

## Nephrolithiasis With Dorzolamide

Carbonic anhydrase inhibitors (CAIs) are an important line of therapy in the treatment of glaucoma. Inhibition of the type II isoenzyme of carbonic anhydrase in the ciliary process results in decreased bicarbonate production with a concurrent decrease in sodium and fluid transport. The net effect is substantially decreased aqueous humor production. The limiting factor in the use of oral CAIs has been the numerous systemic adverse effects including paresthesia, a metallic taste, a malaise complex, gastrointestinal tract dysfunction, metabolic acidosis, hypokalemia, dermatitis, blood dyscrasias, and renal calculi.<sup>1</sup> For this reason, topical CAIs, which theoretically carry minimal risk for systemic complications, represent a significant medical advancement.<sup>2</sup> However, there is little information regarding the possible long-term sequelae of these medications and their potential for producing similar systemic adverse effects as their oral counterparts. We describe 3 patients in whom renal stones occurred following the use of dorzolamide. Cessation of the topical CAI resulted in clinical improvement, and there has been no reoccurrence of renal stones since treatment with this medication was terminated.

**Report of Cases.** *Case 1.* A 17-year-old male adolescent with retinitis pigmentosa and a 3-year history of perifoveal edema developed a renal stone while using acetazolamide. After terminating the use of oral acetazolamide, there were no signs or symptoms of nephrolithiasis until the addition of dorzolamide 2 years later. The patient was not using any other medications and there is no family history of nephrolithiasis. Twenty-one days after beginning treatment with dorzolamide, the patient noted

the onset of a sharp, stabbing pain in the hypogastrum, which radiated into the perineum. He was treated at a local emergency department, where a tentative diagnosis of nephrolithiasis was made based on history and physical examination. Urinalysis showed no abnormalities at this time. He was treated with oral pain medications and fluids. His complaints resolved the following day after passing a small stone. No laboratory analysis was performed on the stone. He has been asymptomatic since terminating the use of dorzolamide 18 months ago.

*Case 2.* A 25-year-old woman with congenital glaucoma had used multiple medications to control her intraocular pressure. She tolerated oral methazolamide without notable adverse effects from age 18 to 21 years. No CAIs were used during the 4 years prior to treatment with dorzolamide. After 8 months of treatment with dorzolamide, she noted polyuria and right flank pain, which prompted her to seek evaluation by a local physician. Although urinalysis showed no abnormalities, she was prescribed trimethoprim-sulfamethoxazole for treatment of symptoms; however, her symptoms progressed until she developed severe right flank pain, polyuria, and dysuria and was seen by a urologist. An intravenous pyelonephrogram revealed the presence of a 3 × 5-mm stone in her right distal ureter, which ultimately required surgical removal. The stone was composed of calcium oxalate. Renal stones have not reoccurred in the past 2.5 years since terminating the use of dorzolamide. This patient had no prior history of nephrolithiasis, and her family history is noncontributory.

*Case 3.* A 71-year-old woman with low-tension glaucoma had a trabeculectomy with mitomycin. Ten months postoperatively she developed endophthalmitis, which necessitated vitrectomy with injection of intravitreal antibiotics. Intraocular

pressure was problematic postoperatively, and dorzolamide was added to her medication regimen; no oral CAIs had been used. Four months after the addition of dorzolamide, she noted the onset of severe, progressive flank pain. An abdominal x-ray film was obtained at a local emergency department, which revealed the presence of renal stones. She was treated with oral pain medication and fluid until she passed a small, sand-colored stone. No laboratory analysis was performed on the stone. Following this episode, the use of dorzolamide was terminated. Renal stones have not reoccurred in the past 28 months since terminating the use of dorzolamide. She had no prior history of nephrolithiasis, and her family history was noncontributory.

