THE OPTOMETRIST'S GUIDE TO FUCHS ENDOTHELIAL CORNEAL DYSTROPHY

Know what to look for, how to look for it, and how to treat it.

BY ALYSSA CALTA, OD, AND SARAH L. BELL, OD

Although corneal dystrophies are considered rare, Fuchs endothelial corneal dystrophy (FECD) is the most common corneal dystrophy affecting the corneal endothelium.[1,2] FECD is a genetic condition inherited in an autosomal dominant fashion with incomplete penetrance.[1,3] Multiple genetic mutations play a role in the development of FECD. However, research suggests environmental factors may increase mutagenesis, as many patients affected by FECD do not report a family history.[1] As is common with most corneal dystrophies, FECD tends to be central, slowly progressive, and bilateral (though it may be asymmetric in some cases).[1] Early-onset FECD can be present at birth, depending on which gene is affected, but it most commonly develops in the sixth decade of life, with a female predilection of nearly 3:1.[1]

PATHOPHYSIOLOGY

Corneal endothelial cells are responsible for maintaining a clear and compact cornea by using active Na+/K+-ATPase and carbonic anhydrase pumps to force water out of the stroma and into the aqueous.[4] These cells are also responsible for maintaining a passive barrier that osmotically draws water out of the stroma and into the aqueous.[4] Although the exact molecular cause of the endothelial cell loss in FECD is unknown, most theories propose it is caused by apoptosis of endothelial cells due to mutated proteins, oxidative stress, or dysfunctional mitochondria.

The hallmark finding of FECD is central corneal guttae, which are small excrescences of Descemet membrane secondary to endothelial cell death.[4] At first, the remaining endothelial cells may expand in size to compensate for the loss of neighboring cells. Over time, the size and number of guttae increase,

leading to disease progression. With fewer endothelial cells, the remaining healthy cells are unable to meet the energy demand needed to maintain corneal deturgescence, allowing aqueous to enter the cornea and causing stromal thickening and edema.[4]

End-stage FECD results in painful bullae that may become infected or scarred, resulting in significant loss of vision or blindness (Figure 1).[4]

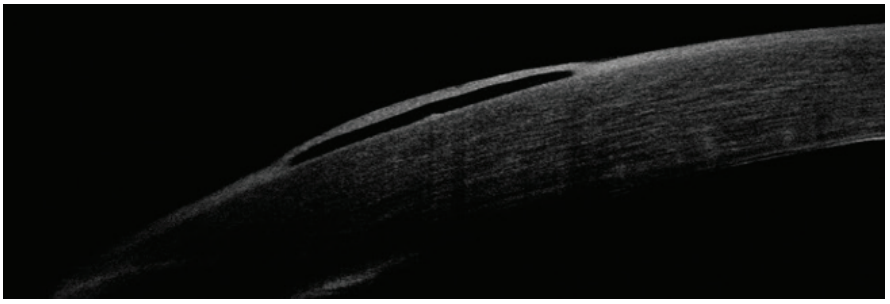

Figure 1. Corneal bullae visualized using anterior segment OCT.

DIAGNOSIS AND CLINICAL SIGNS

Patients with early FECD may be completely asymptomatic. As the disease progresses, symptoms may include glare, halos, and blurry or foggy vision that is worse upon awakening.

Central bilateral cornea guttae are pathognomonic for FECD. These can be visualized with the slit-lamp technique of specular reflection.[5] By separating the light source and oculars by a 60° angle and using high magnification, the corneal endothelium can be visualized, and guttae can be detected (Figure 2). The distribution of guttae can be seen using retroillumination, best visualized when a patient's pupil is dilated.

Specular microscopy can also help detect FECD by imaging the endothelial cells.[5] Not only will a specular analysis give the average endothelial cell density, but it will also show guttae and endothelial cell polymegathism and pleomorphism. Guttae appear as round areas of darkness in a sea of corneal endothelial cells (Figure 3).

