EyeRounds.org

The Best Hits Bookshelf

Volume 1: Popular Cases

First Edition

March 2018

THE UNIVERSITY OF IOWA

About this Book

This first edition book is a compilation of 50 case and tutorial articles featured on our website, EyeRounds.org. These articles have the most online "hits" and were hand-selected for their popularity and impact. They are among some of our most recent and high-yield content. Popularity will, of course, change over time so future editions will likely contain a different mixture of articles.

The content is arranged first by type (case or tutorial) and then subspecialty (Cornea and External Disease, Cataract, Glaucoma, Neuro-Ophthalmology, Oculoplastics, Pediatrics and Strabismus, Retina and Vitreous, and On-Call and Trauma.)

About EyeRounds.org

Ophthalmology Grand Rounds and EyeRounds.org is a website of the University of Iowa Department of Ophthalmology and Visual Sciences in Iowa City, Iowa. On EyeRounds.org, you will find case reports from our daily morning rounds, high-quality atlas images, videos, and online tutorials. EyeRounds.org is an ever-growing resource for students, residents, physicians, and patients. Over time, EyeRounds has gained momentum, now impacting learners all over the globe. Daily, the website receives thousands of hits from over 40 countries.

EyeRounds.org Content

The content on EyeRounds.org is produced by our physicians and is intended for medical students, residents, and physicians.

What is not in this book?

EyeRounds.org atlas images and videos, though very popular with our users, have been excluded from this compilation due to their nature. We invite you to explore the EyeRounds atlas at EyeRounds.org/atlas where you will find hundreds of pages of interesting and educational short items with images of interest. EyeRounds videos can be found at EyeRounds.org/video. Videos have been collected from a variety of sources created over the years by residents, faculty, and fellows of the University of Iowa Department of Ophthalmology & Visual Sciences.

Think before you act…

Disclaimer

Content is made available for review purposes only.

Much of the material from EyeRounds.org is gathered from Grand Rounds presentations.

The intent of Grand Rounds is to initiate discussion and stimulate thought, as a result, EyeRounds articles may contain information that is not medically proven fact and *should not be used to guide treatment*.

Opinions expressed are not necessarily those of the University of Iowa, the Carver College of Medicine, nor the Department of Ophthalmology and Visual Sciences.

For more details, see our terms of use at EyeRounds.org/TOS.htm

Funding Support

EyeRounds.org is partially supported by unrestricted funds from The University of Iowa Department of Ophthalmology and Visual Sciences and from The Iowa Eye Association, neither of whom have influence on the content of this site.

March 8, 2018

Dedication of this Work

Patricia (Trish) Duffel has a B.S. in Pharmacy from the University of Texas, Austin (1976) and an M.A. in Library and Information Science from the University of Iowa (1991). Having earned her pharmacy degree in the days before the Pharm D degree became generally accepted, Trish is a registered pharmacist (RPh). Since 1991, she has been the solo librarian for the Department of Ophthalmology and Visual Sciences at the University of Iowa and the Executive Director and Editor of EyeRounds.org since 2007. In her almost 27 years in the department, she has held many roles including library manager, literature searcher, information chaser, newsletter writer/editor, copy editor, webmaster, and educator.

Trish goes above and beyond, working tirelessly to support and see to the success of residents, fellows, scientists and physicians in the department. Her powerful work ethic, contagious energy, can-do attitude, and unwavering devotion to those around her has made her a favorite among faculty and trainees. She is a treasure trove of knowledge, a forever learner, and a truly incredible human being. For all that she has done for education at the University of Iowa Department of Ophthalmology and Vision Sciences and EyeRounds.org, we dedicate this work to Trish.

Contents

EyeRounds.org

Case Presentations

Cornea and External Disease

Salzmann's Nodular Corneal Degeneration

62-year-old woman presents with 3 years of progressive decrease in vision

Joy N. Carroll, Amanda C. Maltry, MD, Anna S. Kitzmann, MD

September 9, 2013

Chief Complaint

A 62-year-old woman presents with a 3-year history of painless, progressive loss of vision in both eyes.

History of Present Illness

Over the last 3 years, there has been gradual, painless loss of vision in both eyes (right greater than left) at both distance and near. She has had 3 updates of her spectacle prescription that have not provided satisfactory vision. There is no diurnal variation in vision.

Past Ocular History

- Myopia, presbyopia, astigmatism
- Dry eye syndrome, with relief of symptoms with artificial tears
- No ocular surgeries

Medical History

- Hypertension

Medications

- No ocular medications. Systemic medications: metoprolol 50 mg twice daily

Family History

- No family history of glaucoma, macular degeneration, blindness or known ocular diseases.

Social History

- Does not use tobacco or drink alcohol.

Ocular Exam

Visual acuity (VA) with correction

- Right eye (OD): 20/200, pinhole to 20/50-1
- Left eye (OS): 20/25+2, pinhole to 20/20

Manifest Refraction

- OD -2.00 + 5.00 x 20   VA 20/60
- OS -0.75 + 7.50 x 165 VA 20/25

Intraocular pressure (applanation): OD 16 mmHg, OS 18 mmHg

Pupils: Equal, round, 4 mm in dark, 2 mm in light, no relative afferent pupillary defect

Visual fields: Full to confrontation both eyes (OU)

Motility: Full OU

Slit Lamp Exam

- **External**: Normal OU
- **Lids & lashes:** Inspissated meibomian glands with thick waxy secretions and telangiectasia, normal lashes OU
- **Conjunctiva & sclera**: Clear and quiet
- **Cornea**
  - OD: Greyish nodules between the corneal epithelium and Bowman's layer in the paracentral superonasal region extending centrally into the visual axis; iron line at inferior border of the lesion
  - OS: Greyish nodules between the corneal epithelium and Bowman's layer in the paracentral superior and superotemporal regions extending centrally into the visual axis; iron line at inferior border of the lesion. See Figure 1.
- **Anterior chamber**: Deep and quiet OU
- **Iris:** Normal architecture OU
- **Lens**
  - OD: 2-3+ nuclear sclerosis
  - OS: 1-2+ nuclear sclerosis
- **Vitreous:** Normal OU

Dilated Fundus Exam

- **Disc:** Normal, cup-to-disc ratio 0.3 OU
- **Vessels:** Normal OU
- **Macula**: Normal OU
- **Periphery**: Normal OU

Other Tests

Topography was ordered to characterize the corneal nodules seen on slit lamp exam in the setting of significant astigmatism. Figure 2 shows the crab-claw like pattern of irregular astigmatism superiorly on each eye due to the superior Salzmann's nodules. Placido images show irregular mires most noticeable superiorly on each eye corresponding to the Salzmann's nodules.

Diagnosis

A diagnosis of Salzmann's nodular degeneration was made on the basis of the characteristic clinical appearance and the clinical history of progressive increasing irregular

astigmatism associated with worsening of best corrected visual acuity. She was also diagnosed with nuclear sclerotic cataracts on the right greater than left eye.

Figure 1a-b. Slit lamp photos of the left eye before treatment

Figure 2: Topography before treatment.

Treatment and Clinical Course

To improve visual acuity and to decrease the irregular astigmatism a superficial keratectomy was recommended to remove the Salzmann's nodules.

Course

The patient underwent superficial keratectomy on her right eye. Postoperatively, there was complete clearing of the subepithelial opacities with excellent clarity of the underlying stroma. One month later, reliable keratometry and intraocular lens (IOL) calculations were obtained and an uneventful phacoemulsification and implantation of a posterior chamber IOL was performed (see Figure 3). Several months later, she underwent superficial keratectomy on her left eye with similar results, followed by cataract surgery on her left eye one month later. Postoperatively both eyes achieved best corrected visual acuity of 20/20, with substantial reduction in the astigmatic error (Table 1; Figure 4). At the time of this writing, the vision and examination remains stable for 47 months with no recurrence of Salzmann's nodular corneal degeneration. The mild dry eye continues to be well controlled with artificial tears.

Figure 3: Right eye slit lamp photography, after superficial keratectomy, cataract extraction and intraocular lens placement.

Figure 4: Right eye topography after superficial keratectomy. The overall corneal curvature is reduced with substantial reduction of both regular and irregular astigmatism.

http://EyeRounds.org/cases/180-salzmann-nodular-corneal-degeneration.htm

Table 1

Pre-operative Manifest Refraction		
-2.00 + 5.00 x 20	VA 20/60	**OD**
-0.75 + 7.50 x 165	VA 20/25	**OS**
Post-operative Manifest Refraction		
-0.25 + 0.75 x 045	VA 20/20	**OD**
-1.00 + 1.00 x 150	VA 20/20	**OS**

Pathology

Salzmann's nodules are characterized by hyaline deposited anterior to a disrupted or even displaced Bowman's layer, posterior to an atrophic corneal epithelium. Figure 5 for is an example of the typical histopathology of Salzmann's nodules.

Discussion

Salzmann's nodular corneal degeneration was described by Katz in 1930 following a 1925 case series on the condition published by Maximilian Salzmann, although Salzmann concedes that a case published by Ernst Fuchs in 1901 appears to be the first published case of this corneal degeneration [1].

Salzmann's nodular corneal degeneration is characterized by bilateral gray-white elevated nodules anterior to Bowman's layer, which may be visually significant, cause foreign body sensation, or be asymptomatic. It is most common in middle-aged women. The cause of this degeneration is unknown; however, it has been associated with chronic ocular surface inflammation [1-6]. A case series of 152 eyes concluded that the most common associations were, in descending order, meibomian gland dysfunction (MGD), contact lens wear (especially hard contact lenses), peripheral vascularization, pterygium, keratoconjunctivitis sicca, and exposure keratitis [1]. Another case series of 180 eyes also identified MGD as the most common comorbidity [2].

Conservative treatment consists of management of the underlying etiology, such as MGD. Eyelid hygiene and doxycycline may be considered to treat the MGD prior to surgical treatment. Contact lens cessation or re-fitting may also be beneficial. Medical management is successful in preventing the need for surgery in most cases; the indications for surgery are (1) discomfort; (2) reduced vision due to progressive increase in astigmatic error. Surgery is uniformly successful in removal of the nodule and almost invariably successful in reducing the astigmatic error in allowing for improvement in best corrected visual acuity, usually with a much weaker spectacle prescription. Stabilization of the refractive error usually takes 3 to 6 weeks. In rare cases of neglected nodules within the visual axis, anterior stromal haze may compromise the final visual results.

Whereas subtle recurrences are common in most cases over a 5 to 15 year period, visually significant recurrences are uncommon (5 to 20%) and can be minimized with
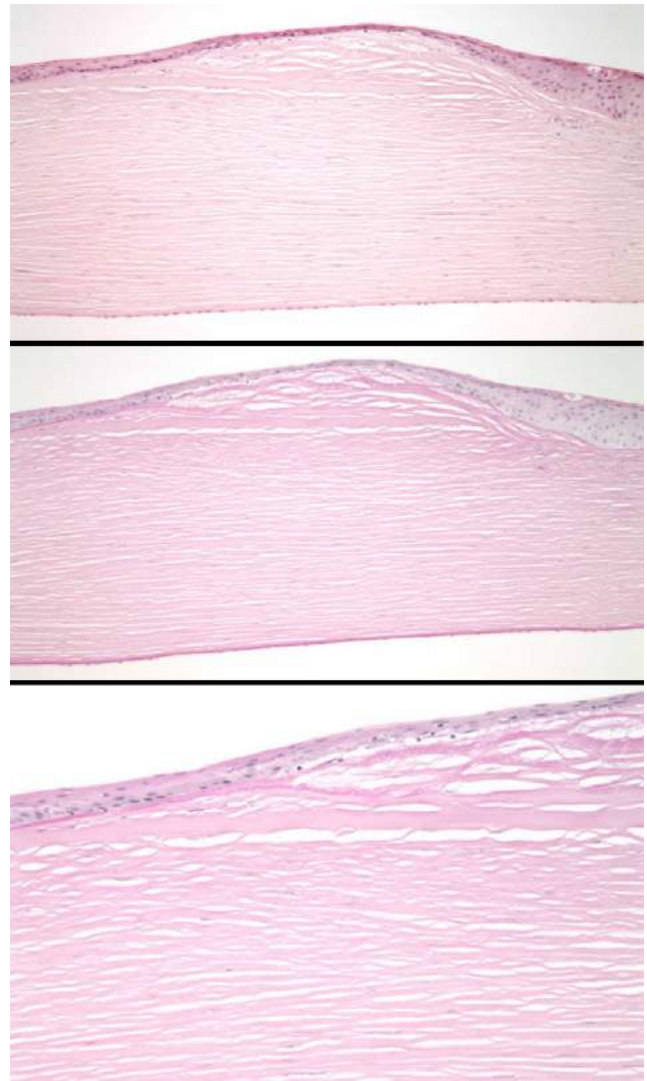
Figure 5: Salzmann's nodule histopathology. A. Atrophic corneal epithelium overlies a nodular, hyalinized fibrous plaque between the epithelium and Bowman's layer. A portion of Bowman's layer is absent at the right side of the lesion. H&E, 50x. B and C. Periodic acid Schiff stain highlights the thickened, irregular epithelial basement membrane.
50x, 100x.

meticulous control of the etiology responsible for the condition [1, 2]. Those cases can be treated with repeat superficial keratectomy. If anterior stromal haze persists in the visual axis after treatment of primary or recurrent nodules, phototherapeutic keratectomy can be offered [1].

Superficial keratectomy of astigmatism-inducing Salzmann's nodules should always be performed prior to cataract surgery. Stable keratometry readings and IOL calculations cannot be reliably obtained until 3 to 6 weeks after surgery. Toric IOLs should be avoided because of the risk of recurrent nodules and induction of post-operative astigmatism.

Examples of Salzmann's nodular corneal degeneration, Figures 6-10
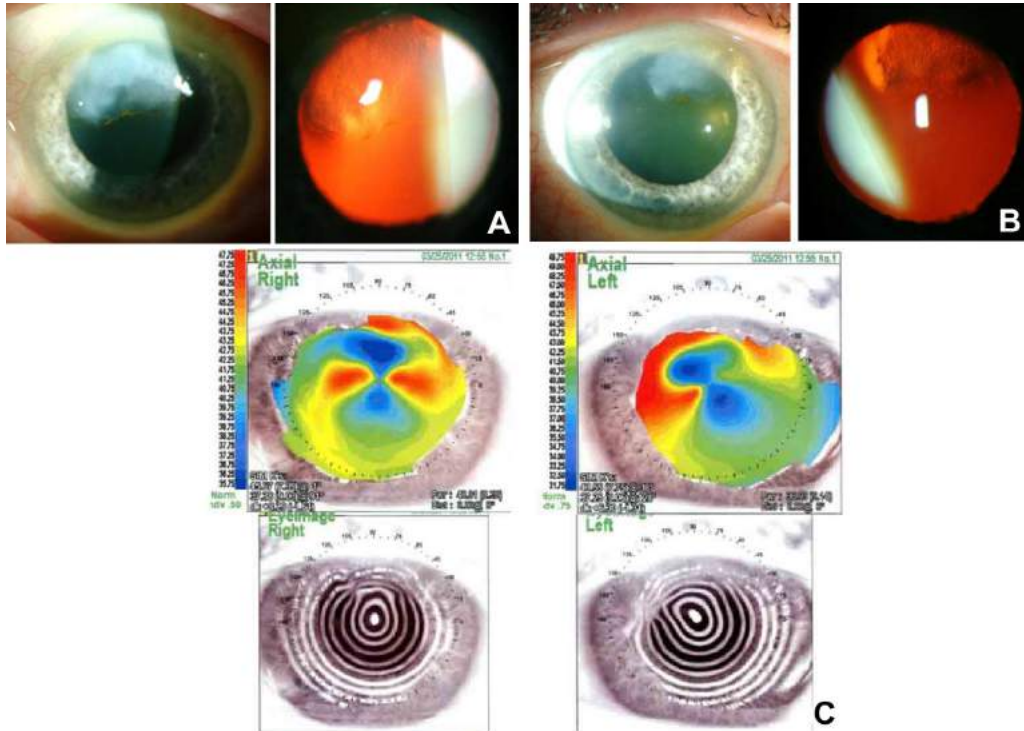
Figure 6

A: Slit lamp photo of the right eye of another patient with a superior Salzmann's nodule.

B: Slit lamp photo of the left eye of another patient with a superior Salzmann's nodule.

C: Corneal topography. The right eye has an against the rule irregular astigmatism with superior steepening. The placido image shows irregular mires superiorly. The left eye has an asymmetric against the rule irregular astigmatism with superonasal steepening and corresponding irregular mires on placido image.
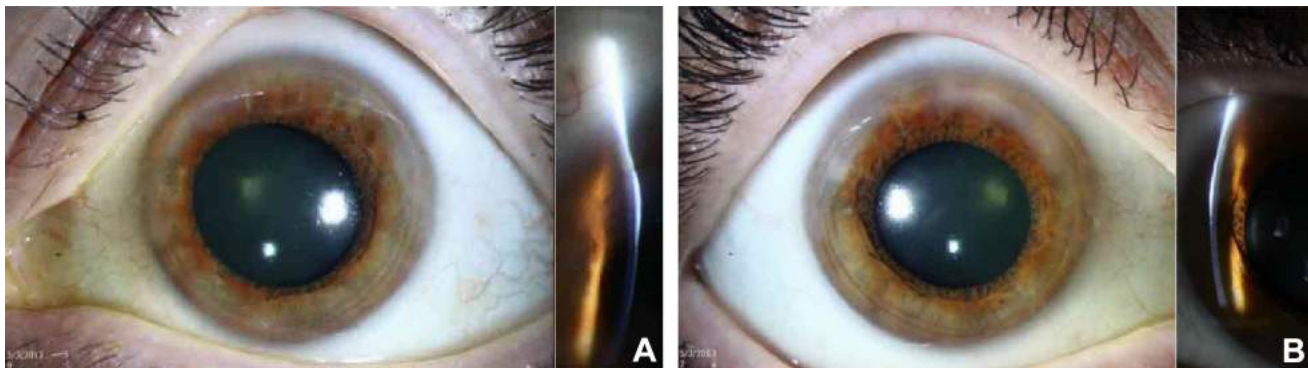
Figure 7a: Slit lamp photo of the left eye of another patient with Salzmann's nodular corneal degeneration. Nodules are peripheral and most evident superonasally and superotemporally in this photo.

Figure 7b: Slit lamp photo of the right eye. Salzmann's nodules are annular in the superior periphery.
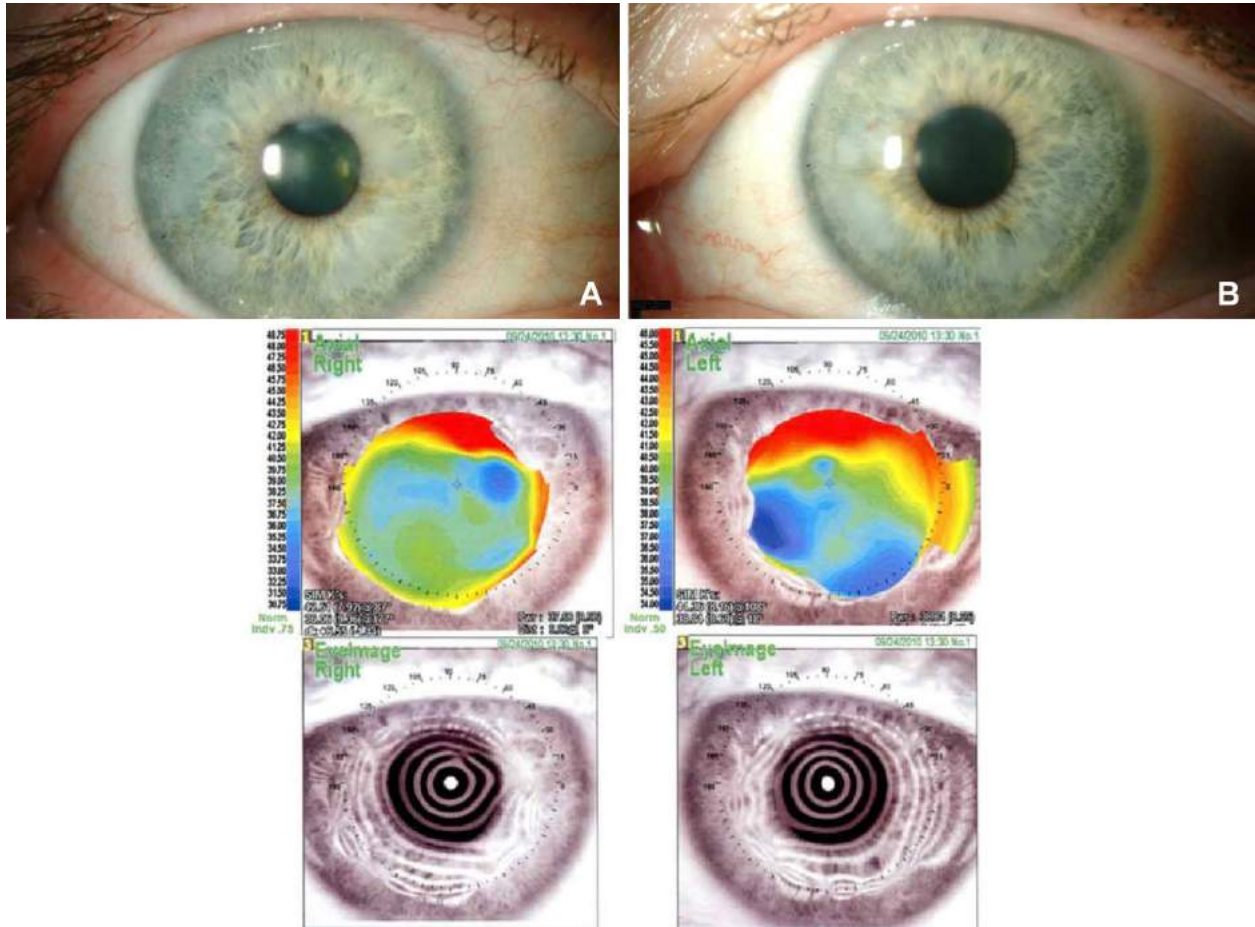
Figure 8a: Slit lamp photo of the right eye of another patient with Salzmann's nodular corneal degeneration. Nodules are annular in the mid-periphery.

Figure 8b: Slit lamp photo of the left eye of another patient with Salzmann's nodular corneal degeneration. Nodules are annular in the interior mid-periphery. F

igure 8c: Corneal topography. The right eye shows a very irregular astigmatism with superior and nasal steepening. Placido image shows irregular mires in the mid-periphery in all directions. The left eye has a very irregular astigmatism with marked superior and temporal steepening. The placido image has irregular mires with some nasal steepening.

Figure 9: Slit lamp photo of the right eye of another patient with Salzmann's Nodular Corneal Degeneration. Nodules are nasal and inferonasal.
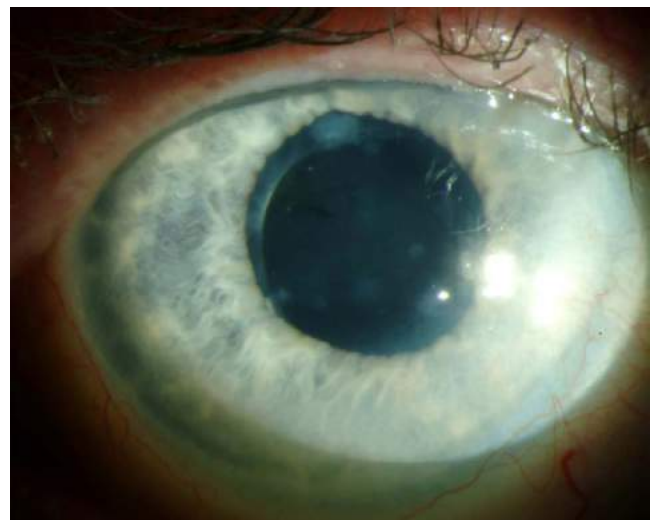
Figure 10: Slit lamp photo of another patient with Salzmann's Nodular Corneal Degeneration. Several small nodules, superior and inferior approach the visual axis.

Summary of the key facts regarding Salzmann's nodular corneal degeneration

Epidemiology	*Signs*

♦ Onset often around 50 years of age, but has been reported in ages 13-92 [2]
♦ Female patients account for 75-90% of all cases [1,2].
♦ Often bilateral [1,2].
♦ Deposits are progressive
♦ Associated chronic ocular surface inflammation
   • Meibomian gland dysfunction
   • Contact lens wear
   • Keratoconjunctivitis sicca
   • Exposure keratitis
   • Trachoma
	♦ Bilateral gray-white elevated corneal subepithelial nodules in the paracentral or central cornea or near the limbus with associated pannus, most commonly in an annular distribution [4].
	♦ There is a subset of Salzmann's nodules with associated vascularization [5].
	
	Symptoms
	
	♦ Decreased visual acuity
	♦ Asymptomatic
	♦ Foreign body sensation

Diagnosis	*Treatment*
♦ Clinical: based on slit lamp exam ♦ Topography: may be helpful for making the diagnosis. Nodules cause irregular astigmatism. ♦ Histopathology: Thin epithelium, thick basement membrane with displaced Bowman layer, and non-specific stromal scarring	♦ Superficial keratectomy (SK) is standard to reduce irregular astigmatism. In a large case series SK was successful in 90.2% of eyes [2]. ♦ Phototherapeutic keratectomy has been used in some cases following SK, and a case review has not identified a significant difference in outcomes compared to repeat SK [1]. ♦ Recurrence after SK is common, in one series recurrence occurred in 21.9% after a mean follow-up time of 61 months [2]. Visually significant recurrences occur in only 5-20% of patients [1].

Conclusion

Salzmann's nodular corneal degeneration is a non-inflammatory, slowly progressive nodular corneal degeneration that may induce ocular surface discomfort and progressive astigmatism with decreased best corrected visual acuity. The diagnosis is based on clinical examination. Topography is helpful in evaluating the contribution of the nodule to visual impairment. Superficial keratectomy is a successful treatment option, and visually significant recurrence afterward is relatively rare.

Differential diagnosis [4]

♦ Corneal scarring
♦ Spheroidal degeneration

References

1. Farjo AA, Halperin GI, Syed N, Sutphin JE, Wagoner MD. Salzmann's Nodular Corneal Degeneration Clinical Characteristics and Surgical Outcomes. Cornea. 2006; 25(1): 11-15. [PMID: 16331034]

2. Graue-Hernandez EO, Mannis MJ, Eliasieh K, Greasby TA, Beckett LA, Bradley JC, Schwab IR. Salzmann Nodular Degeneration. Cornea. 2010; 29(3):283-9. [PMID: 20098304]

3. Nissirios NJ, Barsam A, Nadji E, Donnenfeld ED, Perry HD. Relationship of Bell Phenomenon with Salzmann Nodular Degeneration. Cornea. 2013; 32(7): 939-942. [PMID: 23442252]

4. Das S, Langenbucher A, Pogorelov P, Link B, Seitz B. Long-term outcome of excimer laser phototherapeutic keratectomy for treatment of Salzmann's nodular degeneration.Journal of Cataract & Refractive Surgery. 2005;31(7):1386-1391. [PMID: 16105611]

5. Gore DM, Iovieno A, Connell BJ, Alexander R, Meligonis G, Dart JK. Peripheral hypertrophic subepithelial corneal degeneration: nomenclature, phenotypes, and long-term outcomes. Ophthalmology. 2013;120(5):892-8. [PMID: 23474249]

6. Hamada S, Darrad K, McDonnell PJ. Salzmann's nodular corneal degeneration (SNCD): Clinical findings, risk factors, prognosis and the role of previous contact lens wear. Contact Lens and Anterior Eye. 2011;34(4):173-178. [PMID: 21349758]

Citing this article

Carroll JN, Maltry AC, Kitzmann AS. Salzmann's Nodular Corneal Degeneration: 62-year-old woman presents with 3 years of progressive decrease in vision. EyeRounds.org. September 9, 2013; available from http://EyeRounds.org/cases/180-salzmann-nodular-corneal-degeneration.htm

last updated: 9/9/2013

Treatment of Epithelial Basement Membrane Dystrophy with Manual Superficial Keratectomy

Leslie T. L. Pham, MD; Kenneth M. Goins, MD; John E. Sutphin, MD; Michael D. Wagoner, MD, PhD

February 22, 2010

Epithelial basement membrane dystrophy (EBMD) is the most common type of corneal dystrophy, affecting 2% of the population.[1] Although the majority of patients remain asymptomatic or experience minor episodic subjective discomfort, about 10% will eventually complain of recurrent erosions and/or visual disturbances.[1,2] The clinical course is often biphasic: Recurrent epithelial erosions predominate in the early phase, and visual disturbances occur in the later phase.

The pathophysiologic hallmark of EBMD is an abnormality in the formation and maintenance of the epithelial basement membrane adhesion complex of the corneal epithelium, a phenomenon that accounts for the recurrent erosions that are associated with this disorder. Originally described by Hansen[3] over a century ago, and further characterized by Thygeson[4] a half century later, recurrent erosions are acute disruptions of the corneal epithelium,

which classically occur upon awakening and are associated with severe, sharp pain that may be transient or last for several hours or days, depending upon the surface area of epithelial sloughing. In severe cases, the erosion syndrome may be associated with considerable morbidity and occupational disability. Although erosions may occur in association with prior corneal trauma, EBMD is the most common cause of this disorder.

Initially, there may be few clinical signs associated with EBMD; however, a history of recurrent erosions should suggest this diagnosis, especially if they are bilateral and occur in multiple sites. With continued cycles of epithelial breakdown and aborted efforts at the development of a stable epithelial basement membrane adhesion complex, morphological changes eventually develop, which lead to
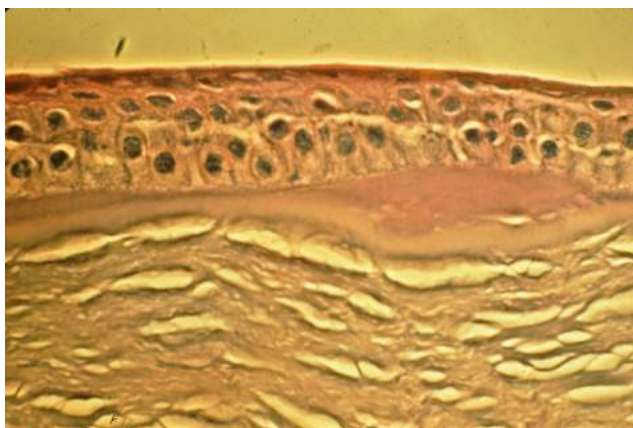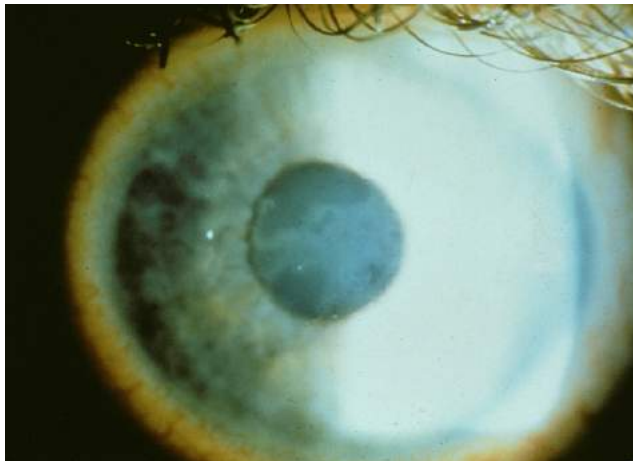
Figure 1. Epithelial basement membrane dystrophy: "map" changes. (A) Clinical appearance. (B) Duplication of the basement membrane correlates with the clinical findings
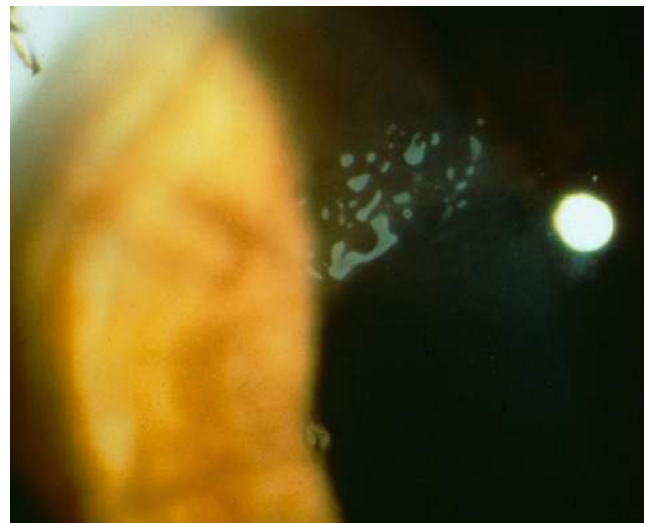
Figure 2. Epithelial basement membrane dystrophy: "dot" changes. (A) Clinical appearance. (B) Intraepithelial deposition of fibrillar material correlates with the clinical findings.

the classic "map-dot-fingerprint" epithelial and subepithelial findings that characterize this disorder (Figures 1-3)[2]. Inadequate formation of hemidesmosomes by the basal epithelial cells results in compensatory aberrant regeneration and duplication of the epithelial basement membrane, a change that is clinically manifested by the "fingerprint" lines. The deposition of fibrogranular material below and above the abnormal basement membrane is responsible for the "map" and "dot" findings, respectively. When present in the visual axis, these epithelial and subepithelial irregularities initially result in irregular astigmatism and induction of higher order optical aberrations, which are subjectively associated with monocular diplopia and visual distortion—often before the development of a decrease in Snellen acuity. However, a progressive decline in Snellen acuity does occur as the morphological abnormalities increase in density, often in association with a paradoxical improvement in the erosion syndrome.

Successful treatment of EBMD is predicated upon optimizing conditions necessary for the formation of stable epithelial basement membrane adhesion complexes throughout the entire cornea, preferably before the development of vision-compromising morphological abnormalities in the visual axis. In most cases of EBMD, recurrent epithelial erosions can be prevented by the bedtime application of a lubricating or hyperosmotic ointment. If mild erosions fre-

quently occur despite bedtime lubrication, the prolonged use of a bandage soft contact lens (SCL) may eliminate or greatly reduce the frequency of symptomatic erosions.

In the event that substantial epithelial erosions develop (Figure 4), more aggressive intervention is indicated. Successful management can be accomplished with manual superficial keratectomy (SK), followed by the reestablishment of an intact corneal epithelium that is firmly adherent and remains optically clear. Clinical and experimental evidence that has accumulated for more than a century regarding the development of the technique of manual SK and its application in this setting is summarized as follows:

♦ **Epithelial debridement**. For more than a century, the treatment of choice for recurrent erosions was the simple debridement of devitalized and poorly adherent epithelium and the use of pressure patching until reepithelialization was complete. Although the prolonged subsequent use of bedtime lubricating ointments subsequently resulted in permanent resolution in many cases, recurrent disease remained quite common. In 1983, Buxton and Fox[5] reported a success rate of 85% with
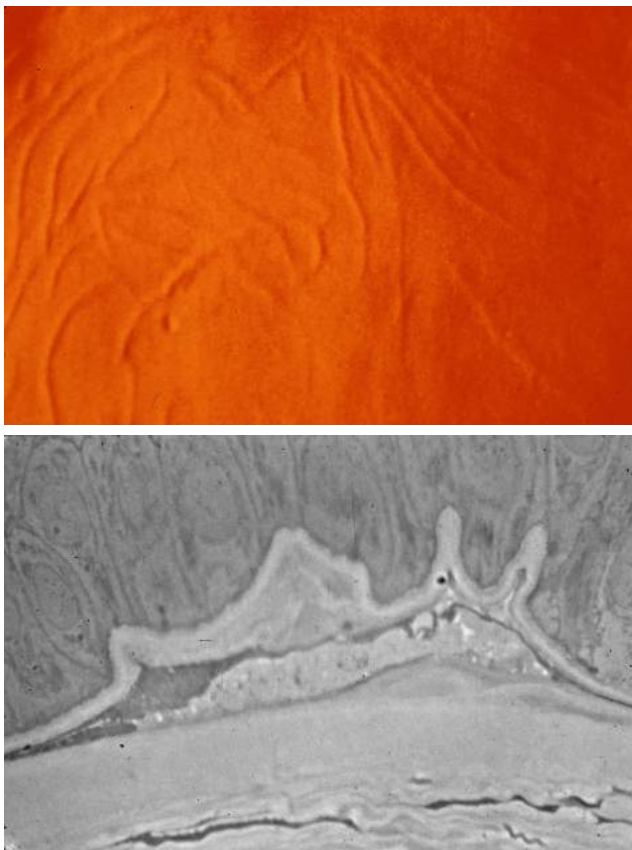
Figure 3. Epithelial basement membrane dystrophy: "fingerprint" changes. (A) These changes are easily seen by retroillumination. (B) Duplication of the epithelial basement membrane correlates with the clinical findings.
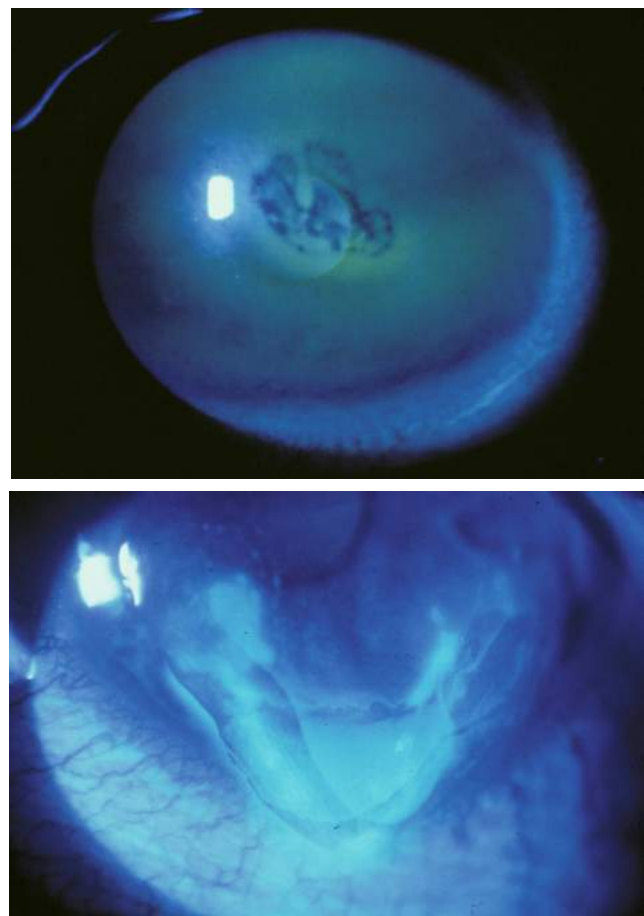
Figure 4. Recurrent corneal epithelial erosions. (A) Small areas of epithelial loss with adjacent areas of rapid tear film breakup associated with poorly adherent corneal epithelium in the axial cornea. (B) Large area of poor adhesion with pseudobullous elevation of the corneal epithelium in the peripheral cornea.

epithelial debridement followed by the extended use of bandage SCL therapy, which facilitated the uninterrupted development of a stable epithelial basement membrane adhesion complex.

♦ **Removal of aberrant basement membrane and subepithelial debris and fibrosis.** Simple epithelial debridement may not be effective in removing all the abnormal basement membrane and may be associated with the recurrence of epithelial erosions even after the discontinuation of extended bandage SCL therapy.[6] As early as 1906, Franke[7] reported a reduced rate of recurrent epithelial erosions when epithelial debridement was followed by the application of chlorinated water. Kenyon and Wagoner[2,8] further emphasized the importance of meticulously cleaning the subepithelial debris as an integral part of the management of this disorder.

♦ **Disruption of Bowman's layer.** Brown and Bron[6] suggested that some disruption of Bowman's layer may be necessary to maximize the opportunity for permanent resolution of recalcitrant epithelial erosions. Anecdotally, it has long been recognized that substantial trauma to Bowman's layer is associated not only with scarring but also with excellent epithelial adhesion. Accordingly, the guiding principle in managing recalcitrant erosions is striking an appropriate balance between sufficient disruption of Bowman's layer to facilitate firm epithelial adhesion and minimization of visually significant scarring. Broad area treatment of Bowman's layer with iodine was reported by Thygeson[4] in 1954, with diathermy by Wood[9] in 1984, with a diamond burr by Buxton and Constad[10] in 1987, with the neodymium:YAG laser by Geggel[11] in 1990, and subsequently with excimer laser phototherapeutic keratectomy (PTK) by numerous authors.[12,13] Focal disruption of Bowman's layer with anterior stromal puncture was demonstrated by McLean et al.[14] to be effective in the management of most cases of recurrent erosion. Although the anterior stromal puncture marks do not seem to be visually compromising, most authors recommend applying this technique aggressively outside the visual axis and either sparingly or not at all in the visual axis.

♦ **Pharmacological control of matrix metalloproteinase-9**. The manual SK techniques of epithelial debridement, removal of aberrant basement membrane and subepithelial debris, and focal disruption of Bowman's layer with stromal puncture, followed by a 6-to-12-week period of bandage SCL therapy, are almost invariably associated with the reestablishment of a firmly adherent corneal epithelium that tends to remain optically clear. However, this outcome is optimized by providing pharmacological intervention that is designed to minimize subepithelial collagenase production and its deleterious impact on the development of the stable epithelial basement membrane adhesion complex during the postoperative period. Durson et al.[15] documented the efficacy of the systemic administration of doxycycline and the topical use of corticosteroids in further improving therapeutic outcomes associated with the medical and surgical management of recurrent erosion syndromes.

In the present study, we reviewed the outcome of treating symptomatic EBMD with manual SK at University of Iowa Hospitals and Clinics (UIHC).

PATIENTS AND METHODS

The medical records of every patient with EBMD who had been treated with manual SK by a member of the Cornea Service at UIHC from January 1, 1998, to December 31, 2007, were retrospectively reviewed. The diagnosis was established by a member of the cornea faculty on the basis of the characteristic clinical findings. Every eye had been treated with at least one mode of medical therapy before undergoing SK, including the use of topical lubrication, hyperosmotic agents, and/or bandage SCL therapy. The indications for surgical intervention were decreased vision and/or recurrent corneal epithelial erosions. Outcome measures included best spectacle-corrected visual acuity (BSCVA), the presence or absence of recurrent erosions, and symptomatic recurrent EBMD. Cases in which more than 3 months of postoperative follow-up were available were included in the statistical analysis. Eyes that had been previously treated with either manual SK or PTK prior to referral to UIHC or before the study period were excluded from the statistical analysis.

Surgical Technique

The surgical procedures were performed with topical anesthesia by members of the cornea faculty (KMG, JES, MDW) in the minor outpatient procedure room. The central corneal epithelium (6.0-8.0 mm) was debrided with a Weck cell sponge in most cases. Occasionally, a no. 57 Beaver blade was required to complete the epithelial removal. Poorly adherent epithelium in the periphery was also debrided when present. A no. 57 Beaver blade was also used to remove the basement membrane and subepithelial fibrosis with gentle scraping. Special precautions were taken to minimize the disturbance of the underlying Bowman's layer. The surface of Bowman's layer was then vigorously smoothed with a Weck cell sponge. In some cases early in the study period, a diamond burr was gently applied to the anterior surface of Bowman's layer. Later in the study period, stromal puncture was directly applied to Bowman's layer outside the visual axis where the epithelium had been debrided and through the epithelium in areas where it remained in place. One surgeon (MDW) applied light treatment in the visual axis in cases where erosions had been documented to occur in this zone or where substantial subepithelial fibrosis had been detected prior to the operative procedure. At the conclusion of the case, a bandage SCL was placed on the eye.

Postoperatively, all patients were treated with topical antibiotics and steroid drops 4 times daily for 1 week. Early in the study period, the bandage SCL therapy was discontinued in most cases after 1 week, the topical antibiotics and steroids were rapidly tapered and discontinued, and bedtime lubricating ointment was continued for at least 3 months. Later in the study period, the bandage SCL therapy was continued for 6 to 12 weeks in most cases, along

with the administration of prophylactic topical antibiotics. In the latter half of the study, most patients were concomitantly treated with systemic doxycycline and topical corticosteroids until the bandage SCL therapy was completed.

RESULTS

Of 20 patients (14 men; 6 women), 22 eyes with EBMD were treated with manual SK for decreased vision (20 eyes) and/or recurrent epithelial erosions (15 eyes). The mean follow-up after surgery was 43.6 months (range, 3.0-115.2 months).

The treatment outcomes for decreased visual acuity are summarized in Table 1. Improvement was detected in BSCVA from a mean preoperative logMAR acuity of 0.313 (Snellen equivalent 20/41) to a best postoperative acuity of 0.038 (20/22) and a final acuity of 0.079 (20/24). A BSCVA of 20/20 or better was achieved in 12 (60.0%) eyes, and the same result was achieved at the most recent examination in 10 (50.0%) eyes. A BSCVA of 20/30 or better was achieved in 20 (100.0%) eyes, and the same result was achieved at the most recent examination in 19 (95.0%) eyes.

All 15 (100.0%) eyes with recurrent erosions had complete resolution of symptoms during the first 6 postoperative months. Between 6 and 60 months after initial treatment, 3 (20.0%) eyes experienced recurrent erosions. Among these, 2 eyes were successfully treated with a course of bandage SCL therapy, and 1 eye was successfully treated with excimer laser PTK.

No surgical complications resulted from any of the manual SK procedures.

DISCUSSION

Our study strongly suggests that manual SK is a safe and effective treatment for visual disturbances and recurrent epithelial erosions associated with EBMD. No complications occurred in any of the 22 eyes treated with manual SK. Furthermore, all 20 eyes treated for visual disturbances experienced a sustained improvement in vision for the entire follow-up period. Although it would be intuitive to anticipate that the same morphological abnormalities would occur postoperatively in this genetic disorder, the establishment of stable epithelial basement membrane adhesion complexes and the reduction of recurrent epithelial erosions in the visual axis either completely prevents or substantially retards the recurrence of these changes and their adverse effects on visual function. Every patient experienced complete relief of recurrent erosion symptoms during the first 6 months, with only 3 experiencing symptoms in the subsequent decade. Among these, 2 cases were relatively minor and were managed with a 3-month course of bandage SCL therapy. One case was troublesome and required treatment of the entire basement membrane of the affected eye with excimer laser PTK.

Obtaining a lasting and satisfactory result with manual SK requires meticulous attention to the surgical technique, especially the thorough removal of all abnormal subepithelial pathology in the visual axis and the use of anterior stromal puncture, prolonged postoperative bandage SCL therapy, and appropriate pharmacological support. This technique is effective in providing a sustained improvement in the spectacle acuity of virtually every patient and relief from recurrent erosions in the vast majority of patients. It is preferred over broad area ablation with the excimer laser because it is much less expensive, is not associated with a hyperopic shift in the baseline refractive error, and is less likely to induce visually significant haze in the visual axis (Table 2).[12,13] Nonetheless, it will occasionally be necessary to offer excimer laser PTK to the small percentage of patients in which manual SK is not completely successful in providing sustained relief from recurrent erosions, as was the case with 1 patient in the present series.

Best Spectacle-corrected Visual Acuity			
Vision	Preoperative	Best Obtained	Final
LogMAR			
Mean	0.313	0.038	0.079
Range	0.097 to 0.903	-0.125 to 0.176	-0.125 to 0.477
Snellen			
Mean	20/41	20/22	20/24
Range	20/25 to 20/160	20/15 to 20/30	20/15 to 20/60
Cumulative, %			
≥20/20	0	60	50
≥20/25	25	85	65
≥20/30	55	100	95
≥20/40	65	100	95

Table 1. Manual Superficial Keratectomy for Decreased Visual Acuity Associated with Epithelial Basement Membrane Dystrophy (n = 20)

	Manual SK	PTK
Cost	Inexpensive	Expensive
Equipment	Simple surgical instruments are sufficient	Excimer laser required
Surgical skill	Minimal training required	Certification course required
Postoperative morbidity	Pain may be present until epithelial defect resolves; minimal risk of corneal infection; virtually no risk of visually significant haze ot scar formation	Pain may be present until epithelial defect resolves; minimal risk of corneal infection; significant haze or scar formation (especially if large refractive errors are treated)
Efficacy	Excellent prognosis for improved vision and resolution of recurrent epithelial erosions	Excellent prognosis for improved vision and resolution of recurrent epithelial erosions
Refractive changes	Little or no change in spherical refractive error	Hyperopic shift may occur
Retreatment	Simple and inexpensive	Simple but expensive

Table 2. Manual Superficial Keratectomy (SK) Versus Excimer Laser Phototherapeutic Keratectomy (PTK) for Treatment of Epithelial Basement Membrane Dystrophy

Excimer laser PTK may be offered in combination with photorefractive keratectomy (PRK) in primary therapy of EBMD if the therapeutic objective is to attain an improvement in uncorrected visual acuity. If this approach is adopted, the treating ophthalmologist must be cognizant of the potential that some of the measured refractive error may be factitiously induced by the epithelial and subepithelial morphological abnormalities associated with EBMD and that the refractive accuracy of PRK cannot be predicted with certainty. In such cases, a more conservative approach would be to perform a 2-stage procedure consisting of manual SK followed by PRK (after the refractive error has stabilized and can be measured accurately).

References

1. Waring GO 3rd, Rodriques MM, Laibson PR. Corneal dystrophies I. Dystrophies of the epithelium, Bowman's layer, and stroma. Surv Ophthalmol. 1978;23:71-122.

2. Kenyon KR, Wagoner MD. Corneal epithelial defects and noninfectious ulceration. In: Albert DM, Jakobiec FA, eds. Principles and Practice of Ophthalmology. Vol 2. 2nd ed. Philadelphia, Pa: WB Saunders; 2000:926-943.

3. Hansen E. Om den intermettirende keratitis vesiculosa neuralgica af traumatisk oprndelse. Hosp Tidende. 1872;15:201-203.

4. Thygeson P. Observations on recurrent epithelial erosion of the cornea. Am J Ophthalmol. 1959;27:48-52.

5. Buxton JN, Fox ML. Superficial keratectomy in the treatment of epithelial basement membrane dystrophy: a preliminary report. Arch Ophthalmol. 1983;101:392-395.

6. Brown N, Bron A. Recurrent erosion of the cornea. Br J Ophthalmol. 1976;60:84-86.

7. Franke E. Uber Erkrankungen des Epithels der Hornhaut. Klin Monastsbl Augenheilkd. 1906;44:508-532.

8. Wagoner MD, Kenyon KR. Keratectomy and lamellar keratoplasty. In: Bruner WE, Stark WJ, Maumenee AE, eds. A Manual of Corneal Surgery. New York, NY: Churchill Livingstone; 1987:29-38.

9. Wood TO. Recurrent erosion. Trans Am Ophthalmol Soc. 1984;82:850-898.

10. Buxton JN, Constad WH. Superficial epithelial keratectomy in the treatment of epithelial basement membrane dystrophy. Ann Ophthalmol. 1987;19:92-96.

11. Geggel HS. Successful treatment of recurrent corneal erosion with Nd:YAG anterior stromal puncture. Am J Ophthalmol. 1990;110:404-407.

12. Hersh PS, Wagoner MD. Excimer Laser Surgery for Corneal Disorders. New York/Stuttgart: Thieme Medical Publishers; 1998.

13. Hersh PS, Klein S, Wagoner MD. Phototherapeutic keratectomy. In: Krachmer JH, Mannis MJ, Holland EJ, eds. Cornea. Vol 2. 2nd ed. St Louis, Mo: Mosby; 2005: 1735-1747.

14. McLean EN, MacRae SM, Rich LF. Recurrent erosion. Treatment by anterior stromal puncture. Ophthalmology. 1986;784-788.

15. Dursun D, Kim MC, Solomon A, Pflugfelder SC. Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9, doxycycline and corticosteroids. Am J Ophthalmol. 2001;132:8-13.

Suggested Citation Format

Acute Corneal Hydrops

Miles F. Greenwald BS, Jesse M. Vislisel MD, Kenneth M. Goins MD

INITIAL PRESENTATION

Chief Complaint

Poor vision and pain in the left eye

History of Present Illness

A 51-year-old male with keratoconus and history of rigid gas permeable (RGP) contact lens wear in the left eye presented with left eye redness, pain, light sensitivity, and tearing for 1 week. He was initially seen at an acute care clinic where he was told he had scratched his conjunctiva. He then presented to his regular ophthalmologist who found him to have acute corneal edema and referred him to the University of Iowa Hospitals and Clinics (UIHC). He was started on ciprofloxacin and hypertonic saline drops by the outside provider. At the time of his presentation, his pain was rated as 7 out of 10 and described as a constant surface irritation and scratchy sensation. He described constant tearing and blurry vision which did not change throughout the day. The patient took out his contact lens when symptoms began.

Past Ocular History

- Keratoconus
- RGP contact lens wear in the left eye, soft contact lens wear in the right eye
- Mild dry eye syndrome, both eyes
- No history of ocular surgery or trauma

Past Medical History

- Non-contributory

Medications

- Ciprofloxacin drops three times daily in the left eye
- Sodium chloride 5% (Muro 128) drops four times daily in the left eye
- Artificial tears as needed in both eyes

Allergies

- None

Family Ocular History

- Mother has had several ocular surgeries and treatment for an unknown disorder

Social History

- Works as an educational product distributor and travels frequently for work

Review of Systems

- Negative except for what is detailed in the history of present illness

OCULAR EXAMINATION

Visual Acuity (Snellen chart)

- Right eye (OD): 20/20 with soft contact lens
- Left eye (OS): 20/100 without correction, pinhole to 20/60

Intraocular Pressure (Tonopen)

- OD: 17 mmHg
- OS: 24 mmHg

Confrontation Visual Fields

- Full in both eyes

Pupils

- No relative afferent pupillary defect in either eye

Extraocular Motility

- Full in both eyes

Pachymetry

- OD: 541 μm
- OS: Unable to measure

External

- Epiphora in left eye, appears to be in discomfort

Slit Lamp Exam OS (Figure 1)

- Lid/lashes: Reactive ptosis
- Conjunctiva/sclera: Diffuse 1+ injection
- Cornea: Inferior conical protrusion, focal area of massive inferior corneal edema with overlying microcystic edema and bullae, epithelium intact, no infiltrates or keratic precipitates
- Anterior chamber: Deep, rare cell
- Iris: Normal architecture, dilated
- Lens: Trace nuclear sclerosis

Differential Diagnosis

- Acute corneal hydrops
- Infectious keratitis
- Autoimmune keratitis
- Traumatic posterior annular keratopathy

- Post-surgical Descemet's membrane detachment
- Fuchs corneal endothelial dystrophy
- Posterior polymorphous corneal dystrophy
- Iridocorneal endothelial syndrome

Additional testing

Anterior Segment Optical Coherence Tomography (OCT) (Figure 2) showed massive inferior corneal edema and overlying epithelial bullae.

Diagnosis

Acute corneal hydrops in the setting of keratoconus

CLINICAL COURSE

Initial conservative management included prednisolone 4 times daily, sodium chloride 5% (Muro 128) drops 4 times daily, and cyclopentolate 2 times daily in the affected eye. A Kontur bandage contact lens was placed for comfort. The patient was placed on timolol once daily to treat the ocular hypertension caused by reactive inflammation.

Placement of an anterior chamber sulfur hexafluoride (SF6) gas bubble was offered to speed his recovery, but due to upcoming travel necessitating air travel and inability to position due to work requirements, he declined.
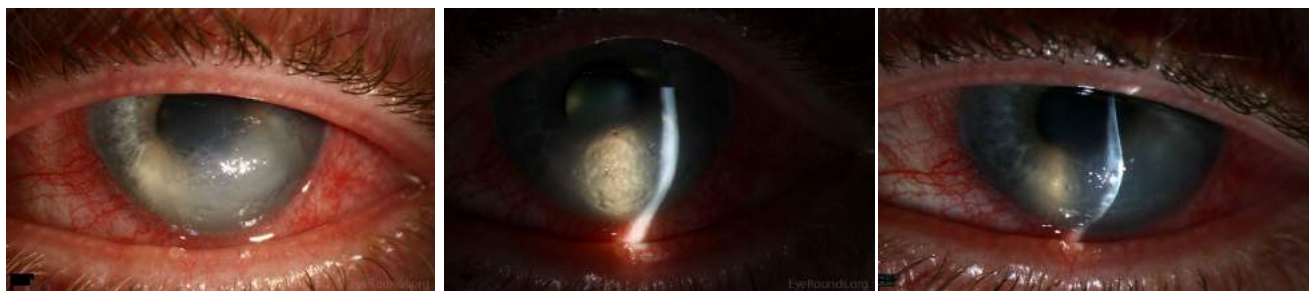
Figure 1
a: Broad illumination of the left eye showing severe, inferior corneal edema.

b: Broad slit beam view of left eye showing microcystic edema and bullae overlying the area of stromal edema.

c: Narrow slit beam demonstrating the inferior conical protrusion and magnitude of corneal edema.
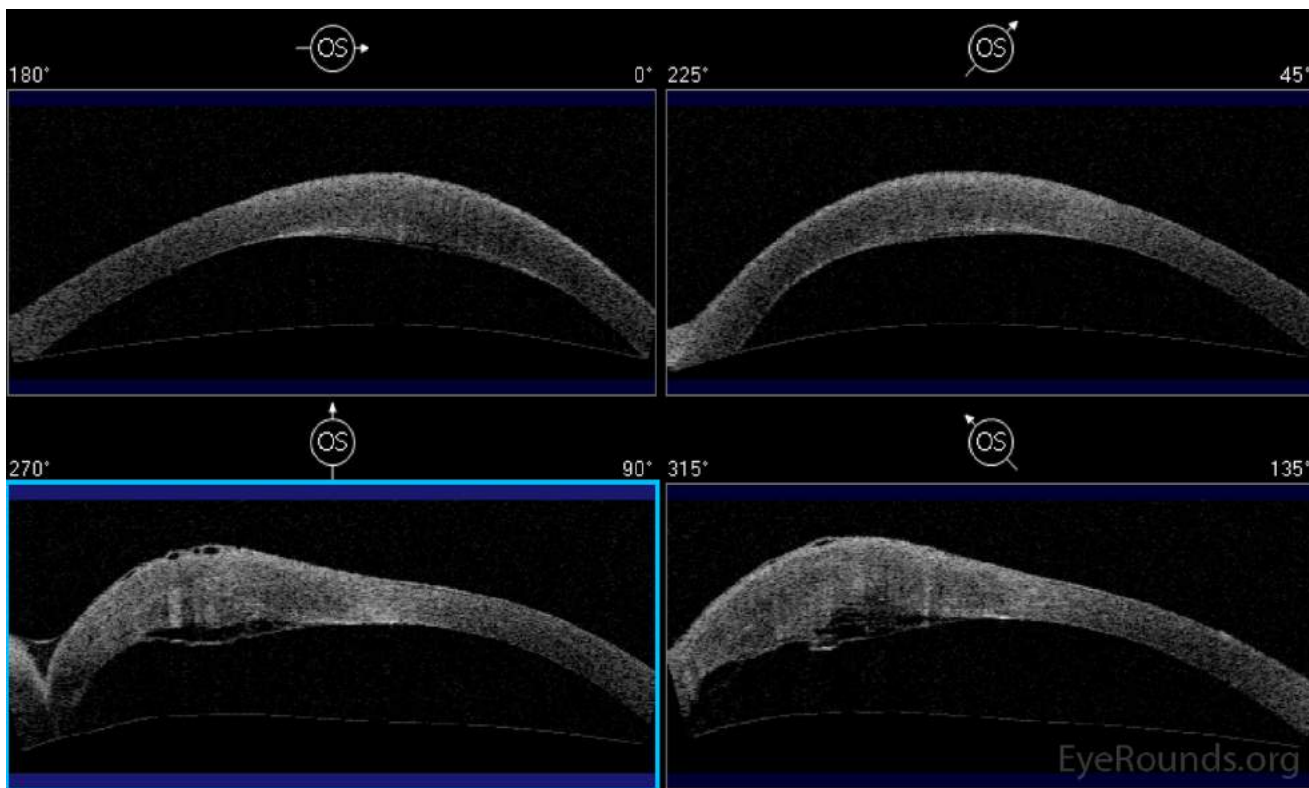
Figure 2: Anterior segment OCT showing massive inferior corneal edema and overlying epithelial bullae. A break in Descemet's membrane with Descemet's membrane detachment is visible below the area of edema.

http://EyeRounds.org/cases/241-acute-corneal-hydrops.htm

The edema gradually improved and 3 weeks later he was found to have some improvement in corneal clarity, but a large amount of scarring and contour irregularity in the area of the hydrops. A penetrating keratoplasty (PK) was performed for restoration of vision.

DISCUSSION

Etiology/Epidemiology

Acute corneal hydrops is caused by the acute disruption of Descemet's membrane in the setting of corneal ectasia. Hydrops is a term used to denote an abnormal accumulation of fluid in a body tissue or cavity. The term is also used to describe fetal swelling in utero, often due to Rh blood group isoimmunization (hydrops fetalis). Acute corneal hydrops occurs in approximately 3% of patients with keratoconus. Although most cases of hydrops are associated with keratoconus due to the prevalence of the disease, the incidence of hydrops is actually higher in other corneal ectatic disorders such as pellucid marginal degeneration (see http://EyeRounds.org/atlas/pages/Pellucid-marginal-degeneration) and keratoglobus, with some reports being as high as 11% [1-2]. The average age of onset is typically around 25 years of age, with males being more commonly affected than females [3]. A history of eye rubbing and seasonal allergies is associated with hydrops development [1,3].

Pathophysiology and Natural History

The focal corneal edema of acute hydrops results from the compromise of the barrier function of Descemet's membrane and subsequent fluid uptake by the overlying corneal stroma. It has been postulated that resolution of hydrops requires two steps. First, the detached Descemet's membrane must reattach to the posterior stroma. This process is dependent on the depth of the detachment. Second, the endothelium must migrate from the reattached Descemet's membrane to cover the gaps between the broken ends. This process depends on the size of the break [4].

Most cases of acute corneal hydrops spontaneously resolve over 2-4 months [5-7]. Depending on the degree of swelling and timeline of resolution, vision-impairing scarring can necessitate the need for corneal transplantation. Larger disruptions of Descemet's membrane are associated with more prolonged resolution of corneal edema, increased risk of neovascularization, and a worsened visual outcome after final resolution of edema compared to smaller disruptions of Descemet's membrane [8].

Signs/Symptoms

Clinical manifestations of acute corneal hydrops include severe corneal edema with a corresponding reduction in visual acuity. Epiphora, photophobia, and pain may also occur. If these manifestations are seen in patients with previously diagnosed corneal ectasia and/or evidence of corneal ectasia, the diagnosis of acute corneal hydrops can be made [9].

Imaging

Anterior segment optical coherence tomography (AS-OCT) is not required for diagnosis but can be helpful to quantify the extent and location of corneal edema and the extent of the break in Descemet's membrane. Imaging techniques such as AS-OCT also allow improved ability to monitor the response to treatment [9].
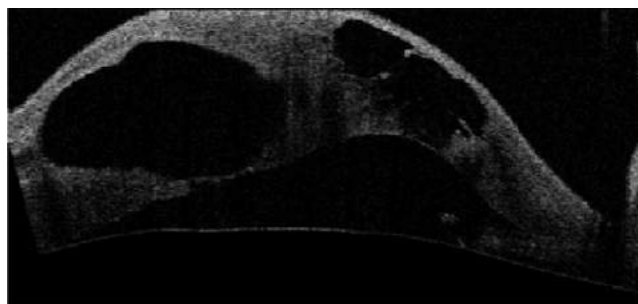
Figure 3: AS-OCT showing large, cystic intrastromal accumulation of fluid in a patient with keratoconus and acute corneal hydrops.

Treatment

Due to the spontaneous resolution of acute corneal hydrops, classical treatment is focused on medical therapy to increase patient comfort and prevent permanent sequelae. Conservative management for acute corneal hydrops includes hypertonic sodium chloride to reduce epithelial edema, and cycloplegia for comfort. Topical steroids are controversial, but we often employ them to reduce the inflammation and subsequent neovascularization that can accompany these episodes. A bandage contact lens can be placed for comfort, but a large diameter soft lens may be necessary to fit the steep contours of these eyes.

Pneumatic descemetopexy, or placement of an anterior chamber air or gas bubble to tamponade the Descemet's membrane break, has been shown to speed recovery following acute hydrops [5-7]. In the last 15 years, this practice has gained popularity because of its ability to significantly reduce the time needed for the resolution of edema. The quicker recovery not only shortens the period of discomfort and poor vision for the patient, but theoretically decreases the risk of visually-significant scarring and need for post-resolution corneal transplantation [5-7,9]. Miyata and colleagues found that the corneal edema lasted an average of 20 days in a group of 9 patients receiving intracameral air compared to 65 days for a control group of 21 patients. The treatment group was able to return to hard contact lens use in one-fourth the time of the control group. However, there was no difference in final best corrected visual acuity after the complete resolution of edema [5]. Panda and colleagues showed that corneal hydrops resolved at an average of 4 weeks in 9 patients who received injections of intracameral SF6 gas compared to 12 weeks

in the control group of 9 patients. This study showed that the treatment group had slightly better best corrected visual acuity, but it was measured at 12 weeks and not after resolution of edema [6]. Basu and colleagues, using C3F8 gas and a much larger group of patients, showed that the edema resolved significantly quicker in the treatment group (57 days for 62 eyes vs. 104 days for 90 control eyes (p<0.0001)). Notably, best corrected visual acuity was not significantly different between the two groups [7]. Ting and Srinivasan reported using C2F6 gas with a similar increase in the rate of edema resolution to the previous studies [10]. No study has yet found a difference in the need for corneal transplantation between those who received a gas or air bubble and those who did not. Several groups have reported using an air bubble along with sutures through Descemet's membrane to even more tightly re-adhere the membrane after hydrops [11-12].

The choice between air and gas depends on the estimated amount of time needed to repair the defect in Descemet's membrane. Air lasts the shortest duration, often only 2-3 days, which may require repeat bubble placement to achieve the desired effect. This was seen in the study by Miyata et al. where 78% of patients required the placement of more than one bubble [5]. At our institution, SF6 is normally utilized with the duration of 7-10 days typically being sufficient to allow for re-apposition and healing of Descemet's membrane.

Penetrating keratoplasty (Figure 4) can be performed to treat the underlying ectatic disorder and any corneal stromal scarring that may result from the hydrops. Deep anterior lamellar keratoplasty (DALK) is extremely challenging to perform following hydrops due to difficulty separating Descemet's membrane from the posterior stroma in the setting of a Descemet's break and the posterior scarring that often accompanies these episodes. Thus, PK is usually our procedure of choice for these patients. When reviewing PK outcomes in ectatic patients who previously developed hydrops, studies have been inconclusive regarding differences in graft survival between grafts with prior episodes of hydrops and grafts without prior hydrops [13-14]. Basu et al. recently compared the allograft survival in the absence of rejection for keratoconus eyes with and without hydrops and found eyes with hydrops had significantly decreased graft survival (83% 5 year rejection-free graft survival in 32 hydrops eyes vs. 98% in 70 non-hydrops eyes) [15]. The proposed mechanism for this increase in graft rejection and failure rates is the presence of intraocular inflammation that accompanies hydrops. While corneal graft success rates decrease somewhat following hydrops, these patients still often have excellent postoperative outcomes.