**Comment.** The CAIs potentiate renal stone formation by producing an alkaline urine that is low in citrate and magnesium. This environment favors calcium oxalate and calcium phosphate stone formation.<sup>1</sup> In 2 of the aforementioned cases the patients had been receiving oral CAIs prior to treatment with dorzolamide; however, each had stopped taking CAIs and had been symptom-free for significant periods prior to the addition of dorzolamide. In case 2, symptoms of nephrolithiasis were present prior to treatment with trimethoprim-sulfamethoxazole. Furthermore, nephrolithiasis is not a commonly reported complication of treatment with this antibiotic, and the composition of the recovered stone is most consistent with a CAI complication. The exclusion of patients with a history of renal impairment from the phase 3 clinical trial of dorzolamide may explain the lack of a significant difference in the rate of nephrolithiasis between patients receiving dorzolamide (approximately 0.14%) and the general population (0.1%-0.2%).<sup>3,4</sup> The cases in this report suggest that there may be an increased risk of nephrolithiasis in patients receiving

topical dorzolamide. Perhaps alternative topical glaucoma medications should be considered in patients with a history of renal calculi.

Jeff Carlsen, BS  
Jane Durcan, MD  
Norm Zabriskie, MD  
Mano Swartz, MD  
Alan Crandall, MD  
Salt Lake City, Utah

This work was supported in part by a grant from Research to Prevent Blindness Inc, New York, NY.

Corresponding author: Jane Durcan, MD, Department of Ophthalmology, John A. Moran Eye Center, 50 N Medical Dr, Salt Lake City, UT 84132.

1. Bartlett JD, Jaanus SD. *Clinical Ocular Pharmacology*. 3rd ed. Newton, Mass: Butterworth-Heinemann; 1995:211-222.
2. Wilkerson M, Cyrilin M, Lipka EA, et al. Four-week safety study and efficacy study of dorzolamide, a novel, active topical carbonic anhydrase inhibitor. *Arch Ophthalmol*. 1993;111:1343-1350.
3. Consensus conference: prevention and treatment of kidney stones. *JAMA*. 1988;260:977-981.
4. Greco MJ. Official release from the Associate Director of Medical Services for the manufacturer of Trusopt, dorzolamide. West Pointe, Pa: Merck & Co Inc; July 18, 1995.

### Incomplete Fibrovascularization of a Hydroxyapatite Orbital Implant 3 Months After Implantation

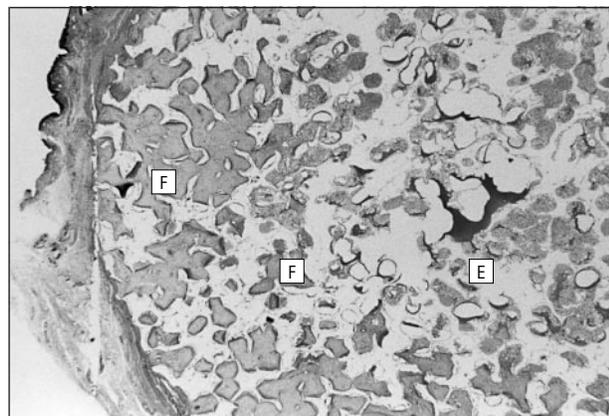
Hydroxyapatite (HA) orbital spheres are the most commonly used implants after primary enucleations.<sup>1</sup>

The wide acceptance of HA implants is due to its high biocompatibility and optimal pore size, which permits host fibrovascular ingrowth. Rapid integration of the implant into the orbital soft tissues offers many potential advantages over nonporous implants, including diminished risk of infection, resistance to implant migration, and enhanced motility with implant peg-prosthesis coupling. We are aware of only 2 histopathologic case reports detailing the degree of host fibrovascularization of a HA sphere (removed because of an orbital malignant neoplasm and not an implant infection) within the first few months after placement of an implant in a human orbit.<sup>2,3</sup> Shields et al<sup>2</sup> reported approximately 3 mm of fibrovascular ingrowth at the sites of precut scleral windows in a 20-mm, scleral-wrapped, HA sphere removed 4 weeks after implantation in a 69-year-old man. Similarly, in a 20-mm, scleral-wrapped, HA implant removed 19 days after implantation in a 9-year-old boy, Rosner et al<sup>3</sup> described a matrix of loose connective tissue extending 6 mm into the sphere in the area of a prefashioned scleral window. Fibrovascularization was most prominent at the surface of the implant. We report herein fibrovascular ingrowth into the paracentral region of a HA implant removed 97 days after implantation.