Serial pachymetry is also helpful in monitoring FECD progression into the later stages of the disease.[5] As the cornea struggles to maintain deturgescence, more fluid accumulates, causing edema and higher pachymetry readings. Corneal thickness can be measured with several optical instruments: an ultrasound pachymeter, anterior segment OCT, tomographer, and specular microscope.[6]

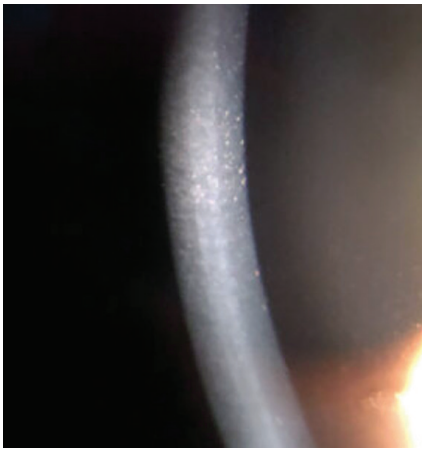

Figure 2. Guttae in early FECD are evident on slit-lamp examination using specular reflection.

MANAGEMENT AND TREATMENT

Medical

In the early stages of FECD, medical intervention may not be needed. Still, document and discuss your findings, especially the genetic component. As the disease progresses, patients may become more symptomatic for fluctuations in vision throughout the day, with hazy vision being worse in the morning. Sodium chloride 5% ointment each night or sodium chloride 5% or 2% ophthalmic drops up to four times daily may be beneficial at this stage. Sodium chloride solution will draw fluid out of the cornea through the epithelium to temporarily stabilize vision by reducing corneal thickness.

More recently, studies suggest the topical use of ripasudil (Glanatec, Kowa Pharmaceuticals), a rho kinase inhibitor, minimizes corneal edema and endothelial cell loss.[7-9] Consideration should be given to starting this drop four times daily in patients with FECD. If OTC options fail to control symptoms, steroid drops dosed four times daily for a month may improve corneal edema due to endothelial decompensation. In vitro improvement of Na+/K+-ATPase

AT A GLANCE

- Fuchs endothelial corneal dystrophy (FECD) is a genetic condition that most commonly affects women and typically develops in the sixth decade of life.
- The hallmark finding of FECD is central corneal guttae, which are small excrescences of Descemet membrane secondary to endothelial cell death that can be seen on imaging.
- If medical intervention fails, surgery may be indicated; recommended treatment is a Descemet stripping endothelial keratoplasty or a Descemet membrane endothelial keratoplasty,

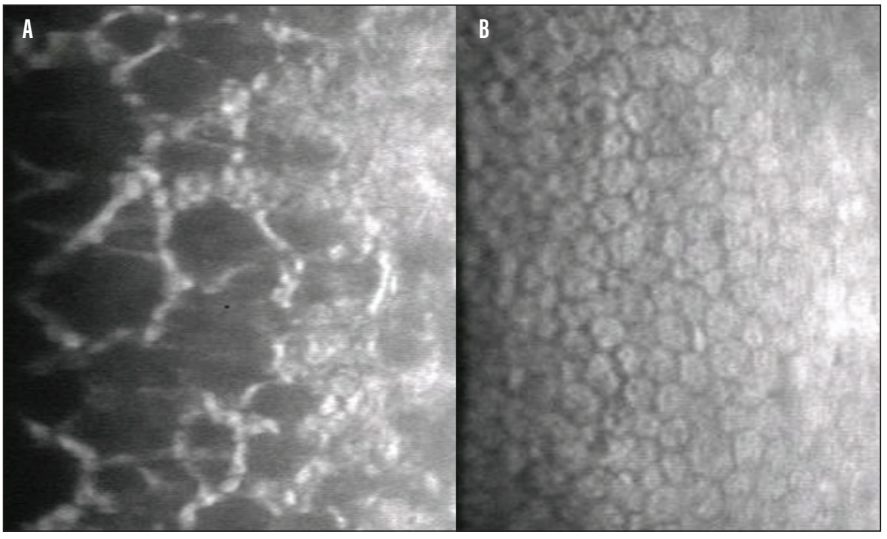

Figure 3. Specular microscopy imaging shows guttae (A) and healthy (B) endothelial cells.

endothelial pump activity with dexamethasone was reported in 2009, but published clinical evidence of improvement using topical steroids is lacking.[10]