Figure 4: Penetrating keratoplasty performed for keratoconus [17]

Treatment/Management Guidelines

EPIDEMIOLOGY	SIGNS
♦ Occurs in 3% of those with keratoconus and 11% of those with pellucid marginal degeneration or keratoglobus ♦ Associated with ocular allergies and eye rubbing	♦ Reduced visual acuity ♦ Conjunctival injection ♦ Corneal edema ♦ Signs of underlying corneal ectasia
SYMPTOMS	TREATMENT/ MANAGEMENT
♦ Decreased vision ♦ Eye pain or irritation ♦ Eye redness ♦ Tearing ♦ Light sensitivity	♦ Conservative treatment • Cycloplegia • Hypertonic saline • Topical steroids • A bandage contact lens may be placed for comfort • Injection of anterior chamber air or gas may accelerate recovery ♦ Penetrating keratoplasty for definitive treatment

REFERENCES

1. Grewal S, Laibson P, Cohen E, et al. Acute hydrops in the corneal ectasias: associated factors and outcomes. Am J Ophthalmol. 2000;129(5):702-3. [PMID 10844084]

2. Sridhar MS, Mahesh S, Bansal AK, et al. Pellucid marginal corneal degeneration. Ophthalmology. 2004;111(6):1102-7. [PMID 15177959]

3. Fan gaskin JC, Good WR, Jordan CA, et al. The Auckland keratoconus study: identifying predictors of acute corneal hydrops in keratoconus. Clin Exp Optom. 2013;96(2):208-13. [PMID 23432147]

4. Basu S, Vaddavalli PK, et. al. Anterior segment optical coherence tomography features of acute corneal hydrops. Cornea. 2012;31(5):479-85. [PMID 15177959]

5. Miyata K, Tsuji H, Tanabe T, et al. Intracameral air injection for acute hydrops in keratoconus. Am J Ophthalmol. 2002;133(6):750-2. [PMID 1203664]

6. Panda A, Aggarwal A, Madhavi P, et al. Management of acute corneal hydrops secondary to keratoconus with intracameral injection of sulfur hexafluoride (SF6). Cornea. 2007;26(9):1067-9.Inoue Y. Review of clinical and basic approaches to corneal endotheliitis. Cornea. 2014;33 Suppl 11:S3-8. [PMID 17893535]

7. Basu S, Vaddavalli PK, Ramappa M, et al. Intracameral perfluoropropane gas in the treatment of acute corneal hydrops. Ophthalmology. 2011;118(5):934-9. [PMID 21211841]

8. Al suhaibani AH, Al-rajhi AA, Al-motowa S, et al. Inverse relationship between age and severity and sequelae of acute corneal hydrops associated with keratoconus. Br J Ophthalmol. 2007;91(7):984-5. [PMID 17576720]

9. Fan gaskin JC, Patel DV, Mcghee CN. Acute corneal hydrops in keratoconus - new perspectives. Am J Ophthalmol. 2014;157(5):921-8. [PMID 24491416]

10. Ting DS, Srinivasan S. Pneumodescemetopexy with perfluoroethane (C2F6) for the treatment of acute hydrops secondary to keratoconus. Eye (Lond). 2014;28(7):847-51. [PMID 23833179]

11. Rajaraman R, Singh S, Raghavan A, Karkhanis A. Efficacy and safety of intracameral perfluoropropane (C3F8) tamponade and compression sutures for the management of acute corneal hydrops. Cornea. 2009;28(3):317-20. [PMID 19387234]

12. Yahia chérif H, Gueudry J, Afriat M, et al. Efficacy and safety of pre-Descemet's membrane sutures for the management of acute corneal hydrops in keratoconus. Br J Ophthalmol. 2015;99(6):773-7. [PMID 25563765]

13. Tuft SJ, Gregory WM, Buckley RJ. Acute corneal hydrops in keratoconus. Ophthalmology. 1994;101(10):1738-44. [PMID 7936572]

14. Akova YA, Dabil H, Kavalcioglu O, Duman S. Clinical features and keratoplasty results in keratoconus complicated by acute hydrops. Ocul Immunol Inflam. 2000;8(2):101-9. [PMID 10980682]

15. Basu S, Reddy JC, Vaddavalli PK, et al. Long-term outcomes of penetrating keratoplasty for keratoconus with resolved corneal hydrops. Cornea. 2012;31(6):615-20 [PMID 22236783]

16. Donaghy CL, Vislisel JM, Greiner MA. An Introduction to Corneal Transplantation. May 21, 2015; Available from: http://EyeRounds.org/tutorials/cornea-transplant-intro/

Suggested Citation Format

Greenwald MF, Vislisel JM, Goins KM. Acute Corneal Hydrops. EyeRounds.org. August 3, 2016; Available from: http://EyeRounds.org/cases/241-acute-corneal-hydrops.htm

last updated: 08/01/2016

Cataract

Marfan Syndrome

Jeffrey Welder, MD; Erik L. Nylen, MSE; Thomas A. Oetting, MS, MD

May 6, 2010

Initial Presentation

Chief Complaint: Decreased vision and glare in both eyes.

History of Present Illness: A 28-year-old female with a history of Marfan syndrome presented to the comprehensive ophthalmology clinic reporting a progressive decrease in vision and worsening glare in both eyes. She had been seen by ophthalmologists in the past, and had been told that her crystalline lenses were subluxed in both eyes. She had not had problems with her vision until recent months.

Medical History: Marfan syndrome with aortic stenosis followed by cardiology

Medications: Oral beta blocker

Family History: No known family members with Marfan Syndrome. Grandmother with glaucoma

Social History: The patient is a graduate student.

Ocular Exam

♦ External Exam Normal.
♦ Visual Acuity (with correction)
  o OD 20/40
  o OS 20/50
♦ Current glasses: OD: 6.75+ 5.00 x 135 OS: -5.25 + 4.25 x 60
♦ Pupils: No anisocoria and no relative afferent pupillary defect
♦ Motility: Ocular motility full OU.
♦ Anterior segment exam
  o Inferiorly subluxed lenses OU (figure 1 and 2).
  o The angle was deep OU and there was no lens apposition to the cornea in either eye.
♦ Dilated funduscopic exam
  o Posterior segment was normal OU with no peripheral retinal degeneration
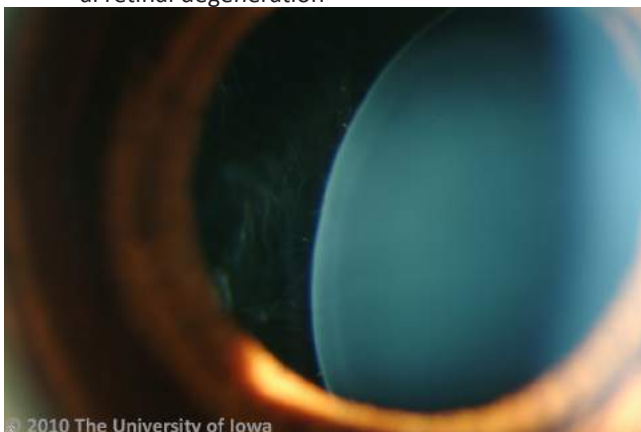
Figure 1: Note the inferiorly subluxed lens.
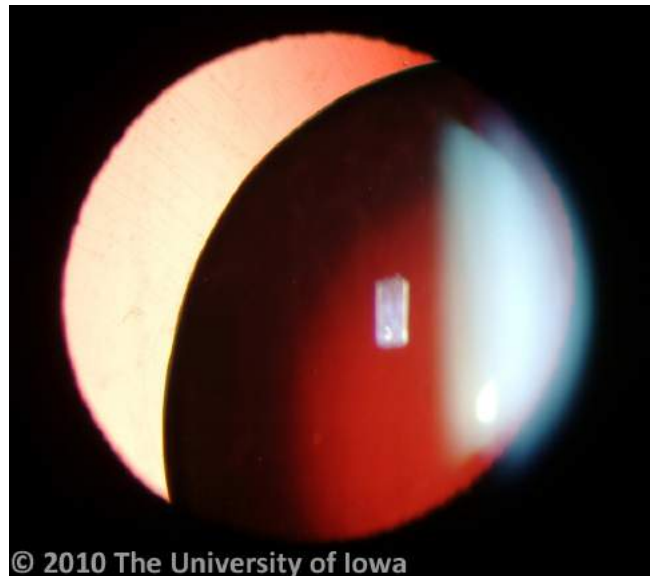
© 2010 The University of Iowa

Figure 2: Inferior lens subluxation highlighted with retroillumination

Clinical Course

The patient's subluxed lenses led to poor vision from peripheral lenticular irregular astigmatism and glare. She was taken to the operating room where her relatively clear lenses were removed and iris sutured intraocular lenses were placed. The surgical video for one eye is shown below.

Video: https://www.facebook.com/cataract.surgery/videos/153379281140/

Her post-operative course was unremarkable with excellent improvement in her visual function. Her iris-sutured intraocular lenses have remained stable for several years as shown in figure 3 and 4.

Discussion

Marfan syndrome is a pleotropic autosomal dominant genetic disorder that results in weakening of connective tissue in the musculoskeletal, cardiovascular and ocular organ systems. It is the second most common inherited connective tissue disorder, with an incidence of between 1/5,000 and 1/20,000. The abnormality in over 80% of Marfan patients involves defects in the protein fibrillin 1 (FBN1) on chromosome 15, a structural component of microfibrils found in connective tissue throughout the body. More than 500 different mutations in the FBN1 gene have been indentified. Another mutation believed to result in the Marfan phenotype is the inactivation of the TGF-β receptor 2 (TGFBR2), thought to disrupt the integration of fibrillin into connective tissue.
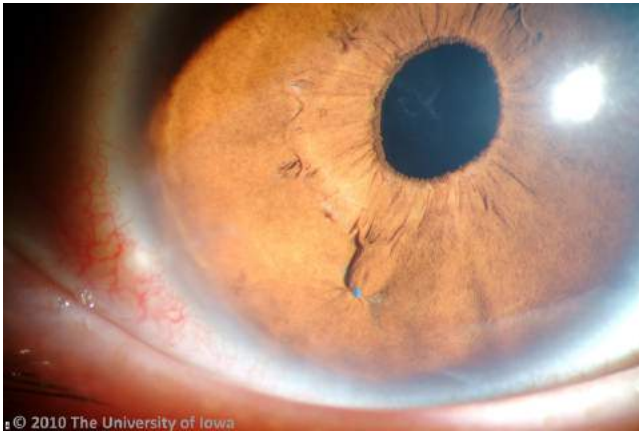
Figure 4: Note the Prolene suture securing the lens to the iris
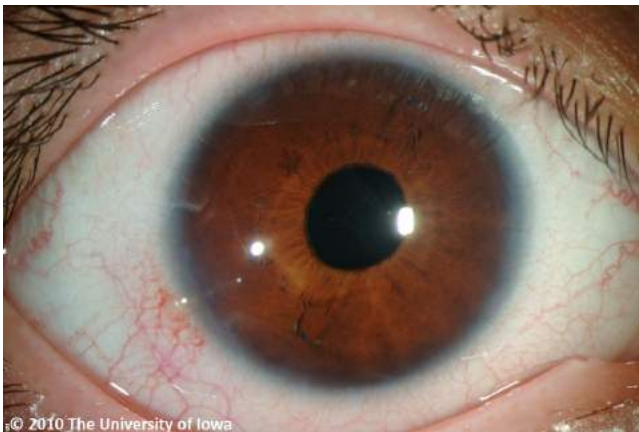
Figure 3: Centered iris-sutured intraocular lens several years after surgery

The diagnosis of Marfan syndrome is complicated by a genotype-phenotype inconsistency that presents with widely variable clinical manifestations. Clinical diagnosis is currently based on Ghent Nosology (1996) which specifies the involvement of at least 3 organ systems (Skeletal, ocular, cardiovascular, dura mater, pulmonary, or skin/integument), 2 of which must meet "major criteria." Marfan syndrome can also be diagnosed with equivocal genetic testing, which can be offered to patients in the context of family planning and pedigree formation.

The systemic manifestations of Marfan syndrome are well-studied, the most obvious of which are the musculoskeletal abnormalities. Again, the common thread in the variety of Marfan phenotypes is the weakness or incompetence of the connective tissues due to defects in fibrillin. The Marfan patient is often very tall with long, flexible extremities and marked scoliosis. They exhibit arachnodactyly (spider fingers, see Figure 5) with the ability to dramatically encircle the wrist (Walker-Murdoch sign). In addition, they often have pectus excavatum, a high-arched palate, and facial abnormalities. The cardiovascular findings range from mild mitral valve prolapse to severe aortic aneurysm or dissection; the severe cardiovascular complications are the primary causes of mortality among Marfan patients.

Figure 5: Arachnodactyly (spider fingers)

Pulmonary diseases include apical blebs or spontaneous pneumothorax.

The major ocular abnormality in Marfan syndrome is ectopia lentis (lens subluxation or dislocation, see Figure 6). While relatively little is known about the exact mechanism of this ocular pathology in Marfan syndrome, a number of theories have been suggested. Wheatley et. al (1995) found that while fibrillin is localized to the superficial capsule and ciliary epithelial surface at the attachment of the zonules in normal eyes, Marfan patients lack such localization and exhibit abnormal ciliary processes with absent or severely disorganized zonules. This pathology was found to be positively correlated with lens subluxation. Clinically, ectopia lentis is bilateral in 60-87% of Marfan patients and is stable from childhood. Symptoms include fluctuating blurred vision, monocular diplopia, and pain. On exam, patients demonstrate refractive instability with myopia and astigmatism, iridodonesis, phacodinesis, and a recessed angle. The most common direction of dislocation on exam
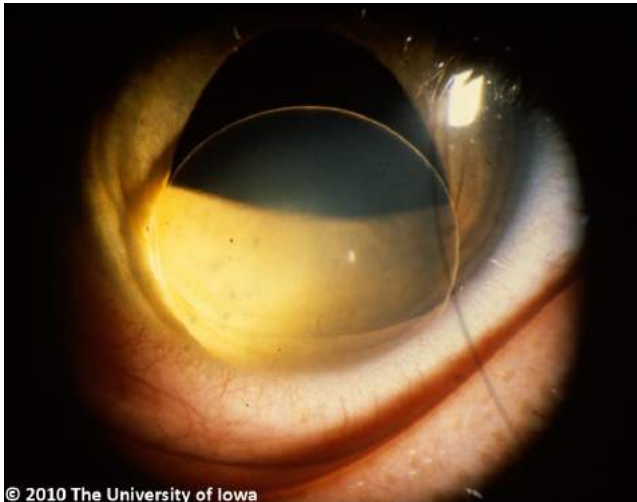
© 2010 The University of Iowa

Figure 6: Ectopia Lentis (lens subluxation or dislocation)

is superotemporal. In addition, there may be secondary complications from lens movement such as phacolytic uveitis from posterior subluxation of the lens to the vitreous.

Retinal tears and detachments are also quite common in patients with Marfan syndrome. The Marfan eye has many risk factors for tears and detachments including high myopia, excess lattice degeneration, vitreous liquefaction, choroidal and scleral thinning, and vitreous traction from ectopia lentis. Each of these changes is thought to be related to fibrillin alterations. Retinal detachment occurs in 5-26.5% of patients with Marfan syndrome and is bilateral in 30-42% of these cases. Rigorous screening and close follow-up of symptoms is important to prevent retinal detachment in these cases.

Other ocular manifestations of Marfan syndrome include flattened cornea (causing astigmatism), keratoconus, increased globe length (causing myopia), iris coloboma, cataracts, glaucoma, strabismus, amblyopia, and vascular malformations. Central to each of these findings is the ubiquitous abnormality of fibrillin in the ocular connective tissue of the Marfan patient.

With regard to ectopia lentis, a number of treatment options exist. Mild subluxation allows for near normal vision with the patient seeing through the phakic portion of the pupil. The other extreme would be severe subluxation in a child which requires urgent surgical correction to avoid irreversible amblyopia. The principle surgical method employed in Marfan syndrome is lens extraction with either IOL placement or contact lens correction. Surgery is indicated when the lens position causes irregular astigmatism and glare, when the lens is posteriorly dislocated into the vitreous, when the lens is dislocated anteriorly and causes secondary glaucoma, or in the setting of cataract formation. Because of the altered anatomy and weakening of the connective tissues in Marfan syndrome, all of the usual complications of lens extraction are amplified. As the capsule is unstable from loss of zonules, the intraocular lens (IOL) must either be placed in the anterior chamber, or be secured to the iris or sclera with permanent Prolene sutures.

One important complication of IOL fixation to the sclera in young patients is that the 10-0 Prolene sutures may break three to ten years following surgery. This has led many surgeons to use larger suture such as 8-O Gortex or 9-O Prolene in the hopes that the suture will last longer. In cases of complete posterior lens dislocation, a pars plana vitreolensectomy can be performed. Another surgical option is to secure the capsule to the sclera using sutured Cionni modified capsular tension rings (CTR from Morcher) or Ahmed capsular tension segments (CTS from Morcher). These surgical interventions, while complicated, have great success in restoring vision in these patients.

Diagnosis: Marfan syndrome with lens dislocation

Differential diagnosis for crystalline lens dislocation

- ♦ Trauma
- ♦ Homocystinuria
- ♦ Sulfite oxidase deficiency
- ♦ Weill-Marchesani Syndrome
- ♦ Hyperlysinemia

Summary

EPIDEMIOLOGY	SIGNS (Ocular)
♦ Incidence: 1/5000 - 1/2000. 60-87% with ectopia lentis. ♦ Gender: Males and females equally represented. ♦ Genetics: Autosomal dominant. 80% from FBN1 mutations on chromosome 15. ♦ Other mutations include TGFBR1 and TGFBR2.	♦ Ectopia lentis (most commonly superotemporal dislocation) ♦ Retinal detachment ♦ Myopia ♦ Hypoplastic iris with miosis ♦ Amblyopia ♦ Strabismus ♦ Keratoconus ♦ Enophthalmos
SYMPTOMS	TREATMENT of ocular complications
♦ Multiple systems including cardiovascular, musculoskeletal, and ocular complaints. ♦ Ocular: blurred vision, monocular diplopia, pain, flashes and floaters.	♦ Lens extraction for ectopia lentis with Contact lens or IOL (anterior chamber, sutured to sclera/iris) ♦ Retinal laser for detachments or tears ♦ Regular screen for myopia, amblyopia, strabismus, keratoconus, and glaucoma.

http://www.EyeRounds.org/cases/110-Marfan.htm

References

1. Abboud E. Retinal detachment surgery in Marfan's syndrome. *Retina* 1998;18:405–409.

2. De Paepe A, Devereux RB, Dietz HC, Hennekam RC, Pyeritz RE. Revised diagnostic criteria for the Marfan Syndrome. *Am J Med Genet* 1996;62(4):417 .

3. Fuchs J. Marfan syndrome and other systemic disorders with congenital ectopia lentis. A Danish national survey. *Acta Paediatr* 1997;86:947-52.

4. Kohnen T, Baumeister M and Bühren J. Scheimpflug imaging of bilateral foldable in-the-bag intraocular lens implantation assisted by a scleral-sutured capsular tension ring in Marfan's syndrome. *J Cataract Refract Surg* 2003;29:598–602.

5. Maumenee I. The eye in the Marfan syndrome. *Trans Am Ophthalmol Soc* 1981;79:684–733.

6. Meire F, Delleman W and Bleeker-Wagemakers E. Ocular manifestations of congenital Marfan syndrome with contractures (CMC syndrome). *Ophthalmic Paediatr Genet* 1991;12: 1–9.

7. Nemet AY, Assia EI, Apple DJ, Barequet, IS. Current Concepts of Ocular Manifestations in Marfan Syndrome. *Sur Ophth* 2006;51(6): 561-575.

8. Pessier A and Potter K. Ocular pathology in bovine Marfan's syndrome with demonstration of altered fibrillin immunoreactivity in explanted ciliary body cells. *Lab Invest* 1996;75:87–95.

9. Pyeritz RE. The Marfan syndrome. *Annu Rev Med* 2000;51:481–510.

10. Remulla JF, Tolentino FI. Retinal detachment in Marfan's syndrome. Int Ophthalmol Clin 2001; 41: 235-40.

11. Robinson PN, Booms P, Katzke S, Ladewig M, Neumann L, Palz M, Pregla R, Tiecke F, Rosenberg T. Mutations of FBN1 and genotype-phenotype correlations in Marfan syndrome and related fibrillinopathies. *Hum Mutat* 2002;20(3):153-61.

12. Siganos D, Siganos C and Popescu C *et al.* Clear lens extraction and intraocular lens implantation in Marfan's syndrome. *J Cataract Refract Surg* 2000;26(5):781-4.

13. Vadalà P, Capozzi P and Fortunato M*et al.* Intraocular lens implantation in Marfan's syndrome. *J Pediatr Ophthalmol Strabismus* 2000;37: 206–208.

14. Weyman AE and Scherrer-Crosbie M. Marfan syndrome and mitral valve prolapse. *J Clin Invest* 2004; 114: 1543–1546.

15. Wheatley H, Traboulsi E and Flowers B *et al.* Immunohistochemical localization of fibrillin in human ocular tissues. Relevance to the Marfan syndrome. *Arch Ophthalmol* 1995;113:103–109.

16. Zhao L, Liang T, Xu J, Lin H, Li D, and Qi Y. Two novel FBN1 mutations associated with ectopia lentis and marfanoid habitus in two Chinese families. *Mol Vis* 2009;15: 826–832.

Suggested citation format

Posterior Polar Cataract

Emily S. Birkholz, MD; Thomas A. Oetting, MD; Anna S. Kitzmann, MD

January 22, 2011

Chief Complaint: 38-year-old male with blurry distance vision

History of Present Illness: The patient noticed blurry distance vision and problems seeing at night for years, more noticeably in his left eye than in his right. When driving at night, he noticed a significant amount of glare from oncoming headlights. On a previous examination 15 years ago, he was informed he had cataracts.

Past Ocular History: The patient wore glasses and had no other ocular history, including no history of amblyopia.

Medical History: No chronic medical conditions, including no diabetes or history of steroid use.

Medications: None

Allergies: No known drug allergies

Family History: Father and brother had posterior polar cataracts.

Social History: The patient smoked but did not drink alcohol.

Review of Systems: A full review of systems was negative.

OCULAR EXAMINATION

Visual acuity in the distance without correction

♦ Right eye (OD): 20/60
♦ Left eye (OS): 20/40

Best Corrected Visual Acuity (BCVA)

♦ OD: 20/20-2
♦ OS: 20/30-2

Glare testing

♦ OD: 20/20-2
♦ OS: 20/40-2

Ocular motility: Full, both eyes (OU), no nystagmus

Intraocular pressure (IOP): 14 mmHg OD, 17 mmHg OS

Pupils: Reactive to light in each eye from 4mm in the dark to 2 mm in the light. No relative afferent pupillary defect (RAPD).

Confrontation visual fields: Full, OD and OS.
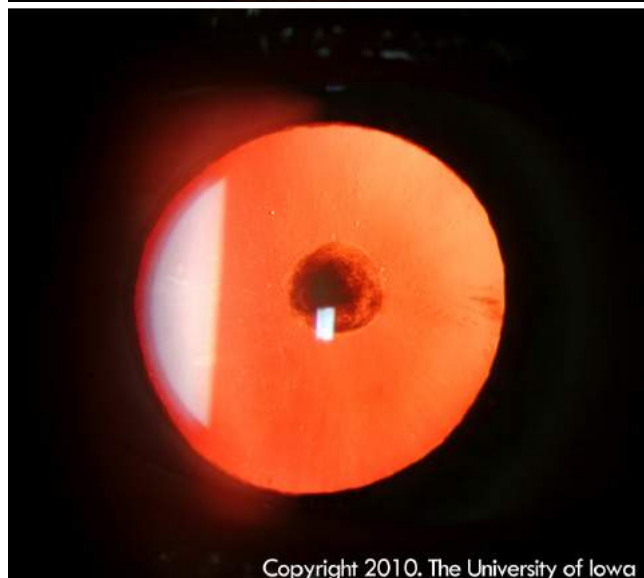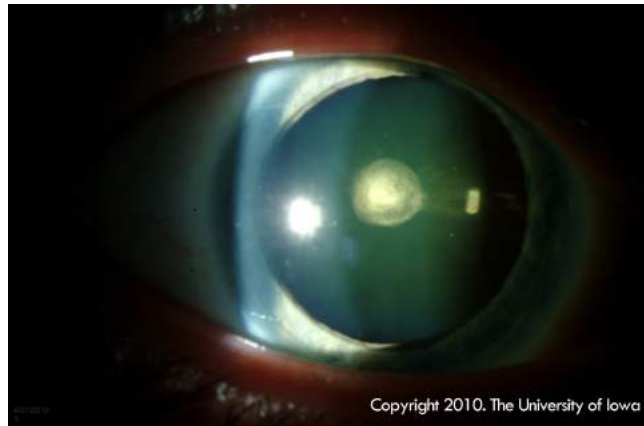
Figure 1. A: Posterior polar cataract of the right eye. B: Slit lamp photo of the posterior polar cataract in the right eye. C: Red reflex showing posterior polar cataract of the right eye

Slit lamp exam (OU)

♦ Normal lids and lashes, quiet conjunctiva, clear corneas. The anterior chambers were deep and quiet. The irides were normal and dilated well.

♦ There was a central 2.5 mm opacity in the posterior aspect of the lens OD (See Figure 1). The lens OS had a central 3.0 mm opacity in the posterior aspect of the lens with surrounding posterior subcapsular cataract and trace anterior subcapsular cataract (See Figure 2). Neither lens had any nuclear sclerosis.
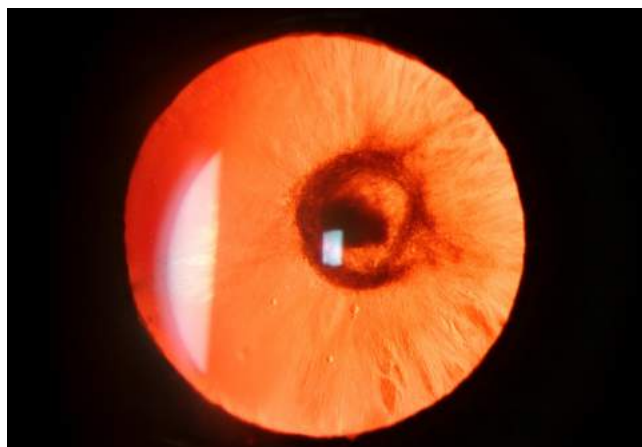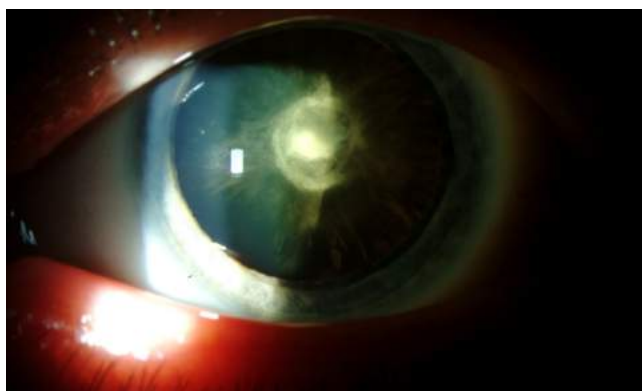
Figure 2. A: Posterior polar cataract of the left eye. B: Slit lamp photo of the posterior polar cataract of the left eye. Note the posterior subcapsular change and anterior subcapsular/cortical spokes. 2C: Red reflex of the left eye demonstrating the posterior polar cataract

Dilated fundus examination (DFE) OU

♦ Clear media, normal healthy optic nerves, normal macula, vessels and periphery

CLINICAL COURSE

The patient's symptoms and anterior segment findings were consistent with posterior polar cataracts. His vision could be improved with refraction to 20/20-2 OD and 20/30-2 OS. Options for management were discussed with the patient including trying a new pair of glasses to improve distance vision or pursuing cataract surgery, which would likely improve distance vision as well as improve symptoms of decreased night vision and glare. Because the cataract was significantly affecting his activities of daily living, the patient opted to pursue cataract surgery for the left eye. The patient was informed that cataract surgery for posterior polar cataracts is associated with increased risk of capsular rupture and vitreous loss that can lead to worse visual outcomes.

Because of the increased complexity of the case, the surgical plan involved obtaining anesthesia with a retrobulbar block, avoiding hydrodissection, sculpting out a bowl in the anterior cortical and nuclear material prior to performing gentle viscodissection, avoiding rotation of the nucleus, and using the anterior vitrector to remove nuclear and cortical material with very low aspiration and slow cut rate settings. In this video you will note that after the cortical material was removed, the surgeon opted not to polish the remaining posterior subcapsular fibers to avoid rupturing the posterior capsule (See Video 1). This remaining material was treated with a Nd:YAG (neodymium yttrium aluminum garnet) laser capsulotomy post-operatively.

Video 1. *Posterior-Polar-Cataract* vimeo.com/18022572

Video 2. *Another surgical video demonstrates a similar technique but uses irrigation and aspiration to remove the cortical material rather than anterior vitrectomy* www.facebook.com/cataract.surgery/videos/454807036140/

Neither case resulted in posterior capsular rupture.

DISCUSSION

Pathophysiology

Posterior polar cataract is a congenital condition that can be sporadic or familial. Sporadic posterior polar cataracts are typically unilateral and associated with remnants of the tunica vasculosa lentis, an embryologic hyaloid structure that fails to regress. Familial posterior polar cataracts are typically bilateral and follow an autosomal dominant pattern of inheritance (Basic and Clinical Science Course, Section 11). More recently, mutations resulting in a 17-base-pair duplication in the PITX 3 gene have been associated with posterior polar cataract. This gene codes for a transcription factor that participates in anterior segment and

lens development (Berry *et al.* 2004, Addison *et al.* 2004). The exact mechanism of how the mutation causes cataract is unknown, but the result is dysplastic, abnormal lens fibers that, as they migrate posteriorly from the equator, form an opacity in the region of the central posterior capsule. The opacity is usually a round discoid plaque, clearly demarcated from the rest of the lens and often associated with vacuoles in the lens surrounding the plaque (Eshaghian and Streeten 1980). Satellite opacities, which may represent fluid entering the lens, can also develop with time around the original plaque. The abnormal lens fibers can become adherent to the central posterior capsule, and the capsule around the plaque is often weakened. Thus, posterior capsular rupture is a feared complication when removing this type of cataract (Osher *et al.* 1990). These cataracts often present in the first few months of life, and if visually significant at an early age, can lead to amblyopia. Most posterior polar cataracts are stationary but can progress in severity over time.

Treatment

When posterior polar cataracts become visually significant (either in infancy if the cataracts are large enough to be amblyogenic, or in adulthood when they cause glare), they can be surgically removed. However, the high risk of posterior capsular rupture makes surgical removal often very difficult. There have been reported rates of posterior capsular rupture in 26-36% of cases depending on the series studied (Osher *et al.* 1990, Vasavada and Singh 1999). More recent studies demonstrate lower rates of posterior capsular rupture (Hayashi 2003). To avoid posterior capsular rupture the following techniques have been described in the literature.

- **Injection of Viscoelastic:** Avoid injecting excessive viscoelastic into the anterior chamber as the increased anterior pressure can cause posterior capsular rupture (Fine 2003).
- **Capsulorhexis**: Avoid a large anterior capsulotomy. In the setting of a posterior capsular rupture, a large opening may not provide enough support for a sulcus intraocular lens (Vasavada and Singh 1999).
- **Hydrodissection**: Avoid hydrodissection as the fluid wave can cause rupture of the weak posterior capsule (Vasavada and Singh 1999, Hayashi 2003). Viscodissection can be safely utilized if the nucleus has been debulked as was demonstrated in the above video.
- **Hydrodelineation**: "Inside-out delineation" is a technique described by Vasavada and Raj. A central bowl or trench is made in the anterior epinuclear material using low phacoemulsification settings [slow motion phacoemulsification utilizes low aspiration flow rate, vacuum, and infusion pressure (Osher 1993)]. The low vacuum level and aspiration flow rate provide a more stable anterior chamber and reduce the risk of surge, which can cause chamber collapse, anterior posterior movement of the iris lens diaphragm, and strain on the zonules and capsule. Low bottle height prevents the posterior capsule from ballooning (Vasavada and Singh 1999). After this initial sculpting, the nuclear material

is hydrodelineated from the epinuclear material by carefully placing the tip of the syringe in the central lens material and slowly injecting fluid in this plane until a golden ring is seen. This "inside-out" hydrodelineation technique can avoid the inadvertent injection of fluid in the subcapsular plane, which can lead to posterior capsular rupture (Vasavada and Raj 2004). Lim and Goh describe another technique called "modified epinucleus pre-chop" for posterior polar cataracts with a dense nucleus. This technique involves pre-chopping the anterior epinucleus using "in situ" chop where the chopper is placed in the mid-periphery of the anterior epinuclear material and repositioned in different meridians with each chop. Once this anterior epinuclear material is removed, hydrodelineation and mobilization of the remaining dense nuclear core can be performed more easily (Lim and Goh 2008).

- **Lens Rotation:** This step should be avoided (Vasavada and Singh 1999).
- **Nucleofractis:** Aspirate the nuclear material if the nucleus is soft, or use slow motion phacoemulsification (example: bottle height 50 cm, vacuum 100 mm Hg, and aspiration flow rate at 20 ml per minute) to gently remove nuclear fragments within the epinuclear shell, which was created by hydrodelineation. Vasavada describes a stop, chop, chop and stuff technique where the vertical chopper is placed more centrally than in traditional chop and small continuous chopping produces small fragments which are then "stuffed" into the phaco tip by the chopper (Vasavada and Desai 1996). The V groove (also known as the "victory") technique described by Kelman in 1994 and "lambda" technique described by Lee and Lee in 2003 involve sculpting the nucleus in the shape of a V or the Greek letter lambda (λ). This is followed by cracking along both "arms" and then removing the central piece first. See Video 3. This offers an advantage of not stretching the capsule while removing the pieces (Kelman 1994, Lee and Lee 2003).

Video 3. www.facebook.com/cataract.surgery/videos/472413536140/

- **Epinucleus removal:** Vasavada and Singh utilize the phacoemulsification probe and low settings to gently strip the epinucleus 360 degrees. The central epinuclear material and plaque are aspirated last (Vasavada and Singh 1999). Fine describes using viscodissection for mobilizing the epinuclear and cortical material (Fine *et al.* 2003). The vitrectomy cutter can also be used to remove the remaining epinucleus. This may provide better control of the anterior chamber, avoids surge, and allows the surgeon to be prepared if the anterior hyaloid face is violated in the setting of posterior capsular rupture.
- **Polish**: Avoid polishing techniques as the posterior polar plaque is very adherent to the capsule, and polishing may lead to rupture of the capsule (Vasavada and Sing, 1999).
- **Lens insertion**: Vasavada and Raj recommend using an AcrySof IOL in the bag if possible, even if there is a small

posterior capsular rupture. In the setting of posterior capsular rupture, the anterior vitreous face can be tamponaded with a dispersive viscoelastic, and then the lens can be gently inserted into the bag. The AcrySof lens unfolds gently, which will reduce the chance of extending a capsular tear. Their technique for manipulating the lens into the bag involves using a Lester manipulator to place the trailing haptic, rather than dialing the lens into place. Irrigation and aspiration to remove the viscoelastic should not be performed posterior to the IOL (Vasavada and Raj 2008).

In summary, there are various surgical techniques that can be utilized to minimize the risk of posterior capsular tear in posterior polar cataract extraction. Avoid hydrodissection, perform hydrodelineation, use slow motion phacoemulsification settings, consider viscodissection of the epinuclear material, and do not polish the remaining posterior polar remnant. Laser posterior capsulotomy can safely be performed post-operatively.

DIAGNOSIS

Posterior Polar Cataracts

Differential Diagnosis

- ♦ Posterior subcapsular cataract
- ♦ Traumatic cataract
- ♦ Mittendorf dot

EPIDEMIOLOGY	SIGNS
♦ Congenital ♦ Sporadic or autosomal dominant inheritance ♦ Unilateral or bilateral ♦ 17 bp duplication in PITX3 gene	♦ Abnormal red reflex ♦ Amblyopia ♦ Central posterior discoid plaque on the lens
SYMPTOMS	TREATMENT
♦ Asymptomatic ♦ Decreased vision ♦ Glare	♦ Surgical removal with care due to high risk of posterior capsular rupture ♦ Avoid hydrodissection ♦ Perform hydrodelineation ♦ Slow motion phacoemulsification (low irrigation, aspiration, bottle height, and phacoemulsification settings) ♦ Viscodissect cortical material ♦ Consider anterior vitrectomy to remove cortical material ♦ Discuss with patient the increased risk of capsular rupture

References

Addison PK, Berry V, Ionides AC, et al. Posterior polar cataract is the predominant consequence of a recurrent mutation in the PITX3 gene. Br J Ophthalmol 2005;89(2):138-141

Berry V, Yang Z, Addison PK, *et al.* Recurrent 17 bp duplication in PITX3 is primarily associated with posterior polar cataract. *J Med Genet* 41(8):e109

Chapter 4. Embryology: Rosenfeld,SI *et al. Section 11. Lens and Cataract. 2007-2008 Basic and Clinical Science Course*. San Francisco: American Academy of Ophthalmology; 2007; p. 34-35.

Eshaghian J, Streeten BW. Human posterior subcapsular cataract; an ultrastructural study of the posteriorly migrating cells. *Arch Ophthalmol* 1980 98:134-143

Fine IH, Packer M, Hoffman RS. Management of posterior polar cataract. *J Cataract Refract Surg* 2003;29:16-19

Hayashi K, Hayashi H, Nakao F, Hayashi F. Outcomes of surgery for posterior polar cataract. *J Cataract Refract Surg* 2003; 29:45-49

Kelman CD. V Groove phaco technique: Fast, easy, safe: Interview with Dr. Kelman. *Ophthalmology Times* 1994;19(18):12

Lee MW, Lee YC. Phacoemulsification of posterior polar cataracts—a surgical challenge. *Br J Ophthalmol* 2003;87(11):1426-1427

Lim Z, Goh J. Modified epinucleus pre-chop for the dense posterior polar cataract. *Ophthalmic Surg Lasers Imaging* 2008;39(2):171-173

Osher RH, Yu BC, Koch DD. Posterior polar cataracts: a predisposition to intraoperative posterior capsular rupture. *J Cataract Refract Surg* 1990;16:157-162

Osher RH. Slow motion phacoemulsification approach (letter). *J Cataract Refract Surg* 1993;19:667

Vasavada A, Singh R. Phacoemulsification in eyes with posterior polar cataract. *J Cataract Refract Surg* 1999;25:238-245

Vasavada AR, Desai JP. Stop, chop, chop and stuff. *J Cataract Refract Surg* 1996;22:526-529

Vasavada AR, Raj SM. Inside-Out delineation*. J Cataract Refract Surg* 2004;30:1167-1169

Vasavada AR, Raj, SM. Posterior polar cataract and pre-existing posterior capsular defect. *Cataract & Refractive Surgery Today Europe* 2008 March:73-77

Citing this article

True Exfoliation Syndrome

Aaron M. Ricca, MD, A. Tim Johnson, MD

posted November 28, 2017

INITIAL PRESENTATION

Chief Complaint

Blurry vision

History of Present Illness

An 84-year-old male presented with gradually worsening blurry vision in both eyes (OU), left worse than right, over a period of several years. He described the vision as hazy and poor in dim lighting. He also reported difficulty with reading, driving, or watching TV. He noted worsening glare and halos with lights, making nighttime driving unsafe.

Past Ocular History

- Ocular hypertension both eyes (OU)
- Removal of numerous metallic corneal foreign bodies OU
- Intermediate non-exudative macular degeneration OU

Past Medical History

- Coronary artery disease status-post left combined coronary artery endarterectomy and bypass
- Myocardial infarction status-post stenting
- Hypertension
- Hyperlipidemia

Medications

- Latanoprost every evening OU
- AREDS2 vitamins
- Atenolol
- Simvastatin
- Spironolactone

Allergies

- No known drug allergies

Family History

- Non-contributory

Social History

- Currently retired, but worked as a metal welder for most of his life

Review of Systems

- Negative except for what is detailed in the history of present illness

OCULAR EXAMINATION

Distance Visual Acuity (with correction)

- Right eye (OD): 20/25-2
- Left eye (OS): 20/30-2

Glare Visual Acuity

- OD: 20/40
- OS: 20/300

Ocular Motility/Alignment

- Full, orthophoric OU

Intraocular Pressure (IOP) by Tonopen®

- OD: 12 mmHg
- OS: 15 mmHg

Confrontation Visual Fields

- OD: small inferonasal field defect by finger counting
- OS: full to finger counting

Slit Lamp Exam

- Lids/lashes: Normal OU
- Conjunctiva/sclera: Clear and quiet OU
- Cornea: Clear OU
- Anterior chamber: Deep and quiet OU
- Iris: Round and flat OU
- Lens
  - OD: 2+ Nuclear sclerosis, 1 + central posterior sub-capsular cataract, elevated scrolled flap of the lens capsule from 4:30 clockwise to 11 (Figures 1 - 3)
  - OS: 3+ Nuclear sclerosis, 1 + central posterior sub-capsular cataract, elevated scrolled flap of the lens capsule from 8:30 clockwise to 4 (Figure 4)

Dilated Fundus Examination

- Vitreous:Quiet OU
- Disc: Normal OU
- Cup-to-disc ratio: 0.2 OU
- Macula
  - OD: Large soft drusen, no heme
  - OS: Subfoveal low-lying fibrovascular PED, large soft drusen, RPE mottling, no heme or subretinal fluid
- Vessels: Normal OU
- Periphery: Normal OU
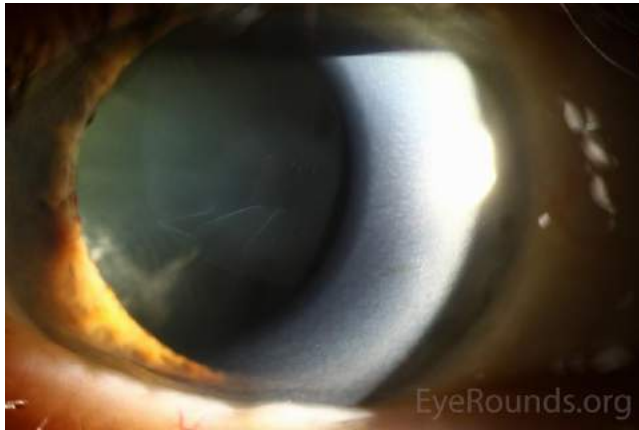
Figure 1: Slit lamp photograph OD demonstrating delamination of the anterior lens capsule with wrinkling of the free-floating flap in the anterior chamber.

Figure 2: Slit lamp photograph OD with slit beam passing through and outlining the free-floating flap of lens capsule schisis.
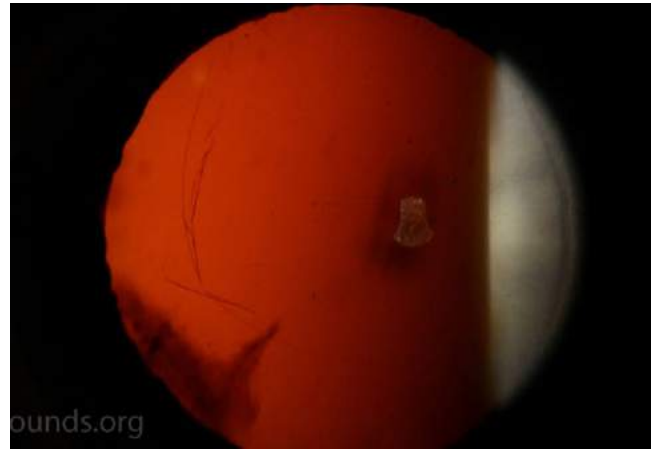
Figure 3: Slit lamp photograph OD with retro-illumination clearly outlining the circular region of schisis with wrinkling of the delaminated free-floating flap.
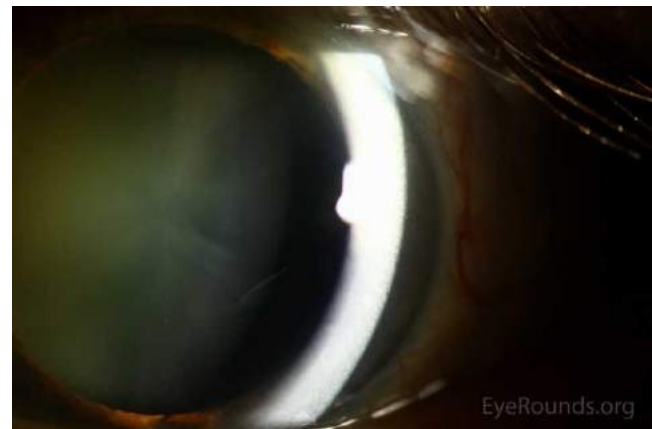
Figure 4: Slit lamp photograph OS demonstrating bilateral disease with the floating rolled edge of the delaminated flap of anterior lens capsule.

Differential Diagnosis

♦ Spontaneous rupture of anterior lens capsule
♦ True exfoliation syndrome
♦ Pseudoexfoliation syndrome eyerounds.org/atlas/pages/pseudoexfoliation-syndrome/

CLINICAL COURSE

The patient underwent cataract extraction by phacoemulsification first OS then OD.

Given the delamination present in the anterior lens capsules that was noted on exam, great care was taken during this procedure, most specifically in performing the continuous curvilinear capsulorrhexis. Trypan blue dye was used to stain the anterior capsule, providing improved visualization. No complications occurred. The patient tolerated the procedures well, and his post-operative visual outcome was excellent.

A video of the surgery is presented at vimeo.com/244672221. *The continuous curvilinear capsulorrhexis is performed in each eye in this patient.*

The pieces of the lens capsule that were removed from each eye during the capsulorrhexis were submitted for histological analysis, and images of these samples are presented below. (Figures 5 and 6)

DIAGNOSIS

True exfoliation syndrome

DISCUSSION

Etiology/Epidemiology

True exfoliation syndrome is a rare disease that was first reported in 1922 by Elschnig; it was initially described in a series of two patients, both of whom were glassblowers [1]. The classic scenario is an asymptomatic glassblower by trade, diagnosed on routine exam. It has been reported in people with other occupational exposures such as steelworkers, blacksmiths, and bakers [2]. The common denominator linking all these professions is excessive exposure to
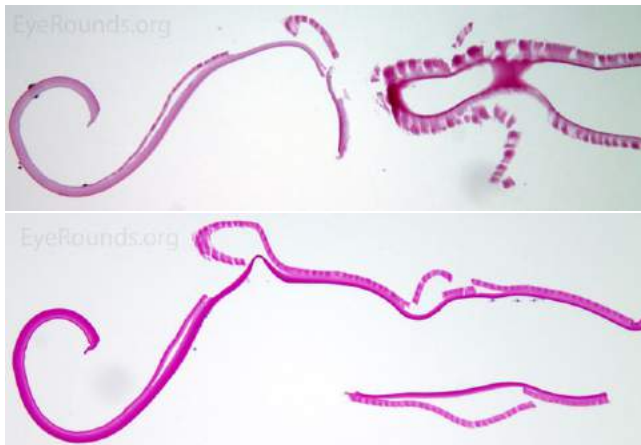
Figure 5: Two images of the anterior lens capsule OS (H&E stain on the top and PAS stain on the bottom image). Both stains clearly demonstrate delamination of the anterior lens capsule with the flap attachment point and breakdown of the anterior delaminated portion.

Figure 6: PAS staining of the anterior lens capsule from the left eye showing early delamination of the anterior capsule with schisis cavities forming and beginning to coalesce.

high heat and infrared radiation. However, there have also been reports of exfoliation associated with inflammation, such as uveitis, and trauma [3], as well as cases of idiopathic exfoliation syndrome seen in elderly patients with no identifiable risk exposures [4 ,5].

Given the rarity of the disease, it is difficult to estimate the incidence or prevalence of this condition. One of the largest case series to date by Teekhasaenee *et al.* demonstrated that 248 out of 259 total cases were idiopathic with no identifiable exposure. In this series, 118 patients were men and 141 patients were women with a combined average age of 75. The overwhelming majority of patients had bilateral disease, and the only statistically significant risk factors identified were age, heat exposure, and trauma [5]. Another smaller case series of 12 patients only identified one with a prior history of infrared exposure or trauma [6]. The mean age at diagnosis in this series was 77.9 and most were bilaterally affected as well, further supporting the idea that this disease is likely age-related in the mod-

ern day population. Some suggest a correlation with the development of glaucoma [4], but most recent data has not borne this out to be true. Some literature reports laser energy as a risk factor, such as that received during a laser peripheral iridotomy, but other reports suggest this is not true [5].

Pathophysiology

The classic theory is that repeated exposure to high levels of infrared radiation causes epithelial damage to the lens capsule with vesicular degeneration. The degeneration leads to capsular dehiscence and schisis, then delamination of the anterior portion of the capsule [3]. It is well known that lens epithelial cells near the equator have the most mitotic activity. These actively dividing cells are also most susceptible to damage from radiation, which may impair the function of future cell generations [2]. It has been shown that areas of zonular disruption are often the location of initial delamination with concomitant progression and zonular damage [5]. Another theory is that the thermal injury directly activates enzymes that are responsible for proteolysis of the collagen in the capsule [7].

Signs/Symptoms

There are often no symptoms reported by the patient when exfoliation occurs, and the diagnosis is commonly made as an incidental finding during physical exam [6]. This is a relatively benign process with the delamination occurring only anteriorly. The integrity of the lens capsule remains intact with no intra-ocular exposure to lens material. True exfoliation can present as a very small linear rent, a very large free-floating flap, or anywhere in between, based on the extent of delamination present [5]. One of the classic signs is known as the double-ring sign (DRS). The DRS is seen when partial splitting of the anterior capsule occurs, giving the appearance of two rings on the capsule [8]. The DRS is diagnostic for true exfoliation syndrome. Another name for this sign is capsulorrhexis masquerade, as it can mimic a partial capsulorrhexis with a free-floating flap of delaminated capsule when DRS has progressed far enough [5]. It is also possible to develop a double delamination where the delaminated flap can split again resulting in parallel flaps [5]. Pigment deposition on the delaminated membrane is a common finding, seen in 68.7% of patients in the case series by Teekhasaenee and colleagues [5].

Testing/Laboratory work-up

The diagnosis is clinical. There are currently no blood tests available to aid in identifying this disease. There is also no known underlying genetic association at this time. Tissue evaluation of the anterior lens capsule after surgical removal during cataract extraction is a common method for definitive diagnosis. When evaluated *via* histology, the section through a lens capsule with true exfoliation syndrome shows a thinned residual capsule, due to loss of tissue from delamination, with an abnormal underlying epithelial layer [2]. Epithelial cells become smaller and spaced out, but the overall thickness of the capsule, when

including the delaminated portion, is increased [2 ,9]. It is possible to see vesicles within the capsule, and the area of splitting often coincides with the highest areas of vesicle concentration [2]. If the capsule sample is well preserved and a portion of the delaminated tissue still attached, the specific area of dehiscence can be seen [2].

Imaging

Numerous recent diagnostic instruments have been used in identifying and investigating exfoliation syndrome with several recent publications documenting the potential benefits. For example, the Pentacam® will provide a cross-sectional image of the anterior chamber and can be used to visualize a floating membrane attached to the anterior capsule [10]. Anterior segment optical coherence tomography (OCT) has also been used to identify true exfoliation, and numerous sources have reported clear display of the split in the capsule with membrane floating in the anterior chamber [2,11]. Newer spectral domain OCT can provide such fine resolution, it may be able to detect subclinical delamination of the anterior capsule prior to developing free-floating flaps [11].

Treatment/Management/Guidelines

True exfoliation of the capsule typically presents no acute issues. As such, it is appropriate to monitor these patients on a routine basis.

Some have proposed grading systems based on the extent of delamination and location of the flap, with the most detailed criteria put forth by Teekhasaenee and colleagues [5]. Clinically, however, there is limited benefit of a breakdown into stages given the lack of impact on management and prognosis. The benefit of staging is that it recognizes the disease is not a static process, and it can be useful in quantifying the extent of exfoliation when presenting early on, as well as documenting the progression.

The major significance of exfoliation is in surgical management and complications during cataract surgery. True exfoliation can make capsulorrhexis difficult and can predispose to radial tears [2,5,10,12]. A radial tear can occur in either the deep or superficial portion of the split capsule [12]. Trypan blue can be used to aid in visualization of the capsule. If possible, the final size of the capsulorrhexis should be larger than the delaminated portion in order to remove all split and weakened tissue [11].

True exfoliation has also been reported to have a relatively high prevalence of phacodonesis and lens dislocation, seen in approximately 10% of patients [5]. This can depend somewhat on the initial location of the split, with more peripheral tears predisposing to zonular weakness.

It is also possible to have true exfoliation concurrent with pseudoexfoliation [13].

EPIDEMIOLOGY OR ETIOLOGY	*SIGNS*
♦ Very rare condition ♦ Average age of presentation: mid-70's [5 ,6] ♦ Proven risk factors: age, heat exposure, trauma [5] ♦ History of glassblowing, steel working, blacksmithing, or any other activities predisposing to recurrent high infrared radiation exposure [2]	♦ Small, partial thickness, linear rent in the anterior capsule [5] ♦ Double ring sign (DRS), AKA capsulorrhexis masquerade [8] ♦ Partial, free-floating flap scrolled in the anterior chamber ♦ Use of anterior segment imaging can aid in diagnosis, i.e. OCT or Pentacam [10 ,11]
SYMPTOMS	*TREATMENT/MANAGEMENT*
♦ Asymptomatic unless the patient develops concurrent lens dislocation	♦ Observation unless the patient develops concurrent lens dislocation, which can occur in up to 10% of patients [5] ♦ Great care when performing intraocular surgery ♦ Use Trypan blue when performing the capsulorrhexis and make final size of rhexis larger than delaminated portion [11]

References

1. Elschnig A. A Detachment of the zonular lamellae in glassblowers. *Klin Monatsbl Augenheilkd* 1922;69:732-734.

2. Cooke CA, Lum DJ, Wheeldon CE, Teoh H, McGhee CN. Surgical approach, histopathology, and pathogenesis in cataract associated with true lens exfoliation. *J Cataract Refract Surg* 2007;33(4):735-738. PubMed.gov/17397753

3. Wong AL, Chan TC, Fong AH, Lam BN, Yuen HK. Clinical characteristics and surgical outcomes of phacoemulsification in true exfoliation syndrome. *J Cataract Refract Surg* 2014;40(1):82-86. PubMed.gov/24238944

4. Cashwell LF, Jr., Holleman IL, Weaver RG, van Rens GH. Idiopathic true exfoliation of the lens capsule. *Ophthalmology* 1989;96(3):348-351. PubMed.gov/2710527

5. Teekhasaenee C, Suwan Y, Supakontanasan W, Tulvatana W, Ritch R. The Clinical Spectrum and a New Theory of Pathogenesis of True Exfoliation Syndrome. *Ophthalmology* 2016;123(11):2328-2337. PubMed.gov/27596291

6. Chen HS, Hsiao CH, Chuang LH, Su WW. Clinicohistopathology of cataract associated with true exfoliation of the lens capsule. *J Cataract Refract Surg* 2011;37(5):969-970. PubMed.gov/21511162

7. Callahan A, Klien BA. Thermal detachment of the anterior lamella of the anterior lens capsule; a clinical and histopathologic study. *AMA Arch Ophthalmol* 1958;59(1):73-80. PubMed.gov/1348699

8. Braude LS, Edward DP. Partial splitting of the anterior lens capsule giving a 'double-ring' sign. *Arch Ophthalmol* 1995;113(6):705-708. PubMed.gov/7786204

9. Kulkarni AR, Al-Ibrahim J, Haider S, Elsherbiny S, Scott R. Phacoemulsification in true exfoliation of the lens capsule: a case series. *Eye (Lond)* 2007;21(6):835-837. PubMed.gov/16751758

10. Chamney SM, Hughes ME, Sinton JE. The use of Pentacam in the assessment of true exfoliation of the lens capsule. *Eur J Ophthalmol* 2015;25(4):e50-52. PubMed.gov/25684157

11. Tan DK, Aung T, Perera SA. Novel method of assessing delamination of the anterior lens capsule using spectral-domain optical coherence tomography. *Clin Ophthalmol* 2012;6:945-948. PubMed.gov/22791977

12. Kim KH, Chung ES, Chung TY. Radial extension of capsulorhexis in true exfoliation patient: a potentially hazardous complication. *J Cataract Refract Surg* 2009;35(3):590-592. PubMed.gov/19251155

13. Kuchle M, Iliff WJ, Green WR. Kombinierte "Feuerlamelle" und Pseudoexfoliation der vorderen Linsenkapsel. [Combined true exfoliation and pseudoexfoliation of the anterior lens capsule]. *Klin Monbl Augenheilkd* 1996;208(2):127-129. PubMed.gov/8648988

Citing this article

Ricca AM, Johnson AT. True exfoliation syndrome. EyeRounds.org. posted November 29, 2017; Available from EyeRounds.org/cases/262-True-Exfoliation-Syndrome.htm

last updated: 11/29/2017

Glaucoma

Aphakic Glaucoma

Nayasha Madhan, BS; Heather A. Stiff, MD; Ze Zhang, MD; Wallace L.M. Alward, MD

posted December 14, 2017

INITIAL PRESENTATION

Chief Complaint

Referral for evaluation of elevated intraocular pressure (IOP) and suspected aphakic glaucoma

History of Present Illness

A 5-year-old female was referred to the University of Iowa Hospitals and Clinics (UIHC) Glaucoma Clinic for evaluation of suspected aphakic glaucoma of the left eye (OS). The patient was born with a congenital cataract OS, which was removed at 7 months of age by an outside provider. She was diagnosed with amblyopia OS and underwent patching of the right eye (OD) for 3 hours per day for a short period of time. At 5 years of age, she was found to have an IOP of 32 mmHg OS and was started on timolol 0.25% twice daily OS. She was then referred for further evaluation.

Past Ocular History

♦ Congenital cataract OS status post extracapsular cataract extraction at 7 months of age
♦ Amblyopia OS
♦ Sensory exotropia OS

Past Medical History

No significant past medical history

Medications

Timolol 0.25%, 1 drop, twice a day, OS

Allergies

No known drug allergies

Family History

No family history of congenital cataracts, glaucoma, or other eye diseases

Social History

Non-contributory

Review of Systems

Negative except for what is listed in the history of present illness

OCULAR EXAMINATION

Visual Acuity with Correction (Snellen)

♦ OD: 20/30
♦ OS: 20/100

Extraocular Motility

♦ OD: Full
♦ OS: 45 prism diopters (PD) left exotropia (Figure 2)

Intraocular Pressure (IOP) by Tonopen®

♦ OD: 14 mmHg
♦ OS: 23 mmHg

Slit Lamp Examination

♦ External: Normal OD, significant buphthalmos OS
♦ Lids: Normal OD, upper and lower eyelid retraction OS
♦ Conjunctiva/sclera: Normal in both eyes (OU)
♦ Cornea: Clear OD, clear with contact lens in place OS
♦ Anterior chamber: Deep and quiet OU
♦ Iris: Normal OD, superotemporal peripheral iridectomy OS
♦ Lens: Normal OD, aphakic OS

Dilated Fundus Examination

♦ Disc: Normal OD, thinning of neuroretinal rim OS
♦ Cup-to-disc ratio: 0.35 OD, 0.7 OS
♦ Macula: Normal OU
♦ Vessels: Normal OU
♦ Periphery: Normal OU

Gonioscopy

Difficult view; appeared to be open for 360 degrees OU

Visual Field

♦ OD: full field
♦ OS: generalized constriction with only a small paracentral island of l2e remaining.
♦ See Figure 1, next page

CLINICAL COURSE

The patient was diagnosed with aphakic glaucoma OS. Because IOP was 23 mmHg, she was switched from timolol 0.25% to timolol-dorzolamide twice daily OS. At 2 months follow-up, IOP was 27 mmHg. Therefore, latano-
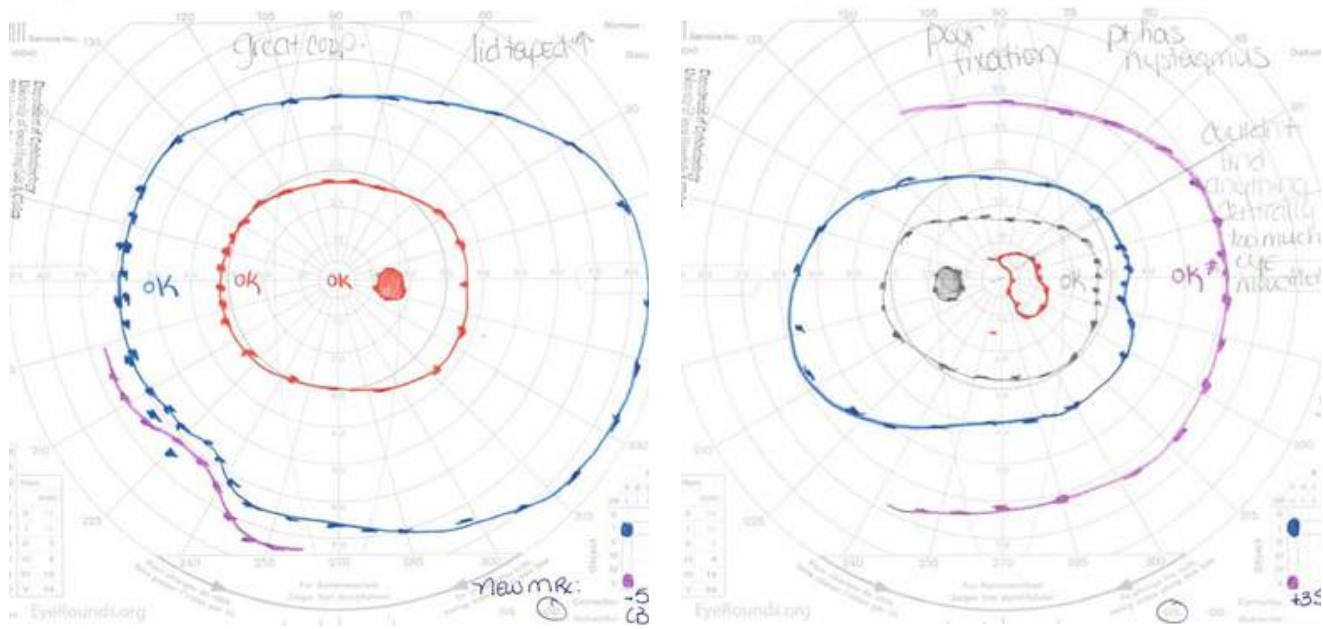
Figure 1. Goldmann visual field (A) OD showing a full field and (B) OS showing generalized constriction with only a small paracentral island of I2e remaining.

prost 0.005% at night was added. She continued to have persistently elevated IOP over the next 2 years, resulting in progressive optic nerve cupping and deterioration of her visual field with a superior arcuate scotoma encroaching on fixation. At this point, it was decided that she would need a surgical procedure. A trabeculectomy was considered, but because she wore contact lenses, the decision was made to precede with a pars plana vitrectomy with insertion of a Baerveldt drainage device. The surgery was performed without complication. IOP decreased to 14 mmHg on timolol-dorzolamide and latanoprost.

Two years after her surgery, she presented with 3 days of pain OS with an IOP of 50 mmHg. She was scheduled for emergent surgical evaluation of her Baerveldt implant. Intra-operative assessment showed drastic anterior migration of the tube, past the posterior capsule and into the iris tissue. During surgery, the tube was freed from the iris, and IOP decreased. The tube was then pulled through the existing peripheral iridectomy and placed on the anterior surface of the iris (Figure 2). The patient did well postoperatively, and her IOP remained in the mid-teens on timolol-dorzolamide and latanoprost.

The patient was followed closely and was later noted to have high myopia and buphthalmos OS (Figure 3). She was referred to the oculoplastic service for proptosis, eyelid retraction, and a large left exotropia (Figure 3). At age 22, she underwent an elective procedure for cosmesis of her proptosis, which involved a medial and lateral orbital wall decompression. At age 23, she underwent large left medial rectus resection for exotropia, taking care to avoid area of the Baerveldt implant superotemporally. Both surgeries were performed without complications (Figure 4).
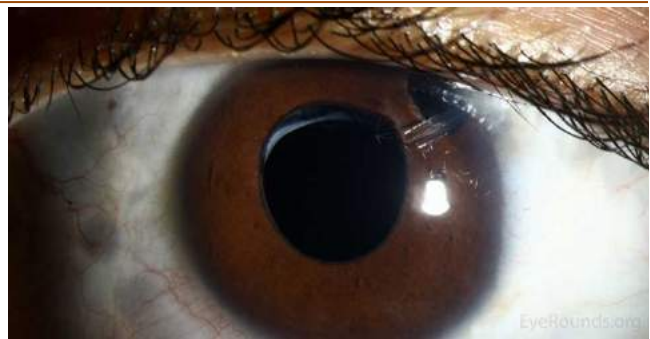
Figure 2. Slit lamp photograph demonstrating Baerveldt tube emerging anteriorly, through the iridectomy.

Figure 3. External photograph demonstrating significant buphthalmos, eyelid retraction, and exotropia OS.

Figure 4. External photograph demonstrating improved eyelid retraction, alignment, and proptosis after orbital decompression and strabismus surgery.
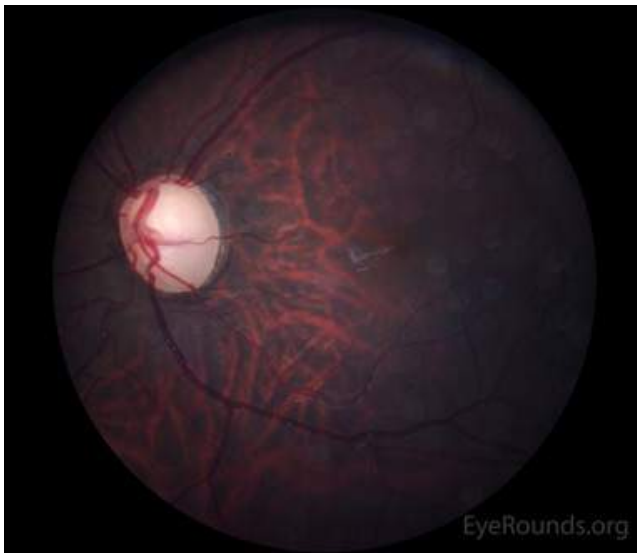
Figure 5. Color fundus photos of left eye (A) Cup-to-disc ratio of 0.9 at age 15 and (B) Cup-to-disc ratio of 0.9 at age 20.
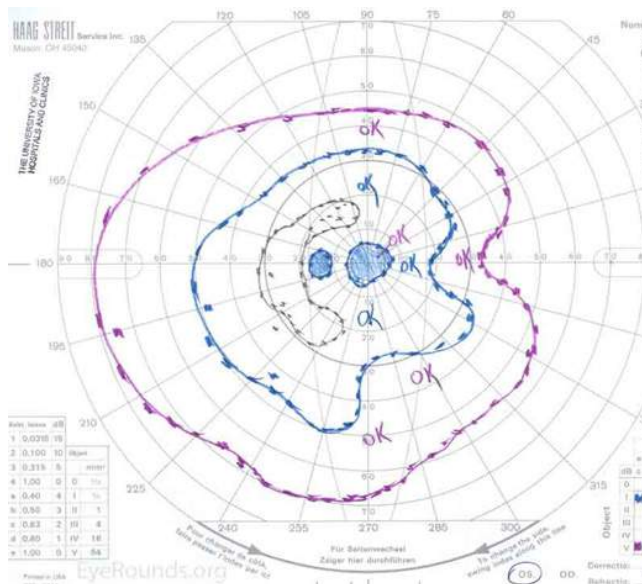
Figure 6. Goldmann visual field OS showing general constriction with superior and inferior arcuate scotomas, along with a central scotoma.

At her most recent appointment, 17 years after her initial presentation, her IOP was 17 mmHg OS on timolol only. Unfortunately, her vision had decreased from 20/100 to 20/1250 OS over her 17-year course. Remarkably, her optic nerves (Figure 5A and B) and OCT of the optic nerves were unchanged over the last 7 years. Her visual field did show some slow progression over time OS (Figure 6).

