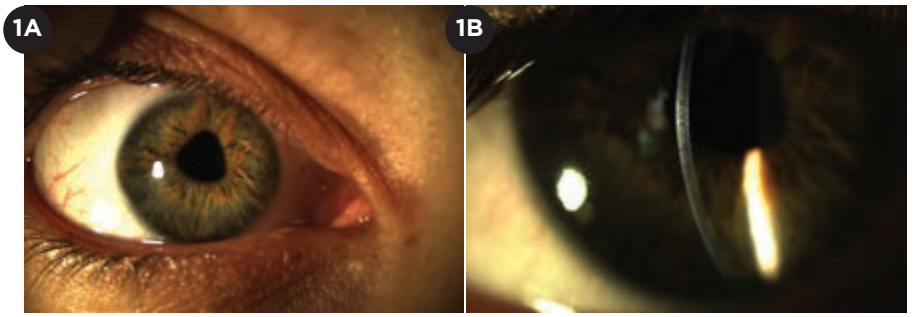
The Strange Case of a Triangular Pupil

On April 1, 2015, Theresa Tippet* was vacationing in Florida with her husband. While relaxing on the beach, the 24-year-old accidentally rubbed sand into her eye. Initially, she did not think much of it. However, at a family gathering 1 week later, her husband noticed that her pupil was now shaped like a teardrop, and they couldn't help but fear that something insidious was occurring.



AT THE SLIT LAMP. *(1A) Right pupil appears triangular in light. Left pupil was normal. There is no heterochromia. (1B) Posterior cornea has a "beaten bronze" appearance.*

The Presentation

When Ms. Tippet presented to our neuro-ophthalmology clinic, she had no relevant medical history. She and her husband were concerned that her misshapen pupil might be the result of a brain tumor. An outside ophthalmologist thought that her pupil might be related to migraines, though she had no complaints of visual changes or headache. She also denied any history of red eye, eye infection, eye surgery, and eye trauma, other than the aforementioned incident at the beach. Of note, her eye required irrigation to remove the sand, but she denied having pain following the event. She also denied photophobia, but stated that "she felt a slight twinge of pain" when moving from darkness to light. Her husband was certain that her pupil had been normal prior to April.

Based on history alone, we initially suspected Adie's tonic pupil, but we were also considering iridocyclitis and trauma in our differential diagnosis.

The Exam

On initial exam, we could appreciate the irregularity of her right pupil in light, but her pupillary constriction was brisk with minimal anisocoria. In darkness, her right pupil was 7.5 mm and her left pupil was 7.0, and constriction to light and convergence were brisk in both eyes. Her intraocular pressure (IOP) was 15 mm Hg in both eyes.

Slit-lamp biomicroscopy showed high peripheral anterior synechiae (PAS) with iris tenting at 1, 5, and 9 o'clock. This unique distribution pulled her pupil into a triangular shape with constriction (Fig. 1A). She also had a "beaten bronze" appearance of her posterior cornea (Fig. 1B). We did not find any stretch holes, iris transillumination defects, cell and flare, or corneal edema.

Gonioscopy confirmed our findings. Her posterior exam was unremarkable.

Following the exam, the diagnosis of Adie's tonic pupil was ruled out. Uveitis and trauma were still possible, but—given her history—seemed unlikely.

Tests and Final Diagnosis

OCT anterior segment imaging was performed to document her anterior synechiae (Fig. 2A). The image also showed formation of a distinct membrane over the iris stroma. On confocal microscopy, Ms. Tippet had swollen-appearing endothelial cells with irregular borders, as well as a moderately decreased cell count in comparison to her left eye. Her endothelial cells had prominent nuclei (Fig. 2B). These findings were typical of, and helped to confirm a diagnosis of, iridocorneal endothelial (ICE) syndrome.

Pathogenesis

ICE syndrome is a sporadic disease characterized by inappropriate proliferation of the corneal endothelium. Though the exact mechanism is not well understood, it is thought that the endothelial cells, which are normally

BY MATTHEW SNIDER AND SANGEETA KHANNA, MD. EDITED BY STEVEN J. GEDDE, MD.