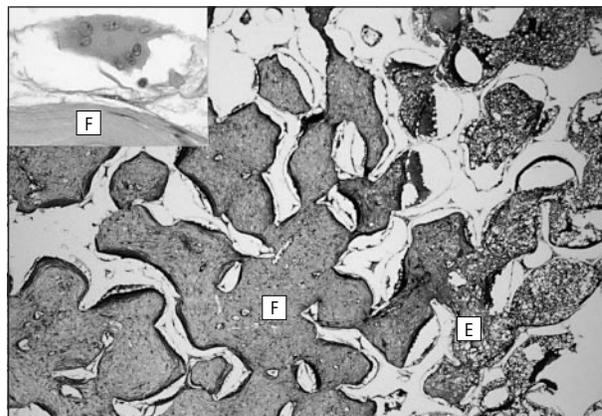
**Report of a Case.** A 55-year-old otherwise healthy man with a blind,

painful right eye due to neovascular glaucoma of unknown cause underwent enucleation with placement of a 20-mm synthetic HA orbital implant (FCI; Issy-Les-Moulineaux, Cedex, France). The sphere was wrapped in polyglactin 910 mesh (Vicryl; Ethicon Inc, Somerville, NJ) and the rectus and inferior oblique muscles were attached as previously described.<sup>4</sup> Histopathologic examination of the enucleated globe revealed an occult ring melanoma of the ciliary body with extensive intraocular invasion and extraocular extension to the episcleral surface with involvement of the perilimbal conjunctiva at the surgical resection margin. Three months postoperatively, a pedunculated conjunctival mass was noted in the patient's anophthalmic socket. The biopsy specimen from the lesion demonstrated recurrence of his ocular melanoma. Orbital exenteration of the right socket was performed 97 days after enucleation.

After decalcification of the exenterated orbital implant, the HA sphere was sectioned anteroposteriorly and examined to determine the degree of host fibrovascular ingrowth. Fibrovascularization, associated with a mild, predominantly chronic, inflammatory cell infiltrate, was evident in the peripheral (outer third) and paracentral (between the outer third and central third) regions of the implant (**Figure 1** and **Figure 2**). The intertrabecular spaces in the central third of the implant were devoid of



**Figure 1.** An anteroposterior section of the implant demonstrates fibrovascularization (F) in the peripheral (outer third) and paracentral (between the outer third and central third) regions of the hydroxyapatite implant. An inflammatory exudate (E) is present more centrally (hematoxylin-eosin, original magnification  $\times 11$ ).



**Figure 2.** The junction between the fibrovascularization (F) and the more central exudate (E) is evident in the paracentral region of the implant (hematoxylin-eosin, original magnification  $\times 30$ ). Inset, Multinucleated foreign body giant cell adjacent to intertrabecular fibrovascular tissue (F) (hematoxylin-eosin, original magnification  $\times 500$ ).

fibrovascular tissue and contained an exudate, with occasional histiocytes, which also was present focally in the paracentral portion of the implant (Figure 1 and Figure 2). The degree of fibrovascular ingrowth occurred approximately equally throughout the circumference of the HA sphere, extending up to 5 mm from the surface toward the center of the implant. Several multinucleated foreign body giant cells were noted adjacent to the trabeculae, mainly toward the periphery of the implant (Figure 2, inset). The external surface of the implant was covered with fibrovascular tissue of variable density and thickness, from which the fibrovascular septa arose, and contained some multinucleated giant cells in which tubular spaces were identified, presumably representing previously digested polyglactin 910 mesh and/or suture material.

