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Grand Rounds

A 48-year-old woman with redness, photophobia, and eye discomfort

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History

A 48-year-old white woman presented to the Bascom Palmer emergency department with redness, photophobia, and discomfort in the left eye of 10 days' duration. Two months previously, she had undergone pars plana vitrectomy with scleral buckle and C3F8 gas at an outside practice to repair a rhegmatogenous detachment. The patient reported, based on conversations with her retinal surgeon, that a dense cataract had begun to develop "almost immediately" after surgery, explaining why her visual acuity did not significantly improve after the gas bubble reabsorbed. Past ocular history was otherwise unremarkable. She had no known chronic medical conditions, and her surgical history included two cesarean sections, functional bladder surgery, and a tonsillectomy. She did not use scheduled medications and had no known allergies. Her family history was notable only for hypertension. She worked as a registered nurse and did not smoke, drink, or use intravenous drugs. Review of systems was negative for arthralgias as well as for gastrointestinal, dermatologic, respiratory, or genitourinary symptoms.

Examination

On initial examination, the patient's uncorrected visual acuity was 20/20 in the right eye and counting fingers in the left eye. Her pupils were 3 mm and reactive with no afferent pupillary defect. Intraocular pressure (IOP) by Goldmann tonometry was 16 mm Hg in the right eye and 31 mm Hg in the left eye. Ocular motility was full in both eyes. The confrontational visual fields were full in the right eye to counting fingers and she was able to detect hand motions in all four quadrants of the left visual field.

Slit-lamp examination of the left eye was notable for 2+ ciliary injection and for 2+ anterior chamber cell and flare accompanied by scattered mutton fat and stellate keratic precipitates in Arlt's triangle. No hypopyon was observed. She was noted to have an intumescent cataract with a prominent vertical cleft (Figure 1). There was no anterior bowing of the iris, and the angle was open to the scleral spur without synechiae on gonioscopy.

The anterior segment examination of her right eye was unremarkable. Dilated fundus examination revealed a sharp, pink disc with a 0.4 cup-to-disc ratio and a healthy fundus. There was no posterior view in the left eye due to the density of her cataract.

Ancillary Testing

A B-scan ultrasound of the right eye revealed small, scattered vitreous opacities without cyclitic membranes or vitreoretinal adhesion, consistent with mild-to-moderate inflammation. There was no evidence of large lens fragments, recurrent retinal detachment, or choroidal thickening.

Treatment

A laboratory workup for anterior uveitis was deferred given the patient's recent surgery and the fact that this was her sentinel inflammatory episode. Based on her ultrasound findings and the lack of profound pain or hypopyon, it was not thought necessary to perform immediate vitreous and/or aqueous tap for gram stain and culture. The patient was initially placed on prednisolone 1% eyedrops every hour, along with brimonidine, dorzolamide, timolol, and cyclopentolate drops. After one week of treatment, the patient's IOP dropped to within normal range and her eye appeared less injected. Subjectively, she was more comfortable but had persistent 1+ to 2+ cell on her anterior segment examination.

Differential Diagnosis

The differential diagnosis for our patient included inflammatory causes such as granulomatous anterior

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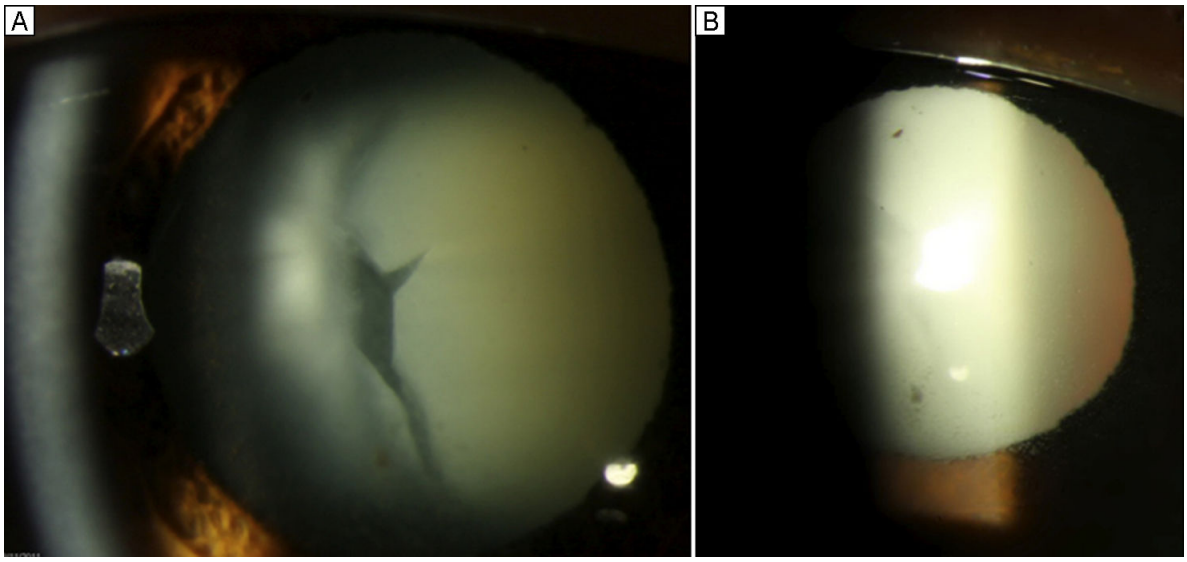