DIAGNOSIS

Aphakic glaucoma

DISCUSSION

Etiology/Epidemiology

Aphakic glaucoma is classified as a secondary form of open angle glaucoma and ranks second as the most common cause of glaucoma in the pediatric population [1]. The following factors have been implicated in its development: surgery within the first year of life, corneal diameter less than 10 mm, retained lens proteins, the presence of other ocular abnormalities, certain cataract types (e.g. complete, nuclear, or persistent hyperplastic vitreous), and a history of secondary surgeries [2]. The most consistent risk factor across the literature has been cataract surgery at a young age [3]. In one study of 137 patients with prior congenital cataract surgery, 12% of patients developed aphakic glaucoma within a mean of 9.6 years following surgery. A meta-analysis using individual patient data on 470 children who underwent cataract surgery in infancy revealed 17% developed glaucoma within a median 4.3 years. The risk was highest in patients who underwent surgery at less than 4 weeks of age or infants with microphthalmos [1]. In an article by Kirwan in 2006, the incidence of aphakic glaucoma following congenital cataract surgery ranged from 15% to 45% [4].

A genetic etiology has also been considered as an explanation for the condition. There are a number of genes that contribute to both the development of cataracts and glaucoma, such as the PAX6 gene [5].

Pathophysiology

As stated above, early cataract surgery has been described as the most commonly identified risk factor for aphakic glaucoma. Early lensectomy is thought to interfere with maturation of the trabecular meshwork. In particular, normal meshwork development requires structural interactions between the native lens, zonules, ciliary body, and trabecular meshwork [6]. Other studies have postulated that aphakic glaucoma may develop from chronic trabecu-

litis secondary to postoperative inflammation or blockade of the trabecular meshwork with retained lens material [7]. Additionally, lens proteins that remain after extraction may degenerate into byproducts that are toxic to the trabecular meshwork [6]. In a retrospective review in 2004, 15% of patients were found to have retained lens material postoperatively; the same study cited literature that reported 41.6% to 78% of patients had residual cortex or lens material [6]. Aphakic glaucoma is typically an open-angle glaucoma, adding weight to the proposition that an interaction occurs between trabecular meshwork cells and lens epithelial cells and/or the vitreous leading to the development of elevated intraocular pressure [8].

There has been some discussion that corticosteroids could contribute to aphakic glaucoma. However, this mechanism has received less support as post-operative steroids are typically used for 1 to 2 months following surgery whereas aphakic glaucoma often develops years later [6].

Signs/Symptoms

Typically, patients develop aphakic glaucoma between 4 to 6 years after cataract surgery and present with elevated IOP, corneal clouding, and excessive loss of hyperopia [8]. Patients often have thick corneas and small anterior segments [9]. Children may present with vague symptoms ranging from irritability to photophobia [8]. However, most commonly, aphakic glaucoma is asymptomatic. Therefore, careful monitoring and surveillance of patients at risk is crucial [4], as IOP elevation may go unrecognized and untreated until fundoscopic exam reveals optic nerve cupping [1].

Workup

IOP measurement in children is commonly performed under general anesthesia. However, general anesthetics can lower IOP, resulting in unreliable readings, and IOP alone is insufficient to make the diagnosis of aphakic glaucoma. A full examination should be performed including cycloplegic refraction, measurement of corneal thickness, gonioscopy, slit lamp exam of the anterior segment, optic nerve head evaluation, visual fields and ocular coherence tomography of the optic nerve if the patient is able. Although aphakic glaucoma is typically an open angle glaucoma, acquired angle defects may be visible on gonioscopy. A retrospective study conducted in 1995 looked at pediatric glaucoma patients who had a history of lensectomy and developed glaucoma two or more years after surgery. Gonioscopy prior to the operation revealed no consistent angle defects, but post-operatively, 96% of patients with glaucoma had an angle defect characterized by blockage of the trabecular meshwork, often caused by pigment or crystalline deposits [6, 10]. Screening for aphakic glaucoma after congenital cataract surgery should occur every 3 months for the first year postoperatively and twice yearly for the next 10 years, after which, annual exams can be resumed [2].

Treatment Guidelines

Treatment of aphakic glaucoma is similar to the treatment of any other secondary open-angle glaucoma. Both medical and surgical treatments play a role, with topical medications serving as the first approach [8].

If patients continue to have consistently elevated IOPs on maximum medical management, surgical management, such as placement of a glaucoma drainage device, becomes necessary. Placement of a drainage device can be difficult in these patients given their thick corneas and small anterior segments. Therefore, a pars plana vitrectomy may be required to facilitate placement of the tube behind the iris [9]. This type of surgery is not without risks, and complications can occur including malpositioning or migration of the tube, endophthalmitis, and corneal decompensation [8]. Trabeculectomy is another option, but these patients often require use of aphakic contact lenses, which may be difficult in the context of a bleb [9]. Many children go on to require subsequent interventions [8].

Summary Table

EPIDEMIOLOGY OR ETIOLOGY	SIGNS
♦ Second most common cause of glaucoma in the pediatric population [1] ♦ Incidence is 15-45% [4] ♦ Cataract surgery at a young age is most consistent risk factor [3] • Early lensectomy may interfere with maturation of the trabecular meshwork [6] ♦ Postoperative inflammation and retained lens material may contribute to the development of disease [6,7]	♦ Elevated IOP, corneal clouding [8] ♦ Excessive loss of hyperopia ♦ Thick cornea and small anterior segment [9] ♦ Open angle but can see obstruction of the trabecular meshwork by pigment or crystalline deposits [6,10] ♦ Optic nerve cupping ♦ Constriction of the visual field ♦ Thinning of the retinal nerve fiber layer on ocular coherence tomography of the optic nerve
SYMPTOMS	TREATMENT/MANAGEMENT
♦ Often asymptomatic ♦ Can present with photophobia or irritability [8]	♦ Topical IOP-lowering medications ♦ Trabeculectomy, although may be difficult in contact lens wearers [9] ♦ Glaucoma drainage devices [9]

References

1. Olitsky SE, Reynolds JD. Overview of glaucoma in infants and children. UpToDate (online resource). Topic 6272, Version 6215.6270. [Last updated Oct 18, 2017; Accessed Nov 4, 2017]:Available from https://www.uptodate.com/contents/overview-of-glaucoma-in-infants-and-children

2. Baily C, O"Keefe M. Paediatric Aphakic Glaucoma. J Clin Exp Ophthalmol 2012; 3:article 203. http://dx.doi.org/210.4172/2155-9570.1000203 .

3. Zhu XJ, Zhang KK, He WW, Sun XH, Meng FR, Lu Y. Diagnosis of pupillary block glaucoma after removal of congenital cataracts with

4. Kirwan C, O'Keefe M. Paediatric aphakic glaucoma. Acta Ophthalmol Scand 2006; 84(6):734-739. https://pubmed.gov/17083529

5. Levin AV. Aphakic glaucoma: a never-ending story? Br J Ophthalmol 2007; 91(12):1574-1575. https://pubmed.gov/18024804

6. Chen TC, Walton DS, Bhatia LS. Aphakic glaucoma after congenital cataract surgery. Arch Ophthalmol 2004; 122(12):1819-1825. https://pubmed.gov/15596586

7. Phelps CD, Arafat NI. Open-angle glaucoma following surgery for congenital cataracts. Arch Ophthalmol 1977; 95(11):1985-1987. https://pubmed.gov/921576

8. Jeganathan VSE, Mulvihill A, Montgomery D. Paediatric Aphakic Glaucoma: A Diagnostic and Management Challenge. Optom Open Access 2016; 1:article 115. http://dx.doi.org/110.4172/2476-2075.1000115 .

9. Alward WLM. Aniridia, Phacomatoses, & other pediatric glaucomas. Iowa Glaucoma Curriculum, [accessed Nov 4, 2017]: Available from http://curriculum.iowaglaucoma.org/chapter/13/video/183 .

10. Walton DS. Pediatric aphakic glaucoma: a study of 65 patients. Trans Am Ophthalmol Soc 1995; 93:403-420. https://pubmed.gov/8719689

Suggested Citation Format

Madhan N, Stiff HA, Zhang Z, Alward WLM. Aphakic Glaucoma. EyeRounds.org. posted December 14, 2017; Available from http://EyeRounds.org/cases/263-aphakic-glaucoma.htm

last updated: 12/14/2017

Uveitis Glaucoma Hyphema (UGH) Syndrome

Cheng Liang, BS, Austin R. Fox,MD, Jason P. Kam, MD, Wallace L.M. Alward, MD

posted October 3, 2017

INITIAL PRESENTATION

Chief Complaint

Elevated intraocular pressure and "cloudy, hazy" vision of the left eye

History of Present Illness

A 54 year-old-man was referred for elevated intraocular pressure (IOP) and decreased vision in the left eye (OS). His ocular history was remarkable for cataract extraction with intraocular lens (IOL) placement in both eyes (OU) and retinal detachment OU repaired by pars plana vitrectomy OU. Eight months prior to presentation, the IOL (Acrysof SN60AT single-piece lens) in the patient's left eye became displaced, and was subsequently repositioned in the ciliary sulcus. The patient developed macular edema in his left eye three months later for which he received a sub-Tenon triamcinolone acetonide injection and started prednisolone acetate eye drops. Two months prior to presentation, the patient developed an IOP of 48 mmHg OS. The patient's left eye was treated with latanoprost every night, timolol-brimonidine (Combigan©) two times a day, and dorzolamide two times a day. He also started oral acetazolamide 500 mg two times a day. One week later, IOP was noted to be in the upper teens, and acetazolamide was discontinued. However, two weeks prior to presentation, his IOP was again elevated to 52 mmHg, and acetazolamide 500 mg two times a day was restarted. Pigment was noted in the anterior chamber one week prior to presentation, and he was restarted on prednisolone acetate eye drops. The patient was referred to the Department of Ophthalmology at the University of Iowa Hospitals and Clinics for evaluation.

Past Ocular History

Traumatic hyphema of right eye (OD) secondary to a bungee cord injury (30 years prior)

Past Ocular Surgeries

Right Eye

- Cataract extraction/posterior chamber IOL placement (18 years prior)
- Pars plana vitrectomy (PPV) for retinal detachment (7 years prior)

Left Eye

- Cataract extraction/posterior chamber IOL placement (16 years prior)
- PPV for retinal detachment (11 years prior)
- PPV, repositioning of single-piece IOL into the ciliary sulcus (1 year prior)

Past Medical History

None

Medications

Clindamycin (tooth abscess)

Allergies

No known drug allergies

Family History

Father with glaucoma, retinal detachment

Social History

Social alcohol use, no tobacco use

Review of Systems

Unremarkable

OCULAR EXAMINATION

Snellen Distance Visual Acuity (with correction)

- OD: 20/20
- OS: 20/20-1

Ocular Motility/Alignment

- OD: Full, Ortho
- OS: Full, Ortho

Intraocular Pressure (Goldmann Applanation)

- OD: 17 mmHg
- OS: 42 mmHg

Pupils

- OD: 5 mm to 3 mm, brisk reaction, no relative afferent pupillary defect (RAPD)
- OS: 5.5mm to 5 mm, minimal reaction, 0.9 log units RAPD by reverse

Pachymetry

- OD: 565 microns
- OS: 556 microns

Confrontation visual fields

- OD: Full to count fingers
- OS: Partial superior temporal, inferior temporal, superior nasal, inferior nasal deficiencies by count fingers

Slit lamp exam

OD

♦ Lids/lashes: Normal
♦ Conjunctiva/sclera: Clear, quiet
♦ Cornea: Clear
♦ Anterior chamber: 1+ pigment, trace flare (post-fluorescein)
♦ Iris: Normal Architecture
♦ Lens: Posterior chamber IOL

OS

♦ Lids/lashes: Normal
♦ Conjunctiva/sclera: Conjunctival scarring at area of previous sclerotomies
♦ Cornea: Krukenberg spindle, no keratic precipitates
♦ Anterior chamber: 1+ pigment, trace flare (post-fluorescein)
♦ Iris: Broad transillumination iris defects in the shape of the IOL (Figure 1)
♦ Lens: Sulcus IOL (single-piece)

Gonioscopy (Spaeth grading system*)

♦ OD Temporal, Nasal, Inferior: E45f 1+; Superior: E45f 2+
♦ OS: Temporal, Nasal, Superior: E50f 3+; Inferior: E50f 4+

*Note: A description of the Spaeth grading system is available at glaucomatoday.com/pdfs/0505_0506.pdf

Dilated fundus examination (DFE)

OD

♦ Vitreous:Optically empty
♦ Disc: Normal
♦ Cup-to-disc ratio: 0.45
♦ Macula: Normal
♦ Vessels: Normal
♦ Periphery: Laser scars inferiorly and nasally

OS

♦ Vitreous:Optically empty
♦ Disc: Vertically cupped, no disc hemorrhage
♦ Cup-to-disc ratio: 0.7
♦ Macula: Normal
♦ Vessels: Normal
♦ Periphery: Laser scars inferiorly and temporally

Additional testing

see figures 1-3

CLINICAL COURSE

The patient underwent a pars plana vitrectomy (23 gauge) with removal of the single-piece IOL and placement of a 3-piece sulcus IOL (Acrysof MA60AC, Alcon Laboratories, Ft. Worth, TX). Immediately following the PPV, an Ahmed
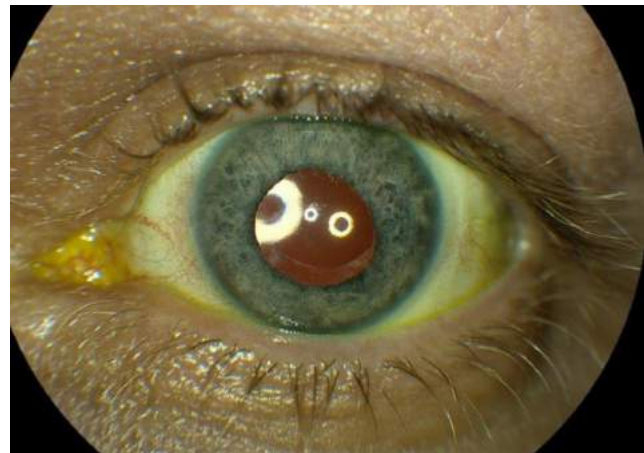
Figure 1: Color and infrared transillumination photos of the left eye. Multiple radial transillumination defects of the iris as well as circumferential defects that match the shape of the IOL haptics.
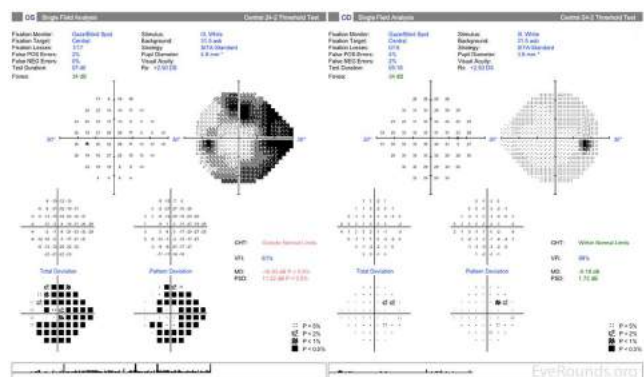
Figure 2: Humphrey Visual Fields (24-2). Left image: Normal visual field OD with good test reliability. Right image: Good test reliability with evidence of severe stage glaucoma with superior and inferior arcuate scotomas OS.

seton (model FP7, New Word Medical, Rancho Cucamonga, CA) was inserted. By post-operative week 16, the visual acuity was 20/25, and IOP was 14 mm Hg on timolol-brimonidine (Combigan©) two times daily.

ONH and RNFL OU Analysis:Optic Disc Cube 200x200   OD ● | ● OS

	OD	OS
Average RNFL Thickness	126 µm	100 µm
RNFL Symmetry	48%	
Rim Area	1.52 mm²	1.08 mm²
Disc Area	2.08 mm²	2.28 mm²
Average C/D Ratio	0.51	0.72
Vertical C/D Ratio	0.41	0.76
Cup Volume	0.107 mm³	0.500 mm³

RNFL Thickness Map · RNFL Deviation Map · Neuro-retinal Rim Thickness · RNFL Thickness · Extracted Horizontal Tomogram · Extracted Vertical Tomogram · RNFL Circular Tomogram · RNFL Quadrants · RNFL Clock Hours

Disc Center(-0.09,0.03)mm   Disc Center(0.15,-0.21)mm

EyeRounds.org

Figure 3: Optical coherence tomography (OCT) of the optic nerve head (ONH) of both eyes. Although the signal strength is poor (6/10 OD and 5/10 OS), the ONH OCT demonstrates robust retinal nerve fiber layer (RNFL) in both eyes. However, the RNFL of the left eye is relatively thinned compared to that of the right eye. There is glaucomatous cupping and a thin neuroretinal rim in the left eye when compared with the right eye.

DIAGNOSIS

Uveitis-Glaucoma-Hyphema-Syndrome

DISCUSSION

Uveitis-glaucoma-hyphema (UGH) syndrome was first described by Ellingson in 1978 and classically included uveitis, glaucoma, and hyphema in the setting of an anterior chamber IOL.[1] However, the term UGH syndrome is often used when one, two, or all three of these entities are present in the setting of any IOL causing irritation of the iris or angle structures.

Epidemiology

Although the incidence is not known, UGH syndrome is thought to be a rare condition that can occur in any patient population, including pediatric populations.[2] UGH syndrome was first associated, and is more commonly associated, with anterior chamber IOLs, single-piece acrylic IOLs, or sulcus lenses;[3] however, it can be seen with any type of IOL, including posterior chamber lenses and cosmetic iris implants.[4] With the predominant use of posterior chamber IOLs and modern advances in lens design, the incidence of UGH syndrome has declined.

Etiology/Pathophysiology

UGH syndrome results from an IOL chafing the iris, irido-corneal angle, or ciliary body, which leads to recurrent trauma to these structures. Uveitis results from mechanical breakdown of the blood aqueous barrier and resultant inflammation. A hyphema results from recurrent damage by the IOL to vascular tissue of the iris, ciliary body, or angle. Intraocular pressure elevation can be caused by pigment dispersion, uveitis, hyphema, direct injury to the aqueous drainage system, or a steroid response to corticosteroids used to treat UGH-related inflammation. Given that IOL irritation underlies the etiology of UGH syndrome, selection of the appropriate lens type, design, and size is crucial to minimize the risk of developing UGH syndrome.

Anterior chamber IOLs have traditionally been associated with UGH syndrome, as they were used when the first cases of UGH syndrome were described. The sizing of an anterior chamber IOL is crucial and should be approximated by measuring the horizontal white-to-white corneal diameter (limbus to limbus) and adding 1 mm. The anterior chamber IOL size and positioning should be assessed following implantation to ensure optimal fit. A small anterior chamber IOL may rotate or tilt to contact iris, whereas a large anterior chamber IOL may directly contact and irritate the iris and angle structures to cause UGH syndrome.

Sulcus IOLs are thought to be a more common cause of UGH syndrome given the close proximity to uveal tissue when intentionally or unintentionally placed in the sulcus.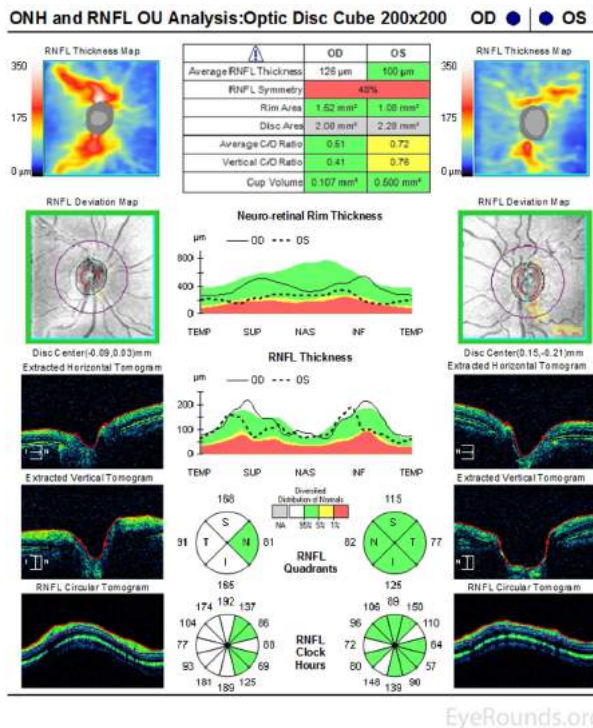 IOLs placed in the sulcus with square optic edges and large, thick, square haptics (*e.g.,* single-piece acrylic IOLs) may contact and irritate iris anteriorly to cause UGH syndrome. In addition, sulcus IOLs with small, planar haptics (*e.g.,* Acrysof SN60AT) may more easily dislocate to contact the uveal tissue.[3] An IOL with a thin, posteriorly angulated haptic and a smooth optic surface with rounded edges would be preferable to minimize iris chafing and the occurrence of UGH syndrome. As with anterior chamber IOLs, proper sizing and positioning of sulcus IOLs are crucial to decrease the contact with uveal tissue and chances of UGH syndrome. It has been recommended that single-piece acrylic IOLs and other IOLs designed for the capsular bag not be placed in the sulcus.[2] However, when placed in the sulcus, IOLs should be secure and clear of the posterior iris surface. UGH syndrome may also occur with sulcus IOLs in the setting of reverse pupillary block, especially in susceptible eyes (*i.e.,* myopia, post-vitrectomy).[5]

Posterior chamber IOLs may or may not be completely positioned in the capsular bag to contact uveal tissue and, though more rare, cause UGH syndrome.[6] In the setting of weakened zonules, such as in exfoliation syndrome or IOL subluxation, UGH syndrome is more likely to occur due to poor zonular support and posterior chamber IOL movement.

Signs/Symptoms

Patients may complain of blurred vision, transient vision loss, ocular pain or ache, erythropsia (*i.e.,* objects take on a reddish hue), or photophobia. Slit lamp examination is

essential to help establish the diagnosis. A poorly positioned IOL optic or haptic contacting uveal tissue may be directly observed. Hyphema, cell and/or flare, transillumination iris defects, synechiae, pseudophacodonesis, or corneal pigment may also be identified on the slit lamp examination. Gonioscopy may demonstrate blood within the inferior angle, signs of mechanical erosion, poorly positioned haptics, or increased pigmentation of the trabecular meshwork. Ocular hypertension is often present, and optic disc cupping and glaucomatous vision loss may be present in advanced cases (Figures 2 and 3).

Testing/Laboratory work-up

Prothrombin time and international normalized ratio should be tested in patients on anticoagulation medications as these patients may have an increased risk of bleeding.

Imaging

Ultrasound biomicroscopy and OCT of the anterior segment may be useful to identify IOL position and contact with the iris or angle structures (Figure 4). Posterior segment ultrasound (B-scan) may be useful to identify a vitreous hemorrhage, if present. UGH plus syndrome is the name given to UGH syndrome in the presence of vitreous hemorrhage.
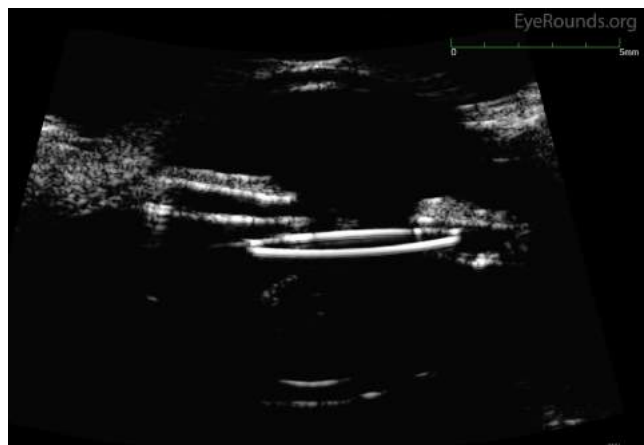
Figure 4: Ultrasound biomicroscopy of the left eye. The nasal optic of an IOL is seen abutting the posterior iris surface in a patient with UGH syndrome. (Note: Figure 4 was obtained from a different patient and is used only for illustration.)

Treatment / Management / Guidelines

Medical Management

Uveitis: Topical corticosteroid drops
Glaucoma: Prostaglandin analogs, beta-blockers, and carbonic anhydrase inhibitors.
Pilocarpine and other cholinergics should be avoided to prevent further chafing of the iris.
Hyphema: Topical corticosteroids drops and cycloplegics (*e.g.,* cyclopentolate)

Surgical Management

Definitive treatment is to secure or exchange the IOL or iris implant. The UGH syndrome is one of the more common indications for IOL exchange surgery, representing 11.9% of IOL exchanges in one study.[7] Laser peripheral iridotomy may be used for the management of UGH syndrome resulting from reverse pupillary block.[5] In addition, serial intracameral anti-VEGF injections have been used to successfully manage UGH syndrome.[8]

EPIDEMIOLOGY OR ETIOLOGY	*SIGNS*
1. Any population with an IOL ○ ACIOL > Sulcus IOL > PCIOL ○ Single-piece IOL > 3-piece IOL 2. Iris implant	♦ Cell and/or flare ♦ Pigment in angle or on cornea ♦ Transillumination iris defects ♦ Displaced lens/haptics ♦ Hyphema or blood in the angle or vitreous ♦ Ocular hypertension ♦ Optic disc cupping ♦ Glaucomatous field changes
SYMPTOMS	*TREATMENT / MANAGEMENT*
♦ Blurred vision ♦ Transient vision loss ♦ Ocular pain ♦ Erythropsia ♦ Photophobia	♦ IOL exchange ♦ Uveitis: topical corticosteroids drops ♦ Glaucoma: Prostaglandin analogs, beta-blockers, Carbonic anhydrase inhibitors ♦ Hyphema: topical corticosteroids drops, cycloplegics

References

1. Ellingson FT. The uveitis-glaucoma-hyphema syndrome associated with the Mark VIII anterior chamber lens implant. *J Am Intraocul Implant Soc* 1978;4(2):50-53. pubmed.gov/701165

2. Lin CJ, Tan CY, Lin SY, Jou JR. Uveitis-glaucoma-hyphema syndrome caused by posterior chamber intraocular lens--a rare complication in pediatric cataract surgery. *Ann Ophthalmol (Skokie)* 2008;40(3-4):183-184. pubmed.gov/19230361

3. Chang DF, Masket S, Miller KM, Braga-Mele R, Little BC, Mamalis N, Oetting TA, Packer M, Committee ACC. Complications of sulcus placement of single-piece acrylic intraocular lenses: recommendations for backup IOL implantation following posterior capsule rupture. *J Cataract Refract Surg* 2009;35(8):1445-1458. pubmed.gov/19631134

4. Arthur SN, Wright MM, Kramarevsky N, Kaufman SC, Grajewski AL. Uveitis-glaucoma-hyphema syndrome and corneal decompensation in association with cosmetic iris implants. *Am J Ophthalmol* 2009;148(5):790-793. pubmed.gov/19660735

5. Singh H, Modabber M, Safran SG, Ahmed, II. Laser iridotomy to treat uveitis-glaucoma-hyphema syndrome secondary to reverse pupillary block in sulcus-placed intraocular lenses: Case series. *J Cataract Refract Surg* 2015;41(10):2215-2223. pubmed.gov/26703298

6. Zhang L, Hood CT, Vrabec JP, Cullen AL, Parrish EA, Moroi SE. Mechanisms for in-the-bag uveitis-glaucoma-hyphema syndrome. *J Cataract Refract Surg* 2014;40(3):490-492. pubmed.gov/24417893

7. Davies EC, Pineda R, 2nd. Intraocular lens exchange surgery at a tertiary referral center: Indications, complications, and visual outcomes. *J Cataract Refract Surg* 2016;42(9):1262-1267. pubmed.gov/27697243

8. Rech L, Heckler L, Damji KF. Serial intracameral bevacizumab for uveitis-glaucoma-hyphema syndrome: a case report. *Can J Ophthalmol* 2014;49(6):e160-162. pubmed.gov/25433757

Citing this article

Cheng L, Fox AR, Kam JP, Alward WLM. Uveitis Glaucoma Hyphema (UGH) Syndrome. EyeRounds.org. posted October 3, 2017; Available from: EyeRounds.org/cases/257-UGH-syndrome.htm

last updated: 10/03/2017

Aqueous Misdirection

Aqueous misdirection synonyms are **malignant glaucoma**, **vitreous block glaucoma**, **ciliary block glaucoma**, **ciliolenticular glaucoma**, or **ciliovitreal block glaucoma**.

Jacob A. Evans, BS; Jaclyn M. Haugsdal, MD; Wallace L. M. Alward, MD

posted September 26, 2016

Initial Presentation

Chief Complaint

Left-sided headache and eye pain

History of Present Illness

An 88-year-old hyperopic female presented with left eye pain rated 10/10 and associated blurred vision, headache, nausea, and vomiting. The pain started approximately 4 hours previously and progressively became worse. She denied other ocular symptoms including tearing and photophobia. The patient had a history of cataract extraction with intraocular lens placement and Nd:YAG (neodymium: yttrium aluminium garnet) capsulotomy bilaterally. She also had a history of having a laser procedure previously for an unknown diagnosis.

Past Ocular History

♦ Pseudophakia
♦ Hyperopia
♦ Pseudoexfoliation syndrome

Past Ocular Surgery

♦ Cataract extraction with posterior chamber intraocular lens in both eyes (OU) (more than 5 years previously)
♦ Nd:YAG laser capsulotomy OU (approximately 1 year previously)
♦ Unknown laser procedure (more than 10 years previously)

Past Medical History

♦ Hypothyroid
♦ Chronic pain
♦ Depression

Medications

♦ Venlafaxine
♦ Levothyroxine
♦ Trazodone
♦ Tramadol
♦ Hydromorphone

Allergies

♦ Iodine contrast

Ocular Family History

♦ Noncontributory

Social History

♦ Former smoker
♦ Uses occasional alcohol

Review of Systems

♦ Per HPI, Otherwise negative

Visual Acuity

♦ Distance without correction
  o Right eye: 20/30 -1
  o Left eye: 20/600
♦ Distance with correction
  o Left eye: 20/60
♦ Near card without correction
  o Right eye: 20/25
  o Left eye: 20/160

Ocular Alignment and Motility

♦ Orthotropic with full motility OU

Intraocular Pressure (IOP)

IOP measured by Tonopen®

♦ Right eye: 11 mmHg
♦ Left eye: 50 mmHg

Pachymetry

♦ Right eye: 518 μm
♦ Left eye: 551 μm

Pupil examination

♦ Right eye: 3 mm in dark → 2 mm in light; brisk but minimal reaction to light
♦ Left eye: 5 mm in dark → 5 mm in light; no reaction to light. 0.9 log unit relative afferent pupillary defect (RAPD)

Slit-lamp examination

♦ Right eye
  o Lids/Lashes: Normal
  o Conjunctiva: Clear and quiet
  o Cornea: Clear
  o Anterior chamber: Quiet and deep
  o Iris: Normal
  o Lens: Posterior chamber intraocular lens with open posterior capsule
  o Vitreous: Normal

- Left eye
  - Lids/Lashes: Normal
  - Conjunctiva: 1+ injection
  - Cornea: Clear
  - Anterior chamber: Shallow anterior chamber with 2 corneal thickness depth centrally and peripheral iridocorneal apposition
  - Iris: Peripheral iridotomy located at 10:30
  - Lens: posterior chamber intraocular lens with open posterior capsule
  - Vitreous: Normal; no cell

Fundus examination

- Right eye
  - Disc: Normal, peripapillary atrophy
  - Cup to disc ratio 0.45
  - Macula: Normal
  - Vessels: Normal
  - Periphery: Normal
- Left Eye
  - Disc: inferior notch, peripapillary atrophy
  - Cup to disc ratio 0.75
  - Macula: Normal
  - Vessels: Normal
  - Periphery: Normal

Gonioscopy

- Right eye: D35f1+ in all directions
- Left eye: A(A)25b in all directions

Ancillary Studies

Standardized ocular echography, left eye

- Mild vitreal opacities seen. Severe excavation of optic nerve. No retinal detachment or mass lesion was visualized.

CLINICAL COURSE

Multiple rounds of topical dorzolamide/timolol, brimonidine, and latanoprost were given to this patient in the emergency room. Additionally, she received dilating drops and intravenous acetazolamide. Her intraocular pressure declined to the low 30's and the anterior chamber started to deepen in the emergency room. She was seen in the eye clinic the following morning. At that time, the anterior chamber had again shallowed and the IOP returned to mid 40's (Left eye) by applanation. The patient received four additional rounds of topical dorzolamide/timolol, brimonidine, latanoprost, and atropine, in addition to immediate release acetazolamide. The IOP was unresponsive, and a pars plana vitrectomy with Ahmed Seton was performed. The day after the procedure, the patient had resolution of headache and eye pain (Left eye). The intraocular pressure was found to be 5. Unfortunately, the intraocular lens had dislocated posteriorly in the postoperative setting, likely

Figure 1: Slitlamp photo, Left eye (Photographer Brice Critser): Using the slit beam to assess anterior chamber depth, there is iridocorneal touch peripherally with approximately two corneal thicknesses deep centrally. The iris does not have the bombé configuration and the anterior chamber is diffusely shallow.

Figure 2: Slitlamp photo, Left eye (Photographer Brice Critser): Using a light aimed from the temporal limbus across the iris plane, a shadow is cast on the nasal aspect of the iris. This is created from the shallowing of the anterior chamber and anterior shift of the iris blocking the passage of light.

secondary to pseudoexfoliation, but vision with +10D lens and pinhole was in 20/40 range. She elected to defer additional surgery at this time.

DIAGNOSIS: Aqueous Misdirection

Differential Diagnosis of flat or shallow anterior chamber and elevated IOP

- Aqueous misdirection
- Pupillary block
- Choroidal effusion/hemorrhage/mass lesion
  - Hemorrhagic, Appositional/Kissing Choroidal Detachment
  - Serous, Appositional/Kissing Choroidal Detachment
- Ciliary body rotation
- Hypotony with applanation of crystalline lens

DISCUSSION

Aqueous misdirection is a form of secondary glaucoma, related to pressure buildup from trapping of aqueous within the vitreous. It typically presents with diffuse shallowing (both central and peripheral) of the anterior chamber in the setting of elevated intraocular pressure, and is considered a diagnosis of exclusion (1, 2).

Etiology/Epidemiology

Aqueous misdirection typically occurs after correctional surgery for angle closure glaucoma. These patients usually have a history of angle closure or peripheral anterior synechiae (3). Aqueous misdirection has infrequently been associated with trauma, inflammation, or an unknown cause (4-6). It may occur days to months postoperatively; one study found median time to diagnosis was 33 days (7).

Pathophysiology

Aqueous misdirection occurs when aqueous is directed posteriorly and becomes trapped within the vitreous (8). This causes compression of the anterior vitreous making it more impermeable to aqueous (6, 9). This impermeability decreases the ability of the aqueous to flow freely forward through the posterior chamber to the anterior chamber, which leads to further trapping of aqueous in the posterior segment (8). The mechanism by which aqueous initially becomes directed posteriorly and trapped is unknown, though many theories have been proposed (9).

Signs/Symptoms

The key features that distinguish aqueous misdirection from similar diagnoses are diffuse shallowing of the anterior chamber (thus absent iris bombe), anterior displacement of the lens-iris diaphragm and a posterior segment free of hemorrhage, masses, or vein occlusion (6). A patent iridotomy/iridectomy in the setting of a flat or shallow anterior chamber is another clue to this diagnosis (4).

Distinguishing aqueous misdirection from other clinical entities can be difficult. Pupillary block presents with a deep central anterior chamber with a shallow periphery, and does not appear in the presence of a patent iridotomy

(4, 6). Pupillary block may be either primary (the most common mechanism of primary angle closure glaucoma) or secondary. Major secondary etiologies include ectopia lentis, cataractous lens intumescence, aphakia/pseudophakia with dislocated intraocular lens, pupillary capture by intraocular lens implant, or posterior synechiae. Pupillary block is uncommon after surgery for angle closure glaucoma.

Anterior rotation of the ciliary body due to swelling, inflammation, medications, or masses can also cause a shallow anterior chamber. Additional testing, such as echography and anterior segment imaging, can be used to look for masses or effusions causing the anterior movement of the ciliary body.

Suprachoroidal hemorrhage is associated with severe eye pain, and hemorrhage will be detected either by dilated fundus exam or with echography (6). The absence of such on B-scan ultrasonography rules out suprachoroidal hemorrhage (1).

Finally, hypotony may be deceptive because it can present with a shallow anterior chamber and the lens may be opposed to the cornea causing artificial elevation of intraocular pressure (6, 10). This entity should be distinguishable from the others simply by palpation of the eye, revealing a hypotonous globe.

Imaging

B-scan ultrasonography is useful to rule out other causes of flat anterior chamber such as choroidal effusions, suprachoroidal hemorrhage, and masses (1). High-resolution ultrasound biomicroscopy may assist in diagnosis by demonstrating anterior displacement of the lens-iris diaphragm, and possibly even anterior rotation of the ciliary body, ciliary processes, and/or zonules (5).

Treatment Guidelines

The first line treatment is medical therapy consisting of cycloplegics and aqueous suppressants (1, 3). Cycloplegia is the most important treatment as it moves the iris-lens diaphragm posteriorly in addition to relieving iris-lens apposition with dilation. A typical regimen includes atropine 1% four times a day (8). Aqueous suppressants include beta blockers, alpha 2 agonists, and oral and topical carbonic anhydrase inhibitors. Osmotic agents can be used to shrink the vitreous (3, 8). Cholinergics should be avoided as these medications tend to shift the lens-iris diaphragm forward. It is possible for up to 50% of cases to be relieved using such a regimen for 5 days, after which the medications may be tapered. However, recurrence is common, and a more definitive treatment may be necessary (8). Other potential treatment options include Nd:YAG laser therapy for aphakic and pseudophakic patients to disrupt the anterior vitreous face.

A pars plana vitrectomy is considered the definitive treatment (1, 3, 11). Removal of the anterior hyaloid is the most critical part of this surgery in order to prevent recurrence (8). Pars plana lensectomy should be added if damage to

Table. Summary: Aqueous Misdirection

EPIDEMIOLOGY	SIGNS

♦ Incidence
0.4 – 4% of eyes after incisional surgery, especially for angle-closure glaucoma (4, 5, 13-16)
♦ Risk factors
   o Hyperopia
   o History of angle closure
   o Trauma or inflammation (4, 6, 7)
   o May occur days to months postoperatively (7)
	♦ *Diffusely* shallow anterior chamber (absent iris bombe) (1, 6)
	♦ Elevated intraocular pressure (2, 6)
	♦ Patent iridotomy/iridectomy (2)
	♦ Dilated fundus exam or echography without choroidal detachment, suprachoroidal hemorrhage, or masses (4)

SYMPTOMS	TREATMENT
♦ Eye pain ♦ Blurry vision/halos ♦ headache/brow ache ♦ nausea or vomiting	♦ Medical management with cycloplegia, aqueous suppressants (topical beta blockers, alpha 2 agonists, and both topical and oral carbonic anhydrase inhibitors), while avoiding cholinergics (3, 6, 8) ♦ Nd:YAG laser capsulotomy (3, 6) ♦ Definitive treatment is pars plana vitrectomy (1, 3, 6, 8, 11)

the crystalline lens occurs or if it is not possible to deepen the anterior chamber by vitrectomy and anterior hyaloidectomy alone (1, 8). Prophylactic pars plana vitrectomy may be considered during intraocular surgery for the fellow eye of a patient with a prior history of aqueous misdirection (12).

Supplemental Information

Gonioscopy gonioscopy.org

Hemorrhagic, Appositional/Kissing Choroidal Detachment eyerounds.org/atlas/pages/choroidal-detachments/HAK.htm

Iowa glaucoma curriculum video on aqueous misdirection: curriculum.iowaglaucoma.org/chapter/19

Serous, Appositional/Kissing Choroidal Detachment eyerounds.org/atlas/pages/choroidal-detachments/SAK.htm

REFERENCES

1. Alvi NP, Cantor LB. Aqueous Misdirection Syndrome. In: Yanoff M, Duker JS, editors. Ophthalmology. London: Elsevier; 2014. p. 1092-3.
2. Kaplowitz K, Yung E, Flynn R, et al. Current concepts in the treatment of vitreous block, also known as aqueous misdirection. Surv Ophthalmol. 2015;60(3):229-41.
3. Ophthalmology AAO. Aqueous Misdirection. Basic and Clinical Science Course: Section 10, 2015-2016 Glaucoma. San Francisco: AAO; 2015. p. 131-3.
4. Foreman-Larkin J, Netland PA, Salim S. Clinical Management of Malignant Glaucoma. J Ophthalmol. 2015;2015:283707.
5. Shen CJ, Chen YY, Sheu SJ. Treatment course of recurrent malignant glaucoma monitoring by ultrasound biomicroscopy: a report of two cases. Kaohsiung J Med Sci. 2008;24(11):608-13.
6. Alward WLM. Aqueous Misdirection. Iowa Glaucoma Curriculum. Updated March 2016. Cited June 30, 2016.; Available from curriculum.iowaglaucoma.org/chapter/19/video/191.
7. Greenfield DS, Tello C, Budenz DL,et al. Aqueous misdirection after glaucoma drainage device implantation. Ophthalmology. 1999;106(5):1035-40.
8. Ramulu PY, Gedde SJ. Aqueous Misdirection. In: Shaarawy TM, Sherwood MB, Hitchings RA, Crowston

JG, editors. Glaucoma. London: Elsevier; 2015. p. 836-46.

9. Epstein DL, Hashimoto JM, Anderson PJ, et al. Experimental perfusions through the anterior and vitreous chambers with possible relationships to malignant glaucoma. Am J Ophthalmol. 1979;88(6):1078-86.

10. Liebmann JM, Weinreb RN, Ritch R. Angle-closure glaucoma associated with occult annular ciliary body detachment. Arch Ophthalmol. 1998;116(6):731-5.

11. Bitrian E, Caprioli J. Pars plana anterior vitrectomy, hyaloido-zonulectomy, and iridectomy for aqueous humor misdirection. Am J Ophthalmol. 2010;150(1):82-7. e1.

12. Chaudhry NA, Flynn HW, Jr., Murray TG, et al. Pars plana vitrectomy during cataract surgery for prevention of aqueous misdirection in high-risk fellow eyes. Am J Ophthalmol. 2000;129(3):387-8.

13. Nguyen QH, Budenz DL, Parrish RK, 2nd. Complications of Baerveldt glaucoma drainage implants. Arch Ophthalmol. 1998;116(5):571-5.

14. Olayanju JA, Hassan MB, Hodge DO, et al. Trabeculectomy-related complications in Olmsted County, Minnesota, 1985 through 2010. JAMA ophthalmology. 2015;133(5):574-80.

15. Jampel HD, Musch DC, Gillespie BW, et al. Perioperative complications of trabeculectomy in the collaborative initial glaucoma treatment study (CIGTS). Am J Ophthalmol. 2005;140(1):16-22.

16. Gedde SJ, Schiffman JC, Feuer WJ, et al. Three-year follow-up of the tube versus trabeculectomy study. Am J Ophthalmol. 2009;148(5):670-84.

Citing this article

Evans JA, Haugsdal JM, Alward WLM. Aqueous Misdirection. EyeRounds.org. September 26, 2016; Available from: EyeRounds.org/cases/244-Aqueous-Misdirection.htm

last updated: 09/26/2016

Hypotony: Late hypotony from trabeculectomy and Ahmed Seton with resulting hypotony maculopathy

Ben J. Janson MD, Jason P. Kam MD, Wallace L.M. Alward MD

INITIAL PRESENTATION

Chief Complaint

Decreased vision in right eye, without pain.

History of Present Illness

A 36-year old female presented with poor vision secondary to a low intraocular pressure (IOP) in her right eye. She had been diagnosed with bilateral idiopathic anterior uveitis in both eyes at age 27 and subsequently developed secondary glaucoma, either due to chronic intraocular steroid use or chronic uveitis, in the right eye (OD) worse than in the left eye (OS). She underwent bilateral trabeculectomies with mitomycin C (MMC) in 2009 and cataract extraction with intraocular lens implantation in 2010 OD and 2011 OS. She was lost to follow up until 2015 when she was found to have an over-filtering bleb with visual acuity (VA) of 20/70 and an IOP of 3 mmHg OD with hypotony maculopathy. She underwent blood patching with temporary improvement in the maculopathy, and another blood patching two months later in the right eye (8/2015 and 10/2015). She was lost to follow-up for another ten months and, in 2016, was urgently referred back with visual acuity in the right eye of 20/60 and IOP of 2 mmHg.

Past Ocular History

♦ Idiopathic bilateral non-granulomatous anterior uveitis
♦ Pseudophakia both eyes (OU)

Past Ocular Surgery

Right Eye

♦ Sub-tenon's triamcinolone (Kenalog®) (10/08)
♦ Trabeculectomy with MMC (3/09)
♦ Phacoemulsification with posterior chamber intraocular lens implant (PCIOL) (2010)
♦ Blood patch x2 (2015)

Left Eye

♦ Trabeculectomy with MMC (07/09)
♦ Phacoemulsification with PCIOL (2011)

Ocular medications

♦ Difluprednate (Durezol®) three times a day (TID) OU

Past Medical History

♦ Intramural leiomyoma of uterus
♦ Depression
♦ Generalized anxiety disorder
♦ Appendectomy
♦ Laparoscopic salpingo-oophorectomy
♦ Cholecystectomy

Medications

♦ Alprazolam 0.5mg, hydrocodone-acetaminophen 5-325mg, zolpidem 10mg

Allergies

♦ Clindamycin, doxycycline, morphine, ibuprofen, naproxen, penicillin, fluoxetine

Family History

♦ Non-contributory

Social History

♦ Smokes 3-4 cigarettes a day

Review of Systems

♦ Negative except for what is detailed in the history of present illness

OCULAR EXAMINATION

Visual Acuity with correction – Linear Snellen

♦ OD: 20/70-1 (pinhole 20/50+2)
♦ OS: 20/20-1

Ocular Motility/Alignment

♦ OD: Full
♦ OS: Full

Intraocular Pressure - Goldmann Applanation

♦ OD: 03 mmHg
♦ OS: 06 mmHg

Pupils

♦ OD: 5 mm in dark, 3 mm in light, no relative afferent pupillary defect (RAPD)
♦ OS: 5 mm in dark, 3 mm in light, no RAPD

Pachymetry

♦ OD: 552 microns
♦ OS: 566 microns

Slit lamp exam

♦ Lids/lashes:Normal OU
♦ Conjunctiva/sclera
  ○ OD: avascular Seidel-negative elevated bleb
  ○ OS: avascular Seidel-negative elevated bleb
♦ Cornea
  ○ OD: Descemet folds
  ○ OS: clear
♦ Anterior chamber: Deep and quiet OU
♦ Iris: Surgical superior iridectomy OU,
♦ Lens: PCIOL OU

Dilated fundus examination (DFE)

♦ Vitreous: Normal OU
♦ Disc
  ○ OD: Relative pallor, no disc hemorrhage
  ○ OS: No disc hemorrhage, healthy rim
♦ Cup-to-disc ratio
  ○ OD: 0.85
  ○ OS: 0.40
♦ Macula
  ○ OD: Striae
  ○ OS: Flat
♦ Vessels: Normal OU
♦ Periphery: Normal OU
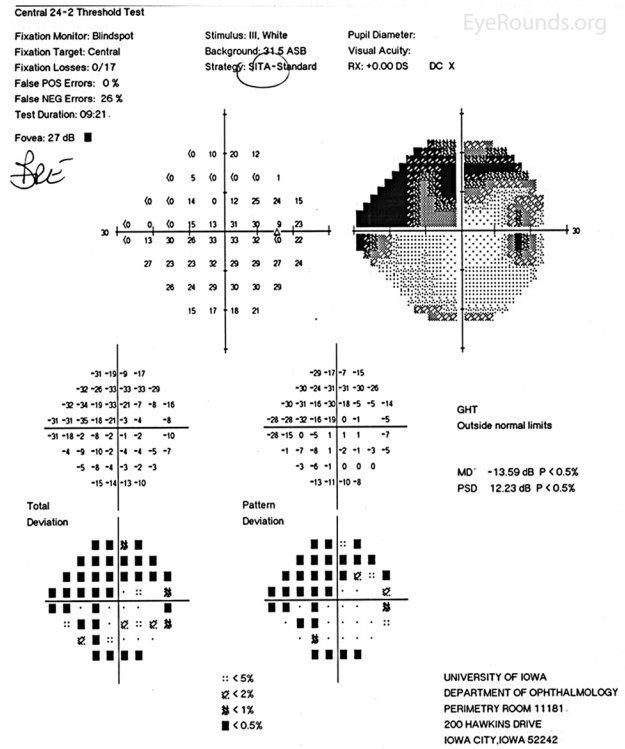
Figure 1: Humphrey Visual Field (HVF) of the right eye. This is a 24-2 visual field commonly used in the screening and monitoring of glaucoma patients. This patient's visual field represents severe stage glaucoma. There are both inferior and superior field defects and these defects approach central vision.
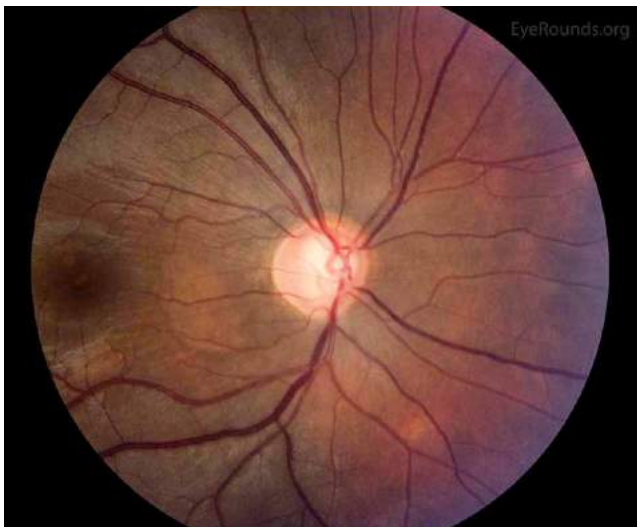
Figure 2: Color fundus photo of the right eye, centered over the optic nerve head. In this photo, the optic nerve appearance is consistent with glaucoma as the cup to disc ratio is increased due to loss of the nerve tissue. The supporting history and other studies support these changes as attributable to glaucoma as compared to other etiologies of enlarged cup to disc ratio.
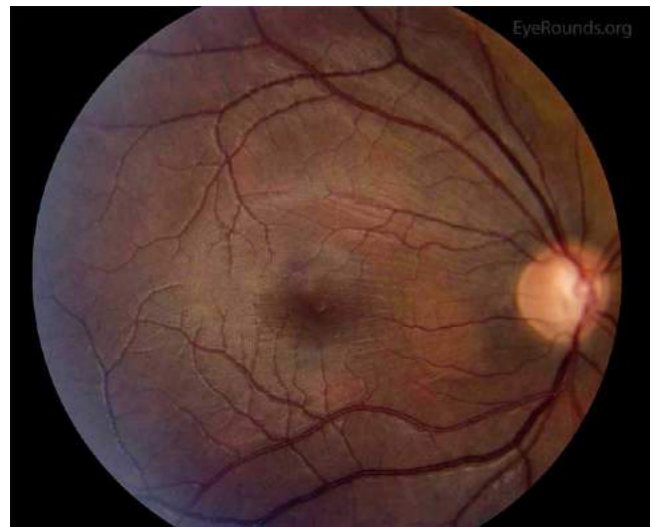
Figure 3: Color fundus photo of the right eye, centered over the macula. In this photo, the wrinkling and striation of the macula is present from the hypotony maculopathy. Due to the low intraocular pressure, folds form in the chorioretinal tissue. There are fine folds radiating out from the fovea and more prominent folds radiating from the optic disc.

Gonioscopy (Spaeth grading system)

♦ OD: B40f1+, scattered peripheral anterior synechiae (PAS)
♦ OS: B40f1+, scattered PAS nasally

Additional testing

Visual Fields (figure 1) and Fundus Photography (figures 2 and 3)

Differential Diagnosis: Hypotony after glaucoma surgery

♦ Overfiltering bleb or inadvertent bleb
♦ Cyclodialysis
♦ Retinal Detachment
♦ Uveitis
♦ Bleb leak
♦ Vascular Occlusion
♦ Ocular ischemia
♦ Infection/inflammation

CLINICAL COURSE

The patient underwent blood patching in the right eye to help raise the IOP in 8/2015, which improved her vision from 20/70 to 20/20 and her IOP from 3 mmHg to 8 mmHg. This improvement was short-lived and blood patching was performed again in 10/2015. Due to insurance and transportation issues, the next evaluation did not occur until 8/2016. At that time the IOP was 2 mmHg in her right eye and she had 20/60 vision. The patient's macular optical coherence tomography (OCT) at the time showed hypotony maculopathy (Image 4). She underwent surgery in 9/2016. During the surgery, the bleb was removed and the trabeculectomy site closed with a scleral patch graft. At the same time an Ahmed seton was inserted and covered with a corneal patch graft.
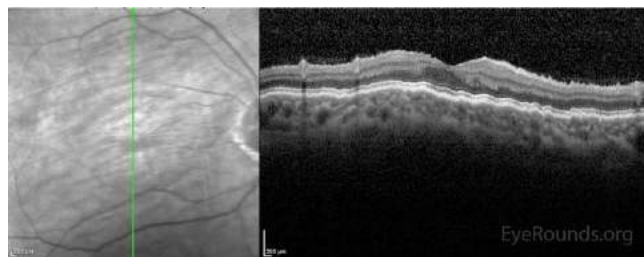
Figure 4: OCT showing hypotony maculopathy. There is a wrinkled appearance to all of the chorioretinal layers.

Post operative course

On post operative day 1, the visual acuity in the right eye was stable at 20/60 with an IOP of 8 mmHg however the following week her vision had dropped to 20/150 and her IOP was 0 with worsening corneal and macular folds and mild choroidal effusions. No retinal detachment was not-

ed. B-scan echography demonstrated a shallow choroidal effusion superiorly (Image 5) and the OCT showed persistent macular folds (Image 6). Atropine was added to her drop regimen to deepen the anterior chamber. There was no change in her weekly exam until she was seen on post operative week 7, at which time her vision had improved to 20/40 (PH 20/25) with an IOP of 9 mmHg, no corneal folds, and improved macular folds. At three months post-operatively her visual acuity was 20/20 and her IOP 7 mmHg. She was off all medications. Her macular folds had completely resolved
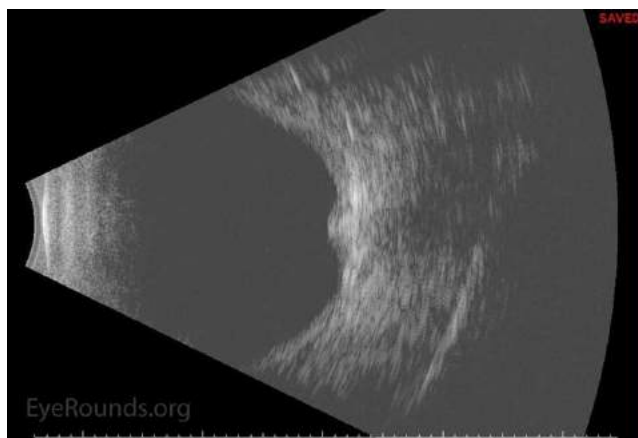
Figure 5: -B-scan echo showing superior shallow choroidal during post-operative course
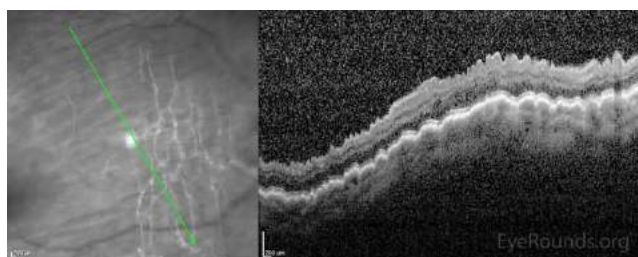
Figure 6: OCT during post-operative course showing worsening macular hypotony as compared to presentation OCT (see Figure 4)

DIAGNOSIS

♦ Hypotony due to overfiltering bleb

DISCUSSION

Etiology/Epidemiology

Hypotony is low intraocular pressure. Some define hypotony as an IOP <5 mmHg. More appropriately it should be considered to be an IOP below which the eye does not maintain its normal shape and may subsequently lose vision. Hypotony can be encountered in the ophthalmologist's practice, with many cases being caused by glaucoma surgery, as in this case report. The causes of hypotony include overfiltering blebs, inadvertent blebs created traumatically or during non-glaucoma surgery, leaking blebs, traumatic or surgically-induced cyclodialysis cleft, retinal

detachment, retinal vascular occlusion, or inflammation. [1] These cases typically present unilaterally, but bilateral cases of hypotony can occur due to systemic disease like myotonic dystrophy, dehydration, uremia, hyperosmotic agents, acidosis, and hyperglycemia.[1, 2]

Modern filtration surgery techniques have reduced the incidence of hypotony, but rates of post-operative hypotony still occur in up to 38% of cases. The risk increases in cases using antifibrotic agents like mitomycin C.[3] Meta-analysis suggests an increased risk of hypotony due to trabeculectomies performed without releasable sutures (RR 4.04) as compared to with releasable sutures (RR 2.57).[4]

Hypotony can occur early (within two weeks of surgery), or late (after two weeks). In one study, late hypotony after primary trabeculectomy with mitomycin C and laser suture lysis occurred in 42.2% of eyes after two years of follow up.[3] Risk factors associated with hypotony include younger age, male gender, myopia, and systemic illness.[3]

Hypotony is associated with a number of complications including hypotony maculopathy, choroidal effusion, cystoid macular edema, optic disc edema, and cataract formation. [1, 3]

Pathophysiology

The principles underlying hypotony can be divided into aqueous underproduction, increased aqueous outflow, or combination of the two.

Overfiltering blebs or leaking blebs are the most common causes of hypotony due to increased aqueous outflow. Increased drainage may also occur due to a cyclodialysis cleft, which is a disinsertion of the ciliary body from the scleral spur. This may develop following trauma or surgery and allows aqueous to drain into the suprachoroidal space. [3, 6]

Inflammation both decreases aqueous production in the ciliary body and increases outflow by increasing uveoscleral tract permeability.[1] Inflammation is not the only cause of decreased aqueous production, however. Aqueous suppressant medications (such as beta-adrenergic antagonists), disruption of the ciliary epithelium, or proliferative downgrowth over the ciliary body can all decrease aqueous production.[3]

Hypotony may cause several secondary structure-related complications which may lead to decreased vision, including ciliochoroidal detachment, hypotony maculopathy, papilledema, and phthisis bulbi. In a chiliochoridal detachment, fluid accumulates in the space between the choroid and sclera due to relative difference between the higher choroidal vascular pressure and the lower intraocular pressure. As the IOP further declines, so too does the structural support to the eye, which can lead to collapse of the scleral wall and development of the hypotony-related macular folds seen in hypotony maculopathy. The redundant retina tissue becomes distorted, leading to a decline in visual acuity. Hypotony maculopathy is most likely to occur in younger individuals whose sclera is thinner, more flexible, and thus more conforming to pressure changes.

[5, 6] Papilledema may also be seen in hypotony, which is thought to be due to constriction of axonal bundles from an anteriorly-bowed lamina cribosa. In severe cases, prolonged hypotony can result in phthisis bulbi.[1, 2]

Signs/Symptoms

Hypotony is not always symptomatic and no IOP cutoff exists below which intervention is indicated. One study found 40% of eyes with low IOP lacked any associated physical signs and two-thirds of eyes maintained visual acuity within two lines of baseline acuity.[5] Individual eyes have a wide range of sensitivity to hypotony.[1] Even patients with a bleb-leak often remain asymptomatic, making objective signs critically important.

However, when symptoms do develop, visual acuity is often affected. The severity of this decline in visual acuity is quite variable, but will usually improve as the IOP improves.[2] The cornea can develop Descemet folds, astigmatism, and edema. The cornea can also decompensate in shallow anterior chambers and lead to cataract formation if contact develops between the lens and cornea.[1] Distinguishing iridocorneal touch from cornea-lenticular touch is important as cornea-lenticular touch can cause deterioration of both the cornea and lens.

Serous choroidal detachments may be visible on exam, but are usually asymptomatic. These serous choroidal detachments may enlarge significantly to the point of retina-to-retina contact, known as "kissing choroidals."[3, 7] (see Related EyeRounds atlas page eyerounds.org/atlas/pages/choroidal-detachments/SAK.htm) However, sudden vision loss and severe, throbbing pain can occur due to breakage of vessels, leading to suprachoroidal hemorrhage. This presence of hemorrhage carries a worse prognosis as compared to serous detachments.[3] Choroidal detachments can be distinguished from retinal detachments as their convex cross sectional appearance extends to the ciliary body, instead of stopping at the ora serrata like a retinal detachment.[7]

The optic nerve head may become edematous due to constriction of axons. With this, the optic nerve head can be mistaken to have a decreased cup to disc ratio as this edema leads to pseudo-reversal of cupping.[1]

The macula may have tortuous vasculature and folds in the chorioretinal tissue. In hypotony maculopathy, there are fine retinal folds radiating out from the fovea and branching chorioretinal folds radiating from the optic disc.

Testing/Laboratory work-up

Slit lamp and dilated fundus examination are important mainstays of the evaluation of hypotony. IOP should be checked by a reliable and accurate method, like Goldmann applanation tonometry. However, false elevations of IOP can occur when the lens contacts the cornea during applanation.[1] Slit lamp examination should include evaluation of trabeculectomy blebs. Seidel testing must be done to test for a leak. However, false negative results occur in slow or intermittent leaks and pressing on the globe may

be necessary.[1] Gonioscopy is utilized to examine for a cyclodialysis cleft and if unsuccessful, other methods like anterior segment OCT or ultrasound biomicroscopy should be utilized.

- OCT for evaluation of retinal and choroidal architecture changes
- B-scan ultrasound for ciliochoroidal effusion
- Ultrasound biomicroscopy or anterior segment OCT for evaluation of angles (if gonioscopy unsuccessful)

Treatment/Management/Guidelines

There are many approaches to the treatment of hypotony and should be tailored to the etiology. In general, it is difficult to increase the IOP. Medications like sodium azide, sodium nitroprusside, cation ionophores, and parasympathetic medications increase IOP, but are too toxic for clinical use.[3] Topical corticosteroids can be introduced, especially in inflammatory etiologies to increase both production of aqueous and create a steroid-induced IOP increase.[3] Atropine can also be used to deepen the anterior chamber and reduce the contact between the iris and cornea.

A recent Cochrane review of interventions of late trabeculectomy bleb leak found no evidence of comparative effectiveness except for one randomized controlled trial which found superiority of conjunctiva advancement technique in sealing leaks compared to amniotic membrane transplant.[8] Other approaches include fibrin glue, autologous blood, cryotherapy, conjunctiva compression sutures, bandage contact lens, Simmons shell, or laser grid treatment.[3, 8] Leaks should be evaluated carefully and treated due to the risk of endophthalmitis. If early after surgery, sometimes pressure patching or aqueous suppressants are enough to allow the epithelium to seal the defect.[1, 3]

Overfiltering blebs can be treated with pressure patches, wound revision, blood injection, trichloroacetic acid, stopping corticosteroids, or tightening the scleral flap with sutures.[1] The trabeculectomy site can also be revised with bleb excision and placement of a full thickness scleral patch graft. In case reports, this approach achieved rapid return of visual acuity, reformation of the filtering bleb, and IOP control without medication.[9] A cyclodialysis cleft can sometimes be closed with laser treatment or can be surgically sutured.[1, 6] Retinal detachments should be repaired surgically. Ciliochoroidal effusions will often spontaneously resolve as the IOP improves, but can be treated with corticosteroids and anticholinergic eye drops.[1] If the ciliochoroidal effusion is large or touching the midline, surgical drainage should be considered.[1]

EPIDEMIOLOGY OR ETIOLOGY	SIGNS
- Overfiltering bleb - Inadvertent bleb (surgical or trauma) - Leaking bleb - Cyclodialysis cleft (trauma or surgical) - Retinal detachment - Retinal vascular occlusion - Inflammation	- Decreased IOP - Corneal/Descemet folds - Astigmatism - Corneal edema - Shallow/flat anterior chamber - Associated signs of ciliochoroidal effusions, suprachoroidal hemorrhage, optic nerve head edema, hypotony maculopathy
SYMPTOMS	TREATMENT/ MANAGEMENT
- Asymptomatic - Decreased visual acuity - Pain	- Varies by etiology - Observation acceptable in some cases - Surgical revision - Autologous blood injection - Fibrin glue - Laser (cyclodialysis cleft)

References

1. Alward WLM. Hypotony. *Iowa Glaucoma Curriculum Version 1.2*. E-published. 2016; Chapter 50, p. 347-355 (itun.es/us/MIXqcb.l OR curriculum.iowaglaucoma.org/)

2. Bowling B. Acquired macular disorders. In Bowling B (eds), *Kanski's Clinical Ophthalmology*, *8th edition.* Philadelphia. Elsevier; 2016; Chapter 14, p. 579-639.

3. Thygesen J. Late Hypotony. In Shaarawy TM, Sherwood MB, Hitchings RA, Cowston JG (eds), *Glaucoma*, 2nd edition. Philadelphia: Elsevier Saunders; 2015; Chapter 88, p. 863-881.

4. Zhou M, W Wang, W Huang, X Zhang. Trabeculectomy with versus without releasable sutures for glaucoma: a meta-analysis of randomized controlled trials. *BMC Ophthalmol* 2014;14(41):1-8. [PMID 24685235]

5. Yun S, Chua B, Clement CI. Does chronic hypotony following trabeculectomy represent treatment failure? *J Curr Glaucoma Pract* 2015;9(10):12-15. [PMID 26997826]

6. Gonzalez-Martin-Moro J, Contreras-Martin I, et al. Cyclodialysis: an update. *Int Ophthalmol* 2016; 37(2):441-457 [PMID 27392912]

7. Guthoff RF, Labriola LT, Stachs O. Diagnostic ophthalmic ultrasound. In Ryan SJ, Sadda SR (eds), *Retina, 5th edition*. Philadelphia: Elsevier Saunders; 2013; Chapter 9, p. 227-284.

8. Bochmann F, Azuara-Blanco A. Interventions for late trabeculectomy bleb leaks. *Cochrane Database Syst Rev*. 2012;9. ID CD006769. Available at dx.doi.org/10.1002/14651858.CD006769.pub2 [PMID 22972097]

9. Haynes WL, Alward WLM. Rapid visual recovery and long-term intraocular pressure control after donor scleral patch grafting for trabeculectomy-induced hypotony maculopathy. *J Glaucoma* 1995:4(3):200-201 [PMID 19920669]

Citing this article

Janson BJ, Kam JP, Alward WLM. Hypotony: Late hypotony from trabeculectomy and Ahmed seton with resulting hypotony maculopathy. EyeRounds.org. posted April 24, 2017; Available from: EyeRounds.org/cases/250-Hypotony.htm

last updated: 04/24/2017

Posner-Schlossman Syndrome (Glaucomatocyclitic Crisis)

Stephanie K. Lynch, MD, Lorraine M. Provencher, MD, Wallace L. M. Alward, MD

Posted August 25, 2016

History of Present Illness (HPI)

A 63-year-old male was evaluated on an urgent basis for pain, redness, and "elevated eye pressure" in the left eye. He described a history of three similar episodes in his left eye, in which he had the same symptoms and his eye pressure was elevated. His first episode occurred approximately 20 years ago (1980s), and at that time, he was diagnosed with acute angle-closure glaucoma (AACG) and treated with a large surgical iridectomy by an outside provider. Review of previous intraocular pressure (IOP) measurements showed an IOP spike to 54 mmHg in 2004 and 54 mmHg again in 2014. Left eye IOP ranged from 11 to 15 in between the episodes of high IOP. He has not required IOP-lowering medications in between episodes.

He denied any history of cold sores, shingles, or other rash. The episodes of pain and high pressure have not been preceded by or accompanied by systemic symptoms or illness.

