

Iridocorneal Endothelial Syndrome: Keys to Diagnosis and Management

A common pathological mechanism explains the corneal, iris, and angle abnormalities that result in a rare but important type of secondary angle-closure glaucoma.

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Iridocorneal endothelial (ICE) syndrome is a disorder with a broad spectrum of clinical manifestations. These are characterized by an abnormal, “beaten metal” appearance of the corneal endothelium, with or without corneal edema, and iris abnormalities of varying degrees of severity ranging from mild stromal atrophy to severe distortion, stretching, and polycoria. The entire spectrum of anterior segment structural abnormalities observed in this syndrome is the result of a transformation of corneal endothelial cells leading to characteristic changes in their morphology and biological behavior. These ICE cells have properties characteristic of transformed epithelial cells, including the ability to proliferate and a failure to respect their normal boundaries. As a result, they cross Schwalbe line and extend over the trabecular meshwork and onto the surface of the iris. As these transformed cells form membranes that contract, variable degrees of distortion of the iris’ architecture occur, and the formation of peripheral anterior synechiae (PAS) often results in the development of secondary angle-closure glaucoma.

CLINICAL PRESENTATION

The clinical findings in ICE syndrome vary greatly from patient to patient. Now thought of as a syndrome with a common fundamental pathophysiological basis but a spectrum of clinical manifestations, it is historically subdivided into essential (progressive) iris atrophy, Chandler syndrome, and Cogan-Reese (iris-nevus) syndrome.¹⁻⁴ Essential iris atrophy (Figure 1) is characterized by severe thinning of the iris with pupillary stretching and the development of multiple holes in the iris. Chandler syndrome is characterized by mild iris abnormalities such as



(All figures courtesy of Robert Rich, MD.)

Figure 1. Essential (progressive) iris atrophy variant of ICE syndrome with severe thinning of the iris, pupillary stretching, and the development of multiple holes in the iris.

stromal atrophy and corectopia as well as more severe corneal edema. Cogan-Reese syndrome (Figure 2) is characterized by the presence of pigmented nodules on the iris’ surface that represent islands of iris tissue pinched off by the contracting ICE membrane. The fine, beaten metal appearance of the cornea and PAS (Figure 3) occur in all three variants of ICE syndrome.

Patients typically present initially with moderately decreased visual acuity and a change in the size and shape of the pupil. Patients with more advanced disease present with symptoms of corneal edema, acutely elevated IOP, or advanced glaucomatous optic neuropathy such as halos around lights, pain, tearing, or decreased peripheral vision.

ICE syndrome occurs more commonly in women than men and is usually diagnosed in the third through fifth

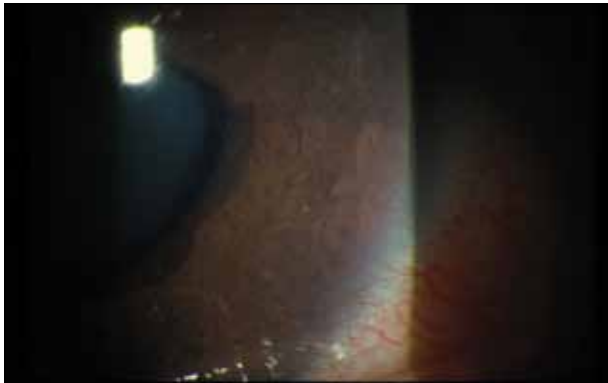


Figure 2. Cogan-Reese (iris-nevus) syndrome with pigmented nodules on the iris' surface that represent islands of iris tissue pinched off by the contracting ICE membrane.

decades of life. Typically, only one eye is clinically affected, but there are several case reports of bilateral involvement, including sequential involvement of the fellow eye years after initial diagnosis.

Glaucoma has been reported to occur in 50% to 80% of patients. The risk of developing glaucoma is higher in eyes with Chandler syndrome and progressive iris atrophy variants. A stronger predictor of the development of glaucoma is the specular or confocal microscopy finding of disseminated or total involvement of the corneal endothelium with ICE cells, which have an irregular size and shape and are readily distinguished from the normal, repeating hexagonal pattern of endothelial cells.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of ICE syndrome includes Axenfeld-Rieger syndrome (a congenital disorder), posterior polymorphous dystrophy, Fuchs endothelial dystrophy (excluded based on the presence of a normal iris, bilaterality, and a hereditary pattern), and iridoschisis (excluded based on older age at onset; the presence of a round, reactive pupil without iris holes; bilaterality; and a normal cornea). If uncertain about the diagnosis of ICE syndrome, one can obtain corneal specular or confocal microscopy. The presence of ICE cells, as described earlier, is pathognomonic.

TREATMENT

Medical Therapy

It is widely held that ICE syndrome has a viral etiology. Based on evidence from polymerase chain reaction of herpes simplex virus DNA in the aqueous humor of affected eyes, that agent is the leading suspect.⁵ Antiviral therapy, however, has not convincingly been shown to be effective in altering the course of the disease.

