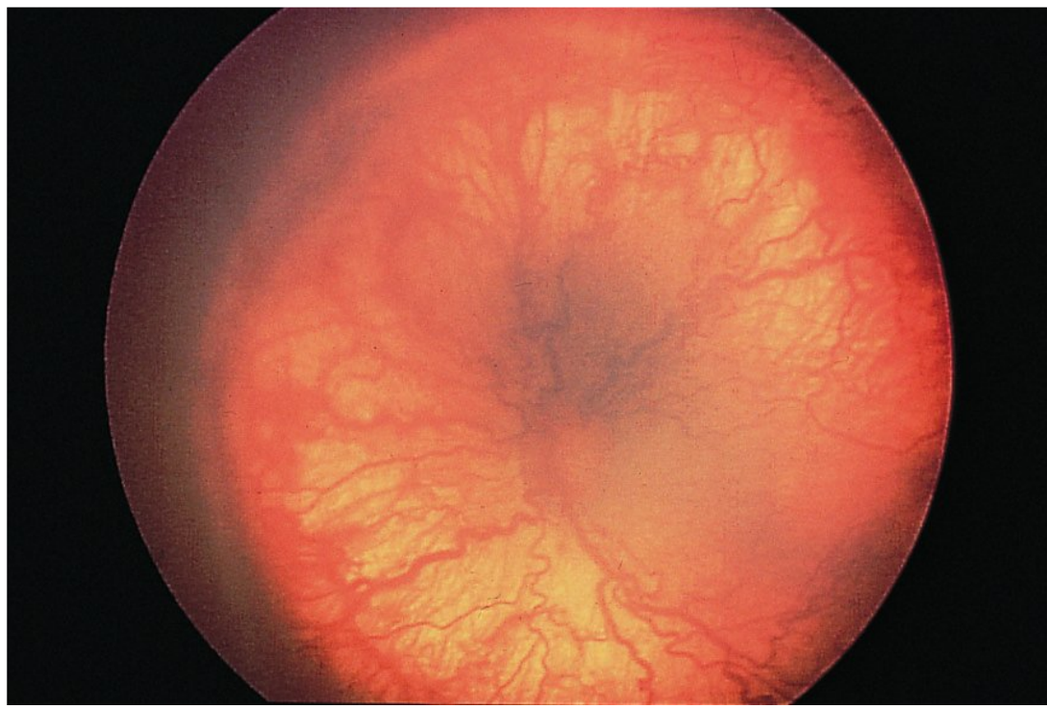

FIGURE 80–1 The retina examined demonstrates Stage 3 ROP with dilation of posterior pole vessels (Plus Disease).

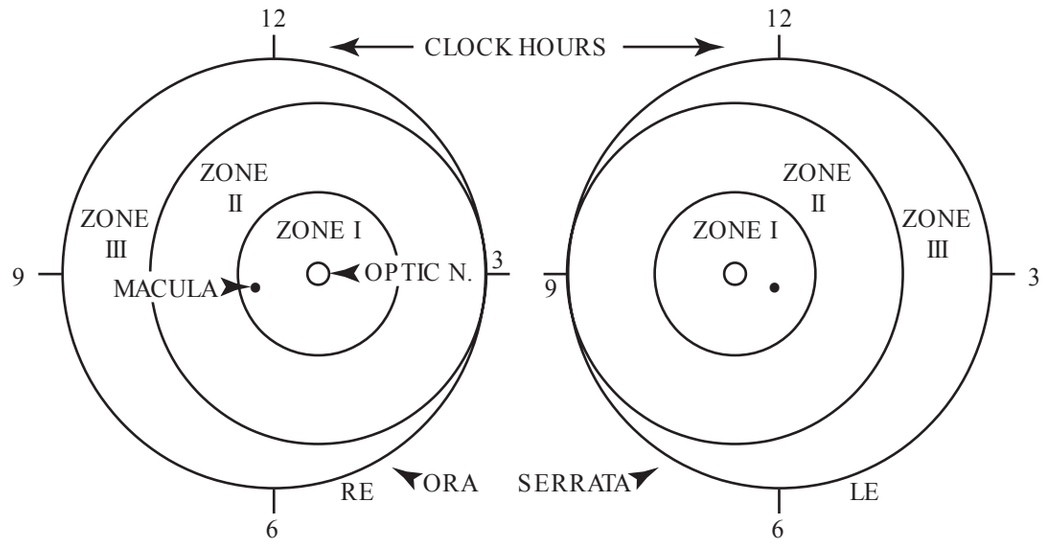

FIGURE 80–2 Zone diagram for ROP, from the International Classification. (From Lee DA and Higginbotham EJ. *Clinical Guide to Comprehensive Ophthalmology*. New York: Thieme, 1999:581, with permission.)

a. History and development: Prior to 1987, ophthalmologists classified ROP by a number of different systems. Because of these different classification systems, it was difficult to compare various study outcomes or decide on common grounds for treatment. In 1987, the International Classification for ROP (ICROP) was published; it has become the preferred classification system. This classification system utilizes several different concepts. The location of disease in the retina is specified by a series of zones. The extent of retinal involvement is recorded by clock hours, and finally, the severity of the disease is recorded according to a system of stages of vascular abnormalities observed. Additionally, the presence or absence of posterior pole retinal vascular dilation and tortuosity, so-called Plus Disease, is noted (Fig. 80–2 and Table 80–1).

b. Zones: The retina is divided into three zones, all centered on the optic nerve. Zone 1 is the area encompassed by a circle with a radius extending from the optic nerve twice the distance between the optic nerve and the macula circumferentially. Zone 2 comprises a doughnut-shaped area of retina extending from Zone 1 to the nasal ora serrata and equally around from the optic nerve to the temporal retina. The remaining temporal crescent of retina is classified as Zone 3.

c. Extent: The extent of retinal involvement is recorded by dividing the retina into clock hours, with the most superior

TABLE 80–1 **International Classification of Retinopathy of Prematurity**

Location	
Zone I	Posterior pole, 2 disc-macula distances around optic nerve
II	Temporal equator and nasal ora serrata
III	Residual crescent anterior to II in temporal periphery
Extent	
Clock hours	
Stage	
1	Demarcation line
2	Ridge
3	Ridge with extraretinal fibrovascular proliferation
4a	Partial retinal detachment excluding the macula
b	Partial retinal detachment including the macula
5	Total retinal detachment
Plus disease	
	Posterior retinal vascular dilation and tortuosity
	Iris engorgement
	Vitreous haze

retina being designated as the 12-o'clock position and going around in clockwise fashion. The number of clock hours of each stage is recorded.

d. Stages: The stage of ROP describes the severity of the vascular abnormalities observed. Stage 1 signifies a demarcation line between vascular and avascular retina. Stage 2 is a fibrovascular ridge occurring between the vascular and avascular retina. Stage 3 is a ridge with extraretinal fibrovascular proliferation. Stage 4 comprises a subtotal retinal detachment; Stage 4A is extrafoveal and Stage 4B includes the fovea. Stage 5 is a total retinal detachment.

e. Plus Disease: Plus Disease describes dilation and tortuosity of the posterior pole retinal vessels. It indicates that the disease is entering a more severe stage and the risk of vision loss is very high.

f. Threshold ROP: Threshold ROP is diagnosed when there is Stage 3 ROP in Zone 1 or 2 for five or more contiguous clock hours or eight cumulative clock hours, in the presence of Plus Disease.

7. Screening criteria: The current screening guidelines for ROP are included in a consensus statement by the American Academy of Ophthalmology, the American Association of Pediatric Ophthalmology and Strabismus, and the American Academy of Pediatrics. These criteria are:

a. All infants with a birth weight of 1500 grams or less, or with a gestational age of 28 weeks or less, as well as those infants over 1500 grams with an unstable clinical course felt to be at high risk by their attending pediatrician or neonatologist.

b. These examinations should be carried out by an ophthalmologist with experience in the examination of preterm infants.

c. The initial examination should be done between 4 and 6 weeks of chronological age or between 31 and 33 weeks postconceptional age. Follow-up examinations for patients with Zone 2 ROP or vascular development should occur at approximately 2- to 4-week intervals. Follow-up examinations for patients with Zone 1 ROP or immature retinal vascularization should occur every 1 to 2 weeks. These follow-up examinations should continue until normal vascularization proceeds to Zone 3 or the risk of attaining threshold conditions has passed.

d. Infants with threshold ROP should be considered candidates for ablative therapy with laser or cryotherapy of at least one eye within 72 hours of diagnosis.

TEST INTERPRETATION

1. Retinal examination: The most important test for an infant at risk for ROP is the appropriately timed retinal examination with scleral depression when needed to visualize the peripheral retina. This patient had mild ROP (in Zone 2) 2 weeks prior to this examination. On the present examination, the infant has Stage 3 retinopathy (extraretinal neovascular tissue) for more than five contiguous clock hours, with Plus Disease (dilation and tortuosity of the posterior pole vessels). This, by definition, is threshold ROP.

2. Important historical features: Factors possibly leading to higher risk in this child include the new onset sepsis since her last examination and the worsening of her respiratory status requiring reintubation and supplemental oxygen. The most important risk factors for ROP in this infant are her extreme prematurity and low birth weight. The overall health status of a premature infant and the postconceptional age should, however, both be considered when deciding the interval for follow-up examination.

3. Postconceptional age: The mean postconceptional age for threshold ROP is 37 weeks overall, but is a few weeks earlier for extremely premature infants like this one, whose postconceptional age at threshold diagnosis is 35 weeks. This infant's follow-up schedule was appropriate because she had

mild ROP 2 weeks prior and was stable at that point. The decrease in her overall health status may have contributed to the rapid progression of the retinopathy and underscores the importance of regular timely follow-up.

4. Prognosis: Prognosis after treatment for ROP depends again on the severity of the threshold ROP. Zone 1 threshold ROP holds a much more guarded prognosis compared with Zone 2 threshold disease. Zone 1 patients are at increased risk of late retinal detachment as well.
5. Ultrasonography: Ultrasonography is sometimes utilized in patients who have had a vitreous hemorrhage and visibility of the retina is poor. During ultrasonography, the examiner is attempting to rule out a retinal detachment.

DIAGNOSIS

Threshold ROP, both eyes.

MEDICAL MANAGEMENT

Many different medical treatment modalities have been tried to manage patients with ROP. Vitamin E, ultraviolet light, and increasing oxygen saturation at prethreshold status have all been tried, with unproven success. Most ophthalmologists feel that these therapies have little utility. Therefore, medical management, other than high quality routine neonatal care, is not the current standard of care.

SURGICAL MANAGEMENT

When a child has threshold ROP, the current standard of care is to ablate the avascular retina with either cryotherapy or laser photoablation. The Multicenter Trial of Cryotherapy for ROP Study in the 1980s showed an approximately 50% reduction of "poor outcome," defined as retinal detachment or posterior retinal fold, in the eyes treated with cryotherapy compared with eyes that went untreated.

Laser photoablation has recently become an increasingly popular treatment modality. Laser ablates the retina as cryotherapy does but has fewer postoperative side effects of conjunctival inflammation, chemosis, and pain. The risks of cryotherapy include vitreous, intraretinal, and subretinal hemorrhage, infection, conjunctival chemosis, apnea, and bradycardia. Potential complications of laser photoablation include cataract and subretinal, intraretinal, and vitreous hemorrhage. Most recent studies have shown the percentage of poor outcomes with laser, as defined in the Cryo-ROP study, to be only 10 to 12% overall. This may be because (1) ophthalmologists are treating ROP earlier, (2) the laser treatment may be more effective, or (3) overall improvement in neonatal care has affected the retinopathy's response to treatment.

REHABILITATION AND FOLLOW-UP

After retinal ablation procedures, the infant should be examined frequently until the disease has regressed. The examiner is evaluating the eyes for involution of the extraretinal fibrovascular proliferation and resolution of Plus Disease. In some unfortunate cases, as involution of the ROP occurs, contraction of this cicatricial tissue causes a traction retinal detachment. This retinal detachment can be partial or total. In some cases, despite adequate laser or cryotherapy treatment, retinal detachment occurs from continued proliferation of ROP. If either of these occurs, consultation with a retinal specialist should ensue immediately for consideration of scleral buckling and/or pars plana vitrectomy procedures.

Ninety percent of ROP resolves spontaneously. Approximately 85 to 90% of ROP treated for threshold disease resolves with good anatomical results. Whether ROP resolves completely or not, long-term follow-up of the child is necessary. The retina should be evaluated at least yearly in the child treated for ROP and slightly less frequently for the child who did not require treatment. It is unknown whether these patients will develop atrophic retinal holes or other retinal complications over their life span.

Premature infants are at risk of developing other serious ophthalmologic problems, including amblyopia, strabismus, and severe refractive error including myopia, astigmatism, and anisometropia. Premature infants should have an examination around the time of their first birthday to evaluate for these entities and, if present, they should be treated accordingly.

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Case 81

CHILDHOOD ESOTROPIA

Evelyn A. Paysse, M.D.

HISTORY

A 5-year-old girl with a history of crossed eyes since 2 months of age presents for an examination. She underwent strabismus surgery at 8 months of age. Her mother reports that her eyes were straight following surgery, until recently when her left eye has been noted to intermittently drift inward, especially when she is tired. She has never been treated with occlusion therapy. Her current glasses are at least 1 year old. Her past medical history is otherwise noncontributory. Family history is notable for a sister with esotropia that required surgical intervention.

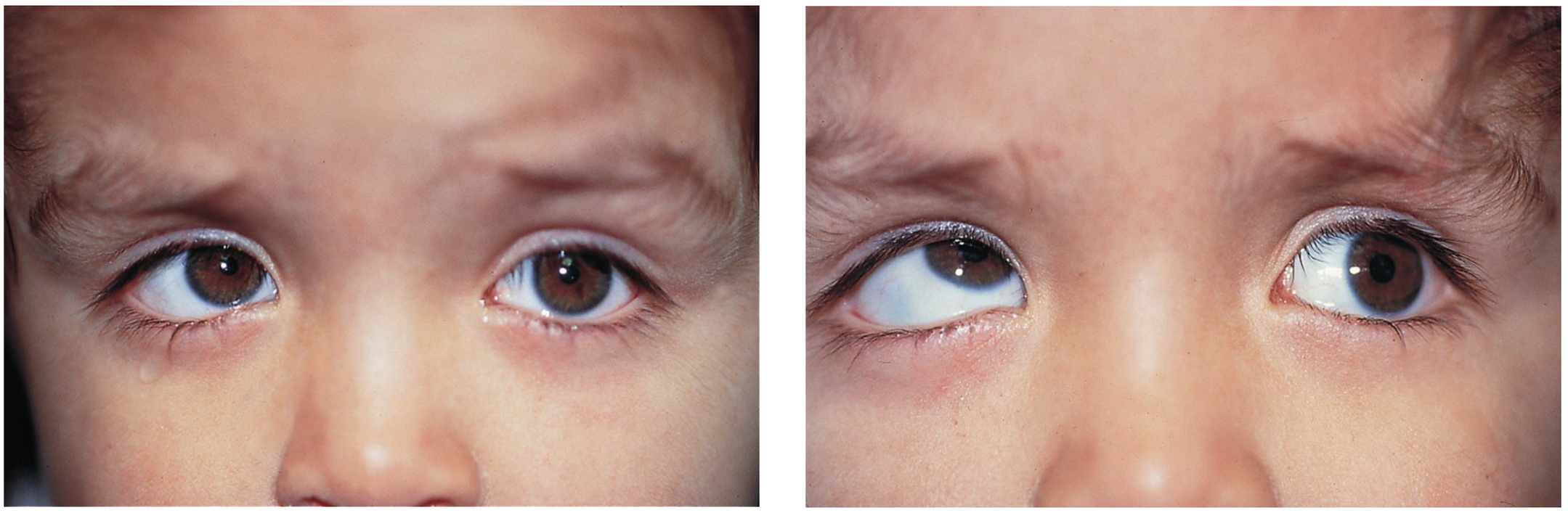
On examination, the child's visual acuity, with her current spectacle correction, is 20/30 OD and 20/50 OS. Her current spectacle prescription is +2.00 OD and +2.50 OS. Motility examination with spectacle correction demonstrates an intermittent esotropia of 5 prism diopters at distance with a left-dissociated vertical deviation of 6 prism diopters. On version testing, moderate inferior oblique muscle overaction is noted in both eyes (Figs. 81–1A, B). A V-pattern is present with esotropia in downgaze increasing to 20 prism diopters and decreasing in upgaze to 5 prism diopters. At near, an intermittent esotropia of 20 prism diopters is seen. Stereopsis testing reveals 3000 seconds of arc stereopsis on the Titmus stereo fly test. Cycloplegic refraction is +3.00 sphere and +3.75 sphere in the right and left eyes, respectively. Optokinetic nystagmus testing is asymmetric, demonstrating a normal response on temporal-to-nasal testing, but a poor nasal-to-temporal response in both eyes. The remainder of the ophthalmologic examination is normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Differential diagnosis. Childhood esotropia can be due to many different entities. It is helpful to divide esotropia into comitant and incomitant deviations. Please see Figure 81–2 and Table 81–1 for differential diagnosis of childhood esotropia.

2. History: It is important when evaluating a child with esotropia to obtain a good history. The examiner must determine the onset of the esotropia, as this will aid in defining the esotropic entity. If the onset is before 6 months of age, the entity could be infantile esotropia; however, accommodative esotropia has also been reported as early as 3 months of age. A host of other esotropia syndromes may also have onset in the first 6 months of life, including Duane syndrome and Moebius' syndrome.

   The quality of the esotropia is also important to elicit from the parents. Intermittent esotropia and esotropia that is greater at near than at distance are more likely to be accommodative in nature. If the deviation is worse in certain positions of gaze, all comitant etiologies will be eliminated from the differential diagnosis. An anomalous head posture with esotropia implies an incomitant (ie, restrictive or paralytic) strabismus such as occurs with a sixth nerve palsy, Ciancia's syndrome (infantile esotropia with nystagmus in abduction), nystagmus blockage syndrome, early onset homonymous hemianopia, Type 1 Duane syndrome, or Moebius' syndrome (Table 81–1).



A B

FIGURE 81–1 (A) Five-year-old child with esotropia. (B) Inferior oblique muscle overaction of the right eye is demonstrated.

Finally, it is also important in the history to determine if there were any preceding events to the esotropia such as a febrile illness, head trauma, or neurologic event. All of these entities can be associated with a sixth nerve palsy. Family history is also important to discuss because strabismus has been shown to be hereditary.

3. Associated ocular motility abnormalities: Inferior oblique muscle overaction, dissociated strabismus complex, A- and V-patterns, and latent nystagmus are other motility abnormalities associated with early onset strabismus, most commonly in association with infantile esotropia. Inferior oblique muscle overaction is diagnosed from the version examination when over-elevation of the eye in adduction occurs. Dissociated strabismus complex is diagnosed with cover testing. The eye under the occluder will elevate, abduct, and excyclotort. Any of these components can predominate and not all components are necessary to have dissociated strabismus complex. If a vertical deviation predominates, it is called dissociated vertical deviation and if a horizontal deviation predominates, it is called dissociated horizontal deviation. Dissociated strabismus complex is often more severe in an amblyopic eye. A- and V-patterns occur when the deviation in upgaze and downgaze differ significantly. An A-pattern esotropia is present when the esotropia is greater in upgaze than downgaze by 10 or more prism diopters. A V-pattern is present when the deviation in upgaze is less than in downgaze by 15 or more prism diopters. Latent nystagmus is present only when one eye is occluded. It is most commonly associated with infantile esotropia.
4. Amblyopia: Amblyopia is commonly associated with strabismus. In strabismus, amblyopia develops in children secondary to the ability to suppress the image in the deviating eye. This suppression is done to avoid diplopia and confusion (see Case 71).

TEST INTERPRETATION

Clinical examination of a strabismic patient is the key to diagnosis. This section will concentrate on the most important parts of the ophthalmologic examination for a patient with esotropia.

1. Stereopsis testing: Stereopsis testing should be the first part of any ophthalmologic examination for a strabismic patient. It will aid in determining the onset of the strabismus and in prognosticating stability of the deviation over time. Stereopsis is the highest form of binocular cooperation. It is the ability to fuse two disparate images into a single impression in depth. With good stereopsis a patient is likely to maintain a more stable

ESOTROPIA

- Inborn error of fusion
  - Infantile esotropia
  - Esotropia with abduction nystagmus, (Ciancia's syndrome)
  - Nystagmus blockage syndrome
- Inborn potential for normal fusion
  - Mechanical
    - Congenital
      - Duane syndrome
      - Congenital fibrosis syndrome
    - Acquired
      - Thyroid related ophthalmopathy
      - Inflammatory
      - Traumatic, blowout fracture
      - Iatrogenic
  - Neurologic
    - Motor
      - Nuclear
        - Congenital
          - Duane I
          - Duane III
          - Moebius syndrome
        - Acquired
          - Sixth nerve palsy (traumatic, microvascular, tumor)
      - Supranuclear
        - Congenital
          - Refractive accommodative esotropia
          - Nonrefractive accommodative esotropia
        - Acquired
          - Central disruption of fusion (Horror fusionus)
      - Postsynaptic
        - Myasthenia gravis
      - Mitochondrial
        - Progressive external ophthalmoplegia
    - Sensory Esotropia

TABLE 81–1 **Differential Diagnoses of Childhood Esotropias**

Incomitant Esotropia
Neurologic
Sixth nerve palsy
Congenital
Acquired (tumor, traumatic, microvascular, inflammatory)
Duane syndrome (Type 1 or 3)
Myasthenia gravis
Progressive external ophthalmoplegia
Moebius' syndrome
Restrictive
Thyroid related ophthalmopathy
Congenital fibrosis syndrome
Duane syndrome (Type 1 or 3)
Iatrogenic (eg, postsurgical)
Posttraumatic (eg, medial orbital wall fracture)
Comitant Esotropias
Infantile esotropia
Ciancia's syndrome
Nystagmus blockage syndrome
Accommodative
Refractive
Nonrefractive (high AC/A)
Horror fusionus
Sensory esotropia

alignment. Poor stereopsis implies early onset strabismus.

2. Motility:

a. Alignment at distance and near. The strabismic deviation must be measured both at distance and near, with and without glasses. If the esotropia is worse at near than distance, especially if intermittent, an accommodative esotropia is the most likely etiology, though this does not always hold true. If the deviation is worse at distance than at near, then divergence insufficiency type esotropia is present. This is often a sign of a sixth nerve paresis, and neuroimaging is indicated to rule out hydrocephalus or an intracranial mass (tumor, arteriovenous malformation, inflammatory lesion, etc.). During this examination, dissociated vertical deviation is also evaluated. Our patient has a constant esotropia that was minimally worse at near than at distance, with dissociated vertical deviation in the left eye. These findings are consistent with infantile esotropia or partially accommodative esotropia.

b. Ductions/versions: Ductions and versions help to distinguish comitant from incomitant deviations. Versions are defined as binocular rotations of the eyes. The examiner has the patient follow a target with his eyes into the six cardinal positions of gaze to evaluate the yoke muscles and oblique muscle function. Next, the examiner has the patient follow the target into upgaze and downgaze to evaluate for an A- or V-pattern. Ductions are defined as monocular rotations of the eye. The examiner has the patient follow a target with one eye covered into the same gaze positions as for versions. If versions are normal, there is no need to test ductions. If, however, there is an incomitant deviation on version testing, ductions should be done to help differentiate a restrictive from a paralytic esotropia. Restrictive etiologies will still have a deficit of duction, whereas a paralytic etiology will often have improved ductions in comparison to versions. Our patient had full versions, inferior oblique muscle overaction, and a V-pattern. All are common findings in infantile esotropia patients as they get older.

3. Cycloplegic refraction: Cycloplegic refraction should be done on every strabismus patient. If it is not performed, latent hyperopia may be overlooked. This is especially important in esotropia patients because of the association of convergence and accommodation. Cycloplegia can be accomplished using cyclopentolate, homatropine, scopalamine, and atropine

FIGURE 81–2 Flow chart of differential diagnosis of esotropia.

drops. Most commonly, cyclopentolate is used because it is shorter-acting. Atropine is the best at achieving cycloplegia but lasts up to 2 weeks. Our child has significant hyperopia that is undercorrected in her current glasses. Her recurrent esotropia may be adequately treated with the increased hyperopic prescription. Hyperopic correction can help maintain ocular alignment or treat small residual deviations.

4. Optokinetic nystagmus (OKN): Patients with early onset esotropia, especially infantile esotropia, typically have asymmetry of optokinetic nystagmus. The temporal-to-nasal direction of this reflex is normal; however, a poor nasal-to-temporal direction nystagmus is present. OKN can be tested with an OKN drum or ribbon. The test should be performed monocularly. Our patient had OKN asymmetry signifying early-onset esotropia.

5. Neuro/orbital imaging. Radiologic imaging is necessary in patients with a divergence insufficiency esotropia to rule out causes of sixth nerve palsy, such as hydrocephalus or intracranial mass. The orbital imaging is also necessary to rule out a mass that could be compressing the peripheral sixth nerve. Neuroimaging should also be considered in a child with late onset, large-angle esotropia or an atypical acquired large-angle esotropia. Our patient did not have any of these findings and, therefore, did not need an imaging study.

DIAGNOSIS

Infantile esotropia status post strabismus surgery, now with recurrent esotropia, dissociated strabismus complex of the left eye, bilateral inferior oblique muscle overaction, and amblyopia of the left eye.

MEDICAL MANAGEMENT

Proper management of this child first involves prescription of new glasses with the full cycloplegic refraction. The examiner should follow-up in 4 to 6 weeks to recheck the ocular alignment. Reduction or elimination of the deviation signifies the presence of a refractive accommodative component to the esotropia. Bifocal treatment can be instituted if the child on follow-up is orthotropic at distance, but still esotropic at near. Bifocals, however, should only be prescribed if fusion or stereopsis is documented. If the remaining esotropia is only 10 to 12 prism diopters, most ophthalmologists believe that this deviation is small enough to develop a stable monofixation syndrome, and no surgery would be indicated. Vision should be monitored at this stage for amblyopia and appropriate treatment instituted.

SURGICAL MANAGEMENT

If the deviation remains greater than 10 to 12 prism diopters at distance, surgical intervention can be performed. Strabismus surgery for esotropia may consist of a bilateral medial rectus recession, a medial rectus recession and ipsilateral lateral rectus resection, or a bilateral lateral rectus resection. The surgical decision depends on the patient's measurements and the surgeon's preference.

REHABILITATION AND FOLLOW-UP

If the eyes are aligned and stereopsis is good with the new spectacle correction, the prognosis is excellent. Regular follow-ups should be performed throughout childhood as amblyopia and/or esotropia can recur. The interval will vary depending on the stability of the angle and visual acuity. Strabismus surgery can be repeated if the deviation recurs or a new deviation develops. The better the stereopsis or fusion present, the more stable the ocular alignment will be.

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Case 82

CHILDHOOD EXOTROPIA

Evelyn A. Paysse, M.D.

HISTORY

A 4-year-old boy presents with a 2-year history of intermittent drifting of the right eye. His mother states that the deviation is worse when the child is tired or when he is looking at distant objects. His mother initially noted this deviation approximately two to three times a day; however, it recently has been getting worse. She states that the eye is now deviated outward approximately 60% of the day. There is no history of antecedent head trauma, febrile episode, or other medical problem. There is no family history of strabismus or amblyopia. Review of systems is notable for right eye closure in sunlight.

On examination, the child's visual acuity is 20/30, OU. On stereopsis testing with the Titmus stereo fly test, the child is able to correctly identify nine of nine circles (40 seconds of arc). The pupils are 3 mm in diameter, round, with brisk response to light. No afferent pupillary defect is detected. External examination is normal, with no evidence of ptosis. An intermittent exotropia of 50 prism diopters at distance is present, with recovery of orthotropia on refixation or blinking (Fig. 82–1). The deviation recurs immediately with occlusion of either eye. A 25-prism diopter poorly controlled intermittent exotropia is present at near. Ductions and versions are full. A 30-minute patch test demonstrates a 50-prism diopter intermittent exotropia at distance and a 45-prism diopter exotropia at near, after removal of the patch. Cycloplegic refraction is +0.50 OD and +0.75 OS. The remainder of the comprehensive examination is unremarkable.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

This is a 4-year-old child with an intermittent exotropia worse at distance than near. No amblyopia is noted, and stereopsis is excellent. The differential diagnosis of exotropia is extensive, but can be quickly narrowed through the use of special tests during the examination.

