Lymphoepitheliomalike Carcinoma of the Orbit

Lymphoepitheliomalike carcinoma (LELC) of the skin is an uncommon cutaneous malignancy with the potential for distant metastasis. We describe a patient with LELC of the mid forehead and an asymptomatic orbital mass, which when biopsied proved to be a lymphoepitheliomalike carcinoma (LELC).

Report of a Case. A 45-year-old man was referred to the Ophthalmology Clinic at the University of Texas M. D. Anderson Cancer Center, Houston, for the evaluation of an asymptomatic right-sided orbital mass that had been identified on recent magnetic resonance imaging (MRI) scans. The patient denied any orbital symptoms or signs except for numbness and paresthesia in the area of the right-sided supraorbital notch, which had been present for at least 2 years. He had a history of a skin nodule on his mid forehead, of which a biopsy specimen had been taken at another institution and diagnosed as LELC of the skin. Subsequently, 2 wide-local excisions with positive margins were performed on the nodule, and biopsy specimens of the skin overlaying the supraorbital notch revealed lymphoepithelioma with perineural invasion.

The ophthalmologic examination results revealed a best-corrected visual acuity of 20/70 OD and 20/15 OS; the visual acuity had been stable in the right eye since a scleral buckle procedure for retinal detachment was performed approximately 18 years prior to this presentation. The external examination revealed quiet globes; the Hertel exophthalmometry measurement was 19 mm in each eye. Results of the extraocular motility examination were normal. The pupils were equal, round, and reactive to light with no afferent pupillary defect. The confrontation visual fields were normal in the left eye, but superior and temporal field defects were found in the right eye; it was not clear whether the field deficit was new or due to the previous retinal detachment in the right eye. The slitlamp examination and applanation tonometry measurements were normal in both eyes. A dilated fundus examination revealed a 0.4 cup-disc ratio in the right eye and a 0.2 cup-disc ratio in the left eye. There was evidence of a scleral buckle band with an attached retina in the right eye; there were no choroidal striae.

High-resolution MRI scans of the orbits were obtained with conventional pulse sequences. They revealed a multilocular cystlike mass in the medial aspect of the right orbit (Figure 1). Other imaging features included fluid-fluid layers within the lesion and peripheral enhancement. A computed tomography scan of the head and neck area that was obtained 6 weeks prior to the MRI scan did not show an orbital mass.

An orbital biopsy of the mass was performed through a modified Lynch incision (supronasal orbitotomy). The cystic mass was identified in the superonasal orbit, approximately 25 mm posterior to the anterior lacrimal crest. The mass extended posteriorly toward the superior orbital fissure, and there was no clearly defined capsule. Partial excision of the mass was performed, and the frozen-section diagnosis was consistent with poorly differentiated LELC. The patient underwent concurrent chemoradiotherapy, consisting of 2 cycles of cisplatin followed by 3 cycles of cisplatin and 5-fluorouracil; external beam radiotherapy was administered in 33 fractions, at a total dose of 6600 rad (66 Gy).

The material from the forehead lesion that was provided by another institution consisted of

Figure 1. A, An axial T1-weighted magnetic resonance imaging (MRI) scan, tailored to the orbits, reveals a multilobular, slightly hyperintense lesion in the upper medial aspect of the right orbit (arrows). B, An axial T2-weighted MRI scan demonstrates a cystlike appearance, with a fluid-fluid layer (arrows) best seen in the anterior component of the tumor. C, An axial postcontrast fat-suppressed T1-weighted image shows peripheral enhancement and a lack of central enhancement.
a skin ellipse containing a dense, nodular infiltrate of the deep dermis (Figure 2A). Islands of large cytologically malignant cells with polygonal, pleomorphic nuclei and prominent nucleoli were identified (Figure 2B). These islands were surrounded by a very dense lymphocytic infiltrate.

The surgical specimen from the orbital biopsy performed at M. D. Anderson Cancer Center consisted of multiple fragments of pink, firm tissue with a combined measurement of 1 × 0.6 × 0.4 cm. The specimen was routinely processed, and additional slides were analyzed by a standard immunohistochemical method. Histologically, there was an infiltrate very similar to that seen in the outside material. An immunohistochemical study showed expression of cytokeratin (Figure 2C), which confirmed the epithelial nature of the malignant cells. This constellation of histologic features is indicative of LELC. Standard in situ hybridization studies failed to reveal evidence of infection by Epstein-Barr virus.

Comment. Lymphoepitheliomas are malignant tumors of epithelial origin with various amounts of reactive lymphocytic infiltrate. Although initially described in the nasopharynx (World Health Organization type 3 nasopharyngeal carcinoma), these tumors have been identified in various locations throughout the body.4–8

Lymphoepitheliomalike carcinoma of the skin is a rare cutaneous malignancy that is probably of adnexal origin.4–8 It is usually a flesh-colored or red, firm nodule or plaque that appears most often on the face. Since the original description by Swanson et al11 in 1988, at least 21 cases have been described. The patient described here is slightly younger than most previously reported patients (older than 50 years) with LELC of the skin.