Figure 1. A, Intumescent cataract with prominent vertical cleft. B, Retro-illumination of cornea demonstrating stellate and mutton fat keratic precipitates.

uveitis (either exacerbated by surgical intervention or coincidental to it), anterior segment ischemia from a tight scleral buckle, or protracted postoperative inflammation. The last two conditions, however, would not be expected to produce typical mutton fat keratic precipitates. As a health care worker, she had PPDs placed annually and had always been nonreactive. Based on her ethnicity, the patient was at low risk for sarcoid. Lyme disease is rare in Miami, and she did not have a history of recent travel to endemic areas. She did not practice high-risk sexual behavior or report any stigmata of syphilis. Likewise, she did not have any respiratory or genitourinary symptoms consistent with Wegener's granulomatosis. Toxoplasmosis was also considered unlikely because her B-scan ultrasound did not reveal evidence of significant posterior uveitis.

Consideration of infectious endophthalmitis from an indolent organism such as *Propionibacterium acnes*, *Staphylococcus epidermidis*, or *Candida parapsilosis* was also warranted because, while such infections do not usually produce granulomatous inflammation, the consequences of missing the diagnosis can be severe. Such infections can initially appear to respond to steroids, so the patient's clinical improvement did not entirely rule them out. Again, however, the patient's clinical presentation and B-scan findings were not typical, and the rates of endophthalmitis after pars plana vitrectomy are quite low with an incidence of approximately 0.02% in a retrospective study by the Pan American Collaborative Retina Study Group.[1]

Given the presence of an intumescent cataract, lens-related etiologies were also carefully considered. Phacomorphic glaucoma was ruled out by confirming that the anterior chamber angle was open on gonioscopy. Phacolytic glaucoma, which involves the leakage of soluble lens proteins through an intact capsular bag in the setting of a mature cataract and usually results in nongranulomatous anterior segment inflammation, was thought less likely than phacoantigenic endophthalmitis, a classically granulomatous autoimmune response to lens proteins. The rapid postoperative development of cataract in our patient might have been due to occult lens capsule trauma during the pars plana vitrectomy.

Diagnosis and Discussion

Once the inflammation quieted further, phacoemulsification with posterior chamber intraocular lens placement was performed. After cortical cleanup, an oval-shaped hole was observed in the posterior lens capsule, corresponding with unrecognized trauma sustained during vitrectomy (Figure 2). This finding supported the presumed clinical diagnosis of phacoantigenic endophthalmitis. The patient's inflammation subsided and her IOP normalized without the need for additional glaucoma drops or for steroids beyond the typical post-cataract extraction course. Unfortunately, the patient developed an occult macular hole, and this limited her final central visual acuity. She pursued further evaluation with the retina service, but has not undergone further surgical intervention to date.