1. Differential diagnosis: The exotropias can be divided into comitant and incomitant deviations (Table 82–1). Comitant exotropias include congenital exotropia, intermittent exotropia, and sensory exotropia. Incomitant exotropias can be divided into neurologic or restrictive entities. The neurologic forms of exotropia include third nerve palsy, progressive external ophthalmoplegia, synergistic divergence, and myasthenia gravis. The restrictive entities that can cause exotropia include congenital fibrosis syndrome, thyroid-related ophthalmopathy (rarely), and posttraumatic or iatrogenic exotropia. Duane syndrome (Types II and III) is unique because it can cause both a neurogenic and restrictive strabismus. This child has a comitant deviation so the differential diagnosis is significantly narrowed.
2. Classification of comitant exotropia: When evaluating a child with a comitant exotropia, the examiner must first classify the deviation in a number of different ways. First, he or she needs to decide if the deviation is intermittent or constant. Then the examiner must evaluate the deviation at distance and near. This allows him or her to classify the deviation either as basic exotropia, divergence excess exotropia, pseudodivergence excess exotropia, or convergence insufficiency exotropia.
3. Comitant exotropias:
   a. Intermittent exotropia occurs as a result of a cortical abnormality of fusion. The eyes are sometimes orthotropic with the patient having normal stereopsis and the eyes are, at other times, exotropic and

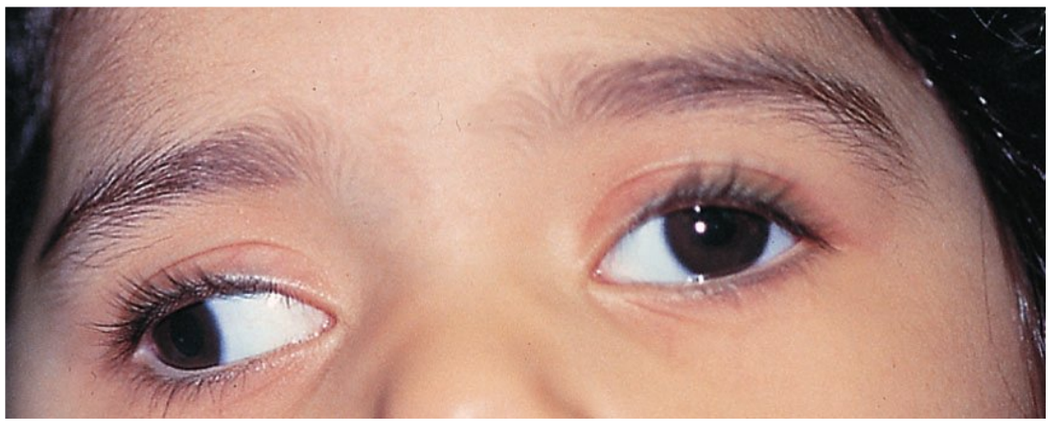

FIGURE 82–1 Exotropia that is often manifest with fixation at distance.

the patient has suppression. Basic exotropia occurs when the deviation is the same at distance and near. Divergence excess exotropia occurs when there is a larger deviation at distance than at near of at least 10 to 15 prism diopters. Convergence insufficiency exotropia occurs when the deviation is worse at near than at distance by 10 or more prism diopters. This form of exotropia is much more common in elderly patients. Pseudodivergence excess exotropia is an exotropia that initially presents in the same way that true divergence excess exotropia does, with a deviation worse at distance than near. After testing with the patch test, which disrupts fusional convergence, a patient with pseudodivergence excess exotropia will have the near deviation increase to within 10 prism diopters of the deviation at distance.

TABLE 82–1 **Types of Childhood Exotropia**

Comitant Exotropia
Essential intermittent exotropia
Basic exotropia
Divergence excess exotropia
Pseudodivergence excess exotropia
Convergence insufficiency exotropia
Congenital exotropia
Sensory exotropia
Myasthenia gravis*
Incomitant Exotropia
Third nerve palsy
Duane's syndrome
Type II
Type III
Chronic progressive external ophthalmoplegia
Synergistic divergence
Myasthenia gravis*
Congenital fibrosis syndrome
Thyroid-related ophthalmopathy**
Iatrogenic
postsurgical
posttrauma

*Myasthenia can cause any type of strabismus, incomitant or comitant.
**Exotropia with thyroid-related ophthalmopathy is rare. It is usually due to concomitant myasthenia.

b. Congenital exotropia, as the name implies, presents at birth or shortly after birth. It is rare and is often associated with intracranial structural abnormalities. Neuroimaging should be considered in these cases.

c. Sensory exotropia occurs after vision loss in one eye. An eye with poor vision tends to drift. If the vision loss occurs before the age of 3, the tendency is for an esotropia to develop. Conversely, if the vision loss occurs after 3 years of age, the tendency is for an exotropia to develop.

d. Myasthenia gravis is characterized by excessive fatigability of striated muscles. It is an autoimmune disease that demonstrates a reduction of available postsynaptic acetylcholine receptors in the end plates of neuromusclar junctions of skeletal muscles. Myasthenia gravis can occur in children and can cause exotropia or any other ocular motility abnormality. It can be comitant or incomitant. Typically, the deviation is variable and worse in the afternoon or when fatigued. It is often associated with ptosis and can also be associated with systemic abnormalities, such as difficulty swallowing, proximal limb weakness, and/or respiratory difficulty.

4. Incomitant Exotropias:

a. A third nerve palsy causes an exotropia and often a hypotropia of the affected eye. It may also be associated with ptosis and mydriasis. A pupil-involving third nerve

palsy is typically due to a compressive lesion, most commonly a posterior communicating artery aneurysm. If a total third nerve palsy is present, complete ptosis, mydriasis, exotropia, and hypotropia of the involved eye will be seen. This strabismus pattern occurs because the third nerve controls four of the six extraocular muscles. The only remaining functional extraocular muscles then are the lateral rectus and superior oblique muscles.

b. Duane syndrome, Types II and III, are conditions of miswiring of the sixth nerve to the lateral rectus muscle and/or the medial rectus muscle. In Duane Type II, an exotropia can occur, associated with a deficit of adduction. Duane syndrome, Type III, causes a deficit of both adduction and abduction and often leaves the eye in an exotropic position.

c. Other exotropias:

Chronic progressive external ophthalmologia is a rare hereditary condition that causes progressive deficits of ocular motility, often associated with ptosis.

Congenital *fi*brosis syndrome is a hereditary condition in which a child is born with fibrotic extraocular muscles and ptosis.

Thyroid-related ophthalmopathy (Graves' ophthalmopathy) can rarely lead to an exotropia due to enlargement of the lateral rectus muscles. Exotropia, however, in a patient with thyroid-related ophthalmopathy, is usually due to concomitant myasthenia gravis, which occurs in 10% of patients with Graves'disease.

Iatrogenic: Exotropia can also result as a consecutive problem after strabismus surgery for esotropia or can be iatrogenically created after surgery for retinal detachment, glaucoma, blowout fracture, or other orbital abnormality.

TEST INTERPRETATION

1. Stereopsis: Stereopsis should be tested first in a strabismic patient as other testing, such as visual acuity or motility evaluations, can be dissociative, causing the patient to temporarily lose the stereopsis and/or fusion that he normally has. Stereopsis testing should be normal in a patient with intermittent exotropia. If stereopsis is reduced in a child with intermittent exotropia, suspicion should be raised toward the other entities that cause exotropia, such as a third nerve paresis.

2. Vision: Visual acuity in children with intermittent exotropia is usually equal in each eye with only about 10% developing amblyopia. Amblyopia then, if present, should raise the examiner's suspicion that other entities, like a third nerve palsy, could be the cause of the exotropia. Visual acuity should be tested with the most sensitive method possible, based on the age of a child.

3. External examination: Because a third nerve palsy can cause exotropia and ptosis, the external examination is important. Any exotropia associated with a ptosis could be a third nerve palsy and special attention should be paid during the ductions and versions examination for an adduction or vertical duction deficit.

4. Pupils: A third nerve palsy can also cause mydriasis of the involved eye, in addition to exotropia and ptosis. Therefore, the examiner needs to carefully evaluate pupil size and, if anisocoria is encountered, perform a full anisocoria workup (see Cases 73, 74, and 75 for anisocoria evaluation).

5. Extraocular motility: In an exotropic patient, ductions and versions should be evaluated for comitance or incomitance. If there is comitance, most of the differential diagnosis can be eliminated. Incomitance of ductions and versions implies a restrictive or paralytic condition. Alternate cover testing should be performed next, first at distance, then at near, in order to classify the type of exotropia present (basic, divergence excess, pseudodivergence excess, or convergence insufficiency).

6. Anomalous head position: Head position should be noted. If a head turn is present a

paralytic or restrictive type of exotropia is usually present.

7. Patch test: When a deviation is found that is comitant and worse at distance than near by 10 to 15 prism diopters or more, the examiner needs to differentiate between pseudodivergence excess exotropia and true divergence excess exotropia by performing a patch test. The patch test works by disrupting fusional convergence. With the patient wearing the correct cycloplegic refraction, an occlusion patch is placed over one eye for approximately 20 to 30 minutes. Next, the examiner carefully removes the patch, paying careful attention to continue to occlude the previously patched eye with his hand or an occlusion paddle to avoid any binocular visual stimulation. Next, the child's ocular alignment is remeasured with alternate cover testing at distance and near. Throughout the entire testing period, the child is not allowed to have binocular stimulation. If the near deviation continues at near to be 10 to 15 prism diopters less than at distance, then a true divergence excess exotropia is diagnosed. If the near deviation has increased to within 10 to 15 prism diopters of the distance deviation, then pseudodivergence excess exotropia is diagnosed. Our patient had an increase of the near deviation to within 10 prism diopters of the distance deviation and, therefore, has a pseudodivergence excess exotropia.

8. Cycloplegic refraction: It is always important to perform a cycloplegic refraction on every child with strabismus. Correction of high hyperopia (+4.00 diopters or more) will improve the control of an exodeviation in some children. This is counterintuitive to general understanding because accommodation (which is required by high hyperopia) typically stimulates convergence. In cases of high hyperopia, however, these children may not be accommodating at all and become exotropic based on a sensory etiology. By giving these children a clear visual world with the hyperopic glasses, their sensory status improves and subsequently their motor alignment improves.

DIAGNOSIS

Pseudodivergence excess type intermittent exotropia.

MEDICAL MANAGEMENT

Medical management is aimed at decreasing the time that the patient is exotropic (ie, increasing fusional control). The actual deviation will usually not change. This sort of management can be divided into either passive management or active management.

1. Passive management is utilized most in younger children (ie, usually less than 4 to 5 years of age), because they usually cannot cooperate or understand the exercises of active management. Overminused spectacles and alternate patching are included in passive management. In overminusing, a child is given glasses with a more myopic correction than he/she needs. Overminusing a spectacle correction stimulates accommodation and subsequently convergence. Overminusing is helpful in some children in order to delay surgical management or while waiting for children to mature enough for active management. It rarely cures the exotropia. Alternate patching is performed by patching alternate eyes on alternate days. A daily patching period of approximately 4 to 6 hours is usually used depending on age and other factors. Alternate patching therapy is based on the theory that it weakens the suppression scotoma that has been set up in a child with intermittent exotropia. This then results in better control of ocular alignment. Base in prism is also helpful in order to increase the time a patient is using fusion.

2. Active management consists of a series of exercises to stimulate convergence and fusion and to increase diplopia awareness. Convergence exercises can only be done with a child who can understand how to perform them. These exercises are fatiguing,

and children less than 5 years of age are usually not able to consistently do them. An easy convergence exercise to perform at home is the "pencil pushup." This exercise is performed by having the child fixate on a small fixation target affixed to a tongue blade, popsicle stick or pencil. Next the parent or child brings the object closer and closer to him/her while converging both eyes on the target until fusion breaks and one eye becomes exotropic. Typically, ten repetitions are done two to three times a day. A number of other convergence exercises can be performed with a red glass or synoptophore. Progressively increasing base-out prism can also be used to stimulate convergence. Convergence exercises are helpful for the conditions of convergence insufficiency exotropia and basic exotropia, but are not typically helpful in patients with divergence excess exotropia.

SURGICAL MANAGEMENT

Surgery is recommended in patients when the control of the exotropic deviation becomes poor. The decision of "poor control" is based on a number of different assessments, including parental impression and clinical examination. Typically, an ophthalmologist will decide to perform strabismus surgery on a child when the deviation is occurring greater than 40 to 50% of the time. Most pediatric ophthalmologists prefer to delay surgery in exotropic patients until 4 years of age, if possible, to avoid the risk of producing an overcorrection before stereopsis is fully developed. The type of surgical procedure performed will depend on the classification of the exotropia and surgeon preference. Bilateral lateral rectus recessions can be performed for divergence excess exotropia, pseudodivergence excess exotropia, and basic exotropia. A lateral rectus recession along with an ipsilateral medial rectus resection can be performed for basic exotropia, pseudodivergence excess exotropia, and convergence insufficiency exotropia. Bilateral medial rectus resections can be performed for convergence insufficiency exotropia.

REHABILITATION AND FOLLOW-UP

Intermittent exotropia is a lifelong condition. Because the cause of intermittent exotropia lies with a cortical defect of fusion, the entity is never "cured." The follow-up interval depends on the level of control. Typically, if medical management is being used, follow-up ranges between 2 and 6 months for reevaluation. If surgery has been performed, healing occurs over approximately 6 weeks. Surgical patients must still be followed long-term, because the deviation can recur. Recurrence of exotropia has been cited in the literature at a rate of 20 to 40%. Surgery can be repeated for symptomatic or cosmetically noticeable deviations. Children with exotropia should be followed for decreasing stereopsis and the onset of amblyopia, both signs of worsening control.

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Case 83

CHILDHOOD PTOSIS

Evelyn A. Paysse, M.D.

HISTORY

A 17-month-old boy presents with a droopy right upper lid. His parents state that this right upper lid has been "lazy" since birth. They also state that he holds his chin up when he is walking or watching TV. No ocular motility disturbance has been noted. His parents also volunteer that occasionally the child lets the lid block his pupil. There is no family history of ptosis, strabismus, or hereditary muscular disorders. The child is otherwise healthy with a negative review of systems.

The child has good fixation and following visual behavior in both eyes (without correction). The child notably has a preferred chin-up head posture of 15 degrees. External examination demonstrates a moderate to severe right upper lid ptosis (Fig. 83–1). The interpalpebral fissure on the right is 6.5 mm and on the left is 10 mm. The eyelid margin-to-reflex distance with the child's head in the primary position is 0.5 mm and 3.5 mm in the right and left eyes, respectively. With a chin-up head posture, the eyelid margin to reflex distance is 2 mm in the right eye and 3 mm in the left eye. Levator function is 6 mm in the right eye and 12 mm in the left eye. No appreciable lid crease is noted in the right upper lid. The pupils are both 3 mm in diameter, round, and briskly reactive to light. There is no afferent pupillary defect. The eyes are orthotropic and have full range of motion in all positions of gaze. Cycloplegic refraction is –0.25 + 1.00 × 90 degrees in the right eye and +0.50 sphere in the left eye. The rest of the comprehensive examination is unremarkable.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. This is a 17-month-old child who has had ptosis of the right upper lid since birth. The history is significant for the lack of variability, lack of previous trauma, lack of strabismus, and lack of anisocoria. Childhood ptosis has an extensive differential diagnosis (Table 83–1).

2. The differential diagnosis of a child with ptosis includes the following:

a. Congenital ptosis occurs from a developmental abnormality of the levator muscle. The levator muscle is hypoplastic with fibrous or fatty infiltration. The degree of the ptosis actually decreases in downgaze relative to the other eye secondary to the fibrotic nature of the levator muscle in this condition. This is helpful to the child who assumes a chin-up posture because the ptotic lid is less ptotic when this position is utilized and better vision is achieved.

b. Horner's syndrome is suspected when its classic triad of miosis, anhydrosis, and mild ptosis of the involved eye are present. Horner's syndrome occurs secondary to dysfunction of the sympathetic chain on the ipsilateral side. Acquired Horner's syndrome requires an evaluation for serious diseases such as neuroblastoma. Congenital Horner's syndrome is typically associated with heterochromia, with the lighter pigmented iris on the involved side. (See Case 74.)

c. *A third nerve palsy* causes a moderate to severe ptosis. It may be associated with vertical strabismus, exotropia, and/or mydriasis. The severity and etiology of the third nerve palsy will determine which of these signs is present. A third nerve palsy can be congenital or it can be acquired due to tumor, trauma, vascular abnormality, or inflammatory lesions of the brainstem or orbit. (See Cases 66 and 67.)

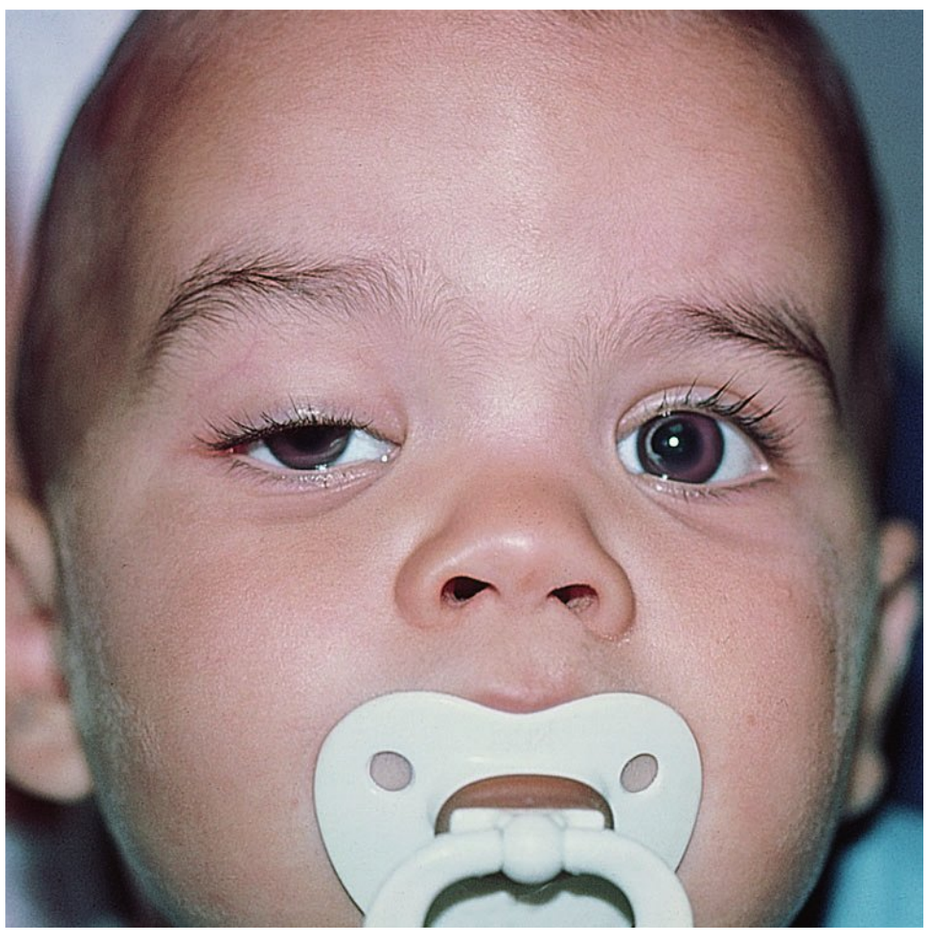

FIGURE 83–1 Facial photograph of the patient demonstrating ptosis of the right upper lid. Note the absence of a lid crease on the affected lid. (From Lee DA and Higginbotham EJ. *Clinical Guide to Comprehensive Ophthalmology*. New York: Thieme,1999:153, with permission.)

d. *Marcus Gunn jaw-winking ptosis* occurs from a synkinesis of the trigeminal (V) nerve to the oculomotor (III) nerve (trigemino-oculomotor synkinesis). Stimulation of the pterygoid branch of the trigeminal nerve, responsible for the muscles of mastication, will also stimulate the levator muscle because of the miswiring and will elevate the upper lid. Pterygoid nerve stimulation occurs most commonly with sucking, swallowing, chewing, or on lateral movement of the jaw. This entity is most commonly diagnosed in the neonatal period when a child is bottle- or breastfeeding but can occasionally be overlooked until later in life.

TABLE 83–1 **Causes of Childhood Ptosis**

- Congenital ptosis
- Horner's syndrome
- Third nerve palsy
- Marcus Gunn jaw-winking ptosis
- Myasthenia gravis
- Double elevator palsy
- Chronic progressive external ophthalmoplegia
- Mechanical ptosis
  - Lid hemangioma
  - Lid neurofibroma
- Levator dehiscence
- Pseudoptosis

e. Other causes of ptosis:

Myasthenia gravis causes ptosis that is variable in severity and timing. It is commonly associated with other extraocular motility abnormalities that do not necessarily follow the rules of neurologic innervation. Myasthenia gravis can be purely ocular or can be ocular and systemic. Systemic findings of myasthenia gravis include respiratory compromise, weakness of proximal extremities, and dysphagia. (See Case 71.)

Ptosis associated with double elevator palsy is typically a severe congenital ptosis, associated with the inability to elevate the eye either in adduction or abduction.

Ptosis associated with chronic progressive external ophthalmoplegia is an acquired ptosis. It is associated with progressive extraocular motility deficits. It can also be associated with other ophthalmologic and systemic abnormalities, such as retinal pigmentary abnormalities and heart block, seen in Kearn-Sayres syndrome.

Mechanical ptosis results from a mass lesion that restricts elevation of the lid such as a large hemangioma, lymphangioma, neurofibroma, or dermoid.

Levator dehiscence occurs secondary to trauma or stretching of the levator muscle, usually over years. It is a slowly progressive, acquired ptosis. The distance between the lid crease and lid margin is increased in this entity.

Pseudoptosis occurs secondary to a primary hypotropia on the involved side with the resultant corresponding upper lid depression. This is not a true ptosis: ie, when the hypotropic eye fixates, the apparent ptosis resolves.

3. Childhood ptosis is associated with several other important ophthalmologic abnormalities. *Amblyopia* is the most important potential problem associated with ptosis. It can occur secondary to one of several mechanisms. The most devastating amblyopia is caused by occlusion of the involved eye due to blockage of the visual axis. This will produce form-vision deprivation amblyopia, such as in a child with a congenital cataract. Amblyopia due to ptosis can also occur secondary to anisometropia. The anisometropia seen in children with congenital ptosis usually occurs secondary to astigmatism, created by the upper lid pressing on the flexible infant cornea. *Strabismus* can occasionally be associated with ptosis and pseudoptosis. This is frequently the case in children with double elevator palsy who have a hypotropia of the involved side and a pseudoptosis.

TEST INTERPRETATION

The major diagnostic considerations in a child with ptosis are related to careful ophthalmologic examination. The following discussion will concentrate on the most relevant parts of an examination.

1. Vision: It is imperative to obtain the best visual acuity or visual behavior (eg, fix and follow; central, steady, maintained) possible in the child. The examiner should perform the most rigorous vision test the child is capable of. Fixation preference should be assessed in addition to visual behavior in a nonverbal or preverbal child. If the child has strabismus, it is easy to assess for fixation preference. The examiner simply covers one eye to gain fixation in the other, then removes the occluder and watches for any refixation movement to the previously covered eye. This would signify a fixation preference for the previously covered eye. Fixation preference is more difficult to ascertain when a child does not have strabismus. The vertical prism test, first described by Wright, can be useful. Several variations of this test exist. One method involves holding a 10- to 14-prism diopter hand-held prism base down in one of the examiner's hands. Next the examiner gains the child's fixation on a small target. The examiner then places the vertical prism in front of one of the child's eyes while watching for a refixation movement. If the child refixates, the examiner will note an upward movement of both eyes as the child switches fixation to the eye looking through the prism. This test should be done several times on one eye and then repeated on the other eye. Typically, if amblyopia is not present, no refixation movement will be noted when the prism is placed in front of either eye. If there is consistent refixation movement when the prism is held before one eye, amblyopia should be suspected. Our child has normal and equal visual acuity in each eye.
2. Pupils: Anisocoria in the presence of ptosis can be due to Horner's syndrome or a third nerve palsy. If anisocoria is noted, the examiner must note whether the anisocoria is worse in lighted or dimly lit conditions, in order to discern whether the iris dilator muscle (ie, sympathetic nervous system) or the iris sphincter (ie, parasympathetic nervous system) is the problematic muscle. If the anisocoria is worse in dimly lit conditions, the dilator muscle is problematic and a Horner's syndrome should be suspected. If the anisocoria is worse in lighted conditions, then the iris sphincter is the problem, and a third nerve palsy may be present. Further workup for each of these entities should be performed. (See Cases 74 and 75.)
3. External examination: Several different measurements should be performed when evaluating every ptosis patient. The palpebral fissure height, the margin reflex distance, and levator function are needed to evaluate ptosis to help determine etiology and to decide on the best management approach. In children, attention to an anomalous head posture is also important. A chin-up head posture is adaptive and usually signifies less risk for

amblyopia than severe ptosis without a chin-up head posture. The distance between the lid crease and the lid margin is also helpful in differentiating the different types of ptosis. If this distance is increased, the ptosis is more likely due to a levator dehiscence. If a lid crease is completely absent or rudimentary, the ptosis is more likely congenital. One must also assess the child for a Bell's phenomenon prior to surgical treatment. Ptosis caused by double elevator palsy, congenital fibrosis syndrome, or progressive external ophthalmoplegia is often associated with a decreased or absent Bell's phenomenon. Patients with an abnormal Bell's phenomenon are at increased risk of exposure keratopathy and other related problems following surgery. Finally, infants should be evaluated while sucking on a bottle and older children should be asked to move their jaw laterally from side to side to rule out trigemino-oculomotor synkinesis. Each of these maneuvers will stimulate the pterygoid branch of the trigeminal nerve and, if jaw winking is present, will stimulate the superior branch of the oculomotor nerve and elevation of the involved lid will occur. Our child has severe ptosis with moderate levator function, absent lid crease, an increase in palpebral tissue height in downgaze, all signs consistent with congenital ptosis.

4. Motility: Motility abnormalities can be associated with ptosis if a third nerve palsy, double elevator palsy, congenital fibrous syndrome, or dense amblyopia (sensory strabismus) is present. A careful motility examination should be done and any abnormalities noted should be addressed.
5. Slit-lamp examination/anterior segment evaluation: If evaluating a mild ptosis for a Horner's syndrome, it is helpful to look for heterochromia. Heterochromia is seen in patients who have a congenital Horner's syndrome. The lighter pigmented iris is on the involved side.
6. Cycloplegic refraction: Significant anisometropia and astigmatism are common sequelae of long-standing ptosis. If significant anisometropia exists, spectacle correction should be prescribed. If amblyopia is detected, appropriate amblyopia treatment should also be instituted. (See Case 77.) Our child has minimal anisometropia with good vision in both eyes.

DIAGNOSIS

Congenital ptosis of the right upper lid with anomalous chin-up head posture and absence of amblyopia.

MEDICAL MANAGEMENT

Medical management is only helpful for the associations of congenital ptosis, namely amblyopia and anisometropia. Amblyopia is typically treated either with occlusion therapy or with pharmacologic or optical penalization. (See Case 77.) The type of amblyopia therapy will depend on patient compliance, cooperation, and physician preference. Anisometropia and astigmatism should be corrected if deemed significant. Vigilant follow-up throughout the childhood years must be done to insure that amblyopia, once treated, does not recur.

SURGICAL MANAGEMENT

Ptosis, if significant, is a surgical disease. Surgery also offers, in addition to an increased visual field and cosmetic benefits, improvement of an anomalous head posture, which could allow for improvement in development and coordination. Surgical treatment goals are to elevate the ptotic lid for better vision and increased visual field, and to reform the lid crease if it is absent or rudimentary for cosmesis. It is important to decrease the surgical dose if the Bell's phenomenon is absent or decreased because of the risk of exposure keratopathy.