Medical therapy with aqueous suppressants may be

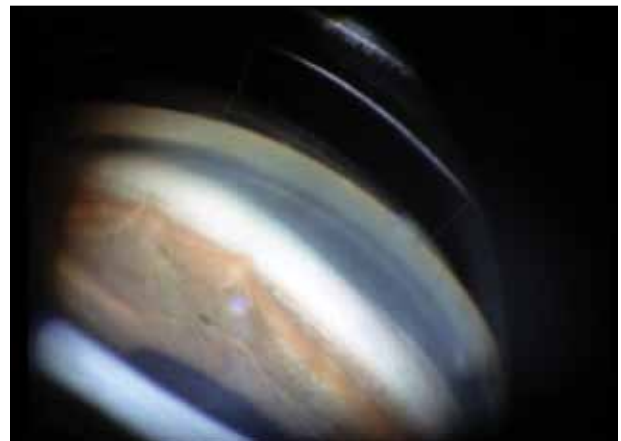


Figure 3. Characteristically broad PAS of ICE syndrome.

of initial benefit. Given the suspected underlying viral etiology of ICE syndrome, it is unclear whether the use of a prostaglandin analogue is safe, because there are case reports of reactivation of herpetic epithelial keratitis with their use. As progressive angle closure occurs due to the development of broad PAS, medical therapy is generally insufficient to control the IOP.

Surgery

Laser trabeculoplasty is ineffective in the setting of ICE syndrome. Trabeculectomy with antifibrotic agents has strong initial success rates. Unfortunately, failure occurs more rapidly than with most other types of glaucoma for a variety of reasons, including the fact that many of these patients are young and have a robust subconjunctival fibrotic response. Some researchers have postulated that patients with ICE syndrome have an intense fibrotic response uniquely attributable to the disease process itself, perhaps due to the presence of proinflammatory mediators in the aqueous humor.⁶ Obstruction of the surgical fistula by PAS or the proliferating membrane itself may also result in trabeculectomy failure. If such a membrane is identified gonioscopically or presumed to be occluding the ostium, Nd:YAG laser treatment may be effective, but recurrent obstruction of the surgical ostium is likely.

Reported success rates for trabeculectomy with antifibrotic agents (most reported cases use 5-fluorouracil) range from 60% to 73% at 1 year and 21% to 29% at 5 years.^{6,7} The intermediate and long-term success rates with the adjunctive use of mitomycin C may be higher, but no evidence supports that concept at this time.

Aqueous shunt surgery is a common first-line surgical approach for glaucoma associated with ICE syndrome. Common complications in this setting include (1) proliferation of the ICE membrane onto the tube

with occlusion of the lumen tip and (2) the formation of iridocorneal adhesions in the area of the tube with forward migration of the tube and obstruction of the lumen tip. Treatment with an Nd:YAG laser may be effective in restoring patency of the tube lumen obstructed by iris tissue or the ICE membrane. The tube frequently must be repositioned.

When initially placing the tube, the surgeon can fashion a long path between the plate and the implantation site to facilitate future repositioning. Positioning the tube in the anterior chamber can be difficult due to the presence of broad, high PAS. Initial placement of the tube into the ciliary sulcus or through the pars plana may be appropriate for pseudophakic eyes. For a pars plana insertion, a thorough pars plana vitrectomy and removal of the vitreous skirt are required. Success rates with drainage device surgery have been reported to be about 70% at 1 year and 53% at 5 years.⁸

Cyclophotocoagulation should be reserved for eyes in which other surgical approaches have failed or eyes with poor visual potential.

PROGNOSIS

IOP control is challenging and may require multiple operations and revisions. Excellent short-term outcomes have been reported in eyes that underwent endothelial keratoplasty for corneal edema. The long-term prognosis is guarded, however, in light of the high risk of failure with glaucoma surgery and corneal grafts.

SUMMARY

ICE syndrome is an acquired disorder of the anterior segment in which corneal endothelial cells take on the characteristics of epithelial cells, fail to respect their

normal boundaries, and proliferate beyond Schwalbe line onto the trabecular meshwork and iris. Sheets of transformed endothelial cells migrate across the anterior chamber angle and onto the iris. When these cellular membranes contract, PAS develop, and characteristic abnormalities of the iris occur.

As a result of the underlying pathology, corneal edema and secondary angle-closure glaucoma may occur. The current treatment of patients with of recalcitrant corneal edema in this disorder is endothelial keratoplasty. Although trabeculectomy has a high initial success rate, a large proportion of these operations fail. The authors' current first-line glaucoma operation for ICE syndrome is aqueous drainage device surgery. This is a challenging disease process to manage and requires close collaboration between the glaucoma and cornea specialists.

As physicians' understanding of the underlying cellular and molecular mechanisms of this disease spectrum improves, new therapies may become available that inhibit further proliferation of the transformed endothelial cell population. Such advances may improve the outcome of the incisional surgical treatment of the associated glaucoma and extend the survival of corneal transplants. ■

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Weigh in on this topic now!



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1. Have you had success treating ICE syndrome with trabeculectomy using adjunctive mitomycin C?

- ☐ Yes
☐ No

2. If yes, have you found this approach to be more successful than trabeculectomy with 5-fluorouracil?

- ☐ Yes
☐ No
☐ The same

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