Past Ocular History

♦ Described above in HPI
♦ Multiple iris nevi, right eye

Family Ocular History

♦ Mother with glaucoma

Past Medical History

♦ Hyperlipidemia
♦ Esophagitis
♦ Allergic rhinitis

Medications

♦ No ocular medications
♦ Atorvastatin, omeprazole, fluticasone nasal spray

Social History

♦ Occupation: real estate appraisal
♦ Rare/occasional alcohol use
♦ Denies tobacco or illicit drug use

Review of Systems

♦ Negative except as stated in HPI

Physical Examination

Visual Acuity (with correction)

♦ 20/20 Right eye (**OD**)
♦ 20/20-2 Left eye (**OS**)

Pupils

♦ **OD**: 3 → 2, brisk, no relative afferent pupillary defect (RAPD)
♦ **OS**: 4 → 4, fixed, 1+ RAPD by reverse

Confrontation Visual Fields

♦ Full to counting fingers both eyes (**OU**)

Extraocular Motility

♦ Full **OU**

Intraocular Pressure (Goldmann applanation tonometry)

♦ **OD**: 20 mmHg
♦ **OS**: 53 mmHg

Pachymetry

♦ **OD**: 553 microns
♦ **OS**: 583 microns

Slit Lamp Examination

Right eye
♦ **Eyelids/lashes**: Normal
♦ **Conjunctiva/Sclera**: Clear and quiet
♦ **Cornea**: Clear
♦ **Anterior Chamber**: Deep and quiet
♦ **Iris**: Multiple small nevi inferotemporally, blue iris
♦ **Lens**: 1+ nuclear sclerosis

Left eye
♦ **Eyelids/lashes**: Normal
♦ **Conjunctiva/Sclera**: 1+ injection, nasal pinguecula
♦ **Cornea**: Trace diffuse microcystic edema, cluster of small keratic precipitates (KP) inferonasally
♦ **Anterior Chamber**: Deep, no flare, a single cell visible
♦ **Iris**: Patent superonasal surgical peripheral iridectomy (PI), mild irregularity of the pupil, blue iris
♦ **Lens**: 2+ nuclear sclerosis, mild pigment on the anterior lens capsule, posterior synechiae at 11 o'clock

Gonioscopy (Spaeth grading system)

- **OD:** D40 f 1+
- **OS:** D40 f 1+ with small area of peripheral anterior synechiae superiorly over the PI

Fundus Examination

OD

- **Vitreous**: Normal, no cell
- **Disc**: Healthy rim, no disc hemorrhages, cup-to-disc ratio: 0.3
- **Macula**: Normal
- **Vessels**: Normal

OS

- **Vitreous**: Normal, no cell
- **Disc**: Mild thinning of inferior rim, no disc hemorrhages, cup-to-disc ratio: 0.4
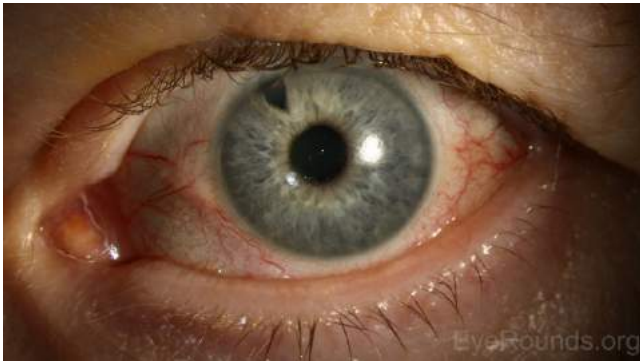- **Macula**: Normal
- **Vessels**: Normal

Figure 1: Slit lamp photograph of the left eye shows mild conjunctival injection. The pupil is irregular with posterior synechiae at 11 o'clock. The cornea is clear. The surgical PI is visible at 11 o'clock.

Figure 2: Slit lamp photograph of the left eye reveals a faint, small KP visible on the corneal endothelium (arrow).
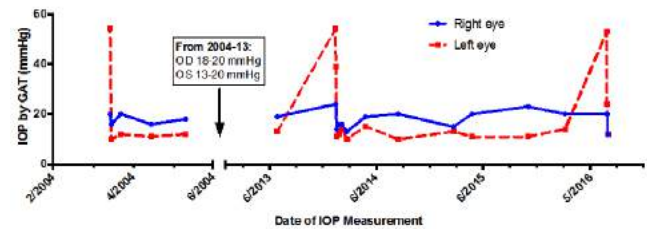
Figure 3: IOP for the patient over several decades with episodes of elevated IOP in 2004, 2014, and 2016. This graph is modeled after a graph by Posner and Schlossman (1948) [1].

Clinical Course

The patient presented with a history of multiple episodes of elevated IOP OS over a period of several decades. IOP returned to normal without medications between spikes (Figure 3). A local provider initially treated our patient for AACG with surgical PI. Given his deep/wide angles on gonioscopy OU, this acute elevation of IOP in the 1980s was likely misdiagnosed as AACG. Outside records surrounding this episode could not be obtained. Our records, which captured two of the past three episodes, indicate that the IOP spiked to the mid-50s with only mild concurrent inflammation. With the episode detailed above, there was again evidence of subtle inflammation, including mild conjunctival injection, faint KP, and trace anterior chamber inflammation.

There was no evidence that his high IOP and inflammation were due to herpes simplex virus (HSV) (i.e., no history of skin lesions, corneal dendrites, transillumination defects, ciliary flush, or decreased corneal sensation). He had previously tested negative for other causes of infectious/inflam-

matory uveitis, including syphilis, sarcoidosis, HLA-B27, tuberculosis, and Lyme disease. The presence of small peripheral anterior synechiae (PAS) was suggestive of prior inflammation. However, despite his history of recurrent episodes, he had very little sequelae of chronic inflammation. Although Fuchs' heterochromic iridocyclitis (FHI) is on the differential for recurrent unilateral inflammatory glaucoma, there was no iris heterochromia, iris transillumination defects, stellate KP, or fine angle neovascularization to suggest this diagnosis.

Humphrey 24-2 visual field testing from a routine follow-up visit five months prior indicated that the patient had a full visual field in both eyes. Cup-to-disc ratio was slightly larger on the left, and optical coherence tomography (OCT) of the retinal nerve fiber layer (RNFL) confirmed mild RNFL thinning and ganglion cell loss in the left eye only. On review of prior IOP records, the pressure in the left

eye appeared to range in the low teens to 20 in between episodes.

For acute management of the patient's elevated IOP, he received three rounds of brimonidine tartrate and timolol-dorzolamide (Cosopt®) every 15 minutes in addition to one dose of 500 mg oral acetazolamide. IOP decreased to 24 mmHg after several hours. Due to the subtle anterior segment inflammation, prednisolone acetate 1% was also started. The patient was instructed to continue timolol-dorzolamide (Cosopt®) twice daily (BID), brimonidine tartrate BID, and prednisolone four times daily OS. One week later, IOP OS had decreased to 12 mmHg. His prednisolone acetate 1% was tapered, and his IOP lowering medications were gradually stopped.

Diagnosis

Posner-Schlossman Syndrome

Discussion

Posner-Schlossman syndrome (PSS), also called glaucomatocyclitic crisis, is a rare inflammatory glaucoma that was first described in 1948 and affects individuals ages 20 to 60 [1]. PSS classically presents as recurrent episodes of unilateral, transient elevations in IOP, ranging in the 40s to 50s mmHg. The IOP elevation is typically out of proportion to the degree of pain and anterior chamber inflammation. IOP as high as 70 mmHg has been reported [2]. Vision loss occurs due to glaucomatous damage, which is thought to accumulate during episodes of markedly raised IOP.

Clinically, scant KP are seen; these may be referred to as "sentinel KPs." In our patient, the anterior chamber inflammation was minimal, and only a small cluster of KP was detected. Generally, peripheral anterior synechiae (PAS), and other severe sequelae of chronic uveitis, are not seen in PSS, unlike in other inflammatory glaucomas. Our patient was noted to have only a small area of PAS. Mild corneal edema due to elevated IOP may also be present on exam, as was noted with our patient.

Some evidence suggests that PSS may be associated with certain human leukocyte antigen (HLA) genes [3]. Several observational studies have investigated the association between PSS and active cytomegalovirus (CMV) infection in the anterior chamber [4-6]. Some uveitis specialists advocate treatment with valganciclovir both during attacks and between attacks as a prophylactic measure. However, a clear causal relationship between CMV infection and attacks of PSS has not been established. Other infectious associations have been proposed, including herpes simplex virus (HSV) [7], varicella zoster virus (VZV) [8], and Helicobacter pylori [9]. Unlike other inflammatory forms of glaucoma, the etiology of increased IOP in PSS cannot be explained completely by trabeculitis and/or inflammatory debris causing obstruction of the trabecular meshwork, as there is minimal anterior segment inflammation. Other explanations that have been postulated include alterations in vascular regulation or autonomic physiology [10-11]. Attacks may last up to several weeks, but they can also resolve within one day when properly treated.

Acute attacks of PSS are managed with IOP-lowering agents (topical +/- oral) as well as anti-inflammatory drops, such as prednisolone. Between episodes of PSS, the IOP is usually within a normal range. This characteristic helps distinguish PSS from other forms of inflammatory glaucoma that include subacute or chronically elevated IOP. The exception to this rule is that some patients with PSS may also have underlying primary open-angle glaucoma [12]. Current research has not clearly established whether treatment with IOP-lowering medications reduces the frequency of future glaucomatocyclic attacks.

In one retrospective case series of 50 patients diagnosed with PSS, the development of glaucomatous visual field changes and optic neuropathy was proportional to the duration of disease [2]. Therefore, patients with PSS should be followed, at minimum, on an annual basis even if their attacks occur on a less frequent basis.

For more photographs and videos, please visit the chapter from the **Iowa Glaucoma Curriculum** on glaucomatocyclic crisis {https://curriculum.iowaglaucoma.org/chapter/24}

EPIDEMIOLOGY	SIGNS
♦ Rare ♦ Most common in the middle decades (30 - 60 years old) ♦ Possible association with CMV virus	♦ Elevated intraocular pressure (30 - 70 mmHg) ♦ Mild conjunctival injection ♦ Scant keratic precipitates ♦ Trace inflammation (cell and flare)
SYMPTOMS	TREATMENT
♦ Decreased vision ♦ Discomfort or pain (brow ache) ♦ Mild injection	♦ Aqueous suppressants during the acute episode ♦ Topical corticosteroids, then taper ♦ Long-term follow-up - important for all patients

Differential Diagnosis for Posner-Schlossman Syndrome

♦ Fuchs heterochromic iridocyclitis https://curriculum.iowaglaucoma.org/chapter/25
♦ Herpetic keratouveitis
♦ Uveitic glaucoma https://curriculum.iowaglaucoma.org/chapter/23
♦ Acute angle-closure glaucoma https://curriculum.iowaglaucoma.org/chapter/17
♦ Chronic angle-closure glaucoma
♦ Primary open-angle glaucoma https://curriculum.iowaglaucoma.org/chapter/14

References

1. Posner A, Schlossman A. Syndrome of unilateral recurrent attacks of glaucoma with cyclitic symptoms. Arch Ophthalmol 1948; 39:517-520.

2. Jap A, Sivakumar M, Chee SP. Is Posner Schlossman syndrome benign? Ophthalmol 2001; 108(5):913-918.

3. Hirose S, Ohno S, Matsuda H. HLA-Bw54 and glaucomatocyclitic crisis. Arch Ophthalmol 1985; 103(12):1837-1839.

4. Chee SP, Bacsal K, Jap A, et al. Clinical features of cytomegalovirus anterior uveitis in immunocompetent patients. Am J Ophthalmol. 2008; 145:834-840.

5. Chee SP, Jap A. Presumed Fuchs heterochromic iridocyclitis and Posner-Schlossman syndrome: comparison of cytomegalovirus-positive and negative eyes. Am J Ophthalmol 2008; 146:883-889.

6. Rodier-Bonifas C, Cornut PL, Billaud G, et al. Cytomegalovirus research using polymerase chain reaction in Posner-Schlossman syndrome. J Fr Ophthalmol 2011; 34:24-29.

7. Yamamoto S, Pavan-Langston D, Tada R, et al. Possible role of herpes simplex virus in the origin of Posner-Schlossman syndrome. Am J Ophthalmol 1995; 119:796-798.

8. Tanaka Y, Harino S, Hara J. Cellular immunity as judged by varicella skin test in Posner-Schlossman syndrome in patients. Folia Jpn 1985; 36:972-976.

9. Choi CY, Kim MS, Kim JM, et al. Association between Helicobacter pylori infection and Posner-Schlossman syndrome. Eye (Lond) 2010; 24(1):64-69.

10. Raitta C, Vannas A. Glaucomatocyclitic Crisis. Arch Ophthalmol 1977; 95(4):608-612.

11. Puri P Verma D. Bilateral glaucomatocyclitic crisis in a patient with Holmes Adie syndrome. J Postgrad Med 1998; 44(3):76-77.

12. Kass MA, Becker B, Kolker AE. Glaucomatocyclitic crisis and primary open-angle glaucoma. Am J Ophthalmol 1973; 75(4):668-673.

Citing this article

Case Presentations

Neuro-Ophthalmology

Functional Visual Loss

John J Chen, MD, PhD and Yanjun (Judy) Chen, MD, PhD

March 6, 2013

Chief complaint: "I can't see anything."

History of Present Illness: A 37-year-old male presented with decreased vision for the past 10-15 years, which had been progressively worsening over the past year. The patient was referred by his local optometrist because he could not read any of the letters on the chart and showed no improvement with refraction. He was referred for visual loss with a high suspicion for functional visual loss.

Past Ocular History: None

Past Medical History: Mild mental retardation and developmental delay, schizophrenia

Medications: Olanzapine

Allergies: None

Family History: Non-contributory

Social History: Disabled, semi-independent living. He denied alcohol or tobacco use.

Review of systems: As above, otherwise negative

Ocular exam

Visual Acuity

- Right eye (OD): Hand motion
- Left eye (OS): Hand motion
    - Despite claiming hand motion vision, he was able to check boxes on a questionnaire sheet. In addition, he was able to ambulate in an unfamiliar environment without difficulty.
    - On formal testing, he claimed that he was unable to see the optokinetic drum. However, he had appropriate nystagmus to the optokinetic drum.
    - He saw two eye charts with a vertical prism placed over one eye.

Pupils: 5→3, no Relative Afferent Pupillary Defect (RAPD), both eyes (OU)

Extraocular movements: Full

Confrontation visual fields: Unable to count fingers, but able to track objects placed in all four quadrants.

Intra-ocular pressure

- OD: 10 mmHg
- OS: 17 mmHg (squeezing)

External: Normal

Slit Lamp Exam: Unremarkable except mild para-central thinning of the cornea in both eyes.

Dilated Fundus Exam

Normal appearing optic nerves with cup-to-disc ratio of 0.2 in both eyes. The maculae were normal. The vessels and peripheral retina were normal.

Retinoscopy was performed given that the evaluation of subjective visual function was unreliable. The retinoscopy exam revealed an irregular reflex with scissoring in both eyes. This finding raised a suspicion of corneal irregularity as the cause of the decreased vision. Corneal topography showed asymmetric inferior steepening consistent with keratoconus or pellucid marginal degeneration (Figure 1).

We were unable to perform a manifest refraction because he stated that things were blurred and refused to acknowledge counting fingers. However, when we gave him a trial frame with the estimated refraction from the corneal topography, he was very satisfied with the outcome. He said he was seeing the best that he had in years. Although his best visual outcome would likely be achieved by the use of rigid gas permeable contact lenses due to his underlying keratoconus, he would be a poor candidate for this option due to his inability to manage contact lenses. Providing astigmatic correction with glasses appeared to have improved his visual acuity and will remain a viable treatment option.

Diagnosis: Keratoconus masked by functional overlay.

Although there was clear functional overlay, the patient had true ocular pathology causing decreased vision. This case was challenging in that the reliability of the visual function testing was limited by his decreased mental capacity and poor cooperation. It would be easy to ignore his complaints of blurred vision because of the obvious discordance between his behavior and expressed visual capacities; although his visual acuity was measured hand motion, he clearly demonstrated ability to ambulate through unfamiliar territory, shake hands, and touch the examiner's finger reliably in various positions.

Keratoconus appeared to contribute to the visual decline, based on ocular exam findings of paracentral corneal thinning and irregular retinoscopic reflex, as well as corneal topography finding of asymmetric steepening inferiorly.

Discussion

Functional visual loss refers to a decrease in visual acuity or loss of visual field with no underlying physiologic or organic basis. Patients with functional visual loss make up 1-5% of the referrals to ophthalmologists.[1,2] The highest incidence occurs in 11-20-year-old patients with a female predominance (63%).[3] The average workup for a patient
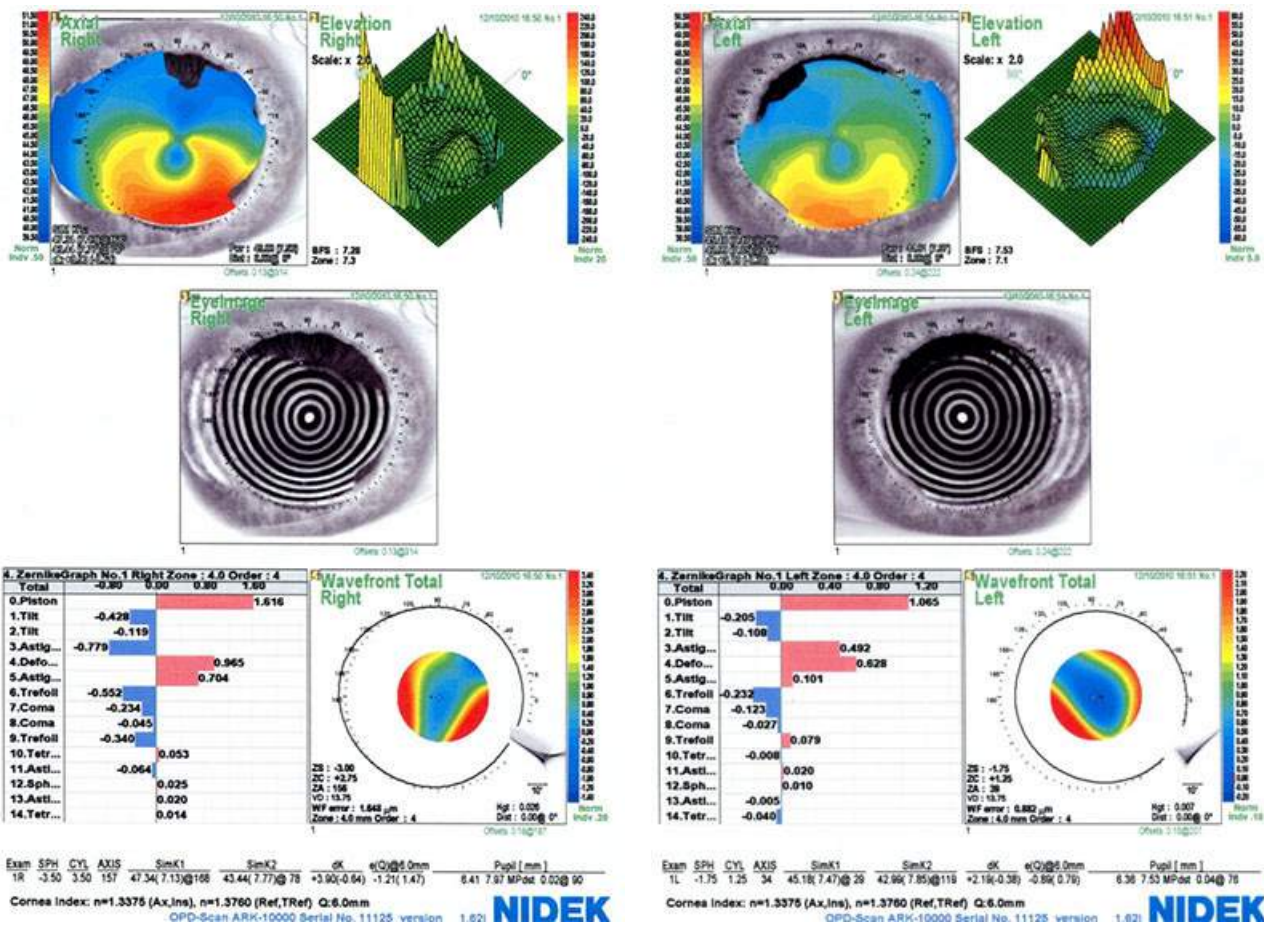
Right eye

Left Eye

Figure 1. Corneal topography showing asymmetric inferior steepening consistent with keratoconus or pellucid marginal degeneration

with functional visual loss is greater than $500 and likely millions of dollars are spent on fraudulent disability claims. [4] A thorough clinical examination can avoid unnecessary investigations and disability expenditures, therefore saving society money as a whole.

First and foremost, the diagnosis of functional or non-organic visual loss is one of exclusion. There is often an underlying true organic visual problem that is masked by functional complaints, and the main goal of any examination is to find the kernel of truth. Functional visual loss can be seen in a variety of patients. There can be a conscious purposeful report of decreased vision in malingering patients, such as patients seeking disability or monetary gain. A nonorganic report of decreased vision can also be part of a somatization disorder. Regardless of the etiology, it is important to have a repertoire of tests to differentiate true functional visual loss from organic visual loss. The approach and tests performed depends on the patient's complaint and can be broken down into two broad categories: decrease in visual acuity and loss of visual field. These can be further stratified between monocular or binocular visual loss and the degree of visual impairment.

Binocular blindness

♦ **Nonvisual tasks**

o The examination starts as the patient walks into the room, observing his ability to navigate to the chair and to shake hands. Appearance and demeanor of the patient can also contribute. For instance, it was shown that patients wearing sunglasses to a tertiary neuro-ophthalmology practice were more likely to have functional visual loss.[5]

o **Fingertip touching:** A patient with true binocular blindness can still touch their index fingers of opposite hands together because this task is based on proprioception and not visual cues. Patients with functional binocular blindness will often claim they are unable to do this.

o **Sign signature**: Same principal as fingertip touching. This can be done in a patient with true binocular blindness.

♦ **Mirror test**

o If the vision is at least light perception, moving a mirror in different angles will result in non-suppressible nystagmoid movements as the eyes follow the moving reflections.

- o Sudden unannounced placement of a mirror in front of the patient may lead to accommodation, convergence, and miosis as the patient focuses on the image of themselves.
- ♦ **Optokinetic nystagmus drum:** Induced jerk nystagmus indicates at least 20/400 vision.
1. **Shock value test**: These include a variety of tests including the menace reflex where the examiner presents visual threats such as a closed fist and observes for blinking or flinching. The examiner can also suddenly drop an object to see if a patient will reflexively react.

Monocular blindness or visual impairment

- ♦ **Relative afferent pupillary defect (RAPD):** This is the most important objective test that can be performed if the patient claims to have a large difference in visual acuity between the two eyes. If there is no refractive error or media opacity causing the disparity in acuity, a RAPD will likely be present in the affected eye if there is true pathology.
- ♦ **Fogging test**
  - o This can be done by placing a plus lens (≥+5.00D over the normal refractive correction) in front of the good/unaffected eye and a lens with minimal power over the affected eye. The patient is then asked to read the chart with both eyes. The patient may not realize that the unaffected eye is fogged and a patient with functional monocular visual loss often reads well with the "affected" eye.
  - o Paired cylinders can also be used. A plus cylinder and a minus cylinder of the same power are placed in parallel in front of the good/unaffected eye. While the patient reads the chart, the axis on one cylinder is rotated 10-15 degrees to fog the good/unaffected eye. If the patient continues to read the chart successfully, they are revealing adequate vision in the "affected" eye.
- ♦ **Titmus stereopsis test:** Stereopsis requires binocular vision. Ability to see 9/9 circles requires 20/20 vision in both eyes. Visual acuity can be estimated based on stereopsis (see Table 1).

Table 1: Relationship of visual acuity and stereopsis

Visual acuity	Average Stereopsis (seconds of arc)	Titmus stereopsis
20/20	40	9/9 circles
20/25	43	8/9 circles
20/30	52	8/9 circles
20/40	61	7/9 circles
20/50	78	6/7 circles
20/70	94	5/9 circles
20/100	124	3/3 animals or 4/9 circles
20/200	160	3/9 circles or 2/3 animals

-Modified from [7]

- ♦ **Prism tests**
  - o **Base-out prism test:** A 10-prism diopter lens placed base-out in front of one eye should normally elicit a movement of both eyes toward the direction of the apex of the prism followed by a shift of the fellow eye back toward the center. A true loss of monocular vision will not result in conjugate movement when the prism is placed over the affected eye.
  - o **Vertical prism dissociation test**: A 4-prism diopter lens is placed base-down in front of the good/unaffected eye. A 20/20 or larger size Snellen is projected. If the patient is able to see two letters of equal clarity, it establishes good vision in the affected eye.[6]
- ♦ **Red-Green duochrome test**: The patient is given red-green glasses with the red lens over the affected eye. The patient is asked to read the red-green duochrome chart with both eyes. The eye behind the red lens is able to see letters on both sides of the chart, whereas the eye behind the green lens can only see letters on the green side of the chart. If the patient is able to read all of the letters, this demonstrates that the affected eye is able to read the letters displayed.
- ♦ **Color plate test**: The patient is given red-green glasses with the red lens over the affected eye. The Ishihara plates cannot be seen by the eye with the green filter. Ability to read the colors indicates at least 20/400 vision in the affected eye.
- ♦ **Cycloplegic test:** For younger patients with the ability to accommodate, a cycloplegic test can be used. Place tropicaimide in only the good eye and saline in the affected eye. After accommodation is paralyzed, check the patient's visual acuity at near with both eyes open. The patient may not realize that they are only reading with the affected eye and may demonstrate good near visual acuity.
  - o Caveat: high myopes will still have good near vision after cycloplegia.

Bilateral visual impairment

- ♦ **Bottom-up visual acuity testing:** Begin with the smallest line (20/10 if available). Progressively increase the size saying that the size is "doubled" in size and express astonishment that the letters cannot be seen. This can often uncover better visual acuity than top-down visual acuity testing in patients with functional vision loss.
- ♦ **"Vision aids":** The patient is given trial frames with four lenses equaling the correct prescription and told that the lenses are special magnifying lenses. This may lead to improvement in visual acuity indicating a nonorganic component.
- ♦ **Near vision testing**: A large discrepancy between near-visual acuity and distance acuity provides evidence of nonorganic disease.
- ♦ **Stereopsis**: see above. As mentioned above, this also can provide an assessment of visual acuity (Table 1).
- ♦ **Size consistency test**: Evaluate a patient's ability to read the Snellen chart at 20 feet and then at 10 feet. The

patient should be able to read letters half the size of the letters read at the full distance. A patient with functional visual loss will often not admit to being able to read the smaller optotypes regardless of the proximity to the target.

Visual field loss

♦ **Saccade test:** Test saccadic eye movements into the reported absent portion of the field. A patient with nonorganic visual field loss may demonstrate accurate saccades to targets in the "nonseeing" field because they are assuming eye movements and not visual fields are being tested.

♦ **Confrontation testing**
  o The examiner asks the patient to count fingers in the "non-seeing" field and instructs to report "none" when none are seen. As the test progresses, the examiner changes to showing fingers silently. A patient response of "none" when the fingers are silently displayed in the "non-seeing" field confirms vision in that area.

♦ **Monocular and binocular visual field testing:** If the patient reports a monocular visual field defect, the visual field test can be repeated with both eyes open. If the field defect is still present under binocular testing, the monocular defect can be assumed nonorganic. This can be done with confrontation visual field testing or with formal evaluation such as Humphrey or Goldmann visual field testing.

♦ **Goldmann visual field testing:** Nonorganic visual fields often demonstrate a spiraling field that becomes smaller as the test object is moved around the field. Crossing isopters or a visual field that remains the same size regardless of the size or brightness of the test stimulus (yielding isopters nearly one on top of another) is also often seen in functional visual field loss.

♦ **Tangent screen**: A tangent screen test can be performed at two different distances from the screen (usually 1 and 2 meters) while maintaining the same ratio of target size to target distance (i.e., larger target at further distance). A patient with organically constricted visual fields will show an increase in the size of the visual field when moved to a farther distance while a patient with functional visual field loss will often report the same absolute size of the field (tubular or gun-barrel field).
  o A nonorganic tubular visual field can also be elicited with repeated confrontation visual field testing at 1 meter and at 2 meters from the patient.

Other tests

In addition to the above examination techniques, retinal imaging and electrophysiological testing can be helpful in elucidating functional vision loss from true organic vision loss. Optical coherence tomography can help identify optic nerve and retinal pathology.[8] In addition, fundus autofluorescence is very sensitive in detecting subtle macular pathology.[9] Multifocal electroretinogram is able to detect focal problems of the rods and/or cones within the macula, although responses can be voluntarily suppressed.

[10,11] Visually evoked potentials, which measure the speed of signal from the optic nerve to the occipital cortex, can also be helpful in some circumstances in differentiating nonorganic vision loss from true pathology.[12-15]

Management

Reassurance alone is the best treatment. Providing non-specific treatments, like glasses or eyedrops, provides a mixed message to the patient and is less effective than reassurance alone.[16,17] It is important to stress a good prognosis, which provides "a way out" and gives the patient the opportunity to recover.[18] Confrontation is rarely helpful.[19] Between 45% and 78% of patients will experience resolution of their visual symptoms with reassurance alone.[3,18,20,21] However, some patients will continue to have persistent functional visual loss, especially in patients with co-existing psychiatric disease or in patients with motivation for material secondary gain. Adults are more likely to have underlying psychiatric illness compared to children. Concomitant psychosocial stressors are more likely in children, while adults often develop functional visual loss after trauma.[3]

Once functional visual loss is diagnosed, it is important to schedule at least one follow-up appointment to maintain a rapport with the patient and also to ensure that there is no organic disease underlying the symptoms. It is estimated that approximately 2% of patients with a diagnosis of functional visual loss have true organic disease.[3] Common masqueraders include keratoconus, cone dystrophy, Stargardt disease, amblyopia, paraneoplastic syndromes, small occipital infarcts, and acute zonal occult outer retinopathy.

Diagnosing functional visual loss is an important skill that can begin the healing process for the functional patient. Using the appropriate clinical tests can obviate the need to perform expensive investigations, such as magnetic resonance imaging, and avoid false disability expenditures, therefore saving society money as a whole.

Differential Diagnosis

True organic disease, commonly keratoconus, cone dystrophy, Stargardt disease, amblyopia, paraneoplastic syndromes, small occipital infarcts, and acute zonal occult outer retinopathy.

Epidemiology	*Symptoms*
♦ 1-5% of referrals to ophthalmologists. ♦ Highest proportion in 11-20-year-old patients, but can occur at any age. ♦ 63% female	♦ Binocular or monocular decreased vision and/or visual field loss
Signs	*Treatment*
♦ See above for clinical tests	♦ Reassurance with appropriate follow-up

References

1. Bose S, Kupersmith MJ. Neuro-ophthalmologic presentations of functional visual disorders. *Neurol Clin* 1995;13(2):321-3

2. Schlaegel TF, Jr., Quilala FV. Hysterical amblyopia; statistical analysis of forty-two cases found in a survey of eight hundred unselected eye patients at a state medical center. *AMA Arch Ophthalmol* 1955;54(6):875-84.

3. Lim SA, Siatkowski RM, Farris BK. Functional visual loss in adults and children patient characteristics, management, and outcomes. *Ophthalmology* 2005;112(10):1821-8.

4. Keltner JL, May WN, Johnson CA, Post RB. The California syndrome. Functional visual complaints with potential economic impact. *Ophthalmology* 1985;92(3):427-35.

5. Bengtzen R, Woodward M, Lynn MJ, Newman NJ, Biousse V. The "sunglasses sign" predicts nonorganic visual loss in neuro-ophthalmologic practice. *Neurology* 2008;70(3):218-21.

6. Golnik KC, Lee AG, Eggenberger ER. The monocular vertical prism dissociation test. *Am J Ophthalmol* 2004;137(1):135-7.

7. Levy NS, Glick EB. Stereoscopic perception and Snellen visual acuity. *Am J Ophthalmol* 1974;78(4):722-4.

8. Sakata LM, Deleon-Ortega J, Sakata V, Girkin CA. Optical coherence tomography of the retina and optic nerve - a review. *Clin Experiment Ophthalmol* 2009;37(1):90-9.

9. Schmitz-Valckenberg S, Holz FG, Bird AC, Spaide RF. Fundus autofluorescence imaging: review and perspectives. *Retina* 2008;28(3):385-409.

10. Lai TY, Chan WM, Lai RY, Ngai JW, Li H, Lam DS. The clinical applications of multifocal electroretinography: a systematic review. *Surv Ophthalmol* 2007;52(1):61-96.

11. Vrabec TR, Affel EL, Gaughan JP, Foroozan R, Tennant MT, Klancnik JM, Jr., et al. Voluntary suppression of the multifocal electroretinogram. *Ophthalmology* 2004;111(1):169-76.

12. Bobak P, Khanna P, Goodwin J, Brigell M. Pattern visual evoked potentials in cases of ambiguous acuity loss. *Doc Ophthalmol* 1993;85(2):185-92.

13. Gundogan FC, Sobaci G, Bayer A. Pattern visual evoked potentials in the assessment of visual acuity in malingering. *Ophthalmology* 2007;114(12):2332-7.

14. Leavitt JA. Diagnosis and management of functional visual deficits. *Curr Treat Options Neurol* 2006;8(1):45-51.

15. Rover J, Bach M. Pattern electroretinogram plus visual evoked potential: a decisive test in patients suspected of malingering. *Doc Ophthalmol* 1987;66(3):245-51.

16. Kathol RG, Cox TA, Corbett JJ, Thompson HS. Functional visual loss. Follow-up of 42 cases. *Arch Ophthalmol* 1983;101(5):729-35.

17. Thompson HS. Functional visual loss. *Am J Ophthalmol* 1985;100(1):209-13.

18. Chen CS, Lee AW, Karagiannis A, Crompton JL, Selva D. Practical clinical approaches to functional visual loss. *J Clin Neurosci* 2007;14(1):1-7.

19. Gross MP, Sloan SH. Patients with eye symptoms and no organic illness: an interdisciplinary study. *Psychiatry Med* 1971;2(4):298-307.

20. Kathol RG, Cox TA, Corbett JJ, Thompson HS, Clancy J. Functional visual loss: II. Psychiatric aspects in 42 patients followed for 4 years. *Psychol Med* 1983;13(2):315-24.

21. Sletteberg O, Bertelsen T, Hovding G. The prognosis of patients with hysterical visual impairment. *Acta Ophthalmol (Copenh)* 1989;67(2):159-63.

Citing this article

Ocular Tilt Reaction

53-year-old female complaining of vertical diplopia following a stroke and found to have a skew deviation, fundus torsion, and torticollis

Christopher A. Kirkpatrick MD; Matthew J. Thurtell MBBS, MSc

December 31, 2014

Chief Complaint: "Double vision"

History of Present Illness

A 53-year-old female presents as a referral from her neurosurgeon with a complaint of double vision. It was acute in onset, painless, and first noticed two weeks prior, immediately upon awakening from a cerebral angiogram with aneurysm stenting and coiling. She has a history of a dissecting left posterior cerebral artery (PCA) aneurysm and underwent coil embolization 5 months prior to presentation. Unfortunately, only 80% of the aneurysm was coiled, which led to her repeat cerebral angiogram with stenting and re-coiling of the remaining aneurysm. The procedure was complicated by decreased flow in several of the posterior circulation arteries, a small thrombus at the origin of the left PCA, and a complicated deployment of the pipeline stent. Following the procedure, she was noted to have a deteriorating neurologic status and an MRI was obtained that showed multiple subacute infarcts in the bilateral thalami, right occipital pole, right paramedian midbrain, cerebellar vermis, and both cerebellar hemispheres (Figure 1).

She complains of binocular diplopia that is vertical in nature. It has been constant and non-progressive since the onset. It is relieved with closing of either eye. The diplopia is unchanged in any particular gaze direction or head positioning and is similar for both distance and near.

Past Ocular History

♦ Refractive error and presbyopia for which she wears bifocal glasses
♦ No prior eye surgery or trauma
♦ No history of childhood strabismus

Past Medical History

♦ Left PCA aneurysm (as above)
♦ Breast cancer status post bilateral mastectomy with subsequent breast reconstruction
♦ Osteoarthritis status post right total hip replacement
♦ Hypertension
♦ Hyperlipidemia
♦ Anxiety

Medications

♦ Alprazolam   ♦ Clopidogrel
♦ Anastrozole   ♦ Quinapril
♦ Aspirin   ♦ Simvastatin
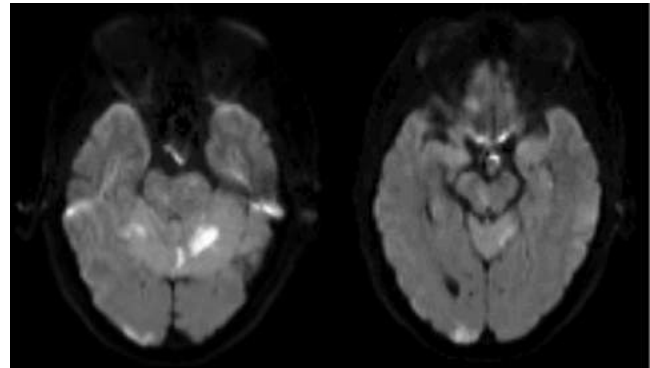
Figure 1: MRI axial diffusion-weighted imaging (DWI) showing hyperintensity (diffusion restriction) in the cerebellum, right occipital lobe, and right paramedian midbrain.

Family History

♦ Non-contributory

Social History

♦ She endorses very rare alcohol consumption and denies any current or past tobacco or illicit drug use.

Review of Systems

♦ She specifically denies noticing any ptosis, anisocoria, or loss of peripheral vision.

Ocular Exam

Visual Acuity (with correction)

♦ Right eye (OD): 20/25
♦ Left eye (OS): 20/25

Pupils

Both eyes (OU): 3 mm in dark, 2 mm in light, no relative afferent pupillary defect (RAPD)

Intraocular Pressure (IOP)

♦ OD: 11 mmHg
♦ OS: 12 mmHg

Confrontation Visual Fields

♦ Full OU

Motility

♦ Full OU

Alignment (Figure 2)

♦ Alternate head position: right head tilt
♦ A 7-8 prism diopter comitant left hypertropia
♦ 5 degrees of excyclotorsion OD and 7 degrees of incyclotorsion OS on double Maddox rod testing

Slit Lamp Exam

♦ External/Lids/Lashes: Normal OU
♦ Conjunctiva/Sclera: Clear and quiet OU
♦ Cornea: Clear OU
♦ Anterior Chamber: Deep and quiet OU
♦ Iris: Normal OU
♦ Lens: 1+ nuclear sclerosis OU

Figure 2: The patient had a very small angle, comitant left hypertropia (LHT). She adopted a compensatory right head tilt (not shown) and there was 5 degrees of excyclotorsion OD and 7 degrees of incyclotorsion OS with double Maddox rod (DMR) testing (see Figure 3). The alignment did not improve with earth neutral positioning.

Dilated Fundus Exam (Figure 3)

♦ Excyclotorsion OD and incyclotorsion OS
♦ Vitreous: Normal OU
♦ Disc: Normal OU
♦ Cup to Disc Ratio: 0.2 OU
♦ Macula: Normal OU
♦ Vessels: Normal OU
♦ Periphery: Normal OU

Diagnosis

Right ocular tilt reaction – skew deviation, fundus torsion, and torticollis, secondary to posterior circulation infarction

Clinical Course

The patient was able to achieve sensory fusion with 7 prism diopters of base down prism over her left eye. A Fresnel prism of this strength was placed on the left lens of her glasses. Given the comitant nature of her deviation, she was able to fuse well in all directions of gaze. She was scheduled to follow-up in the Neuro-ophthalmology clinic in 3 months time to assess for any change in her alignment or resolution of her diplopia.

DISCUSSION

A skew deviation is a vertical misalignment of the eyes that is caused by damage to the otolithic input to the ocular motor nuclei. When accompanied by binocular torsion, torticollis, and a tilt in the subjective visual vertical, it is termed the ocular tilt reaction. Lesions causing this are classically localized to the posterior fossa and can be from a variety of causes, but are many times a result of an acute lesion, such as ischemic stroke, demyelination, trauma, iatrogenic/post-surgical, hemorrhage, or tumor affecting the brainstem, cerebellum, or vestibular structures or pathways. It is thought that the ocular tilt reaction is likely
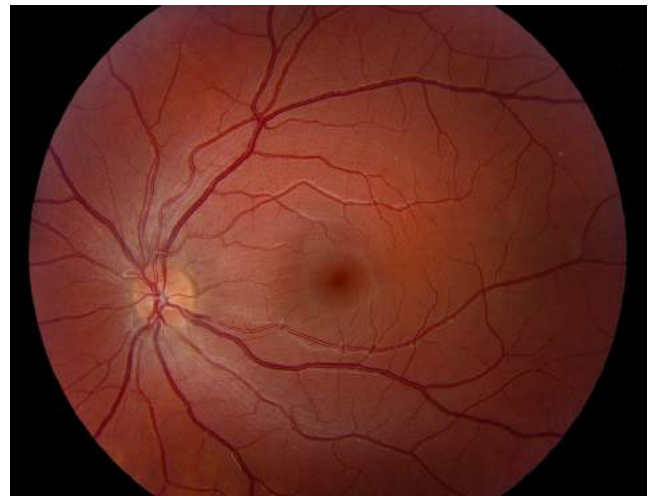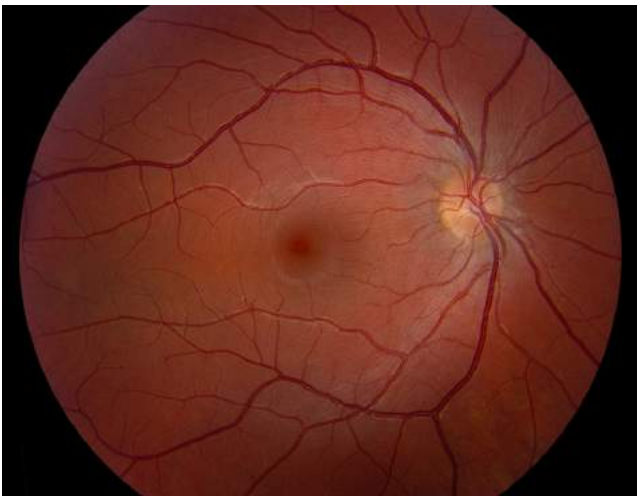

Figure 3: Excyclotorsion OD and incyclotorsion OS

a vestigial remnant of the primitive otolithic righting reflex that is tonically suppressed under normal physiologic conditions in frontal-eyed species (i.e., humans) in the interest of single binocular vision and only becomes manifest in the presence of pathology.

Pathophysiology

The vestibular system plays a major role in control of head-eye posture in the roll plane – the plane in which the head or body tilt or rotate from side to side. The vestibulo-ocular system has a primary function to maintain eye position and stabilize fixation during movements of the head or whole body in this plane. In the labyrinth of the inner ear, the semi-circular canals sense angular acceleration while the otoliths (saccules and utricles) sense linear acceleration of the head in space. Bilateral input from these structures projects to the central vestibular system that in-turn modulates extraocular muscle tone (via the vestibulo-ocular reflex) to maintain eye position and stable foveation during changes in head position. Input from this system also plays a role in spatial perception and in postural tonus of the head and body (via the vestibulo-spinal reflex).

Under normal physiologic conditions, a change in head or body position in the roll plane initiates asymmetric sensory input from the vertical semicircular canals and utricle to the central vestibular system as a response. For example, consider a leftward body tilt in the roll plane (Figure 4). Physiologically, this would initiate a compensatory rightward ocular tilt reaction. If the body is tilted to the left, it causes the left eye to be lower in space than the right. The compensatory skew deviation will cause subsequent upward rotation of the lowermost left eye and downward rotation of the uppermost right eye to realign them. Also, when the body is tilted to the left, there is a torsional deviation of both eyes toward the left. The compensatory ocular counter-roll results in incyclotorsion of the left eye and excyclotorsion of the right eye relative to the head, so that there is no torsion of the eyes relative to space. The third component of the physiologic ocular tilt reaction is the compensatory head tilt or torticollis that will more closely realign the head with the gravitational vertical. In the example of a leftward body tilt in the roll plane, this will result in a compensatory rightward head tilt.

In a pathologic ocular tilt reaction, a unilateral lesion (or stimulation) of the utricle or its pathways will result in asymmetric vestibular input to the central nervous system (CNS) that mimics a change in body position in the roll plane as sensed by the CNS (Figure 4). This will result in two main findings: 1) an ocular tilt reaction in the absence of any true body tilt in the roll plane - this can be tonic or paroxysmal and can be a complete ocular tilt reaction or partial with only certain components becoming manifest (i.e., only a skew deviation or only synkinetic ocular torsion), and 2) a tilt in the subjective visual vertical – a perception by the patient that vertical orientation is different from what is true vertical. Patients are usually asymptomatic from this and do not perceive a tilt in their perception of the world until placed in artificial testing situations that eliminate external cues. Given that the ocular torsion is in
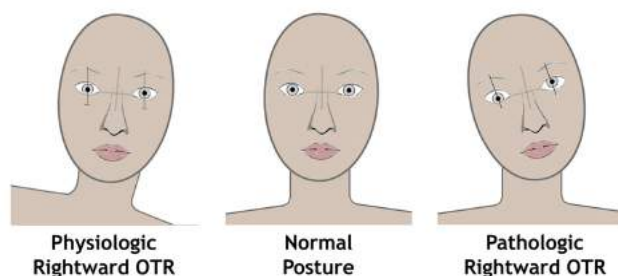

Figure 4: Left: A physiologic ocular tilt reaction (OTR) in response to a left body tilt in the roll plane – there is a compensatory right head tilt with downward rotation and excyclotorsion of the right eye and upward rotation and incyclotorsion of the left eye. Right: A pathologic OTR will have the same changes in head posture, eye position and rotation as the physiologic OTR in the absence of a change in body position in the roll plane to stimulate it. [adapted from 1]

the same direction as the patient's perception of vertical, it is thought that this may be the driving force for all components of the ocular tilt reaction – to realign the eyes and body with the subjective and CNS perception of true gravitational vertical.

Neuroanatomy and Localization

The otolithic and graviceptive pathways that mediate vestibular input and modulate the vestibulo-ocular reflex begin peripherally with sensory organs of the otoliths in the labyrinth of the inner ear and project to the ipsilateral vestibulocochlear nucleus (CN VIII) at the ponto-medullary junction via the vestibular portion of CN VIII (Figure 5). This pathway then decussates to the contralateral side at the level of the pons to ascend the brainstem in the medial longitudinal fasciculus (MLF) to the supranuclear centers for vertical-torsional eye movements in the rostral midbrain. The rostral interstitial nucleus of the medial longitudinal fasciculus (riMLF) contains the excitatory burst neurons that generate vertical and torsional saccades. The interstitial nucleus of Cajal (INC) contains the inhibitory burst neurons for vertical and torsional saccades and also acts as the neural integrator for vertical and torsional gaze holding; it likely plays a major role in producing the ocular tilt reaction. These nuclei send signals to the ocular motor nuclei (oculomotor nucleus (CN III), trochlear nucleus (CN IV) and abducens nucleus (CN VI)) that will in-turn modulate extraocular muscle tone and eye position.

Knowing the above anatomy of the pathway can help with localization of a causative lesion. For example, diminished input from the right utricle anywhere along the pathway will cause asymmetric vestibular input from the right and will result in the CNS perception that the head is being tilted to the left in the roll plane thereby producing a right ocular tilt reaction (Figure 5). The causative lesion will be ipsilateral if it is located caudal to the decussation of the otolithic pathway in the pons and will be contralateral if is located rostral to the decussation. For example, an ipsilateral ocular tilt reaction can occur with lesions of
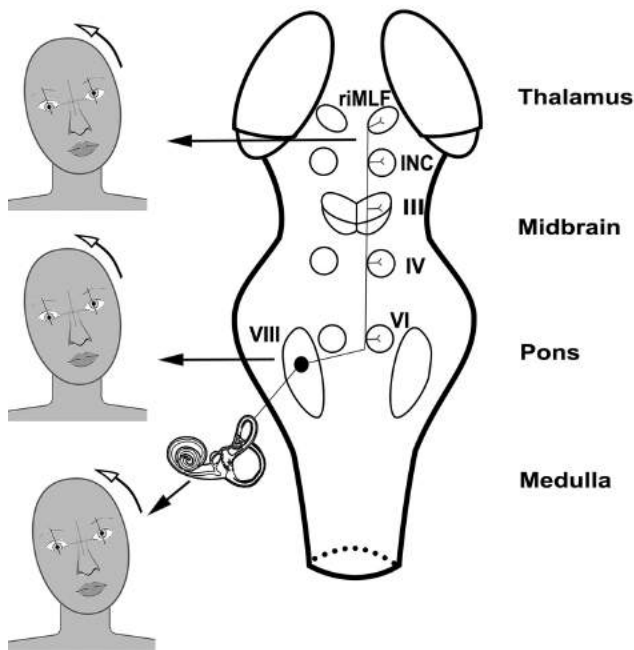
Figure 5: A schematic showing the pathway of vestibular input to the vestibulo-ocular reflex (VOR) (see Neuro-anatomy and Localization section in the article for more detailed information). Note that the schematic on the left is showing a right ocular tilt reaction resulting from an ipsilateral lesion of the pathway if it is caudal to the decussation in the pons or resulting from a contralateral lesion of the pathway if it is rostral to this decussation. [adapted from 3]

the utricle/labyrinth, vestibular nerve, or lateral medulla (i.e., in Wallenberg syndrome) that are all caudal to the decussation of the graviceptive pathway fibers in the pons; a contralateral ocular tilt reaction can occur with lesions that affect the rostral pons, MLF (i.e., in conjunction with internuclear ophthalmoplegia), the midbrain or INC (i.e., in dorsal midbrain syndrome) that are all rostral to the decussation of the graviceptive pathway fibers in the pons. There are a variety of etiologies that can affect these areas, but, as stated previously, stroke, demyelination, trauma, iatrogenic/post-surgical, and tumor are common etiologies. Furthermore, there are multiple otolithic projections to the cerebellum. Lesions of the cerebellum are also known to cause complete or partial ocular tilt reactions.

Presentation

Patients with lesions affecting the otolithic input to the ocular motor nuclei do not always present with the entire spectrum of the ocular tilt reaction (i.e., skew deviation, ocular torsion, and torticollis), but can present with variable components and severity of each. An isolated skew deviation typically presents as a fairly comitant, acquired, vertical misalignment of the eyes with a full range of extraocular movements. There is usually some degree of incyclotorsion of the hypertropic eye or excyclotorsion of the hypotropic eye (or both), which help differentiate it from CN IV palsy. These patients typically report vertical diplopia. There are variations of skew deviation including comitant, incomitant, paroxysmal, periodic alternating, lateral alternating, and transient neonatal that will not be discussed in this article. As discussed above, synkinetic cyclorotation of the eyes and a tilt in the subjective visual vertical may be asymptomatic to patients, and can easily be missed on examination unless specifically sought.

The direction of torsion of the eyes will be the same as the direction of the ocular tilt reaction (i.e., in a right ocular tilt reaction there will be incyclotorsion of the left eye, excyclotorsion of the right eye, or both – torsion of the eyes to the right). This is also true of the head tilt (i.e., a right ocular tilt reaction will have a right head tilt). The hypotropic eye in the skew deviation will correspond to the side of the ocular tilt reaction (i.e., a hypotropic right eye will be present in a right ocular tilt reaction with a corresponding skew deviation).

Treatment and Prognosis

The majority of ocular tilt reactions are transient with spontaneous recovery in many cases. As a temporizing symptomatic measure, the vertical diplopia can be treated with prisms and is typically very amenable to this therapy given the comitant nature of the vertical deviation. Botulinum toxin injections into the extraocular muscles have also been used with some success. In patients with persistent skew deviation with vertical diplopia, prism, repeated botulinum toxin, or strabismus surgery (typically vertical rectus muscle recession) can be offered. It is important to note that these treatments will not eliminate the head tilt component of the ocular tilt reaction, as this, along with the synkinetic ocular torsion, are a compensatory mechanism to realign the head and eyes with gravitational vertical.

Etiology	Signs
♦ Damage to the vestibular pathways that mediate head-eye posture in the roll plane ♦ Localization: utricle/labyrinth, vestibular nerve, brainstem, or cerebellum ♦ Causative lesion: variable, but commonly stroke, demyelination, trauma, iatrogenic/post-surgical, hemorrhage, or tumor	♦ Skew deviation – comitant vertical misalignment of the eyes (comitant hypertropia) ♦ Synkinetic ocular torsion – incyclotorsion of the hypertropic eye and excyclotorsion of the hypotropic eye, torsion in the same direction as the head tilt ♦ Head tilt – tilt in the direction of the ocular torsion and/or toward the hypotropic eye
Symptoms	**Treatment**
♦ Vertical diplopia ♦ Tilt in the subjective visual vertical	♦ Observation ♦ Prism ♦ Botulinum toxin injection ♦ Strabismus surgery

Differential Diagnosis

♦ Superior oblique palsy (with or without spread of comitance)
♦ Inferior oblique palsy
♦ CN III palsy (superior division, inferior division)
♦ Myasthenia Gravis
♦ Thyroid eye disease
♦ Cranial dysinnervation syndromes (i.e., CFEOM)
♦ Chronic progressive external ophthalmoplegia (CPEO)
♦ Brown syndrome
♦ Monocular elevation deficiency (e.g., due to orbital floor fracture with inferior rectus entrapment or iatrogenic inferior rectus fibrosis following retrobulbar block)
♦ Ocular neuromyotonia

References

1. Brodsky, MC, Donahue, SP, Vaphiades, M, Brandt, T. Skew Deviation Revisited. Surv Ophthalmol. 2006; 51(2):105-128. PMID:16500212
2. Brodsky, MC. Dissociated vertical divergence: a righting reflex gone wrong. Arch Ophthalmol. 1999;117(9):1216-1222. PMID:10496394
3. Brandt T, Dieterich M. Vestibular syndromes in the roll plane: topographic diagnosis from brainstem to cortex. Ann Neurol. 1994;36(3):337-47. PMID: 8080241

Suggested Citation Format

Kirkpatrick CA, Thurtell MJ. Ocular Tilt Reaction: 53-year-old female complaining of vertical diplopia following a stroke and found to have a skew deviation, fundus torsion, and torticollis. Dec 31, 2014; Available from: http://EyeRounds.org/cases/200-OTR.htm

last updated: 12/31/2014

Ethambutol Toxicity and Optic Neuropathy

60-year-old female with bilateral painless central vision loss

Elizabeth M. Grace and Andrew G. Lee, MD

November 5 , 2007

Chief Complaint: 60-year-old Caucasian, diabetic female with subacute awareness of bilateral blurry central vision.

History of Present Illness: The patient had been on ethambutol as part of treatment for her recent diagnosis of Mycobacterium avium intracellulare (see Medical History below). Months after initiation of therapy, the patient noted increasing glare with bright lights in her left eye and arranged an appointment to visit an eye doctor. However, only days before the appointment she fell down a flight of stairs, resulting in a fracture of the C2/C3 vertebrae. She was hospitalized at another facility and placed in a stabilizing "halo" for 12 weeks. A few days into her hospitalization, the patient awakened from sedation and noticed blurry central vision in both eyes, which she described as "whited out". This was not addressed at the time and her medications were continued, including ethambutol. The blurry vision worsened over the next couple months. The patient saw an optometrist two months after the fall, who documented her vision to be 20/400 in each eye. The optometrist noted no disc edema referred the patient to a retinal specialist.

One month later the patient was examined by a local retinal specialist who noted that her vision had slowly worsened to CF at 2-3 feet in both eyes. The patient also reported dyschromatopsia with difficulty distinguishing brown from green and light blue from pink. The notes from that visit document a normal slit lamp examination, no afferent pupillary defect (RAPD), and intraocular pressures of 24 and 25 mmHg in the right and left eyes, respectively. On ophthalmoscopy 2-3+ disc pallor was evident in both optic nerves, with spontaneous venous pulsations noted. An MRI of the brain and orbits was performed and showed no optic abnormality (see Figure 1). She returned to the retinal specialist who also performed a FDT 30-2 Threshold visual field test, which showed bilateral dense central scotomas (see Figure 2). The patient was then referred to the University of Iowa for further evaluation within two weeks.

Past Ocular History: Refractive error (corrected with trifocals). No ocular history of eye disease, surgery or trauma.

Medical History: The patient had a known history of pulmonary Mycobacterium avium intracellulare (MAI) ten months prior to presentation. She was initially treated with azithromycin, rifampin, and ethambutol. The rifampin was discontinued after the patient developed a rash during the first months of therapy. The ethambutol was started at 25 mg/kg/day for 2 months and then decreased to a maintenance dose of 15 mg/kg/day (800 mg daily). At the time she was seen at UIHC her ethambutol dose was 14.4 mg/kg/day (800 mg daily).

In addition, the patient had auto-immune Addison's disease diagnosed 3 years ago, an 11-year history of diabetes mellitus, and a history of hypothyroidism. There were no other health issues. Recent PPD and HIV testing was negative.

Medications: Synthroid, Fludrocortisone, Hydrocortisone, Actonel, Lantus, Humalog, Ethambutol, Azithromycin, and PRN medications (Protonix, Tylenol, multivitamin, calcium)

Allergies: Codeine and sulfa medications. (Prednisone has caused erosive esophagitis as a side-effect in the past).

Family History: Diabetes Mellitus in mother and brother. Denies any history of glaucoma.

Social History: Denies smoking cigarettes or drinking alcohol.

Review of Systems: Unremarkable. Specifically negative for renal or liver disease.

Ocular Examination

- ♦ **General**: Pleasant female wearing a soft neck collar and visually assisted by her daughter
- ♦ **Visual Acuity**: Right eye (OD)--Count fingers at 2 feet; Left eye (OS)--Count fingers at 1 foot
- ♦ **Ocular motility:** Full, both eyes (OU). No nystagmus
- ♦ **Intraocular pressure (IOP):** 32 mmHg OD and OS
  - ○ drops of brimonidine and dorzolamide/timolol (Cosopt) were given immediately in each eye. Repeat IOP was 21 OD and 19 OS.
  - ○ Gonioscopy: Open bilaterally (Spaeth grading 25-30R with 2+ pigment). No peripheral anterior synechiae (PAS).
- ♦ **Pupils**: Reactive to light in each eye from 6mm in the dark to 4mm in the light. No relative afferent pupillary defect (RAPD).
- ♦ **Slit lamp examination (OU)**
  - ○ Quiet anterior chambers with no cell or flare, open angles, mild cataract, and no pseudoexfoliation (PXF), no pigment dispersion syndrome (PDS).
- ♦ **Goldmann visual fields (GVF)**: Dense central scotomas with relatively full peripheral fields bilaterally (see Figure 3).
- ♦ **Dilated fundus examination (DFE), OU**
  - ○ Normal , dry macula with no bull's eye maculopathy. Normal vessels and periphery in each eye. Cup-to-disc ratio was 0.5 in each eye, with a sloping to the rim, and bilateral mild temporal pallor (see Figure 4).
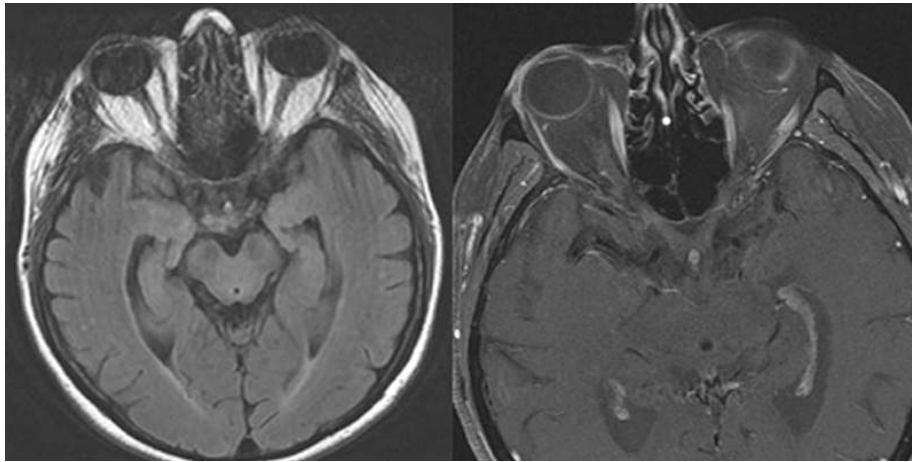
Figure 1: MRI of the brain and orbits - flare and T1 images demonstrate extensive non-enhancing white matter disease consistent with small vessel ischemic changes. However, there were no abnormalities of the orbit and no optic nerve enhancement.
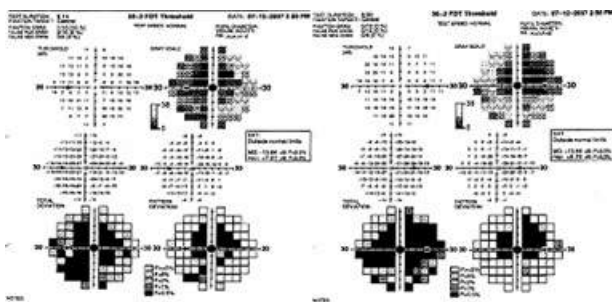

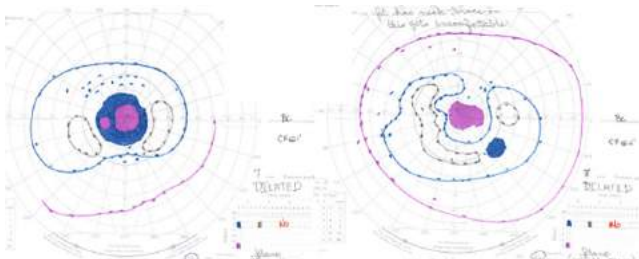*Figure 2: FDT 30-2 Threshold Test, demonstrating bilateral dense central scotomas.*

Figure 3: Goldmann Visual Fields indicate dense central scotomas with relatively full peripheral field, OD and OS.
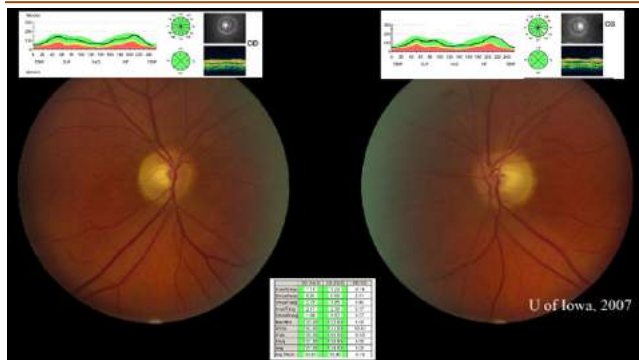

Figure 4: Fundus photos, showing a cup-to-disc ratio of 0.5 in each eye, a sloping rim, and mild temporal pallor. Superimposed OCT shows an average retinal nerve fiber layer thickness in both eyes, with no focal thinning.

Course

In summary, this is a 60-year-old female with a history of mycobacterium avium intracellulare (MAI) treated with ethambutol for 2 months at 25 mg/kg/day and then 8 months at 15 mg/kg/day, now with subacute bilateral central vision loss, with associated bilateral temporal optic disc pallor. OCT was obtained to investigate possible visual recovery via the nerve fiber layer thickness. A normal thickness of the retinal nerve fiber layer was seen in both eyes with no areas of focal thinning, average 95.83 OD and 95.99 OS (see Figure 4). The patient stopped the ethambutol immediately upon examination at the University of Iowa and her infectious disease physician was contacted about the toxic optic neuropathy. On follow-up with her infectious disease physician, the azithromycin treatment was continued and ciprofloxacin was added to the anti-MAI regimen. At her 3 week follow-up, the patient reported her vision slowly "lightening" with less dark shadows. She continues to have poor central vision, and difficulty distinguishing colors. On exam, color plate testing was poor, with 0/14 plates correct in each eye. Her visual acuity had improved to 20/400 OD and CF at 3 feet OS. Repeat Goldmann visual fields were performed at 3 and 6 weeks, showing some visual improvement of the dense central scotomas (see Figure 5).
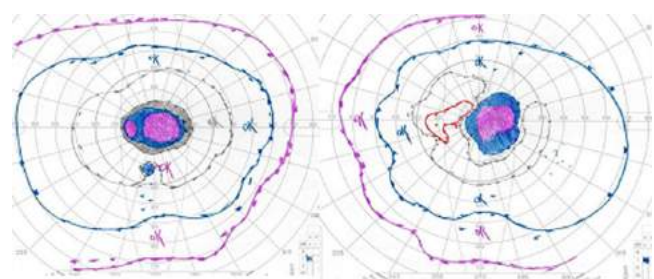

Figure 5: Goldmann Visual Fields 6 weeks after discontinuing ethambutol, demonstrating improving dense bilateral central scotomas.

The patient was evaluated in our Glaucoma Clinic for the high IOP measured previously. The patient used the latanoprost drops daily for 3 weeks and her pressure measured 28 in both eyes. Gonioscopy showed D35R, 1+ pigment in both eyes, and no synechiae. As no secondary causes of glaucoma were found, she likely has steroid induced ocular hypertension. It is believed the pressures were not contributing to her bilateral central visual field loss. Because of the optic neuropathy, a target IOP ≤ 20 was made by adding Timolol OD, Cosopt OS, and continuing the latanoprost OU. The patient returned for follow-up 3 weeks later. She had responded well to this medical therapy; her pressures were 16 in each eye. Also, a multi-focal electroretinogram (MERG) was obtained to ascertain whether there was a combination of retinal and optic nerve damage, as previously reported in cases of ethambutol-related optic neuropathies (Kardon et al., 2006). Her MERG showed a paracentral depression, especially superiorly in the first order waveforms of both eyes, thus demonstrating evidence of retinal involvement in addition to the optic neuropathy (see Figure 6).
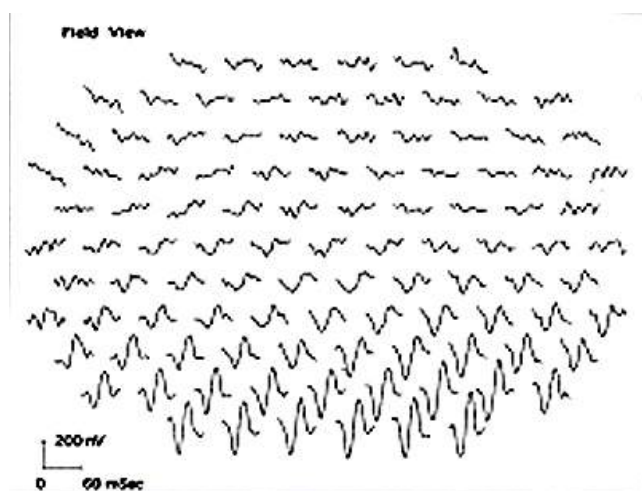

Figure 6: Multifocal electroretinogram (MERG) 6 weeks after discontinuing ethambutol, showing paracentral depression of first order waveforms especially superiorly (right eye shown).

Discussion

Toxic and metabolic optic neuropathies include the broad category of visual loss from medications, environmental toxins, and nutritional deficiencies. Recognition of these conditions is important because they are potentially reversible, particularly when caught early. Because the onset of these optic neuropathies is insidiously slow, most patients will already be symptomatic for weeks or months before being seen by a medical professional. Thus evaluation is recommended within 2 weeks of presentation, except for acute methanol toxicity, which is a medical and visual emergency (Levin et al., 2005).