Several different surgical treatment approaches are possible. The choice of procedure depends on the severity of the ptosis and levator function. The Fasanella-Servat procedure is used

for small ptosis of 2 mm or less. A small wedge of conjunctiva, superior tarsus, levator palpebrae, and Müller's muscle are resected in this procedure. This is an excellent procedure for a Horner's syndrome–associated ptosis. The levator resection is the most versatile procedure and gives an excellent cosmetic result. It can be performed for mild, moderate, and severe ptosis. The frontalis suspension procedure is typically reserved only for severe ptosis with significant residual levator function. As its name implies, it is a suspension procedure in which material is threaded through the upper lid and attached to the frontalis muscle. The material acts as a sling to hold the lid up. Different materials, including a variety of sutures (Supramid, nylon, prolene, Gore-Tex), silicone rods, and organic materials, such as banked or autogenous fascia lata or palmaris longus tendon, have been utilized as the suspension material. The best long-term results are found with the use of an autogenous fascia lata. Results with banked fascia lata are almost as long-lasting. All synthetic materials have been shown to have a shorter life span and increased risk for late complications such as granuloma formation and other inflammatory reactions. The potential complications of ptosis surgery, though infrequent, include early and late infection, suture granuloma, exposure keratopathy, retrobulbar hemorrhage, and overcorrections.

REHABILITATION AND FOLLOW-UP

A child with congenital ptosis needs to be followed throughout childhood for the associated problems of amblyopia and anisometropia. Once treated, amblyopia can recur until a child is age 7 to 10 years old. Therefore, surveillance must continue. Following surgical repair of ptosis, healing will occur over approximately 1 month. It is common after surgery for the child to have some lagophthalmos when sleeping. Ocular lubrication at night helps for the first month, and can usually be abandoned thereafter, as children adapt very well to the small amount of lagophthalmos that occurs from these procedures. When the Bell's reflex is absent, lubrication is usually needed permanently after surgery. Lid height should be followed over time, as ptosis can recur.

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Case 84

THE APPARENTLY BLIND INFANT

David K. Coats, M.D.
Evelyn A. Paysse, M.D.

HISTORY

A 3-month-old girl is brought to her ophthalmologist by her parents because of concerns that she may be blind. They report that she has poor eye contact, that she does not respond to parental facial expressions, and that she does not appear to be able to tell the difference between light and dark. The child's prenatal and birth histories are unremarkable. Her past ophthalmologic and medical histories are unremarkable. The child has two normal siblings, ages 2 years and 5 years old, who saw much better at 3 months of age than the patient does and who are developmentally and visually normal at this time. The review of systems is completely negative, with the exception of poor visual attention. The child appears grossly normal from a developmental standpoint, though the child has not been seen by her pediatrician in several weeks.

On examination, a healthy-appearing 3-month-old girl is sitting on her mother's lap. The ocular adnexal and other facial features appear normal. The child does not fixate on or follow any target and does not respond to facial gestures. She does blink when a bright light is directed into her eyes. Opticokinetic (OKN) testing is done and demonstrates an occasional beat of nystagmus, but attention is poor and the test results are equivocal. The eyes are orthotropic with full versions to oculocephalic testing. Spontaneous nystagmus is not seen. The pupillary examination reveals pupils that are 5 mm in size and moderately reactive to light with no afferent pupillary defect and no paradoxical pupillary reaction. Anterior segment and fundus examinations are normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Poor vision in a child requires consideration of an extensive differential diagnosis. In general, poor vision in an infant should be divided into poor vision without nystagmus and poor vision with nystagmus. If nystagmus is present, the differential diagnosis includes bilateral structural abnormalities of the cornea lens, retina, or optic nerve leading to a bilateral severe, afferent dysfunction. Idiopathic infantile nystagmus is also a consideration if nystagmus is present. The absence of nystagmus strongly supports a cortical-based abnormality.

2. Delayed visual maturation (DVM) is an interesting and troubling problem that is not infrequently encountered in young infants. In general, the absence of fixation behavior in a child of 4 to 6 weeks of age is rarely alarming to pediatricians or parents. If obvious visual fixation behavior is not present after this time, however, parents and pediatricians alike tend to become very concerned. DVM can be classified into three major groups: (1) isolated DVM; (2) DVM with associated central nervous system (CNS) disease; (3) DVM with associated structural eye abnormalities. In isolated DVM, the absence of obvious visual behavior is the only abnormality noted. The child is developmentally and neurologically normal and typically has normal electrophysiologic testing results. DVM can also coexist with systemic disease and/or mental retardation or with ocular disease such as optic nerve hypoplasia and albinism. The etiology of the DVM is unknown, but some have suggested that

delayed myelination of the optic nerves and/or tracts or delayed synaptogenesis in the visual pathways may be the etiology.

3. Cortical visual impairment (CVI) is another important condition that must be considered. A child with CVI will appear clinically similar to the child with DVM. Typically, the child with CVI, however, has a history of perinatal hypoxia or another serious neurological event suggesting the possibility of hypoxic brain injury and typically also has concurrent neurologic and/or systemic abnormalities.
4. Structural abnormalities of the eye must be carefully ruled out. In general, bilateral structural abnormalities that are severe enough to produce blindness typically will present with concurrent nystagmus. Affected patients may initially appear similar to the child with DVM because nystagmus may not develop until the child is several months of age. Careful ophthalmologic examination will usually eliminate the confusion.

TEST INTERPRETATION

The ophthalmologist should work in conjunction with the child's pediatrician or neurologist. The child suspected of having DVM should undergo a careful developmental assessment. If the developmental milestones are normal, isolated DVM is the likely diagnosis. Time will allow this diagnosis to be confirmed as the child begins to develop normal visual behavior with age. This child is developmentally normal (Fig. 84–1).

A neurological assessment is also important and can be conducted by the child's pediatrician or a neurologist. The presence of neurologic abnormalities can coexist with DVM. The prognosis, however, for DVM with neurologic abnormalities is not as good and vision is often slower to improve compared with isolated DVM. This patient had a normal screening neurological examination.

In general, unless neurologic and/or systemic abnormalities are found, the child with isolated DVM does not need to undergo electrophysiologic testing. If tested, however, the child's EEG must be normal. If the EEG is abnormal, the child does *not* have isolated DVM. The visual evoked potential test in a child with isolated DVM may be mildly delayed and attenuated or may be normal. The test is useful in predicting eventual development of good vision. The electroretinogram is also normal in children with isolated DVM. This child's parents requested a VEP and the results are shown in Figure 84–2.

It is of paramount importance for the ophthalmologist to interact appropriately with parents, pediatricians, and neurologists. It is wrong to declare an infant blind at an early age, as many will prove to have normal vision as the visual system matures. Alleviating parental and referring physician fear is a major role of the ophthalmologist early on in treating infants with this condition. An extensive workup, however, is not initially needed if the infant is developmentally and neurologically normal.

DIAGNOSIS

Isolated DVM.

MEDICAL MANAGEMENT

The child should undergo a careful initial developmental and neurologic assessment. Periodic assessments of development and neurologic function should also be undertaken by the child's pediatrician. Continued normal development is strongly suggestive of isolated DVM and the likelihood of eventual improvement of vision.

SURGICAL MANAGEMENT

No surgical treatment is indicated.

REHABILITATION AND FOLLOW-UP

For the typical infant with isolated DVM, vision typically will become normal by the time the infant is 6 to 8 months old. At this point, no

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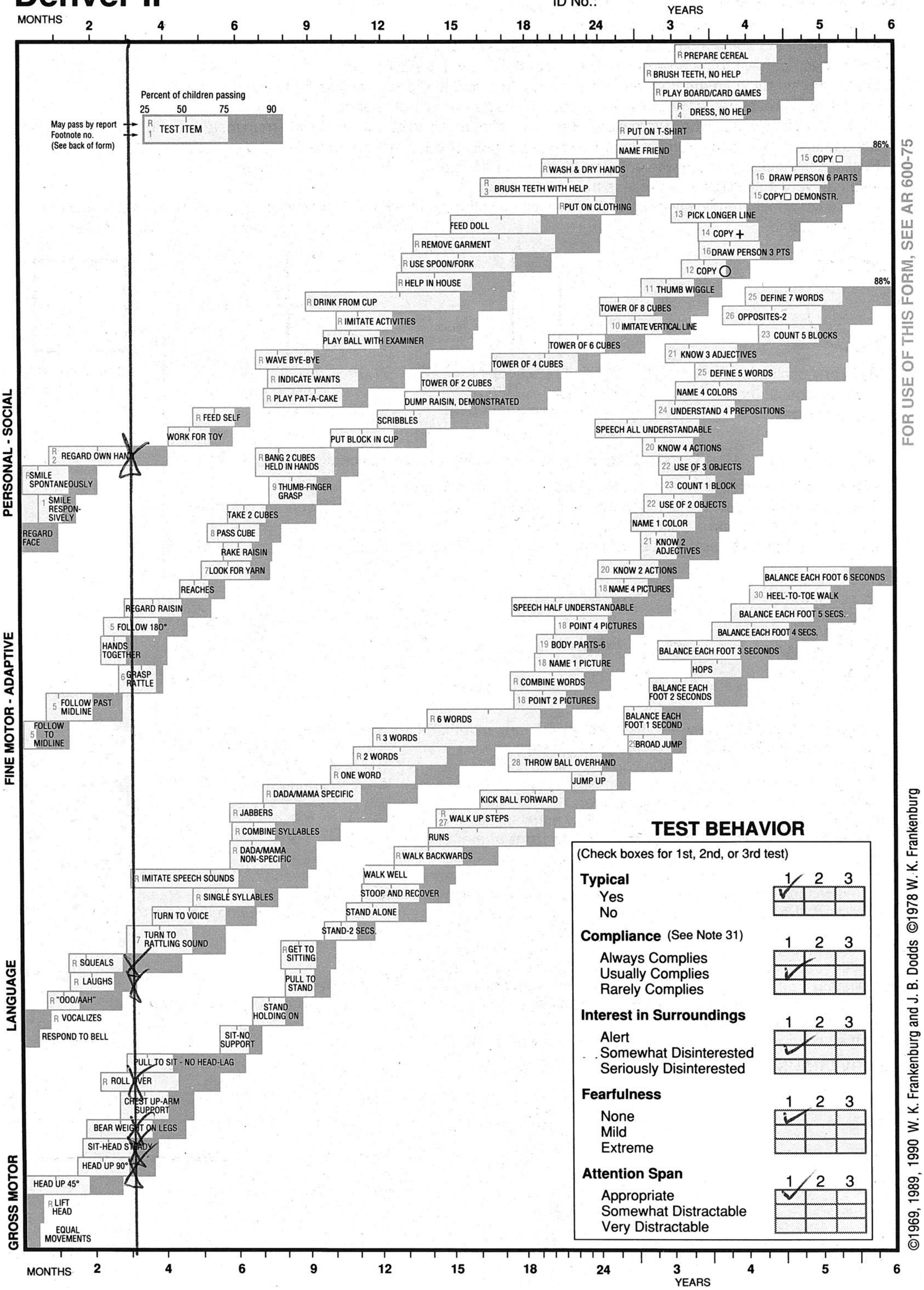
Denver II

Examiner:
Date:

Name:
Birthdate:
ID No.:



TEST BEHAVIOR

(Check boxes for 1st, 2nd, or 3rd test)

	1	2	3
Typical			
Yes	✓		
No			
Compliance (See Note 31)			
Always Complies			
Usually Complies	✓		
Rarely Complies			
Interest in Surroundings			
Alert			
Somewhat Disinterested	✓		
Seriously Disinterested			
Fearfulness			
None	✓		
Mild			
Extreme			
Attention Span			
Appropriate	✓		
Somewhat Distractable			
Very Distractable			

FOR USE OF THIS FORM, SEE AR 600-75

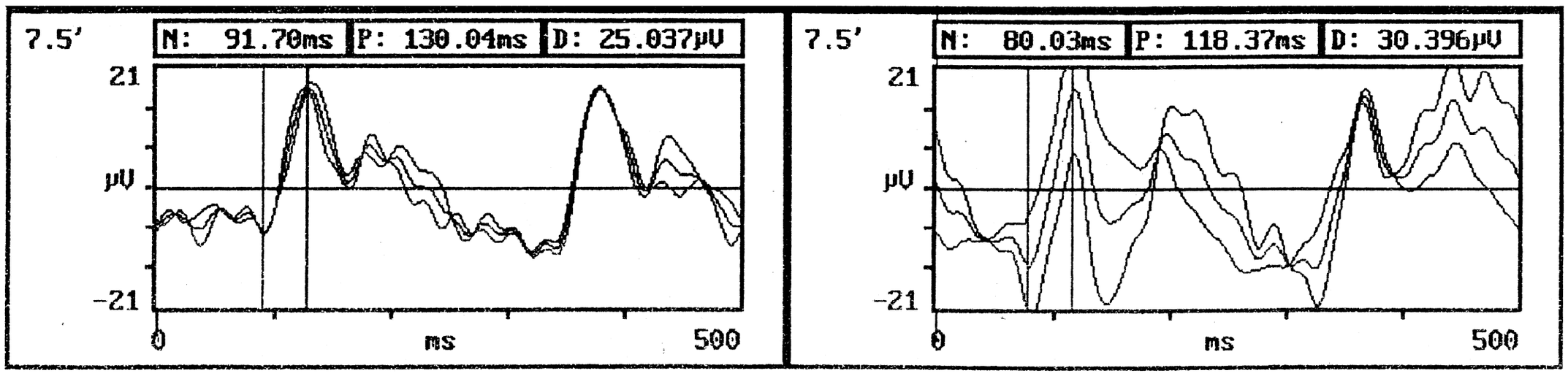


FIGURE 84–2 Pattern visual evoked potential test on child with (left) DVM, and (right) normal visual development. The peak (P100) is prolonged in the child with DVM. (Courtesy of Thomas C. Prager, Ph.D., M.P.H., Houston, TX.)

further evaluation or intervention is required, and such a child can be expected to do well. On the other hand, if the vision fails to improve by 6 to 8 months of age, further evaluation including electrophysiologic testing and neuroimaging is indicated. In a child with DVM associated with neurologic abnormalities, developmental delay, and/or ocular abnormalities, visual response may be delayed until as late as 1 to 2 years of age.

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Case 85

OPTIC NERVE HYPOPLASIA

David K. Coats, M.D.
Evelyn Paysse, M.D.

HISTORY

A 3-year-old male is referred by another ophthalmologist. The child was diagnosed with esotropia and amblyopia in the right eye at age 2 years. The referring ophthalmologist prescribed full-time patching of the left eye, which was done sporadically for approximately 6 months. No improvement in the child's vision was noted prompting referral for a second opinion and treatment recommendations.

The child's medical history is notable for a weight and height in the 15th percentile, but is otherwise unremarkable. The review of systems is completely negative with the exception of the ophthalmologic complaints and there is no family history of strabismus or amblyopia.

The patient is shown in Figure 85–1. Best corrected visual acuity is 20/200 in the right eye and 20/30 in the left eye. Motility evaluation reveals an esotropia of 25 prism diopters at distance and near with full ductions and versions. Pupillary testing reveals a 1+ relative afferent pupillary defect (RAPD) in the right eye. Cycloplegic refraction is +1.25 diopters in both eyes and initial evaluation of the posterior pole reveals a normal disc, macula, and vessels. The ophthalmogist is concerned by the presence of the RAPD and performs a more careful evaluation of the posterior pole. The disc of the right eye appears pale, the vessels crowded, the disc diameter is small, and a double ring sign is noted (Figs. 85–2A and B). The left disc is also slightly smaller than normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. A RAPD should always be a tip-off that amblyopia is *not* the problem and a careful evaluation to determine the etiology of the afferent abnormality should be carried out. While it is true that trace RAPDs may occasionally be seen in children with amblyopia, the presence of an easily identifiable RAPD is not consistent with a diagnosis of amblyopia. The examiner must explain its presence and is advised to refer the child for a second opinion if a plausible explanation cannot be found.

2. Optic nerve hypoplasia is a not uncommon congenital anomaly of the optic nerves. It may occur in one or both eyes and may be isolated or may be associated with central nervous system (CNS) and endocrine abnormalities. The condition is difficult to diagnose in an uncooperative child. Nevertheless, a detailed and magnified view of the disc must be obtained. The so-called double ring sign may or may not be present, and when present, may be mistaken for a normal-sized optic nerve. This is especially true if indirect ophthalmoscopy, which offers only minimal magnification, is the only technique used to examine the discs. Often, an anomalous configuration of retinal vessels on the disc is the first tip-off that there is a problem with the optic nerve, prompting a more detailed look.

Vision can vary from 20/20 to no light perception. Many children with severe optic nerve hypoplasia appear completely blind at birth but demonstrate useful vision later in life. When severe and bilateral optic nerve hypoplasia is present, the child will also have nystagmus and presents a less formidable diagnostic challenge.

3. Optic nerve hypoplasia is commonly associated with midline CNS defects such as absence of the septum pellucidum and/or corpus callosum and posterior pituitary ectopia. Hemispheric migrational anomalies

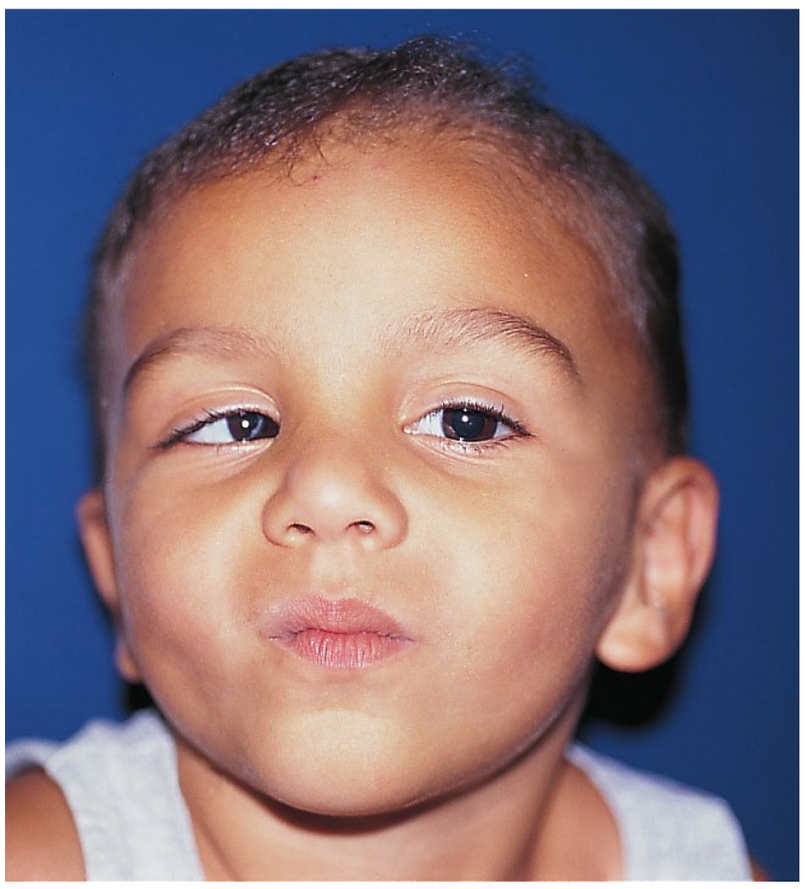


FIGURE 85–1 Esotropia noted in a patient on initial examination. (Courtesy of Andrew G. Lee, M.D., Iowa City, IA.)

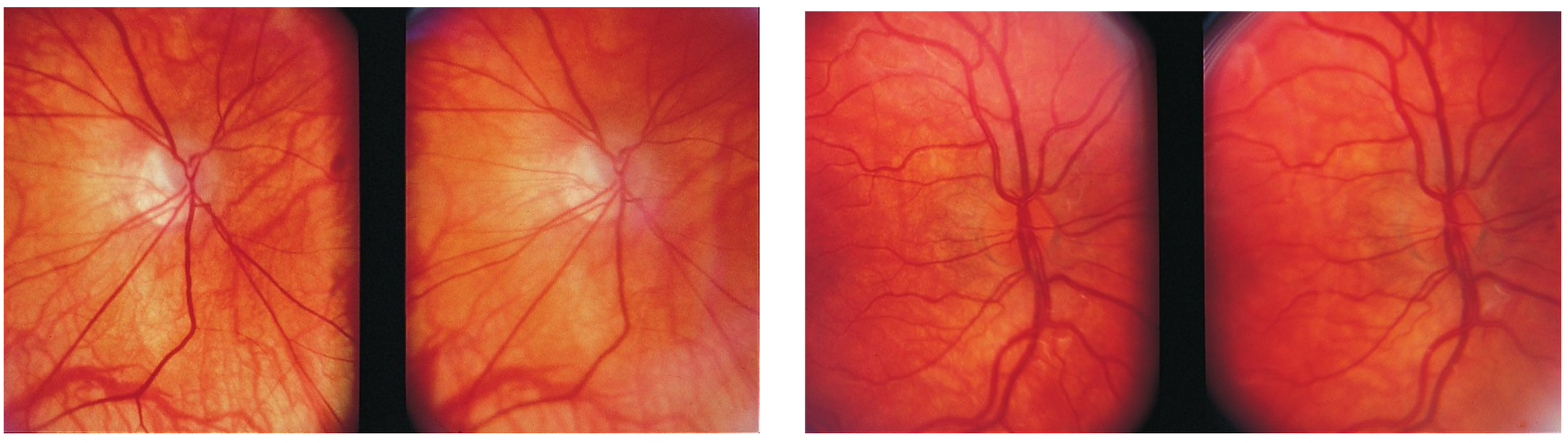
may also be present. When optic nerve hypoplasia coexists with these midline CNS defects, the terms *septo-optic dysplasia* or *De Morsier syndrome* have been utilized.

Patients with septo-optic dysplasia may suffer a variety of pituitary hormone abnormalities, including abnormalities of growth hormone and of the adrenocorticosteroid axis. It is important to recognize this condition because corticotropin deficiency has been associated with sudden death in children with septo-optic dysplasia following an otherwise uneventful febrile illness, and growth hormone deficiency can result in severe growth retardation. Endocrine abnormalities are most likely to occur in children with posterior pituitary ectopia and hemispheric migrational abnormalities.

4. Optic neuritis and optic atrophy are included in the differential diagnosis of this child with poor vision in one eye and a RAPD. These conditions can be ruled out on clinical examination.

TEST INTERPRETATION

1. When a RAPD was noted in this child, careful scrutiny of the optic discs became paramount. Several methods can be utilized to obtain a better view of the posterior pole in an uncooperative or marginally cooperative child. These measures include the use of direct ophthalmoscopy, or indirect ophthalmoscopy using a 14-diopter lens. Both of these techniques offer greater magnification compared to indirect ophthalmoscopy with a 20-diopter lens but have the disadvantage of being either difficult to perform on an uncooperative child (direct ophthalmoscopy) or not readily available (14-diopter lens) in most ophthalmology practices. Modified (monocular) indirect ophthalmoscopy offers a useful imaging option. With this technique, a standard 20-diopter lens is held 5 to 6 cm in front of the child's eye. The direct ophthalmoscope is then held approximately



A B

FIGURE 85–2 (A) Small right optic nerve with "double ring" sign. (B) Normal left optic nerve of another patient for comparison. (Courtesy of Andrew G. Lee, M.D., Iowa City, IA.)

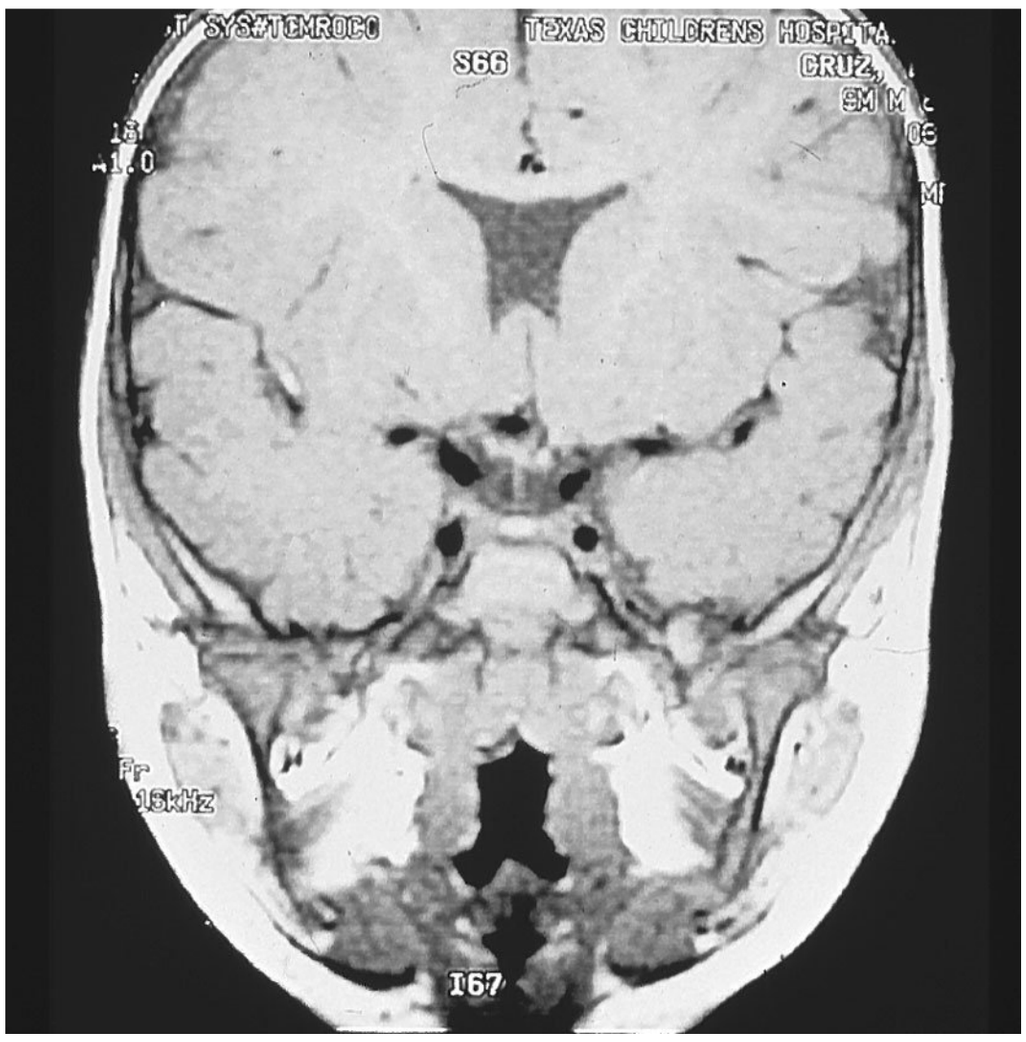


FIGURE 85–3 Magnetic resonance scan demonstrating absence of the septum pellicidum. (Courtesy of Andrew G. Lee, M.D., Iowa City, IA.)

18 cm away. The aerial image produced by the 20-diopter lens is then focused with the direct ophthalmoscope. This technique allows adequate magnification to accurately assess the optic nerves without requiring the close proximity to the child as required for direct ophthalmoscopy. Examination of the eyes under anesthesia is sometimes required in particularly uncooperative children. The potential for serious problems due to corticotropin deficiency should be considered and steroids administered before anesthesia if this problem is strongly suspected.

2. Magnetic resonance imaging of the brain is the preferred neuroimaging study to rule out midline CNS defects and hemispheric migrational abnormalities, but computed tomography (CT) scan may be adequate. Specifically, the examiner should review the scan for absence of the corpus callosum or septum pellucidum and for pituitary abnormalities. Ectopia of the posterior pituitary bright spot is highly suggestive of current or future endocrine abnormalities. This child's MR scan is shown in Figure 85–3.

Endocrine testing should be conducted by an endocrinologist or the child's pediatrician. This patient had a markedly reduced growth hormone level. The most common endocrine abnormalities that present in septo-optic dysplasia are growth hormone and corticotropin deficiency. These conditions should be detected early in the disease course to prevent a potential medical disaster. The child's pediatrician should be advised of the child's condition and the need to follow growth and endocrine parameters carefully and frequently.

DIAGNOSIS

Septo-optic dysplasia, with bilateral, asymmetric optic nerve hypoplasia. The child is also suffering from a growth hormone deficiency with resulting short stature and low weight.

MEDICAL TREATMENT

The child should be under the care of an endocrinologist and should undergo growth hormone replacement with close follow-up of his growth parameters. Despite the fact that the child has optic nerve hypoplasia, there is still the potential to improve the vision in his right eye if a component of functional amblyopia coexists with the anatomical defect. Such patients should receive a trial of amblyopia therapy before concluding that the visual impairment is irreversible.