Lymphoepitheliomalike carcinoma of the skin is microscopically distinct from other primary cutaneous neoplasms. Although poorly differentiated squamous cell carcinoma could conceivably be associated with a prominent lymphoid infiltration, the latter is usually concentrated in the superficial dermis and has connections with the epi- dermis. Furthermore, squamous cell carcinoma is usually associated with at least focal evidence of cytoplasmic keratinization.

Cases of LELC of the skin associated with a metastatic or satellite lesion in the orbit are extremely rare. The only mention in the literature is in a study of 1422 orbital tumors analyzed at the eye pathology laboratory at the Shanghai Medical University, Shanghai, China.12 The authors list an LELC of the skin metastatic to the orbit in one of the 1422 cases reviewed in their article, but no further description of the histologic findings or the clinical findings is provided.

In the case described here, the orbital mass was an incidental finding on an MRI scan after the diagnosis of LELC of the forehead skin with perineural invasion. It is likely that the orbital mass represents a metastatic lesion secondary to the forehead lesion, though the possibility of a direct extension into the orbit or a primary orbital tumor with subsequent cutaneous metastasis cannot be completely ruled out. It is interesting that the radiologic features of the orbital mass were suggestive of a benign cystic lesion. Although there were minimal to no orbital signs or visual symptoms of a mass in this patient, and the radiologic features suggested a benign process, the orbital biopsy was undertaken to rule out metastasis. Performing the orbital biopsy was a crucial step, and it changed the staging and treatment of this disease.

This case underscores the importance of a thorough systemic workup for patients with LELC of the skin. The orbital mass was identified during an MRI scan of the head and neck, which was obtained to rule out involvement of the paranasal sinuses or the oropharynx. In general, because of the close histologic similarity to nasopharyngeal lymphoepithelioma, patients with suspected LELC of the skin should have a thorough otolaryngological examination, including indirect laryngoscopy, to rule out metastasis to the skin. The differential diagnosis also includes Merkel cell tumor; lymphoma; pseudolymphoma; and metastatic lymphoepithelioma from the salivary gland, thymus, cervix, lung, vulva, stomach, or tonsil. These may be excluded by history, physical examination findings, and the results of histological studies, including immunohistochemical analysis. Lymphoma and pseudolymphoma can be excluded because of the expression of lymphoid markers and the lack of cytokeratin expression. Merkel cell carcinoma is characterized by malignant epithelial cells with a lesser degree of pleomorphism than is seen in LELC of the skin; also, the nuclei in Merkel cell carcinoma characteristically have finely dispersed (“salt-and-pepper”) chromatin.
We recommend an imaging study of the head and neck in all patients with lymphoepithelioma of the pericocular skin not only to rule out nasopharyngeal carcinoma, but also to rule out the possibility of orbital metastasis, as was the case in this patient.

The association of LELC and the Epstein-Barr virus varies in different organs and in different geographical regions. The Epstein-Barr virus is definitively associated with LELC from the stomach, salivary gland, lung, and thymus. The association of Epstein-Barr virus with LELC is restricted to Asian patients with tumors of the salivary gland and lung; whereas association of Epstein-Barr virus with gastric and thymic LELC is independent of race. As was the case in our patient, in the skin, there is no apparent association between LELC and Epstein-Barr virus. The treatment of choice for LELC of the skin is complete surgical excision whenever possible.1, 2, 15 Radiotherapy is also an effective modality for the treatment of lymphoepitheliomas, particularly in patients in whom complete surgical excision of the cancer is not possible.16 In the patient whose case we describe, the forehead lesion had recurred twice and was found to be associated with perineural invasion. The orbital mass could not be completely excised without total sacrifice of the intraorbital contents because it extended posteriorly almost to the superior orbital fissure. Externally, beam radiotherapy was the best treatment option for this patient with extensive skin, perineural, and orbital lymphoepithelioma.

M. Amir Ahmadi, MD
Victor G. Prieto, MD, PhD
Gary L. Clayman, MD
Lawrence E. Ginsberg, MD
Bita Esmaeli, MD
Houston, Tex

Corresponding author and reprint requests: Bita Esmaeli, MD, Ophthalmology Section, Department of Plastic Surgery, University of Texas M. D. Anderson Cancer Center, Box 443, 1515 Holcombe Blvd, Houston, TX 77030 (e-mail: besmaeli@mdanderson.org).

References


Orbital Cavitary Rhabdomyosarcoma Masquerading as Lymphangioma

Rhabdomyosarcoma is the most common primary orbital malignant neoplasm of childhood. However, it constitutes only 4% of all orbital lesions studied by biopsy in children.1 As it is a highly malignant tumor, prompt diagnosis and treatment are imperative. Current therapeutic regimens of radiation and chemotherapy have provided 93% 3-year survival.2 We herein report a rare variant of orbital rhabdomyosarcoma that showed magnetic resonance (MR) imaging findings of central cavitation, simulating an orbital lymphangioma.

Report of a Case. An otherwise healthy 4-year-old girl was referred to us because of abrupt-onset proptosis of her right eye (Figure 1). The parents had noted mild painless swelling of the right upper eyelid during the previous 3 weeks.