FURTHER CLUES. *(2A) On anterior OCT, we noted high PAS with membrane pulling on iris and abnormal endothelial cell layer on iris. (2B) On confocal microscopy, we observed endothelial cells with irregular borders and prominent nuclei in the right eye and (2C) normal endothelial cell appearance in the left.*

locked in the G1 phase of the cell cycle, are able to proliferate and grow onto the iris. This causes diffuse PAS, as well as damage to the iris. The cells are said to behave and appear more like epithelial cells. There is some evidence to suggest that the disease may be related to herpes simplex virus (HSV) infection, though the association is not certain.[1,2] It is possible that inflammation from a virus may promote abnormal epithelial-like behavior of the endothelial cells, causing migration onto the trabecular meshwork and the iris. There is no current research on whether treatment for HSV might help the long-term prognosis of ICE.

Typical Presentations

This rare disease typically presents unilaterally, though occasionally bilaterally, in women in their 20s to 40s.

There are 3 variants described in the literature, and though there is considerable overlap between them, each has a hallmark trait that predominates:

- Chandler syndrome is the most common variant, and its hallmark is corneal edema.
- Essential iris atrophy's hallmark is large stretch holes and irregularities of the iris.
- Cogan-Reese syndrome's hallmark is pigmented, pedunculated iris masses; Cogan-Reese is the least common of the variants.

Other characteristics that may occur in any of the variants include increased IOP, "beaten bronze" appearance of endothelium, and diffuse PAS.

Confocal or specular microscopy is particularly useful in diagnosis. On confocal microscopy, look for light to dark inversion, prominent endothelial nuclei, decreased endothelial cell count, and irregular endothelial borders.

Differential Diagnosis

Diagnosis can be challenging and will vary based on the presentation. This disease is most often confused with posterior polymorphous dystrophy, which is more often bilateral and familial. For this reason, lack of family history can be a useful clue when differentiating between these 2 diseases.

Another common misdiagnosis occurs when ICE is confused with unilateral primary open-angle glaucoma. This misdiagnosis could be particularly easy to make in a case like ours, which has a paucity of symptoms. Of course, our case lacked elevated IOP.

The differential diagnosis is highly dependent on the variant and exam findings. For example, in a case with the predominant feature of pedunculated iris nodules, neurofibromatosis would be high on the differential; however, in a patient presenting primarily with corneal edema, Fuchs endothelial dystrophy would be placed higher on the differential. Because of the broad differential, confocal microscopy is a useful tool to help differentiate between other etiologies on the basis of the features described above.

Complications and Management

Unfortunately, there is no cure for ICE syndrome. The most serious complications of ICE are glaucoma and corneal edema. For this reason, these patients must have lifelong, regular visits to an ophthalmologist for monitoring of disease progression.

In these patients, glaucoma can be particularly difficult to manage and often requires surgical treatment. While medical management with aqueous production suppressants is a reasonable choice to decrease IOP as well as corneal edema, these patients will often require a shunting procedure or trabeculectomy to help control IOP. Because the endothelial cells will continue to grow abnormally, failure rate for surgery is high, and the need for further procedures should be anticipated.

Similarly, many patients with corneal edema will ultimately require corneal transplantation. Penetrating keratoplasty and endothelial keratoplasty are the 2 most common procedures on these patients.

Finally, it is important to stress that prognosis is highly variable and case dependent.

Our Patient

Ms. Tipper was advised to follow up with her primary ophthalmologist every 6 months to monitor IOP. We also discussed the questionable role of antivirals in this disease and she chose observation at this time.

* Patient name is fictitious.

1 Alvarado JA et al. *Arch Ophthalmol.* 1994; 112(12):1601-1609.
2 Sacchetti M et al. *Biomed Res Int.* 2015;2005: 763093. doi:10.1155/2015/763093.

Dr. Khanna is an assistant professor of ophthalmology and **Matthew Snider** is a fourth-year medical student; both are at the Saint Louis University School of Medicine, St. Louis, Mo.
They report no financial disclosures.