SURGICAL TREATMENT

Strabismus surgery or botulinum toxin injection can be offered to repair the child's esotropia. The child's parents should be advised, however, that strabismus may recur following surgery for sensory strabismus. Surgery should be deferred until amblyopia treatment has been maximized.

REHABILITATION AND FOLLOW-UP

As with all functionally monocular patients, polycarbonate safety spectacles should be

prescribed to protect the child's better-seeing eye. In children with optic nerve hypoplasia, ongoing evaluation of growth and endocrine parameters should continue throughout early childhood, even if the child appears to be growing normally at initial diagnosis. Endocrine abnormalities have been detected and problems have been noted with delayed onset as late as 3 to 4 years of age. Stress doses of corticosteroids should be administered in patients with corticotropin abnormalities in situations such as acute illness, surgery, or serious injury.

[Note: The child described in this case is a composite of several children used to demonstrate common findings of optic nerve hypoplasia.]

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Case 86

CHILDHOOD OPTIC PATHWAY GLIOMA

Evelyn A. Paysse, M.D.
David K. Coats, M.D.

HISTORY

A 4-year-old girl presents to the office after having failed a vision screening examination in her pediatrician's office. Her visual acuity in the right eye is 20/60 and in the left eye is 20/30. She has no complaints of blurred vision, pain, redness, or discharge. Her mother has not noted any crossing or drifting of the eyes. Her mother stated, however, that her right eye has appeared to be getting "larger" than her left eye for at least 1 year. The child has not been complaining of headaches nor has she had nausea, vomiting, fever, cough, or any other symptoms. The child is otherwise healthy. There is no family history of hereditary eye disease or developmental problems.

On examination, a healthy-appearing 4-year-old girl is sitting in the examination chair. Her best corrected visual acuity is 20/60 in the right eye and 20/25 in the left eye. Her cycloplegic refractive error is +0.50 sphere in both eyes. Two millimeters of proptosis and increased resistance to retropulsion of the right eye are noted (Fig. 86–1). There is no lid retraction or lagophthalmos. Pupils are 4 mm in diameter, round, and briskly reactive to light. An afferent pupillary defect is present in the right eye. Motility evaluation reveals orthotropia with full versions. Visual fields are not reliable due to the child's age. Slit-lamp examination is entirely normal in both eyes. Moderate optic nerve pallor is noted bilaterally, slightly worse in the right eye than in the left eye. The remainder of the comprehensive ophthalmologic exam is unremarkable.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Differential diagnosis: This is a young child with slowly progressive proptosis, decreased vision in the right eye, and bilateral optic atrophy. The differential diagnosis is vast and includes life-threatening and vision-threatening conditions, including various neoplasms, inflammatory lesions, vascular anomalies, and thyroid-related ophthalmopathy (Table 86–1).

2. Presentation of optic pathway glioma: The slow, progressive nature of this child's problem is characteristic of a slow-growing tumor, like an optic pathway glioma. Optic pathway glioma presents with or without proptosis depending on location. If there is orbital involvement, slowly progressive proptosis can be present with or without restriction of motility, and with or without an optic neuropathy. No inflammatory reaction of the ocular adnexa or lids is present and lagophthalmos is not seen. The most common symptoms of optic pathway glioma at time of diagnosis include visual difficulty, headache, diplopia, lethargy, imbalance, and failure to thrive. Optic pathway glioma causes damage by local compression. Vision loss is the most common sequela. The most common signs at diagnosis depend on the glioma's location and include decreased vision in one or both eyes, homonymous hemianopia, optic atrophy, optic disc edema, and proptosis (Table 86–2). Panhypopituitarism and diabetes insipidus can also occur, especially if the posterior chiasm is involved. Approximately 80% of optic pathway gliomas involve the chiasm. Optic gliomas may also involve the hypothalamus and pituitary gland, third ventricle, and posterior optic tracts.

3. Association with neurofibromatosis: Optic pathway glioma is associated with Type I neurofibromatosis in 30 to 40% of cases.

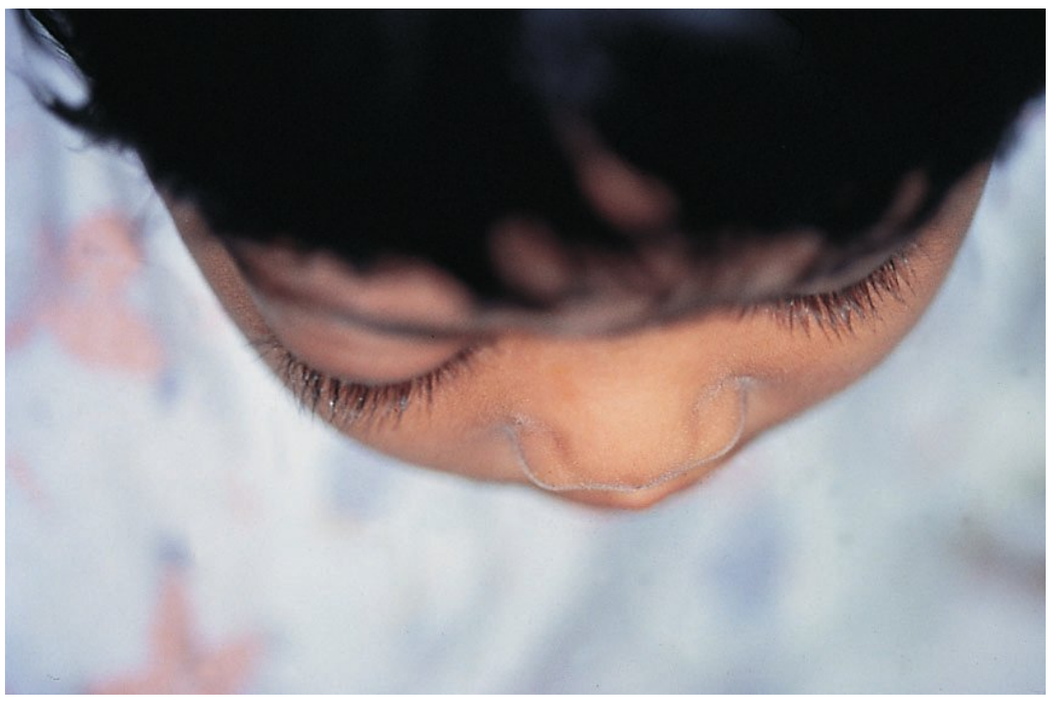

FIGURE 86–1 Child with proptosis of the right eye.

Patients with neurofibromatosis tend to have less aggressive optic pathway gliomas. It is, therefore, important to inquire about family history and also to examine the patient for café au lait spots, peripheral neurofibromas, axillary freckling Lisch nodules, and other signs of Type I neurofibromatosis. Optic pathway gliomas associated with neurofibromatosis hold a better prognosis for survival than isolated optic pathway gliomas. Malignant transformation of a glioma can occur, but does so more commonly in patients with isolated gliomas.

TABLE 86–1 **Differential Diagnosis of Proptosis in Childhood**

Neoplasms
• Hemangioma
• Rhabdomyosarcoma
• Dermoid
• Optic pathway glioma
• Plexiform neurofibroma
• Meningioma
• Lymphoma
• Metastatic (eg, neuroblastoma)
Inflammatory abnormalities
• Orbital cellulitis
• Orbital pseudotumor/myositis
• Mucocele
• Cavernous sinus thrombosis
Vascular anomalies
• Arteriovenous malformation
• Orbital varices
• Carotid-cavernous fistula
Thyroid-related ophthalmopathy
Hematoma

TEST INTERPRETATION

The major diagnostic considerations in this patient are based on a careful comprehensive ophthalmologic examination, neuroimaging, and family history. This child has slowly progressive proptosis of the right eye, decreased vision in the right eye, and bilateral optic atrophy. If there is any indication of a systemic disorder related to the ophthalmologic findings, appropriate pediatric and/or neurologic consultation should be obtained.

1. External examination: Detailed examination of the ocular adnexa is critical to help differentiate the possible etiologies. The examiner should evaluate for signs of thyroid-related ophthalmopathy, which include lagophthalmos of the upper lid on downgaze (von Graefe's sign), lid retraction, and generalized lid fullness. These signs are absent in our patient. Next, retropulsion should be performed by having the patient first close his eyes. The examiner then gently palpates each globe, pushing the globe posteriorly. Comparison is made of the resistance of the globe to this retropulsion maneuver. If a retrobulbar orbital mass is present, increased resistance to retropulsion will be appreciated. Next, the examiner should evaluate the patient for external signs of neurofibromatosis, such as café au lait spots, peripheral neurofibromas, and axillary freckling. Lastly, exophthalmometry should be performed to evaluate for proptosis and to establish baseline data.
2. Optic nerve function: Vision loss is common with many orbital diseases, including optic pathway glioma. An optic neuropathy can occur from compression, inflammation, or infiltration. An afferent pupillary defect is indicative of optic nerve dysfunction. Other signs of optic neuropathy include

TABLE 86–2 **Clinical Characteristics of Optic Pathway Gliomas**

Age	8.8 years mean
Gender distribution	M = F
Association with neurofibromatosis 1	29%
Tumor location	
Chiasm	75.7%
Chiasm alone	6.6%
Chiasm + optic nerve	47.2%
Chiasm + brain	46.2%
Optic nerve alone	24%
Optic disc	1.6%
Visual loss at presentation	87.5%
Optic disc edema	35%
Optic disc atrophy	59%
Proptosis	
Orbital involvement glioma	94%
Chiasmal glioma	18%
Ophthalmoplegia	
Orbital involvement glioma	27%
Chiasmal glioma	21%
Nystagmus	23%
Hypothalamic signs	26%
Headache	28%

(From Lee AG, Dutton JJ. A practice pathway for the management of gliomas of the anterior visual pathway: an update and an evidence-based approach. *Neuro-ophthalmology*. 1999;22:139–155.)

decreased subjective color vision, decreased brightness sense, visual field defects, and optic disc pallor. Our patient had an afferent pupillary defect and bilateral optic atrophy.

3. Slit-lamp examination: In patients with optic pathway glioma, it is important for prognostic considerations to diagnose neurofibromatosis if it is present. The prognosis for survival may be better for neurofibromatosis-associated optic pathway glioma than for isolated optic pathway glioma. Lisch nodules, which are hematomas on the iris, are easily visible on slit-lamp examination.
4. Neuroimaging: Computed tomography (CT) or magnetic resonance imaging (MRI) will aid in narrowing the differential diagnosis. The examiner should obtain imaging of the brain as well as the orbit to evaluate for intracranial involvement. The MRI scan is shown in Figure 86–2. It demonstrates the typical appearance of a chiasmal glioma extending into the right orbit. An optic pathway glioma can involve only the optic nerve

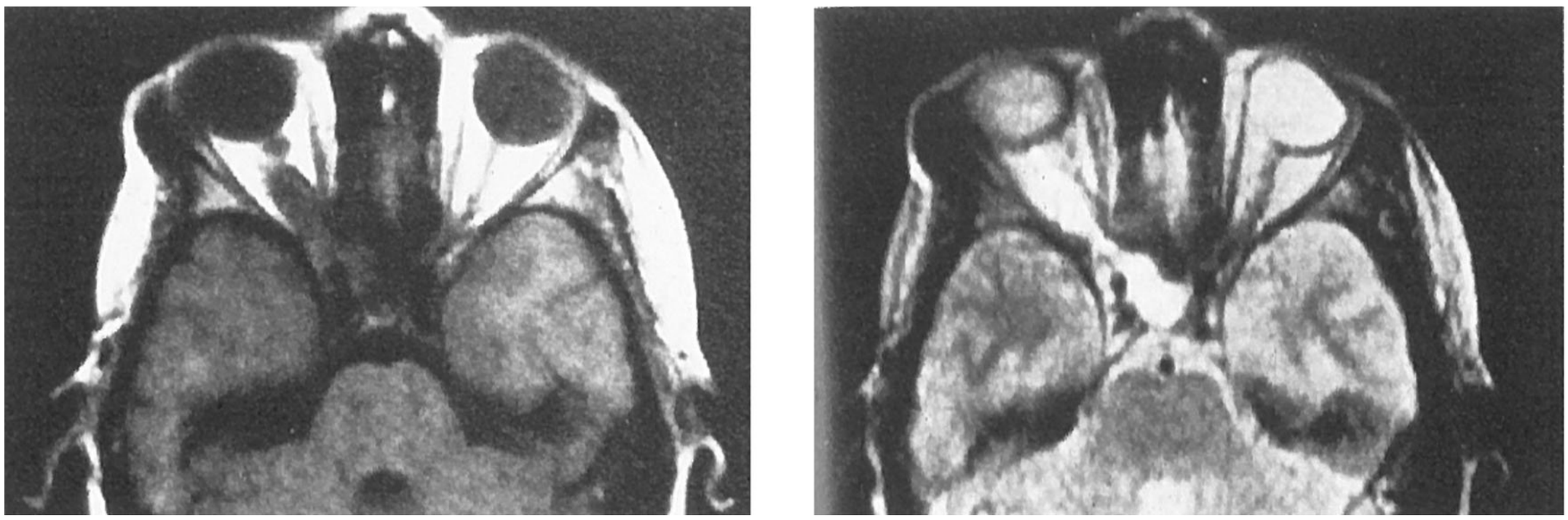

FIGURE 86–2 MR image T1-weighted (left) and T2-weighted (right) of retrobulbar mass of the right orbit, intrinsic to the optic nerve.

or may involve the optic nerve and chiasm. The optic nerve on neuro/orbital imaging will have an intrinsic enlargement of its caliber, with or without extension through the optic canal to involve the chiasm. A glioma will enhance with contrast on CT or MRI. If the posterior chiasm is involved, the pituitary and hypothalamus are also commonly affected. Bony erosion is not seen.

5. Other presenting signs and symptoms: Nystagmus (most commonly see-saw) can occur when there is chiasmal involvement and extension into the diencephalon. Precocious puberty may be seen at presentation in patients with optic pathway gliomas. Other endocrine abnormalities such as panhypopituitarism, isolated growth hormone deficiency, diabetes insipidus, or failure to thrive typically present following treatment, because of damage from surgery or radiation therapy.
6. Histopathology: Biopsy is usually not needed for clinical diagnosis. However, most optic pathway gliomas are classified as juvenile pilocytic astrocytomas and have a benign appearance (Fig. 86–3).

DIAGNOSIS

Isolated optic chiasmal glioma with extension to the right optic nerve.

MEDICAL MANAGEMENT

An optic pathway glioma can be medically managed using a variety of techniques. Optic pathway gliomas may respond to radiation therapy, if they are to be treated medically. Variable positive responses to radiation therapy have been reported in the literature, ranging from 18 to 45% at 24 to 60 months' follow-up. Chemotherapy has been found to be variably effective in the treatment of optic pathway gliomas. It can, however, be attempted in those tumors unresponsive to radiation therapy.

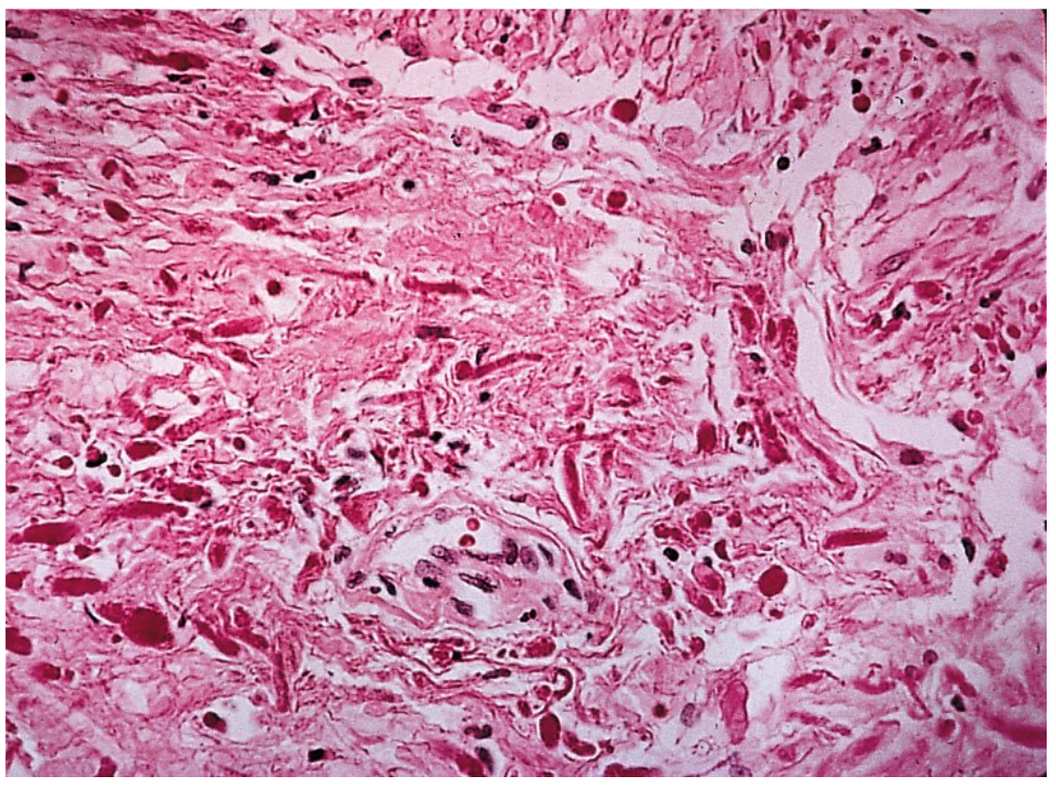

FIGURE 86–3 Histopathology of optic pathway gliomas. (Courtesy of Ramon Font, M.D., Baylor College of Medicine, Department of Ophthalmology, Houston, TX.)

Endocrine abnormalities are much more common posttreatment than pretreatment; therefore appropriate endocrine evaluation and follow-up should be performed.

SURGICAL MANAGEMENT

If an optic pathway glioma involves solely the optic nerve, total resection of the optic nerve can result in a cure. The globe itself can be left intact. Of course, with resection of the optic nerve, complete loss of vision in the eye will occur. Subtotal resection of a chiasmal glioma can be considered if the tumor has an exophytic component. A total resection of the tumor, however, is not possible if chiasmal involvement is present because of the proximity to other critical structures. Subtotal resection of a chiasmal glioma carries a significantly increased risk of bilateral vision loss.

REHABILITATION AND FOLLOW-UP

There are varying reports of survival of patients with optic pathway gliomas ranging from 60 to 89% survival at 10 years. Prognosis for survival of patients with chiasmal gliomas is worse than for patients with optic nerve gliomas because of the more aggressive nature of the tumor and the side effects of a large mass potentially compressing the hypothalamus, pituitary gland, third ventricle, and posterior optic tracts. The prognosis for patients with optic pathway glioma and neurofibromatosis might be better than for those with isolated optic pathway glioma because of the less aggressive nature of the tumor.

The visual prognosis has also been reported to be variable. Many studies have reported consistent loss of vision with any treatment, while others have reported stable or improving visual acuity after radiation treatment. The importance of long-term follow-up cannot be overemphasized as there are many reports of late onset progression after 10 years of being progression-free. Intellectual deficits are common in long-term survivors secondary to hydrocephalus or radiation side effects.

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Section XI

ORBIT/ OCULOPLASTICS

87. Ptosis
88. Thyroid Eye Disease
89. Ectropion
90. Entropion
91. Trichiasis
92. Dacryocystitis
93. Orbital Pseudotumor
94. Orbital Cellulitis
95. Dacryoadenitis
96. Orbital Tumors of Childhood
97. Orbital Tumors in Adults
98. Benign Tumors of the Eyelid
99. Malignant Tumors of the Eyelid

Case 87

PTOSIS

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 72-year-old woman was referred for drooping of her upper eyelids. The patient stated that the drooping had slowly progressed over the last 3 to 4 years. The drooping was now severe enough to interfere with her vision, and she often found herself manually lifting her lids to improve her visual field. There was no previous history of periocular trauma or surgery. She had undergone bilateral cataract extraction with placement of intraocular lenses 4 years previously. There was no history of muscle weakness or fatigue, and she had no known neurologic disease. She did not complain of diplopia or significant fluctuation of the lid position during the day. Inspection of old photographs did not show the presence of ptosis.

Examination showed corrected visual acuity of 20/20 OU. The patient was orthophoric with full ductions and versions on motility examination. Ptosis of both upper eyelids was present, with the right upper lid being lower than the left upper lid in both primary position and downgaze. The palpebral fissures measured 5 mm on the right and 6 mm on the left (Fig. 87–1). The marginal reflex distances were 0 on the right and +1 on the left. The levator function measured 14 mm on both sides. Inspection of the tarsal conjunctiva on both sides showed no significant abnormalities and no orbital masses were palpated. The upper eyelid creases were effaced on both sides, and the superior sulci were deepened.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. In this patient, there is bilateral ptosis, which has been slowly progressive. There is good preservation of levator function, and the absent upper eyelid crease and the deep superior sulci are consistent with an aponeurotic ptosis. The more ptotic eyelid is lower in downgaze, which contrasts with congenital ptosis. Furthermore, the opportunity to inspect previous photographs confirms the acquired nature of the lid malposition.

Aponeurotic ptosis results from a disinsertion of the levator aponeurosis from its normal attachment on the anterior tarsus. While levator disinsertion may occur following trauma or severe edema, it is most commonly an age-related change in the eyelid. The presence of good lid excursion (greater than 12 mm) indicates preservation of levator function and is important in distinguishing aponeurotic ptosis from other types of ptosis.

2. Neurogenic ptosis results from interruption of the innervation to the levator aponeurosis (cranial nerve III) or disruption of the sympathetic innervation to Mueller's muscle. It may be congenital or acquired. Horner's syndrome, myasthenia gravis, or other neurologic conditions may cause acquired ptosis. Careful pupil examination and testing with topical cocaine and Paredrine will confirm the presence of Horner's syndrome. Tensilon testing should be performed if myasthenia gravis is suspected.

3. Myogenic ptosis may also be congenital or acquired. Myogenic congenital ptosis results from abnormal development and fibrosis of the levator muscle and may be unilateral or bilateral. In contrast to aponeurotic ptosis, the ptotic lid will be higher in downgaze and the levator function is severely reduced, usually measuring less than 7 mm.

Acquired myogenic ptosis occurs in muscular diseases such as muscular dystrophy, progressive external ophthalmoplegia

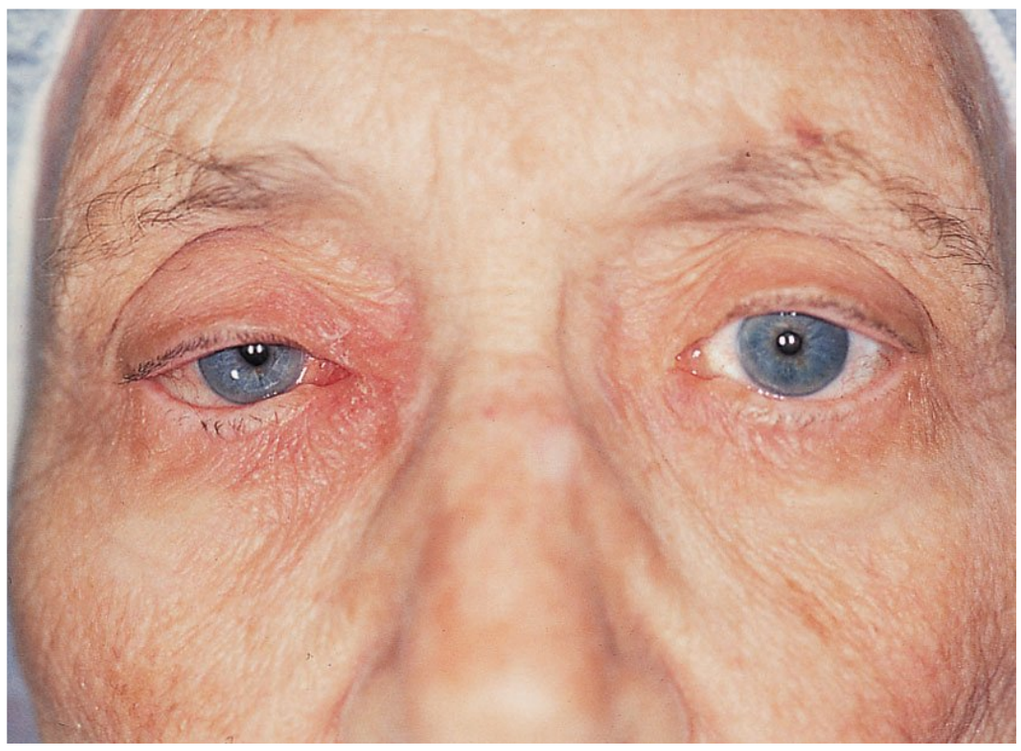

FIGURE 87–1 Clinical photograph depicting bilateral ptosis of the eyelids that is more marked on the right side. Note the absent lid crease and the deep superior sulcus on both sides.

(Kearns-Sayre syndrome), or oculopharyngeal dystrophy. The levator function is markedly diminished, and ocular motility is often severely impaired.

4. Mechanical ptosis results from the presence of a mass within the eyelid. The mass may be congenital or acquired and may be inflammatory or neoplastic. The ptotic lid should be everted to allow examination of the tarsal conjunctiva and fornix. Palpation of the orbit may reveal a mass superiorly. More commonly, severe blepharochalasis may produce mechanical ptosis.
5. Conditions that may mimic the presence of eyelid ptosis should be included in the differential diagnosis. The eyelid may appear ptotic if the globe is small (phthisis bulbi) or displaced posteriorly (enophthalmos). Eyelid retraction on one side may simulate ptosis of the contralateral lid.

TEST INTERPRETATION

If neurogenic or myogenic ptosis is suspected, appropriate testing as discussed above should be performed. It is critical to establish the correct diagnosis, not only to allow the correct management of the lid malposition, but also to ensure that any systemic disease is identified and addressed appropriately.

DIAGNOSIS

Ptosis of both upper eyelids due to levator aponeurosis disinsertion.

MEDICAL MANAGEMENT

If ptosis is mild and the patient is asymptomatic, no treatment is indicated. If ptosis is severe enough to cause symptomatic visual field impairment, taping of the lid or the use of eyelid crutches attached to the patient's spectacles may be tried. In most patients, these measures are only temporizing, and surgical correction of the lid malposition is required to effect a long-term solution.

SURGICAL MANAGEMENT

Most cases of severe aponeurotic ptosis will require surgical treatment to achieve long-term satisfactory results. The most common procedure used is reattachment or advancement of the dehisced levator aponeurosis to the anterior tarsus. This is accomplished through an external approach that also allows for reestablishment of the eyelid crease. Complications of surgery include undercorrection or overcorrection, asymmetric or unsatisfactory lid contour, and lagopthalmos with secondary exposure symptoms.

REHABILITATION AND FOLLOW-UP

The patient underwent external levator advancement on both upper eyelids. The procedure was performed using local infiltrative anesthesia allowing for intraoperative adjustment of lid height and contour. Postoperatively, the patient

noted an improvement in her visual field, and she has suffered no complications from the surgical procedure.

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Case 88

THYROID EYE DISEASE

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 44-year-old woman was referred for evaluation of pain around both eyes. The pain was especially severe with eye movement. She had noted increasing prominence of both eyes over the past 18 months and complained that both eyes felt "gritty." She had no complaints of diplopia or blurred vision, and there was no previous ocular history of surgery or trauma. Her medical history was unremarkable, and there was no previous history of thyroid dysfunction. Her review of symptoms was significant for heat and cold intolerance, but she reported no recent change in weight, body hair growth or loss, or change in the quality of her voice. There was no known cardiovascular or neurologic disease.

Examination showed corrected visual acuity of 20/20 in each eye. Normal color vision defect was detected with Hardy-Rand-Rittler color plates. Both pupils reacted normally, and there was no relative afferent pupil defect. The motility exam showed orthophoria with mild (−1) restriction of upgaze on both sides. There was no subjective diplopia. Upper and lower eyelid retraction was present with palpebral fissures measuring 16 and 15 mm on the right and left sides, respectively (Fig. 88–1). Temporal flaring of the upper lids was noted, and 2 mm of lagophthalmos was present bilaterally. There was increased resistance to retropulsion of both globes; no orbital masses were palpated. Exophthalmometry measurements were 22 mm on the right side and 21 mm on the left (Fig. 88–2). Slit-lamp examination showed scattered punctate epithelial erosions of both corneas inferiorly. Mild bulbar conjunctival injection was present bilaterally. The anterior segments were otherwise unremarkable. Dilated fundus exam showed both optic discs to be flat without pallor. The retina appeared normal, and there were no choroidal striae.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. One of the most common causes of proptosis in middle-aged adults is thyroid eye disease (Graves' disease), and this patient demonstrates many of the salient features of this condition.