The visual acuity was 20/20 in each eye. There was 6 mm of right proptosis. Motility was restricted in all gazes, and the right eye was displaced inferiorly and temporally. Subtle subcutaneous ecchymosis was present at the inferotemporal orbital rim. There was a dilated clear ocular fundus with conjunctival hyperemia superonasally.

An MR image showed a superonasal heterogeneous soft tissue mass with no bone erosion. On T1-weighted gadolinium-enhanced images, the central area of the mass was hypointense, suggestive of proteinaceous material. A peripheral hyperintense rim indicated vascularized tissue. There was a thin septum dividing the central “cystic” area, but fluid-fluid levels were not seen (Figure 2A). T2-weighted images disclosed an irregular isointense rim and central area of extreme hyperintense signal (Figure 2B). These findings were suggestive of lymphangioma with proteinaceous fluid and hemorrhage.

A diagnosis of lymphangioma was favored in light of the rapid development of proptosis, dilated conjunctival lymphatics, subcutaneous ecchymosis, and the presence of presumed cystic, rather than solid, structures on MR imaging. Cautious observation was advised, but 10 days later, worsening of the proptosis and eyelid swelling prompted a biopsy. Intraoperatively, a multicystic blue mass was found and aspiration of 1 mL of internal serosanguineous fluid collapsed the mass. Near-total excision of the remaining mass was performed. These findings continued to suggest the diagnosis of hemorrhagic lymphangioma.

Histopathologic examination disclosed undifferentiated small round cells with hyperchromatic nuclei (Figure 3), high nuclear-to-cytoplasmic ratio, and brisk mitotic activity. Immunohistochemistry

©2001 American Medical Association. All rights reserved.
demonstrated intense immunoreactivity for smooth muscle actin and desmin. These findings confirmed the diagnosis of rhabdomyosarcoma. Radiotherapy (4500 rad [45 Gy]) and chemotherapy with cyclophosphamide, dactinomycin, and vincristine sulfate were instituted by means of the Intergroup Rhabdomyosarcoma Study Committee protocol. The patient continued to demonstrate complete tumor regression at 20 months' follow-up.

Comment. Orbital rhabdomyosarcoma typically occurs as a unilateral solid mass in the superonasal part of the orbit. The average age at diagnosis is 8 years. Proptosis and displacement of the globe usually develop during a period of weeks. Lymphangioma also occurs in a similar age group, about 4 to 10 years of age. Bleeding into lymphangioma can produce sudden proptosis and ecchymosis. Frequently, conjunctival involvement is found.

Rhabdomyosarcoma can usually be differentiated from lymphangioma by MR imaging. Rhabdomyosarcoma characteristically shows a solid homogeneous mass that is isointense to vitreous on T1-weighted images. Lymphangioma demonstrates a multicystic mass with lobulated margins, showing hypointensity to vitreous on T1-weighted images and hyperintensity to vitreous on T2-weighted images. The rim of lymphangioma can enhance minimally. Our case had MR imaging characteristics most consistent with lymphangioma.

Cavitation can occur within other ocular tumors secondary to hemorrhage, necrosis, and mucoid degeneration. However, cavitation within rhabdomyosarcoma is distinctly unusual. To our knowledge, this finding has not been previously reported. In a review of 250 orbital childhood tumors by Shields and associates, there were no rhabdomyosarcomas with cavitation.

Our case presented a diagnostic dilemma. Rhabdomyosarcoma and lymphangioma occur in similar age groups and are seen with similar clinical findings. The malignant nature of rhabdomyosarcoma vs the benign course of lymphangioma underscores the importance of correct diagnosis. Although conservative management of lymphangioma is generally advised, proper follow-up should be performed. If the suspected lymphangioma fails to demonstrate resolution or shows progression, biopsy should be considered to rule out rhabdomyosarcoma.

Douglas R. Fetkenhour, BS
Carol L. Shields, MD
An N. Chao, MD
Jerry A. Shields, MD
Philadelphia, Pa
Carl B. Guterman, MD
Hackensack, NJ
Ralph C. Eagle, Jr, MD
Philadelphia
Uveal Effusion and Secondary Angle-Closure Glaucoma Associated With Topiramate Use

Rarely, drugs, mostly sulfila-related compounds, have produced uveal effusions, forward rotation of the iris, lens diaphragm, transient myopia, and secondary angle closure. \(^1\) We have recently encountered 2 cases in which uveal effusions have occurred after administration of topiramate (Topamax; Ortho-McNeil Pharmaceutical, Raritan, Nj), a new anticonvulsant medication.

**Report of Cases.** Case 1. A 34-year-old white woman was seen in our emergency department with severe headaches and progressively blurry vision in both eyes. Her medical history was notable for depression. Her ocular history was unremarkable, she had never worn glasses, and she denied ocular disease within the family. Her medications included clonazepam, buspirone hydrochloride, citalopram hydrobromide, orlistat, fluvoxamine maleate (a selective serotonin reuptake inhibitor [SSRI], which she started 2 days prior to initial examination), and topiramate (which she started 2 weeks prior to initial examination).