Toxic Optic Neuropathy Symptoms
♦ Subacute, painless, bilateral central vision loss
♦ Color desaturation
♦ May be neurologic symptoms of "stocking and glove" peripheral neuropathy and cognitive decline in patients with vitamin B12 deficienies

Toxic Optic Neuropathy Signs
♦ Bilateral visual acuity affected because the papillomacular bundle is preferentially affected, severity is variable
♦ Visual fields demonstrate bilateral central or cecocentral scotomas, rarely bitemporal scotomas can be seen with ethambutol toxicity
♦ Pupils may react sluggishly, however there should be no RAPD because of symmetrical visual loss
♦ Optic discs may look normal initially or slight hyperemic, (similar to Leber's HON) over time temporal pallor develops

Differential Diagnoses of painless bilateral central vision loss with mild temporal disc pallor in an adult
♦ Toxic optic neuropathy (medications, environmental)
♦ Nutritional optic neuropathy
♦ Inflammatory optic neuropathy
♦ Leber's hereditary optic neuropathy (LHON)
♦ Compressive/infiltrative process

Table 1. Toxins, Medications, Deficiencies Associated with Optic Neuropathy

TOXINS	MEDICATIONS	VITAMIN DEFICIENCIES
♦ Arsenics ♦ Carbon disulfide/tetrachloride ♦ Ethyl alcohol ♦ Ethylene glycol ♦ Methanol ♦ Thallium ♦ Tobacco	♦ Amiodarone ♦ Cyclosporine ♦ Chlorambucil ♦ Chloramphenicol ♦ Cisplatin ♦ Disulfiram ♦ Ethambutol ♦ Halogenated hydroxyquinolones ♦ Isoniazid ♦ Penicillamine ♦ Sildenafil ♦ Streptomycin	♦ B12 ♦ B1 (Thiamin deficiency = beriberi) ♦ B6 ♦ Nicotinic Acid (Niacin deficiency = pellagra)

There are numerous medications and toxins as well as nutritional deficiencies that can cause optic neuropathies, stressing the importance of taking a proper history and collecting an accurate medication list as well. Table 1 is an abbreviated list of substances and vitamin deficiencies associated with optic neuropathy.

Depending on the patient's presentation some ancillary tests may need to be performed. If suspicious for a nutritional optic neuropathy a CBC, serum B12, and RBC folate levels (provides a general index of nutritional status better than an isolated folate level) should be obtained, along with consideration for hematology consult if there is no underlying etiology for the vitamin deficiency. If concerned about alternate retinal cause of visual loss, a multifocal electroretinogram (MERG) and fluorescein angiogram may be appropriate to order. Lastly, an MRI may be necessary if the presentation is atypical (i.e. bitemporal visual field depression). The MRI should be ordered with contrast and orbital view with fat suppression to look for any demyelinating lesions and exclude compressive lesions (Levin et al., 2005).

Mycobacterium avium complex (MAC) encompasses two closely related organisms, *M. avium* and *M. intracellulare*. In patients with an intact immune system the major syndrome is pulmonary disease, whereas disseminated disease and cervical lymphadenitis is more commonly seen with advanced HIV infection. The clinical presentation of pulmonary MAC disease is quite non-specific and looks similar to other mycobacterial infections and COPD. Diagnosis is based on a complicated clinical case definition of chest scans, histopathologic specimen, positive sputum cultures, and positive bronchial wash cultures set forth by the American Thoracic Society. Successful treatment is based on multi-drug therapy similar to tuberculosis. The preferred regimens for pulmonary MAC is three drug therapy including a macrolide, either clarithromycin or azithromycin, ethambutol, and rifabutin. Once the sputum cultures are negative most experts treat for at least another 12 months, with most patient with pulmonary MAC receiving a total of 18 to 24 months of therapy (Gordin et al., 2005).

Ethambutol is a bacteriostatic antimicrobial medication used as a first line defense against tuberculosis (TB) and MAC. Ethambutol's therapeutic action is hypothesized to act as a chelating agent that disrupts a metal containing enzyme system in the mycobacteria. Inside the human mitochondria, the chelation of copper or zinc containing enzymes has been suggested as a optic neuropathy mechanism.

Since its beginning uses as a treatment for TB, ethambutol's potential optic neuropathy toxicity was well recognized. Early animal studies showed that ethambutol caused lesions in the optic nerves and the optic chiasm, causing a diminished visual acuity in an often normal fundus exam (Miller et al., 2005).

The regimens of ethambutol doses vary by disease. The TB regimens can begin at either 50 mg/kg/day (maximum 4 grams) for 2 weeks or 25-30 mg/kg/day (maximum 2

grams) for 3 weeks, and then patients are maintained at 15-20 mg/kg/day (max 2 grams). For MAC regimens the maintenance dose is 15 mg/kg/day (maximum 2.5 grams). However depending on the species of mycobacteria a patient may be treated with a loading dose of 25 mg/kg/day for the first two months of therapy (Mandell et al., 2005; Micromedex 2007).

Ethambutol optic toxicity is known to be dose related. Leibold first described the dose dependent nature of ethambutol's toxicity in the 1960s. He reported 18% of patients receiving high doses of ethambutol, > 35 mg/kg/day had vision loss, whereas only 3.3% of low dose therapy, < 30 mg/kg/day had vision loss (1966). Citron further characterized the ethambutol toxicities at 6% of patients receiving doses of 25 mg/kg/day and only 1% of patients on doses of 15 mg/kg/day had vision loss (1969). Because ethambutol is cleared mainly by the kidneys, doses need to be adjusted accordingly in any patient with renal insufficiency, based on their GFR (Micromedex 2007). If you recall, our patient did have a history of diabetes, however upon review of her chart she had no renal insufficiency based on normal creatinine values.

Once ethambutol toxicity is recognized and the medication is stopped many patients recover vision slowly over several months. Although medical literature suggests that the toxic effects of ethambutol are completely reversible with discontinuation, there have been numerous case reports of non-reversible vision loss after ethambutol use. Kumar described a series of 7 consecutive patients with severe vision loss caused by ethambutol at 25 mg/kg/day. After an average follow up of 8.3 months, only 3 of the 7 patients achieved visual recovery better than 20/200, with none of the patients having any predisposing risk factors to contribute to a poor prognosis (1993). Other investigators have also documented poor visual acuity recovery despite discontinuation of ethambutol at the onset of visual symptoms (Melamud et al., 2003).

When starting ethambutol, every patient should be warned about the potential visual toxicity. If patients have any symptoms of decreased acuity, reduced color discrimination, or visual field loss, the medication should be discontinued immediately and the prescribing physician notified. There are differing recommendations for monitoring the ethambutol related optic toxicity. The manufacturer recommends patients receiving ethambutol should have visual acuity testing before initiation of therapy and then periodically. Also the manufacturer recommends monthly eye examinations in patients receiving doses of 25 mg/kg/day or greater (Micromedex 2007). Recommendations for the routine visual acuity assessment prior to starting ethambutol have also been made by the Joint Tuberculosis Committee of the American and British Thoracic Societies (Thorax 1998; Bass et al., 1994). However, the committee no longer recommends visual acuity assessment during routine follow-up. Assessment of red-green color vision prior to treatment is also recommended by the American Thoracic Society. The TB and Chest Service of the Department of Health of Hong Kong also published guidelines recommending baseline vision tests for both visual acuity

(Snellen chart) and red-green color vision (Ishihara chart), however these tests do not require an ophthalmologist's expertise (Hong Kong Annual Report 2002).

In summary, we present a classic case of ethambutol related toxic optic neuropathy. Our patient presented with painless, progressive, bilateral central vision loss and blue-yellow dyschromatopsia. The patient's visual acuity was count fingers at 2 feet in both eyes and her visual fields demonstrated bilateral central scotomas. Ophthalmoscopy demonstrated a mild temporal pallor of both optic discs, however her OCT was promising with a normal average nerve fiber thickness seen in both eyes. Upon presentation she was taking 14.4 mg/kg/day of ethambutol. According to previous reports only 1% of patients on this dose would experience toxic optic neuropathy. She appropriately discontinued the ethambutol and continued monitoring of her visual acuity recovery and her MAC infection. This case is being presented to remind practitioners of the importance of knowing a patient's past medical history and medication list when evaluating vision loss. Lastly, the importance of proper counseling of the visual side effects when starting a medication like ethambutol is imperative. The need to discontinue the medication immediately at the onset of any visual disturbances and follow-up with the treating physician should be reinforced with every patient taking these antibiotics.

Diagnosis: Ethambutol-Related Toxic Optic Neuropathy

Differential Diagnoses of painless bilateral central vision loss with mild temporal disc pallor in an adult

- ♦ Toxic optic neuropathy (medications, environmental)
- ♦ Nutritional optic neuropathy
- ♦ Inflammatory optic neuropathy
- ♦ Leber hereditary optic neuropathy (LHON)
- ♦ Compressive/infiltrative process

EPIDEMIOLOGY	SIGNS
♦ See Table 1. Toxins, Medications, and Vitamin deficiencies above	♦ Bilateral visual acuity affected because the papillomacular bundle is preferentially affected, severity is variable ♦ Visual fields demonstrate bilateral central or cecocentral scotomas, rarely bitemporal scotomas can be seen with ethambutol toxicity ♦ Pupils may react sluggishly, however there should be no RAPD because of symmetrical visual loss ♦ Optic discs may look normal initially or slight hyperemic, (similar to Leber's hereditary optic neuropathy) o over time temporal pallor develops
SYMPTOMS	TREATMENT

♦ Often asymptomatic early in course; symptoms may include
   o Subacute, painless, bilateral central vision loss
   o Color desaturation
   o May be neurologic symptoms of "stocking and glove" peripheral neuropathy and cognitive decline in patients with vitamin B12 deficienies
	♦ In most cases of medication-related optic neuropathy, immediate cessation of the offending agent is the only treatment option
	♦ Vitamin replacement is essential in cases of optic neuropathy related to deficiency
	♦ Specific anti-toxins may be indicated in cases of optic neuropathy related to environmental toxins

References

1. Kardon RH, Morrisey MC, Lee AG. Abnormal multifocal electroretinogram (mfERG) in ethambutol toxicity. Semin Ophthalmol 2006;21(4):215-222. PubMed.gov/17182409. DOI: 10.1080/08820530600987454

2. Levin L, Arnold A. Chapter 25: Toxic and Metabolic Optic Neuropathies. Neuro-ophthalmology: The Practical Guide. New York: Thieme Medical Publishers; 2005.

3. Gordin FM, Horsburgh CR. Chapter 250: Mycobacterium avium Complex. In: Mandell GL, Bennet JE, Dolin R, editors. Principles and Practice of Infectious Diseases, 6th Edition. London: Churchill Livingstone; 2005.

4. Miller NR. Toxic and Deficiency Optic Neuropathies. 2005:. In: Biousse V, editor. Walsh and Hoyt's Clinical Neuro-Ophthalmology. 6th Edition.: Lippincott Williams & Wilkins; 2005; p. 455-456.

5. Leibold JE. The ocular toxicity of ethambutol and its relation to dose. Ann N Y Acad Sci 1966;135(2):904-909. PubMed.gov/5220245

http://www.EyeRounds.org/cases/75-Ethambutol-Toxicity-Optic-Neuropathy.htm

6. Citron KM. Ethambutol: a review with special reference to ocular toxicity. Tubercle 1969;50:Suppl:32-36. PubMed.gov/4918612

7. Kumar A, Sandramouli S, Verma L, Tewari HK, Khosla PK. Ocular ethambutol toxicity: is it reversible? J Clin Neuroophthalmol 1993;13(1):15-17. PubMed.gov/8501256

8. Melamud A, Kosmorsky GS, Lee MS. Ocular ethambutol toxicity. Mayo Clin Proc 2003;78(11):1409-1411. PubMed.gov/14601701. DOI: 10.4065/78.11.1409

9. Chemotherapy and management of tuberculosis in the United Kingdom: recommendations 1998. Joint Tuberculosis Committee of the British Thoracic Society. Thorax 1998;53(7):536-548. PubMed.gov/9797751

10. Bass JB, Jr., Farer LS, Hopewell PC, O'Brien R, Jacobs RF, Ruben F, Snider DE, Jr., Thornton G. Treatment of tuberculosis and tuberculosis infection in adults and children. American Thoracic Society and The Centers for Disease Control and Prevention. Am J Respir Crit Care Med 1994;149(5):1359-1374. PubMed.gov/8173779. DOI: 10.1164/ajrccm.149.5.8173779

11. Tuberculosis & Chest Service of the Department of Health of the Government of the Hong Kong SAR. Preventive measures against drug-induced ocular toxicity during anti-tuberculosis treatment (general recommendations) [TB&CS/DH0208]. 2002. [Last rev. on 2002; accessed on 05 Nov. 2007] Available at www.info.gov.hk/tb_chest/doc/Prevent_ocutox_TBRx.pdf.

12. National Library of Medicine, National Institutes of Health. Ethambutol. : TOXNET Toxicology Data Network, 2008. [Last rev. on 14 Apr 2008; accessed access verified 2 March 2018] National Library of Medicine, Narional Institutes of Health. Ethambutol. TOXNET Toxicology Data Network. Available online at National Library of Medicine. Toxnet.nlm.nih.gov. [bit.ly/2tb-Vqqk].

Citing this article

Grace EM, Lee AG: Ocular Sarcoidosis: Ethambutol Toxicity and Optic Neuropathy: 60-year-old female with bilateral painless central vision loss. EyeRounds.org. November 5, 2007; Available from: www.EyeRounds.org/cases/75-Ethambutol-Toxicity-Optic-Neuropathy.htm.

last updated: 11-05-2007

Optic Neuritis

Pavlina S. Kemp, MD, Kimberly M. Winges, MD, Michael Wall, MD

September 30, 2012

Chief complaint: 40-year-old female with cloudy vision of the right eye

History of Present Illness: The patient is a 40-year-old female who was well until two weeks prior to her clinic visit when she noticed visual loss in her right eye. It was accompanied by pain with eye movements and a dull retro-orbital ache. She also noted decreased perception of color and contrast. She denied weakness, numbness, tingling, double vision or headache. She recalled one episode of similarly blurred vision in the left eye one year ago, which resolved spontaneously.

Past Ocular History

♦ Recurrent corneal abrasion in the right eye
♦ Prism in glasses since age 8

Past Medical History

♦ Migraine headaches
♦ No history of hypertension, hyperlipidemia, or diabetes

Medications

♦ Fexofenadine-pseudoephedrine (Allegra-D®)
♦ Multivitamin

Allergies

♦ Azithromycin - stomach pain
♦ Betamethasone - hives
♦ Sulfadoxine - headaches

Family History

♦ Sister with multiple sclerosis, diagnosed 10 years ago, with a history of optic neuritis.
♦ Mother with amblyopia in right eye (OD), migraine
♦ Maternal and paternal grandfathers with glaucoma

Social History

♦ 1-2 alcoholic beverages per week
♦ No history of smoking
Review of Systems: As above, otherwise negative.

Ocular Exam

Best-Corrected Visual Acuity
♦ Right eye (OD): 20/20
♦ Left eye (OS): 20/20

Pupils
♦ OD: 3 mm (dark) to 2 mm (light), slow, 0.3-0.6 log unit relative afferent pupillary defect
♦ OS: 3 mm (dark) to 2 mm (light), brisk, no relative afferent pupillary defect

Intraocular pressure (applanation): OD: 15 mmHg, OS: 15 mmHg

Extraocular motility: Full OD and OS, pain with adduction and abduction OD, 4 prism diopters of comitant esophoria

Confrontation visual fields
♦ Full to finger confrontation OD and OS
♦ Red target testing revealed red desaturation OD temporally and centrally, normal OS
External: Normal both eyes (OU)

Slit Lamp Exam
♦ Lids/lashes: Normal OU
♦ Conjunctiva/sclera: Normal OU
♦ Cornea: Clear OU
♦ Anterior chamber: Deep and quiet OU
♦ Iris: Normal architecture OU
♦ Lens: Clear OU
♦ Vitreous: Normal OU

Dilated Fundus Exam (shown in Figure 1)
♦ Optic nerves: No pallor or edema OU, small cup:disc OD>OS
♦ Macula: Normal OU
♦ Vessels: Normal course and caliber OU
♦ Periphery: Normal OU

Goldmann perimetry (Figure 2)
♦ OD: Inconsistent answers and mild constriction of I2e and I1e isopters
♦ OS: Full

Spectral-domain optical coherence tomography (SD-OCT) of the optic nerve heads (Figure 3)
♦ No thinning of retinal nerve fiber layer OU. Smaller cup-to-disc ratio OD than OS

Optical coherence tomography of ganglion cell + inner plexiform layer (Figure 4)
♦ OD: Normal ganglion cell layer thickness
♦ OS: Reduced ganglion cell layer thickness inferiorly

Critical flicker fusion
♦ OD: 17.9 (standard deviation 0.8) (depressed)
♦ OS: 24.2 (standard deviation 1.6)
♦ Magnetic resonance imaging (MRI) of the orbits and brain with and without contrast show contrast enhancement of the right optic nerve, and multiple ovoid periventricular white matter lesions, seen in Figures 5 and 6.

Figure 1: Color fundus photographs of the right and left eye show no optic disc edema. There is temporal pallor of the optic disc in the left eye.
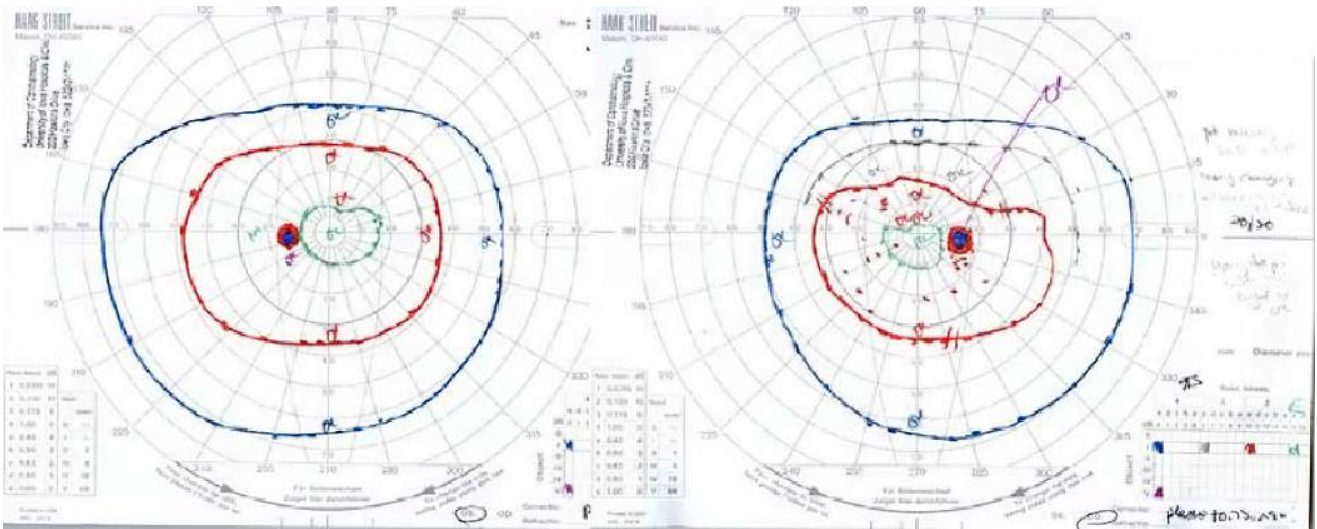

Figure 2: Goldmann perimetry OS (left) and OD (right).

Diagnosis: Optic neuritis of the right eye with a prior bout of optic neuritis in the left eye

Discussion

Optic neuritis is defined as inflammation of the optic nerve, which can be anterior, in which optic disc swelling is visible, or more commonly retrobulbar, in which inflammation is posterior to the globe without optic disc edema. The etiology of optic neuritis can be secondary to demyelination, vasculitis (such as secondary to systemic lupus erythematosus), infection (such as syphilis or post-viral optic neuritis, most commonly seen in children) or a granulomatous process (such as Wegener's granulomatosis or sarcoidosis). Demyelination may be isolated or associated with multiple sclerosis (MS) (Thurtell, 2012).

Presenting symptoms include subacute vision loss over a few days to 2 weeks, with recovery typically beginning by one month with the majority of recovery completed by two months. Pain with eye movement is seen in 92% of patients, and often precedes visual loss. Decreased color vision and color desaturation with loss of contrast is common, and is often more severe than Snellen acuity loss. Patients may describe phosphenes (light flashes with eye movement) or photisms (light induced by noise, smell, taste or touch) (BCSC Section 5 - Chapter 4, 2011).

Exam findings of optic neuritis include decreased visual acuity ranging from 20/20 to no light perception. A relative afferent pupillary defect is usually present unless optic neuropathy is bilateral. Optic disc edema is seen in about one-third of adult patients, although subtle disc edema can be seen in a higher percentage of patients if OCT is used. Visual field testing can show various nerve fiber bundle defects. In a study of 448 patients with acute optic neuritis, 48.2% of affected eyes had diffuse visual field loss, 20.1% of eyes had altitudinal or other nerve fiber bundle-type defects, and 8.3% had central or cecocentral scotomas (Keltner, 1993). Please refer to Keltner et al. for exemplary
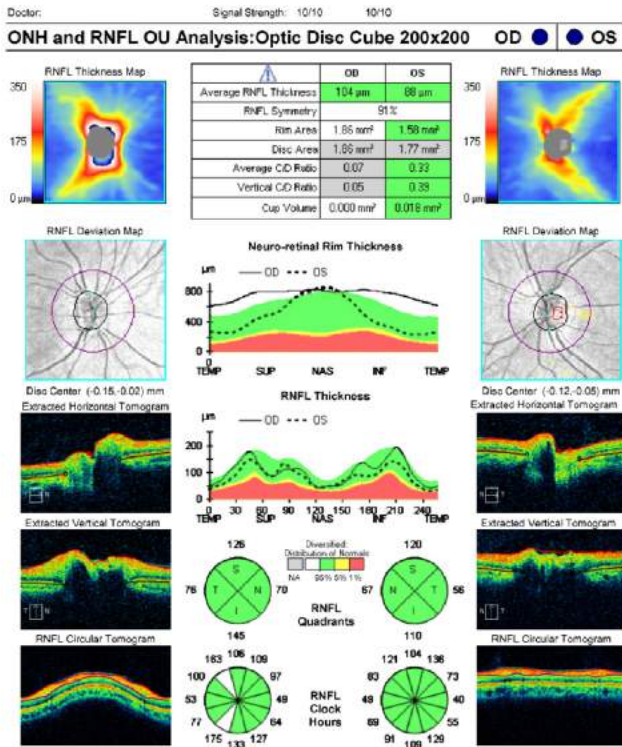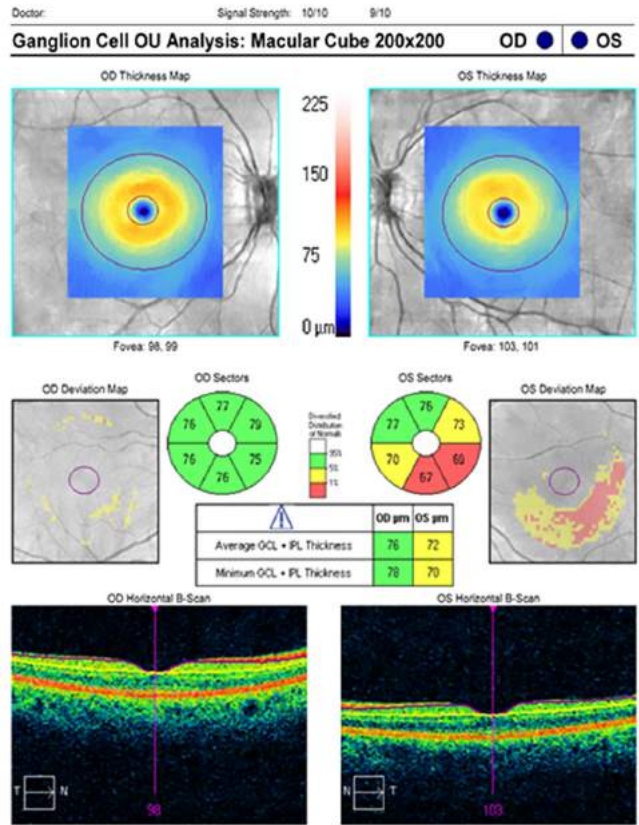
Figure 3: SD-OCT of optic nerve heads.

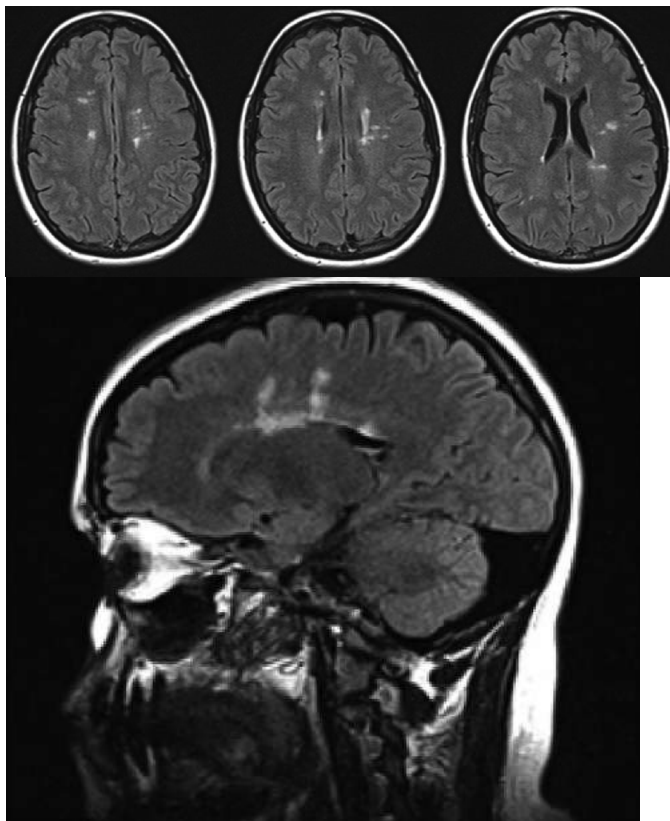Figure 4: SD-OCT of ganglion cell + inner plexiform layer.

Figure 5: Axial (A) and sagittal (B) T2 - FLAIR sequence showing multiple "Dawson's Fingers": vertically oriented ovoid periventricular white matter lesions.
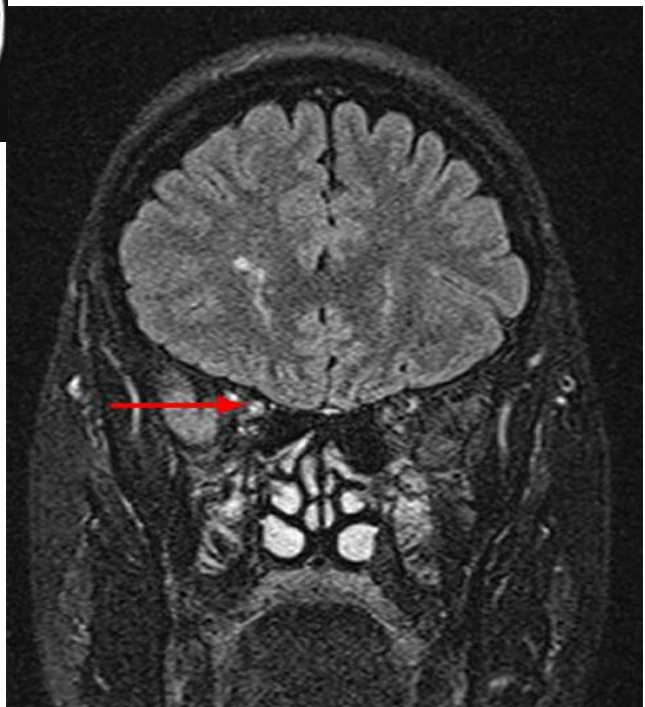

Figure 6: Coronal T2 - FLAIR sequence showing enhancement of the right optic nerve (arrow).

images of the visual field defects typically seen with acute optic neuritis. Of note, our patient's case is typical in all clinical respects except for her visual field defect; most patients have one of the patterns of visual loss listed above, whereas our patient's visual field had a mild relative paracentral defect.

Several eponymic signs and symptoms of demyelinating disease can be sought. Pulfrich's phenomenon represents an altered perception of motion; to a patient with unilateral optic neuritis, a swinging pendulum appears to trace an elliptical pathway rather than its true single-plane oscillation. This is due to a conduction delay in one optic nerve, causing a slowing in neuronal transmission compared with the other optic nerve (BCSC Section 5 - Chapter 6, 2011). Uhthoff's phenomenon describes worsening of vision or other demyelinating disease symptoms with physical activity or elevation in body temperature. L'Hermitte's sign describes an electrical "shock-like sensation" that runs down the spine and into the upper extremities with forward flexion of the neck (BCSC Section 5 - Chapter 14, 2011).

Optic neuritis should follow its typical course or other causes should be sought. Typically, optic neuritis worsens over days to several weeks, stabilizes and gradually improves over one to two months. If there is no substantial spontaneous improvement by one month, others causes should be considered. Further workup may include CSF studies of cell count, glucose, protein, VDRL and electrophoresis evaluating for oligoclonal bands. VDRL and FTA-ABS for syphilis, Lyme disease antibody titers, chest X-ray and serum angiotensin-converting enzyme levels for sarcoidosis and ANA for systemic lupus erythematosus and vasculitic disorders should be considered (BCSC Section 5 - Chapter 4, 2011).

MRI of the brain is performed when optic neuritis is suspected. If there are one or more white matter lesions typical for multiple sclerosis, a course of IV methyl prednisolone followed by an oral tapering dosage is considered (see below). When ordering brain MRI scans, the FLAIR (fluid-attenuated inversion recovery) sequence should be obtained, and gadolinium contrast should be used to look for active lesions in which the blood- brain barrier has broken down. Fat suppression should be used for sequences looking at the orbits. Demyelinating lesions in the brain are seen as periventricular, ovoid hyper-intensities in the white matter, which are best seen on T2-weighted or FLAIR images (Thurtell, 2012). There is no role for CT scanning in optic neuritis. If there is uncertainty about the diagnosis of optic neuritis, MRI of the orbits with fat suppression and gadolinium are performed.

According to the Optic Neuritis Treatment Trial (Optic Neuritis Study Group, 2008), patients with no brain lesions on MRI had a 25% risk of progression to multiple sclerosis within 15 years, as compared to a 72% risk of progression in the same time period in patients with at least one demyelinating lesion seen on MRI. In this study, patients with normal MRIs who had not developed multiple sclerosis by year 10 had only a 2% risk of developing the disease by year 15. The highest rate of conversion to multiple sclerosis occurred in the first 5 years. Patients had a lower risk of

developing future multiple sclerosis if they had a normal baseline MRI, were male, had optic disc swelling, no pain, or if exam showed no light perception vision, peripapillary hemorrhages or retinal exudates, as these are atypical features of optic neuritis. Recovery of vision was not found to be related to the presence of pain, optic disc swelling or severity of visual loss. At 10 years, recovery of visual acuity to ≥20/20 and =20/40 occurred in 74% and 92% of optic neuritis patients respectively, although most patients remain aware of residual abnormalities in contrast sensitivity, light brightness, visual field or color vision. Only 3% of patients had visual acuity worse than 20/200 in the Optic Neuritis Treatment Trial at 10 years. Recurrence of optic neuritis in the same eye or fellow eye is not uncommon, occurring in 35% of patients at 10 years according to the Optic Neuritis Treatment Trial.

Treatment for optic neuritis is based on the Optic Neuritis Treatment Trial protocol (Beck, 1992), which used IV methylprednisolone 250 mg q 6 hours x 3 days, followed by oral prednisone 1 mg/kg/day for 11 days. This therapy was shown to speed recovery by 1-2 weeks, although there was no long-term benefit for vision. In the group of patients with 2 or more white matter lesions, 16 % of optic neuritis patients who were treated with this corticosteroid regimen developed multiple sclerosis, compared with 36% of untreated optic neuritis patients over a two year period. However, this difference equalized by year 3 of the trial (Beck, 1993). Interestingly, patients treated with oral prednisone had a higher rate of recurrence of optic neuritis and therefore is not recommended.

In patients with newly diagnosed optic neuritis, the question of a diagnosis of multiple sclerosis is often raised. In 15-20% of cases, optic neuritis is the initial manifestation of multiple sclerosis. Since it is important not to incorrectly give a patient the diagnosis of multiple sclerosis and commit the patient to lifelong disease modifying treatment, the best and safest criteria for diagnosing multiple sclerosis requires two or more clinical events typical for multiple sclerosis that are separated in time and space with related MRI lesions, as shown in Table 1 (adapted from Ropper, 2009). Table 2 (adapted from McDonald, 2001) shows the McDonald criteria for the diagnosis of multiple sclerosis, applying the classic multiple sclerosis criteria to specific clinical situations. The McDonald criteria were developed for use in research protocols, which remains their most appropriate use. Recurring optic neuritis in the absence of other clinical or laboratory manifestations is not sufficient diagnosis of multiple sclerosis; autoimmune optic neuritis should be considered.

The Controlled High-Risk Subjects Avonex Multiple sclerosis Prevention Study (CHAMPS) (O'Connor, 2003), evaluated patients without clinically definite multiple sclerosis who are at high risk for developing the disease, based on a single demyelinating event. The single demyelinating event could be any one or more of: optic neuritis, spinal cord syndrome, or brainstem cerebellar syndrome, and 2 or more white matter lesions on MRI. This study found that patients treated with Avonex® (interferon beta-1a) were 44% less likely to develop clinically definite multiple sclero-

sis or to have progression of disability than those treated with placebo over a two-year period. The BENEFIT study showed similar results for Betaseron® (interferon beta-1b) (Kappos, 2007). Initiating immuno-modulating therapy in patients with a single demyelinating event remains controversial however, as this often means a lifetime of therapy in patients that may have a benign disease course without treatment. Many neurologists will follow the patient with repeat brain MRI every six months and decide on treatment based on the presence of the demyelinating activity observed.

In the case above, as is customary in our eye clinic when a patient presents with optic neuritis and has one or more typical demyelinating lesions on brain MRI, we treat based on the Optic Neuritis Treatment Trial protocol. We give 3 daily doses of 1 gram IV Solu-Medrol (methylprednisolone sodium succinate), followed by 1 mg of oral prednisone per kilogram of body weight per day for 11 days (rounded to the nearest 10 mg) followed by a tapering regimen of prednisone consisting of 20 mg on day 15 and 10 mg on days 16 and 18. Treatment should begin within 8 days of the onset of visual symptoms. We consulted neurology for evaluation for treatment with immuno-modulating therapy for multiple sclerosis, based on 2 episodes of optic neuritis (showing dissemination in time) and multiple periventricular white matter lesions (showing dissemination in space).

Summary

This case describes a 40-year-old female with subacute onset of decreased vision in the right eye, associated with pain with right eye movement, 0.3 - 0.6 relative afferent pupillary defect OD, and a fundus exam notable for temporal pallor OS. Her diagnosis is retrobulbar optic neuritis of the right eye. In retrospect, the patient had similar symptoms in the left eye one year prior that had resolved spontaneously, which is presumed to be from a prior episode of optic neuritis. During the workup of this episode, she was found to have multiple periventricular white matter lesions on MRI, consistent with a diagnosis of multiple sclerosis.

Table 1: Diagnosis of multiple sclerosis based on dissemination in time and space (adapted from Ropper, 2009).

Dissemination in Time	Dissemination in Space
Any new cerebral or spinal T2 lesion on follow-up MRI at any time	One or more lesions in 2 or more characteristic sites ♦ periventricular, juxtacortical, posterior fossa, spinal cord ♦ excluding symptomatic brainstem and cord lesions

Table 2: Diagnosis of multiple sclerosis based on the McDonald criteria (adapted from McDonald, 2001).

Clinical Presentation	Additional Data Needed for Multiple Sclerosis Diagnosis
Two or more attacks; objective clinical evidence of 2 or more lesions	None
Two or more attacks; objective clinical evidence of 1 lesion	Dissemination in space, demonstrated by MRI *or* 2 or more MRI-detected lesions consistent with MS plus positive cerebrospinal fluid (CSF) *or* await further clinical attack implicating a different site
One attack; objective clinical evidence of 2 or more lesions	Dissemination in time, demonstrated by MRI *or* second clinical attack
One attack; objective clinical evidence of 1 lesion (monosymptomatic presentation; clinically isolated syndrome)	Dissemination in space, demonstrated by MRI *or* 2 or more MRI-detected lesions consistent with MS plus positive CSF *and* dissemination in time, demonstrated by MRI *or* second clinical attack
Insidious neurological progression suggestive of multiple sclerosis	Positive CSF *and* dissemination in space, demonstrated by 1. 9 or more T2 lesions in brain or 2. 2 or more lesions in spinal cord, or 3. 4-8 brain plus 1 spinal cord lesion or 4. abnormal visual evoked potential associated with 4-8 brain lesions, or 5. with fewer than 4 brain lesions plus 1 spinal cord lesion demonstrated by MRI and dissemination in time, demonstrated by MRI or continued progression for one year

Differential Diagnosis	Signs

♦ Optic neuritis
   o Secondary to demyelination
   o Secondary to infectious causes: Lyme disease, syphilis, tuberculosis
   o Secondary to vasculitis such as lupus
♦ Neuromyelitis optica (Devic's Disease)
♦ Compressive optic neuropathy
♦ Infiltrative optic neuropathy from granulomatous disease or malignancy
	♦ Decreased visual acuity
	   o 20/20 to no light perception
	♦ Visual field defect
	   o Diffuse visual field loss most common, followed by altitudinal or other nerve fiber bundle-type defects
	♦ Relative afferent pupillary defect
	♦ Optic disc edema about one-third of adults
	♦ Pulfrich's and Uhthoff's phenomena

Symptoms	Treatment
♦ Subacute vision loss over 1-2 weeks, with spontaneous recovery over weeks to months ♦ Pain with eye movement ♦ Decreased color vision	♦ IV methylprednisolone 250 mg every 6 hours x 3 days, then ♦ Oral prednisone 1 mg/kg/day for 11 days, then ♦ Taper off over next 4 days

References

Beck RW, Cleary PA, Anderson MM Jr, Keltner JL, Shults WT, Kaufman DI, Buckley EG, Corbett JJ, Kupersmith MJ, Miller NR, et al. A randomized, controlled trial of corticosteroids in the treatment of acute optic neuritis. The Optic Neuritis Study Group. *N Engl J Med*. 1992;326(9):581-8.

Beck RW, Cleary PA, Trobe JD, et al. The effect of corticosteroids for acute optic neuritis on the subsequent development of multiple sclerosis. The Optic Neuritis Study Group. *N Engl J Med*. 1993; 329(24):1764-1769.

Chapters 4, 6 and 14: The Patient with Decreased Vision: Classification and Management Retrobulbar optic neuritis. *BCSC Section 5: Neuro-Ophthalmology.* San Francisco: American Academy of Ophthalmology, 2011.

Kappos L, Freedman MS, Polman CH, Edan G, Hartung HP, Miller DH, Montalban X, Barkhof F, Rade EW, Bauer L, Dahms S, Lanius V, Pohl C, Sandbrink R; BENEFIT Study Group. Effect of early versus delayed interferon beta-1b treatment on disability after a first clinical event suggestive of multiple sclerosis: a 3-year follow-up analysis of the BENEFIT study. *Lancet*. 2007;370(9585):389-97.

Keltner JL, Johnson CA, Spurr JO, Beck RW. Baseline visual field profile of optic neuritis. The experience of the optic neuritis treatment trial. Optic Neuritis Study Group. *Arch Ophthalmol*. 1993;111(2):231-4.

McDonald WI, Compston A, Edan G, et al. Recommended diagnostic criteria for multiple sclerosis: guidelines from the International Panel on the Diagnosis of multiple sclerosis. *Ann Neurol*. 2001;50(1):121-127.

O'Connor P; CHAMPS. The effects of intramuscular interferon beta-1a in patients with high risk for development of multiple sclerosis: a post hoc analysis of data from CHAMPS. *Clin Ther*. 2003;25(11);2865-2874.

Optic Neuritis Study Group. Visual function 15 years after optic neuritis: a final follow-up report from the Optic Neuritis Treatment Trial. *Ophthalmology*. 2008; 115(6):1079-1082.e5.

Chapter 36: Multiple Sclerosis and Allied Demyelinating Diseases. IN: Ropper AH, Samuels MA. *Adams and Victor's principles of neurology. 9th ed*. New York: McGraw-Hill Medical; 2009.

Chapter 1: Optic Neuritis. IN: Thurtell MJ, Tomsak RL, Daroff RB. *Neuro-Ophthalmology: What do I do now?* Oxford; New York: Oxford University Press; 2012.

Citing this article

Kemp PS, Winges, KM, Wall M. Optic neuritis. EyeRounds.org. Posted Sept. 30, 2012. Available from http://www.EyeRounds.org/cases/159-optic-neuritis.htm

last updated: 12/29/2012

Case Presentations

Oculoplastic Surgery

EyeRounds.org

83

"I Can't Open My Eyes": A Case of Blepharospasm and Apraxia of Eyelid Opening

Imran Jivraj, MD; Meredith Baker, MD; Erin Shriver, MD, FACS

February 23, 2015

Initial Presentation

Chief Complaint: Difficulty Opening Eyes

History of Present Illness: A 72-year-old man presented to the oculoplastic clinic reporting an increasingly frequent difficulty opening his eyes for the past two years. He described being unable to open his eyes voluntarily, sometimes thrusting his head backwards or rubbing his brow with his fingers during these episodes. He was also bothered by frequent contractions of the muscles around the eyes on both sides of his face which caused forcible eyelid closure. He believes his inability to control eyelid opening was responsible for a driving accident a few months prior.

Past Ocular History: The patient suffered from bilateral ocular surface irritation, worse upon waking, for which he used preservative-free artificial tears.

Medical History: Previously repaired hip fracture after a motor vehicle accident.

Medications: None.

Family History: None.

Social History: Lives with his wife in a two-bedroom apartment. No smoking or alcohol consumption.

Physical Exam

- **Visual Acuity** (with correction): 20/25 Right eye (OD) and Left eye (OS)
- **Extraocular Motility**: Full both eyes (OU)
- **Pupils**: 4 mm dark, 2 mm light OD; 4 mm dark, 2 mm light OS, no RAPD OU
- **Intraocular Pressure**: 15 mmHg OU
- **Confrontation Visual Fields**: Full OU
- **Hertel Exophthalmometry**: 14 mm OU
- **External Examination**: Bilateral brow ptosis and dermatochalasis. Frequent spasms of the orbicularis oculi muscles, procerus, corrugators bilaterally, causing forcible eyelid closure. The patient had other episodes where he was unable to open his eyes voluntarily even in the absence of obvious contractions of the protractor muscles; during these moments, he would rub his temples or brows or thrust his head backwards. The upper eyelids were easily everted.
- **Slit Lamp Examination**: Mild inferior superficial punctate erosions and conjunctival hyperemia OU
- **Dilated Funduscopic Exam**: Normal disc, macula, vessels, and periphery OU

Course

The patient had evidence of blepharospasm with concurrent apraxia of eyelid opening (ALO). He also demonstrated brow ptosis, floppy eyelids, and dermatochalasis which were likely worsened by blepharospasm. The patient received 5 unit injections of botulinum toxin A into the procerus, corrugator, and at the medial and lateral junctions of the pretarsal and preseptal orbicularis in the upper lids. Injections of botulinum toxin offered symptomatic improvement and an obvious reduction in both the blepharospasm and ALO, although he required increased doses of botulinum toxin at subsequent follow-up appointments. When botulinum toxin failed to produce adequate functional improvements, the patient received bilateral upper eyelid blepharoplasty, pentagonal wedge resection for floppy eyelids, and limited myectomy of both upper lids. Three years later, he underwent bilateral direct browplasty.

He was lost to follow up and presented several years later after sustaining injuries from a motor vehicle collision which he attributed to his reduced visual function from blepharospasm and apraxia of eyelid opening. He underwent additional injections of botulinum toxin A in the pretarsal orbicularis and glabella. One month after the injections he noted significant improvement in his visual function with decreased blepharospasm and apraxia of lid opening. See video: vimeo.com/119006289

Discussion

Blepharospasm is characterized by bilateral, uncontrolled, involuntary spasms of the eyelid protractor muscles and brows, sometimes triggered by stress, intense light, or fatigue. Contractions of the procerus, corrugator, and orbicularis oculi are readily observed on clinical examination with depression of the brow (Charcot sign). During spasms, patients are unable to open their eyes. However, once obvious contractions cease, patients are able to readily initiate eyelid opening. Blepharospasm may occur independently or in association with other disorders of the orofacial muscles (Meige's Syndrome) or cervical muscles (Brüeghel's Syndrome). While the etiology is unclear, associations with essential tremor and Parkinson's disease suggest that blepharospasm may arise from dysfunction of the basal ganglia, although lesions at other cortical and subcortical structures have been identified as well.[1, 2] Because of the coexistence of ocular surface disease, lubrication with artificial tears and blepharitis management with warm compresses and eyelid scrubs should be considered prior to instituting more invasive modalities. FL-41 rose-tinted lenses have been shown to improve discomfort from photophobia as well as reduce blink rate and

eyelid contraction force in patients with blepharospasm.[3] Blepharospasm is exquisitely sensitive to botulinum toxin injection into the eyelid protractors and this is often administered every three months. True failures of botulinum are rare, occurring in fewer than 2% of patients.[4, 5]

Apraxia of eyelid lid opening (ALO) is a condition which may occur concurrently with blepharospasm, or rarely, as an independent condition. Blepharospasm and ALO are frequently observed together in patients with advanced Parkinson's disease (PD) and Progressive Supranuclear Palsy (PSP). A separate review on the diverse ophthalmological features of PD can be found on EyeRounds at eyerounds.org/cases/206-I-cannot-read.htm

ALO is characterized by the intermittent inability to open the eyelids after closure in the absence of apparent contraction of the orbicularis oculi muscle. Unlike blepharospasm, where visible contractions of the eyelid protractors are easily witnessed, patients with ALO exhibit contractions of the frontalis muscle which elevates the brow, employ motor tics such as backward thrusting of the head, or palpate the periocular skin to encourage eyelid opening. ALO is not a true eyelid apraxia; it is better considered a focal eyelid dystonia because the patient's motor system is temporarily prevented from contracting despite normal understanding of the command.[6-8]

Two mechanisms are thought to be at work in ALO. The first is prolonged, involuntary pretarsal orbicularis contraction, where there is persistence of tone in the pretarsal orbicularis muscle despite a command to open the eyelids. The levator palpebrae superioris is unable to overcome its antagonist muscle and eyelid opening is prevented. The second mechanism involves involuntary levator palpebrae inhibition, where initiation of levator contraction is delayed after the command to open the eyelid is initiated.[6, 8, 9]

Botulinum injections into the orbicularis muscle have been largely successful in the management of ALO. Krack and Marion treated 34 patients with ALO, either isolated or coexistent with blepharospasm, PD, or PSP with approximately 30 units of onabotulinumtoxin A per side and found improvements in 83% of patients in all groups.[8] They also suggested that the junction of the pretarsal and preseptal portions of the orbicularis is a more efficacious site of injection, favoring it over injections in the orbital component. Boghen et al. found that lid metrics, such as lid opening latency and lid movement durations were prolonged in patients with ALO and improved by 30-38% in patients who were treated with botulinum injections.[10] In a review on the role of botulinum toxin, Jankovic et al. summarized the strong evidence for the use of botulinum toxin into the pretarsal orbicularis muscle for patients with ALO, particularly if coexistent with blepharospasm.[11]

The role of systemic dopaminergic therapy as another treatment for ALO has been suggested in select case reports. Lee et al. described a patient with PD who developed ALO after the dose of levodopa/carbidopa was reduced.[12] When therapy was resumed, the ALO resolved. Yamada et al. described a patient with PSP whose ALO was resistant to injections of higher doses of botulinum toxin, but responded to an augmented dose of levodopa/benserazide.[13] The mechanism at play is not well understood, but it is likely that supplementary dopamine at the level of the basal ganglia may improve the component of ALO resulting from involuntary inhibition of the levator muscle.

Deep brain stimulation of the subthalamic nucleus has been used as a therapeutic modality for PD and has been shown to induce ALO in some patients while improving pre-existing ALO in others.[14-16] The varied impact of subthalamic stimulation on ALO has not yet been explained, but it may relate to creating a lesion of unique structural and functional components within the subthalamic nucleus whose role on ALO is not yet understood. Another possibility is that electrical current from deep brain stimulation spreads to adjacent structures which impacts ALO.

In patients whose blepharospasm does not respond satisfactorily to botulinum toxin, the possibility of unwitnessed ALO must be considered. As mentioned, true failures of botulinum toxin are exceedingly rare, and it has been suggested that most patients whose blepharospasm does not respond to botulinum toxin have coexistent ALO. Rana et al. described two patients with ALO and blepharospasm and PSP who responded to an initial treatment with botulinum toxin but later stopped responding satisfactorily despite increased doses. Only after a partial orbicularis myectomy was performed in one, and eyelid crutches instituted in the other, did persistent botulinum toxin injections offer therapeutic benefit.[17] An approach which combines treatment modalities with botulinum toxin may be considered in patients with ALO who are refractory to botulinum alone.

Anderson et al. have been strong proponents for the role of surgical myectomy in patients with ALO coexistent with blepharospasm who are refractory to botulinum toxin. [5, 18, 19] They conducted a retrospective chart review of patients in whom blepharospasm was refractory to botulinum injections. Patients underwent a full orbicularis myectomy of the upper eyelids with removal of every filament of orbicularis muscle as well as removal of the procerus, corrugator, depressor supraciliaris, repair of associated eyelid malpositions, as well as punctal occlusion. Forty-five of the 51 patients had concurrent ALO, and 33% of patients had a completed "cure" of ALO, while 50% experienced some improvement in ALO symptoms. Complications from the surgery included orbital hemorrhage, post-operative ocular surface disease, forehead numbness, and the need for further surgery. This study was retrospective and subject to recall bias; moreover, the surgical procedure was not standardized as surgery for eyelid malposition and/or punctal occlusion was offered simultaneously. Despite these weaknesses, the study suggests a role for surgical myectomy in improving ALO refractory to botulinum toxin. [5]

Selected case reports have identified a potential role for brow lifting in patients who are refractory to botulinum and surgical myectomy. However, compromise of an already tenuous ocular surface from brow elevation must

be strongly weighed against the potential benefit on ALO symptoms in patients with PD.[20]

Blepharospasm, characterized by bilateral involuntary contractions of the eyelid protractors, is exquisitely sensitive to injections of botulinum toxin. True failures of botulinum toxin are rare, and ALO must be suspected in these cases. ALO, better described as an eyelid dystonia, is often responsive to botulinum toxin injections into the pretarsal orbicularis muscle or at the junction of the pretarsal and preseptal orbicularis muscle. In patients who are refractory to botulinum toxin injections, other complementary therapies, such as eyelid crutches and surgical myectomy should be considered. Patients suffering from PD may benefit from augmented systemic dopaminergic therapy in consultation with the patient's neurologist. The role of more invasive treatments, such as deep brain stimulation of the subthalamic nucleus, remains to be elucidated. Further research which seeks to quantify the electromyographic components of ALO will allow ophthalmologists to better understand the mechanisms at play in an individual patient's ALO and offer targeted treatments to improve patients' visual function and quality of life.

References

1. Coscarelli JM. Essential blepharospasm. Semin Ophthalmol 2010;25(3):104-8.[PMID: 20590421].

2. Khooshnoodi MA, Factor SA, Jinnah HA. Secondary blepharospasm associated with structural lesions of the brain. J Neurol Sci 2013;331(1-2):98-101.[PMID: 23747003].

3. Blackburn MK et al. FL-41 tint improves blink frequency, light sensitivity, and functional limitations in patients with benign essential blepharospasm. Ophthalmology 2009;116(5):997-1001.[PMID: 19410958].

4. Forget R. et al. Botulinum toxin improves lid opening delays in blepharospasm-associated apraxia of lid opening. Neurology 2002;58(12):1843-6.[PMID: 12084888].

5. Georgescu D et al. Upper eyelid myectomy in blepharospasm with associated apraxia of lid opening. Am J Ophthalmol 2008;145(3):541-547.[PMID: 18191096].

6. Ugarte M. and Teimory M. Apraxia of lid opening. Br J Ophthalmol 2007;91(7):854.[PMID: 17576707].

7. Jankovic J. Apraxia of lid opening. Mov Disord 1995;10(5):686-7.[PMID: 8552131].

8. Krack P., Marion MH. Apraxia of lid opening, a focal eyelid dystonia: clinical study of 32 patients. Mov Disord 1994;9(6): 610-5.[PMID: 7845400].

9. Esteban A. and Gimenez-Roldan S. Involuntary closure of eyelids in parkinsonism. Electrophysiological evidence for prolonged inhibition of the levator palpebrae muscles. J Neurol Sci 1988;85(3):333-45.[PMID: 3210029].

10. Boghen D. Apraxia of lid opening: a review. Neurology 1997;48(6):1491-4.[PMID: 9191752].

11. Jankovic J. Disease-oriented approach to botulinum toxin use. Toxicon 2009;54(5):614-23.[PMID: 19073203].

12. Lee KC, Finley R, and Miller B. Apraxia of lid opening: dose-dependent response to carbidopa-levodopa. Pharmacotherapy 2004;24(3):401-3.[PMID: 15040654].

13. Yamada S., et al. The effects of levodopa on apraxia of lid opening: A case report. Neurology 2004;62(5):830-1.[PMID: 15007147].

14. Fuss G. et al. Improvement of apraxia of lid opening by STN-stimulation in a 70-year-old patient with Parkinson's disease: A case report. Minim Invasive Neurosurg 2004; 47(1):58-60.[PMID: 15100935].

15. Tommasi G et al. Effects of varying subthalamic nucleus stimulation on apraxia of lid opening in Parkinson's disease. J Neurol 2012;259(9):1944-50.[PMID: 22349870].

16. Goto S et al. Apraxia of lid opening is alleviated by pallidal stimulation in a patient with Parkinson's disease. Eur J Neurol 2000;7(3):337-40.[PMID: 10886319].

17. Rana AQ and Shah R. Combination of blepharospasm and apraxia of eyelid opening: a condition resistant to treatment. Acta Neurol Belg 2012;112(1):95-6.[PMID: 22427299].

18. Jordan DR, Anderson RL, and Digre KB. Apraxia of lid opening in blepharospasm. Ophthalmic Surg 1990;21(5):331-4.[PMID: 2381654].

19. Pariseau B. Worley MW, and Anderson RL. Myectomy for blepharospasm 2013. Curr Opin Ophthalmol 2013;24(5):488-93.[PMID: 23925062].

20. Nicoletti AG, Pereira IC, and S. Matayoshi. Browlifting as an alternative procedure for apraxia of eyelid opening. Ophthal Plast Reconstr Surg 2009;25(1):46-7. [PMID: 19273924].

Suggested Citation Format

Carotid Cavernous Fistula

Alex W. Cohen, MD, PhD; Richard Allen, MD, PhD

May 14, 2010

Initial Presentation

Chief Complaint: Double vision.

History of Present Illness: A 46-year-old female patient presented to the Oculoplastics Clinic reporting double vision and visual distortion. The patient first noticed binocular horizontal diplopia two months prior to her visit. She described diplopia in primary position that worsened in right gaze and she had resorted to wearing an occlusive patch in order to control her symptoms. Three months prior to the current visit the patient noted the presence of a large blood vessel above her right eye. She also reported a whooshing sound in her right ear for 2-3 months.

Past Ocular History: The patient was in a bicycle accident four months prior during which she sustained a small zygomaticomalar complex fracture (Figure 1). The patient was seen in the ophthalmology clinic three weeks later and was noted to have no diplopia, no gaze restriction, and a normal eye exam. She was asked to follow up two months later.

Medical History: Alcohol dependency and depression

Medications: Claritin® (loratadine)

Family History: Substance abuse, neck cancer, heart disease.
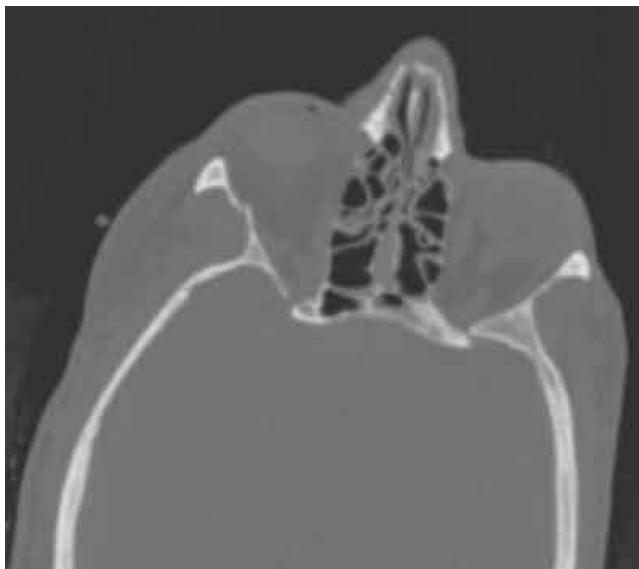
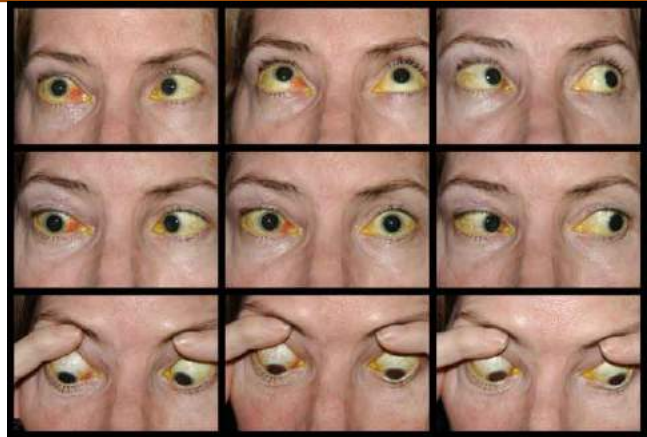**Social History:** Alcohol dependency

Figure 2: Motility photos: Note the abduction deficit in the right eye.

Figure 3: External Examination four months after initial injury. Note the dilated veins on the upper and lower right eyelids as well as the engorged nasal conjunctival vessels.

Figure 1: CAT scan obtained on initial presentation after biking injury. Note the small ZMC fracture on the right side (arrow)

Physical Exam

- Visual Acuity (without correction)
  - 20/20 Right eye (OD)
  - 20/20 Left eye (OS)
- Extraocular motility: -3 abduction deficit OD and Full OS (see figure 2)
- Pupils: OD 6mm dark, 4 mm light; OS 6 mm dark, 4 mm light; No relative afferent pupillary defect (RAPD)
- Intra-ocular pressure: 14 mmHg OD, 12 mmHg OS
- Confrontation visual fields (CVF): Full OD and OS
- Hertel: 21 mm OD, 17 mm OS, base 95 mm
- External examination: Venous engorgement of the right upper and lower eyelids; Orbital bruit present over the right eye (see Figure 3).
- Anterior segment examination: Conjunctival injection OD. Otherwise normal examination, both eyes (OU)
- Dilated funduscopic exam: Normal macula, vasculature and periphery OU

Course

A presumptive diagnosis of right-sided carotid cavernous fistula (CCF) was made based on clinical suspicion and the findings of proptosis, venous engorgement, orbital bruit, and abduction deficit. The patient was sent for MRI/MRA imaging of the brain that afternoon. The images demonstrated a right CCF as well as a markedly dilated right superior ophthalmic vein (Figures 4, 5, and 6). The patient was then seen in the Neurointerventional Clinic and scheduled for coiling of the fistula later that week.

The patient underwent coiling of the right internal carotid artery (Figures 7 and 8). During the procedure, a high flow, expansive connection between the artery and the cavernous sinus and collateral veins was noted. There was also extensive arterial damage to the right cavernous internal carotid artery consistent with dissection. Good flow was seen to cross a patent anterior communicating artery so the fistula was treated with right internal carotid artery sacrifice, using coil embolization. Fortunately, the right ophthalmic artery remained perfused via collateral circulation. After the procedure the patient had an unremarkable hospital course and she was discharged home six days later.

Discussion

A carotid-cavernous fistula (CCF) is an abnormal communication between the venous cavernous sinus and the carotid artery. The fistula may occur spontaneously but usually occurs following some sort of head trauma, as jn

the case of our patient. In one retrospective study, the time to presentation following injury ranged from one day to as late as 2 years.

There are four distinct types of fistulas (types A-D). A type A fistula is a direct, high flow fistula between the cavernous internal carotid artery and the cavernous sinus. It is the most common CCF following head trauma. Direct fistulas are thought to form from a traumatic tear in the wall of the cavernous internal carotid artery or following rupture of an aneurysm. Thus high pressure arterial blood gains rapid access to the venous system and leads to venous hypertension.

Type B-D, or indirect fistulas, occur between meningeal branches of the external or internal carotid artery and the cavernous sinus. These are low-flow fistulas. The etiology of types B-D is unclear, but they have been associated with pregnancy, sinusitis, age, and trauma. Symptoms are usually mild and may include dilated conjunctival and episcleral vessels and mild proptosis. These low flow fistulas generally resolve without treatment.

The onset of symptoms with a Type A fistula is usually rapid and can be very dramatic. Patients with a direct Type A fistula generally present with varied complaints, including unilateral visual loss, proptosis, lid swelling, pulsatile tinnitus and/or diplopia. A triad of clinical findings has been described as exophthalmos, orbital bruit, and dilated conjunctival vessels. Clinical findings include venous congestion of the eyelids, conjunctiva and episcleral vessels, cranial nerve palsies (3, 4, or 6), visual loss, proptosis, elevated intraocular pressure, optic disc edema, and dilated and tortuous retinal vessels.
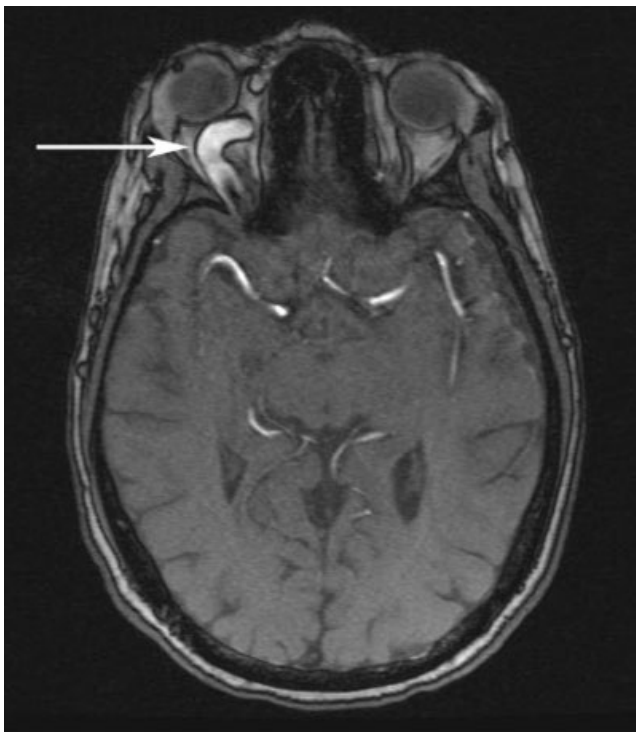

Figure 4: Magnetic Resonance Angiogram (MRA) image demonstrating an enlarged superior ophthalmic vein (arrow).
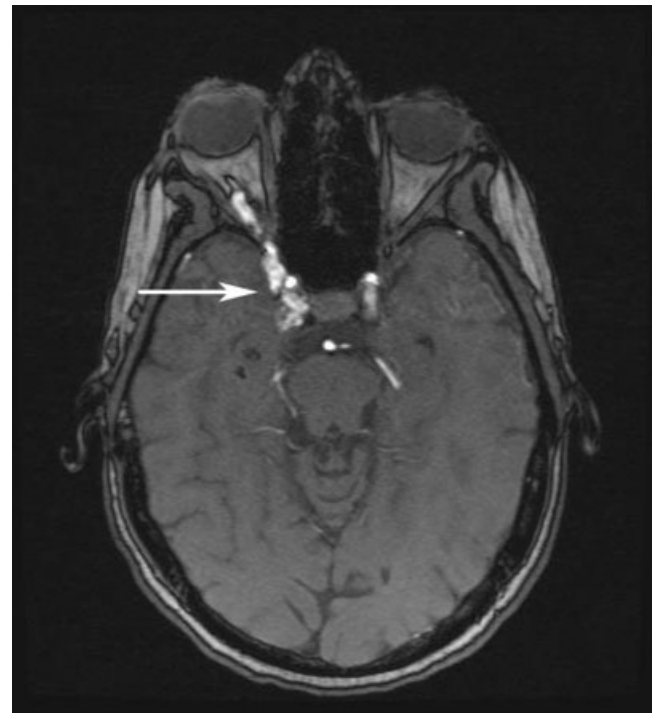

Figure 5: MRA demonstrating a right carotid cavernous fistula (arrow)

In one retrospective study of 11 traumatic CC fistulas the most common clinical signs were proptosis, dilated conjunctival vessels, and an orbital bruit, all of which were found in 100% of the patients (Brosnahan, 1992). The second most common clinical finding was conjunctival chemosis, occurring in 10/11 patients. 8/11 patients has a sixth nerve palsy while 5/11 patients had a third nerve palsy and 5/11 had a fourth nerve palsy. An efferent pupillary defect secondary to a third nerve palsy was present in 5/11 patients. Less common findings included elevated intraocular pressure (range 26-30 mmHg.3/11 patients), loss of vision(2/11 patients), optic disc edema (2/11 patients), and dilated retinal vessels (4/11 patients).

Once a direct CCF is identified it is important to direct the patient to the appropriate treating specialist, either an interventional neurologist or neurosurgeon. Direct fistulas

always require treatment. The literature is replete with different treatment modalities, including transarterial or transvenous embolization with coils, liquid embolic agents, balloon embolization, and stent placement. The success rate of closing the fistula with these treatments ranges from 55-99%. Potential complications of treatment include worsening of an oculomotor nerve palsy and loss of vision.

Diagnosis

Carotid Cavernous Fistula

EPIDEMIOLOGY	SIGNS
♦ Trauma ♦ Ruptured aneurysm	♦ Orbital bruit ♦ Dilated conjunctival vessels ♦ Exophthalmos ♦ Blood is Schlemm's Canal ♦ Elevated intraocular pressure ♦ Oculomotor nerve palsy
SYMPTOMS	TREATMENT
♦ Decreased vision ♦ Pulsatile tinnitus ♦ Diplopia ♦ Proptosis	♦ Endovascular coiling ♦ Observation

Figure 6: Three dimensional reconstructed image showing the CC fistula (arrow)
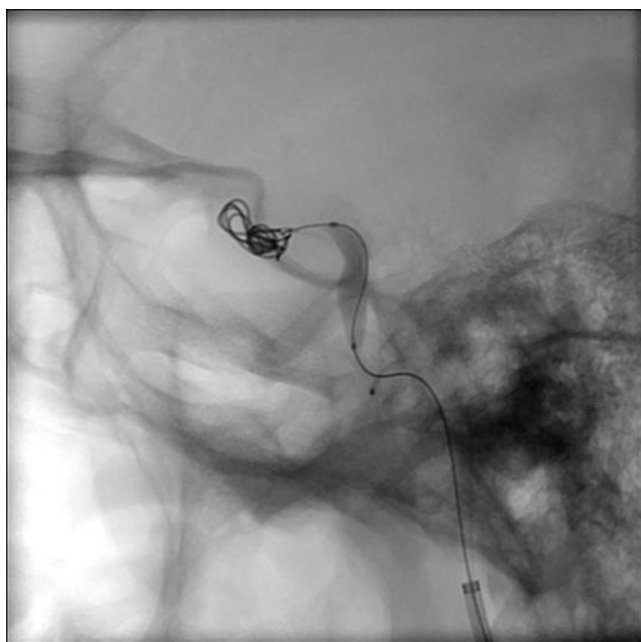

Figure 7: Intraoperative image demonstrating coil being deployed within the internal carotid system

Figure 8: Postoperative image showing coils within the internal carotid artery

Differential Diagnoses

- Dural Cavernous Fistula
- Orbital Hemorrhage
- Orbital Tumor
- Orbital Varix

References

1. Brosnahan D, McFadzean RM, and Teasdale E. Neuro-ophthalmic features of carotid cavernous fistulas and their treatment by endoarterial balloon embolisation. Journal of Neurosurgery, Neurosurgery, and Psychiatry; 1992, Vol. 55:553-556.
2. Gemmete JJ, Ansari SA, Gandhi DM. Endovascular techniques for treatment of carotid-cavernous fistula. J Neuro-Ophthalmology. 2009, Vol 29: 62-71.
3. Uysal E, Kizilkili O, Ulusay M, Basak M. Endovascular trapping of direct carotid-cavernous fistula. J Clin Neurosci. 2010 Mar;17(3):392-4.
4. Wadlington VR, Terry JB. Endovascular therapy of traumatic carotid-cavernous fistulas. Crit Care Clin. 1999 Vol 15(4):831-54.