**Comment.** Histologic evaluation of the rate of host fibrovascular ingrowth of HA orbital implants has been mainly limited to animal studies, where fibrovascularization has been noted to extend to the center of a 12-mm polyglactin 910-wrapped HA implant by 1 month.<sup>5</sup> Fibrovascular ingrowth in both the coralline HA implant (Bio-eye; Integrated Orbital Implants Inc, San Diego, Calif) and synthetic HA implant (FCI) has been shown in a rabbit model to occur at a similar rate.<sup>6</sup> To our knowledge, our case represents the third report of a HA spherical implant removed from a human orbit due to an orbital malignant neoplasm in the early postoperative period and prior to complete fibrovascularization to the center of the implant. In both of the previously reported cases, the coralline HA implants were wrapped in sclera and removed within the first month after implantation.<sup>2,3</sup> The synthetic HA implant described in our patient was wrapped in polyglactin 910 mesh and not removed until day 97 after implantation, but it demonstrated a similar tissue response as previously noted in the coralline HA implants.<sup>2,3</sup> Prominent fibrovascular ingrowth was evident uniformly to the paracentral zone of the implant. The center of the implant

did not demonstrate fibrovascularization. A better understanding of the rate at which fibrovascular ingrowth occurs in HA orbital implants is important in establishing the appropriate time for implant drilling and motility peg placement. The generally accepted guideline of waiting at least 6 months after implantation to drill HA implants is supported by the absence of central vascularization in our patient 3 months after implantation of a synthetic HA sphere.<sup>7</sup>

Stephen R. Klapper, MD  
David R. Jordan, MD  
Seymour Brownstein, MD  
Karim Punja, MD  
Ottawa, Ontario

Corresponding author: David R. Jordan, MD, 340 McLeod St, Suite 104, Ottawa, Ontario, Canada K2P 1A4.

1. Hornblass A, Biesman BS, Eviatar JA. Current techniques of enucleation: a survey of 5,439 intraorbital implants and a review of the literature. *Ophthalmic Plast Reconstr Surg.* 1995;11:77-88.
2. Shields CL, Shields JA, Eagle Jr RC, De Potter P. Histopathologic evidence of fibrovascular ingrowth four weeks after placement of the hydroxyapatite orbital implant. *Am J Ophthalmol.* 1991;111:363-366.
3. Rosner M, Edward DP, Tso MOM. Foreign-body giant-cell reaction to the hydroxyapatite orbital implant. *Arch Ophthalmol.* 1992;110:173-174.
4. Jordan DR, Allen LH, Ells A, et al. The use of Vicryl mesh (polyglactin 910) for implantation of hydroxyapatite orbital implants. *Ophthalmic Plast Reconstr Surg.* 1995;11:95-99.
5. Jordan DR, Ells A, Brownstein S, et al. The use of Vicryl mesh to implant hydroxyapatite orbital implants: an animal model. *Can J Ophthalmol.* 1995;30:241-246.
6. Jordan DR, Munro SM, Brownstein S, Gilberg SM, Grahovac SZ. The synthetic hydroxyapatite implant: the so-called counterfeit implant. *Ophthalmic Plast Reconstr Surg.* 1998;14:244-249.
7. Jordan DR, Chan S, Mawn L, Gilberg SM, Brownstein S, Hill V. Complications associated with pegging hydroxyapatite implants. *Ophthalmology.* 1999;106:505-512.

### **Intraorbital Needle Fragment: A Rare Complication of Retrobulbar Injection**

A rare case of retained intraorbital needle fragment complicating retrobulbar anesthesia is reported. Prompt combined open exploration, removal of the needle fragment, and subsequent phacoemulsification and intraocular lens

implantation resulted in uneventful recovery with a best-corrected visual acuity of 20/30 OD. Although serious needle-related complications are not common, they could be sight- or even life-threatening. The "needle-free" techniques of administering local anesthesia by topical drops or by sub-Tenon infusion with a plastic cannula may eliminate such complications and are therefore worth considering.

**Report of a Case.** A 71-year-old Chinese woman originally scheduled for cataract surgery on the right eye was referred to us for further management of a retained intraorbital fragment from a broken retrobulbar needle following the retrobulbar injection of the anesthetic solution. The needle was a metallic reusable 25-gauge retrobulbar needle that was 3.8 cm long. The needle had broken at the hub-needle junction with its shaft left intraorbitally. The patient experienced nausea and diminished movements of the right eye, but no impairment of vision.