On examination her visual acuity was 20/250 OU. Slitlamp examination revealed trace conjunctival injection and chemosis, relatively clear corneas, and shallow anterior chambers (approximately 2 corneal thickness deep centrally). The pupils were widely dilated, and the lenses were clear. Intraocular pressures measured 51 mm Hg OD and 45 mm Hg OS. Funduscopic examination findings were normal with a cup-disc ratio of 0.3 OU. No choroidal effusions were seen by indirect ophthalmoscopy. On gonioscopy there was a deep iris convexity with appositional angle closure. With compression, trabecular meshwork was seen in both eyes without peripheral anterior synechiae.

The diagnosis of bilateral angle closure glaucoma was made. The patient was treated with 0.5% timolol maleate, dorzolamide hydrochloride, brimonidine tartrate, oral acetazolamide (500 mg), and latanoprost. Her pressures eventually decreased to 28 mm Hg OD and 27 mm Hg OS. 1% Pilocarpine was added to alleviate the pupillary mydriasis.

She was seen the following day with examination findings relatively unchanged, except that her pupils were now mid-dilated and tensions were 29 mm Hg OD and 32 mm Hg OS. The anterior chambers were still shallow in both eyes. A manifest refraction revealed the formerly emmetropic patient now had measurements of −8.75 sphere OD and −7.25 sphere OS. A B scan was performed and demonstrated a separation between the choroidal layer and the sclera 360° with the crystalline lens shifted anteriorly (Figure, D). Ultrasound biomicroscopy was also performed and demonstrated a closed angle with a forward shift of the ciliary body (Figure, A and B).

A diagnosis of bilateral uveal effusion was made. Pilocarpine hydrochloride was discontinued and scopolamine hydrocholoride was administered. An oral steroid taper was also started to decrease the inflammatory response within the suprachoroidal space. After consultation with her psychiatrists, she stopped receiving fluvoxamine maleate and the topiramate was tapered over 2 weeks. She was seen every 2 to 3 days. She reported alleviation of her symptoms by the sixth day after initial examination. By then, her myopic shift had resolved and her chambers were deep. On gonioscopy, she was open to ciliary body band without synechiae in both eyes. Her intraocular pressures were 11 to 14 mm Hg OU. She finished her prednisone taper and stopped receiving the antiglaucoma medications within 1 week. Subsequently, the scopolamine was stopped, and her pupils returned to normal size. Her vision returned to 20/25 OU without correction. Repeated B scans and ultrasound biomicroscopy were performed 3 weeks after initial examination, which revealed a resolution of the effusion (Figure, C and E). Her axial lengths were 23.54 mm OD and 23.74 mm OS.

Case 2. A 53-year-old white woman with blurry vision in both eyes on awakening was seen at another clinic. Her medical history was notable for depression and high cholesterol levels. Her medications included premarin, venlafaxine hydrochloride (an SSRI), atorvastatin calcium, and topiramate (which she started 10 days prior to the onset of her symptoms).

Her vision was recorded as counting fingers OD and 20/160 OS. Slitlamp examination revealed chemosis, diffuse corneal edema, and diffusely shallow anterior chambers. Her intraocular pressures were recorded as 72 mm Hg OD and 74 mm Hg OS. Funduscopic examination findings were reported as normal with normal-appearing optic nerves. A diagnosis of bilateral angle closure was made.

Peripheral iridotomies were performed that same day in both eyes, and medications were administered without reduction of her intraocular pressures. One hour postlaser, paracenteses were made to both eyes to relieve the pressure and then repeated several hours later with reduction of her intraocular pressure to 45 mm Hg OD and 48 mm Hg OS.
mm Hg OS. The patient continued to receive topical and oral antiglaucoma medications. She discontinued only the topiramate since this was the only recent change to her medications. She was seen the next day. Her anterior chambers were deeper centrally but still shallow peripherally. Her intraocular pressure was 25 mm Hg OU. Gonioscopy revealed no angle structures, and funduscopic examination did not show clinically evident choroidal effusions. Tropicamide was administered. By the next day, her intraocular pressure was 12 mm Hg OU, and her anterior chambers were deep. Repeated gonioscopy revealed angles open to scleral spur.

She was seen at our service 1 month after her initial presentation. Her vision was 20/25 OU uncorrected. Slitlamp examination revealed clear corneas with deep, quiet anterior chambers in both eyes. Intraocular pressure was 14 mm Hg OU, and gonioscopy revealed grade III open angles without synechiae in both eyes. Funduscopic examination revealed a cup-disc ratio of 0.6 with temporal pallor.

Comment. Spontaneous uveal effusions are most common in individuals with microphthalmic eyes or with abnormal sclera. Drug-induced uveal effusions have been cited, although they also occur rarely. Both of our patients received topiramate as adjunctive therapy for depression approximately 2 weeks prior to presentation. We feel that topiramate has some relation to the cause of the patients’ bilateral uveal effusions, though it is unclear whether it is topiramate alone or in conjunction with an SSRI.