For purposes of evaluation and management, the ophthalmic findings of thyroid eye disease can be divided into three categories: optic nerve function, motility disturbance, and eyelid retraction. The most common causes of vision loss in Graves' disease are compressive optic neuropathy and corneal exposure. Restrictive motility disturbances in Graves' disease result from inflammation and swelling of the extraocular muscles, followed by fibrosis. The inferior rectus muscle is most frequently involved, followed by the medial, superior, and lateral rectus muscles. Radiographically, there is fusiform enlargement of the involved muscle with relative sparing of the tendon. Many authors divide thyroid orbitopathy into two categories. Type I orbitopathy consists of symmetric proptosis and eyelid retraction with minimal restrictive myopathy. Symptoms of severe orbital inflammation are not present. In contrast, patients with Type II orbitopathy display marked inflammatory changes with restrictive myopathy and an increased incidence of compressive optic neuropathy. Involvement of the levator and Mueller's muscle in the upper eyelid and the lid retractors in the lower eyelid causes upper and lower eyelid retraction. Scleral show and lagophthalmos leading to severe corneal exposure may result.

The diagnosis of thyroid related ophthalmopathy is made on clinical grounds, and confirmed radiographically. In addition to demonstrating the enlarged extraocular

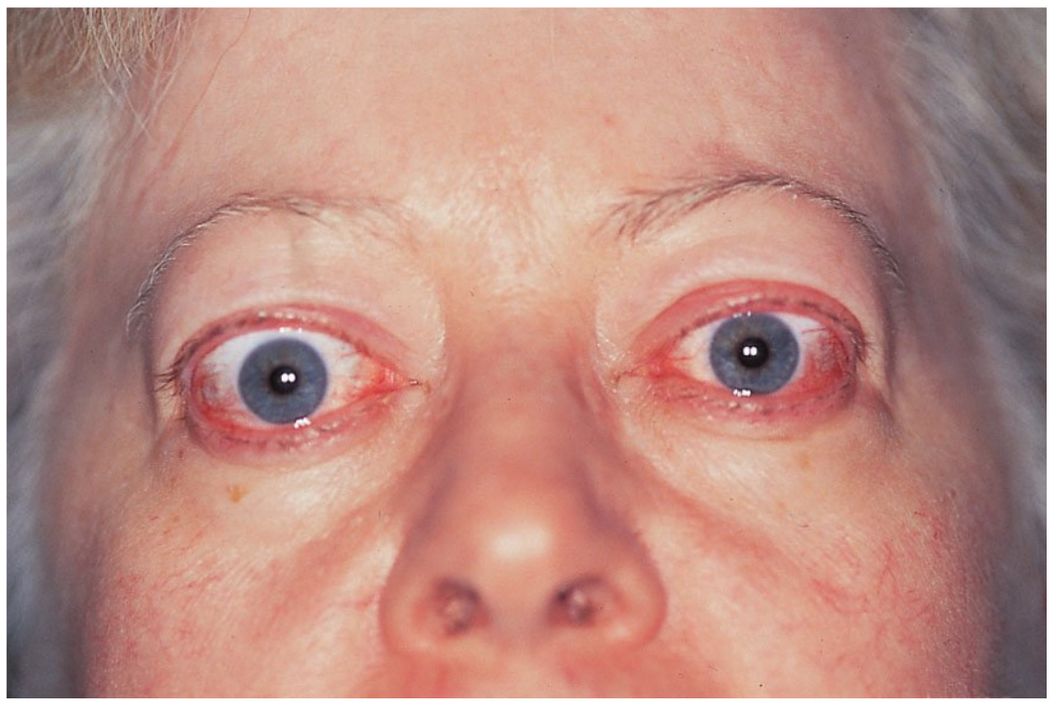

FIGURE 88–1 Clinical photograph depicting marked eyelid retraction with widened palpebral fissures and scleral show.

muscles, the computed tomography (CT) or magnetic resonance imaging (MRI) allows assessment of the optic nerve near the orbit apex. Consultation with an internist or endocrinologist should be sought to evaluate the patient's thyroid status. The ophthalmic disease and thyroid dysfunction, if present, often run independent courses, and the patients should be thoroughly educated in this regard.

2. Orbital inflammatory pseudotumor may also occur as bilateral disease and may even produce a localized myositis. In orbital pseudotumor, the CT scan will show enlargement of the entire muscle, including the tendon. This contrasts with the tendon sparing typically seen in Graves' disease (see Case 93).

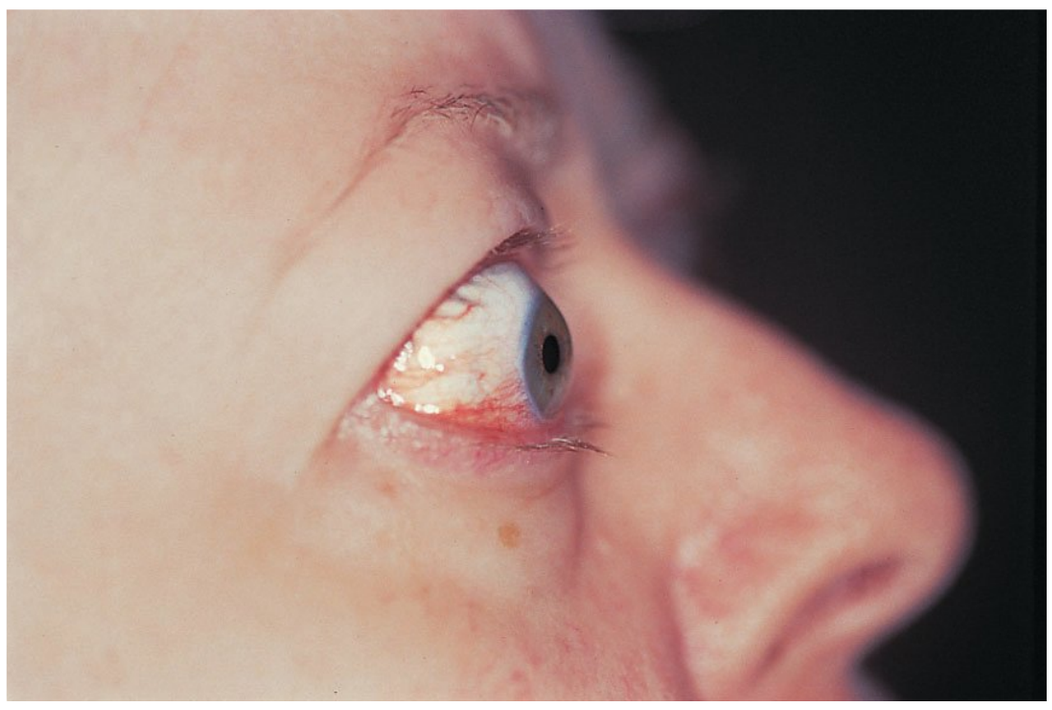

FIGURE 88–2 Lateral view demonstrates proptosis of the globe.

3. Other causes of bilateral proptosis include bilateral orbital metastasis from a distant primary malignancy and diffuse orbital infiltrative processes such as amyloidosis. A detailed clinical history and radiographic evaluation of the orbits will help distinguish these entities from Graves' disease.

TEST INTERPRETATION

Humphrey visual field testing was performed that showed no significant abnormalities. A CT scan of the orbits demonstrated mild to moderate extraocular muscle enlargement of both inferior rectus muscles and the left medial rectus muscle. Tendon sparing, typical of Graves' disease, was present. Posteriorly, the optic nerves did not appear compressed.

DIAGNOSIS

Graves' orbitopathy (Type I) with eyelid retraction and bilateral proptosis.

MEDICAL MANAGEMENT

Corneal exposure changes may be treated with frequent instillation of artificial tears or lubricating ointment. Punctal occlusion, either temporary or permanent, may be considered. Wearing of a moisture shield at bedtime may help ameliorate nocturnal drying due to lagophthalmos and decreased Bell's phenomenon.

Active orbital inflammation, especially if there is evidence of compressive optic neuropathy, may be treated with high doses of oral corticosteroids (prednisone 80 to 100 mg daily). Limiting treatment to 2 to 4 weeks may minimize the unwanted side effect of the steroids, namely Cushingoid syndrome and immune suppression. The steroids can be tapered while carefully monitoring optic nerve function. Patients who cannot be successfully tapered should be considered for radiation therapy or surgical decompression of the orbit.

Most patients with symptomatic restrictive strabismus will eventually require strabismus surgery. During the active inflammatory phase, wearing a patch over one eye may relieve the patient's symptoms. Prisms are usually not effective because of the noncomitant nature of the motility disturbance. Motility measurements should be stable for at least 3 to 4 months before strabismus surgery is performed.

SURGICAL MANAGEMENT

Patients with compressive optic neuropathy that is unresponsive to steroid therapy or radiation treatment or in whom the steroids cannot be successfully tapered may be considered for orbit decompression. In addition, patients with severe proptosis leading to corneal exposure may be considered for orbit decompression, even in the absence of compressive optic neuropathy. There continues to be debate regarding the optimal surgical approach for decompression as well as the number of orbital walls that should be removed, with some authors advocating two-wall and others supporting three-wall decompression. Orbit decompression may cause exacerbation of existing diplopia or creation of diplopia in a patient without previous symptoms. The patient must be fully apprised of this risk and must understand that subsequent strabismus surgery may be required.

Strabismus surgery may be indicated in thyroid eye disease if symptomatic diplopia is present. Motility measurements should be stable for at least 3 to 4 months before surgery to ensure that the patient is not in an active inflammatory phase. Additionally, strabismus surgery should follow orbit decompression surgery because the motility pattern may be altered after orbit surgery.

Severe eyelid retraction is addressed only after any needed orbit or muscle surgery. Eyelid retraction can cause severe functional as well as cosmetic problems, and again, treatment must be individualized. Recession of the levator aponeurosis in the upper eyelid and of the lower lid retractors in the lower lids allows for improved coverage of the bulbar surface and improved cosmesis.

REHABILITATION AND FOLLOW-UP

The patient maintained good visual acuity and did not develop significant diplopia. She was treated initially with frequent artificial tears and punctal occlusion to improve the corneal surface. After 4 months of stable symptoms, she underwent recession of all four eyelids. There were no intraoperative or postoperative complications, and the patient was satisfied with the cosmetic result as well as the relief of her exposure symptoms. Endocrinology evaluation revealed hypothyroidism, and the patient has been maintained on thyroid hormone replacement therapy.

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Case 89

ECTROPION

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 70-year-old man presented with complaints of left eye irritation of at least 1 year's duration. He had bilateral cataract surgery 3 years previously and there was no other history of ocular disease or trauma.

Examination showed a corrected vision of 20/20 OD and 20/25 OS. The external examination showed a marked "out-turning" of the left lower eyelid with associated tarsal conjunctival injection diffusely (Figs. 89–1A and B). No masses were palpated. There was mild dermatochalasis of both upper lids. Both lower lids exhibited moderate horizontal laxity. The remainder of the eye examination was within normal limits.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The patient has an ectropion of the left lower eyelid. In this age group, the most common cause of ectropion is related to involutional (age-related) changes within the eyelid. The most prominent change relates to increased laxity of the tarso-ligamentous sling that normally supports the eyelid. As the laxity of the lid progresses, the eyelid will commonly develop a medial ectropion first. At this stage, the patient may complain of epiphora due to eversion of the lower lid punctum. If untreated, the eyelid will eventually develop a generalized ectropion involving the entire lid. Prolonged eyelid eversion may then result in conjunctival hypertrophy as well as keratinization of the exposed tarsal conjunctival surface.

2. Cicatricial ectropion must be included in the differential diagnosis of an out-turning eyelid. This condition results from a vertical shortening of the anterior lamella of the lid, which may occur after surgical or accidental trauma to the lid or cheek area. Excision of malignant skin cancers or overaggressive skin removal during a lower lid blepharoplasty may produce a cicatricial ectropion. To determine if the anterior lamella is vertically shortened, a manual attempt to lift the lid into its normal position should be made. Inability to easily lift the lid to its normal position indicates the presence of a cicatricial component. This shortening of the anterior lamella must be addressed in any surgical correction of the lid malposition.

3. A mechanical ectropion is usually easily identified by the presence of a tumor or other mass on the lid causing the lid margin to be displaced downward. Less common causes of mechanical ectropion include edema of the lid or herniation of orbital fat.

4. Paralytic ectropion most commonly occurs following temporary or permanent seventh nerve palsy. The presence of other accompanying signs of seventh nerve impairment, including facial weakness on the ipsilateral side, makes the diagnosis apparent.

TEST INTERPRETATION

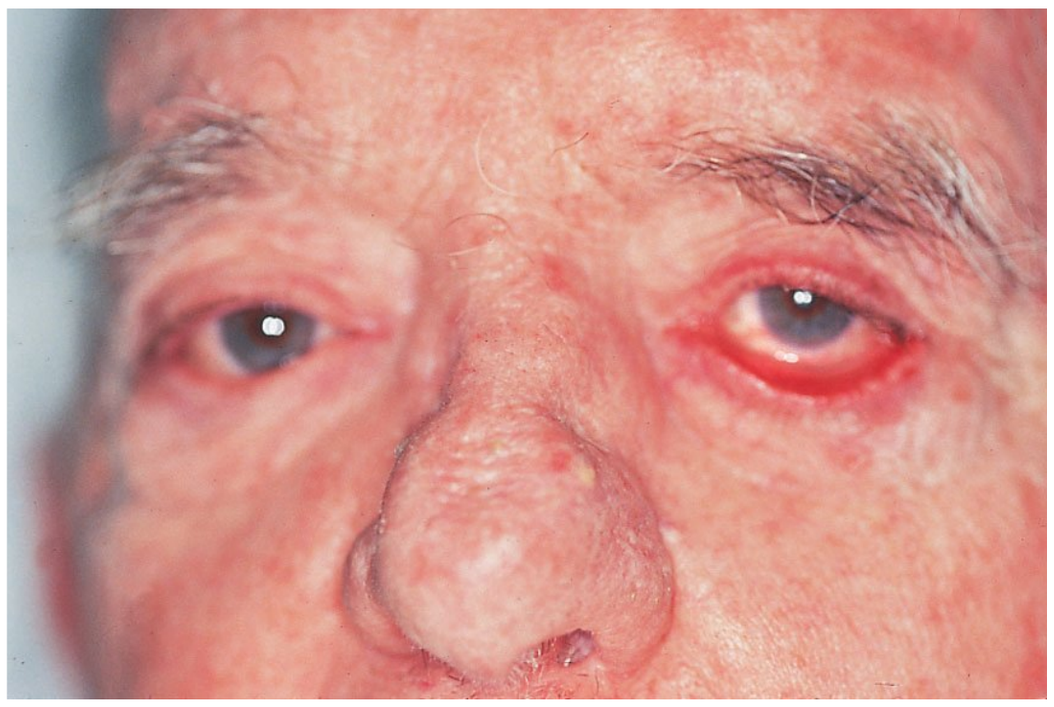
Inability to lift the eyelid manually might suggest cicatricial or restrictive etiology.

DIAGNOSIS

Involutional ectropion of the left lower eyelid with resultant ocular irritation.

MEDICAL MANAGEMENT

Mild involutional ectropion may be treated with artificial tears or lubricating ointment. If the condition is progressive, then surgical management is the definitive treatment.



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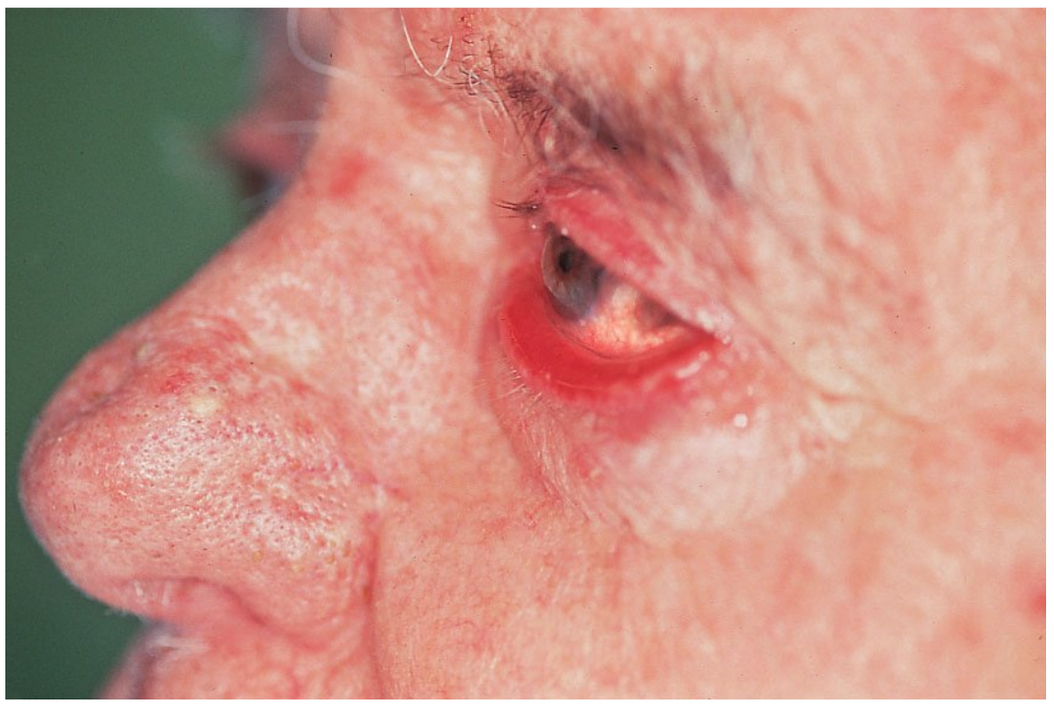

B

FIGURE 89–1 Clinical appearance of lower lid ectropion (A). Injection of the exposed tarsal conjunctiva is best seen on lateral view (B).

SURGICAL MANAGEMENT

The correct type of ectropion must be diagnosed so that the appropriate surgical procedure can be employed. If a cicatricial component exists, the anterior lamella of the lid must be vertically elongated through the use of a free, full-thickness skin graft. Paralytic ectropion is most commonly addressed using a lateral tarsorrhaphy or medial or lateral canthoplasties.

The surgical treatment for involutional ectropion most commonly employs one of several horizontal shortening procedures, such as the lateral tarsal strip procedure or a full-thickness wedge resection of the eyelid. If the ectropion is primarily medial, the "lazy-T" procedure may be efficacious. This procedure includes a full-thickness pentagonal wedge resection immediately lateral to the lower lid punctum combined with an elliptical excision of tarsal conjunctiva and retractors posterior to the punctum (medial spindle procedure). If medial canthal laxity comprises a significant contribution to the lid malposition, a medial canthal plication may be performed.

REHABILITATION AND FOLLOW-UP

The patient underwent a lateral tarsal strip procedure in conjunction with a medial spindle procedure. The corrected eyelid position ameliorated the patient's symptoms of ocular irritation.

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Case 90

ENTROPION

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 75-year-old woman presented with complaints of severe right eye pain. Her symptoms began intermittently approximately 2 years previously and have now progressed such that she is constantly cognizant of right eye pain and discomfort. The patient has discovered that she can alleviate her pain if she manually retracts her right lower eyelid.

Examination shows 2 mm of ptosis of both upper eyelids with deep superior sulci and preservation of levator function. There is "in-turning" of the right lower eyelid causing the lashes to rub against the epibulbar surface (Fig. 90–1). Moderate horizontal laxity of the lower lid is present. With gentle downward traction on the right lower eyelid, the lid margin can be restored to its normal position; however, the in-turning recurs when the patient blinks.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The patient has an entropion of the right lower eyelid. Involutional entropion is the most common type of entropion in this clinical setting. Age-related changes that contribute to the development of the condition include the following: (1) horizontal laxity of the eyelid; (2) disinsertion or dehiscence of the lower eyelid retractors; (3) overriding of the preseptal orbicularis; (4) relative enophthalmos of the globe due to atrophic changes of the orbital soft tissues. All of these features are present in the current case and must be considered in the surgical approach to correcting the patient's condition.

2. Other causes of entropion should be considered and ruled out before proceeding with treatment. Ocular irritation or lid edema may cause a temporary spastic entropion. This condition occurs after intraocular surgery or other trauma to the lid that produces edema of the periocular soft tissues. The combination of lid edema, orbicularis spasm, and underlying involutional changes can result in a spastic entropion. Taping the eyelid to evert the lid margin may palliate the patient's symptoms. Placement of Quickert-Rathbun sutures to evert the lid may also be helpful in relieving the patient's discomfort. The condition may improve once the underlying cause of the edema is corrected; however, it may be necessary to correct the involutional changes surgically to effect a permanent correction of the lid malposition.

3. Cicatricial entropion occurs when there is vertical shortening of the posterior lamella of the eyelid. This condition may result from a variety of conditions including Stevens-Johnson syndrome, cicatricial pemphigoid, or posttrauma scarring after chemical or thermal burns. The digital eversion test, or the ability to easily rotate the lid margin to its normal position using downward traction on the lid, allows the examiner to determine if a cicatricial condition is present. The posterior tarsus should be inspected for evidence of scarring or loss of the inferior fornix. Treatment of cicatricial entropion includes tarsal fracture with placement of everting sutures for mild cases. More severe cases in which the tarsus is severely scarred and distorted may require tarsal and mucus membrane grafting. Available materials for grafting include hard-palate mucosa, preserved scleral grafts, and autogenous ear cartilage.

TEST INTERPRETATION

The lid was not restricted, suggesting involutional entropion.

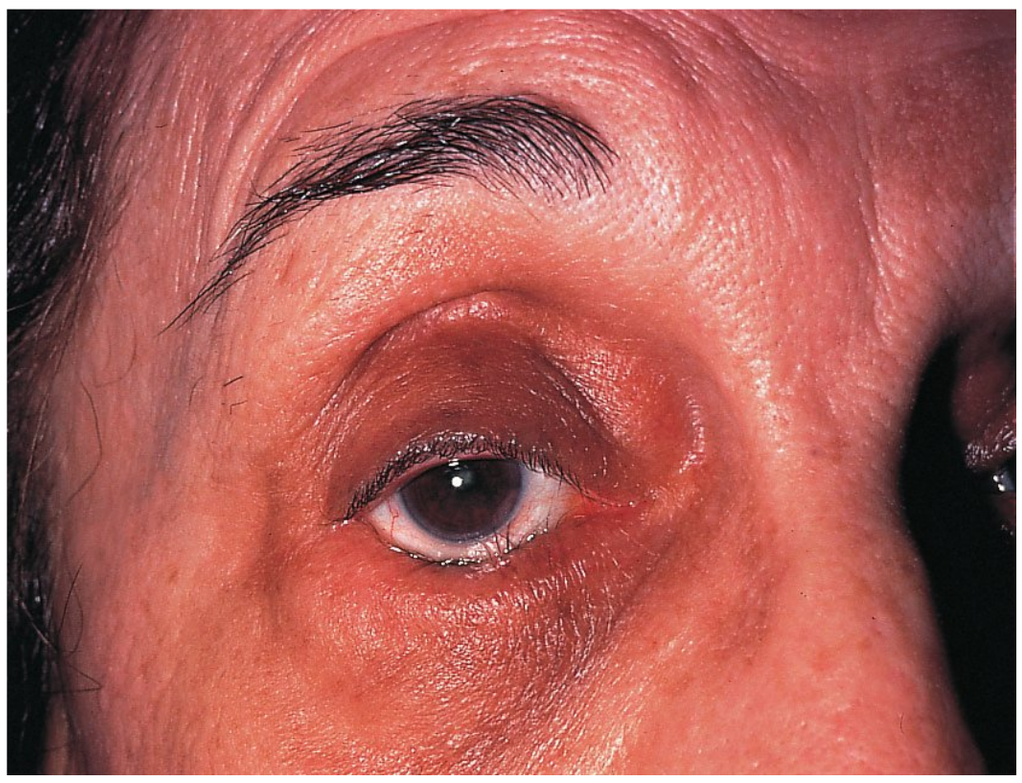

FIGURE 90–1 Clinical appearance of lower lid entropion. Overriding of the preseptal orbicularis can be seen.

DIAGNOSIS

Involutional entropion of the right lower eyelid.

MEDICAL MANAGEMENT

Taping the lid may provide acute relief of the patient's symptoms; however, this is rarely satisfactory over the long-term.

SURGICAL MANAGEMENT

Temporizing everting sutures (Quickert-Rathbun sutures) may be used to effect immediate relief of the patient's discomfort. To achieve a more permanent correction, surgical management directed toward the primary cause(s) of the entropion is indicated. Horizontal tightening of the lid using a lateral tarsal strip procedure will often satisfactorily correct the entropion. The Wies procedure, in which a full-thickness horizontal incision is used to create an adhesion between the anterior and posterior lamellae of the lid, is another option. Lastly, direct repair of the lower lid retractors can be performed through a skin-orbicularis incision. This procedure may be combined with a horizontal shortening procedure.

REHABILITATION AND FOLLOW-UP

The patient underwent a Wies procedure of the lower eyelid with satisfactory correction of the lid entropion. She has experienced no postoperative complications.

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Case 91

TRICHIASIS

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 64-year-old woman presented with complaints of chronic irritation of the left eye. The problem had been present intermittently over the past 2 to 3 years but had become more constant over the previous few months. There was no previous history of ocular surgery, disease, or trauma.

Ophthalmic examination was normal except for the external exam. There was an entropion of the left lower eyelid (Fig. 91–1). The lid was easily returned to its normal position using gentle manual downward pressure. The tarsal conjunctiva showed mild erythema without evidence of cicatricial changes, and the inferior fornix was deep without symblepharon. When the lid was in its normal position, an abnormal row of fine nonpigmented lashes was present posterior to the gray line. These lashes were in contact with the epibulbar surface. Mild punctate corneal changes were present inferiorly. The inferior bulbar conjunctiva showed rose bengal staining in the areas associated with the abnormal lashes. Diffuse thickening of the lid margin was noted as well as the presence of fine telangiectatic vessels. Scattered debris, including collarettes, were present on the lashes of all four eyelids.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. This patient has ocular irritation due to two components. The first is the eyelid malposition, or entropion of the lid. Entropion of the eyelid is discussed in Case 90. The second component is the abnormal row of lashes present posterior to the gray line. In the face of chronic prolonged inflammation, the meibomian glands may undergo metaplastic transformation to hair follicles. This transformation results in the presence of fine lashes emanating from the previous meibomian gland orifices, a condition referred to as distichiasis. These abnormal lashes may, in turn, rub the globe and cause trichiasis.
2. Trichiasis may result from misdirection of the lashes secondary to eyelid malposition. It occurs commonly when posterior lamella scarring is present and may be diffuse or segmental.
3. Ocular irritation may be produced by ocular surface disorders such as Sjögren's syndrome, blepharitis, or meibomian gland dysfunction. Careful evaluation of the ocular tear film should be performed including assessment of the tear breakup time. Instituting a lid hygiene program, frequent use of artificial tears, and consideration of punctal occlusion may help these disorders.

TEST INTERPRETATION

Schirmer's testing may provide some quantitative measurement of tear production. The use of rose bengal dye aids in the identification of abnormal dry areas of the epibulbar surface.

DIAGNOSIS

1. Trichiasis of the lower eyelid due to aberrant lashes (distichiasis) and lower lid entropion.
2. Blepharitis and meibomian gland dysfunction of all four eyelids.

MEDICAL MANAGEMENT

Treatment of misdirected lashes may be challenging, and recurrence is frequent regardless of the modality used.