Suggested citation format

Cohen AW, Allen R. Carotid Cavernous Fistula. EyeRounds.org. May 14, 2010; Available from: http://www.EyeRounds.org/cases/111-Carotid-Cavernous-Fistula.htm.

last updated: 05-14-2010

Chalazion

Acute presentation and recurrence in a 4-year-old female

Justin Kuiper, BA, Jesse M. Vislisel, MD, Thomas A. Oetting, MD

August 23, 2014

History of Present Illness (HPI)

The patient is a 4-year-old female patient who was referred to the pediatric ophthalmology and strabismus clinic at the University of Iowa for evaluation of a bump of the right lower lid. The parents first noticed it about two weeks prior. There was no recollection of prior trauma or insect bites to the area. They were seen at their local family care center and were given oral Bactrim (trimethoprim/sulfamethoxazole). The patient had taken the medication for four days, but there was no improvement of the area. The patient was acting well and did not report any pain in the area.

Past Ocular History: No other ocular history.

Family Ocular History: Negative for ocular problems.

Past Medical History:
Normal growth and development and no history of illness.

Ocular medications:
Bactrim (trimethoprim/sulfamethoxazole) suspension 10 ml, by mouth (PO), twice daily (BID) for 10 days, currently on day four.

Systemic medications: None.

Social History:
The patient lives at home with her parents. She does not have siblings. The family recently moved to Iowa from Florida.

Review of Systems:
A complete review of systems is negative except as in HPI.

OCULAR EXAMINATION

Visual acuity (LEA symbols) without correction
♦ Right eye (OD): 20/30
♦ Left eye (OS): 20/25
Pupils: 4 mm in dark, 2 mm in light, no relative afferent pupillary defect both eyes (OU).

Alignment: Orthophoric

Extraocular movements: Full OU

Figure 1. Initial presentation showed a 1.0 mm x 0.7 mm firm nodule on the lateral aspect of the right lower lid with superficial overlying skin breakdown and erythema.

Slit Lamp Exam (Figure 1)
Right eye
♦ Eyelids: 1.0 mm x 0.7 mm firm nodule on the lateral aspect of the right lower lid with superficial overlying skin breakdown and erythema. No periorbital erythema or edema.
♦ Conjunctiva: white and quiet
♦ Cornea: clear
♦ Anterior chamber: deep and quiet
♦ Iris: round and regular
♦ Lens: clear
Left eye
♦ Eyelids: normal
♦ Conjunctiva: white and quiet
♦ Cornea: clear
♦ Anterior chamber: deep and quiet
♦ Iris: clear
♦ Lens: clear

Clinical Course

The patient was diagnosed with a chalazion of the right lower eyelid. She was sent out with a plan for conservative management including warm compresses and topical erythromycin ointment. She was seen for follow-up 10 days later with continued enlargement of the lesion, so she was taken to the operating room for incision and drainage.

Following the procedure, the chalazion appeared significantly improved (Figure 2) and it eventually resolved completely. She presented again nine months after her initial presentation, this time for a left upper lid lesion, also thought to be a chalazion (Figure 3), which later resolved with conservative treatment.

Figure 2. Post-operative appearance 1 week after chalazion incision and drainage showed significant improvement of the right lower lid.

Figure 3. Clinical appearance 9 months after incision and drainage of the initial lesion. Note the complete resolution of the chalazion on the right lower lid. Since the procedure, the patient developed a large left upper lid chalazion.

DISCUSSION

A chalazion is a localized, lipogranulomatous lesion of the eyelid. It is an inflammatory process, caused by an obstruction of the sebaceous glands of the eyelid (meibomian and Zeiss) from inflammatory disease (eg, acne rosacea), infection (eg, seborrheic dermatitis), or neoplasm (eg, sebaceous gland carcinoma or Merkel cell carcinoma) (1). This obstruction causes secreted lipids to accumulate and leak into the collagenous stroma of the tarsal plate, triggering an immune reaction first made up of neutrophils, and later lymphocytes, plasma cells, macrophages, mononuclear cells, eosinophils, and multinucleated giant cells. Pathology of the lesion shows that acutely it presents with a suppurative pattern (mainly neutrophils), but may develop into a more chronic granulomatous pattern over time (2).

A chalazion is the most common inflammatory lesion of the eyelids (3). Patients often present with a persistent (often more than 2 weeks), initially painless nodule in the eyelid (Figure 4). The lesion may grow and distort the lid causing discomfort in the surrounding tissue (4). Chalazia can induce reversible vision changes from astigmatism and corneal irregularly due to compression of the cornea (5). This presentation is fairly consistent; a retrospective study of over 1000 cases showed that ophthalmologists are able to correctly diagnose chalazia by clinical symptoms nearly 94% of the time (3).

Other lesions can look similar to a chalazion, however in the setting of recurrent or difficult to treat chalazia in older patients, it is important to rule out neoplasm (6). One common mimic is sebaceous cell carcinoma. This also presents most commonly as a small, rubbery, firm nodule, and diagnosis is further complicated because sometimes there is true chalazion formation secondary to obstruction of the meibomian ducts from the carcinoma (7). Another lesion that can present similarly to a chalazion is a hordeolum (commonly referred to as "stye"). Although a chalazion and hordeolum are similar clinically, the underlying pathology is different. An internal hordeolum is an acute, painful, inflamed lesion near the eyelid margin caused by infection (predominantly staphylococcal) of the tarsal meibomian glands, which leads to a small abscess. An external hordeolum is also an abscess (predominantly staphylococcal), but it is located in the eyelash follicles and surrounding sebaceous and apocrine glands (Zeis and Moll) (1).

Although many patients wait for an acute chalazion to heal without any intervention, there are reports that this only occurs roughly 25-50% of the time (8-9). For patients that present to clinic, depending on how advanced the lesion is at presentation, most ophthalmologists recommend a trial of conservative management before surgical intervention. Conservative management includes some combination of frequent warm compresses, massage of the lesion, and lid scrubs. This increases clearance of acute inflammation to 40-80% (10-11).

If a patient fails conservative management, the two most common interventions are steroid injections and incision and drainage (I&D) (summary in Table 1). Steroid injections are usually performed with triamcinolone acetomide which may be injected transcutaneously or transconjunctivally. Steroid injections are effective at reducing the size of the lesion or curing it completely 60-84 % of the time with one treatment (9, 12-14), but success increases to as high as 77-89% with two or more injections (9, 15). The most common adverse reaction to this treatment is skin

Figure 4. Examples of chalazia in three separate patients.

92

depigmentation (particularly in darkly pigmented patients), but using a transconjunctival approach to injection reduces this risk. Other possible risks include atrophy of the orbital and subcutaneous fat, increased intraocular pressure, and accidental intraocular injection (13). This treatment is less invasive than I&D and is generally considered more convenient for patients (9). It may also be safer in the setting of multiple chalazia or in those located near the lacrimal puncta (12).

The other common option for management is incision and drainage (Figure 5). This is performed by securing the lesion with a chalazion clamp, everting the eyelid, opening the conjunctiva over the lesion with a scalpel, and curetting out the granulomatous substance inside (Video 1). Risks of the operation include infection, bleeding, and damage to lid structures. Older children and adults can often undergo the procedure under local anesthesia, but general anesthesia is required in young children. It is highly effective; there is improvement of the lesion or complete resolution at a rate of 79-87% with a single operation (9, 12, 13) and as high as 90% with two operations (13, 15). There is reported to be an increased rate of complete resolution or "cure" compared to steroid injections (16). An additional benefit of I&D is that tissue may be sent to pathology to confirm the diagnosis, which is particularly useful in situations where the lesions are recurrent or clinically do not appear clearly to be a chalazion. Even with appropriate treatment of chalazia, recurrence is common. It is difficult estimate the incidence however, as patients with resolution are often lost to follow up and chalazia can recur years after treatment, thus requiring a study with a very long follow up period. One study by Sendrowski and Maher showed that 22-26% of patients who have one chalazion treated with incision and drainage developed recurrence during the course of a two-year follow up period (17).

Diagnosis: **Chalazion**

Differential Diagnosis

- Hordeolum
- Sebaceous cell carcinoma
- Merkel cell tumor
- Sebhorreic keratosis
- Basal cell carcinoma
- Squamous cell carcinoma
- Keratoacanthoma
- Epithelial inclusion cyst
- Pyogenic granuloma
- Preseptal cellulitis

Table 1. Comparison of steroid injection vs. I&D for management of chalazion

	Steroid Injection	Incision and Drainage
Efficacy - Single treatment	◆ 60-84 % (9,12-14)	◆ 79-87% (9,12,13)
- Second treatment	◆ 77-89% (9,15)	◆ >90% (13,15)
Pros	◆ More convenient ◆ Less invasive ◆ Good for multiple lesions or near puncta	◆ Highly effective ◆ Pathological diagnosis ◆ Higher rate of complete cure
Cons	◆ Risk of skin depigmentation ◆ May be less convenient if multiple treatments are required	◆ Less convenient ◆ Higher risks of bleeding and infection

EPIDEMIOLOGY	*SIGNS*
◆ Most common inflammatory lesion of the eyelid ◆ 13.4% of all benign lid lesions are chalazia (18)	◆ Firm, persistent nodule of the eyelid which may progress to become edematous with overlying erythema
SYMPTOMS	*TREATMENT*
◆ Typically painless, but eyelid discomfort and swelling can develop if the lesion progresses to a large size ◆ May cause astigmatism and visual distortion	◆ Warm compresses and lid hygiene ◆ Triamcinolone injection ◆ Incision and drainage

See video demonstration of chalazion incision and drainage at www.youtube.com/watch?v=Zlaeh8CBJXc {http://bit.ly/2t7Mmmq}
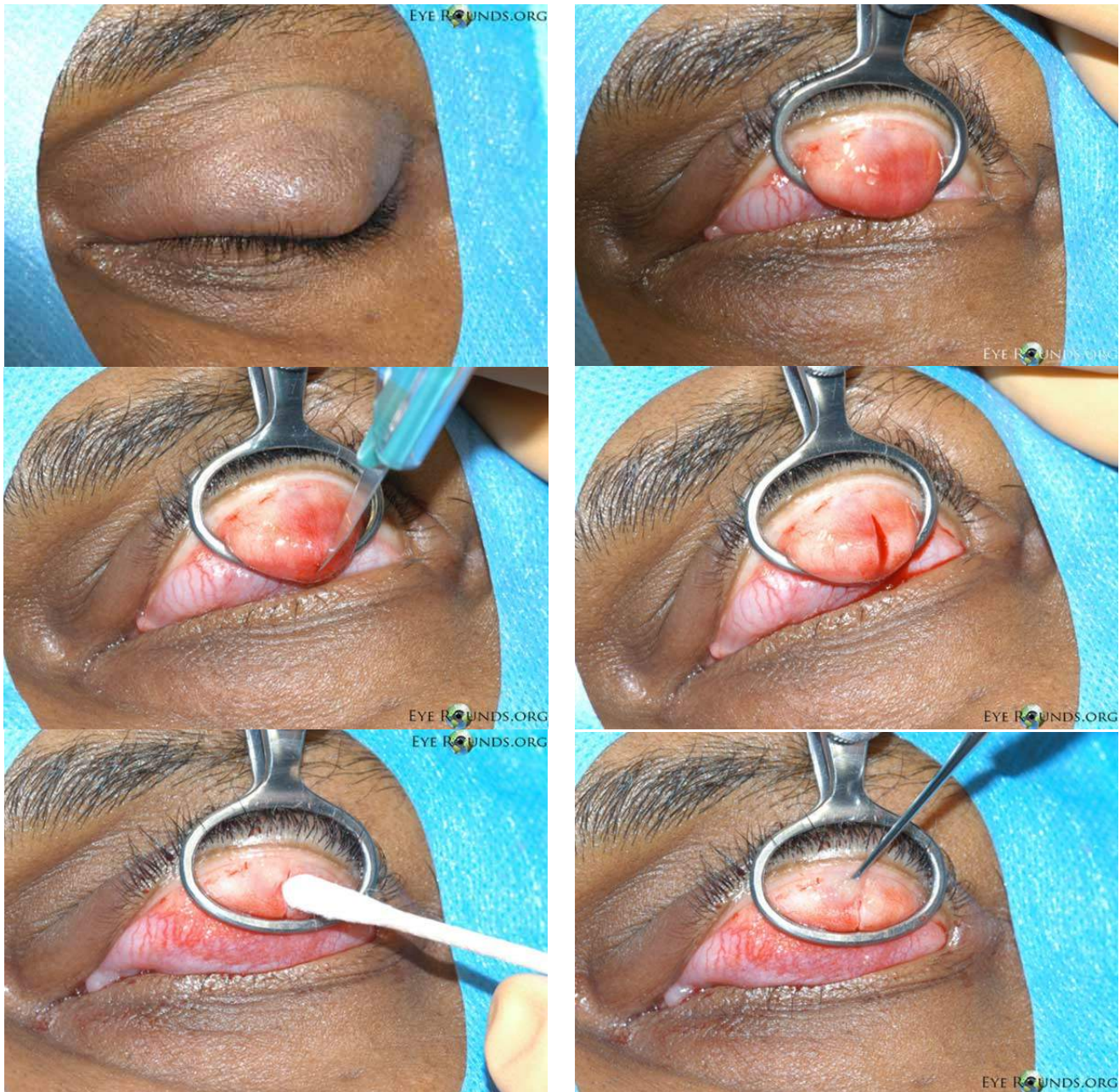
Figure 5. Procedural photographs for the incision and drainage of a chalazion.

(A) Draping of the patient with sufficient exposure of the lesion in the left upper lid. First, the eye is anesthetized topically. Then a mixture of lidocaine and epinephrine is injected into the eyelid to provide local anesthesia.

(B) A chalazion clamp is placed and tightened with the lesion in the center of the ring and the eyelid is everted. This exposes the lesion and helps with hemostasis.

(C) A size 11 scalpel blade is used to incise across the center of the lesion, dissecting down to the level of the tarsal plate.

(D) The lesion may be opened with a single, vertical incision as shown here, or with two perpendicular incisions forming an "x" shape. We usually prefer the single incision as there is less potential for disruption of adjacent meibomian glands.

(E) Some contents may be drained with gentle pressure from a cotton tip applicator.

(F) A curette is inserted into the lesion to thoroughly excise the remaining contents and break adhesions. Westcott scissors may be used to remove any excessive scar tissue within the lesion. Gentle electrocautery may be used to assist with hemostasis. The clamp is then removed and the incision is left open to encourage further drainage.

References

1. Skorin, L. Hordeolum and chalazion treatment: the full gamut. *Optometry Today.* 2002; 25-27.

2. Dhaliwal, U, Arora, VK, Singh, N, Bhatia, A. Cytopathology of Chalazia. *Diagnostic Cytopathology*. 2004; 31:118-122.

3. Ozdal, PC, Codere, F, Callejo, S, Caissie, AL, Burnier, MN. Accuracy of clinical diagnosis of chalazion. *Eye*. 2004; 18:135-138.

4. Wald, E. Periobital and orbital infections. *Infect Dis Clin N Am.* 2007; 21:393-408.

5. Bagheri, A, Hasani, HR, Karimian, F, Abrishami, M, Yazdani, S. Effect of chalazion excision on refractive error and corneal topography. *Eur J Ophthalmol*. 2009; 19:521-526.

6. Mueller, JB, McStay, CM. Ocular Infection and Inflammation. *Emerg Med Clin N Am*. 2008; 26:57-72.

7. Johnson, S, Nerad, JA, Syed NA. Sebaceous Cell Carcinoma: A Masquerade Syndrome. *EyeRounds. org*. January 23, 2007; Available from: eyerounds.org/cases/62-Sebaceous-Cell-Carcinoma-A-Masquerade-Syndrome.htm.

8. Cottrell, DG, Bosanquet, RC, Fawcett, IM. Chalazions: the frequency of spontaneous resolution. *British Medical Journal*. 1983; 287:1595.

9. Goawalla, A, Lee, V. A prospective randomized treatment study comparing three treatment options for chalazia: triamcinolone acetonide injections, incision and curettage and treatment with hot compresses. *Clin Exp Ophthalmol.* 2007; 35(8):706 –712.

10. Garrett GW, Gillespie ME, Mannix BC. Adrenocorticosteroid injection vs. conservative therapy in the treatment of chalazia. *Am J Ophthal*. 1978; 85:818-821.

11. Perry, HD, Serniuk, RA. Conservative treatment of chalazia. *Ophthalmology*. 1980; 87(3):218-221.

12. Simon, GB, Rosen, N, Rosner, M, Spierer, A. Triamcinolone Acetonide Injetion Versus Incision and Curettage for Primary Chalazia: A Prospective, Randomized Study. *Am J Ophthal.* 2011; 151:714-718.

13. Ahmad, S, Baig, MA, Khan, MA, Khan, IU, Janjua, TA. Intra-lesional corticosteroid injection vs surgical treatment of chalazia in pigmented patients. *J Coll Physicians Surg Pak* 2006; 16:42–44.

14. Vidaurri, LJ, Pe'er, J. Corticosteroid Treatment of Chalazia. *Ann Ophthalmol*. 1986; 18:339-340.

15. Watson, AP, Austin, DJ. Treatment of chalazions with injection steroid suspension. *Br J Ophthalmol* 1984; 68:833–835.

16. Jacobs, PM, Thaller, VT, Wong, D. Intralesional corticosteroid therapy of chalazia: a comparison vs. incision and curettage*. Br J Ophthalmol.* 1984; 68:836-837.

17. Sendrowski, DP, Maher, JF. Thermal Cautery After Chalazion Surgery and Its Effect on Recurrence Rates. *Optom Vis Sci.* 2000; 77(11): 605-607.

18. Tesluk, G. Eyelid lesions: incidence and comparison of benign and malignant lesions. *Ann Ophthalmol*. 1985; 17:704-707.

Suggested Citation format

Bell's Palsy Treated with Facial Nerve Decompression

Nicholas S Andresen, BA; Thomas JE Clark, MD; Daniel Q Sun, MD; Marlan R Hansen, MD; Erin M Shriver, MD

Initial Presentation

Chief Complaint

Facial droop and slurred speech

History of Present Illness

A 68-year-old man presented to the eye clinic with five days of right-sided facial droop, which was associated with the inability to fully close the right eye and slurred speech. Approximately two to three days before the onset of the facial droop, he noted a sharp, severe, retroauricular pain with intermittent radiation into the right side of his face. He also noted altered and diminished taste on the right side of his tongue. He denied any other proceeding symptoms. He was evaluated at an outside hospital, where a head computed tomography (CT) was negative. He was then transferred to the University of Iowa Hospitals and Clinics (UIHC) with concern for acute cerebrovascular accident. Upon evaluation in the UIHC Emergency Department, an isolated facial nerve palsy was identified. He was diagnosed with Bell's palsy and started on oral prednisone (60 mg daily), lubricating eye drops, and ophthalmic ointment with a plan for outpatient follow-up with Ophthalmology and Otolaryngology.

Upon evaluation in the Oculoplastics clinic, he reported using tape to keep his right eye closed. He denied eye pain or diplopia but stated that the vision in his right eye was slightly blurred.

Past Ocular History

♦ Metallic, non-penetrating, corneal foreign body, Left eye

Past Medical History

♦ Non-contributory

Medications

♦ Prednisone, oral, 60 mg daily
♦ Erythromycin 0.5% ophthalmic ointment, 3 times daily, Right eye
♦ Preservative free artificial tears, 3 times daily, Right eye

Allergies

♦ No known allergies

Family History

♦ Non-contributory

Social History

♦ Non-contributory

Review of Systems

♦ Negative, except for as described in the history of present illness. No recent tick bites or rash. No vestibular symptoms.

Ocular Examination

Visual Acuity with correction (Snellen)

♦ Right eye: 20/30
♦ Left eye: 20/40 -1

Manifest Refraction

♦ Right eye: +1.50 sphere
♦ Left eye: +1.25 sphere

Ocular Motility and Alignment

♦ Full, both eyes
♦ Orthotropic

Intraocular Pressure (IOP)

♦ Right eye: 13 mmHg
♦ Left eye: 14 mmHg

Pupils

♦ Right eye: 3 mm in dark, 2 mm in light. Briskly reactive. No relative afferent pupillary defect (RAPD).
♦ Left eye: 3 mm in dark, 2 mm in light. Briskly reactive. No RAPD.

Confrontation Visual Fields

♦ Full, Both eyes

External Exam (figure 1)

♦ Right eye: complete right-sided facial paralysis, incomplete blink, strong Bell's phenomenon
♦ Left eye: normal

Figure 1. External photo demonstrates right-sided facial droop, brow ptosis, and lower eyelid ectropion.

Slit Lamp Examination

♦ Lids/Lashes
 o Right eye: upper eyelid retraction with mild lower eyelid ectropion
 o Left eye: normal
♦ Conjunctiva/Sclera
 o Right eye: minimally injected
 o Left eye: clear and quiet
♦ Cornea
 o Right eye: decreased tear meniscus, irregular tear film, diffuse superficial punctate keratitis (SPK), worse inferiorly with mild, diffuse stromal haze
 o Left eye: inferior SPK, faint, circular, subepithelial scar in superonasal periphery
♦ Anterior Chamber
 o Deep and quiet, both eyes
♦ Iris
 o Normal architecture, both eyes
♦ Lens
 o 1+ nuclear sclerosis, both eyes

Dilated Fundus Examination (DFE)

♦ Unremarkable, both eyes

Clinical Course

Upon evaluation in the Oculoplastics clinic, a video demonstrating the complete nature of the patient's facial nerve dysfunction was sent to the Otolaryngology resident on-call. The Otolaryngology team asked to see the patient immediately and electroneuronography (ENoG) and electromyography (EMG) were ordered to evaluate candidacy for surgical decompression of the facial nerve. ENoG revealed 100% loss of facial nerve function and EMG showed absent motor unit potential of the orbicularis oris and orbicularis oculi despite maximal effort. Right facial nerve decompression via a middle cranial fossa (MCF) approach was performed 12 days after the onset of symptoms. Following decompression, the facial nerve was found to be anatomically intact but it did not respond to electrical stimulation.

3 Month Post-Operative Visit

Figures 2 and 3

The patient continued to experience a significant degree of lagophthalmos and had to continue eyelid taping. He remained incapable of producing a complete blink or fully closing his right eye. Lower eyelid ectropion secondary to laxity was also present. Despite significant lagophthalmos, only minimal exposure keratopathy was present. At this point, the patient chose to defer placement of an eyelid weight so an external, stick-on weight was ordered instead.

Figure 2. External photo at 3 month post-operative visit showing right brow ptosis and lower eyelid ectropion.

Figure 3. Lateral view of right eyelid with BlinkEze® eyelid weight in place.

6 Month Post-Operative Visit

When evaluated six months post-operatively, the patient had discontinued use of the weight as he felt his eyelid function had improved significantly. He also noted that he had begun to experience epiphora. On physical exam, lagophthalmos and ectropion were present but improved compared to his one month post-operative visit. No exposure keratopathy was present. The continued use of preservative-free artificial tears and lubricating eye gel at night was recommended.

Figure 4. External photo at 6 month post-operative visit showing improved right brow ptosis and lower eyelid ectropion.

Figure 5. External photo at 10 month post-operative visit showing mild residual right brow ptosis and lower eyelid ectropion.

10 Month Post-Operative Visit

When asked, the patient was able to fully close the right eye, but he continued to have an incomplete reflexive blink. Lower eyelid laxity, ectropion, and epiphora were still present. No exposure keratopathy was noted.

Figure 6. External photo at 18 month post-operative visit showing resolution of right brow ptosis and lower eyelid ectropion, as well as an increased tear lake height

18 Month Post-Operative Visit

The patient continued to experience epiphora. He demonstrated a full reflexive blink with good orbicularis oculi tone. There was only mild eyelid laxity remaining, with a high tear lake and no ectropion. No keratopathy was noted.

Diagnosis

Bell's palsy, status post (s/p) facial nerve decompression. Complete facial nerve paralysis was present upon presentation that improved to House-Brackmann Grade II paralysis one year post-operatively.

Discussion

Etiology and Clinical Features

For detailed information regarding the etiology and clinical features of Bell's palsy, please refer to the EyeRounds article Facial Nerve Palsy: Ocular Complications and Management[1] at eyerounds.org/cases/215-facial-nerve.htm

Care should be taken to differentiate Bell's palsy from Ramsey Hunt syndrome, which is characterized by otalgia and the presence of a vesicular rash on the postauricular skin, ear canal, or tympanic membrane [2]. Ramsey Hunt syndrome may also involve other cranial nerves, particularly the auditory and vestibular nerves leading to acute, unilateral, sensorineural hearing loss or vertigo, respectively. The natural history of Ramsey Hunt syndrome is different from that of Bell's palsy and requires different management.

Management of Bell's Palsy

Imaging and Initial Work-up

Patients with a history and physical exam highly suggestive of Bell's palsy may not always require magnetic resonance imaging (MRI) or computed tomography (CT). However, patients with otorrhea, vestibular complaints, or hearing loss should be evaluated with both MRI and high-resolution CT [2]. An atypical presentation, such as a slow onset of symptoms, recurrent episodes of acute paralysis, evidence of synkinesis, or a proceeding facial twitch should also prompt imaging studies, as these symptoms may suggest an alternative diagnosis (e.g. tumor) [3]. Planned surgical decompression or persistent, severe paralysis after 6 months are also indications for imaging [2].

Further steps should be taken during the initial evaluation depending upon individual patient characteristics. For patients living in areas endemic for Lyme disease, serologic testing (IgM, IgG) should be obtained [2]. Patients with vestibular complaints require evaluation with an electronystagmogram (ENG), and those with complete facial nerve paralysis require electrophysiologic testing (EMG, ENoG) in order to assess candidacy for facial nerve decompression. Further details regarding these tests are beyond the scope of this discussion.

Steroids

The mainstay of acute treatment for Bell's palsy is early treatment with oral glucocorticoids for all patients [4-7]. Several double-blind, placebo-controlled, randomized trials support the effectiveness of early, short-term, oral glucocorticoid therapy for all patients within 3-7 days of symptom onset, demonstrating a quicker and more complete recovery of facial nerve function [8-13]. Patients in these trials were treated with 10-day courses of oral prednisone 50-80 mg daily, with or without a taper after day five of treatment. There is no evidence to support one particular steroid-dosing regimen over another. At our institution, patients who present within 7 days of symptom onset are treated with a 10-14-day course of 60-80 mg/day of oral prednisone.

Antivirals

Bell's palsy was first described as a facial nerve palsy without a known etiology [14]. However, recent studies indicate that herpes simplex virus (HSV) may play a role in the pathogenesis of Bell's palsy. Evidence of HSV type 1 (HSV-1) infection has been found in patients with Bell's palsy, [15-18] and HSV-1 inoculation has been shown to cause

facial paralysis in mice [19 ,20]. Consequently, antiviral therapy has been proposed as one potential treatment for Bell's palsy.

Antiviral therapy may be used alone or in addition to glucocorticoid therapy. Data supporting the use of antiviral therapy are mixed. Two large clinical trials have been performed that randomized 496 and 829 patients, respectively, to receive placebo, steroids alone, antivirals alone (acyclovir or valacyclovir), or steroids and antivirals [11 ,12]. Both studies showed no significant difference in the recovery of facial nerve function between groups that received placebo or antivirals alone. Similarly, no difference was found between groups that received steroids alone or steroids and antivirals. However, both of these studies included patients with all degrees of facial weakness. It is known that patients with mild facial paresis have a high rate of recovery without treatment. Thus, any benefit of antiviral therapy for patients with more severe paresis or paralysis may have been masked by the subset of patients with mild degrees of weakness expected to demonstrate recovery even without treatment.

Several smaller trials have demonstrated a trend towards benefit with antiviral therapy [8 ,13], and one trial showed a benefit to receiving both antiviral (valacyclovir) and steroid therapy compared to steroids alone [9]. Furthermore, a 2015 Cochrane review that pooled results from 10 trials, including all of the studies mentioned above, found antiviral and steroid therapy to be superior to steroid therapy alone [21]. Importantly, no serious adverse effects have been documented in any study using antivirals for Bell's palsy to date. Patients who present to our institution within 7 days of symptom onset are treated with valacyclovir 500 mg orally 3 times per day for 10 days in addition to steroid therapy.

Physical Therapy

Physical therapy is another potential treatment for facial paresis that includes exercises, massage, electrical stimulation, acupuncture, and biofeedback. A recent Cochrane review found only twelve low to moderate quality studies that evaluated the efficacy of physical therapy for facial paresis due to Bell's palsy [22]. One of these studies showed that facial exercises reduce the rate of synkinesis (involuntary facial movement that occurs with voluntary movement of a different facial muscle group) at three months [23]. Another trial showed some benefit for facial exercises for patients that have had persistent nerve palsy for nine months or longer [24]. While physical therapy may provide some benefit for patients, the evidence supporting its use remains relatively weak, and it should only be considered as an adjuvant therapy. At our institution, practice patterns vary in term of the use of physical therapy. Electrical physical therapy is not used, as it may cause an increased rate of complications [22].

Facial Nerve Decompression

The facial nerve enters the temporal bone through the internal acoustic meatus and travels through Fallopian canal of the temporal bone before exiting the skull via
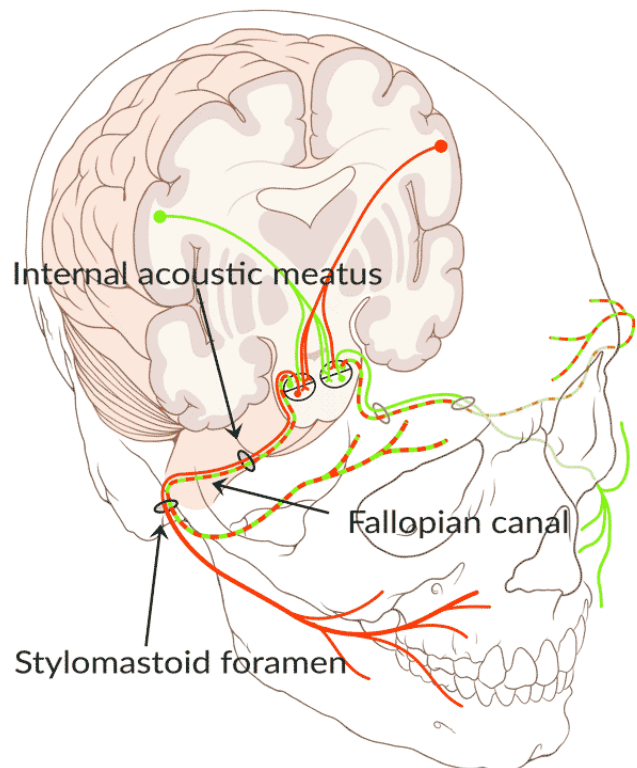
By Patrick J. Lynch, medical illustrator (Patrick J. Lynch, medical illustrator) [CC BY 2.5 (http://creativecommons.org/licenses/by/2.5)], via Wikimedia Commons

Figure 7. Route of the facial nerve as it enters the temporal bone through the internal acoustic meatus, travels through the Fallopian canal, and exits via the stylomastoid foramen. The Fallopian canal can be further divided into labyrinthine, tympanic, and mastoidal segments (not shown here). Image by Patrick J. Lynch, medical illustrator [CC BY 2.5 (creativecommons.org/licenses/by/2.5)], via Wikimedia Commons

the stylomastoid foramen (Figure 7). The Fallopian canal contains labyrinthine, tympanic, and mastoidal segments. It is believed that Bell's palsy is related to neural edema and compression within the labyrinthine segment of the Fallopian canal. Thus, decompression of the labyrinthine and perigeniculate segments of the facial nerve has been proposed as one potential treatment for Bell's palsy (Figure 8).

Controversy currently exists as to the role of surgical decompression due to good outcomes with observation alone in patients with incomplete paralysis, the lack of large trials, and the complications associated with surgical intervention [5]. Consequently, surgical therapy is not currently recommended for the majority of patients with Bell's palsy [5 ,25 ,26].

Surgical intervention is reserved for patients who have a poor prognosis with observation or medical therapy alone. One study found that patients with complete loss of facial nerve function, 90% or greater loss on ENoG testing, and absent volitional nerve activity on EMG have a 58% chance of a poor outcome (House-Brackmann III or IV [27]) at 7 months [28]. Several other studies have also supported the prognostic value of ENoG testing and the association
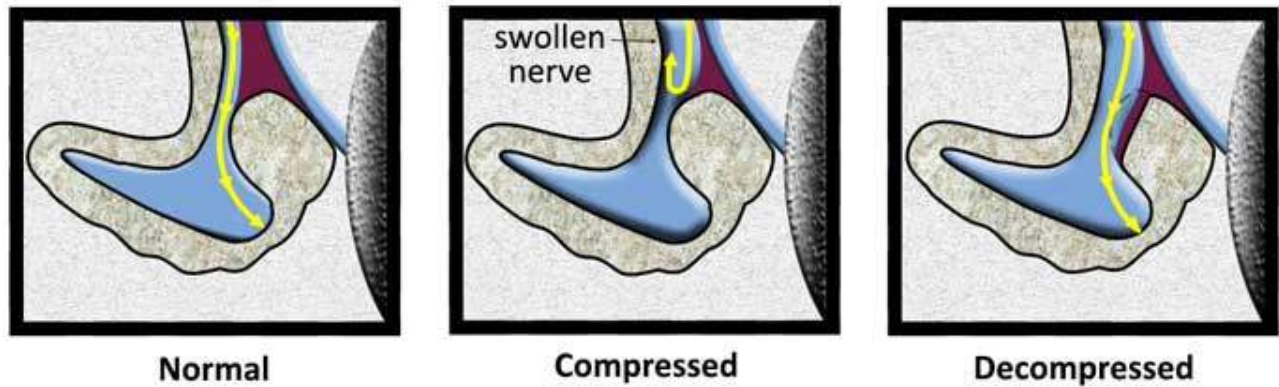
Figure 8. Schematic showing facial nerve decompression. Panel A shows a normal facial nerve within the Fallopian canal of the temporal bone. Panel B shows the facial nerve compressed within the labyrinthine segment of the Fallopian canal. Panel C shows the facial nerve after decompression of the labyrinthine segment of the Fallopian canal.

of 90% or greater functional loss on ENoG testing with poor outcomes with medical management alone [29 ,30]. Surgical intervention may be beneficial for these patients in improving the likelihood of recovery of good facial nerve function.

Facial nerve decompression has been described via either a transmastoid or middle cranial fossa (MCF) approach. The MCF approach has demonstrated the greatest promise, [28] as it provides access for decompression of the labyrinthine segment of the facial nerve. Transmastoid approaches do not provide access to this region of the Fallopian canal and are not currently used for the treatment of Bell's palsy. One

multi-center, case-control study demonstrated near complete recovery of facial nerve function (House-Brackmann I-II) for 31 of 34 (91%) patients treated with facial nerve decompression via an MCF approach as compared to 15 of 36 (42%) patients treated with steroids alone [28]. All patients who underwent surgery had >90% reduction in amplitude on ENoG, absent voluntary facial nerve activity, and were able to undergo surgery within 3-14 days of symptom onset. The efficacy of a MCF approach has also been validated by an additional report [31].

Awareness of the window of opportunity for facial nerve decompression is critical. Providers in primary care clinics,

Epidemiology [36-38]	Signs and Symptoms of Bell's Palsy
♦ Incidence (estimated) 20–42 per 100,000 annually ♦ Lifetime risk, 1 in 65 ♦ Highest incidence in ages 39 and 50 years ♦ Higher incidence in summer ♦ Recurrence more likely in first 1.5 years after first incidence occurrence	♦ Acute onset (<24-48 hours) of unilateral facial weakness or paralysis ♦ Loss of forehead wrinkling ♦ Brow ptosis ♦ Incomplete eyelid closure with possible exposure keratopathy ♦ Drooping of the mouth with possible drooling ♦ Absence of pain, vesicles, dizziness or hearing loss
Work-up for Facial Nerve Paralysis *Imaging (CT or MRI)* ♦ Clinical course, signs, and symptoms inconsistent with classic Bell's palsy ♦ Waxing and waning course ♦ Presence of otorrhea, vestibular complaints, or hearing loss ♦ Severe paralysis for >6 months ♦ Planning for surgical decompression *Electrophysiologic testing (ENG, EMG, or ENoG)* ♦ Vestibular symptoms or complete paralysis *Serologic Lyme disease testing* ♦ Vestibular symptoms or complete paralysis	**Treatment Recommendations** ♦ For patients presenting 7-10 days after symptom onset with stable or improving motor function: no treatment ♦ For patients presenting within 7 days of symptom onset: Steroid (oral prednisone, 60-80 mg/day, 10-14 days) and antiviral (oral valacyclovir, 500 mg, 3 times per day for 10 days) ♦ Electrodiagnostic testing is unnecessary for patients with voluntary facial movements (paresis) ♦ Patients with complete paralysis should be referred for electrodiagnostic testing in order to evaluate candidacy for facial nerve decompression

emergency departments, and eye clinics must recognize that patients with complete or near-complete facial nerve paralysis need urgent referral so that appropriate diagnostic testing (ENoG and EMG) may be attained and surgical intervention completed within 14 days of symptom onset [28].

All patients with complete facial nerve paralysis should be referred to a center with expertise in MCF surgery [2]. Identifying and maintaining appropriate referral pathways is important as the number of neuro-otologists who regularly perform procedures via the MCF approach remains limited [32]. Additionally, the MCF approach is a technically demanding procedure that can be associated with severe complications (e.g. cerebrospinal fluid leak, hearing loss, facial nerve injury) [33-35]. These factors should be considered and discussed when choosing to proceed with facial nerve decompression.

References

1. Welder JD, Allen RC, Shriver EM. Facial Nerve Palsy: Ocular Complications and Management. EyeRounds.org. Posted July 14, 2015; Available from: www.EyeRounds.org/cases/215-facial-nerve.htm. 2015.

2. Gantz BJ, Sun DQ, Roche JP. Idiopathic Facial Paralysis and Herpes Zoster Oticus. *Glasscock-Shambaugh Surgery of the Ear*. 7th ed; 2017.

3. Gilden DH. Clinical practice. Bell's Palsy. *N Engl J Med* 2004;351(13):1323-1331. PubMed.gov/15385659

4. Gronseth GS, Paduga R, American Academy of N. Evidence-based guideline update: steroids and antivirals for Bell palsy: report of the Guideline Development Subcommittee of the American Academy of Neurology. *Neurology* 2012;79(22):2209-2213. PubMed.gov/23136264

5. Baugh RF, Basura GJ, Ishii LE, Schwartz SR, Drumheller CM, Burkholder R, Deckard NA, Dawson C, Driscoll C, Gillespie MB, Gurgel RK, Halperin J, Khalid AN, Kumar KA, Micco A, Munsell D, Rosenbaum S, Vaughan W. Clinical practice guideline: Bell's palsy. *Otolaryngol Head Neck Surg* 2013;149(3 Suppl):S1-27. PubMed.gov/24189771

6. de Almeida JR, Guyatt GH, Sud S, Dorion J, Hill MD, Kolber MR, Lea J, Reg SL, Somogyi BK, Westerberg BD, White C, Chen JM, Bell Palsy Working Group CSoOH, Neck S, Canadian Neurological Sciences F. Management of Bell palsy: clinical practice guideline. *CMAJ* 2014;186(12):917-922. PubMed.gov/24934895

7. Schwartz SR, Jones SL, Getchius TS, Gronseth GS. Reconciling the clinical practice guidelines on Bell's palsy from the AAO-HNSF and the AAN. *Neurology* 2014;82(21):1927-1929. PubMed.gov/24793182

8. Adour KK, Ruboyianes JM, Von Doersten PG, Byl FM, Trent CS, Quesenberry CP, Jr., Hitchcock T. Bell's palsy treatment with acyclovir and prednisone compared with prednisone alone: a double-blind, randomized, controlled trial. *Ann Otol Rhinol Laryngol* 1996;105(5):371-378. PubMed.gov/8651631

9. Hato N, Yamada H, Kohno H, Matsumoto S, Honda N, Gyo K, Fukuda S, Furuta Y, Ohtani F, Aizawa H, Aoyagi M, Inamura H, Nakashima T, Nakata S, Murakami S, Kiguchi J, Yamano K, Takeda T, Hamada M, Yamakawa K. Valacyclovir and prednisolone treatment for Bell's palsy: a multicenter, randomized, placebo-controlled study. *Otol Neurotol* 2007;28(3):408-413. PubMed.gov/17414047

10. Kawaguchi K, Inamura H, Abe Y, Koshu H, Takashita E, Muraki Y, Matsuzaki Y, Nishimura H, Ishikawa H, Fukao A, Hongo S, Aoyagi M. Reactivation of herpes simplex virus type 1 and varicella-zoster virus and therapeutic effects of combination therapy with prednisolone and valacyclovir in patients with Bell's palsy. *Laryngoscope* 2007;117(1):147-156. PubMed.gov/17202945

11. Sullivan FM, Swan IR, Donnan PT, Morrison JM, Smith BH, McKinstry B, Davenport RJ, Vale LD, Clarkson JE, Hammersley V, Hayavi S, McAteer A, Stewart K, Daly F. Early treatment with prednisolone or acyclovir in Bell's palsy. *N Engl J Med* 2007;357(16):1598-1607. PubMed.gov/17942873

12. Engström M, Berg T, Stjernquist-Desatnik A, Axelsson S, Pitkäranta A, Hultcrantz M, Kanerva M, Hanner P, Jonsson L. Prednisolone and valaciclovir in Bell's palsy: a randomised, double-blind, placebo-controlled, multicentre trial. *Lancet Neurol* 2008;7(11):993-1000. PubMed.gov/18849193

13. Yeo SG, Lee YC, Park DC, Cha CI. Acyclovir plus steroid vs steroid alone in the treatment of Bell's palsy. *Am J Otolaryngol* 2008;29(3):163-166. PubMed.gov/18439948

14. Bell C. On the Nerves; Giving an Account of Some Experiments on Their Structure and Functions, Which Lead to a New Arrangement of the System. *Philosophical Transactions of the Royal Society of London* 1821;111:398-424.

15. Burgess RC, Michaels L, Bale JF, Jr., Smith RJ. Polymerase chain reaction amplification of herpes simplex viral DNA from the geniculate ganglion of a patient with Bell's palsy. *Ann Otol Rhinol Laryngol* 1994;103(10):775-779. PubMed.gov/7944168

16. Murakami S, Mizobuchi M, Nakashiro Y, Doi T, Hato N, Yanagihara N. Bell palsy and herpes simplex virus: identification of viral DNA in endoneurial fluid and muscle. *Ann Intern Med* 1996;124(1 Pt 1):27-30. PubMed.gov/7503474

17. Furuta Y, Fukuda S, Chida E, Takasu T, Ohtani F, Inuyama Y, Nagashima K. Reactivation of herpes simplex virus type 1 in patients with Bell's palsy. *J Med Virol* 1998;54(3):162-166. PubMed.gov/9515763

18. Lazarini PR, Vianna MF, Alcantara MP, Scalia RA, Caiaffa Filho HH. Herpes simplex virus in the saliva of peripheral Bell's palsy patients. *Braz J Otorhinolaryngol* 2006;72(1):7-11. PubMed.gov/16917546

19. Liston SL, Kleid MS. Histopathology of Bell's palsy. *Laryngoscope* 1989;99(1):23-26. PubMed.gov/2642582

20. Sugita T, Murakami S, Yanagihara N, Fujiwara Y, Hirata Y, Kurata T. Facial nerve paralysis induced by herpes simplex virus in mice: an animal model of acute and

transient facial paralysis. *Ann Otol Rhinol Laryngol* 1995;104(7):574-581. PubMed.gov/7598372

21. Gagyor I, Madhok VB, Daly F, Somasundara D, Sullivan M, Gammie F, Sullivan F. Antiviral treatment for Bell's palsy (idiopathic facial paralysis). *Cochrane Database Syst Rev*2015;10.1002/14651858.CD001869.pub8(11):CD001869. PubMed.gov/26559436

22. Teixeira LJ, Valbuza JS, Prado GF. Physical therapy for Bell's palsy (idiopathic facial paralysis). *Cochrane Database Syst Rev*2011;10.1002/14651858.CD006283.pub3(12):CD006283. PubMed.gov/22161401

23. Wen C-M, Zhang B-C. [Effect of rehabilitation training at different degree in the treatment of idiopathic facial palsy: a randomized controlled comparison] (in Chinese). *Zhongguo Linchuang Kangfu [Chinese Journal of Clinical Rehabilitation]*2004;8(13):2446-2447.

24. Beurskens CH, Heymans PG. Positive effects of mime therapy on sequelae of facial paralysis: stiffness, lip mobility, and social and physical aspects of facial disability. *Otol Neurotol* 2003;24(4):677-681. PubMed.gov/12851564

25. Grogan PM, Gronseth GS. Practice parameter: Steroids, acyclovir, and surgery for Bell's palsy (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2001;56(7):830-836. PubMed.gov/11294918

26. McAllister K, Walker D, Donnan PT, Swan I. Surgical interventions for the early management of Bell's palsy. *Cochrane Database Syst Rev*2013;10.1002/14651858.CD007468.pub3(10):CD007468. PubMed.gov/24132718

27. House JW, Brackmann DE. Facial nerve grading system. *Otolaryngol Head Neck Surg*1985;93(2):146-147. PubMed.gov/3921901

28. Gantz BJ, Rubinstein JT, Gidley P, Woodworth GG. Surgical management of Bell's palsy. *Laryngoscope* 1999;109(8):1177-1188. PubMed.gov/10443817

29. Takemoto N, Horii A, Sakata Y, Inohara H. Prognostic factors of peripheral facial palsy: multivariate analysis followed by receiver operating characteristic and Kaplan-Meier analyses. *Otol Neurotol* 2011;32(6):1031-1036. PubMed.gov/21725266

30. Byun H, Cho YS, Jang JY, Chung KW, Hwang S, Chung WH, Hong SH. Value of electroneurography as a prognostic indicator for recovery in acute severe inflammatory facial paralysis: a prospective study of Bell's palsy and Ramsay Hunt syndrome. *Laryngoscope* 2013;123(10):2526-2532. PubMed.gov/23918352

31. Kim IS, Shin SH, Kim J, Lee WS, Lee HK. Correlation between MRI and operative findings in Bell's palsy and Ramsay Hunt syndrome. *Yonsei Med J* 2007;48(6):963-968. PubMed.gov/18159587

32. Smouha E, Toh E, Schaitkin BM. Surgical treatment of Bell's palsy: current attitudes. *Laryngoscope* 2011;121(9):1965-1970. PubMed.gov/22024853

33. Glasscock ME, McKennan KX, Levine SC. Acoustic neuroma surgery: the results of hearing conservation surgery. *Laryngoscope* 1987;97(7 Pt 1):785-789. PubMed.gov/3600130

34. Shelton C, Brackmann DE, House WF, Hitselberger WE. Middle fossa acoustic tumor surgery: results in 106 cases. *Laryngoscope* 1989;99(4):405-408. PubMed.gov/2927217

35. Brackmann DE, House JR, 3rd, Hitselberger WE. Technical modifications to the middle fossa craniotomy approach in removal of acoustic neuromas. *Am J Otol* 1994;15(5):614-619. PubMed.gov/8572061

36. Campbell KE, Brundage JF. Effects of climate, latitude, and season on the incidence of Bell's palsy in the US Armed Forces, October 1997 to September 1999. Am J Epidemiol 2002;156(1):32-39. PubMed.gov/12076886

37. Rowlands S, Hooper R, Hughes R, Burney P. The epidemiology and treatment of Bell's palsy in the UK. Eur J Neurol 2002;9(1):63-67. PubMed.gov/11784378

38. Zhao H, Zhang X, Tang YD, Zhu J, Wang XH, Li ST. Bell's Palsy: Clinical Analysis of 372 Cases and Review of Related Literature. Eur Neurol 2017;77(3-4):168-172. PubMed.gov/28118632.

Citing this Article

Andresen NS, Clark TJE, Sun DQ, Hansen MR, Shriver EM. Bell's Palsy Treated With Facial Nerve Decompression, EyeRounds.org. posted August 1, 2017; Available from: EyeRounds.org/cases/256-Bells-Palsy.htm

last updated: 08/10/2017

Vertical Oscillopsia: A Case of Superior Oblique Myokymia

Lucas T. Lenci MD, Elizabeth A. Thompson, Matthew J. Thurtell MBBS

January 4, 2016

INITIAL PRESENTATION

Chief Complaint: "Shaking vision in my left eye"

History of Present Illness (HPI)

A 39-year-old male presents to our general ophthalmology clinic for a third opinion regarding intermittent episodes of objects bouncing up and down in his vision in his left eye. The episodes have been occurring for the past two months and last for several seconds to minutes. Bright lights, caffeine, and looking down to read seem to exacerbate these episodes. At times, these symptoms have made it difficult for him to work. He recalls having similar difficulties with his vision 3 years prior, but his symptoms resolved within a week after their onset. He denies double vision, redness, or pain with eye movement.

Past Ocular History

- Refractive error, contact lens wearer since age 14
- No eye trauma or surgeries

Past Medical History

- Guillain-Barré Syndrome (GBS) and subsequent pulmonary embolism, which required hospitalization for 4 months, 15 years prior to presentation
- Obstructive sleep apnea

Past Surgical History

- Cholecystectomy
- Motorcycle accident in 1994 with significant trauma to his leg and several orthopedic reconstructions of the left hip and leg

Medications: Fluticasone 50 mcg nasal spray

Allergies: None

Family History: Brother with Charcot-Marie-Tooth syndrome

Social History

- Significant smoking history; typically smoked 1-1.5 packs per day for 20-25 years, but at times, up to 3 packs per day; currently smoking 4-5 cigarettes per day
- No alcohol or illicit drug use

Review of Systems: Negative except as listed in HPI

OCULAR EXAMINATION

Visual Acuity

- Right eye (OD): 20/15
- Left eye (OS): 20/20-2

Ocular Motility

Full, no ocular misalignment on cross cover testing. No nystagmus. Intermittent, low-amplitude, vertical-torsional movements were observed at the slit lamp in the left eye. [Video 1, see vimeo.com/149334342]

Intraocular Pressure (IOP)

- OD: 12
- OS: 10

Pupils

- OD: 5 mm in dark → 4 mm in light, no afferent pupillary defect (RAPD)
- OS: 5 mm in dark → 3 mm in light, no RAPD

Confrontation visual fields: Full to counting fingers both eyes (OU)

Slit lamp exam

Both eyes (OU)

- External/Eyelid: Meibomian gland dysfunction, no blepharospasm, no facial spasms
- Conjunctiva: Clear and quiet
- Cornea: Clear
- Anterior chamber: Deep and quiet
- Iris: Normal architecture
- Lens: Clear

Dilated fundus examination (DFE)

OU: Normal apart from intermittent vertical-torsional movements of fundus OS

DIAGNOSIS

Superior oblique myokymia

CLINICAL COURSE

Based on the patient's history of intermittent, brief episodes of vertical oscillopsia and the low-amplitude vertical-torsional movements of the left eye on examination, the patient was diagnosed with superior oblique myokymia. Since the patient had previously sought the opinion of two other eye care providers, he was particularly pleased to learn of a diagnosis and to hear that treatment options were available. He was started on carbamazepine 100 mg orally three times a day and scheduled to follow-up in the neuro-ophthalmology clinic.

He returned 1 month later with significant improvement of his symptoms. He experienced several side effects (drows-

iness, dizziness, and upset stomach) while taking carbamazepine 100 mg three times a day, so he had reduced the dose. When he returned for his follow-up, he was taking 50 mg two times a day, which he felt provided 70% relief of symptoms. There was further discussion with the patient regarding other treatment options and he expressed interest in trying a topical agent. He was started on 1 drop of timolol in the left eye twice a day. He was told that if the timolol was effective, the carbamazepine could be tapered to an even lower dose or perhaps discontinued. An MRI of the brain with contrast and an MRA of the head were recommended to evaluate for an underlying structural lesion—most commonly, a small vascular loop compressing the left fourth nerve. The MRI and MRA were normal and did not show any vascular abnormalities. The patient was scheduled to return for routine follow-up in 4-6 months.

DISCUSSION

Superior oblique myokymia (SOM) is an uncommon disorder characterized by rapid, low-amplitude, high frequency contractions of the superior oblique muscle, which results in monocular vertical-torsional oscillopsia. Duane first described the disease in 1906 and he termed it a 'unilateral rotatory nystagmus' (1). In 1970, Hoyt and Keane were the first to use the term superior oblique myokymia after describing the clinical presentations of five patients (2). Affected patients are typically healthy, young to middle-aged adults without ocular or neurologic disease. Patients may report visual disturbances such as spontaneous image tilt, a fluttering or trembling sensation, and recurrent episodes of vertical-torsional oscillopsia, often described as "shaking, " "shimmering, " "vibrating, " "jiggling, " "dancing, " or "jumping" (1, 2, 3, 4). The episodes are brief, only lasting a few seconds to minutes, and recur sporadically. A patient may experience multiple episodes in one day for several weeks and then have symptoms disappear suddenly. The symptoms may recur weeks, months, or even years later, with a different frequency and duration (2). The characteristic symptoms allow for the diagnosis to be strongly suspected based on the history alone. The pathognomonic eye movements can often be observed with mild to moderate magnification at the slit lamp, although it is relatively uncommon to see these movements in clinic. The movements can occasionally be elicited by having the patient gaze in the direction of action of the superior oblique muscle—down and in (3, 5, 6).

The pathogenesis of SOM remains uncertain, although several mechanisms have been proposed (2, 7, 8, 9). At present, the pathogenesis is thought to be similar to that of other paroxysmal cranial nerve disorders (such as trigeminal neuralgia and hemifacial spasm) and due to compression of the nerve by a vascular loop near the nerve root exit zone (10). Vascular compression is defined by the absence of a detectable layer of cerebrospinal fluid between the fourth nerve and an adjacent blood vessel (typically a branch of the superior cerebellar or posterior cerebral artery) most easily seen on thinly sliced (1-2 mm) MRI images (6, 10). SOM can occasionally be caused by a structural lesion (e.g., tumor) or brainstem demyelination

(8, 10, 11, 12, 13, 14). Although an underlying structural lesion is not often identified, most neuro-ophthalmologists will recommend an MRI with and without contrast and, if available, an MR angiogram with contrast to evaluate for an underlying structural lesion and possible vascular compression of the fourth nerve (3).

Treatment

The vast majority of SOM cases follow a benign, relapsing and remitting course (2, 3, 4, 8, 15). In the setting of normal neuro-imaging, observation and reassurance may be appropriate for patients with mild or infrequent symptoms. For patients with persistent or bothersome symptoms, a variety of oral and topical medications may be considered (4). Carbamazepine provides symptomatic improvement in the majority of patients (5, 15). However, it is often poorly tolerated and has potentially severe adverse effects including leukopenia, acute renal failure, thromboembolism, and arrhythmias (4, 5, 7, 16). For this reason, some have proposed using gabapentin as a first line therapy, given the improved tolerability and safer side-effect profile (6, 17). Many other drugs, including oxcarbazepine, phenytoin, clonazepam, baclofen, oral and topical beta-blockers, mirtazapine, and memantine have been tried with varying degrees of success (3, 4, 5, 6, 7, 8, 16, 17, 18, 19). Botulinum toxin injection into the superior oblique muscle has also been proposed as a treatment, but provides only temporary relief and carries a risk of affecting other extraocular muscles (20).

Surgical intervention is reserved for patients with intolerable symptoms who fail to get an adequate response to medical management (5, 20). The first surgical treatments attempted were tenotomy or complete severance of the superior oblique tendon with subsequent recession (reattachment of the eye muscle at a different location to weaken its action) and myectomy—removal of a portion of the muscle belly of the ipsilateral inferior oblique to weaken its action (1 2, 5, 21). Other studies report a benefit from tenectomy or partial severance of the superior oblique tendon followed by myectomy of the ipsilateral inferior oblique. While this approach is typically very successful in eliminating oscillopsia, it may produce an iatrogenic superior oblique palsy in about a third of patients. Prism correction may alleviate this complication (8, 21, 22, 23). The Harada Ito procedure has also been used to treat SOM (24). In patients with intractable symptoms who have evidence of vascular compression of the fourth nerve on imaging, microvascular decompression of the fourth nerve could be considered as a last resort (25, 26, 27, 28).

Summary

A 39-year-old healthy male reported having episodic oscillopsia lasting for seconds to minutes for the previous two months. He recalled having similar episodes three years prior to presentation with spontaneous resolution. On slit-lamp examination, low amplitude and high frequency vertical-torsional movements were noted in the left eye, consistent with superior oblique myokymia. In most patients, superior oblique myokymia is a benign, relapsing

and remitting condition. Neuroimaging is usually obtained to evaluate for an underlying structural lesion. Superior oblique myokymia often responds to oral medications, such as carbamazepine. Topical beta-blockers have also been used with varying degrees of success. Surgical treatments, such as strabismus surgery and microvascular decompression of the fourth nerve, are reserved for patients with severe and intractable symptoms.

Differential Diagnosis

♦ Monocular nystagmus
♦ Heimann-Bielschowsky phenomenon
♦ Voluntary nystagmus
♦ Blepharospasm

EPIDEMIOLOGY	*SIGNS*
♦ Typically, young to middle-aged otherwise healthy adults ♦ Men and women appear to be equally affected ♦ May have a history of mild ocular, orbital, or head trauma	♦ Unilateral, intermittent, vertical-torsional eye movements that occur for seconds to minutes at a time ♦ Not always seen in clinic, but may be appreciated using magnification with a slit lamp or 20 D lens ♦ Movements classically precipitated by downward and inward movement of affected eye
SYMPTOMS	*TREATMENT*

♦ Recurrent brief episodes of vertical-torsional oscillopsia, often described as "shaking", "shimmering", "quivering", "vibrating", "jiggling", or "jumping" images
♦ Episodic image tilt in one eye
♦ Intermittent vertical or mixed vertical-torsional diplopia
♦ Reported trigger factors and associations: stress, fatigue, alcohol, caffeine, nicotine, fluorescent lighting
	Observation and reassurance
	
	Consider obtaining MRI brain and MRA head
	
	### Medical management
	
	♦ Carbamazepine
	  ○ Start at 100 mg orally twice daily
	  ○ Titrate up to 200 mg orally three times daily, as tolerated
	♦ Gabapentin
	  ○ Starting at 100 mg orally daily or twice daily
	  ○ Effective dose range: 300-600 mg daily, but 600-900 mg may be required in some cases
	♦ Topical beta-blocker
	  ○ 1-2 drops daily in the affected eye
	♦ Others: Oxcarbazepine, phenytoin, clonazepam, baclofen, mirtazapine, and memantine
	
	### Surgical Intervention
	
	♦ Strabismus surgery
	♦ Microvascular decompression of fourth nerve

References

1. Duane A. Unilateral rotary nystagmus. Trans Am Ophthalmol Soc 1906;11(Pt 1):63-67.
2. Hoyt WF, Keane JR. Superior Oblique Myokymia. Arch Ophthal 1970;84(4):461-467.
3. Foroozan R, Buono LM, Sergott RC, and Kawasaki A. Jumping Jack Flash. Surv Ophthalmol 2006;51(1):63-67.
4. Williams PE, Purvin VA, and Kawasaki A. Superior oblique myokymia: Efficacy of medical treatment. J AAPOS 2007;11(3):254-257.
5. Susac JO, Smith JL, Schatz NF. Superior oblique myokymia. Arch Neurol 1973;29(6):432-434.
6. Kattah JC and FitzGibbon EJ. Superior Oblique Myokymia. Current Neurology and Neuroscience Reports 2003;3(5):395-400.
7. Wu L, Tsai T, Hu F. Treatment of superior oblique myokymia with oxcarbazepine. Taiwan J Ophthalmol 2014;4:49-51.
8. Brazis PW, Miller NR, Henderer JD, and Lee AG. The Natural History and Results of Treatment of Superior Oblique Myokymia. Arch Ophthalmol 1994;112(8):1063-1067.

9. Breen LA, Gutman L, Riggs JE. Superior Oblique myokymia. A misnomer. J Clin Neuroophthalmol 1983;3(2):131-32.

10. Hashimoto M, Ohtsuka K, and Hoyt WF. Vascular Compression as a Cause of Superior Oblique Myokymia Disclosed by Thin-Slice Magnetic Resonance Imaging. Am J Ophthalmol 2001;131(5):676-677.

11. Mehta AM, Demer JL. Magnetic resonance imaging of the superior oblique muscle in superior oblique myokymia. J Pediatr Ophthalmol Strabismus 1994;31(6):378-383.

12. Geis TC, Newman NK, Dawson RC. Superior oblique myokymia associated with a dural arteriovenous fistula. J Neuroophthalmol 1996;16(1):41-43.

13. Meyers C, Murphy MA. Superior oblique myokymia following endoscopic arterial ligation for epistaxis. J Neuroophthalmol 2010;30(2):169.

14. Abhinav K, Park ND, Patel NK. Trochlear myokymia secondary to cerebellopontine angle arachnoid cyst. Br J Neurosurg 2012;26(5):754-755.

15. Rosenberg ML, Glaser JS. Superior oblique myokymia. Ann Neurol 1983;13(6):667-669.

16. Jain S, Farooq SJ, and Gottlob I. Resolution of superior oblique myokymia with memantine. J AAPOS 2008;12(1):87-88.

17. Tomsak RL, Kosmorsky GS, and Leigh RJ. Gabapentin Attenuates Superior Oblique Myokymia. Am J Ophthalmol 2002;133(5):721-723.

18. Tyler TD, Ruiz RS. Propranolol in the treatment of superior oblique myokymia. Arch Ophthalmol 1990;108(2):175-176.

19. Bibby K, Deane JS, Farnworth, and Cappin J. Superior oblique myokymia—a topical solution? Br J Ophthalmol 1994;78(11):882.

20. Ruttum MS, Harris GJ. Superior oblique myectomy and trochlectomy in recurrent superior oblique myokymia. Graefes Arch Clin Exp Ophthalmol 1988;226(2):145-147.

21. Agarwal S, Kushner BJ. Results of extraocular muscle surgery for superior oblique myokymia. J AAPOS 2009;13:472-476.

22. de Sa LC, Good WV, Hoyt CS. Surgical management of myokymia of the superior oblique muscle. Am J Ophthalmoml 1992;114(6):693-696.

23. Ruttum MS., Harris GJj. Superior oblique myectomy and trochlear resection for superior oblique myokymia. Am J Ophthalmol 2009;148(4):563-565.

24. Kosmorsky GS, Ellis BD, Fogt N, Leigh RJ. The treatment of superior oblique myokymia utilizing the Harada-Ito procedure. J Neuroophthalmol 1995;15(3):142-146.

25. Samii M, Rosahl SK, Carvalho GA, Krzizok T. Microvascular decompression for superior oblique myokymia: first experience. Case report. J Neurosurg 1998;89(6):1020-4.

26. Scharwey K, Krzizok T, Samii M, Rosahl SK, Kaufmann H. Remission of superior oblique myokymia after microvascular decompression. Ophthalmologica 2000;214(6):426-8.

27. Mikami T, Minamida Y, Ohtsuka K, Houkin K. Resolution of superior oblique myokymia following microvascular decompression of trochlear nerve. Acta Neurochir (Wien) 2005;147(9):1005-1006.

28. Fam MD, Scott C, Forster A, Kamel MH. Microvascular decompression for superior oblique myokymia: case report. Br J Neurosurg 2014;28(4):552-555.

Citing this article

Pediatric Ophthalmology & Strabismus

Orbital Cellulitis in a Child

Esther S. Hong, MD, Richard C. Allen, MD, PhD

January 12, 2010

Chief Complaint: Swollen left eye and sinus infection

History of Present Illness: 9-year-old female with left nasal pain 4 days prior to presentation. Her left eye was swollen and red and seemed to be worsening. The patient also stated that it had been more difficult to open her left eye and there had been some mattering on her eyelids. She also noticed diplopia in all gazes.

She initially presented to her pediatrician who thought she had a preseptal cellulitis and started her on amoxicillin.

However, after one day on amoxicillin, the patient returned to her pediatrician because her symptoms were worsening. She was switched to Augmentin and had 5 doses when she presented to our institution.

The patient's pediatrician also ordered a maxillofacial CT at her return visit. (see below)

Past Ocular History: none

Medical History: none

Medications
♦ Augmentin ® (amoxicillin with clavulanate potassium)
♦ Tylenol ® (acetaminophen) as needed
♦ Tylenol #3 ® (acetaminophen and codeine) as needed

Figure 1. Photo of patient

Allergies: none

Family History: Noncontributory.