Topiramate is a sulfamate-substituted monosaccharide, used primarily as an antiepileptic medication. Topiramate is thought to possess a state-dependent sodium channel-blocking action. It also potentiates the activity of GABA (g-aminobutyric acid) and antagonizes the ability of kainate to activate the kainate/AMPA (alpha-amino-3-hydroxy-5-methylisoxazole-4-propionic acid) subtype of excitatory amino acid receptor. Topiramate also has a weak carbonic anhydrase inhibition. These mechanisms of action help explain the antiepileptic nature of the drug, though the mechanism of choroidal effusions remains unclear. Topiramate does cross the blood-brain barrier and has also been detected in the vitreous.

To our knowledge, these are the first reported cases of choroidal effusions associated with topiramate. It is therefore our suggestion that if a patient is seen with bilateral angle-closure glaucoma, a history of topiramate usage should be sought.

Prithvi S. Sankar, MD
Louis Robert Pasquale, MD
Cynthia L. Grosskreutz, MD, PhD
Boston, Mass

We thank Herbert Knauf, MD, for his clinical information and Danny Gauthier, MD, and Lois Hart, RD, MS, for their technical assistance.

Corresponding author: Cynthia L. Grosskreutz, MD, PhD, Department of Ophthalmology, Glaucoma Consultation Service, Massachusetts Eye and Ear Infirmary, 243 Charles St, Boston, MA 02114-3096.

Ghost Cell Glaucoma Related to Snake Poisoning

The presence of blood or blood debris in the anterior chamber can increase intraocular pressure (IOP). Vitreous hemorrhage can also lead to secondary glaucoma, producing a “ghost cell glaucoma” (GCG).1,2 Ghost cells (GCs) are degenerated spherical erythrocytes that partially lose their hemoglobin content by aging for a long period in the vitreous. Changes begin after a few days and are usually completed within 3 weeks. Hemoglobin abandons the red blood cell and forms clumps that adhere to vitreous bands. Hemoglobin that remains in the red blood cell becomes denatured and binds to the internal surface of the cell membrane, forming granules (Heinz bodies).3 Once formed, GCs may remain intact for months, moving freely within the vitreous. Neither fresh erythrocytes nor GCs are able to pass through an intact anterior hyaloid membrane; thus, a hyaloid injury must be present for these cells to be found in the anterior segment.2,3 Since GCs are rigid, they have difficulty passing through the trabecular meshwork. They tend to accumulate in its middle and external portions, whereas fresh erythrocytes pass 3 times more easily to the external portion and from there to the Schlemm canal.1,3

Increased IOP usually occurs about 2 to 4 weeks after the injury, but it may also take from 1 week to many months to develop.2,3 It is a complication that often requires surgical intervention with profuse and repeated lavage of the anterior chamber or vitrectomy to remove the hemorrhagic tissue.2,4

We describe a patient who developed vitreous hemorrhage and GCG after a snake bite. There was no evidence of anatomic alteration of the anterior hyaloids.

Report of a Case. A 44-year-old male farmer was seen in the emergency department of our institution (Hospital San Juan de Dios, National University of Colombia, Bogotá) 72 hours after sustaining a snake bite (Bothrops atrox) in his right foot. The patient was admitted to the hospital and treated for respiratory distress syndrome and hemorrhagic syndrome with renal and cerebral involvement. Two days later, after recovery from respiratory distress and renal failure, he complained of bilateral visual loss.

On examination, his visual acuity was hand motions in the right eye and light perception in the left eye. The left eye showed inferior and temporal subconjunctival hemorrhage (Figure 1), stromal and epithelial corneal edema, ++++ cells and flare in the anterior chamber, and dense anterior vitreous hemorrhage (Figure 2). The IOP was 17 mm Hg OD and 40 mm Hg OS. Dilated indirect opthalmoscopy showed a dense vitreous hemorrhage in both eyes. Results of B-scan ultrasonography confirmed bilateral vitreous hemorrhage with incomplete posterior vitreous detachment.

With an initial diagnosis of GCG in the left eye, a paracentesis and aqueous sampling were performed in the left eye. Cytologic examination of the aqueous humor disclosed the presence of GCs. Meanwhile, the IOP in the right eye rose to 28 mm Hg, and treatment was begun with 0.4% apraclonidine hydrochloride twice daily, 0.4% timolol maleate twice daily, and a prostaglandin deriva-
Figure 3. Spherical erythrocytes with vacuoles and partial loss of hemoglobin (ghost cells) in vitreous (Papanicolaou, original magnification ×100).

Bilateral GCG secondarily to snake poisoning has not yet been described in the literature, based on our MEDLINE search of the medical literature since the initial description of GCG in 1976 to the present.

Comment. Bilateral GCG secondarily to snake poisoning has not yet been described in the literature, based on our MEDLINE search of the medical literature since the initial description of GCG in 1976 to the present.

Ophthalmologists should be aware that snake bite can cause visual loss. Early diagnosis and prompt treatment to reduce the number of blood cells and GCs may increase the potential for recovery.