On ophthalmic examination, visual acuity was 20/400 OD and there was an immature cataract. The pupillary reactions were normal and there was no evidence of globe perforation. The needle entry wound was at the junction of the lateral one third and medial two thirds of the orbital floor. No trace of the needle fragment could be seen or felt. The needle fragment was clearly shown by orbital radiograph (**Figure 1**). An axial orbital computed tomographic scan (**Figure 2**) demonstrated that the needle fragment was situated just beneath the optic nerve. No retrobulbar soft tissue abnormality was evident. Prompt surgical exploration and removal of the needle fragment were followed by phacoemulsification and intraocular lens implantation. No intraoperative or postoperative complications were encountered. Four months postoperatively, the best-corrected visual acuity was 20/30 OD and the patient was doing well.

**Comment.** A retained intraorbital needle fragment complicating retrobulbar anesthesia is rare and, to the best of our knowledge, has not been previously reported in the English-

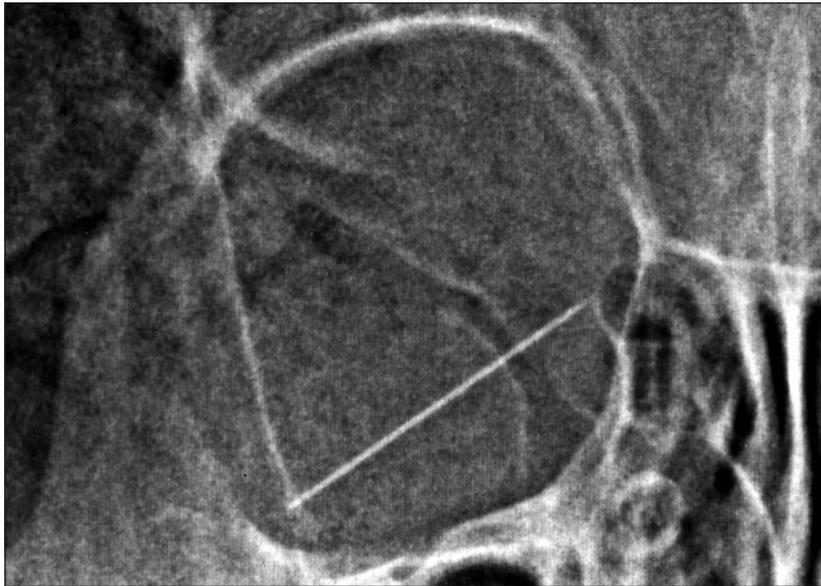


Figure 1. Anteroposterior view of an orbital x-ray film showing the radiopaque needle fragment.

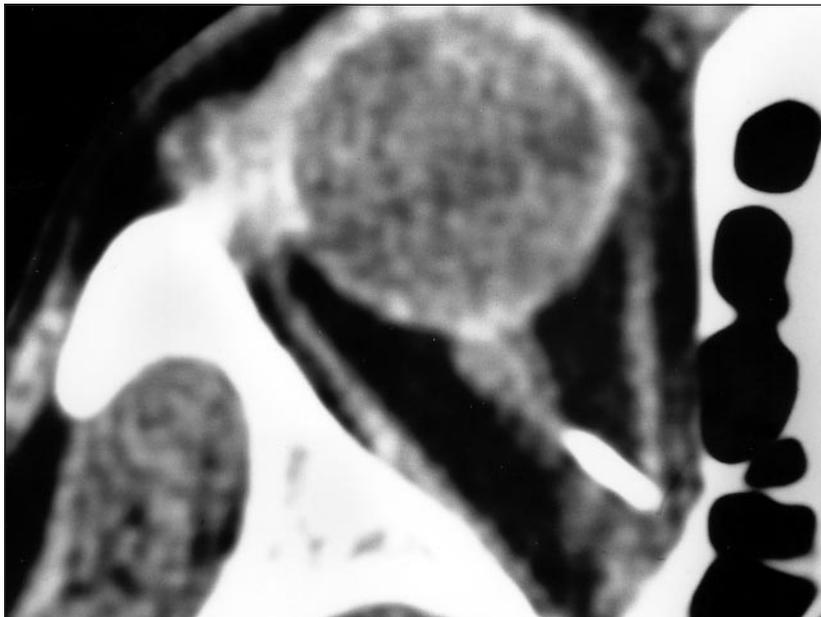


Figure 2. Axial orbital computed tomographic scan showing a portion of the retained needle fragment located intraconally and adjacent to the optic nerve.