Review of Systems: Afebrile, mild headache, clear mild rhinorrhea, no neck stiffness

Ocular Exam

♦ Visual Acuity, with best correction
  o OD 20/20
  o OS 20/20
♦ Pupils: 4mm → 2mm, brisk, equal, no RAPD OU
♦ Motility
  o OD — normal
  o OS — -0.5 adduction and superior gaze, -1.5 abduction
  o (Notes diplopia in all field of gaze)
♦ Intraocular pressure applanation: OD — 23, OS — 14
♦ Confrontational visual fields: Full OD/OS

External Exam
♦ Hertels: OD 13mm, OS 15mm, base 93mm
♦ Palpebral Fissure: OD 9mm, OS 7mm
♦ Marginal Reflex Distance: OD 5mm, OS 3mm

EXTERNAL/SLIT LAMP EXAM
♦ Lids/Lashes
  o OD normal
  o OS erythematous/edematous upper and lower lids, proptosis
♦ Conjunctiva/Sclera: normal OD/OS
♦ Cornea: normal OD/OS
♦ AC: formed, no cell/flare OD/OS
♦ Lens: normal OD/OS
♦ Vitreous: No cell OD/OS

Vital signs: BP 115/68, Pulse 76, T 36.9

Laboratory tests
♦ CBC
  o *WBC 11.6 K/mm3*
♦ Differential
  o *Neutrophils 8050/mm3*
  o Lymphocytes 2010/mm3
  o *Monocytes 880/mm3*
  o Eosinophils 60/mm3
  o Basophils 40/mm3
♦ Hgb: 12.5 G/DL
♦ Platelets: 294 K/mm3
♦ *ESR: 65*
♦ *CRP: 4.6*

(Elevated abnormal values are *in ITALICS*)

Figure 2: Motility Assessment on presentation

Figure 3. 2mm Proptosis OS

Figure 5. Post treatment photo

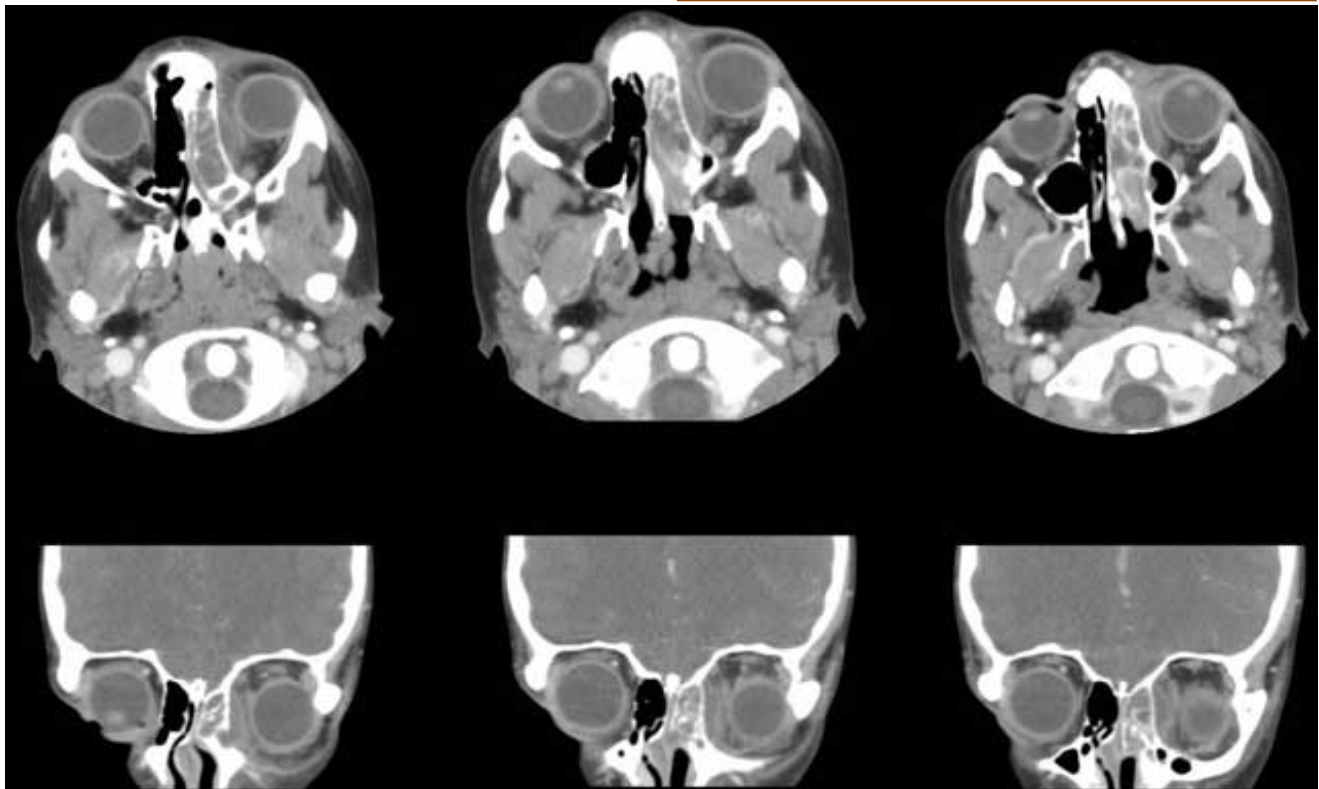
Figure 6. Post treatment motility assessment

Figure 4. CT max/face: Subperiosteal abscess formation adjacent to the lamina papyracea of the left orbit with extensive sinusitis involving the left ethmoid sinus

Hospital Course: The patient was admitted into the hospital and treated with IV ceftriaxone and clindamycin. She was also treated with Afrin® (oxymetazoline) spray. Otolaryngology was consulted to address the sinusitis.

Her symptoms improved quickly after the initiation of IV antibiotics treatment. Her motility was almost full after one day of treatment. The patient was monitored every 12 hours by ophthalmology. By admission day 3, the patient was feeling better with full motility and much improved erythema and edema of her left eye. Diplopia was resolved.

Her sinus symptoms had also improved.

The patient was discharged home on hospital admission day 4 with a two-week course of clindamycin and nasal steroids.

Discussion

Orbital cellulitis is an infection of the soft orbital tissue posterior to the orbital septum. This is in contrast to preseptal cellulitis which is a soft tissue infection of the eyelids anterior to the orbital septum. If a diagnosis of preseptal cellulitis is entertained, a well-defined event should be elicited from the patient (e.g. injury, stye, bug bite, etc). If a convincing event cannot be elicited, an orbital etiology should always be investigated with orbital imaging. The patient in this case was diagnosed initially with a preseptal cellulitis with no predisposing event.

The most common bacterial organisms in orbital cellulitis include *Streptococcus* species, *Staphylococcus* aureus, *Pseudomonas*, *Enterococcus*, *Klebsiella*, and *Haemophilus influenzae* type B. Methocillin-resistant staph aureus is becoming more common in orbital cellulitis. If a fungal infection is suspected, consider *Mucor* and *Aspergillus* species.

90% of cases occur as a secondary extension of acute or chronic bacterial sinusitis, especially the ethmoid sinuses. Other extensions of periorbital structures include the face/eyelids, dacryocystitis and dental infections. Exogenous causes include trauma and orbital/periorbital surgery. An orbital foreign body (specifically organic) should always be entertained in the setting of an orbital cellulitis that is not responding to antibiotic therapy. Endogenous causes include septic embolization from bacteremia. There may also be intraorbital causes including endophthalmitis and dacryoadenitis.

Orbital clinical findings include proptosis, ptosis, restriction of ocular motility, ocular pain, and chemosis. If there is decreased visual acuity, or a visual field or relative afferent pupillary defect, one must consider compressive optic neuropathy which warrants urgent aggressive management.

Systemic clinical findings are essential in the workup of possible orbital cellulitis. Pertinent findings include leukocytosis and fever. In this patient, she had already been treated with a four day course of antibiotics which explains her afebrile state as well as her normal WBC count. However she still exemplified elevated neutrophils, monocytes, ESR and CRP which also demonstrate an infectious etiology.

CT of the orbits and the paranasal sinuses is essential. Evidence of sinusitis mandates otolaryngology involvement. Lumbar puncture is necessary if meningeal signs and symptoms develop. Conjunctival cultures add very little information. Nasal cultures may be appropriate if there is significant nasal discharge in the setting of sinusitis. Blood cultures are appropriate in the setting of septicemia. If surgical drainage of the orbita and/or sinus is performed, cultures should be obtained.

Surgical intervention is less likely in orbital cellulitis in children (≤ 9 years old) because the infection is caused by a single gram positive organism. IV antibiotic therapy is the initial treatment of choice. Progression (worsening motility deficit, pain, optic nerve dysfunction) in a child after 24-48 hours of IV antibiotic therapy would lead one to drain the abscess. However, if this were an adult patient, with evidence of an abscess formation, early surgical intervention to drain the involved sinus and orbital abscess is usually indicated along with medical therapy given that the infection is more likely to be polymicrobial.

Consider surgical management if the patient has any of the following
- ♦ > 9 years old
- ♦ Frontal sinusitis
- ♦ Non medial location of the subperiosteal abscess
- ♦ Large subperiosteal abscess
- ♦ Presence of gas in the abscess on CT suggesting an anaerobic etiology
- ♦ Recurrent episode of subperiosteal abscess
- ♦ Nasal polyps which suggest chronic sinusitis
- ♦ Evidence of acute optic neuropathy
- ♦ Dental infection (likely an anaerobic infection)

Clinical improvement does not correlate accurately with repeat CT scan analysis. It may take 48-72 hrs for the abscess to improve on imaging.

The majority of patients respond well to medical and/or surgical treatments. Rarely, orbital cellulitis may spread posteriorly to the cavernous sinus, meninges and the brain parenchyma.

Diagnosis: Orbital Cellulitis

Differential Diagnoses

Infectious orbital inflammation
- ♦ Preseptal cellulitis
- ♦ Orbital cellulitis
  - o Bacterial
  - o Fungal
- ♦ Dacryocystitis
- ♦ Dacryoadenitis
- ♦ Endophthalmitis

Non-infectious orbital inflammation
- ♦ Thyroid eye disease
- ♦ Wegener 's granulomatosis
- ♦ Sarcoidosis
- ♦ Churg-Strauss
- ♦ Malignancy
- ♦ Idiopathic orbital inflammatory syndrome

EPIDEMIOLOGY	SIGNS
♦ Increased incidence during the winter due to the increased incidence of sinusitis ♦ No ethnic preferences ♦ Blindness occurs in up to 11% of cases ♦ In children, twice as common in males ♦ More common in children than adults: mean age 7-12 years old.	♦ Proptosis ♦ Ptosis ♦ Chemosis ♦ Lid erythema/edema ♦ Motility restriction
SYMPTOMS	TREATMENT
♦ Ocular/periorbital pain ♦ Decreased vision ♦ Diplopia ♦ Nasal discharge ♦ Worsening pain on eye movement ♦ Nasal tenderness	**In children** ♦ Inpatient - broad spectrum IV antibiotics which is narrowed or tailored to the most likely or documented organism. Consider covering for MRSA. If the patient is afebrile and improving x 48hrs, may switch to oral antibiotics. ♦ Outpatient oral antibiotics for 2-3 weeks ♦ Consider surgical management if worsening on IV antibiotics or have the special conditions listed above in the Discussion section **In adults** ♦ Inpatient - surgical debridement of orbital abscess and associated sinus along with IV antibiotics. ♦ Outpatient oral antibiotics for 2-3 weeks

References

1. Garcia GH., et al. Criteria for nonsurgical management of subperiosteal abscess of the orbit. Ophthalmology. 2000;107:1454-1458. PubMed.gov/10919887

2. Harris GJ. Subperiosteal abscess of the orbit: age as a factor in the bacteriology and response to treatment. Ophthalmology. 1994;101:585-595. hPubMed.gov/8127580

3. Basic and Clinical Science Course, Section 6. Orbit, Eyelids and Lacrimal System. American Academy of Ophthalmology. 2009, pp.231-233.

4. McKinley SH., et al. Microbiology of pediatric orbital cellulitis. Am J Ophthalmol. 2007;144:497-501 PubMed.gov/17698020

5. Nageswaran S., et al. Orbital cellulitis in children. Pediatr Infect Dis J. 2006;25:695-699. PubMed.gov/16874168

Citing this Article

Hong ES, Allen RC. Orbital Cellulitis in a Child. EyeRounds.org. January 12, 2010; Available from: http://www.EyeRounds.org/cases/103-Pediatric-Orbital-Cellulitis.htm

last updated: 01-12-2010

Congenital dacryocystocele with spontaneous resolution

Elizabeth H. Gauger, MD and Susannah Q. Longmuir, MD

March 7, 2013

Chief complaint: Full-term 10 day-old female referred to the pediatric ophthalmology clinic by dermatologist for a bluish mass inferior to the right medial canthus.

History of present illness: Initially a cystic lesion was noted on the fetus' face on a 28-week ultrasound. At birth, an elevated, bluish lesion was noted just inferior to the right medial canthus. The lesion did not seem to bother the patient, and it had not changed in size or appearance since birth. The local pediatrician was concerned it was a hemangioma and referred the patient to dermatology. Dermatology subsequently evaluated the patient and referred her to pediatric ophthalmology for further management.

Past Ocular History: Unremarkable

Past Medical History: Unremarkable

Medications: None

Allergies: No known drug allergies

Family History: No known eye disease

Ocular Exam

- ♦ **External Exam** (Figure 1):
  - ○ **Right eye (OD)**: 12mm horizontal by 15mm vertical elevated, bluish cystic lesion at medial canthus below medial canthal tendon. Punctum present inferiorly. Punctum not visualized superiorly.
  - ○ **Left eye (OS)**: Normal
- ♦ **Visual Acuity:** Winces to light OD and OS
- ♦ **Pupils**: Reactive. No anisocoria and no relative afferent pupillary defect
- ♦ **Intraocular pressure:** Physiologic by palpation

- ♦ **Alignment**: Ortho by Hirschberg
- ♦ **Anterior segment exam**: Within normal limits
- ♦ **Dilated funduscopic exam**: Deferred until examination under anesthesia (EUA)

Clinical Course

The clinical exam features were felt to be classic for and consistent with a congenital dacryocystocele. An examination under anesthesia and probing of the lacrimal system on the right side was planned for three days later. The patient was started on oral Augmentin (amoxicillin/clavulanate), due to concern for early infection of the dacryocystocele.

On the morning of the procedure, the child was seen in the pre-operative area. The mother reported that the prior evening, there had been a large amount of discharge from the medial canthal area, and the swollen, blue cystic area had spontaneously decompressed.

Given that the dacryocystocele had spontaneously decompressed, probing of the nasolacrimal system was deferred. Tobradex (tobramycin/dexamethasone ophthalmic suspension) drops four times a day to the right eye were prescribed for prophylaxis. The child was to follow-up in clinic in one week for further evaluation. No further complications or problems occurred in this infant.

Discussion

Presentation of congenital dacryocystocele

Congenital dacryocystocele, also known as a *dacryocele*, often presents shortly after birth. It is an infrequent variant

A. External exam of infant. Note the purplish swelling inferior to the medial canthal tendon.
Figure 1: External exam of infant.

B. The mass is causing upward slanting/displacement of the palpebral fissure nasally.

of nasolacrimal duct obstruction (NLDO) and found in only about 1.0% of infants with congenital NLDO.[1]

Congenital dacryocystocele often presents as a bluish, cystic, firm mass inferior to the medial canthus. One study cited the median age of presentation as 7 days of life.[2] It is most commonly unilateral but may be bilateral. Multiple studies have found that the condition is more common in females than in males, secondary to females having a more narrow nasolacrimal duct than males.[2]

Patients with a dacryocystocele may have difficulty breathing or develop infection of the site. Parents may notice that the child has difficulty breastfeeding and develops respiratory difficulty when feeding on the breast ipsilateral to the dacryocystocele.[2]

Diagnosis

Often, the diagnosis of congenital dacryocystocele can be made based on clinical findings alone. However, if the diagnosis is in question, a computed tomography (CT) scan or magnetic resonance imaging (MRI) can be used to confirm the diagnosis. Interestingly, the diagnosis can also be made prenatally with ultrasonography.[3] Items that should be considered in the differential diagnosis include: encephalocele, meningocele, and encephalomeningocele. These generally occur superior to the medial canthus, however. These are potentially life-threatening diagnoses that should be promptly evaluated.

Congenital dacryocystocele can be considered a subcategory of congenital NLDO. In both, there is improper drainage of tears; however, they differ in the site of the blockage. In NLDO, the blockage generally occurs distally at the valve of Hasner. Thus, there is backlog of the drainage system leading to a watery eye and epiphora. With a dacryocystocele, there is a functional blockage proximally as well as a blockage distally. This leads to fluid accumulation (amniotic fluid and mucous produced by the lacrimal sac glands) causing distention (Figure 2). The proximal blockage is thought to be caused by failure of the mesoderm to properly canalize during development.[2]
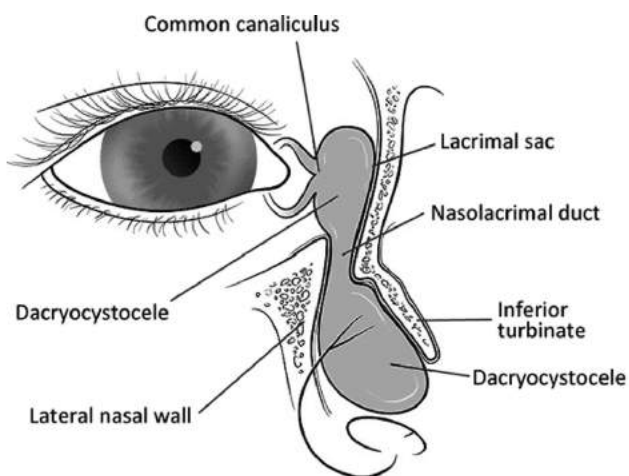
Treatment

Treatment options for dacryocystocele range from conservative, non-surgical management (massage, observation) to surgical (probing of nasolacrimal system).[3] Initially conservative measures should be tried. This includes digital massage over the area of elevation and prophylactic topical antibiotics. If no response to treatment is seen within 1-2 weeks, probing and irrigation of the lacrimal system either in the clinic or operating room is recommended (Figures 3 and 4). One study reported that approximately 22% of cases spontaneously resolved, while the remainder required surgical intervention.[2]

Should the dacryocystocele progress to dacryocystitis, antibiotics are indicated.[2] As children who develop dacryocystitis are often one month of age or younger, admission to the hospital may be recommended depending on age, medical co-morbidities, and follow-up. Sepsis is a life threatening complication if the infection goes without treatment. If there is an intranasal component (endonasal cyst), marsupialization of the cyst is recommended, and an otolaryngology consult may be appropriate depending on the surgeons experience.[4]

Complications

There are several complications that can occur as a result of a dacryocystocele. These include: dacryocystitis, cellulitis, and respiratory compromise. In cases of infection, the child may experience life-threatening sepsis. Therefore, it is important if the child develops concurrent dacryocystitis and cellulitis that they be hospitalized for observation and administration of intravenous antibiotics.[3] Once the infection subsides, probing with or without stent placement is advised.

Rarely, dacryocystocele can be associated with an intranasal cyst. If one opts to try conservative management initially, these children must be monitored for signs of infection or breathing difficulty. Consultation with an otolaryngologist or endoscopic nasal endoscopy should be performed at the time of probing. Should any of the above complications occur, prompt management (antibiotics, probing, surgery) is required.[2]

Figure 2: Schematic drawing of a congenital dacryocystocele. (Used with permission)[3]

Figure 3: Example of a congenital dacryocystocele in a newborn.

A. Decompression of dacryocystocele in the operating room.

Figure 4

B. Subsequent probing and irrigation.

Epidemiology	Signs
♦ Presents within first several days to weeks of life (median age = 7 days of life)[2] ♦ Usually unilateral	♦ Elevated purplish mass *inferior* to medial canthal tendon ♦ Epiphora, mattering (generally unilateral)
Symptoms	**Treatment**
♦ Tearing ♦ Mattering	♦ Conservative: Digital massage, ♦ Surgical: Probing and irrigation
Differential Diagnosis	**Complications**
♦ Hemangioma: Usually presents later, softer to touch ♦ Encephalocele: Usually *superior* to medial canthal tendon ♦ Dermoid: Usually *superior* to medial canthal tendon ♦ Nasal glioma	♦ Dacryocystitis ♦ Cellulitis ♦ Respiratory compromise ♦ Sepsis CT or MRI should be performed if more serious etiology suspected

Diagnosis: Congenital Dacryocystocele

References

1. MacEwen CJ, Young JD. Epiphora during the first year of life. Eye (Lond) 1991;5(Pt 5):596-600.
2. Wong RK, VanderVeen DK. Presentation and management of congenital dacryocystocele. Pediatrics 2008;122:e1108-12.
3. Becker BB. The treatment of congenital dacryocystocele. Am J Ophthalmol 2006;142:835-8.
4. Lueder GT. Endoscopic treatment of intranasal abnormalities associated with nasolacrimal duct obstruction. J AAPOS 2004;8:128-32.

Citing this Article

Phlyctenular Keratoconjunctivitis

12-year-old Female with Staphylococcal Blepharitis

Arpitha Muthialu, MD; Lauren E. Jensen; Michael Wagoner, MD, PhD

February 27, 2009

Chief Complaint: Blurry vision and discomfort in the right eye.

History of Present Illness: A 12-year-old female complains of blurry vision, foreign body sensation, and photophobia in her right eye. While she has had chronic problems for years in both eyes, she has noted the acute onset and progressive worsening of the symptoms in the right eye for one week.

Past Ocular History: Since the age of 6, the patient has struggled with meibomian gland dysfunction and chronic staphylococcal blepharoconjunctivitis, as well as seasonal allergic conjunctivitis. She has been treated with topical corticosteroids, antibiotics, and antihistamines since age 8 and systemic doxycycline since age 9.

Medical History: Otherwise healthy.

Medications: Since her last exam 8 months prior to this presentation, she was completely asymptomatic on a regimen of

- Doxycycline (100mg orally once daily)
- Prednisolone acetate 1.0% (twice daily drops)
- TobraDex (Tobramycin and Dexamethasone) ointment nightly

The patient had discontinued all of these systemic and topical medications one month prior to the current episode upon the suggestion of a maternal aunt who recommended adoption of a "holistic and naturalistic" approach to the management of her chronic ocular disorders.

Family History: Noncontributory

Physical and Ocular Examination

- General: healthy-appearing young female
- Visual Acuity, without correction
  - Right eye (OD)--20/80 (with pinhole improves to 20/50)
  - Left eye (OS)--20/20
- Extraocular Motility: Full, both eyes (OU)
- Intra-ocular pressure: OD -- 17mmHg; OS -- 14 mmHg
- External and anterior segment examination (see Figure 1A-C and Figure 2A-B)
  - Right eye
    - Lids/adnexa: mild anterior blepharitis
    - Conjunctiva/sclera: 2+ diffuse conjunctival injection
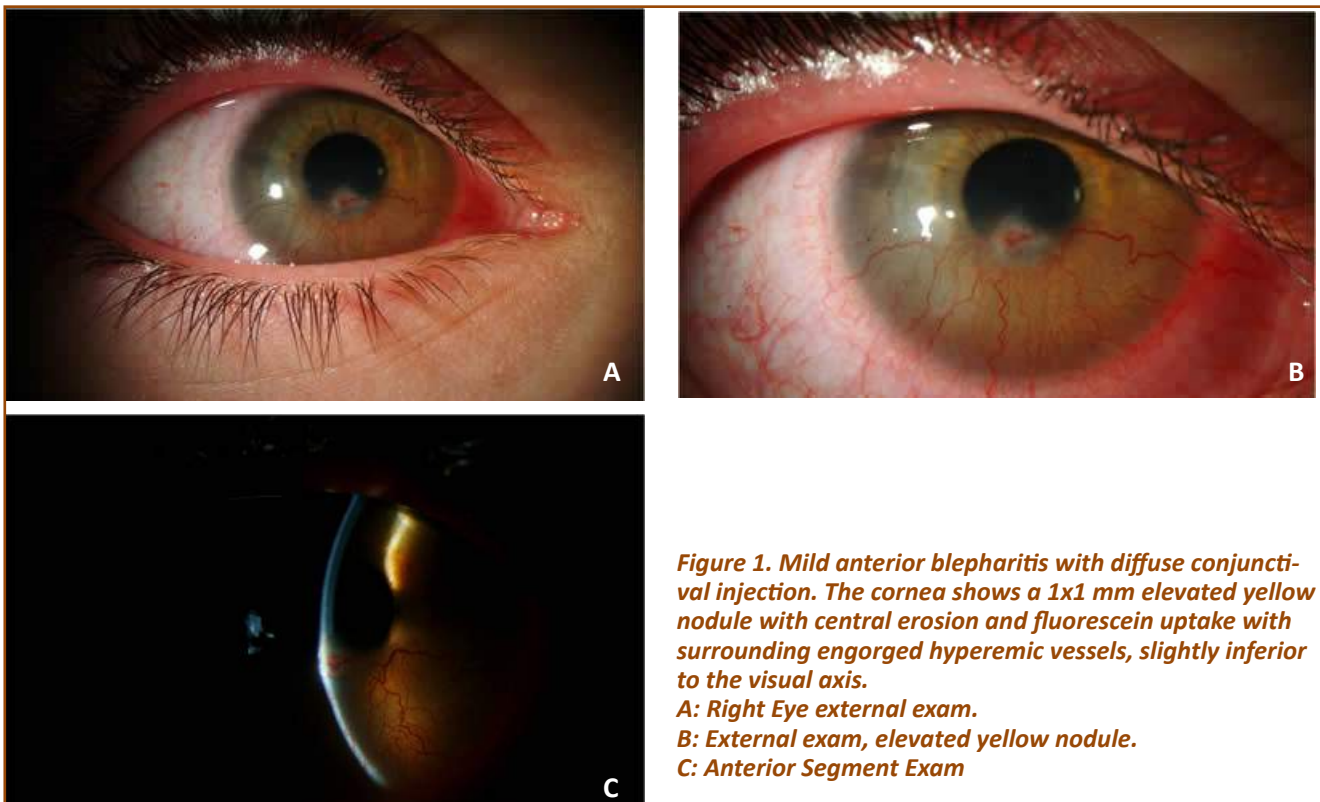
Figure 1. Mild anterior blepharitis with diffuse conjunctival injection. The cornea shows a 1x1 mm elevated yellow nodule with central erosion and fluorescein uptake with surrounding engorged hyperemic vessels, slightly inferior to the visual axis.
A: Right Eye external exam.
B: External exam, elevated yellow nodule.
C: Anterior Segment Exam

- Cornea: 1x1 mm elevated yellow nodule with central erosion and fluorescein uptake with surrounding engorged hyperemic vessels, slightly inferior to the visual axis; there is 360 degree limbal pannus
- Anterior chamber: deep and quiet
- Iris is normal and lens is clear
- Left eye
  - Lids/adnexa: mild anterior blepharitis
  - Conjunctiva/sclera: quiet and white
  - Cornea: 360 degree limbal pannus
  - Anterior chamber: deep and quiet
  - Iris is normal and lens is clear
- Dilated fundus exam (DFE): No pallor or edema of either disc. Normal macula, vessels, and periphery, OU

Mild anterior blepharitis with diffuse conjunctival injection. The cornea shows a 1x1 mm elevated yellow nodule with central erosion and fluorescein uptake with surrounding engorged hyperemic vessels, slightly inferior to the visual axis.

Discussion

Phlyctenular keratoconjunctivitis (PKC) is a localized noninfectious inflammatory/ hypersensitivity disorder of the ocular surface characterized by subepithelial nodules of the conjunctiva and/or cornea. These "phlyctenules," are derived from "phlyctena," the Greek word for "blister." The blister characterization was likely chosen due to the tendency for the nodules to ulcerate once necrosis occurs. Histopathologically, phlyctenules are subepithelial inflammatory nodules containing histiocytes, lymphocytes, plasma cells, and neutrophils. Mononuclear phagocytes, dendrites Langerhans cells, and neutrophils make up the majority of the inflammatory cells in the epithelium overlying the phlyctenule.

The pathogenesis of PKC is thought to be a hypersensitivity reaction to an antigen of bacterial origin. PKC has been classically associated with *M. tuberculosis* (especially in developing countries). However, *Staphylococcus aureus* is the cause in majority of cases in the United States. A number of other organisms are also associated with PKC (Table 1).

Table 1: Organisms Implicated in the Pathogenesis of Phlyctenular Keratoconjunctivitis

- Mycobacterium tuberculosis
- Staphylococcus aureus
- Chlamydia trachomatis
- Neisseria gonorrhea
- Coccidiodes immitis
- Bacillus spp.
- Herpes simplex virus
- Leishmaniasis Ascaris lubricoides
- Hymenlepsis nana
- Candida spp.

Most often, phlyctenulosis is a corneal sequelae of chronic Staphylococcal blepharitis, a disorder that often presents in the clinic as chronic conjunctivitis or keratitis characterized by punctate epithelial keratopathy, and/or marginal corneal infiltrates (Table 2). When present, symptoms of PKC depend upon the location of the lesion. Conjunctival lesions usually present with mild to moderate symptoms, including foreign body sensation, tearing, photophobia, burning, and itching. Corneal lesions typically present with more severe symptoms of the same variety.

Corneal phlyctenules usually begin at the limbus and spread centrally, perpendicular to the limbus, leaving no clear zone between the lesion and the limbus. The vessels run in a straight course from the limbus. They can become necrotic and ulcerate centrally or spontaneously involute within 2 to 3 weeks. Upon resolution, a wedge-shaped fibrovascular scar may remain. Centripetal migration of successive inflammatory lesions may develop as in this case. Rarely, inflammation associated can lead to keratolysis and perforation.

Treatment

Management of PKC requires both anti-inflammatory and anti-bacterial management, as well as management of chronic blepharitis. Control of inflammation can be achieved with topical corticosteroids, which should be tapered very slowly to avoid recurrences. Antibacterial measures may include a several week course of application of topical antibiotics to the eyelid margin and conjunctiva,

Figure 2A: External Exam. Left eye.

Figure 2B: External Exam of left eye shows mild anterior blepharitis
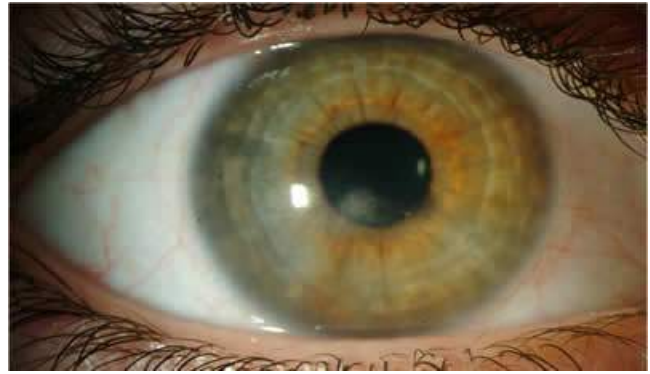
Figure 3A: Right eye, post-treatment

Figure 3B: Right eye, post-treatment

igure 3C: post-treatment

Figure 3D: post-treatment anterior eye exam.

especially at bedtime. Management of chronic blepharitis requires a consistent regimen of lid hygiene and warm compresses, as well as systemic administration of tetracycline derivatives, such as Doxycycline for patients without contraindications. Tetracyclines should not be used in children under age 8 because permanent tooth discoloration can occur. In addition, tetracycline is teratogenic and should be avoided in pregnant women, as well as in nursing mothers.

Follow-up Course

Our patient responded dramatically to topical prednisolone acetate 1% which was initially used every 2 hours while awake. She was treated with a 1 week course of topical gatifloxacin drops four times daily (to prevent infection at the epithelial defect) and a 3 week course of TobraDex® ointment at bedtime. Management of chronic blepharitis was achieved by reinstating a strict program of lid hygiene and warm compresses, along with reinstituting doxycycline 100 mg orally twice daily for one month and then once daily thereafter. Within 1 week, she responded readily to this treatment with improved vision and decreased discomfort (post-treatment images Figure 3A-D), after which topical corticosteroid therapy was gradually tapered.

Diagnosis

Phlyctenular keratoconjunctivitis

Differential Diagnoses for Corneal nodule and irritation

♦ Staphylococcal marginal keratitis with phlyctenule
♦ Microbial keratitis
♦ Inflamed pseudopterygium
♦ Salzmann's nodule
♦ Corneal foreign body

http://www.eyerounds.org/cases/89_Phlyctenular-Keratoconjunctivitis-Staphylococcal-Blepharitis.htm

EPIDEMIOLOGY	SIGNS
♦ Predominantly young individuals	♦ Staphylococcal blepharitis ♦ Inflammation of cornea or conjunctiva ♦ Wedge-shaped nodular lesion and engorged hyper-emic vessels at or near the limbus, bulbar conjunctiva, or cornea
SYMPTOMS	**TREATMENT**

♦ Redness, foreign body sensation, morning crusting, photophobia, itching
♦ Decreased vision
	♦ Antibacterial
	  • Eyelid hygiene
	  • Ointment to lid margin (i.e. TobraDex)
	  • Topical antibiotics initially (i.e. gatifloxacin)
	♦ Anti-inflammatory
	  • Topical corticosteroids (i.e. prednisolone 1% q2-q4 hours)
	♦ Treat the blepharitis
	  • Eyelid hygiene
	  • Warm compresses
	  • Oral doxycycline (100mg Daily to BID)

References

1. Albert DM, Jakobiec FA, eds. Principles and Practice of Ophthalmology. 2nd ed. Philadelphia: Saunders; 2000. p. 1093-1099.

2. Gokhale J et al. Etiology of Phlyctenulosis. Indian Journal of Ophthalmology. 1965. Vol 13 (2): 65-67.

3. Jackson WB. Blepharitis: Current strategies for diagnosis and management. Can J Ophthalmol. 2008: 43(2):170-9.

4. Krachmer JH, Mannis MJ, Holland EF, eds. Cornea. 2nd ed. Philadelphia: Elsevier Mosby; 2005. p. 1235-1238.

5. Rapuano CJ, Luchs JI, Kim T. Anterior Segment: The Requisites in Ophthalmology. St. Louis: Mosby; 2000. p. 165-168.

Additional Reading

Wagoner MD, Bajart AM, Allansmith MR. Phlyctenulosis. In: Fraunfelder FT, Roy FH *Current Ocular Thearapy 3*. Philadelphia, PA; W.B. Saunders Co. 1990. p. 454-445

Citing this article

Muthialu A, Jensen LE, Wagoner M. Phlyctenular Keratoconjunctivitis: 12-year-old Female with Staphylococcal Blepharitis. EyeRounds.org. February 27, 2009; Available from: http://www.eyerounds.org/cases/89_Phlyctenular-Keratoconjunctivitis-Staphylococcal-Blepharitis.htm

last updated: 02-27-2009

Retina & Vitreous

Intraocular Foreign Body

A Classic Case of Metal on Metal Eye Injury

Paul Abrams, B.S. (M4), Emily S. Birkholz M.D., Ryan M. Tarantola M.D., Thomas A. Oetting M.D., Stephen R. Russell M.D.

May 24, 2011

Chief Complaint: Acute right eye pain

History of Present Illness: A 36-year-old male presented with right eye pain immediately after he had been pounding a metal object with a metal chisel. He was not wearing safety glasses and felt something strike his right eye. This was followed by tearing and blurred vision. He continued working for a few hours, but when the vision and tearing did not improve he went to a local emergency room. He was diagnosed with a corneal abrasion and sent home on topical antibiotics. An appointment with a local ophthalmologist was made for the following morning where his vision was found to be hand motions, a traumatic cataract had developed, and there was suspicion of an intraocular foreign body (IOFB). He was then referred emergently to the University of Iowa Ophthalmology On Call Service.

Past Ocular History: The patient had no previous eye trauma, disease, or surgery.

Medical History: Unremarkable

Medications: Moxifloxacin eye drops

Family and Social History: Noncontributory

Review of Systems: Negative

OCULAR EXAMINATION

Visual acuity
- Right eye (OD) HM
- Left eye (OS) 20/20
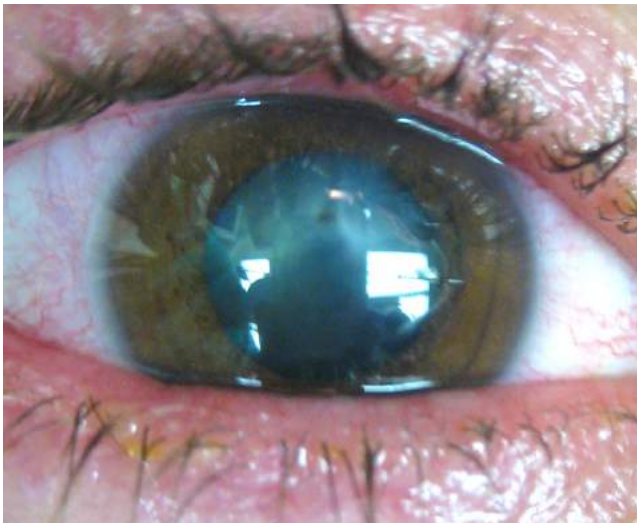
Figure 1: Right eye at presentation. Note the traumatic cataract

Intraocular pressure
- OD 16 mmHg
- OS 17 mmHg

Pupils: Dilated upon arrival by outside ophthalmologist

External and anterior segment examination (see Figure 1)
- OD: Conjunctiva mildly injected, no conjunctival lacerations, no subconjunctival hemorrhage. Cornea with central 1 mm Seidel-negative full-thickness laceration. Anterior chamber formed, 1+ cell, no hypopyon or hyphema. Dense traumatic cataract with disruption of anterior lens capsule. No view of the anterior vitreous.
- OS: Normal

Dilated fundus exam (DFE)
- OD: No view due to cataract
- OS: Normal

Since there was no view to the posterior pole and we suspected an IOFB due to the presence of the cataract and the mechanism of injury, the patient underwent echography of the right globe. (See Figure 2.)

CLINICAL COURSE

The patient was diagnosed with a corneal laceration, traumatic cataract, and a metallic IOFB. He was brought to the
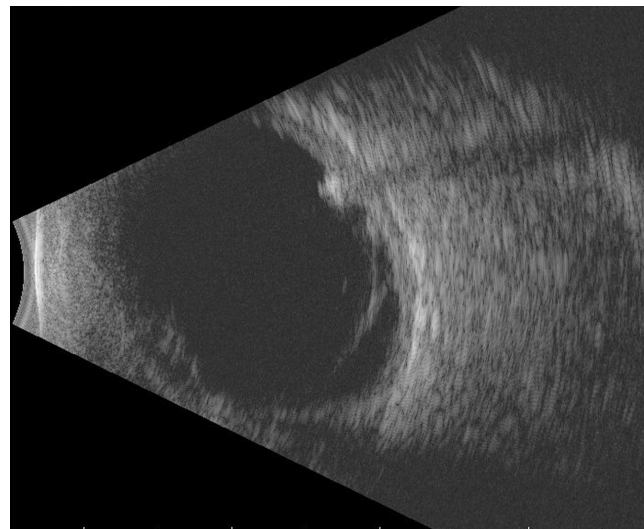

Figure 2: Ultrasound imaging revealed a dense cataract, mild vitreous hemorrhage with a tract-like membrane extending posteriorly, and a highly reflective mobile-appearing opacity lying posteriorly near the optic nerve with shadowing. There was no retinal detachment and no choroidal hemorrhage. The posterior scleral wall was intact. A posterior vitreous detachment was also present.

operating room urgently for corneal laceration repair, pars plana vitrectomy, lensectomy, and removal of the metallic IOFB. Prior to surgical repair, the patient received one dose of intravenous antibiotics (cefazolin 1000 mg and vancomycin 1250 mg) and had his tetanus shot updated.

Please View Video at: **vimeo.com/258087704**

Creating a water-tight globe was the first priority, which was accomplished by closing the corneal laceration with 2 10-0 nylon sutures (see Figure 3A). A peritomy was performed, followed by scleral incisions for 20-gauge vitrectomy. Using the vitrector, the cataract and posterior capsule were removed with care to preserve the anterior capsule for future intraocular lens placement. A core and periph-
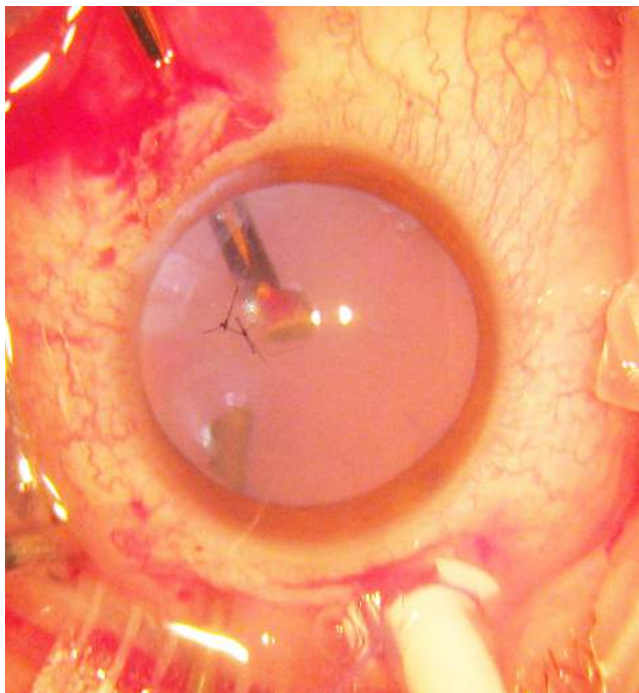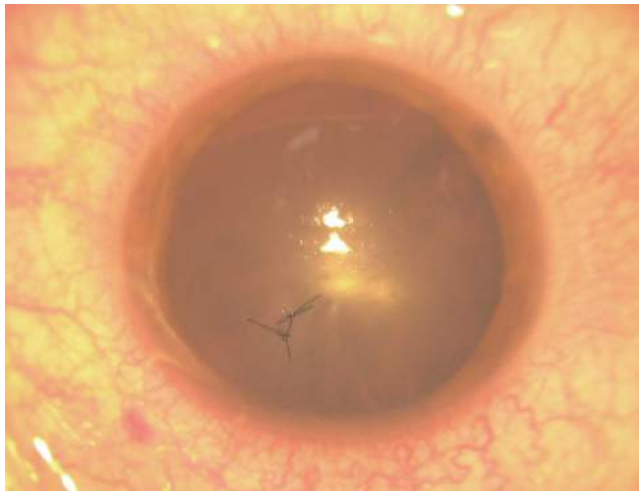
Figure 3. A. Photo in the operating room showing the 10-0 nylon sutures sealing the corneal laceration. B. Photo in the operating room of the intraocular rare earth magnet holding the metallic IOFB

eral vitrectomy were then performed. The retina was then examined and a metallic object with a surrounding inflammatory capsule was found embedded in the retina, temporal to the macula. Laser demarcation of the retina surrounding the metallic IOFB was performed using an endolaser. An intraocular rare earth magnet was inserted into the eye and used to engage and lift the IOFB anteriorly into the vitreous cavity (see Figure 3B). Forceps were then inserted to grab the IOFB from the magnet and remove it from the eye. A careful indented peripheral retinal examination was performed, which did not reveal any other retinal breaks or impact sites. The scleral and conjunctival incisions were closed with 7-0 Vicryl suture. Fifty mg of cefazolin and 10 mg of dexamethasone were injected beneath the conjunctiva.

Post-operatively the patient was instructed to use scopolamine twice daily and tobramycin-dexamethasone ointment 4 times daily in the operative eye. At the first post-operative week, vision in the right eye had improved to 20/60-1 with a +10.00 diopter (D) lens. At his 8 week follow-up, the patient's vision improved to 20/25-3 with a +10.0D lens.

He is to undergo secondary intraocular lens placement after all inflammation has subsided and his corneal stitches are removed. Until his secondary intraocular lens is placed, he will continue to wear a +13.00D contact lens in this aphakic right eye.

DISCUSSION

This case illustrates the stereotypical history for a metallic IOFB--a young male who is hammering or chiseling metal on metal and feels something strike the eye. Based on the history alone, the possibility of an IOFB should be thoroughly investigated, or the diagnosis can easily be missed due to the sometimes underwhelming external clinical appearance. Although he was evaluated in the emergency room on the day of his injury, this patient did not undergo a dilated exam, an ophthalmologist was not consulted the day of his injury, nor did he have any imaging to evaluate for the possibility of an IOFB. He was diagnosed with a corneal abrasion and no further work-up was done. The possibility of IOFB was not considered until the follow up visit with an ophthalmologist more than 16 hours after the injury. This delay in diagnosis can lead to a worse prognosis depending upon the location of the IOFB and the development of associated endophthalmitis, particularly if the IOFB is organic material or if the injury is sustained in a rural environment (Boldt 1989).

Epidemiology: Foreign bodies are one of the most common causes for ophthalmologic emergencies, which represent 3% of all United States emergency room visits (Babineau 2008). Risk factors include being male, not wearing eye protection, and performing a metal-on-metal task (hammering or chiseling a metal object) (Ehlers 2008, Babar, 2007, Napora 2009). The mean age at which injury occurred was 33 years. The foreign body most frequently enters the cornea, and approximately 65% of them land in the posterior segment (Ehlers 2008).

Treatment: Treatment depends on the location and scope of the injury but usually involves emergent removal of the IOFB with repair of any damaged structures. This may involve an anterior approach if the IOFB is located in the anterior chamber and may include corneal laceration repair, lensectomy, and/or anterior vitrectomy. A very careful retinal examination must be performed to identify an IOFB, the impact site of the IOFB, the presence of multiple IOFBs, and any other retinal damage including tears or detachments that may have occurred. If visualization of the retina is not possible due to a cataract or vitreous hemorrhage, imaging via a CT of the orbits or ultrasound of the globe is essential to evaluate for an IOFB. If the posterior segment is involved, a pars plana approach is utilized. The IOFB can be removed (if metallic) using an external or internal magnet or forceps. Typically, a pars plana vitrectomy is also performed. If a retinal tear or detachment is identified it is often repaired at the time of IOFB removal. If the IOFB is organic, or if the injury occurs in a rural setting, one may choose to culture the vitreous and IOFB and inject intravitreal antibiotics at the time of surgery as well.

Complications: One of the most common complications of an IOFB is a retinal detachment (14-26%). Other complications include: endophthalmitis (4-6%), corneal scar, cataract, angle recession glaucoma, vitreous hemorrhage, retained IOFB, blind/painful eye, and sympathetic ophthalmia (Ehlers 2008).

Prognostic factors: Patients with smaller wound lengths (under 2mm), IOFBs that are located in the anterior segment only, and those with a normal lens at presentation have the best prognosis. Negative prognostic factors include a longer wound length (greater than 3.5mm), posterior segment IOFB, poor initial visual acuity, and the presence of complications arising from IOFB (retinal detachment, endophthalmitis) (Ehlers 2008, Bai 2010, Unver 2009).

Endophthalmitis: Endophthalmitis is a concern with any type of IOFB. If the foreign body contains organic matter, intravitreal injection of gentamycin and either vancomycin or clindamycin was previously suggested (Boldt 1989); however, the use of ceftazidime has now largely replaced that of gentamycin in order to avoid aminogylcoside toxicity. Foreign bodies that result from metal-on-metal activity are less likely to contain organic material or bacterial contamination. In theory, the heat of the object as well as the anti-bacterial nature of ionized metals makes it difficult for bacteria to survive. It is still reasonable, however, to culture and treat with intravitreal antibiotic injections at the conclusion of the surgery.

DIAGNOSIS: Intraocular Foreign Body

EPIDEMIOLOGY	SIGNS
♦ Mean age 33 years ♦ Male ♦ Metal on metal mechanism of injury ♦ No eye protection	♦ Penetrating corneal or scleral injury ♦ Traumatic cataract ♦ Iris defect, peaked pupil ♦ Vitreous hemorrhage ♦ Retinal tear/detachment ♦ Commotio retinae ♦ Ultrasound or CT showing highly reflective/hyperintense object
SYMPTOMS	**TREATMENT**
♦ Decreased vision ♦ Eye pain ♦ Eye redness	♦ Complete ocular examination including detailed retinal examination ♦ Suture of corneal or scleral entrance wound ♦ IOFB removal using magnet or forceps, anterior or posterior approach depending on location of IOFB ♦ Possible pars plana vitrectomy ♦ Possible lensectomy if traumatic cataract ♦ Possible repair of retinal detachment

References

Babar TF, Khan MT, Marwat MZ, Shah SA, Murad Y, Khan MD. Patterns of ocular trauma. *J Coll Physicians Surg Pak* 2007;17(3):148-153. PubMed.gov/17374300. DOI: 03.2007/JCPSP.148153

Babineau MR, Sanchez LD. Ophthalmologic procedures in the emergency department. *Emerg Med Clin North Am* 2008;26(1):17-34, v-vi. PubMed.gov/18249255. DOI: 10.1016/j.emc.2007.11.003

Bai HQ, Yao L, Meng XX, Wang YX, Wang DB. Visual outcome following intraocular foreign bodies: a retrospective review of 5-year clinical experience. *Eur J Ophthalmol* 2011;21(1):98-103. PubMed.gov/20544679

Boldt HC, Pulido JS, Blodi CF, Folk JC, Weingeist TA. Rural endophthalmitis. *Ophthalmology* 1989;96(12):1722-1726. PubMed.gov/2622617

Ehlers JP, Kunimoto DY, Ittoop S, Maguire JI, Ho AC, Regillo CD. Metallic intraocular foreign bodies: characteristics, interventions, and prognostic factors for visual outcome and globe survival. *Am J Ophthalmol* 2008;146(3):427-433. PubMed.gov/18614135. DOI: 10.1016/j.ajo.2008.05.021

Napora KJ, Obuchowska I, Sidorowicz A, Mariak Z. [Intraocular and intraorbital foreign bodies characteristics in patients with penetrating ocular injury]. *Klin Oczna* 2009;111(10-12):307-312. PubMed.gov/20169884

Unver YB, Acar N, Kapran Z, Altan T. Prognostic factors in severely traumatized eyes with posterior segment involvement. *Ulus Travma Acil Cerrahi Derg* 2009;15(3):271-276. PubMed.gov/19562551

Additional Reading

Bouraoui R, Bouladi M, Mghaieth F, Chaker N, Sammouda T, El Matri L. A metallic intraocular foreign body discovered 26 years after ocular injury. *Tunis Med* 2016;94(3):245-246. PubMed.gov/27575512

Bypareddy R, Sagar P, Chawla R, Temkar S. Intraocular metallic foreign body causing branch retinal vein occlusion. *BMJ Case Rep* 2016;2016. PubMed.gov/26994054. DOI: 10.1136/bcr-2016-214745

Ishii K, Nakanishi M, Akimoto M. Removal of intracameral metallic foreign body by encapsulation with an intraocular lens injector. *J Cataract Refract Surg* 2015;41(12):2605-2608. PubMed.gov/26796440. DOI: 10.1016/j.jcrs.2015.10.046

Lawrence DA, Lipman AT, Gupta SK, Nacey NC. Undetected intraocular metallic foreign body causing hyphema in a patient undergoing MRI: a rare occurrence demonstrating the limitations of pre-MRI safety screening. *Magn Reson Imaging* 2015;33(3):358-361. PubMed.gov/25523608. DOI: 10.1016/j.mri.2014.12.009

Sindal MD, Sengupta S, Vasavada D, Balamurugan S. Retained intraocular iron foreign body presenting with acute retinal necrosis. *Indian J Ophthalmol* 2017;65(10):1036-1038. PubMed.gov/29044081. DOI: 10.4103/ijo.IJO_363_17

Citing this article

Idiopathic Juxtafoveal Telangiectasia Type II (Macular Telangiectasia type 2)

John J Chen, MD, PhD; Angela R McAllister, MD; Elliott H Sohn, MD
February 17, 2014

Chief complaint: Decreased vision and a central scotoma in both eyes (OU)

History of Present Illness: The patient is a 43-year-old male who presented with decreased vision and a central scotoma OU for the past 10 years, which has been getting progressively worse. He describes the vision as having a blurred spot in central of his vision bilaterally. The patient saw an optometrist two years ago and could not be refracted better than 20/40 in either eye. The patient has had intermittent photopsias in both eyes over the past two years. He denies floaters.

Past Ocular History: None

Past Medical History: Depression

Medications: sertraline, fish oil

Allergies: None

Family History: Non-contributory

Social History: The patient works as a chef. He does not smoke or drink alcohol.

Review of systems: All negative except for HPI

Ocular exam

Visual Acuity
♦ Right eye (OD): 20/60
♦ Left eye (OS): 20/60

Pupils: 5→3, no RAPD OU

Extraocular movements: Full OU

Confrontation visual fields: Full OU

Intra-ocular pressure:
♦ OD: 21 mmHg
♦ OS: 19 mmHg

External
Slit Lamp Exam
♦ Lid/Lashes: Normal OU
♦ Conjunctiva/Sclera: Normal OU
♦ Cornea: Clear OU
♦ Anterior Chamber: Deep and quiet OU
♦ Iris: Normal OU
♦ Lens: Clear OU
♦ Vitreous: Normal OU

Dilated Fundus Exam
The optic nerves have a cup-to-disc ratio of 0.2 OU. The macula of both eyes have a greyish sheen with superficial crystals, right angle venules, and telangiectatic vessels that are more prominent temporally. The vessels and peripheral retina are normal OU. There is no posterior vitreous detachment (Figure 1).

Ancillary Tests
Fundus photos demonstrate a greyish sheen with superficial crystals, right angle venules, and telangiectatic vessels that are more prominent temporally in the macula of both the right (A) and left (B) eyes (Figure 1).

Fluorescein angiography (FA) demonstrates telangiectatic vessels surrounding the fovea more prominent temporally with leakage OU (Figure 2).

Spectral domain optical coherence tomography (OCT) demonstrates small foveal cystoid cavities in both the right (A) and left (B) eyes. The central macular thickness is 331 microns OD and 320 microns OS (Figure 3).
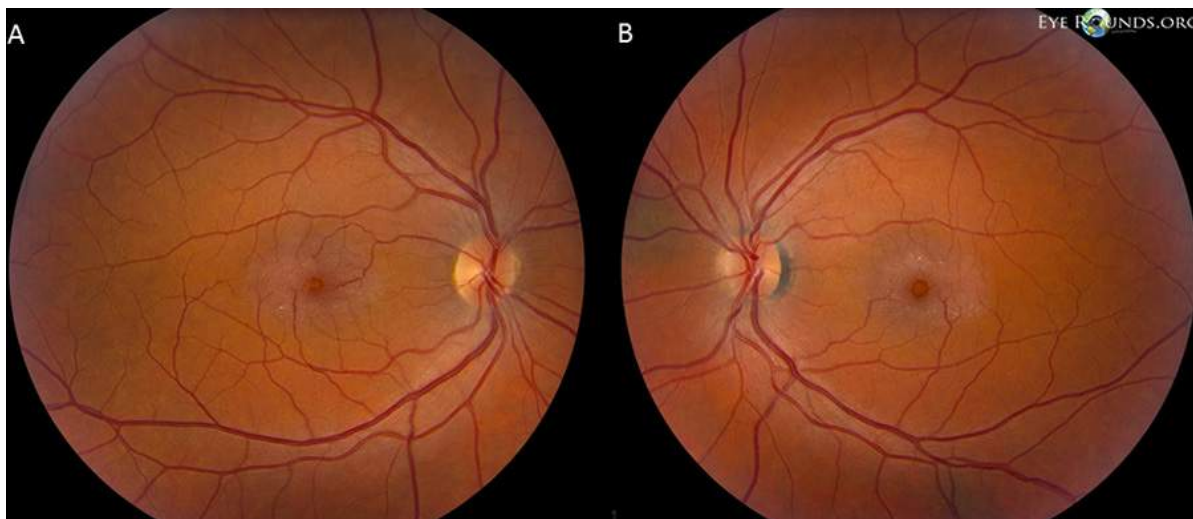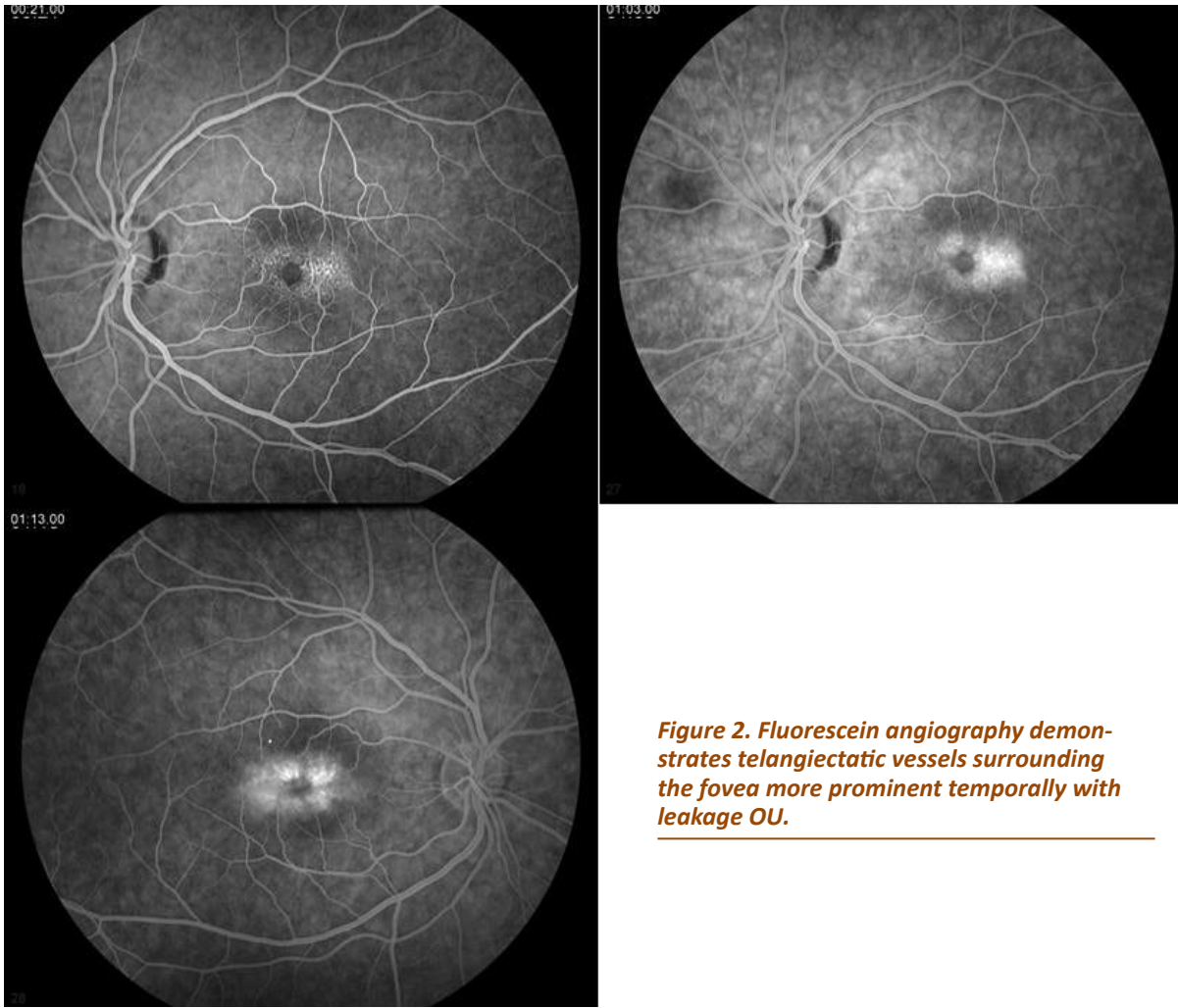

Figure 1. Fundus photos demonstrate a greyish sheen with superficial crystals, right angle venules, and telangiectatic vessels that are more prominent temporally in the macula of both the right (A) and left (B) eyes.

Figure 2. Fluorescein angiography demonstrates telangiectatic vessels surrounding the fovea more prominent temporally with leakage OU.
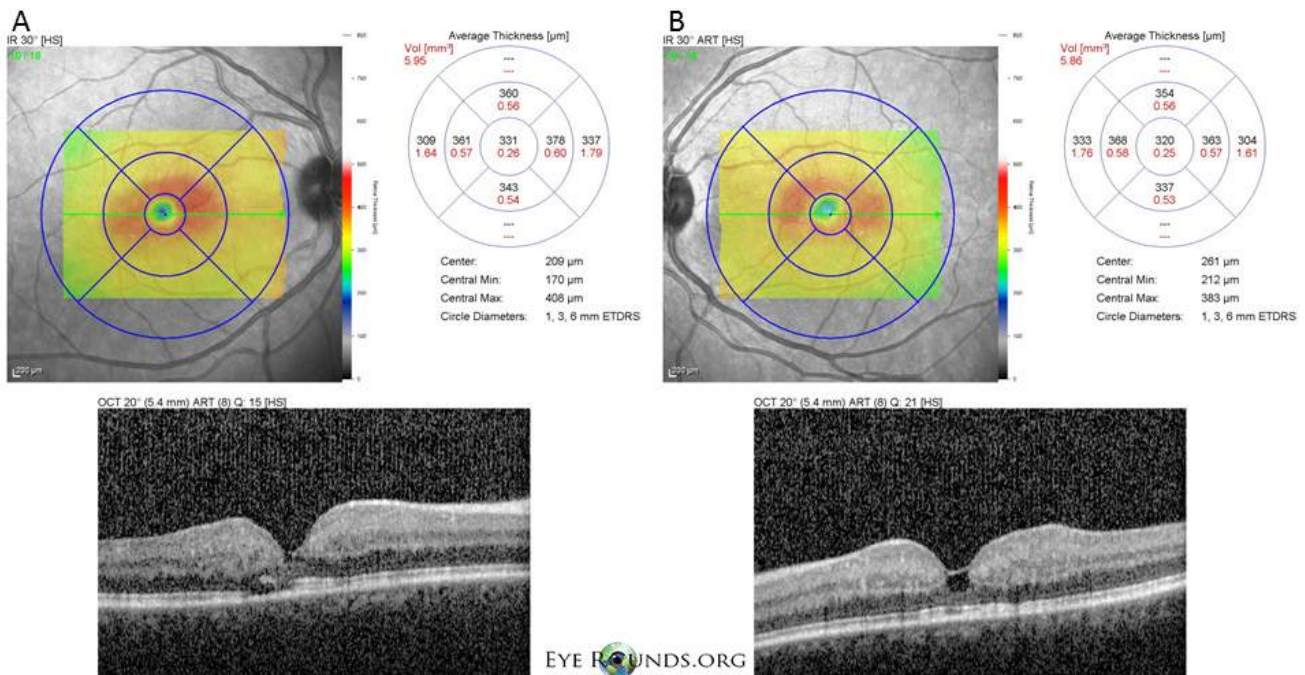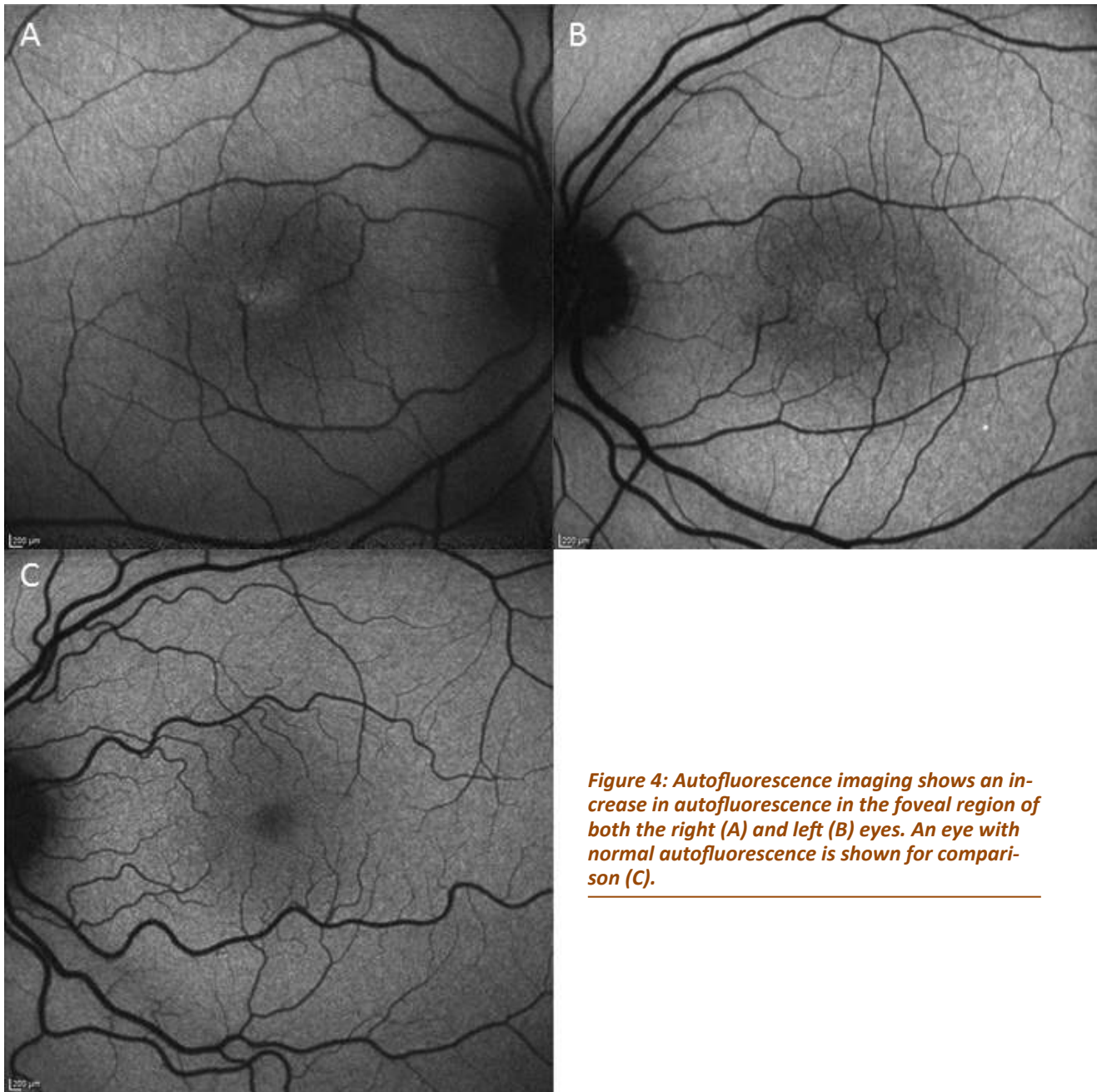

Figure 3: Spectral domain optical coherence tomography (OCT) demonstrates small foveal cystoid cavities in both the right (A) and left (B) eyes. The central macular thickness is 331 μm OD and 320 μm OS.

Figure 4: Autofluorescence imaging shows an increase in autofluorescence in the foveal region of both the right (A) and left (B) eyes. An eye with normal autofluorescence is shown for comparison (C).

Autofluorescence imaging shows a mild increase in autofluorescence in the foveal region of both the right (A) and left (B) eyes (Figure 4).

Diagnosis

Idiopathic Juxtafoveal telangiectasia, type II (Macular Telangiectasia type 2 or Mac Tel 2)

Discussion

Idiopathic juxtafoveal telangiectasia (IJFT), also known as idiopathic macular telangiectasia[1], is an uncommon disorder characterized by telangiectatic vessels in the juxtafoveolar region of one or both eyes. According to Gass, IJFT can be divided into three groups based upon phenotype:[2] type I is typically a unilateral disease characterized by parafoveal dilation of capillaries, microaneurysms, leakage, and lipid deposition; type II is the most common form of IJFT and typically presents with bilateral juxtafoveal telangiectasias with minimal exudate; type III is extremely rare and is characterized by occlusive telangiectasia. This review will focus on IJFT type II (macular telangiectasia type 2 or Mac Tel 2).

The prevalence of IJFT type II is not entirely known, but one large study estimated a prevalence of 1-5 in 22,062 while another study estimated it may be has high as 0.1%

in some populations.[3 ,4] Although IJFT can occur at any age, the mean age of onset is 55 years old. There is no predilection for gender and no known racial predilection. Although there are a few case reports of monozygotic twins with IJFT type II raising the possibility of genetic component, there is currently insufficient evidence from population studies to support genetic association. Several studies suggest that smoking may worsen disease.

IJFT type II is a bilateral disease, but can be asymmetric and may appear as a unilateral process early in the disease. Patients often present with complaints of blurred vision, metamorphopsia, or paracentral scotomas.

Early changes seen with IJFT type II include parafoveal graying of the retina, superficial crystalline deposits, subfoveal cystoid cavities, parafoveal telangiectasias, and right-angle vessels. Visual acuity decreases slowly and is often associated with hyperplasia of the retinal pigment epithelium (RPE). In approximately one-third of patients, deep retinal neovascularization with retinal feeders, subretinal neovascularization (SRNV), may occur as an acute complication and is then called the proliferative form.[1 ,5] The natural progression of the disease results in significant visual loss in the majority of patients with IJFT type II.[5] In a paper by Watzke et al., 15 or 20 eyes developed either central RPE hyperplasia or SRNV with decreased vision of 20/70 or worse over 15 years.[5]

Fundus findings of IJFT type II on biomicroscopy can be subtle, especially early in the disease process, and therefore imaging with FA, OCT, and fundus autofluorescence are important in making the diagnosis. FA highlights the parafoveal telangiectatic vessels, which demonstrate early hyperfluorescence with leakage. These are often more prominent temporal to the fovea. OCT demonstrates subfoveal cystoid spaces, usually without cystoid macular edema.[6 ,7] In more advanced disease, photoreceptor disruption and outer retinal atrophy are present on OCT.[7] Fundus autofluorescence findings are pathognenmonic for MacTel II, showing a loss of the physiologic hypoautofluorescence—i.e. increased autofluorescence—in the fovea. [8 ,9]

The pathogenesis of IJFT type II is unclear, but may involve abnormalities in the parafoveolar Muller cells rather than a primary abnormality of retinal capillaries.[10] Muller cells are important for the health of the retinal capillary endothelium and the surrounding retina.[11 ,12] It has been postulated that Muller cell dysfunction in IJFT type II results in endothelial degeneration, which may lead to retinal capillary proliferation and telangiectasia.[6 ,7] In support of this, perifoveal depletion of Muller cells has been seen on histopathology of patients with IJFT type II.[13] The superficial crystals seen in patients with IJFT type II are thought to represent to footplates of degenerated Muller cells.[7 ,14] In addition, it has been speculated that the spaces seen on OCT in IJFT type II represent tissue loss from retinal degeneration, specifically due to the dysfunction or loss of Muller cells, rather than fluid filled cystic spaces.[1,12,13]

A better understanding of the disease mechanism in IJFT type II is important because there remains no definitive treatment for the visual loss seen in the nonproliferative form of IJFT II. Bevacizumab has been shown to be effective in the treatment of the SRNV associated with IJFT type II, but does not appear to consistently affect the course or cystic changes in nonproliferative IJFT.[15-19] Similarly, ranibizumab failed to show a functional benefit in a prospective interventional trial of patients with nonproliferative IJFT type II, although was shown to cause a significant reduction in retinal thickness and a decrease in leakage on FA.[20] Oral carbonic anhydrase inhibitors were also shown to cause a significant reduction in retinal thickness, but did not significantly improve visual acuity.[21] Multiple other interventions have been tried, including focal grid laser,[22] photodynamic therapy,[23] and intravitreal triamcinolone,[24] with no clear improvement in either the cystoid cavities or the visual acuity in patients with IJFT type II. Finding an effective treatment is important because the majority of patients with IJFT type II develop a significant decline in vision over time.