Ledy Rojas, MD
Gabriel Ortiz, MD
Myrian Gutiérrez, MD
Sonia Corredor, MD
Bogotá, Colombia


Recurrent Transient Visual Loss After Deep Sclerectomy

Recurrent transient visual loss in the elderly is mostly associated with cardiovascular disorders. Other causes include giant cell arteritis, migraine, increased intracranial pressure, orbital mass, and idiopathy. We describe a patient with unusual recurrent transient visual loss after deep sclerectomy with collagen implant (DSCI).

Report of a Case. A 75-year-old woman was referred for investigation of possible amaurosis fugax. She complained of recurrent painless blurred vision in her left eye for the past 6 months. Her medical history was relevant for common migraine and systemic hypertension. Systemic medications included losartan potassium, hydrochlorothiazide, lorazepam, carvedilol, and aspirin. Severe bilateral glaucoma necessitated trabeculectomy in the right eye in 1994 and DSCI in the left eye in 1996. Both procedures were uneventful.
The episodes of visual loss in the left eye occurred on average once a week, lasted up to 24 hours, and affected her ability to read. Some episodes occurred after performing gymnastic exercises, after bending forward, and once after sneezing. She had no symptoms or signs suggesting giant cell arteritis.

Best-corrected visual acuity was 20/40 OD and 20/25 OS. Pupil examination revealed a 2+ right relative afferent defect. Intraocular pressure (IOP) was 11 mm Hg in the right eye and 14 mm Hg in the left. Fundus examination revealed bilateral glaucomatous disc atrophy that was severe in the right eye (cup-disc ratio, 0.9) and moderate in the left eye (cup-disc ratio, 0.5). Visual field defect was severe in the right eye and moderate in the left.

Results of investigations, including a complete blood cell count, erythrocyte sedimentation rate, cardiovascular examination, precerebral Doppler and cerebral magnetic resonance imaging, and angiography, were normal.

Several similar episodes have occurred since she was examined. A few hours after onset of the latest episode, examination of the left eye showed visual acuity of 20/50−2, 2 mm of hyphema (Figure 1), and IOP of 38 mm Hg; gonioscopy revealed active bleeding through a microperforation in the trabeculo-Descemet membrane at the site of surgery (Figure 2).

Because of repeated bleeding episodes and increased IOP in the left eye, the site of DSCI underwent reoperation. Many actively bleeding blood vessels surrounding the Schlemm canal orifice were found and coagulated. No further bleeding has occurred since, and the IOP remained less than 15 mm Hg without therapy.

Comment. Transient visual loss secondary to recurrent hyphema has been reported after trabeculectomy and after cataract surgery with either an iris suture or an anterior chamber implant but not after nonpenetrating filtering surgery. Nowadays, DSCI is becoming a common technique to safely lower IOP and is believed to be less traumatic than trabeculectomy because of the nonpenetrating technique. More than 1500 patients have undergone DSCI in our department (unpublished data); however, recurrent hyphema occurred only in the present case. During surgery, no obvious perforation was noted, but we cannot rule out the possibility of a microperforation of the trabeculo-Descemet membrane.

Recurrent hyphema after DSCI could result from spontaneous bleeding of anomalous scleral blood vessels at the site of surgery (such as in the present case), venous hypertension (Valsalva phenomenon) with blood reflux in the Schlemm canal, or a combination of both. Aspirin therapy might have also contributed to the bleeding.

History of previous filtering surgery in the setting of transient visual loss should then prompt gonioscopy and a careful anterior chamber examination for the presence of hyphema or blood reflux through the trabeculo-Descemet membrane.

Aude Ambresin, MD
François-Xavier Borruat, MD
André Mermoud, MD
Lausanne, Switzerland

Corresponding author: François-Xavier Borruat, MD, Hôpital Oph-
Anterior Ischemic Optic Neuropathy Following Acute Angle-Closure Glaucoma

Nonarteritic anterior ischemic optic neuropathy (NAION) is believed to be caused by acute occlusion of small vessels to the optic nerve, resulting in lacunar infarction. Most involved optic nerves are anatomically crowded with a cup-disc ratio that is small and usually less than 30%. Nonarteritic anterior ischemic optic neuropathy may also follow other episodes of hemodynamic instability, such as cerebral hypoperfusion (shock optic neuropathy) or blood loss. It has been described after uncomplicated cataract extraction, in which it is presumed to be due to perioperative elevation of intraocular pressure. We report a case of NAION developing in each eye of a man with sequential acute angle-closure glaucoma. In each eye, the vision loss followed the bout of glaucoma by approximately 2½ weeks.