language literature. A small inert intraorbital foreign body (FB) that is not causing vision impairment can be left in place.<sup>1</sup> For our patient, however, we considered that prompt removal was needed because it seemed that subsequent damage to the optic nerve or other intraorbital tissue would be likely. Removal of a retained orbital needle is not always easy. Endoscopic removal of a retained orbital FB has been reported to be successful with only minimal additional trauma.<sup>2,3</sup> The instrument is passed along the wound tract until the FB is located

and removed with forceps.<sup>3</sup> However, the needle track created by a 25-gauge needle is so small that introducing an endoscope would be very difficult. Open surgical exploration seems preferable. Subsequent cataract surgery can be performed safely to enable early visual rehabilitation. The keys to success for intraorbital FB removal include accurate preoperative localization, careful exploration with an operating microscope, and gentle instrumentation to avoid pushing the FB further into the orbit. Last but not least, prevention is the best treat-

ment. The use of disposable retrobulbar needles is encouraged to lower the risk of needle breakage from metal fatigue caused by repeated sterilization. "Needle-free" techniques of administering local anesthesia by topical drops or by sub-Tenon infusion with a plastic cannula<sup>4</sup> have the advantage of avoiding needle-related complications.

Dennis S. C. Lam, FRCS,  
 FRCOphth  
 Ricky W. K. Law, FRCS  
 Alfred T. S. Leung, FRCS  
 Wai-Man Chan, FRCS  
 Arthur C. K. Cheng, MBBS  
 Wai-Kiu Shum, FRCS  
 Shatin, Hong Kong

This work was supported in part by the Mrs Annie Wong Eye Foundation, Hong Kong.

Reprints: Dennis S. C. Lam, FRCS, FRCOphth, Department of Ophthalmology & Visual Sciences, Eye Unit, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin NT, Hong Kong (e-mail: dennislam@cuhk.edu.hk).

1. Duke-Elder S, MacFaul PA. Retained foreign bodies. In: Duke-Elder S, ed. *System of Ophthalmology*. London, England: Henry Kimpton; 1972: 655-670.
2. Norris JL, Cleasby GW. An endoscope for ophthalmology. *Am J Ophthalmol*. 1978;85:420-422.
3. Norris JL. Endoscopic orbital surgery: report of a case. *Arch Ophthalmol*. 1981;99:1400-1401.
4. Greenbaum S. Parabolbar anesthesia. *Am J Ophthalmol*. 1992;114:776.

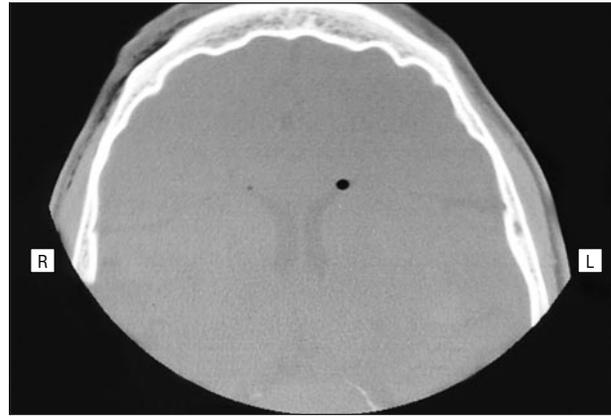
### Intracerebral Air Caused by Conjunctival Laceration With Air Hose

Air compressor injuries have been implicated in numerous reported cases of facial and eye trauma. Severe facial trauma may result in fracture of the orbits or sinuses, leading to the accumulation of air within the orbit or even within the brain.<sup>1</sup> We report a case in which trauma to the conjunctiva (without compromise of the skull, bony orbits, or sinuses) led to accumulation of air within the brain.