Our patient highlights all of the early findings of non-proliferative IJFT type II, including parafoveal graying of the retina, superficial crystalline retinal deposits, right angle vessels, and parafoveal telangiectasias (Figure 1). FA further highlighted the parafoveal telangiectasias, which demonstrated prominent leakage and staining of the retina (Figure 2). OCT demonstrated characteristic subfoveal cystoid spaces (Figure 3). Finally, fundus autofluorescence showed a mild increase in foveal autofluorescence consistent with IJFT type II (Figure 4). Fortunately, our patient did not show signs of more advanced disease, including no evidence of retinal pigment epithelium hyperplasia or SRNV. The patient was initially started on PO methazolamide 50mg bid and demonstrated a decrease in macular thickness within 1.5 months of treatment (Figure 5). He was then changed to PO acetazolamide secondary to insurance and had a continued decrease in macular thickness and subfoveal cysts over the next year despite only tolerating 125mg bid (Figure 5). There was also a mild non-significant improvement in visual acuity to 20/50 OD and 20/40 OS at the most recent follow-up.

Differential Diagnosis

♦ diabetic macular edema
♦ pseudophakic macular edema
♦ lamellar/macular hole
♦ Coats disease
♦ retinal vein occlusion
♦ radiation retinopathy
♦ Eales disease
♦ ocular ischemic syndrome
♦ crystalline retinopathy
♦ IJFT type I and III (see table).
♦ Proliferative disease can be mistaken for choroidal neovascularization from age-related macular degeneration.
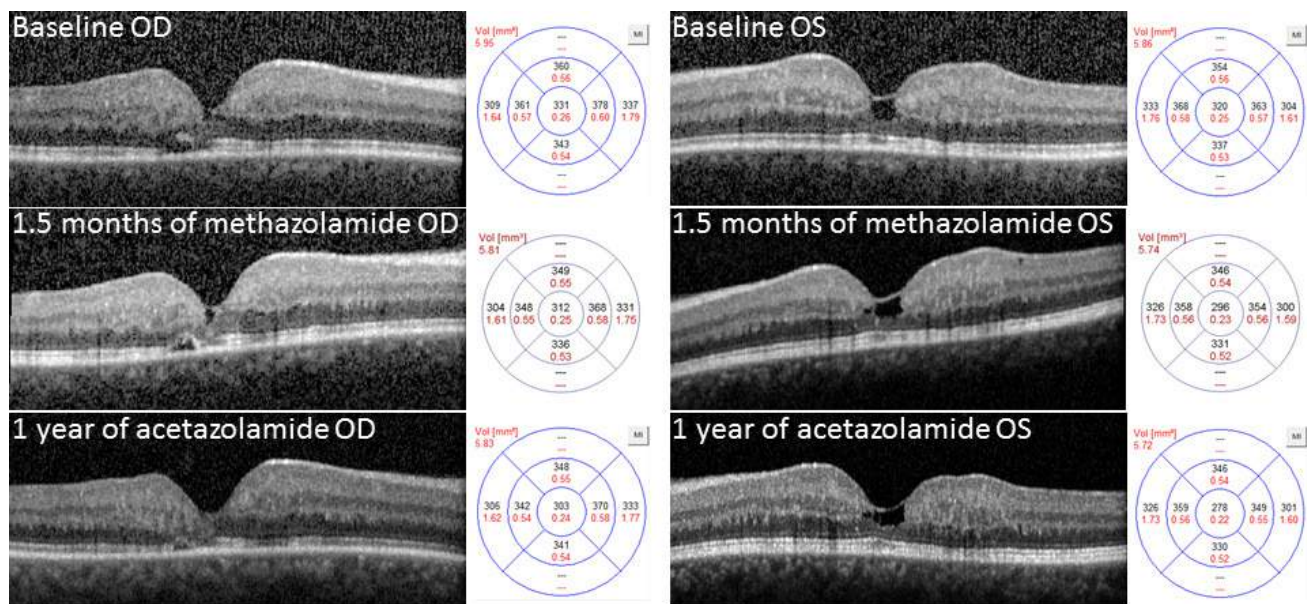
Figure 5: Spectral domain optical coherence tomography (OCT) demonstrates subfoveal cyst-like spaces OU at baseline. The retinal thickness map is shown to the right (CMT = 331 μm OD, CMT = 320 μm OS). After 1.5 months of methazolamide, there was a reduction in the macular thickness (CMT = 312 μm OD, CMT = 296 μm OS). After one year of treatment with acetazolamide, there was a further decrease in the cystic spaces and macular thickness (CMT = 303 μm OD, CMT = 278 μm OS). Images were obtained in the same meridian and registered to the original visit.

Types of IJFT*	Epidemiology	Signs and symptoms	Treatment	Prognosis
IJFT type I	Predominantly male. Mean age 40yo.	Unilateral prominent visible telangiectatic retinal capillaries with macular edema and lipid deposition/exudate.	Laser photocoagulation may reduce exudation and stabilize vision.	Variable, majority progress to 20/70 or worse if untreated
IJFT type II	Equal gender predilection. Mean age 55yo.	Bilateral parafoveal graying of the retina, superficial crystalline deposits, subfoveal cystoid cavities, parafoveal telangiectasias (more evident on FA), right-angle vessels, hyperplasia of the RPE. SRNV develops in approximately 1/3 of patients.	No known treatment for non-proliferative IJFT type II. Intravitreal anti-VEGF for SRNV.	Variable, 2/3 of eyes will progress to 20/70 or worse associated with RPE hyperplasia or SRNV.
IJFT type III	Very rare	Bilateral perifoveal capillary obliteration, capillary telangiectasia, and minimal exudation, associated with systemic or cerebral disease.	Unknown due to its rarity	Variable, mostly unknown due to its rarity

* Idiopathic juxtafoveal telangiectasia (IJFT) is also known as idiopathic macular telangiectasia. According to the idiopathic macular telangiectasia classification, IJFT type I is named aneurysmal telangiectasia and IJFT type II is named perifoveal telangiectasia. Because of its rarity, IJFT type III has been omitted from the idiopathic macular telangiectasia classification.[1]

Table: Characteristics of the three types of idiopathic juxtafoveolar telangiectasia

Epidemiology (IJFT type II)	Symptoms
♦ Prevalence: 1-5 in 22,062, but may be has high as 0.1%. ♦ Mean age of presentation is 55 years old ♦ Equal gender predilection ♦ Bilateral disease	♦ Decreased vision ♦ Central or parafoveal scotoma ♦ Metamorphopsia
Signs	**Treatment**

♦ Non-proliferative IJFT type II: bilateral parafoveal graying of the retina, superficial crystalline deposits, subfoveal cystoid cavities, parafoveal telangiectasias (more evident on FA), right-angle vessels, hyperplasia of the retinal pigment epithelium. Findings are often more prominent in the temporal parafoveal region, especially early in the disease.
  • FA demonstrates parafoveal telangiectatic capillaries with leakage, often more prominent temporally.
  • OCT demonstrates subfoveal cystoid cavities. In more advanced disease, photoreceptor disruption and outer retinal atrophy are present.
  • Fundus autofluorescence demonstrates increased foveal autofluorescence.
♦ Proliferative IJFT type II: subretinal neovascularization.
	♦ For the non-proliferative form with macular cystoid cavities, oral carbonic anhydrase inhibitors have been shown to cause a significant reduction in retinal thickness, but did not significantly improve visual acuity.[21] Otherwise, no proven treatment exists.
	♦ Anti-VEGF therapy, ranibizumab or bevacizumab, are effective in the treatment of subretinal neovascularization seen in the proliferative form of IJFT type II.
	♦ Smoking may be a modifiable risk factor.

References

1. Yannuzzi LA, Bardal AM, Freund KB, Chen KJ, Eandi CM, Blodi B. Idiopathic macular telangiectasia. Arch Ophthalmol 2006;124(4):450-60.
2. Gass JD, Blodi BA. Idiopathic juxtafoveolar retinal telangiectasis. Update of classification and follow-up study. Ophthalmology 1993;100(10):1536-46.
3. Aung KZ, Wickremasinghe SS, Makeyeva G, Robman L, Guymer RH. The prevalence estimates of macular telangiectasia type 2: the Melbourne Collaborative Cohort Study. Retina 2010;30(3):473-8.
4. Klein R, Blodi BA, Meuer SM, Myers CE, Chew EY, Klein BE. The prevalence of macular telangiectasia type 2 in the Beaver Dam eye study. Am J Ophthalmol 2010;150(1):55-62 e2.
5. Watzke RC, Klein ML, Folk JC, Farmer SG, Munsen RS, Champfer RJ, Sletten KR. Long-term juxtafoveal retinal telangiectasia. Retina 2005;25(6):727-35.
6. Nowilaty SR, Al-Shamsi HN, Al-Khars W. Idiopathic juxtafoveolar retinal telangiectasis: a current review. Middle East Afr J Ophthalmol 2010;17(3):224-41.
7. Cohen SM, Cohen ML, El-Jabali F, Pautler SE. Optical coherence tomography findings in nonproliferative group 2a idiopathic juxtafoveal retinal telangiectasis. Retina2007;27(1):59-66.
8. Schmitz-Valckenberg S, Fan K, Nugent A, Rubin GS, Peto T, Tufail A, Egan C, Bird AC, Fitzke FW. Correlation of functional impairment and morphological alterations in patients with group 2A idiopathic juxtafoveal retinal telangiectasia. Arch Ophthalmol2008;126(3):330-5.
9. Wong WT, Forooghian F, Majumdar Z, Bonner RF, Cunningham D, Chew EY. Fundus autofluorescence in type 2 idiopathic macular telangiectasia: correlation with optical coherence tomography and microperimetry. Am J Ophthalmol 2009;148(4):573-83.
10. Gass JD. Histopathologic study of presumed parafoveal telangiectasis. Retina2000;20(2):226-7.
11. Tout S, Chan-Ling T, Hollander H, Stone J. The role of Muller cells in the formation of the blood-retinal barrier. Neuroscience 1993;55(1):291-301.
12. Newman E, Reichenbach A. The Muller cell: a functional element of the retina. Trends Neurosci 1996;19(8):307-12.
13. Powner MB, Gillies MC, Tretiach M, Scott A, Guymer RH, Hageman GS, Fruttiger M. Perifoveal muller cell depletion in a case of macular telangiectasia type 2. Ophthalmology 2010;117(12):2407-16.
14. Gass JDM. Stereoscopic atlas of macular diseases : diagnosis and treatment. 4th ed. St. Louis: Mosby, 1997.
15. Roller AB, Folk JC, Patel NM, Boldt HC, Russell SR, Abramoff MD, Mahajan VB. Intravitreal bevacizumab for treatment of proliferative and nonproliferative type 2 idiopathic macular telangiectasia. Retina 2011;31(9):1848-55.

16. Mandal S, Venkatesh P, Abbas Z, Vohra R, Garg S. Intravitreal bevacizumab (Avastin) for subretinal neovascularization secondary to type 2A idiopathic juxtafoveal telangiectasia. Graefes Arch Clin Exp Ophthalmol 2007;245(12):1825-9.

17. Konstantinidis L, Mantel I, Zografos L, Ambresin A. Intravitreal ranibizumab as primary treatment for neovascular membrane associated with idiopathic juxtafoveal retinal telangiectasia. Graefes Arch Clin Exp Ophthalmol 2009;247(11):1567-9.

18. Matsumoto Y, Yuzawa M. Intravitreal bevacizumab therapy for idiopathic macular telangiectasia. Jpn J Ophthalmol 2010;54(4):320-4.

19. Kovach JL, Rosenfeld PJ. Bevacizumab (avastin) therapy for idiopathic macular telangiectasia type II. Retina 2009;29(1):27-32.

20. Charbel Issa P, Finger RP, Kruse K, Baumuller S, Scholl HP, Holz FG. Monthly ranibizumab for nonproliferative macular telangiectasia type 2: a 12-month prospective study. Am J Ophthalmol 2011;151(5):876-886 e1.

21. Chen JJ, Sohn EH, Folk JC, Mahajan VB, Kay CN, Boldt HC, Russell SR. Decreased Macular Thickness in Nonproliferative Macular Telangiectasia Type 2 with Oral Carbonic Anhydrase Inhibitors. Retina 2014;34(7):1400-6. doi: 10.1097/IAE.0000000000000093

22. Park DW, Schatz H, McDonald HR, Johnson RN. Grid laser photocoagulation for macular edema in bilateral juxtafoveal telangiectasis. Ophthalmology 1997;104(11):1838-46.

23. De Lahitte GD, Cohen SY, Gaudric A. Lack of apparent short-term benefit of photodynamic therapy in bilateral, acquired, parafoveal telangiectasis without subretinal neovascularization. Am J Ophthalmol 2004;138(5):892-4.

24. Wu L, Evans T, Arevalo JF, Berrocal MH, Rodriguez FJ, Hsu M, Sanchez JG. Long-term effect of intravitreal triamcinolone in the nonproliferative stage of type II idiopathic parafoveal telangiectasia. Retina 2008;28(2):314-9.

Suggested Citation Format

Chen JJ, McAllister, AR, Sohn EH. Idiopathic Juxtafoveal Telangiectasia Type II (Macular Telangiectasia type 2). EyeRounds.org. February 17, 2014; Available from: Eyerounds.org/cases/185-JXT.htm

last updated: 2/17/2014

Vitreous Syneresis:
An Impending Posterior Vitreous Detachment (PVD)

Elizabeth Gauger, MD; Eric K. Chin, MD; Elliott H. Sohn, MD

Nov 17, 2014

Chief Complaint

New flashing lights and floating "spots"

History of Present Illness

A 60-year-old female presented to the eye clinic with flashing lights and new floaters in the left eye for the past four days. The floaters were described as "large and stringy", and the flashing lights occurred in the temporal periphery "like a camera flash going off repeatedly". The flashes of light were also worse in a dimly lit environment. She denied any "shades" or "curtains" in her peripheral vision. She denied any recent head trauma or falls. She had no known personal or family history of retinal tears or detachment, and she had no complaints in her right eye. She had no other complaints at presentation.

Past Ocular History

- Glaucoma suspect based on mild optic nerve cupping
- Myopia, recent manifest refraction = -3.75 right eye, -2.75 left eye
- No prior ocular surgeries

Eye Drops: None

Past Medical History: Unremarkable

Medications: None

Allergies: No known drug allergies

Family History: No known eye disease

Ocular Exam

Visual Acuity (Snellen) at distance with correction

- Right eye (OD): 20/25, no improvement with pinhole
- Left eye (OS): 20/20, no improvement with pinhole

Ocular motility: Full both eyes (OU)

Intraocular Pressure (IOP), via Tonopen: 21 mm Hg OD, 20 mm Hg OS

Pupils: Equally reactive in each eye from 4 mm in the dark to 2 mm in the light. No relative afferent pupillary defect in either eye.

Slit Lamp Exam

- **OD:** Mild nuclear sclerosis.
- **OS:** Mild nuclear sclerosis. Vitreous syneresis, but negative Shafer's sign/no "tobacco dust" (Figure 1).
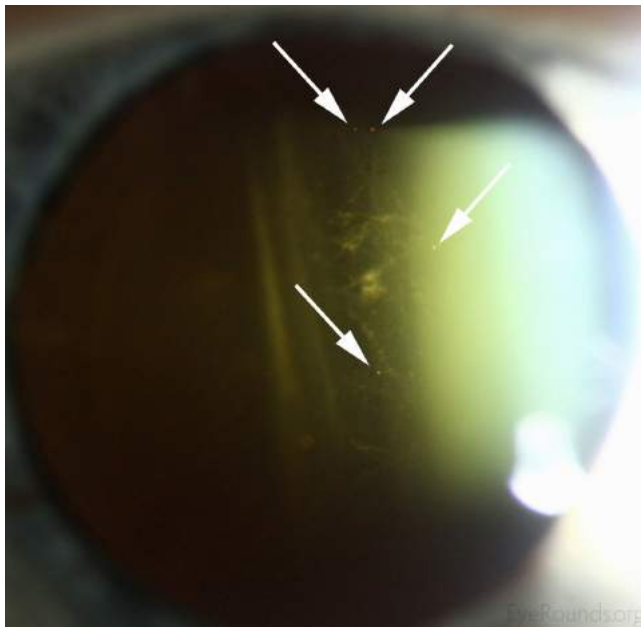
Figure 1: White arrows demonstrate a positive Shafer's sign in a different patient. This patient had strands of vitreous syneresis, which are seen as wispy material just below the white arrows. Our patient did not have Shafer's sign.
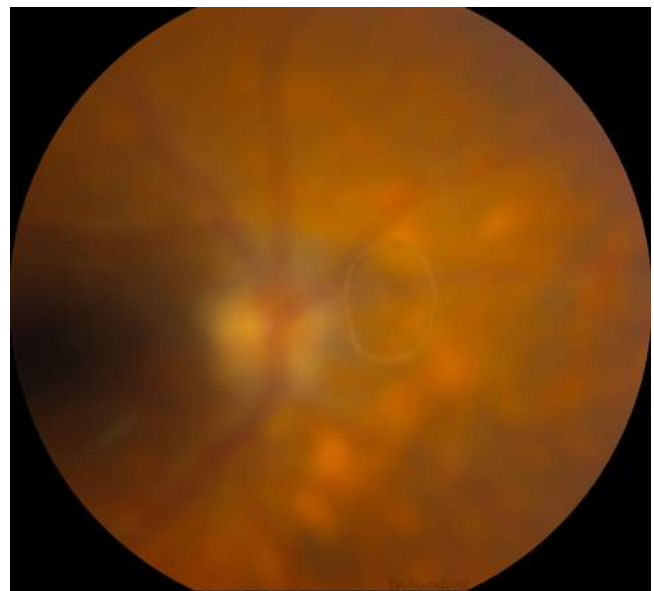

Figure 2: Example of a Weiss ring, indicating detachment of the vitreous from the optic nerve. The optic nerve, retina, and retinal vessels are purposely out of focus because the Weiss ring is located more anteriorly in the vitreous. Photo Credit: Matt Weed, MD.

Dilated Fundus Exam

- ♦ OD
  - Vitreous: Normal; no Weiss ring
  - Optic nerve: 0.5 cup:disc ratio
  - Macula: Normal
  - Vessels: Normal
  - Periphery: No holes, tears, or subretinal fluid on 360 degree scleral depressed examination
- ♦ OS
  - Vitreous: syneresis; no Weiss ring (Figure 2).
  - Optic nerve: 0.5 cup:disc ratio
  - Macula: Normal
  - Vessels: Normal
  - Periphery: No holes, tears, or subretinal fluid on 360 degree scleral depressed examination

Clinical Course

The patient had no evidence of a retinal tear or detachment in either eye on 360 degree scleral depressed examination. There was suggestion of an evolving posterior vitreous detachment based on the vitreous syneresis seen in the anterior vitreous and symptoms consistent with separation of the vitreous from the retina. The patient was instructed to monitor her symptoms closely. She was instructed to specifically watch for an increase in amount of severity of her flashes and floaters, or the development of new "curtains" in the periphery of her vision. Follow-up was scheduled for one month for repeat scleral depressed examination in both eyes, sooner if needed.

Discussion

A posterior vitreous detachment (PVD) is defined as the separation of the posterior hyaloid face from the neurosensory retina. At birth, the vitreous "gel" fills the back of the eye and normally has Jello-like consistency. As one ages, the vitreous undergoes "syneresis," in which it becomes more fluid or liquid-like. The pockets of fluid in the vitreous cavity give the patient a sensation of "floaters" or "cobwebs." As the pockets of fluid collapse on themselves, they gently pull on the retina giving the patient a sensation of "flashes of light" or photopsias. Eventually, the vitreous may completely separate from the neurosensory retina, which is called a *posterior vitreous detachment* or "PVD" that is confirmed clinically with observation of Weiss ring on funduscopic examination. This usually occurs in one eye at a time, but a PVD in the contralateral eye often occur 6 to 24 months later (6). In high myopia, PVD develops increasingly with age and the degree of myopia (7). As the vitreous gel separates, it may cause a tear in the neurosensory retina which is fragile and thin like a piece of tissue paper. A retinal tear can allow the liquid part of the vitreous to escape behind the retina and separate the retina from its underlying attachments (and blood supply). This is known as a rhegmatogenous retinal detachment. Typically, however, the vitreous separates without any ill effects on the retina.

Risk Factors

Patients are at greatest risk for a symptomatic PVD in the 5th to 7th decade of life, although it can occur much earlier. Most often patients are myopic (near-sighted). High myopes (i.e. refraction of -6.00 or greater) are at increased risk of complications related to a PVD due to thinning of the retina as it is stretched along a longer eye. Other predisposing risk factors for a PVD include a family history of retinal tears or detachments, intraocular inflammation (uveitis), trauma, and previous eye surgery.

Signs and Symptoms

The patient in this case exhibited the typical signs and symptoms of an acutely evolving posterior vitreous detachment, including new onset of flashes and floaters. The flashes of light (or photopsias) are often described as a camera flash going off repeatedly in the patient's peripheral vision. The photopsias tend to be more noticeable in dimly lit environments. They are caused by mechanical traction on the retina, caused by the vitreous gel "tugging" on the underlying neurosensory retina.

Patients may also endorse new floaters. Generally these are described by patients as large, wispy objects moving around when they move their eye in different directions of gaze. Sometimes, they will even describe it as something "running" across their vision, like a small mouse, fly, or cobweb in the central or peripheral vision. These are generally a nuisance to the patient, but benign and require only reassurance when in isolation.

Worrisome signs suggestive of a complication related to a retinal tear or detachment may include many, new, *tiny* floaters often described as "gnats" or "pepper" in the patient's vision. Often these new floaters are "too many to count." This is a worrisome sign, because this may indicate pigment released from the retina and surrounding structures, or red blood cells from a broken retinal vessel. This may indicate that the part of the retina has been torn or detached. Other worrisome signs include a shade or a curtain of vision, which may indicate a retinal detachment where the neurosensory retina has been detached from its underlying connections.

Causes

An acute PVD is most commonly caused by the natural process of vitreous shrinkage and liquefaction over time. As mentioned above, as the gel liquefies, the vitreous body collapses and peels off areas of adhesion to the neurosensory retina. The vitreous is normally most strongly adherent to the vitreous base (peripherally and anteriorly), optic nerve, retinal vessels, and fovea center. Other areas of strong adherence are to retinal scars or lattice degeneration. With an acute PVD, symptoms often develop without warning or inciting event. However, in cases of ocular or head trauma, a "traumatic PVD" may occur.

Types of PVD

Generally, an acute PVD develops suddenly, but becomes complete within weeks of onset of symptoms. A PVD is considered "partial" when the vitreous jelly is still attached at the macula/optic nerve head and "complete" once total separation of the jelly from the optic nerve head has occurred. Figure 3 shows a horizontal cross section of the neurosensory retina through the fovea center with partial separation of the vitreous gel from the underlying retina. Notice that it is still attached to the optic nerve (right). Accurate staging of this PVD would require evaluation of the peripheral retina; however, OCT confirms that it is only a partial PVD and a complete Weiss ring is unlikely to be present. When a PVD is "complete," the examiner will classically observe a Weiss ring on exam (Figure 2). A "Weiss ring" is the circular peripapillary attachment that is visible within the vitreous after it has become detached from the optic nerve head.

PVDs can also be associated with vitreous hemorrhage. The presence of blood in the vitreous cavity can make the patient's vision quite poor, and some patients will describe seeing "tiny red floaters" from the red blood cells. It usually is caused by the tearing of a retinal vessel at the time of the vitreous gel peeling off the retina. Spontaneous vitreous hemorrhage in the setting of an acute PVD strongly suggests there may be a retinal tear or detachment. While the blood will likely clear slowly over time, the clinician should have a high index of suspicion for a retinal tear or detachment. The patient should be followed closely to ensure that this is not the case. B-scan ultrasonography may be necessary to assess for retinal tears and detachments if the vitreous hemorrhage is severe enough to obscure the examiner's view.

Complications

Retinal Tear/Detachment

Retinal tears (Figure 4) occur in 10-15% of patients with acute, symptomatic PVDs. For this reason, it is important to have a dilated scleral depressed examination. If a retinal tear occurs, this in and of itself does not have a poor prognosis. Complications arise when the liquefied vitreous escapes through the tear and behind the retina resulting in a neurosensory retinal detachment. If a tear is discovered early, laser demarcation (i.e. "laser barricade" or "laser retinopexy") is a procedure that can be performed in the clinic to prevent progression to a retinal detachment. However, if a rhegmatogenous retinal detachment (Figure 5) results, the patient may need to undergo a more involved surgery to reattach the retina. In addition to being a more involved procedure that often warrants going to the operating room, the prognosis may be worse depending on the detachment's severity.

Vitreous hemorrhage

A hemorrhagic PVD (i.e. vitreous hemorrhage secondary to a PVD) can occur in about 7.5% of PVDs. This occurs when a retinal blood vessel is torn during vitreous separation. The risk of having an underlying retinal tear increases to nearly 70% in the case of a hemorrhagic PVD. Symptoms of a hemorrhagic PVD may include a more significant decrease in vision secondary to the blood dispersed throughout the vitreous cavity.

Recommendations

If one experiences similar symptoms as the patient above (e.g. sudden onset of many new floaters and/or flashes of lights), it is recommended the patient undergo a dilated fundus examination with complete 360 degree scleral
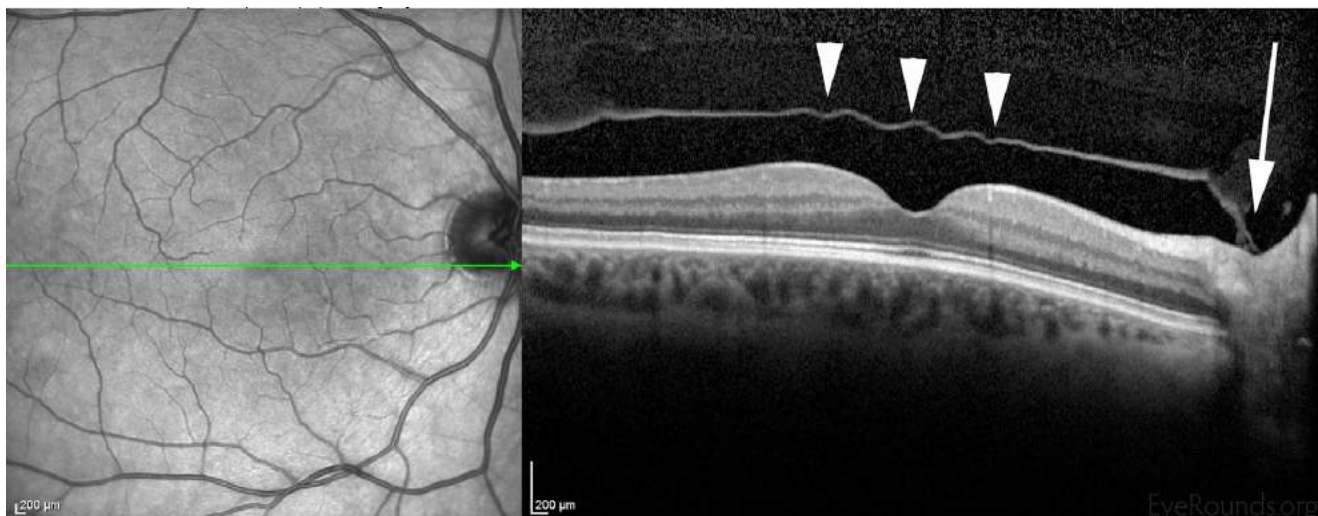

Figure 3: Optical coherence tomography (OCT) of the macula from a patient who had complete separation of the vitreous (arrowhead) from the fovea center. Note that the vitreous is still attached at the optic nerve (right side, large arrow), indicating only a partial PVD has occurred.
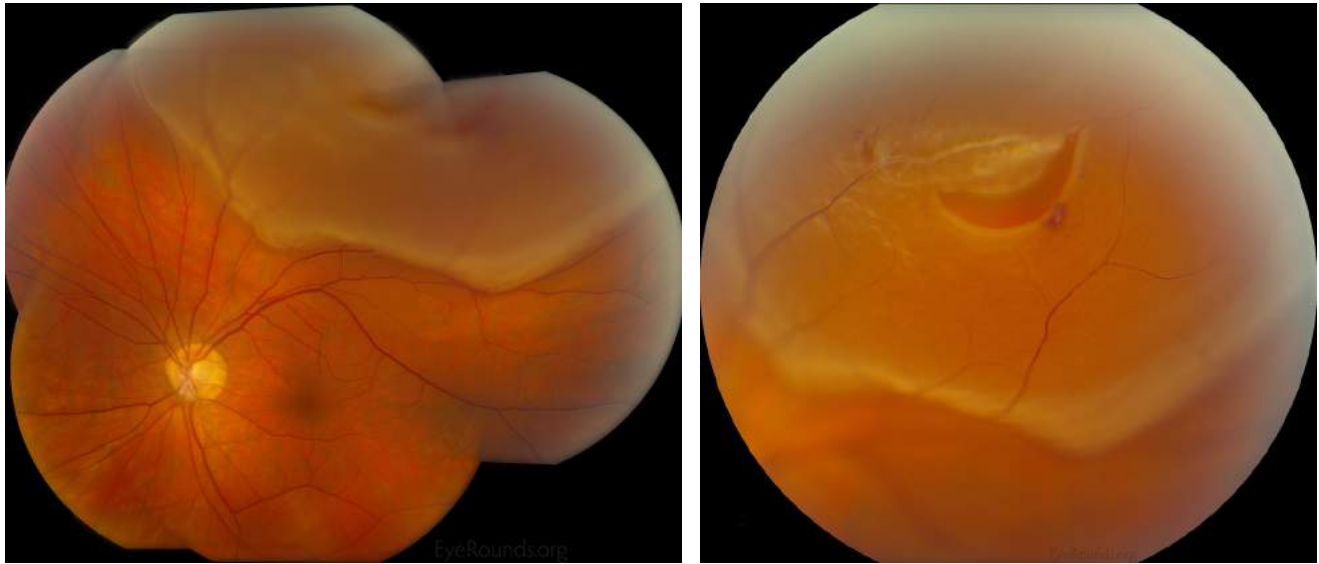
http://EyeRounds.org/cases/196-PVD.htm

Figure 4: High magnification of a peripheral horseshoe retinal tear adjacent to lattice degeneration, a retinal vessel, and specks of intraretinal hemorrhage. Photo credit: Jesse Vislisel, MD.
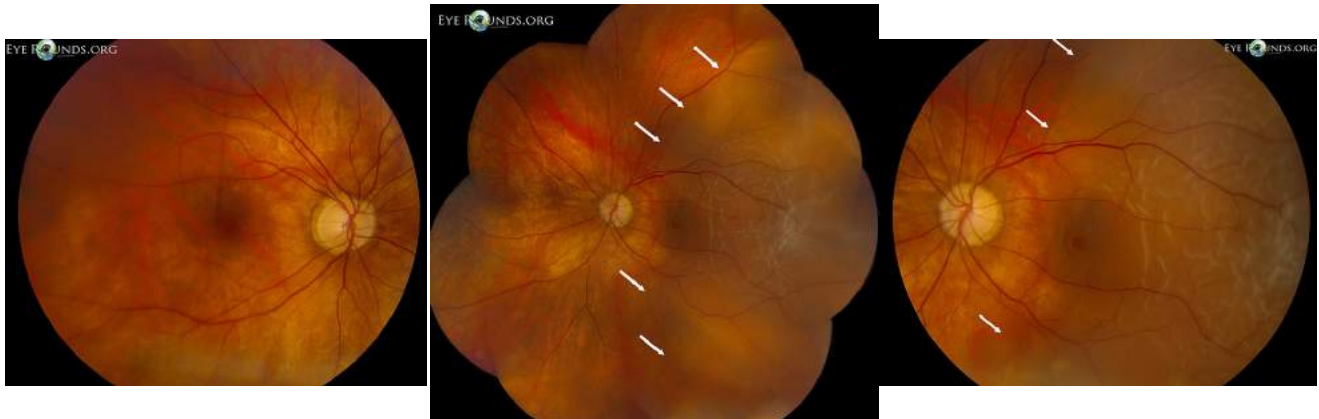

Figure 5: Low magnification montage, rhegmatogenous macula-off retinal detachment (temporal to the white arrows). Photo Credit: Eric Chin, MD.

depressed examination within 12-24 hours. The examiner should be an eye physician who feels confident in examining the peripheral retina, as this is typically where retinal tears and detachments originate. The examiner will likely examine both eyes thoroughly, even the asymptomatic eye, to ensure no pathology exists. Often times, having a tear in one eye may suggest a predisposition to having additional tears or retinal pathology in the same or contralateral eye. If an isolated retinal tear is found, laser demarcation will likely be advised. If a retinal detachment is present, immediate referral to a retina specialist is warranted.

If an evolving acute PVD is found without any retinal tears or detachments, it is commonly advised to have a follow-up scleral depressed examination approximately one month later. Follow-up varies based on severity, symptoms, and other risk factors. If the PVD is hemorrhagic, or other more concerning signs are present on exam, the examiner may recommend follow-up at more frequent intervals. Although there are no preventative measures, it is gener-

ally recommended that the patient avoids heavy exertion, lifting, or bending over in the setting of acute PVD with vitreous hemorrhage so that the blood in the vitreous cavity can settle inferiorly away from the center vision. Elevating the head of the bed will allow gravity to settle the blood inferiorly, out of the visual axis. Patients may continue their blood-thinning medications, as there is no evidence that the discontinuation of antiplatelet or anticoagulant agents speeds the recovery of vitreous hemorrhage.

When to call your eye doctor

After the initial examination, the symptoms may persist but hopefully diminish with time. Follow-up at one month is typically adequate barring any new or changing symptoms. Symptoms which would require a more urgent follow-up exam, include many, new, tiny floaters (like "gnats" or "pepper") in the vision, new or increasing frequency of flashes in the vision, or a new shade or curtain of darkness in the visual field.

Table 1. Acute Posterior Vitreous Detachment (PVD)

Risk factors	Older age (5th and 7th decades of life)
	Myopia
	Intraocular inflammation
	Trauma
	Previous intraocular surgery (such as cataract extraction)
Symptoms	Photopsias (flashes of light), generally unilateral
	New floaters
Examination	Dilated fundus exam with 360 degree scleral depression to assess for presence retinal tears or detachments.
Treatment	No treatment warranted for an isolated PVD
	If a retinal tear is found, laser retinopexy is often indicated
	If rhegmatogenous retinal detachment is present, surgery is often required
Complications	Vitreous hemorrhage
	Retinal tear(s)
	Rhegmatogenous retinal detachment
Follow up	Repeat dilated fundus examination within 4-6 weeks for an uncomplicated, non-hemorrhagic PVD, sooner as needed.
	Call your eye doctor earlier for repeat examination if you experience many, new, tiny floaters, new or increasing flashes, or a shade or curtain obscuring your vision.

References

1. Hayreh SS, Jonas JB. Posterior vitreous detachment: clinical correlations. *Ophthalmologica* 2004;218:333-43.

2. Hollands H, Johnson D, Brox AC et al. Acute-onset floaters and flashes: is this patient at risk for retinal detachment? *JAMA* 2009;302:2243-9.

3. Margo CE, Harman LE. Posterior vitreous detachment: How to approach sudden-onset floaters and flashing lights. *Postgrad Med* 2005;117:37-42.

4. Ryan SJ. Ryan: Retina, 5th ed. Saunders/Elsevier. 2012.

5. Sarrafizadeh R, Hassan TS, Ruby AJ et al. Incidence of retinal detachment and visual outcome in eyes presenting with posterior vitreous separation and dense fundus-obscuring vitreous hemorrhage. *Ophthalmology* 2001;108:2273-8.

6. Hikichi T, Yoshida A. Time course of development of posterior vitreous detachment in the fellow eye after development in the first eye. Ophthalmology 2004;111:1705-7.

7. Akiba J. Prevalence of posterior vitreous detachment in high myopia. Ophthalmology 1993;100:1384-8.

Suggested Citation Format

Fungal endophthalmitis

Hematogenous seeding in an immune suppressed patient with positive fungal and bacterial blood cultures

Aaron M. Ricca MD, Elaine M. Binkley MD, H. Culver Boldt MD

posted December 15, 2017

INITIAL PRESENTATION

Chief Complaint

Floaters and blurred vision of the right eye

History of Present Illness

A 23-year-old male was referred to the University of Iowa Hospitals and Clinics Department of Ophthalmology and Visual Sciences for evaluation of possible ocular extension of T-cell lymphoma to the right eye. The patient had a history of T-cell lymphoblastic lymphoma with associated CNS disease, actively being treated with systemic chemotherapy. He reported that 3 days prior to presentation to an outside ophthalmologist he noted an acute onset of new floaters and blurred vision in the right eye. He denied photopsias but reported photophobia and eye pain. The referring ophthalmologist noted a white lesion nasal to the disc and started prednisolone drops every 1-hour to the right eye while awake due to concern for ocular extension of his lymphoma. The patient's vision continued to decline in the right eye prompting referral for further evaluation.

While on chemotherapy, the patient had a history of opportunistic infections such as *Aerococcus* and *Acinetobacter*, in addition to thrombocytopenia, which required platelet transfusions. Additionally, he had a Hickman catheter placed, which is a chronic indwelling central venous line. He denied fevers, chills, or night sweats.

Past Ocular History

♦ Refractive error

Past Medical History

♦ T-cell acute lymphoblastic lymphoma (NOTCH1-mutated; RAS/PTEN-wt)
♦ Atrial flutter with RVR
♦ Leukemic meningitis
♦ Recurrent pulmonary embolism, chronically anti-coagulated
♦ Non-ischemic cardiomyopathy
♦ Hypogammaglobulinemia
♦ Pancytopenia secondary to chemotherapy
♦ MRSA (Methicillin Resistant *Staph aureus*) and VRE (Vancomycin Resistant *Enterococcus*) colonization

Medications

♦ Chemotherapy with delayed intensification (model arm D of COG AALL0434 -Clinicaltrials.Gov Identifier: NCT00408005- see bit.ly/2talmm7) including pegaspargase, cyclophosphamide, cytarabine, nelarabine, thioguanine, intrathecal methotrexate, and dexamethasone
♦ Acyclovir 400mg by mouth twice daily
♦ Bupropion 100mg by mouth twice a day
♦ Dronabinol 2.5-5mg by mouth daily
♦ Lovenox 120mg subcutaneously daily
♦ Fluconazole 100mg by mouth daily
♦ Furosemide 40mg by mouth daily
♦ Gabapentin 600mg by mouth twice a day
♦ Hydrocortisone 10mg by mouth twice a day
♦ Hydromorphone 2mg by mouth as needed
♦ Levofloxacin 500mg by mouth daily
♦ Lisinopril 2.5mg by mouth daily
♦ Metoprolol succinate 100mg by mouth daily
♦ Ondansetron 4-8mg by mouth every 8 hours as needed
♦ Sildenafil 25mg by mouth as needed
♦ Thiamine 100mg by mouth daily
♦ Trazodone 50mg by mouth every evening as needed

Allergies

Sulfonamides

Family History

No family history of lymphoma, leukemia, heart disease, or lung disease

Social History

Rarely uses cigarettes, occasionally uses chewing tobacco, social alcohol use, and no illicit drug use

Review of Systems

Negative except for what is detailed in the history of present illness

OCULAR EXAMINATION

Visual Acuity with/without correction (Snellen)

- Right eye (OD): 20/100 -1 with eccentric fixation
- Left eye (OS): 20/20

Ocular Motility/Alignment

- OD: Full, Orthotropic
- OS: Full, Orthotropic

Intraocular Pressure (IOP) by Goldmann Applanation

- OD: 8 mmHg
- OS: 9 mmHg

Pupils

- OD: 8mm in dark, 7mm in light, minimally reactive and no relative afferent pupillary defect
- OS: 6mm in dark, 5mm in light, no relative afferent pupillary defect

Confrontation visual fields

- OD: Total superotemporal and partial inferotemporal defects
- OS: Full to count fingers

Slit lamp exam

Right eye
- Lids/lashes: Normal
- Conjunctiva/sclera: Trace injection
- Cornea: Fine white blood cell on the inferior 25% of the corneal endothelium
- Anterior chamber: 4+ white blood cells, 2+ flare
- Iris: Dilated, no lesions, no neovascularization
- Lens: Clear

Left eye
- Lids/lashes: Normal
- Conjunctiva/sclera: Clear and quiet
- Cornea: Clear
- Anterior chamber: Deep and quiet
- Iris: Dilated, normal architecture
- Lens: Clear

Dilated fundus examination (DFE)

Right eye
- Vitreous: 3+ anterior vitreous cell
- Disc: Poor view, obscured by white infiltrate and hazy vitreous
- Cup-to-disc ratio: Poor view
- Macula: Poor view
- Vessels: Poor view

- Periphery: There was a 20/100 view with vitreous opacities. White infiltrates obscured the optic nerve. The white infiltrates extended nasally into the mid-periphery. There were retinal hemorrhages superonasal to the optic nerve. There was a white, pre-retinal opacity measuring 4 x 3 x 2 mm in the inferior mid-periphery. The temporal retina appeared grossly normal.

Left eye
- Vitreous: No anterior vitreous cell
- Disc: Pink and sharp
- Cup-to-disc ratio: 0.1
- Macula: Normal, no heme, good foveal reflex
- Vessels: Normal in course and caliber
- Periphery: Normal, no heme, no cotton wool spots
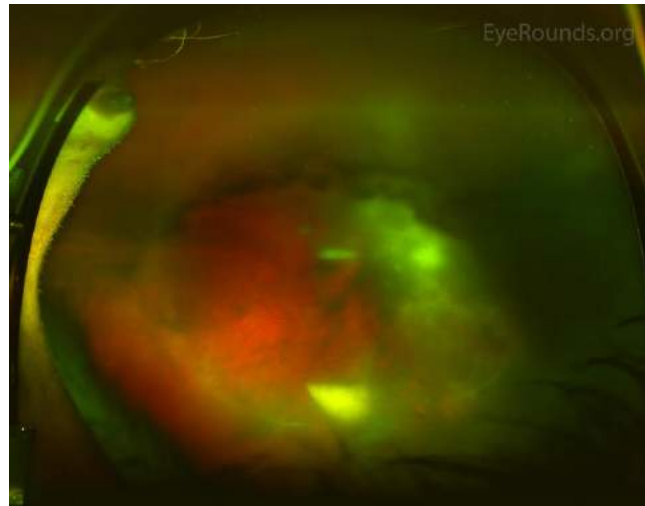
Figure 1. Optos photo of the right eye on presentation demonstrated the significant anterior vitreous cell, dense white vitreous opacities, and very poor view of most of the fundus.

Additional testing

Standardized echography (figure 2)

Differential Diagnosis

- T-cell leukemic infiltrate
- Bacterial endophthalmitis eyerounds.org/cases/45-Endophthalmitis-After-Cataract-Surgery.htm
- Fungal endophthalmitis EyeRounds.org /cases/264-fungal-endophthalmitis.htm
- Viral endophthalmitis
- Tuberculosis eyerounds.org/cases/case6.htm
- Toxoplasma Chorioretinitis eyerounds.org/cases/74-Acquired-Toxoplasmosis-Retina.htm
- Sarcoidosis eyerounds.org/cases/248-unilateral-optic-nerve-granuloma.htm
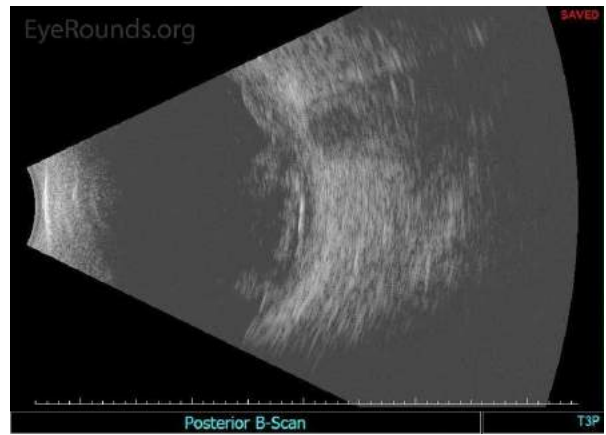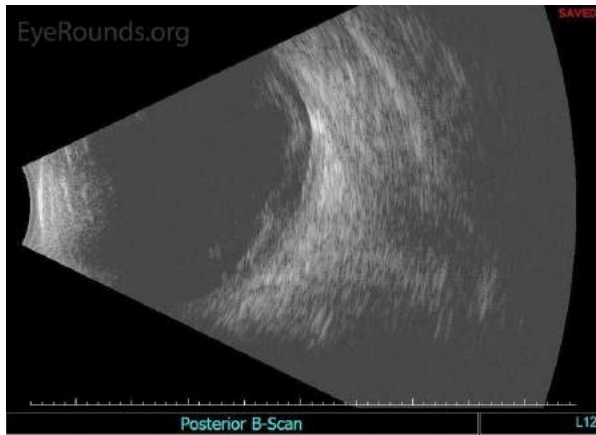- Syphilis eyerounds.org/cases/157-Ocular-Syphilis.htm

Figure 2. Echography of the right eye demonstrated dense irregular vitreous opacities that were concentrated posteriorly along the fundus and surrounding the optic disc. There was irregular retinochoroidal layer thickening. The retina was attached.

CLINICAL COURSE

(Figures 3-5)

Given the high concern for infectious endophthalmitis due to the patient's immune suppression and indwelling catheter, on the day of presentation, the patient was taken to the operating room for urgent pars plana vitrectomy with injection of intravitreal antibiotics (vancomycin and ceftazidime), antivirals (foscarnet), and antifungals (amphotericin B). A vitreous biopsy was obtained and sent for cytology, culture, and polymerase chain reaction (PCR).

The patient had daily follow up immediately post operatively. On post-operative day 2 the pathology from the vitreous biopsy returned with hyphae on the aerobic smear. Vitreous cultures were still pending and blood cultures showed no-growth. At this time, a repeat vitreous tap and inject of amphotericin B was performed. The patient was started on nightly intravenous amphotericin B managed in coordination with the hematology/oncology team. By the
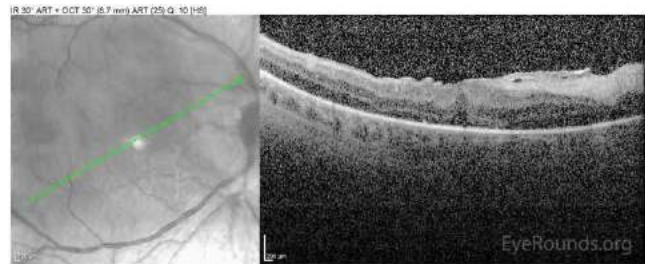
Figure 4. Spectral-domain OCT obtained the same day as the above photograph demonstrating development of an epiretinal membrane with distortion of the foveal contour.
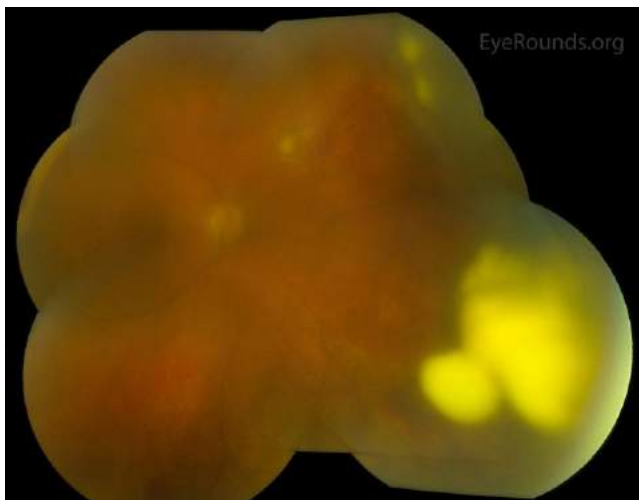
Figure 3. Color fundus photo montage demonstrating consolidation of the nasal vitreous opacities with resolution of the opacities overlying the optic disc.
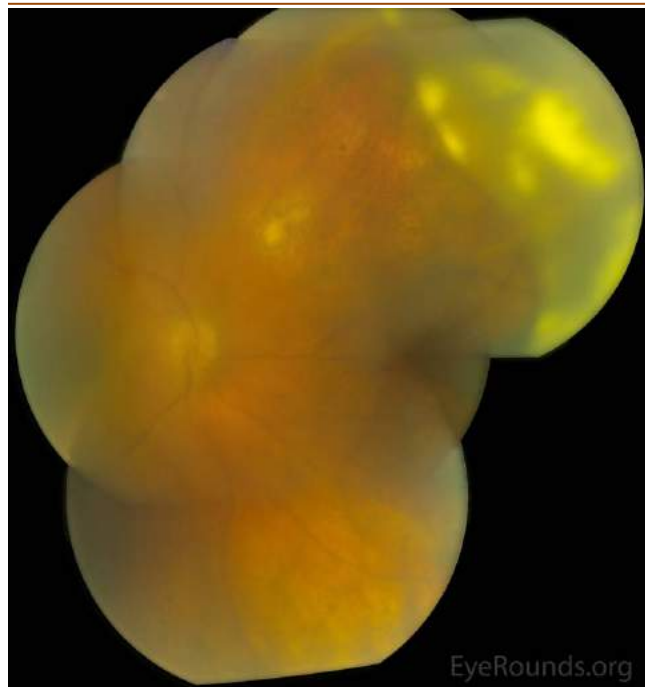
Figure 5. Color fundus photo montage part-way through the treatment course demonstrating improved media opacity and yellow-white colored pre-retinal opacities nasally and inferiorly

https://EyeRounds.org/cases/264-Fungal-Endophthalmitis.htm

following day, vitreous biopsy cultures grew *Aspergillus fumigatus* and the intravenous medication was switched to voriconazole. Repeat intravitreal tap and injections of amphotericin B, then eventually voriconazole, were continued every other day for a total of 3 weeks. Throughout this time, echography was used for serial monitoring given the poor view to the posterior pole due to the vitreous debris. The Hickman catheter was presumed to be the source for the infection and was removed, as is standard of care for source control with presumed colonization of the catheter. The infection cleared and vitreous debris slowly improved. Unfortunately, the vision did not improve beyond counting fingers. After several months of follow-up the vision has remained stable and the inflammation and infection have not recurred.

DIAGNOSIS

Fungal endophthalmitis due to *Aspergillus fumigatus* in the setting of T-cell lymphoblastic lymphoma

DISCUSSION

Etiology/Epidemiology

Endophthalmitis is the disease process where the vitreous and/or the aqueous humors are infected by bacteria or fungi. Endophthalmitis can be exogenous, due to an external penetrating source via trauma or surgery, or endogenous, due to hematogenous seeding of the microbe. Fungal endophthalmitis is overall much less common than bacterial endophthalmitis, however endogenous endophthalmitis is due to a fungus over half of the time with *Candida* being the most common and *Aspergillus* the second most common causative species.[1-3] Males and females are equally effected and the disease is initially unilateral in 75% of patients, although a quarter of that population progresses to develop bilateral disease.[4] Predisposing factors include those commonly associated with the development of fungemia such as central venous catheters, history of gastrointestinal (GI) trauma or surgery, use of broad-spectrum antibiotic therapy, hyperalimentation, neutropenia, IV drug abuse, corticosteroid therapy, and diabetes mellitus.[1,5] The presence of candida endophthalmitis in patients with multiple comorbidities is thought to be an indicator of high mortality risk.[1]

Endogenous endophthalmitis due to a mold is relatively rare; the two most common causative molds are *Aspergillus* and *Fusarium*.[5] *Aspergillus* is a saprophytic mold and is present in the soil across the globe. Humans are ubiquitously exposed to conidia (spores) via inhalation. Immunocompetent individuals rarely develop infection.[6] *Aspergillus fumigatus* is the most common subspecies of *Aspergillus* responsible for causing endophthalmitis as in this case. Other species known to cause infections include *A. flavus, A. terreus, A. niger,* and *A. nidulans*.[6] One large collection of 84 patients with *Aspergillus* endophthalmitis found that over 90% of the time there was at least one un-derlying condition leading to immunodeficiency, and often there were multiple conditions present.[4] In this same study there was no significant difference in infection rates between males and females and all ages were involved.

The most common risk factor for developing *Aspergillus* endophthalmitis is IV drug abuse; other factors strongly associated with developing this disease include recent hospitalizations, immunosuppression due to organ transplants, malignancy, and lung disease.[2,4,6] *Aspergillus* is also known cause keratitis and orbital cellulitis.

Pathophysiology

Aspergillus endophthalmitis is typically endogenous and acquired by hematogenous seeding in most cases. The most common sources of hematogenous seeding are the lungs or via IV drug abuse.[4] The conidia travel via the blood to the choroid where they seed and then migrate to infect multiple tissues in the eye.

Signs/Symptoms

The presenting symptoms of fungal endophthalmitis are often non-specific, with the most common complaint being decreased vision.[5] Other symptoms commonly reported include severe eye pain, ipsilateral headache, redness, eye swelling, photophobia, and floaters.[2,4] The presenting vision can be relatively preserved but is often decreased to counting fingers or light perception.[4,6] Anterior chamber reaction with cells in the aqueous plus/minus a hypopyon is often present.[4,6] On dilated fundus exam one sees vitritis; followed by yellowish, fluffy exudative chorioretinal infiltrates with ill-defined borders. These lesions are commonly located in the macula. The vitreous also often contains fluffy, irregular, yellowish exudative masses.[4,6,7] Intraretinal hemorrhages are frequently present, as is often the case in any form of endophthalmitis.[6] *Aspergillus* endophthalmitis is associated with infection of other organs, such as the lungs and heart. For this reason a thorough review of systems is crucial and often elicits other positive symptoms suggestive of systemic involvement.[4]

Testing/Laboratory work-up

The appropriate workup is patient dependent and based on the clinical picture at the time of presentation. Cultures of the aqueous or vitreous fluid can prove useful in confirming the diagnosis as well as establishing antimicrobial sensitivities.[4,6] Histological analysis and evaluation by polymerase chain reaction (PCR) can also be helpful in identifying the causative organism faster than routine cultures.[7] Several papers document the benefit of performing a pars plana vitrectomy for diagnostic as well as therapeutic purposes.[2,6] Should medical or surgical correction prove futile, diagnosis can be made via histological analysis of enucleated eyes with stain and culture.[4] Blood and sputum cultures can also prove useful. Most commonly, a full systemic workup is required to screen for other areas of infection or causes of immunodeficiency, to be coordinated with colleagues in internal medicine.

Imaging

B-scan echography is useful for monitoring patients, as in this case where the view to the posterior pole was limited by vitreous opacities. Color fundus photography is an additional modality that may be used to document the diagnosis and to monitor the patients' progress at subsequent visits, as was evident in this patient. Spectral-domain OCT (optical coherence tomography) imaging of fungal endophthalmitis demonstrates a diffusely thick choroid with subretinal exudation in the presence of a mostly normally organized neurosensory retina.[8] Many infectious or malignant causes of chorioretinal infiltrates with similar appearance to *Aspergillus* show disruption and loss of the normal retinal layers on OCT, further enhancing diagnostic yield.[8] It has been shown that *Aspergillus* produces a predominantly choroidal infiltrate, which is contrary to common viral or protozoal uveitidies where there is widespread involvement of the neurosensory retina. [8] Wide-field angiography can assist in ruling out viral or autoimmune diseases that present with diffuse vasculitis, as the vasculitis present in *Aspergillus* infection is localized to near the chorioretinal lesions.[8]

Treatment/Management/Guidelines

Given the rarity of this disease process, there are no well-executed randomized controlled trials comparing early vitrectomy versus intravitreal injection with or without systemic therapy. As such, the management of endophthalmitis secondary to *Aspergillus* is approached in a case-by-case basis with some combination of the aforementioned interventions. In the presence of vitritis, chorioretinitis involving the macula, or endophthalmitis it is advantageous to treat with intravitreal antifungal medications with or without early vitrectomy.[9] Many providers attempt treatment with intravitreal antifungals initially. Amphotericin B has traditionally been the intravitreal antifungal of choice with an initial dose of 5-10 mcg, with some clinicians giving as much as 20 mcg, however there are risks of adverse effects at higher concentrations, such as retinal toxicity.[2,6] Intravenous and intravitreal voriconazole is well tolerated by patients with few adverse effects. The recommended dose for intravitreal voriconazole is 100 mcg and the number of injections depends on the patients response.[10] The use of topical or oral corticosteroids is controversial. Some providers feel that they are not indicated while others use them once the infection is being adequately treated. Steroids should never be used as first line therapy without adequate anti-microbial coverage as this can worsen the infection. These patients require frequent follow up as repeat injections are often warranted and performed within days to weeks, again depending on patient response.[6] One study documented the efficacy of intravitreal voriconazole in treating patients with culture proven, fluconazole and amphotericin resistant fungal endophthalmitis with complete resolution of the disease. [11] Several recent manuscripts have documented the benefits and efficacy of treating Aspergillus with intravitreal voriconazole with or without early vitrectomy with good outcomes.[12,13] A recent study in a guinea pig model of Aspergillus endophthalmitis showed greater efficacy with intravitreal voriconazole therapy over intravitreal amphotericin B.[14] If the anterior segment is involved the patient may benefit from intracameral voriconazole and anterior segment washout.[11]

Historically, many patients were initially treated first with intravenous amphotericin B.[4] However, the significant adverse effects of systemically administered amphotericin B, such as hypertension and nephrotoxicity, limited the management potential with this drug.[9] Prior to the advent of new-generation triazoles including posaconazole, voriconazole, and ravuconazole, intravenous and intravitreal amphotericin B was the preferred therapy.[10]Currently, systemic anti-fungal therapy often involves a newer generation azole with amphotericin B being used less frequently. Voriconazole has good oral bioavailability as well as excellent ocular penetration. This, combined with the limited systemic side effect profile when compared to other antifungals, often makes it the first-line when oral therapy is pursued.[7] It has also been suggested that oral antifungal therapy with second generation azoles can be used as monotherapy in cases of limited fungal chorioretinitis not involving the macula.[10] Recommended dosing with oral voriconazole for systemic therapy is 6 mg/kg for 2 doses, then 4 mg/kg twice daily. The duration of treatment should last for approximately 4-6 weeks, or longer depending on the observed response by funduscopic exam. [10] The infectious disease service is often consulted to assist with dosing and medication administration as well as laboratory monitoring.

Careful observation of the clinical course is warranted and the importance of a multidisciplinary approach to the overall management of the patient should be emphasized.[10] Treatment plans are adjusted throughout the course of the disease and largely depend on changes in visual acuity and clinical exam findings. Fundus photography and B-scan ultrasonography can be used to track disease process and document response to therapy. Late complications, such as retinal detachment from tears at the edge of the chorioretinal scars, epiretinal membranes, and cataract have been described.[15] Despite the various effective treatment modalities for fungal endophthalmitis, infections due to Aspergillus are some of the most severe and have poorer visual outcomes than infections due to other fungi such as *Candida*.[3]

EPIDEMIOLOGY	RISK FACTORS
♦ Fungal endophthalmitis is less common than bacterial, however >50% of endogenous endophthalmitis is due to a fungus[1-3] ♦ *Candida* is the most common and *Aspergillus* the second most common causative organism[1-3] ♦ The 2 most common causative molds are *Aspergillus* and *Fusarium* [5] ♦ Males and females are equally affected[4] ♦ 75% of the time patients present with unilateral disease; 25% of that population progresses to develop bilateral disease[4]	♦ >90% of the time there is at least one cause of immuno-deficiency, and often there are multiple causes[4] ♦ Risk factors for fungemia include central venous catheters, history of GI trauma or surgery, use of broad-spectrum antibiotic therapy, hyperalimentation, neutropenia, IV drug abuse, corticosteroid therapy, and diabetes mellitus[1,5] ♦ Risk factors associated specifically with *Aspergillus* include IV drug abuse, recent hospitalizations, immuno-suppression, and lung disease[2,4,6]
SIGNS/SYMPTOMS	TREATMENT/MANAGEMENT
♦ Most common presenting complaint is decreased vision[5] ♦ Other common symptoms include severe eye pain, ipsilateral headache, redness, eye swelling, photophobia, and floaters[2,4] ♦ Vision is frequently very poor at initial presentation ♦ Anterior chamber reaction plus/minus hypopyon is frequently present[4,6] ♦ Vitritis present in almost all cases[4,6,7] ♦ Yellowish, fluffy exudative chorioretinal infiltrates with ill-defined borders that are commonly located in the macula[4,6,7] ♦ Vitreous masses appear as fluffy, irregular, yellowish exudative masses[4,6,7] ♦ Intraretinal hemorrhages are frequently present[6] ♦ Review of systems is almost always positive, suggestive of comorbidities or systemic involvement	♦ Fundus photographs and B-scan for monitoring of disease progression and efficacy of treatment ♦ Vitreous tap or diagnostic and therapeutic vitrectomy with gram stain and culture is beneficial in determining chorioretinitis vs. endophthalmitis ♦ Intravitreal injection with voriconazole (recommended dose is 100 mcg) or amphotericin B with or without early vitrectomy in cases of endophthalmitis or chorioretinitis involving the macula is warranted [10] ♦ Systemic antifungal therapy (fluconazole, amphotericin, or voriconazole) can be used as adjuvant, or sole therapy in limited chorioretinitis not involving the macula. Recommended dosing with oral voriconazole for systemic therapy is 6 mg/kg for 2 doses, then 4 mg/kg twice daily for 4-6 weeks, or longer as needed[10] ♦ AC washout and intracameral anti-fungal therapy in cases of AC involvement[11]

References

1. Khan FA, Slain D, Khakoo RA. Candida endophthalmitis: focus on current and future antifungal treatment options. *Pharmacotherapy* 2007;27(12):1711-1721. www.ncbi.nlm.nih.gov/pubmed/18041891

2. William A, Spitzer MS, Deuter C, Blumenstock G, Partsch M, Voykov B, Ziemssen F, Bartz-Schmidt KU, Doycheva D. Outcomes of Primary Transconjunctival 23-Gauge Vitrectomy in the Diagnosis and Treatment of Presumed Endogenous Fungal Endophthalmitis. *Ocul Immunol Inflamm* 2017;25(2):239-245. www.ncbi.nlm.nih.gov/pubmed/26829468

3. Essman TF, Flynn HW, Jr., Smiddy WE, Brod RD, Murray TG, Davis JL, Rubsamen PE. Treatment outcomes in a 10-year study of endogenous fungal endophthalmitis. *Ophthalmic Surg Lasers* 1997;28(3):185-194. www.ncbi.nlm.nih.gov/pubmed/9076791

4. Riddell J, McNeil SA, Johnson TM, Bradley SF, Kazanjian PH, Kauffman CA. Endogenous Aspergillus endophthalmitis: report of 3 cases and review of the literature. *Medicine (Baltimore)* 2002;81(4):311-320. www.ncbi.nlm.nih.gov/pubmed/12169886

5. Durand ML. Bacterial and Fungal Endophthalmitis. *Clin Microbiol Rev* 2017;30(3):597-613. www.ncbi.nlm.nih.gov/pubmed/28356323

6. Weishaar PD, Flynn HW, Jr., Murray TG, Davis JL, Barr CC, Gross JG, Mein CE, McLean WC, Jr., Killian JH. Endogenous Aspergillus endophthalmitis. Clinical features and treatment outcomes. *Ophthalmology* 1998;105(1):57-65. www.ncbi.nlm.nih.gov/pubmed/9442779

7. Gruener AM, Allen F, Stanford MR, Graham EM. Aspergillus fumigatus Endophthalmitis with Necrotizing Scleritis following Pars Plana Vitrectomy. *Case Rep Ophthalmol Med* 2016;2016:9289532. www.ncbi.nlm.nih.gov/pubmed/27379189

8. Adam CR, Sigler EJ. Multimodal imaging findings in endogenous Aspergillus endophthalmitis. *Retina* 2014;34(9):1914-1915. www.ncbi.nlm.nih.gov/pubmed/24695061

9. Shah CP, McKey J, Spirn MJ, Maguire J. Ocular candidiasis: a review. *Br J Ophthalmol* 2008;92(4):466-468. www.ncbi.nlm.nih.gov/pubmed/18369061

10. Riddell J, Comer GM, Kauffman CA. Treatment of endogenous fungal endophthalmitis: focus on new antifungal agents. *Clin Infect Dis* 2011;52(5):648-653. www.ncbi.nlm.nih.gov/pubmed/21239843

11. Sen P, Gopal L, Sen PR. Intravitreal voriconazole for drug-resistant fungal endophthalmitis: case series. *Retina* 2006;26(8):935-939. www.ncbi.nlm.nih.gov/pubmed/17031296

12. Kramer M, Kramer MR, Blau H, Bishara J, Axer-Siegel R, Weinberger D. Intravitreal voriconazole for the treatment of endogenous Aspergillus endophthalmitis. *Ophthalmology* 2006;113(7):1184-1186. www.ncbi.nlm.nih.gov/pubmed/16713628

13. Ferreira TB, Vaz F, Rodrigues A, Donato S. Intravitreal voriconazole as primary treatment for endogenous Aspergillus endophthalmitis. *BMJ Case Rep* 2009;2009:bcr1020081110. www.ncbi.nlm.nih.gov/pubmed/21687050

14. Zhao J, Cheng Y, Song X, Wang C, Su G, Liu Z. A Comparative Treatment Study of Intravitreal Voriconazole and Liposomal Amphotericin B in an Aspergillus fumigatus Endophthalmitis Model. *Invest Ophthalmol Vis Sci* 2015;56(12):7369-7376. www.ncbi.nlm.nih.gov/pubmed/26574795

15. Dave VP, Pathengay A, Relhan N, Sharma P, Jalali S, Pappuru RR, Tyagi M, Narayanan R, Chhablani J, Das T, Flynn HW, Jr. Endophthalmitis and Concurrent or Delayed-Onset Rhegmatogenous Retinal Detachment Managed With Pars Plana Vitrectomy, Intravitreal Antibiotics, and Silicone Oil. *Ophthalmic Surg Lasers Imaging Retina* 2017;48(7):546-551. www.ncbi.nlm.nih.gov/pubmed/28728182

16. Perlmutter Cancer Center. Clinical Trials and Research Studies. "COG-AALL0434: Intensified Methotrexate Nelarabine (Compound 506U78; IND# 52611) and Augmented BFM Therapy for Children and Young Adults with Newly Diagnosed T-cell Acute Lymphoblastic Leukemia (ALL) or T-cell Lymphoblastic." Available at clinicaltrials.med.nyu.edu/cancer/clinicaltrial/107/cog-aall0434-intensified-methotrexate/

Citing this article

Ricca AM, Binkley EM, Boldt HC. Fungal endophthalmitis: Hematogenous seeding in an immune suppressed patient with positive fungal and bacterial blood cultures. EyeRounds.org. posted December 15, 2017; Available from EyeRounds.org/cases/264-Fungal-Endophthalmitis.htm

last updated: 12/15/2017

Index