Report of a Case. A 70-year-old man with angina pectoris and hypercholesterolemia developed acute pain and markedly diminished vision in his left eye due to angle-closure glaucoma. Visual acuity was noted to be 5/200, corneal edema was present, and intraocular pressure was 30 mm Hg. Medications (timolol maleate, brimonidine tartrate, latanoprost, 1% pilocarpine hydrochloride, prednisolone, and oral acetazolamide), and subsequent laser iridotomies were successful in reversing the process. He was maintained on timolol and latanoprost after the third day. Visual acuity was noted to be 20/40 after 11 days. Ophthalmoscopy showed a healthy left optic nerve with a 0.1 cup-disc ratio. At this time, the patient was advised, but refused, to have prophylactic iridotomy in the fellow eye. One week later, vision loss in the left eye recurred. There was no associated eye pain, headache, jaw claudication, or polyamyagia rheumatica. On examination, visual acuity was hand movements, and a remaining inferotemporal island of vision was detected on confrontation visual field testing. Slitlamp examination results were unremarkable, and intraocular pressure was normal. A left afferent pupil defect was noted. The left optic nerve was swollen with overlying hemorrhages. Westergren erythrocyte sedimentation rate was normal. Left NAION was diagnosed.

One month after the bout of angle-closure glaucoma in the left eye, the patient experienced sudden vision loss in the right eye due to angle-closure glaucoma. The intraocular tension was 56 mm Hg. Medications (the same used as in fellow eye) and laser iridotomy again were successfully employed, and 10 days later, visual acuity recovered to 20/50. One week later, however, there was marked worsening of vision in the right eye. Neuro-ophthalmologic consultation was sought, and examination revealed a best-corrected visual acuity of 20/200 OD and 2/200 OS. Each pupil was dilated and unresponsive to light. Glaucomflecken was noted on the left lens. Goldmann visual fields showed bilateral central scotomas with peripheral inferior extension. Ophthalmoscopy revealed pale swelling of the right optic disc and resolving optic disc edema in the left eye, with marked optic atrophy. Retinal arterioles were attenuated bilaterally. Sequential NAION was diagnosed. On subsequent follow-up there was no improvement of visual acuity or visual fields in either eye, and bilateral optic atrophy was noted.

Comment. In our case, vision loss due to NAION was most likely precipitated by hemodynamic instability to the optic nerve from the marked rise and subsequent stabilization of intraocular pressure. Although permanent vision loss, which occurs at the time of angle-closure glaucoma, is thought to be caused by an ischemic event to the optic nerve, NAION following such a bout has not (to our knowledge) previously been reported. The explanation for the duration between the angle-closure episode and the onset of NAION is unknown. We postulate that in our case, subclinical low-grade optic nerve ischemia occurred at the time of the pressure rise with subsequent progressive ischemia until frank vision loss ensued. Perhaps a vicious cycle consisting of ischemia, optic disc swelling, and additional ischemia occurred. Hayreh has described several cases of subclinical optic disc edema resulting in frank bouts of symptomatic NAION months later. Perhaps our case and those of Hayreh shed some light on the possible mechanism as to why some cases of NAION following cataract extraction have a demonstrable interval between surgery and vision loss. In any event, acute rise in intraocular pressure is to be considered a risk factor in NAION. Whenever possible, precautions should be taken to avoid pressure rise, especially in eyes with optic discs that are developmentally small, with small cup-disc ratios.

Michael L. Slavin, MD
Michael Margulis, MD
Great Neck, NY

Corresponding author and reprints: Michael L. Slavin, MD, Division of Neuro-ophthalmology, Department of Ophthalmology, Long Island Jewish Medical Center, the Albert Einstein College of Medicine, 600 Northern Blvd, Great Neck, NY 11021 (e-mail: DrSlavin4@aol.com).

Contractile Peripapillary Staphyloma With Light Stimulus to the Contralateral Eye

A peripapillary staphyloma is a sporadic, unilateral, congenital defect characterized by an excavation surrounding a usually normal optic disc and often accompanied by decreased vision or by enlargement of the blind spot. A less common occurrence is when the wall of the peripapillary staphyloma is contractile, which is caused by 1 of 2 possible mechanisms, “pressure balance” or “muscular contraction.” This article provides the first documentation of a contractile peripapillary staphyloma through sequential pictures and discusses the main differential diagnosis and the possible pathophysiological mechanism.

Report of a Case. A 23-year-old white woman was referred for evaluation after undergoing a vitrectomy on the left eye for removal of a peripapillary cisticercus, which disappeared after retrobulbar anesthesia. The best-corrected visual acuity was 20/25 OD and 20/30 OS. The pupillary reflexes were normal. The left eye had a peripapillary staphyloma showing circular-type contractile movements characterized by a short time delay, following the light stimulus to the contralateral eye. The correlations were negative with the Valsalva maneuver, neck venous compression, forced lid closure, increase of ocular pressure with contact lens, respiratory movements, accommodation, and illumination of the affected eye.

The visual field showed enlargement of the blind spot. Fluorescein angiography revealed a window defect in the peripapillary region. Optical coherence tomography, B-scan ultrasonography, computed tomography, and nuclear magnetic resonance in combination revealed a parietal ectasia. The orbital Doppler was normal. No retrobulbar tumors, inflammation, abnormal vessels, or other congenital anomalies were identified. Changes in size and shape affecting the disc and the peripapillary zone were documented by serial photographs and video documentation obtained from biomicroscopy and scanning laser ophthalmoscopy (Figure 1 and Figure 2).