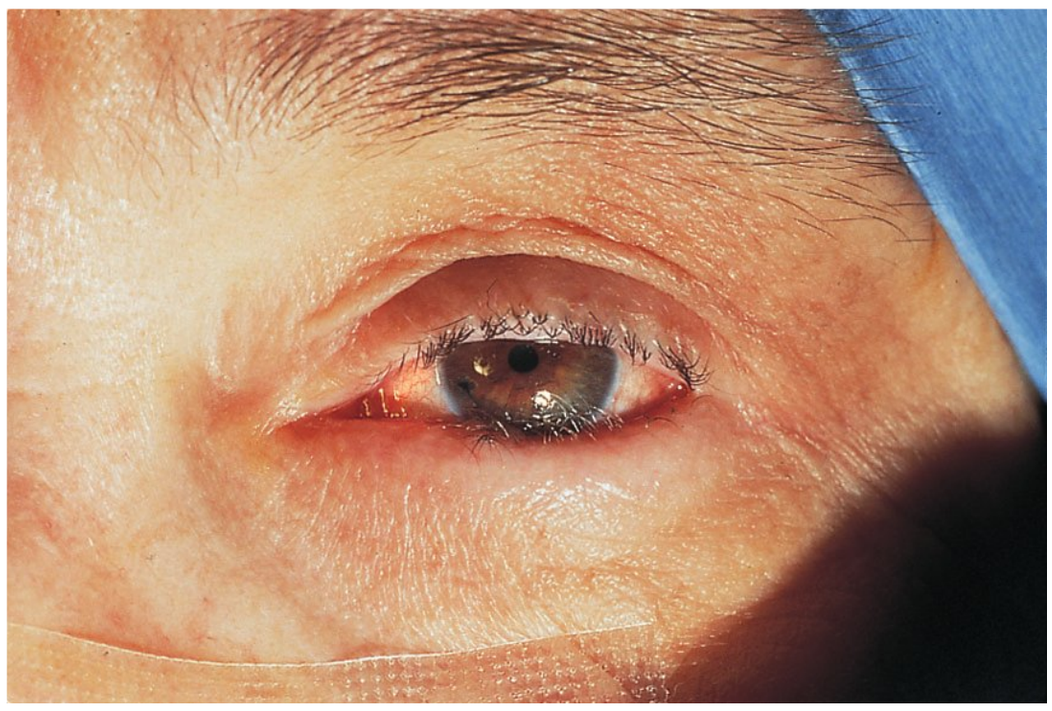

FIGURE 91–1 Clinical photograph showing entropion of the left lower eyelid with trichiasis.

If only a few abnormal lashes are present, simple epilation may be performed. While this will effect immediate relief of the patient's symptoms, the lashes will almost always recur, and consideration of other treatments is usually required:

- Electrolysis may be used for focal areas of trichiasis. The recurrence rate is high, and extensive use of electrolysis may result in scarring of the eyelid margin.
- Cryotherapy is one of the more effective treatments for trichiasis. It may be performed using a local infiltrative anesthetic. A nitrous oxide probe is applied to the area of aberrant lashes using a double freeze-thaw technique. The concomitant use of a thermocoupler allows for monitoring of the eyelid temperature and helps avoid overtreatment. Bringing the eyelid tissues to −20°C will effect ablation of the hair follicle without damage to the surrounding tissues. Complications include loss of skin pigmentation and eyelid notching. If some of the aberrant lashes recur, the procedure can be repeated.
- Argon laser ablation has been used to treat focal areas of aberrant lashes. The laser is less effective than cryotherapy but does not result in the posttreatment edema produced after cryotherapy. This may be particularly important in patients with existing inflammatory lid conditions such as ocular cicatricial pemphigoid.

SURGICAL MANAGEMENT

The lower lid entropion may be surgically corrected as discussed elsewhere (see Case 90).

Surgical management of trichiasis may be considered if the lashes are grouped in one area of the eyelid and there is sufficient horizontal laxity of the lid. Under these circumstances, a full-thickness pentagonal wedge containing the area of aberrant lashes may be excised. The lid defect is repaired in the standard fashion, and a cantholysis can be performed to allow closure of the defect without undue tension.

A lid-splitting procedure can also be used in which the lid is split between the anterior and posterior lamella. The bulbs of the hair follicles can then be identified within the tarsus and removed, or the cryoprobe can be applied directly to the tarsal plate.

REHABILITATION AND FOLLOW-UP

The patient underwent a Wies procedure to correct the lower eyelid entropion. At the same time, cryotherapy was applied to the aberrant lashes. Postoperatively, the patient did well, with only focal recurrence of the distichitic lashes. These were re-treated with additional cryotherapy in the office. A lid hygiene program to address the patient's blepharitis and meibomian gland dysfunction was also instituted.

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Case 92

DACRYOCYSTITIS

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 44-year-old woman was referred for evaluation of tearing and inflammation of the right lower eyelid medially. Her past medical history was significant for lethal midline granuloma (midfacial necrotizing lesion) for which she had undergone at least three previous procedures, which included removal of the nasal septum and fronto-ethmoidectomies. She reported constant epiphora of the right eye since the time of her surgeries and had more recently noted intermittent redness of the right lower eyelid. These episodes of redness were associated with lid tenderness and mucous discharge from the eye. She had been previously treated with an unknown ophthalmic antibiotic drop.

Examination showed erythema of the right lower lid medially with associated tenderness (Fig. 92–1). No definite masses were palpated in the lacrimal sac region. There was a whitish mucoid discharge present, and the conjunctiva was mildly injected. The puncta of the right upper and lower eyelid were present and appeared patent. There was a well-healed surgical incision over the nose with residual distortion of the nose architecture. The remainder of the ophthalmic examination was completely normal. Nasolacrimal irrigation was performed that demonstrated complete obstruction of the distal nasal lacrimal system. The upper system was patent as demonstrated by the reflux of irrigating solution through the upper and lower puncta. Inspection of the inner nose showed a large nasal defect with an absent septum.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

Dacryocystitis, or inflammation of the lacrimal sac, may be caused by a wide variety of disorders. The common denominator is obstruction of the nasal lacrimal duct (NLD) causing impaired drainage of tears from the lacrimal sac. The affected patient will complain of epiphora, and repeated episodes of dacryocystis may ensue due to the chronic stasis of tears in the lacrimal sac and resultant infection.

1. Congenital nasal lacrimal duct obstruction occurs in approximately 5% of full-term newborns and may lead to acute dacryocystitis. The cause is usually a thin residual mucosal membrane at the lower end of the lacrimal duct causing impaired drainage of tears.
2. In adults, acquired NLD obstruction more commonly occurs at the junction of the lacrimal sac and the duct. Chronic inflammation from adjacent sinus disease, viral infections, autoimmune disorders, and use of some medications such as 5-fluorouracil or phospholine iodide may contribute to the development of NLD obstruction. A careful history to rule out previous facial or canalicular trauma or surgery should be obtained. Rarely, tumors of the lacrimal sac may produce epiphora and dacryocystitis. A palpable mass within the lacrimal sac, particularly with extension above the level of the medial canthal tendon, should raise the suspicion of a neoplasm.
3. Preseptal cellulitis and orbital cellulitis may initially present as a dacryocystitis. The infection may extend to involve the periocular tissues both anterior and posterior to the orbital septum. Preseptal and orbital cellulitis are discussed elsewhere in the text. (See Case 94.)

TEST INTERPRETATION

Many authors recommend delaying NLD irrigation until the acute infection has resolved, although gentle irrigation may be safely performed if the infection does not appear too severe. The presence of the obstruction should be demonstrated, and the level of the obstruction (NLD, canalicular) must be determined. Passage of the Bowman probe into the canaliculus and sac will

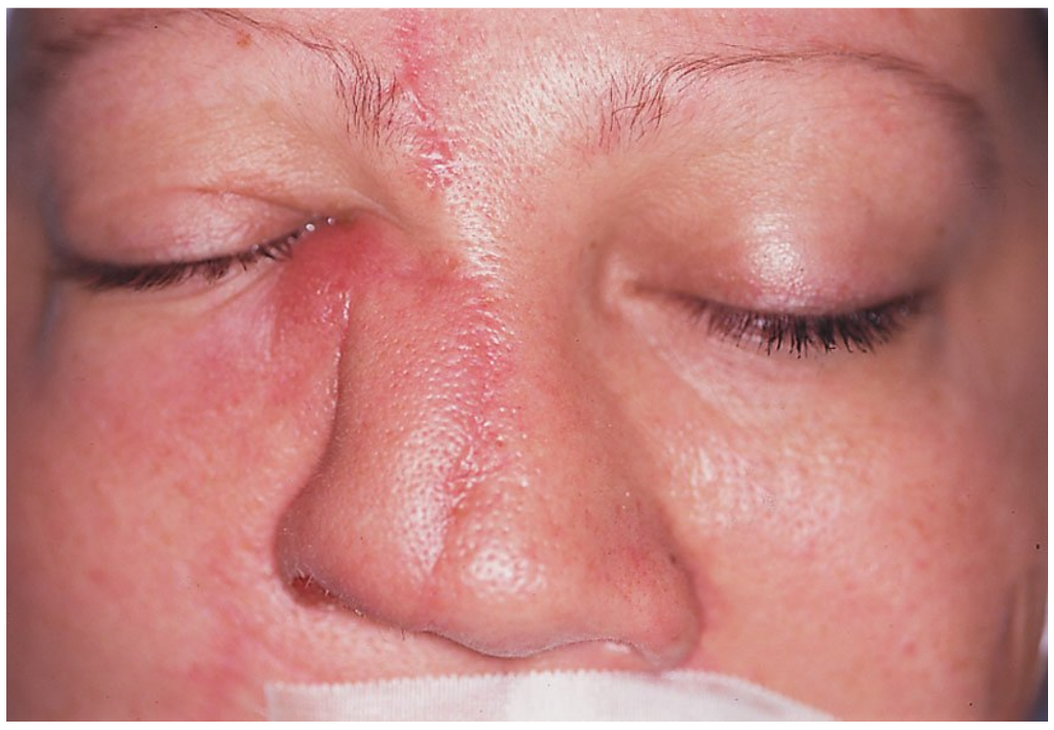

FIGURE 92–1 Clinical appearance of patient with erythema and mild edema of the right lower eyelid over the region of the lacrimal sac. The previous surgical incision over the nose is visible.

reveal any obstruction at this level. Observation of reflux through the upper and lower puncta signifies patency of the upper lacrimal system. Failure of the irrigant to reach the nose confirms the presence of an NLD obstruction.

Other tests that may be of use in evaluating the lacrimal system include dacryocystography and scintigraphy. In dacryocystography, radiopaque dye is injected into the canaliculi, and an x-ray is subsequently obtained. If an obstruction is present, the dye will be visualized remaining within the lacrimal sac. To perform dacryoscintigraphy, a drop containing a radioactive marker is placed on the conjunctival surface, and sequential scans are obtained. The passage of the marker into the canaliculi, lacrimal sac, and duct can thus be documented. The advantage of this latter test is that it more closely mimics physiologic conditions and may demonstrate functional obstruction of the lacrimal system when other testing methods have demonstrated anatomic patency.

DIAGNOSIS

Dacryocystitis, right side, secondary to disrupted or absent NLD as a result of the patient's previous midline disease and surgery.

MEDICAL MANAGEMENT

The acute infection should be treated with oral or intravenous antibiotics, depending on the severity of the infection. If a pyocele or abscess is present, aspiration may yield material for smears and cultures to guide antibiotic therapy. The patient should be instructed to apply warm compresses frequently to the inflamed site. Addition of antibiotic ophthalmic drops is of limited value and is usually not needed.

SURGICAL MANAGEMENT

Most patients with dacryocystitis will eventually require dacryocystorhinostomy (DCR) to prevent further episodes of infection. Surgery is best deferred until resolution of the infectious process. In a few patients, however, medical management will not totally resolve the infection, and a DCR will need to be performed while active inflammation is still present.

REHABILITATION AND FOLLOW-UP

The patient was treated with oral antibiotics resulting in rapid resolution of the inflammation. She subsequently underwent a DCR with placement of silicone tubing, with good resolution of her epiphora. She continues under the care of her ear, nose, and throat physician and oncologist for treatment of the lethal midline disease.

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Case 93

ORBITAL PSEUDOTUMOR

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 63-year-old man presented with a 2-day history of left eye pain and decreased vision. There was no previous history of ophthalmic disease, surgery, or injury. His past medical history was significant for poorly controlled hypertension. The review of systems revealed no history of rheumatoid disease or collagen vascular disease. There was no history of diabetes mellitus.

Examination showed best corrected vision of 20/20 OD and 20/400 OS. There was a 2+ relative afferent pupillary defect of the left pupil. Marked periorbital edema and erythema with 3 mm of left globe proptois was noted. There was increased resistance to retropulsion of the left globe and diffuse restriction of left globe motility with associated pain. The conjunctiva of the left eye showed 3+ erythema and diffuse chemosis (Fig. 93–1). Both anterior chambers were quiet, and no cell or flare was present. There was mild nuclear sclerosis of both lenses noted. The dilated fundus exam of the left eye showed diffuse choroidal thickening. The fundus of the right eye was unremarkable.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. This older patient presents with signs and symptoms of diffuse orbital inflammation of acute onset. Inflammatory processes, either infectious or noninfectious, should be strongly considered. The absence of known risk factors such as diabetes mellitus, malignancy, history of immunosuppressive therapy, or recent trauma lowers the suspicion for an infectious process.

Orbital pseudotumor may present in several forms: Acute anterior orbital in*fl*ammation in which the inflammatory process primarily affects the globe, especially the sclera, Tenon's capsule, and the immediate adjacent orbital structures. The differential diagnosis includes a ruptured dermoid cyst, acute hemorrhage into an orbital lymphangioma, orbital cellulitis, leukemic infiltrate, and collagen vascular disease. Orbital pseudotumor may also present as diffuse idiopathic orbital in*fl*ammation in which the majority of the orbital structures are involved in the inflammatory process. On occasion, the inflammation may be confined primarily to one orbital structure; for example, an orbital myositis may occur when an extraocular muscle is preferentially affected, and dacryoadenitis may occur if the orbital inflammation is centered in the lacrimal gland. These latter patients present with eyelid edema, and a diffusely enlarged, painful, lacrimal gland. The enlarged lacrimal gland can be readily visualized by manually lifting the lid and inspecting the superotemporal forniceal region. Other causes of lacrimal gland enlargement include bacterial infections, sarcoidosis, and lyphomatous infiltration of the gland.

2. Thyroid-related orbital inflammation must be considered in any case of orbital inflammation with proptosis. A careful medical history and review of symptoms will reveal a concurrent history of thyroid disease or symptoms suggestive of thyroid dysfunction such as heat/cold intolerance, unexplained changes in body weight, changes in body hair or voice quality. The neck should be carefully palpated for evidence of an enlarged thyroid gland. Orbital imaging by either computed tomography or magnetic resonance imaging (MRI) will show extraocular muscle enlargement with sparing of the tendon insertions of the muscles. While thyroid-related orbital inflammation is often asym- metric, there will usually be radiographic evidence of bilateral disease.

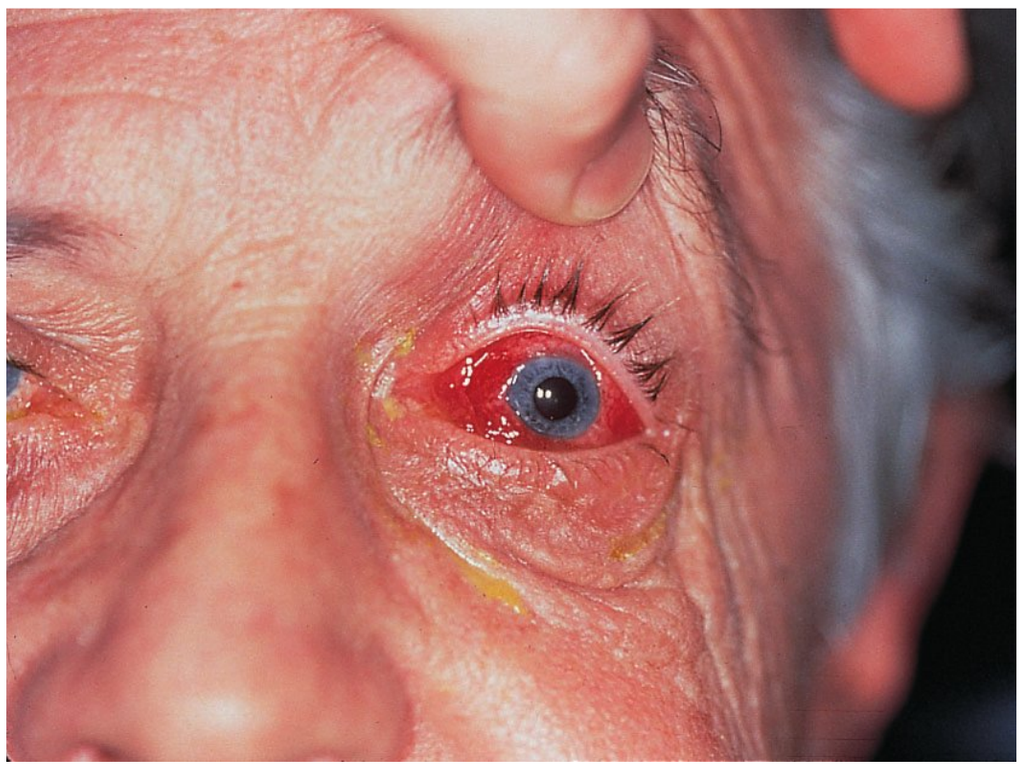

FIGURE 93–1 Clinical photograph demonstrating left periorbital inflammation and conjunctival injection.

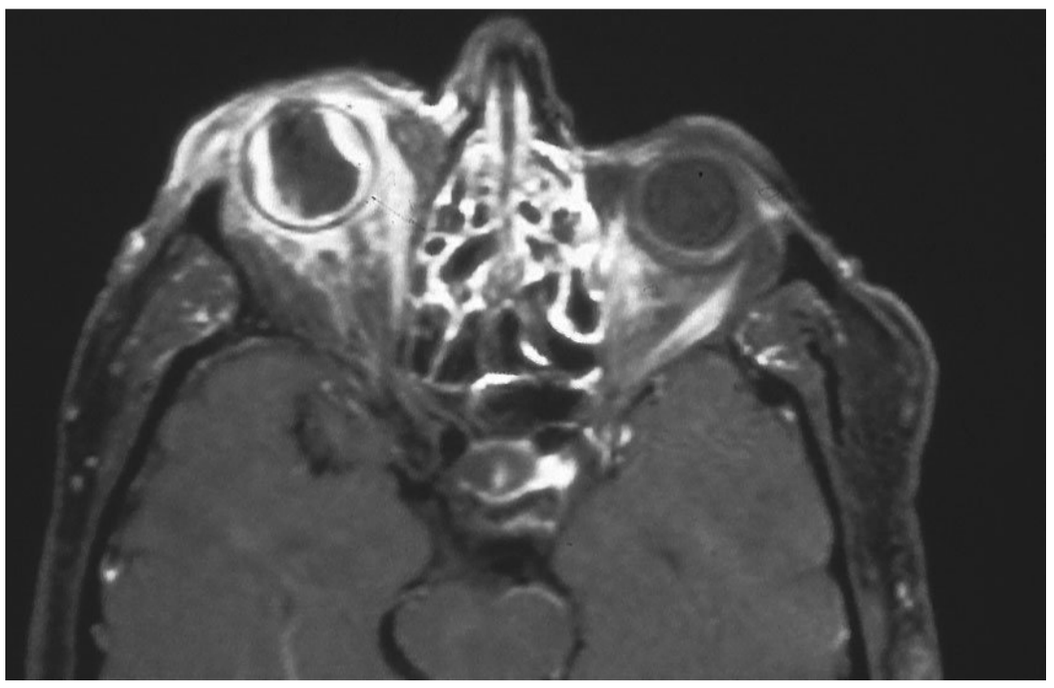

FIGURE 93–2 Post-gadolinium magnetic resonance imaging shows diffuse thickening of the sclera and episcleral tissues as well as the presence of choroidal thickening.

3. Orbital inflammation may be a manifestation of systemic collagen-vascular disease, such as polyarteritis nodosa or Wegener's granulomatosis. A review of systems will often reveal a history of renal or pulmonary disease. Systemic evaluation should include assessment of serum antineutrophil cytoplasmic antibody including both the cytoplasmic pattern and the perinuclear pattern (c-ANCA and p-ANCA), rheumatoid factor, and ANA testing.
4. Unsuspected orbital infections may result in pronounced signs of orbit inflammation. Most bacterial infections are the result of penetrating trauma to the orbit. Fungal infections may occur both in the setting of ocular trauma and in immunosuppressed individuals such as patients with diabetes mellitus or patients receiving chemotherapy. Immunosuppressed patients may be susceptible to orbital infections caused by Mucor or Aspergillus. Lastly, the possibility of a retained orbital foreign body, with or without associated infection, must be excluded. The clinical history is paramount in guiding the subsequent evaluation and workup.

TEST INTERPRETATION

An MRI of the orbit, before and after administration of gadolinium contrast material, was obtained (Fig. 93–2). There was diffuse anterior orbital inflammation with diffuse scleral thickening, especially posteriorly. Inflammation of the adjacent tissues was noted. The choroidal thickening seen on the funduscopic exam was well demonstrated. There was no evidence of a discrete neoplastic process.

DIAGNOSIS

Orbital pseudotumor with associated scleritis and secondary choroidal effusion.

MEDICAL MANAGEMENT

The patient was afebrile and the white blood cell count was normal. Systemic evaluation revealed no evidence of collagen-vascular disease. IV steroid treatment (methylprednisolone, 250 mg every 6 hours) was instituted. Within 24 hours there was marked improvement in the orbital inflammation, and the patient reported resolution of his pain. By 48 hours, the vision in the left eye was 20/40, and the relative afferent pupil defect had resolved. The patient was converted to oral prednisone and discharged from the hospital. At subsequent follow-up examination, his vision had returned to normal, and all of the orbital inflammatory signs had resolved. A follow-up MRI was obtained to rule out the possibility of inflammation masking an

underlying neoplastic process. The MRI was normal.

SURGICAL MANAGEMENT

In the current case, the patient's orbital disease responded promptly and dramatically to the institution of steroid therapy. If clinical improvement had not been seen after 48 hours of steroid treatment, orbital exploration and biopsy to obtain tissue for histopathologic and microbiologic studies would have been indicated.

REHABILITATION AND FOLLOW-UP

The patient was referred for systemic evaluation for collagen-vascular disease or lymphoma. All studies were negative, and the patient did well as the oral steroid therapy was slowly tapered. He has not experienced further episodes of orbital inflammation.

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Case 94

ORBITAL CELLULITIS

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 7-year-old boy was referred for further evaluation and treatment of right-sided lid swelling, right eye pain, and fever. His symptoms had begun approximately 4 days previously when his parents noted progressive redness and swelling of the right upper eyelid. The boy complained of pain around the right eye. No definite complaint of decreased vision was elicited. The presumptive diagnosis of preseptal cellulitis had been made, and the patient had been placed on oral antibiotics. Two days later, the child was reevaluated and found to have further progression of the right upper lid edema, now causing a complete ptosis of the lid. Because of the disease progression while on oral antibiotic treatment, the patient was referred to a tertiary care center.

Upon his arrival, it was noted that the child was somewhat lethargic and continued to complain of pain around the right eye. The patient's temperature, taken orally, was 100°. There was marked periorbital edema and erythema with complete ptosis of the eyelid (Fig. 94–1). Enlarged preauricular and submandibular lymph nodes were palpated. The eyelid was gently lifted to allow for testing of the visual acuity, which was found to be 20/25 OD and 20/20 OS. The conjunctiva appeared diffusely injected, and there was decreased motility of the right globe in all directions of gaze. No conjunctival discharge was noted. Mild proptosis of the globe appeared to be present; however, the diffuse lid edema and tenderness precluded formal exophthalmometry measurements. The pupils reacted normally with no relative afferent defect. The anterior segments were quiet, and the dilated fundus exam showed no significant abnormalities.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Preseptal cellulitis produces inflammation and infection of the eyelids and periorbital tissues anterior to the orbital septum. The condition most commonly results from periocular trauma or a skin infection. Clinical findings include marked erythema and edema of the eyelids and periocular soft tissues. Conjunctival discharge and regional lymphadenopathy may be present. The globe is not involved, and pupillary function, visual acuity, and ocular motility remain undisturbed. Conjunctival cultures should be obtained, and treatment with oral antibiotics instituted. If an abscess is present or develops during the course of the disease, it may be surgically drained. Care must be taken to avoid violating the orbital septum as this may allow seeding of the deeper orbital structures by the infection. The most common organism causing preseptal cellulitis is Staphylococcus aureus, and use of a penicillinase-resistant penicillin, such as oxacillin, results in prompt resolution of the infection.

2. Orbital cellulitis results from inflammation and infection of the orbital tissues posterior to the orbital septum. Orbital cellulitis is most commonly caused by secondary extension of acute or chronic bacterial sinusitis. Less commonly, preseptal cellulitis, dacryocystitis, or dental infection may progress to an orbital cellulitis. Clinical findings include the changes associated with preseptal cellulitis including eyelid edema and erythema. In addition, there are conjunctival chemosis, ocular motility restriction, and pain with eye movement. Decreased vision and pupillary abnormalities may be present in severe cases. The patient may be febrile and lethargic. Immediate radiographic imaging, preferably computed tomography (CT) scan, is indicated to evaluate the paranasal sinuses and the extent of the orbital disease. The presence of a subperiosteal abscess may be an indication for surgical drainage. Recent reports of successful medical management of

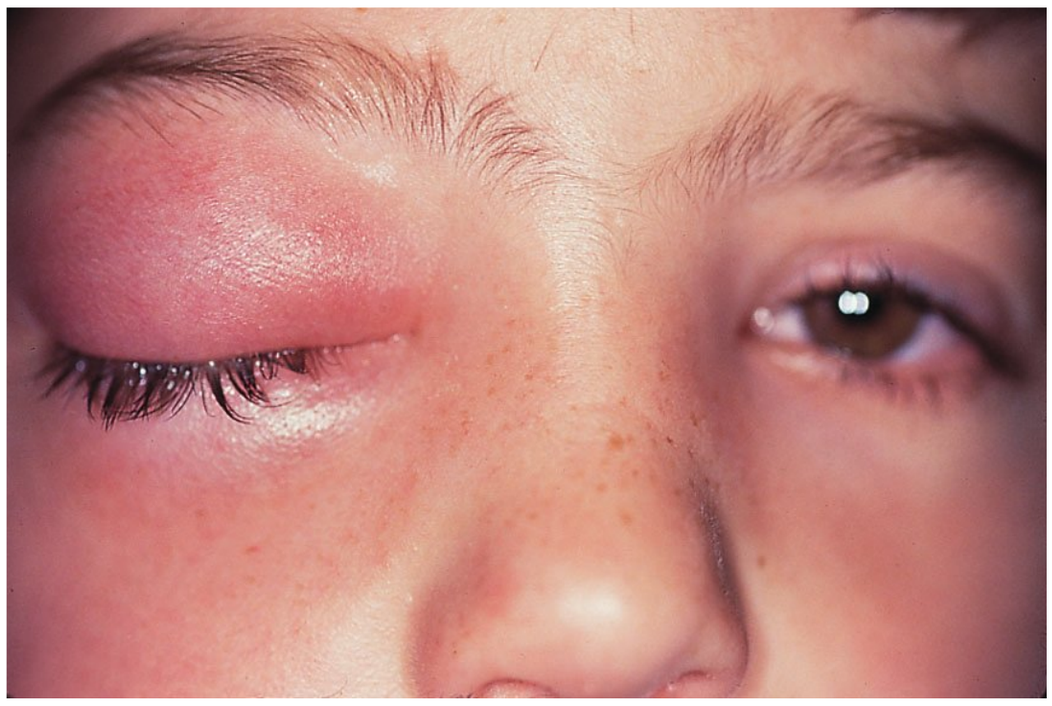

FIGURE 94–1 Clinical photograph depicting marked erythema and edema of the right eyelid producing secondary ptosis of the right upper eyelid.

children with subperiosteal abscesses have prompted re-evaluation of the best treatment protocol for these patients. It may be appropriate to institute antibiotic therapy and observe the patient carefully. Worsening of the visual acuity or ocular motility, or failure to show clinical improvement after 48 hours of treatment, are indications to proceed to surgical drainage of the subperiosteal abscess. This should be performed in conjunction with an ear, nose, and throat (ENT) surgeon if significant sinusitis is present. In children, orbital cellulits is commonly caused by a single microorganism (Streptococcus sp or Hemophilus in*fl*uenzae) whereas in adults, multiple organisms, including anaerobes, are often isolated. With the advent of the Hemophilus in*fl*uenzae type-B vaccine (HiB), there has been a decreasing incidence of H. in*fl*uenzae–associated cases of orbital cellulitis in children.