**Report of a Case.** A healthy 47-year-old white man was disconnecting an air compressor hose (120 psi) when the free end suddenly popped off and



**Figure 1.** Axial computed tomographic scan showing extensive soft tissue swelling. There is air within the soft tissues and orbit and shrouding the optic nerve. Air is also present within the suprasellar cistern.



**Figure 2.** Axial computed tomographic scan demonstrating air within the frontal horn of the lateral ventricle.

struck him in the right eye. The patient complained of severe pain and experienced swelling of the eyelids and bleeding from the eye socket. He was evaluated in the emergency department.

Uncorrected visual acuity was 20/100 OD and 20/20 OS. External examination revealed extensive edema and echymoses of the right eyelids. The right palpebral fissure opened only 3 mm with voluntary effort. Motility examination was normal. The nasal conjunctiva had a large (10-mm) jagged laceration with intermixed mucoid debris and Tenon fascia. The sclera was completely intact. The cornea was clear with no epithelial defect or laceration. The anterior chamber showed cell (1+) and flare. The lens and vitreous cavity were normal. The optic disc was also normal. The retina showed evidence of peripheral and macular commotio. There were no retinal breaks or detachment noted. The left eye and adnexa were completely normal.

A computed tomographic scan of the head and orbits was obtained (**Figure 1**). There were no bony fractures in the face, orbits, sinuses, or skull. There was extensive soft tissue swelling of the face, particularly in the region of the right orbit. In addition to swelling, there was an accumulation of air within the soft tissues of the eyelid, face, and right orbit. Interestingly, air was also

noted within the optic canal, within the subarachnoid space, and within the third and fourth ventricles of the brain (**Figure 2**). Air was also present near the base of the skull in the region of the circle of Willis.

The patient underwent irrigation and debridement of his conjunctival wound under topical anesthesia. No sutures were placed. The patient was prescribed oral cephalexin as well as a topical combination product of dexamethasone, neomycin sulfate, and polymyxin B sulfate drops and ointment. A tetanus toxoid injection was also given. During the next several weeks, the patient's eyelid and soft tissue swelling resolved, as did his mild iritis and commotio retinae. Visual acuity returned to an uncorrected 20/25 OD. The conjunctival wound has healed with minimal visible scarring.

**Comment.** Air within the cranial cavity (pneumocephalus) has been described in several clinical situations including facial trauma.<sup>2,3</sup> Given the lack of bony fractures in this patient, it is presumed that the air within the brain arrived there by an unusual route; dissection beneath the Tenon fascia, around the optic nerve, and through the optic canal into the subarachnoid space and ventricles. This pathway is possible because the cerebrospinal fluid surrounding the optic nerve is in

continuity with the intracranial subarachnoid space. Intracerebral air is generally well tolerated, although its presence in the setting of bony fracture can signify increased risk of intracranial pressure or meningitis.<sup>4</sup> A similar case was reported in 1977, in which a 12-year-old boy had air demonstrated on x-ray films in the region of the sella turcica after lacerating his conjunctiva with an air-compressor tip.<sup>5</sup> To our knowledge, our case is the first to confirm this unusual mechanism of traumatic pneumocephalus using the more sophisticated technique of computed tomographic imaging.

T. Reginald Williams, MD  
Nicholas Frankel, MD  
Hickory, NC

Reprints: T. Reginald Williams, MD, Graystone Ophthalmology Associates, PO Box 2588, Hickory, NC 28603 (e-mail: retina@twave.net).

1. Waring GO, Flanagan JC. Pneumocephalus: a sign of intracranial involvement in orbital fracture. *Arch Ophthalmol.* 1975;93:847-850.
2. Orebaugh SL, Margolis JH. Post-traumatic intracerebral pneumatocele: case report. *J Trauma.* 1990;30:1577-1580.
3. Dandy WE. Pneumocephalus (intracranial pneumatocele or arocele). *Arch Surg.* 1926;12:949-982.
4. Keskil S, Baykaner K, Ceviker N, et al. Clinical significance of acute traumatic intracranial pneumocephalus. *Neurosurg Rev.* 1998;21:10-13.
5. Koenig RP. Traumatic eye and intracranial air-movement from a subconjunctival to an intracranial position. *Am J Ophthalmol.* 1977;83:915-917.