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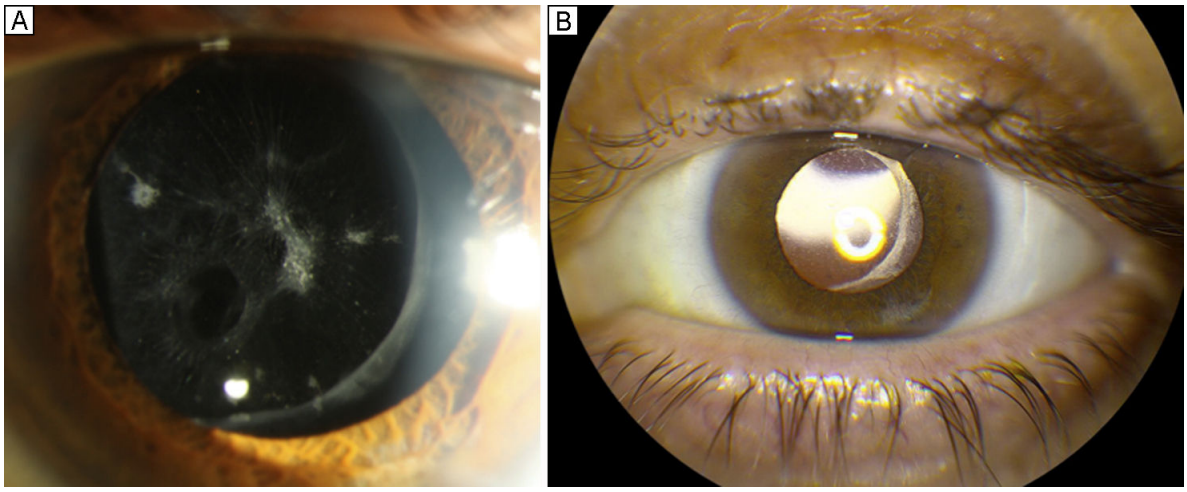

Figure 2. A, Oval hole in the inferonasal posterior capsule from unrecognized intraoperative vitrector trauma. B, Result after placement of posterior chamber intraocular lens.

Phacoantigenic endophthalmitis is a rare granulomatous uveitis caused by altered immune tolerance to lens proteins following capsular disruption. The traditional term, "phacoanaphylactic endophthalmitis," is misleading because inflammation results from immune complex formation rather than IgE crosslinking and histamine release. When first described by Straub in 1919, basic immunologic mechanisms were not yet understood, and "anaphylaxis" was used to describe all sudden-onset inflammation.[2,3]

Until the 1980s, it was erroneously believed that the immune system attacked antigens previously sequestered by the lens capsule. Lens-related antigens have since been identified in organs throughout the body and lens proteins are known to be present in low concentrations in the aqueous of normal individuals.[4] There are many cases in which the lens capsule is disrupted without inciting inflammation. Disruption is therefore necessary but not alone sufficient to cause an immunologic response. The exact stimulus for alloimmunization remains unclear, but the process of immune complex formation and inflammatory cell recruitment has been well elucidated.[5]

Ultrasound findings consistent with a fulminant infectious endophthalmitis include abundant vitreous debris, often in loculated pockets, inflammatory membranes, and occasionally retinal or choroidal detachment. While B-scans in early endophthalmitis may not demonstrate classical findings, this paucity would be unusual in a patient presenting within 10 days of symptoms.

Phacoantigenic endophthalmitis most often follows surgical or traumatic penetration of the lens capsule but also has been described after spontaneous capsular rupture resulting from advanced, swollen cataracts. Inflammation often develops within days to weeks of the inciting event, but latency periods of up to 59 years have been reported.[4] Peak incidence is in the fifth to seventh decades despite higher rates of ocular trauma in younger individuals.[2,4]

Though rare, phacoantigenic endophthalmitis seems to be an under-recognized condition. In a series of 144 cases of histopathologically confirmed phacoantigenic endophthalmitis, Thatch et al[2] found that the pre-enucleation diagnosis was correct in only 5% of cases. Clinically, phacoantigenic endophthalmitis can be difficult to distinguish from other forms of postoperative uveitis. Patients often present with photophobia and ciliary reaction. Findings can range from mild anterior uveitis to fulminant endophthalmitis with hypopyon. Mutton fat keratic precipitates and peripheral anterior synechiae are characteristic but not universal. Most manifestations of phacoantigenic endophthalmitis are anterior, but late sequellae may include mononuclear choroiditis, optic atrophy, retinal perivasculitis, or retinal detachment.[4]

If clinical suspicion is high, early evaluation and treatment for infectious endophthalmitis is critical. Several recent studies report the utility of anterior chamber paracentesis for cytologic evaluation and/or western blot quantification of lens protein concentration, but these procedures are not standard clinical practice.[6,7] Histopathology is not practical or necessary in many cases, but when performed, it typically reveals a zonal granulomatous pattern with concentric rings of polymorphonuclear

leukocytes, epithelioid and giant cells, and mononuclear cells.

In cases of granulomatous anterior uveitis associated with lens capsule disruption, patients are initially treated with steroids. When only small lens fragments are retained, as after phacoemulsification, inflammation may subside with medical management alone. When phacoantigenic endophthalmitis follows lens trauma, as with our patient, surgery is required for definitive treatment.

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