Complications of orbital cellulitis can ensue if appropriate evaluation and management are delayed. These include orbital apex syndrome, blindness, brain abscess, cavernous sinus thrombosis, and even death.

3. Infiltration of the orbit by leukemic cells or extraocular extension of retinoblastoma may mimic an orbital cellulitis. Appropriate radiographic imaging and a complete ophthalmic examination, including dilated fundus exam, must be performed in all patients with presumed orbital cellulitis.

TEST INTERPRETATION

A CT scan of the orbits and paranasal sinuses was obtained emergently. The scan showed a large subperiosteal abscess in the superomedial aspect of the right orbit. There was extensive thickening of the ethmoid sinus mucosa consistent with sinusitis. No bony abnormalities were present.

DIAGNOSIS

Orbital cellulitis with associated sinusitis.

MEDICAL MANAGEMENT

Systemic antibiotic treatment is indicated and infectious disease consult may be helpful.

SURGICAL MANAGEMENT

Because the patient had failed to improve on previous therapy, he was taken to the operating room where the large subperiosteal orbital abscess was drained, and an ethmoidectomy was performed by an ENT surgeon. Preoperative blood cultures obtained and intraoperative cultures of the purulent material within the abscess failed to reveal a causative organism. The patient was treated with intravenous ceftriaxone and clindamycin on the recommendation of the pediatric infectious disease consultation.

REHABILITATION AND FOLLOW-UP

The patient showed marked improvement of his clinical findings, and he remained afebrile. After 48 hours of intravenous antibiotics, treatment was converted to oral antibiotics, and he was discharged. Subsequent follow-up examination showed complete resolution of the periorbital swelling and motility restriction.

SUGGESTED READING

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Case 95

DACRYOADENITIS

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 12-year-old boy presented with a 1-week history of swelling of the left upper eyelid. The boy was otherwise healthy without known chronic medical disease. On examination, there was redness and fullness of the temporal aspect of the left upper lid that created an "S-shaped" deformity of the eyelid (Fig. 95–1). Manual elevation and slight eversion of the left upper eyelid revealed marked injection and chemosis of the bulbar conjunctiva laterally, as well as enlargement and erythema of the palpebral lobe of the lacrimal gland (Fig. 95–2). There was moderate tenderness over the enlarged lacrimal gland. Mild enlargement of the regional lymph nodes was also noted. The remainder of the ocular examination, including motility, was normal. There was no evidence of intraocular inflammation.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The clinical course and physical findings of inflammation centered within the lacrimal gland strongly suggest the diagnosis of acute dacryoadenitis. Patients with acute dacryoadenitis typically present with rapid enlargement and inflammation of the lacrimal gland. The clinical examination reveals erythema and edema of the temporal aspect of the upper eyelid as well as the temporal aspect of the tarsal and bulbar conjunctiva. Palpation of the superotemporal orbit shows the lacrimal gland to be diffusely enlarged and tender. Regional lymhpadenopathy is often present.

Before the advent of widespread childhood immunization, mumps represented the leading cause of acute dacryoadenitis. More recent studies have demonstrated an association between recent Epstein-Barr virus (EBV) infection and episodes of dacryoadenitis. Up to one-third of patients with clinical acute dacryoadenitis will have serologic evidence of EBV infection. Antibodies to viral capsid antigen are detectable with the onset of clinical symptoms about 6 weeks after exposure. Viral capsid antigen IgM falls to low levels after several weeks, while viral capsid antigen IgG will persist indefinitely. Antibodies to EBV nuclear antigen increase a few weeks after the onset of clinical infection and remain detectable for years. Thus, the presence of antiviral capsid antigen antibodies with absent or rising anti-EBV nuclear antigen antibodies is diagnostic for recent EBV infection.

2. Other infectious causes of acute dacryoadenitis have been identified. These include staphylococci, streptococci, and gonococci. The presence of a purulent discharge, in addition to evidence of acute inflammation of the lacrimal gland, should prompt obtaining cultures of the ocular surface. Empiric antibiotic therapy, both topical and systemic, may be instituted until culture results are available to guide further therapy.

3. Idiopathic orbital inflammation (pseudotumor) may involve the lacrimal gland preferentially, producing a clinical picture of acute dacryoadenitis. While eyelid erythema and edema may occur, additional orbital signs such as orbital pain, restricted eye movement, and proptosis will also be present. Such orbital signs should prompt computed tomography (CT) or magnetic resonance imaging (MRI) of the orbits, which will depict not only diffuse enlargement of the lacrimal gland, but also evidence of anterior orbital soft tissue inflammation. Extraocular muscle enlargement may also be demonstrated. Orbital pseudotumor is discussed in Case 93.

4. Primary and secondary lacrimal gland tumors may also cause enlargement of the lacrimal gland. Primary lacrimal gland tumors include

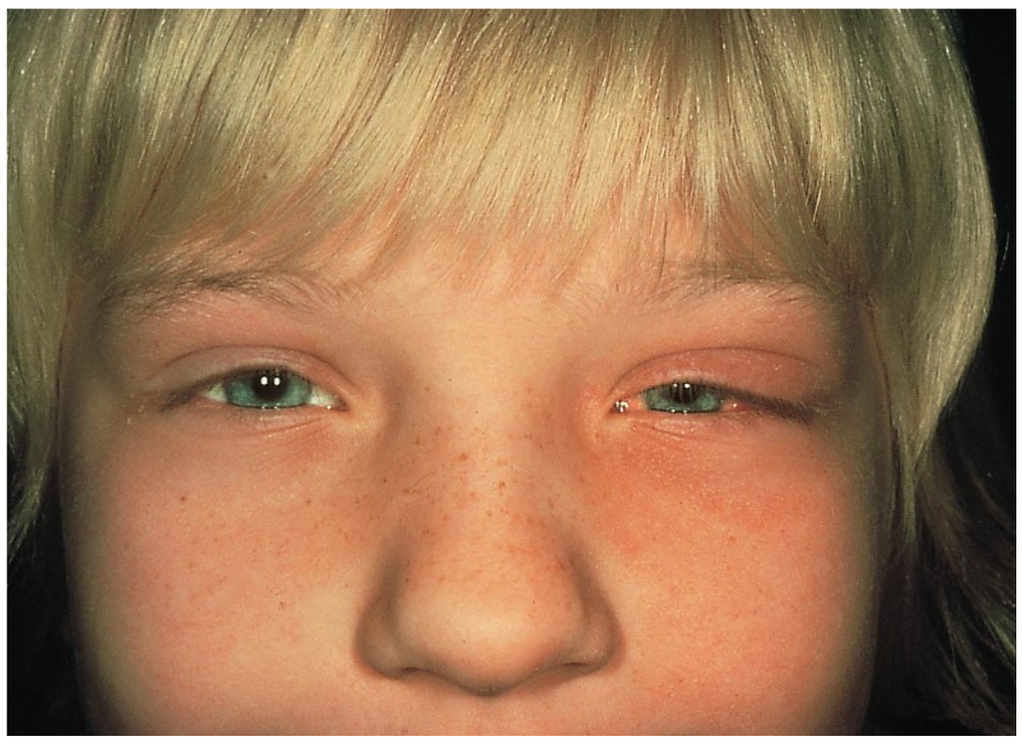

FIGURE 95–1 Clinical appearance showing "S-shaped" deformity of the left upper eyelid. (Figure courtesy of Robert R. Waller, M.D.)

both epithelial and nonepithelial lesions. The lacrimal gland may also be secondarily involved by direct extension of a tumor from an adjacent orbital or paranasal site, or by hematogenous spread of a metastatic lesion. Lacrimal gland tumors are discussed in detail elsewhere.

TEST INTERPRETATION

CT or MR scan of the orbit might show a mass inflammation, or infection.

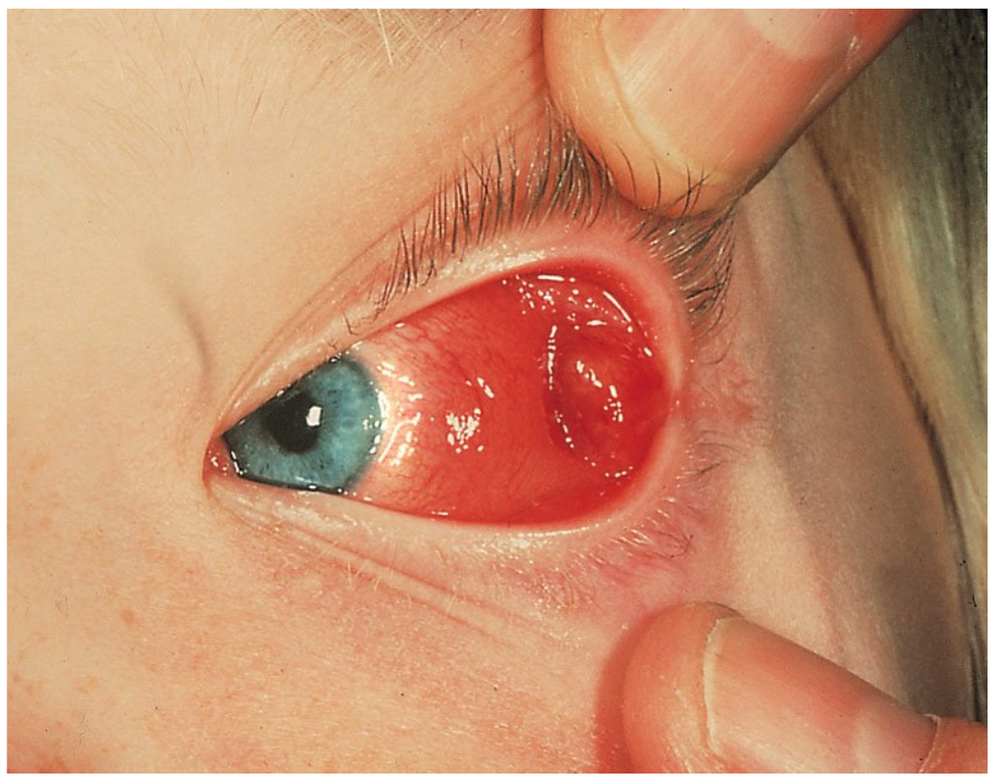

FIGURE 95–2 Enlargement of the palpebral lobe of the lacrimal gland of the left eye with associated conjunctival injection and chemosis. Note the absence of purulent discharge. (Figure courtesy of Robert R. Waller, M.D.)

DIAGNOSIS

Acute dacryoadenitis, presumably secondary to EBV infection.

MEDICAL MANAGEMENT

In the present case, the clinical picture is highly characteristic of acute dacryoadenitis, and the patient had no accompanying orbital signs or symptoms. Serologic evaluation was positive for anti-EBV capsid antigen antibodies and negative for antiviral nuclear antigen antibodies, thereby establishing the diagnosis of acute dacryoadenitis secondary to EBV infection. Management may include anti-inflammatory therapy with topical or oral corticosteroid medication. The disease is self-limited, however, and it is not firmly established that such palliative measures actually serve to shorten the course of the disease.

SURGICAL MANAGEMENT

There is no proven role for surgical management of this problem.

REHABILITATION AND FOLLOW-UP

Follow-up for resolution of symptoms is reasonable.

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Case 96

ORBITAL TUMORS OF CHILDHOOD

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

An 8-month-old healthy boy presented for evaluation of a mass over the right eye. The mass had been present since shortly after birth, and the parents reported a slow continual enlargement of the mass. The child had been born at full-term after an uncomplicated pregnancy. He was otherwise healthy with no known medical problems. There was no associated change in color or size of the mass with crying or Valsalva's maneuvers.

Examination showed central fixation and following in each eye. The motility was full and both pupils were normal. Both anterior segments were quiet to slit-lamp examination, and the dilated funduscopic exam showed no abnormalities. There was a moderately firm mass present over the superotemporal aspect of the right orbit (Fig. 96–1). The mass measured approximately 20 mm × 10 mm × 5 mm and was fixed to the underlying tissues. The overlying skin was intact without discoloration or ulceration. Careful palpation of the superior orbital rim revealed no discernable defect. There was no measureable proptosis, and both orbits were normal to retropulsion. No other masses were palpated.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. Orbital tumors in children, as in adults, may be subdivided into primary tumors and secondary tumors. The most common primary orbital tumors in children are the cystic lesions, dermoids, and epidermoids. Many authors consider these tumors to be choristomas, and they are most likely congenital with variable age of presentation related to their slow growth.

Histologically, dermoids are cystic structures lined by keratinized epithelium with adnexal structures, such as hair follicles or sweat glands, contained within the cyst wall. Epidermoid cysts have a similar histologic appearance except that adnexal structures are not present. Dermoids most commonly occur at the superotemporal orbital rim at the zygomatico-frontal suture. Less commonly they may be present at the superonasal aspect of the orbit. While these lesions are benign, they tend to slowly enlarge. They may also rupture as the result of minor trauma to the area, inciting a severe granulomatous inflammation of the surrounding tissues. Therefore it is recommended that these lesions be excised surgically, making certain that the entire cyst wall and its contents are removed.

2. Vascular lesions of the orbit also occur commonly in children. The most common of these is the capillary hemangioma, which may involve the eyelids or orbit. There is an associated reddish discoloration of the overlying skin, and the size of the lesion may enlarge with crying or Valsalva's maneuvers. Hemangiomas may be of sufficient size as to induce visually significant astigmatism or obstruct the visual axis, with the risk of developing amblyopia. Thus, although these tumors are benign, the child should be followed carefully for any evidence of developing amblyopia. The natural history of these lesions is that they often slowly and spontaneously involute. If, however, the risk of amblyopia is imminent, treatment may be required. This may include surgical extirpation to effect a debulking of the tumor. Systemic or intralesional steroids may provide an alternate treatment approach. Other modalities that

FIGURE 96–1 Clinical photograph showing well-circumscribed mass in the superotemporal right orbit. The overlying skin is intact.

have been employed include radiotherapy, cryotherapy, and laser (CO_2, Nd:YAG, argon) ablation.

Lymphangioma is another vascular tumor that may involve the orbit in children. These lesions may wax and wane in size and may undergo rapid enlargement in association with upper respiratory infections. They are also prone to spontaneous hemorrhage that can cause tumors to enlarge dramatically. If the lesion involves the anterior orbital structures, a dark-colored cystic lesion may be evident beneath the conjunctiva. Hemorrhage within a deep orbital lymphangioma may produce sudden proptosis of the affected globe. Lymphangiomas are typically poorly circumscribed tumors that interdigitate with the surrounding orbital structures, thereby precluding complete surgical extirpation. They can, however, be surgically reduced by excising a portion of the cyst wall and evacuating the hemorrhagic material. This material has a characteristic dark-brown color giving rise to the clinical appearance of a "chocolate cyst."

3. Neural tumors include optic nerve glioma and neurofibroma. Both of these tumors occur with increasing frequency in children with neurofibromatosis. Optic nerve glioma may cause slowly progressive axial proptosis with variable effects on the visual acuity and visual field. Radiographically, these tumors create a characteristic fusiform enlargement of the optic nerve. The appropriate management of these tumors remains controversial. Careful monitoring of vision and the amount of proptosis is indicated. Periodic radiographic evaluation should also be performed to evaluate for extension of the glioma to involve the intracanalicular portion of the optic nerve. Surgical removal of an optic nerve glioma involving the intracanalicular optic nerve or threatening the optic chiasm may be indicated.

Plexiform neurofibromas of the eyelid and orbit are considered pathognomic for neurofibomatosis Type 1. These tumors may cause a mechanical ptosis of the eyelid as well as cosmetic deformity. The lesion often interdigitates with other eyelid structures, including the levator aponeurosis, thereby making complete surgical extirpation unfeasible. The surgical approach involves debulking the tumor while maintaining as much function of the eyelid and eye as possible.

4. Rhabdomyosarcoma should be included in the differential diagnosis of a childhood orbital tumor. This tumor represents the most common primary orbital malignancy of childhood. Typically, these lesions will present with rapidly progressive proptosis, and prompt radiographic evaluation and surgical biopsy are indicated. Adequate tissue should be obtained to allow for special testing, including immunohistochemical studies and transmission electron microscopy to demonstrate the presence of diagnostic cross striations. Treatment must be coordinated with oncologists and radiotherapists and usually includes radiotherapy and chemotherapy.

5. Secondary tumors of the orbit include retinoblastoma with extraocular extension into the orbit. Therefore, a complete ophthalmic examination is mandatory in the evaluation of a child with a suspected orbital tumor. Malignancies may also metastasize to secondarily involve the orbit. In children, neuroblastoma is the most common metastatic orbital tumor, producing sudden proptosis, often associated with ecchymosis, that

may be bilateral. A thorough physical examination may reveal a palpable abdominal mass. Treatment may include a combination of surgery, chemotherapy, and radiation. Despite treatment, the prognosis for metastatic neuroblastoma is poor. Other malignancies that may metastasize to the orbit in children include Ewing's sarcoma and osteosarcoma.

TEST INTERPRETATION

Computed tomography or magnetic resonance scan of the orbit will better delineate the lesion.

DIAGNOSIS

Dermoid cyst of the right orbit.

MEDICAL MANAGEMENT

There is no medical treatment for this condition.

SURGICAL MANAGEMENT

As discussed previously, surgical removal of a dermoid cyst is recommended due to the risk of traumatic rupture and resultant inflammatory response. Some authors recommend delaying surgery until the infant is at least 6 months old to decrease the risk of anesthesia. In the current case, the tumor was approached through a lid crease incision to allow for a cosmetically acceptable inconspicuous scar. The lesion was dissected from the surrounding tissues and removed in toto (Fig. 96–2). The patient has done well without further sequelae.

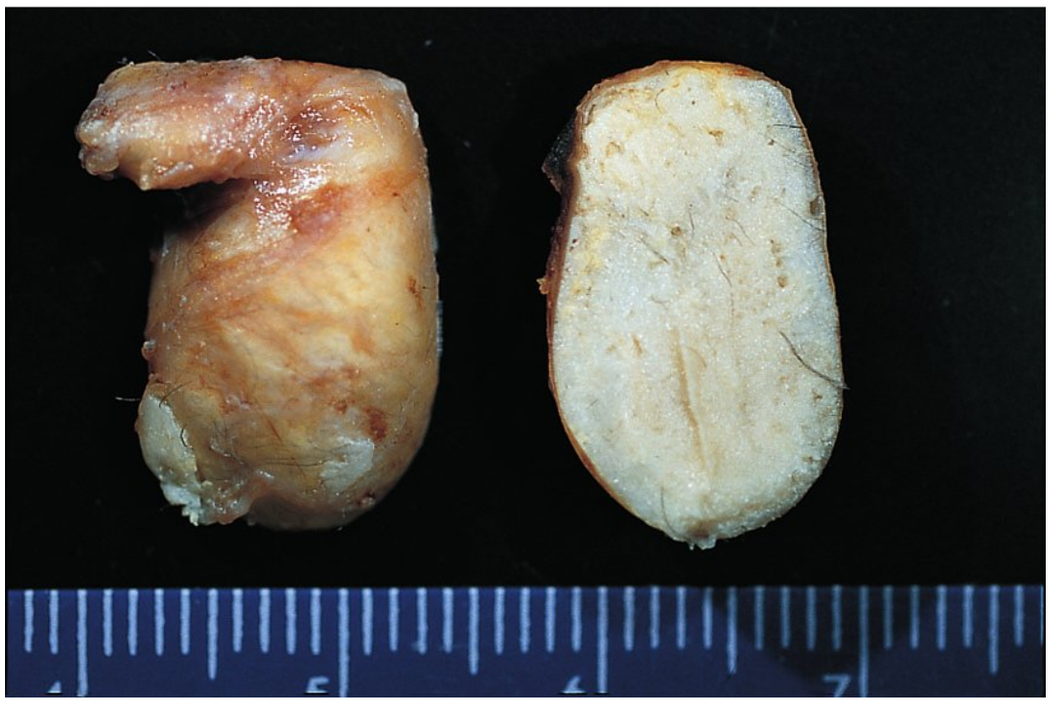

FIGURE 96–2 Gross appearance of dermoid cyst showing keratinous debris with hair filling the cyst cavity.

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Case 97

ORBITAL TUMORS IN ADULTS

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 44-year-old man was referred for evaluation of proptosis of the left eye. The patient was in good health and took no medications. Ophthalmic history was negative for previous surgery, trauma, or disease. He reported increasing prominence of the left eye without associated pain or diplopia. His glasses prescription had been changed twice in the past year.

Examination showed visual acuity of 20/20 OU with a manifest refraction of −2.25 D OD and +1.00 D OS. Motility and pupil examination were within normal limits. The palpebral fissure was widened on the left side, and Hertel exophthalmometry readings were 20 mm OD and 24 mm OS (base 95) (Fig. 97–1). There was increased resistance of the left globe to retropulsion. No bony defects or definite masses were palpated. There was no regional lymphadenopathy, and no bruits were auscultated over the orbits. The anterior segments were quiet by slit-lamp examination; the bulbar conjunctiva was unremarkable without evidence of abnormal vascularity. Dilated examination of the left fundus revealed choroidal striae of the posterior pole. The optic nerve was normal, and no hemorrhage or exudate was present. The right fundus was normal.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. This patient presents with evidence of a mass lesion of the left orbit, namely progressive proptosis and a decrease in his myopic refractive error. Tumors may arise within the orbit primarily, or they may involve the orbit secondarily. Secondary orbital tumors may extend directly into the orbit from adjacent structures such as paranasal sinuses, or malignancies may metastasize to the orbit hematogenously from a distant site.

The most common primary orbital tumor in adults is the cavernous hemangioma. Patients are typically middle-aged and present with painless proptosis. Radiographically, cavernous hemangiomas are well-circumscribed, retrobulbar lesions that may show irregular enhancement after injection of contrast material. Ultrasound examination reveals medium to high internal reflectivity. Because of the typical clinical and radiographic appearance, biopsy is usually not required to establish a diagnosis, and treatment is not required if the proptosis is minimal and the patient is asymptomatic. If treatment is indicated, the tumor can be removed in toto via a medial or lateral orbital approach. Because the cavernous hemangioma has limited communication with the systemic circulation, preoperative arteriography is not indicated. Histopathologically, these tumors are encapsulated and contain numerous endothelial-lined vascular channels containing red blood cells.

2. Hemangiopericytoma is another vascular orbital tumor that arises in middle-aged adults. The tumor arises from pericytes, and although it may radiographically and grossly appear well-circumscribed, hemangiopericytoma is an infiltrative lesion that may produce proptosis, motility abnormalities, or conjunctival prolapse. The treatment is complete surgical extirpation. Local tumor recurrence may occur and is not predictable based on the histopathologic features of the lesion. Treatment of recurrent hemangiopericytoma is problematic, and there is a risk of malignant

FIGURE 97–1 Clinical photograph showing proptosis of the left eye.

transformation. Surgical debulking procedures in combination with radiation treatment have been employed to treat tumor recurrences with mixed results.

3. Lymphoproliferative lesions of the orbit range from reactive lymphoid hyperplasia to orbital lymphoma. These lesions have a variety of clinical appearances, depending on the exact orbital structures that are involved. Diagnosis usually requires tissue biopsy with special studies (eg, immunohistochemistry, flow cytometry, gene rearrangement studies) to determine the presence of a clonal population of lymphocytes. Lymphoma may be limited to the orbit or may involve the orbit as part of a systemic process.

4. Neural tumors that may involve the orbit in adults include meningioma and schwannoma. Meningiomas may arise from the optic nerve sheath and involve the orbit primarily. More commonly, the meningioma arises intracranially and extends to involve the orbit secondarily. Meningiomas typically present in middle-aged women, with the clinical findings determined by the tumor location. Primary meningiomas of the optic nerve cause early visual symptoms with axial proptosis. Computed tomography (CT) imaging shows a diffusely thickened optic nerve that may contain calcifications. Injection of contrast material may give rise to the characteristic "railroad track" appearance of the enlarged optic nerve sheath. In contrast, secondary orbital meningiomas may have little effect on the vision until the tumor has achieved significant size. If the tumor is arising from the lateral portion of the sphenoid, the patient may present with a temporal fossa mass in addition to proptosis.

Schwannomas, which are composed of proliferations of Schwann cells, often arise from the sensory nerves of cranial nerve V, but may arise from any peripheral nerve sheath. Orbital schwannomas are typically intraconal, well-circumscribed tumors, and multiple tumors may be present. Symptoms and signs are determined by the tumor location. Because of their encapsulation, schwannomas are amenable to complete surgical removal.

5. Fibrous histiocytoma is the most common primary mesenchymal orbital tumor in adults. These tumors infiltrate the surrounding orbital structures making them difficult to remove completely. Fibrous histiocytomas may be locally aggressive leading to frequent recurrences. There are benign and malignant forms of fibrous histiocytoma, and histopathologic study of the tumor is necessary for accurate diagnosis. Cases of malignant transformation of a previous benign tumor have also been reported.

6. Lacrimal gland tumors generally fall into two categories: epithelial and nonepithelial. Within these two categories, both benign and malignant variants exist. Of the nonepithelial lesions, the vast majority are inflammatory and may be infectious or noninfectious. Noninfectious inflammatory entities include sarcoid, Wegener's granulomatosis, and orbital pseudotumor.

The most common epithelial neoplasm of the lacrimal gland is the pleomorphic adenoma. Other epithelial tumors of the lacrimal gland include adenoid cystic carcinoma, squamous carcinoma, and

mucoepidermoid carcinoma. Epithelial lacrimal gland tumors present as a mass in the lacrimal fossa and produce downward displacement and proptosis of the globe. Bony erosion of the lacrimal fossa is often seen on CT scan. If an epithelial lacrimal gland tumor is suspected preoperatively, a lateral orbitotomy should be performed and the entire tumor removed without prior incisional biopsy. Failure to preserve the surrounding capsule intact results in an increased risk of recurrence and malignant transformation. Malignant epithelial lacrimal gland tumors have the capacity to metastasize widely and to cause death.

7. A wide variety of visceral carcinomas as well as cutaneous melanomas may involve the orbit secondarily by metastatic spread. However, breast and lung carcinomas account for the majority of orbital metastatic tumors. A previous history of malignancy exists in 75% of patients presenting with metastatic orbit disease. Thus, in 25% of patients, the orbital tumor is the first manifestation of the patient's malignancy. In a patient with a previously established cancer diagnosis, a fine-needle aspiration biopsy may be performed to confirm the orbit diagnosis before the patient proceeds with therapy. Some orbital lesions may not be amenable to fine-needle biopsy; this is particularly true for fibrotic tumors, such as scirrhous breast carcinoma or tumors that are posteriorly located in the orbit adjacent to the optic nerve.

TEST INTERPRETATION

An orbital CT scan demonstrated a well-circumscribed retrobulbar tumor pressing on the posterior aspect of the globe (Fig. 97–2). There were no associated bony changes, and the tumor showed only marginal enhancement with contrast material.

DIAGNOSIS

Probable cavernous hemangioma of the left orbit.