Comment. The condition described herein must be distinguished from coloboma of the optic disc, in which the defect is within the nerve head, or myopic conus, in which the defect is usually secondary to an abnormal disc. In this case report, an error during embryological development seems likely. An area that should have become sclera may have become a circular muscle instead, using concentrically oriented smooth strands and forming an incomplete ring around the nerve.

We favor a neuromuscular contraction mechanism as the basis for the observed phenomenon. A circular, heterotopic smooth muscle situated at the posterior pole of the eye, associated with an autonomic cholinergic reflex, and innervated by a ciliary nerve is, in our estimation, the most likely cause for these intracocular motions. The contraction was noticeably changed by retrobulbar anesthesia. The relevant mechanism may be rudimentary and may explain the nonsynchronous re-

---

Figure 1. Serial fundus photographs of the peripapillary staphyloma, showing its contractile movements and shape and size modifications in response to light stimulation to the contralateral eye. A, Normal appearance of the ectasia with an indefinite nasal margin of the disc. B, Initial contraction of the anomaly, allowing a partial identification of the nasal margin of the disc. C, Progressive contraction revealing a normal shape of the disc. D, Final appearance of the region after a circular contraction pattern.

Figure 2. Serial ultrasonographic pictures, revealing changes of ectasia deepness at the nasal aspect of the peripapillary staphyloma. A, Initial appearance after the light stimulus in the contralateral eye. B-D, Progressive contraction following the provocative test.
spontaneous pupillary constriction with a latency period after the pupillary reflex and the negative correlation to direct illumination.

Michel E. Farah, MD
Fausto Uno, MD
Pedro P. Bonomo, MD
Mario Nobrega, MD
Ana L. Höfling-Lima
São Paulo, Brazil

We thank Tercio Guia for the serial pictures and video documentation.

Corresponding author: Michel E. Farah, MD, Avenida Ibirapuera, 331, 4° andar, CEP 04524-020, São Paulo-SP, Brazil (e-mail: michelfarah@uol.com.br).


**Shrinkage: Fact or Fiction?**

The diagnosis of giant cell arteritis (GCA) is confirmed by finding characteristic histological changes in the disease in an anterior segment, such as the superficial temporal artery. The length of the arterial specimen is crucial because of the presence of “skip lesions”1 (areas of no inflammation) in GCA. Recently, there has been discussion concerning the required length of an arterial specimen to securely confirm or exclude the diagnosis of GCA.2-5 It is generally accepted that 20 mm is an adequate specimen length for a unilateral biopsy. In a “Letter to the Editor” in the Journal of the American Medical Association, the issue has been raised as to whether this is a prefixation or postfixation measurement guideline and whether formalin fixation reduces the effective length of a temporal artery biopsy specimen.4 This is a potentially important question since the accuracy of the histological diagnosis of GCA is believed to be strongly correlated to the length of the fixed artery specimen that is available for pathological assessment. We report the first available data that directly address this question.

**Report of a Case.** All patients undergoing temporal artery biopsy at Wills Eye Hospital (Philadelphia, Pa) between January 15 and July 1, 1999, were prospectively enrolled. Immediately upon excision of the temporal artery segment and prior to the placement of the specimen in 10% neutral buffered formalin fixative, the length of the specimen was measured in the operating room by the surgeon. It was later remeasured after fixation before sectioning by the pathologist, who was masked as to the initial measurement. Both sets of measurements were done using the same standardized millimeter rulers with measurements being made to the nearest tenth of a millimeter.

Twenty-eight temporal artery biopsies were performed. Fifteen were positive and 13 were negative for shrinkage. The average prefixation length was 28.4 mm (SD, 6.0 mm), whereas the average postfixation length was 26.0 mm (SD, 5.5 mm), representing a mean shrinkage of 2.4 mm (95% confidence interval, 1.6-3.1 mm; P<.001, 2-tailed test) or a mean reduction of about 8% (6%-13%). Twenty-two biopsy specimens were measured between 3 and 6 hours of being placed in fixation, and 6 were measured within 12 hours of fixation. No statistical difference was detected between these 2 groups.

**Comment.** Our study shows that shrinkage of temporal artery biopsy specimens does occur following formalin fixation. This observation suggests that clinicians may need to take slightly longer temporal artery biopsy specimens than previously recommended to insure that shrinkage due to chemical fixatives does not reduce diagnostic accuracy in the investigation of this treatable but potentially sight-threatening condition. While a 20-mm sample of temporal artery is generally considered to be an adequate biopsy specimen, because of the presence of skip lesions, the shorter the biopsy specimen, the more important the shrinkage factor is to diagnosis.

Helen V. Danesh-Meyer, FRACO
Auckland, New Zealand
Philadelphia, Pa
Peter J. Savino, MD
Jurij R. Bilyk, MD
Ralph C. Eagle, MD
Robert C. Sergott, MD
Philadelphia, Pa

Corresponding author: Helen V. Danesh-Meyer, MD, Discipline of Ophthalmology, University of Auckland, Private Bag 92019, Auckland, New Zealand (e-mail: h.daneshmeyer@auckland.ac.nz).