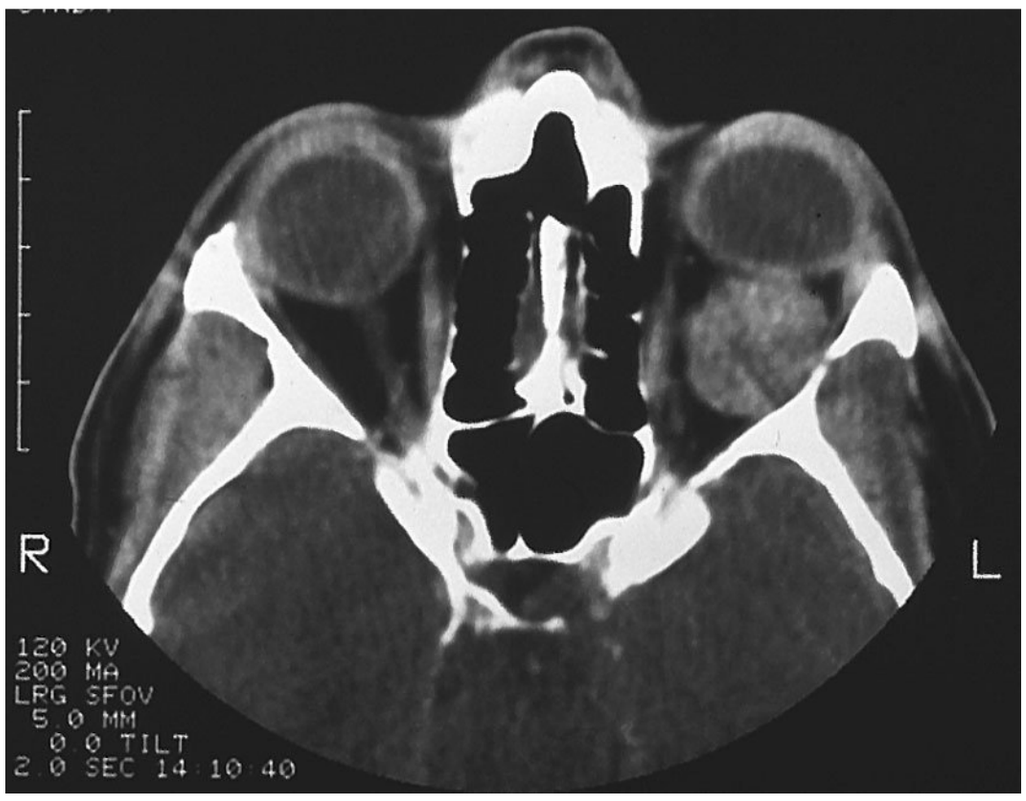

FIGURE 97–2 CT scan demonstrating the well-circumscribed retrobulbar tumor in the left orbit. The mass is pressing on the posterior aspect of the left eye.

MEDICAL MANAGEMENT

There is no medical treatment for this condition.

SURGICAL MANAGEMENT

Because of the patient's progressive proptosis and changing refractive error, surgical excision was recommended. A lateral orbitotomy was performed and a dark-red encapsulated tumor was removed in toto (Fig. 97–3). Histopathologic evaluation confirmed the diagnosis of cavernous hemangioma.

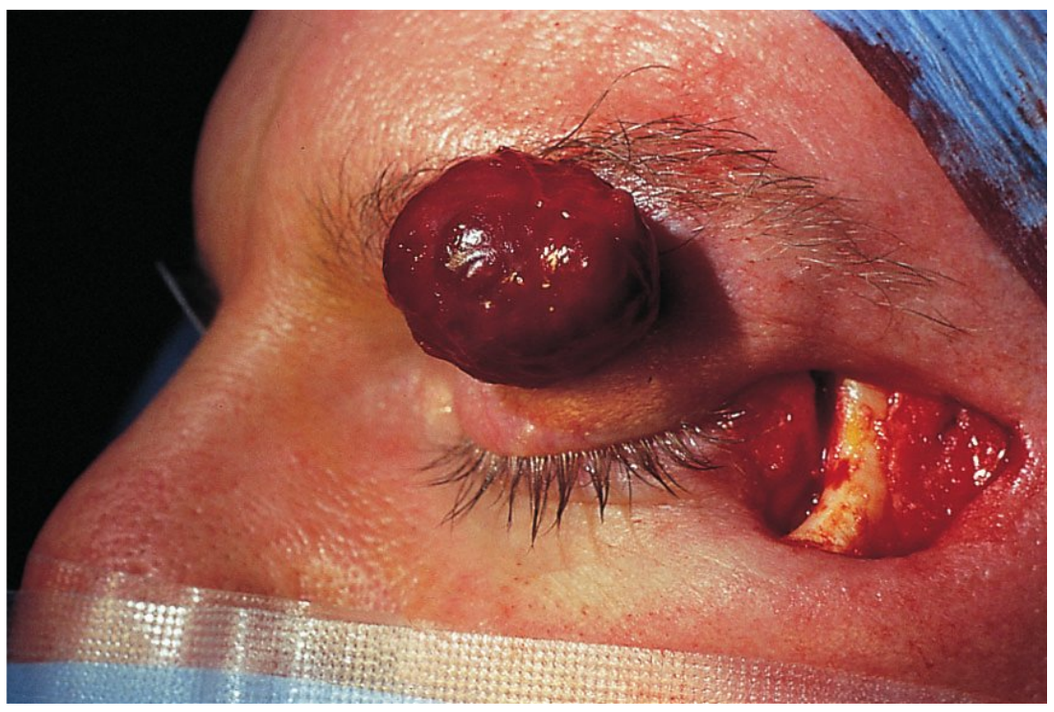

FIGURE 97–3 Intraoperative photography showing the lateral orbitotomy and the excised reddish well-circumscribed tumor.

REHABILITATION AND FOLLOW-UP

The patient did well postoperatively. The refractive error in his left eye stabilized at −2.00 D, and the choroidal striae in the left eye slowly resolved.

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Case 98

BENIGN TUMORS OF THE EYELID

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 32-year-old man presented for evaluation of a left upper eyelid lesion. He reported the lesion being present for several years, but had noted slow painless enlargement over the past few months. He reported no associated redness or bleeding from the lesion and there was no history of previous skin disease or skin cancer. He was in good health and took no medications. His ophthalmic examination was within normal limits with the exception of the external exam. There was a 10 mm × 8 mm × 5 mm smooth dome-shaped skin lesion involving the preseptal eyelid skin of the left upper lid (Fig. 98–1). The tumor was amelanotic, and the overlying skin was intact without ulceration or telangiectasia. There was no regional lymphadenopathy, and no other skin lesions were present on the head and neck region.

DIFFERENTIAL DIAGNOSIS

1. The very slow growth over many years, and the lack of skin ulceration, scaling, or telangiectasia support the benign nature of this tumor. Nevi are melanocytic lesions that may appear pigmented or amelanotic, and they are among the most common benign eyelid tumors. Histopathologically, nevi are divided into three categories, depending on the depth of the nevus cells. In junctional nevi, the nevus cells are grouped at the epidermal–dermal junction. As some of the nevus cells drop into the deeper dermis, the lesion is categorized as a compound nevus. Lastly, when all of the nevus cells are present in the dermis, the term intradermal nevus is employed. Nevi are most likely present at birth and may acquire melanin pigment over time, particularly in association with puberty. They may also display slow growth over time. Nevi frequently occur at or near the eyelid margin, but do not cause loss of cilia or significant distortion of the eyelid architecture. Changes in pigmentation of the lesion may raise the concern of possible melanoma, or nevi may cause cosmetic concerns due to their location on the eyelid or eyelid margin. Nevi are amenable to an excisional biopsy or shave biopsy, and the specimen should be submitted for histopathologic evaluation to confirm the clinical diagnosis.

2. Benign epithelial lesions occur often on the eyelid and should be considered in the differential diagnosis. Squamous papilloma appears as a well-circumscribed nonpigmented lesion on the eyelid or eyelid margin. In contrast to the smooth surface of an intradermal nevus, the papilloma has an irregular frond-like surface. Examination of the lesion under magnification at the slit lamp will usually reveal small pinpoint vessels at the tip of each frond. Histopathologically, papillomas are composed of thickened, or acanthotic, epidermis, overlying numerous fibrovascular cores. The normal maturation pattern of the epidermis is not disturbed.

Seborrheic keratosis is another common benign tumor that affects sun-exposed skin including the eyelids. These lesions may be appear variably pigmented and have an oily crusty appearance. The lesions are sessile and appear to “sit” on the epidermal surface. Histopathologcially, acanthosis, hyperkeratosis, and papillomatosis are present. Additionally, pseudohorn cysts, representing infoldings of the epidermis, are frequently observed.

Inverted follicular keratosis is considered by most pathologists to represent an inflamed variant of seborrheic keratosis. These lesions may display exuberant hyperkeratosis

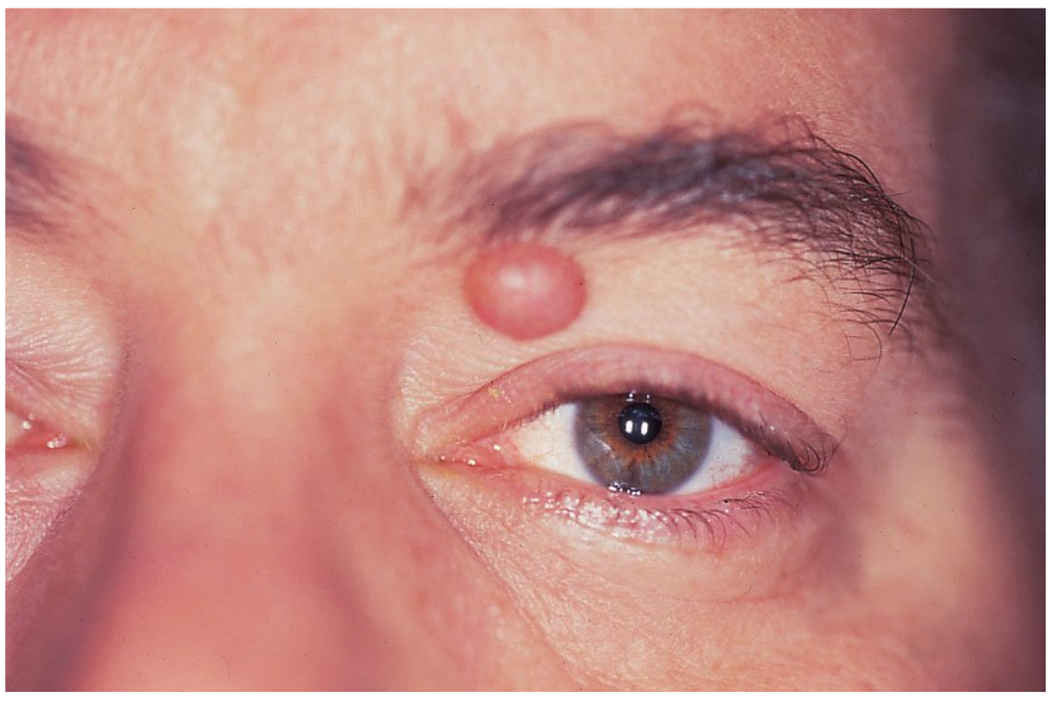

FIGURE 98–1 Clinical photograph showing non-pigmented smooth dome-shaped lesion of the upper eyelid.

creating a cutaneous horn. At the base of the lesion, the acanthotic epithelium contains numerous whorls of keratin, referred to as squamoid eddies.

Actinic keratosis appears as reddish flat, slightly scaly lesions on sun-exposed skin of the face, including the eyelids. Histopathologically, they display hyperkeratosis and parakeratosis, or abnormal retention of squamous cell nuclei in the surface keratin. Additionally, there is disruption of the normal orderly maturation pattern of the epidermis, and increased mitotic activity is present. Actinic keratoses are considered premalignant lesions, meaning that if left untreated, they may transform to a squamous cell carcinoma. Complete surgical excision is therefore indicated.

Keratoacanthomas may display relatively rapid growth and display a keratin-filled central crater surrounded by an elevated thickened epidermal margin. These lesions are self-limited and will often spontaneously involute after 4 to 6 weeks. Surgical excision may be indicated for histologic confirmation or for cosmetic concerns.

Epithelium may proliferate beneath the skin surface where it may form epidermal inclusion cysts. These cysts grow slowly and form a firm subcutaneous nodule. Epidermal inclusion cysts may arise from the infundibulum of the hair follicle or from entrapped epithelial rests that become implanted during minor trauma. Histologically, the cysts are lined by stratified squamous epithelium and are filled with keratin debris.

3. The adnexal structures of the skin may give rise to a number of benign eyelid tumors. Of these lesions, syringomas, arising from the sweat glands, are the most common. Clinically, these tumors appear as multiple yellowish papules. Histologically, numerous proliferating ductal structures, lined by a double row of cuboidal epithelium, are present. Some of the ductal structures have a characteristic "comma" shape, and there may be extensive fibrosis of the surrounding stroma.

Hidrocystomas may arise from either eccrine or apocrine sweat glands and appear as translucent cysts beneath the skin surface. Eccrine hidrocystomas frequently appear as multiple small cysts, whereas the apocrine hidrocystoma is most often a solitary nodule. Hidrocystomas occur most commonly at the lateral canthus or are associated with the eyelid margin.

Pilomatrixoma is a tumor that occurs more frequently in children or young adults. The lesion has a reddish-blue color, and there may be a history of minor trauma to the area. Microscopically, the tumor is composed of islands of basophilic cells with interposed "shadow" cells. Areas of dystropic calcification are scattered throughout the lesion, and associated granulomatous inflammation is often present.

TEST INTERPRETATION

The morphologic appearance of the lesion is usually characteristic, but tissue diagnosis by pathologic examination is recommended in suspicious cases.

DIAGNOSIS

Benign eyelid tumor, most likely intradermal nevus.

MEDICAL MANAGEMENT

There is no medical treatment for this condition.

SURGICAL MANAGEMENT

Because of the apparent benign nature of the tumor, no further ancillary testing is indicated. The lesion may be observed, or it may be surgically excised. In most cases, the procedure can be performed as an office procedure using a local infiltrative anesthetic. The resulting small defect can be repaired primarily or allowed to heal by secondary intention. Care must be taken not to create distortion of the eyelid margin or significant shortening of the anterior lamella of the eyelid. Any excised specimen should be sent for histopathologic confirmation.

REHABILITATION AND FOLLOW-UP

The patient underwent excisional biopsy of the upper eyelid lesion, and histopathologic examination of the specimen confirmed the diagnosis of intradermal nevus (Fig. 98–2). The patient has done well without evidence of recurrence.

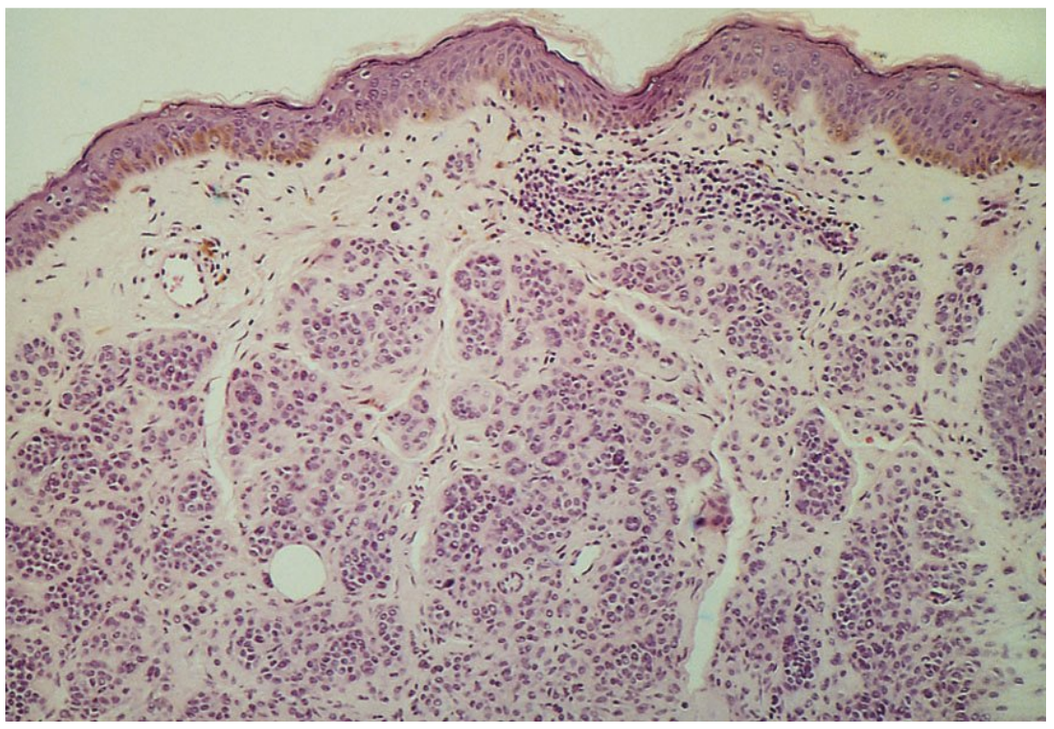

FIGURE 98–2 Low-power photomicrograph showing nests of nevus cells within the superficial and deep dermis (H & E; original magnification ×13.2).

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Case 99

MALIGNANT TUMORS OF THE EYELID

Debra Shetlar, M.D.
Milton Boniuk, M.D.

HISTORY

A 55-year-old man presented for evaluation of an enlarging skin nodule of his right upper eyelid. The lesion had been present for approximately 8 months and had grown fairly rapidly. The patient recalled one episode of bleeding from the area after he had picked at the lesion. While there was no previous history of skin cancer, the patient reported an extensive sun-exposure history, having been an avid sailor. His ophthalmic examination was within normal limits except for the external examination. There was a large elevated nonpigmented nodule involving the skin of the right upper eyelid near the medial canthal region (Fig. 99–1). The nodule measured 15 mm × 12 mm × 7 mm and showed numerous small telangiectatic vessels on its surface. The edges of the tumor had a thickened pearly appearance. There was no ulceration present. The skin underlying the lesion was freely moveable, and the tumor did not appear fixed to the underlying deep structures. There was no regional lymphadenopathy. The skin of the patient's face showed diffuse sun-exposure changes consisting of fine wrinkles and telangiectatic vessels and scattered areas of crusting.

DIFFERENTIAL DIAGNOSIS—KEY POINTS

1. The relative rapid growth of this lesion, the history of previous bleeding, and the clinical features suggest a malignant tumor. Basal cell carcinoma is the most common malignancy of the eyelid and most commonly involves the lower eyelid and the medial canthal region. Risk factors for basal cell carcinoma include fair skin, northern European ancestry, history of extensive sun exposure, or history of previous basal cell carcinoma. Patients with a family history of skin cancer may be at an increased risk for developing basal cell carcinoma.

Clinically, basal cell carcinomas are categorized as nodular, nodular-ulcerative, or morpheaform. Microscopically, basal cell carcinomas are composed of nests and cords of proliferating epidermal basilar cells. Palisading of the nuclei at the periphery nests is a characteristic feature. In the morpheaform variant, the tumor nests invade the deep dermis and are associated with a marked stromal fibrosis. Other pathologic variants of basal cell carcinoma include basosquamous, adenoid, and cystic types.

The treatment for basal cell carcinoma is complete surgical extirpation of the tumor. The lesion should be excised with a margin of uninvolved adjacent tissue, and the free margins should be confirmed pathologically. Reconstruction should ensue only after complete removal of the malignancy is verified. On occasion, the basal cell carcinoma may be very extensive and involve deep vital structures such that complete removal is not possible. In such cases, radiation therapy and chemotherapy have been employed after surgical debulking of the tumor.

2. The second most common malignancy of the eyelid is squamous cell carcinoma. The ratio of basal cell carcinoma to squamous cell carcinoma frequency is approximately 40 to 1. In contrast to basal cell carcinoma, squamous cell carcinoma more frequently involves the upper eyelid and behaves more aggressively. The tumor may have an ulcerative appearance and may show crusting or hyperkeratosis. Squamous cell carcinoma may invade adjacent structures such as the orbit or lacrimal drainage system and may

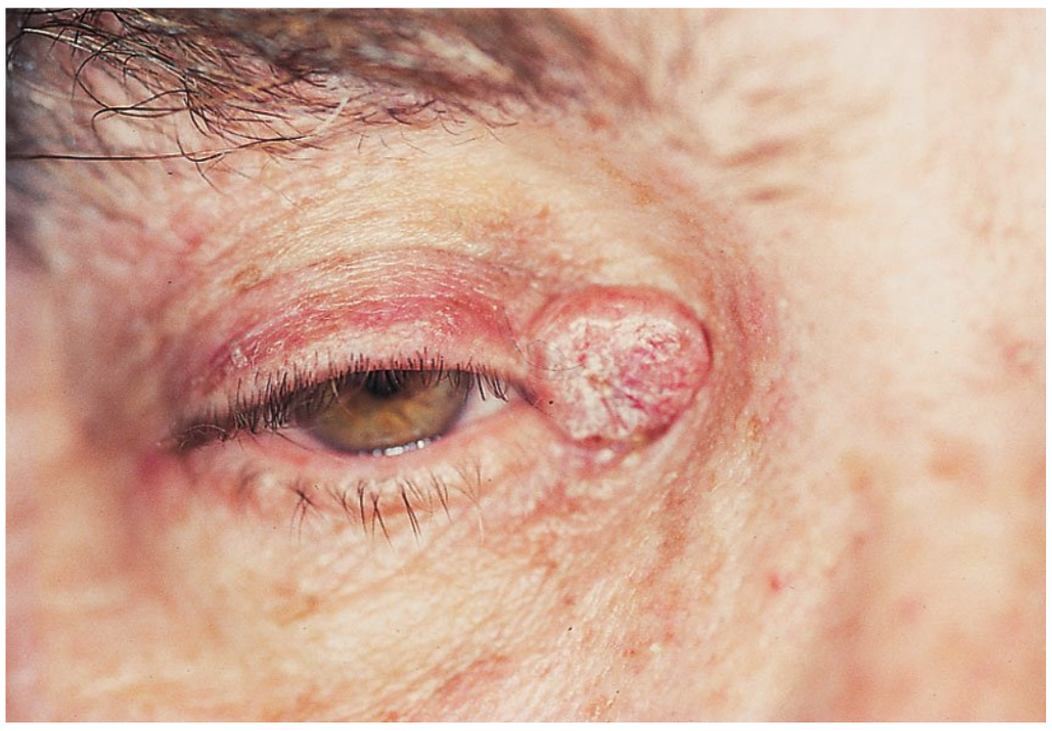

FIGURE 99–1 Clinical photograph showing non-pigmented elevated lesion over the medial canthal region. There is irregular crusting over the surface of the lesion.

metastasize to regional lymph nodes or spread hematogenously to distant sites.

As with basal cell carcinoma, the treatment for squamous cell carcinoma is complete surgical removal. A wide margin of uninvolved tissues should be obtained. There is a higher recurrence rate for squamous cell carcinoma as compared to basal cell carcinoma. If there is orbital invasion, exenteration may be required to achieve complete removal of the tumor.

3. Sebaceous carcinoma accounts for less than 0.8% of eyelid tumors; however, its protean clinical appearance causes this entity to be frequently confused with inflammatory lesions or other eyelid disorders, thereby delaying correct diagnosis and appropriate treatment. Sebaceous carcinoma arises from the meibomian glands or, less frequently, from the glands of Zeiss. It may also arise from sebaceous units within the caruncle or eyebrow. Patients are usually over 50 years old, and the tumor may masquerade as a chalazion, chronic blepharitis, ocular cicatricial pemphigoid, basal cell carcinoma, or squamous carcinoma. Therefore, the clinician should maintain a high level of suspicion for possible sebaceous carcinoma in an older patient with a recurrent chalazion or chronic unilateral blepharitis that is refractory to treatment.

Biopsies of suspicious lesions should be sent to the pathology laboratory with a request for special lipid stains. These include oil red O and Sudan black stains and must be performed on frozen tissue, because routine processing of the tissue will dissolve any lipid that is present. Good communication between the clinician and the pathologist is therefore of paramount importance. Because many general pathologists lack familiarity with this entity, the clinician should not hesitate to seek outside consultation if there is a high clinical suspicion of sebaceous gland carcinoma.

Wide surgical excision of the tumor is indicated once the diagnosis is established. Because sebaceous gland carcinoma can metastasize widely, a complete metastatic evaluation should also be obtained. Incomplete excision will leave the patient at risk for local recurrence as well as metastatic dissemination. Radiation treatment has been employed for palliative therapy but is not effective as a primary treatment modality.

4. Malignant melanoma may arise in the eyelid, just as it may occur in the skin or mucus membranes throughout the body. Cutaneous melanomas may be subclassified as lentigo maligna, superficial spreading melanoma, and nodular melanoma. The nodular melanoma is the most common type affecting the eyelid and has a more aggressive clinical course. The eyelid can be secondarily involved from primary melanoma arising in the conjunctiva or by metastasis of melanoma from other sites.

The treatment for cutaneous melanoma is wide surgical excision with microscopic verification of clear margins. The finding of lymphatic or vascular invasion on microscopic evaluation should prompt referral for possible regional lymph node dissection. As with cutaneous melanomas arising elsewhere, an invasion depth of greater than 1.5 mm portends a higher risk for recurrence and the development of metastatic disease.

TEST INTERPRETATION

Morphologic appearance is suspicious, but tissue diagnosis is required for confirmation of malignancy.

DIAGNOSIS

Lesion of the right upper eyelid (medial canthal region); probable basal cell carcinoma.

MEDICAL MANAGEMENT

There is no medical treatment for this condition.

SURGICAL MANAGEMENT

Ancillary testing is not indicated prior to establishing the diagnosis by incisional or excisional biopsy. Once the diagnosis is known, patients with sebaceous carcinoma or cutaneous melanoma should undergo a complete metastatic evaluation. This is usually conducted under the supervision of an internist or oncologist. If complete removal of the tumor will require extensive reconstructive procedures, an incisional biopsy can be performed first to correctly establish the diagnosis. Small lesions, however, may be removed in toto at the time of initial biopsy. Many surgeons advocate the use of cryotherapy to the margins of the resulting defect to decrease the risk of tumor recurrence. Reconstruction procedures are dictated by the size and location of the defect once clear surgical margins have been verified.

The current patient underwent excisional biopsy of the lesion due to the high clinical suspicion of basal cell carcinoma. Intraoperative frozen section analysis confirmed the diagnosis of basal cell carcinoma with free surgical margins (Fig. 99–2). Because of the location of the defect, a full-thickness skin graft was used to repair the defect to avoid creating lagophthalmos or webbing of the medial canthal region.

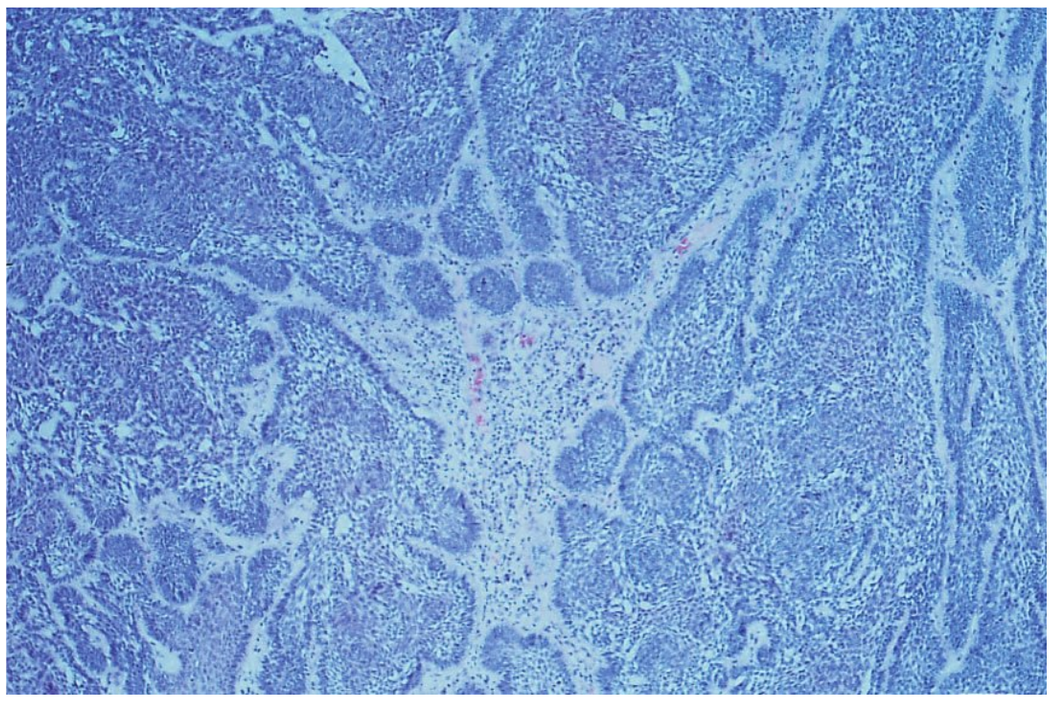

FIGURE 99–2 Histopathology of the tumor showing a nodular basal cell carcinoma. The nuclear palisading around the periphery of the nests is apparent (H & E. original magnification ×13.2).

REHABILITATION AND FOLLOW-UP

The patient did well postoperatively with a satisfactory functional and cosmetic result. He has been educated about his increased risk for the development of new skin malignancies and is under the care of a dermatologist for continued surveillance.

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