Surgical

If medical treatment is insufficient, a referral for an endothelial keratoplasty may be indicated. Surgical intervention should be considered in cases of poor vision affecting daily activities or eye pain due to microcystic edema or bullae (Figure 4). Most commonly, recommended treatment is a Descemet stripping endothelial keratoplasty (DSEK) or a Descemet membrane endothelial keratoplasty (DMEK). The visual outcome of a DMEK tends to be more optically clear than that of a DSEK due to the reduced thickness of DMEK tissue. Therefore, a DSEK is typically reserved for more complicated cases and those with lower acuity potential due to concurrent disease.[11]

Some surgeons may elect to perform a triple DMEK, a combination of cataract extraction, IOL implantation, and a DMEK, if the patient is still phakic. Others may prefer a staged procedure with cataract surgery then a DMEK. Studies present conflicting results as to whether endothelial cell loss and visual outcome is equal between the two methods, but a triple procedure tends to have a higher complication rate.[12-14]

A new technique, Descemet stripping only/descemetorhexis without endothelial keratoplasty, has recently emerged.[8] In this procedure, the poorly functioning central endothelium is stripped to allow healthy peripheral endothelial cells to migrate centrally to restore vision. Trials have reported positive results, especially when combined with topical rho kinase inhibitors.[15,16] In addition, quarter DMEKs have been trialed, in which a patient receives a quarter of the donor's cornea.[17]

KNOWLEDGE IS POWER

Patients diagnosed with FECD should be educated about its hereditary nature and their family members monitored for it. The condition may not significantly progress in some cases depending on genetic disposition,[3] but in others, medical treatment followed by surgical intervention may be necessary for clear, comfortable vision. Clinical guidelines recommend patients with FECD be observed every 6 months or sooner if symptoms worsen.[1] Being aware of the appropriate medical and surgical treatments can not only aid in patient management, but also in patient education prior to referral to a cornea specialist. ■

1. Moshirfar M, Somani AN, Vaidyanathan U, Patel BC. Fuchs endothelial dystrophy. In: *StatPearls* [Internet]. Treasure Island, FL: StatPearls Publishing. July 31, 2023. Accessed August 5, 2024. www.ncbi.nlm.nih.gov/books/NBK545248/

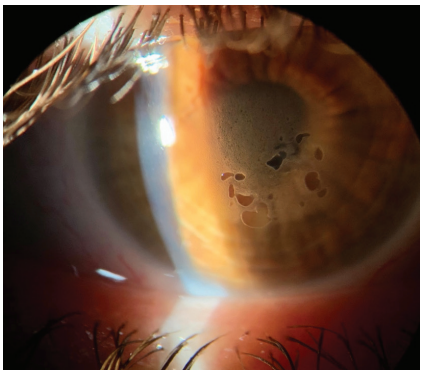

Figure 4. Bullous keratopathy, such as that pictured here, can result from end-stage FECD.

2. Vedana G, Villarreal G Jr, Jun AS. Fuchs endothelial corneal dystrophy: current perspectives. *Clin Ophthalmol*. 2016;10:321-330.
3. Iliff BW, Riazuddin SA, Gottsch JD. The genetics of Fuchs' corneal dystrophy. *Expert Rev Ophthalmol*. 2012;7(4):363-375.
4. Tone SO, Kocaba V, Böhm M, Wylegala A, White TL, Jurkunas UV. Fuchs endothelial corneal dystrophy: the vicious cycle of Fuchs pathogenesis. *Prog Retin Eye Res*. 2021;80:100863.
5. Tone SO, Jurkunas U. Imaging the corneal endothelium in Fuchs corneal endothelial dystrophy. *Semin Ophthalmol*. 2019;34(4):340-346.
6. Camburu G, Zemba M, Tătaru CP, Purcărea VL. The measurement of central corneal thickness. *Rom J Ophthalmol*. 2023;67(2):168-174.
7. Fujimoto H, Setoguchi Y, Kiryu J. The ROCK Inhibitor ripasudil shows an endothelial protective effect in patients with low corneal endothelial cell density after cataract surgery. *Trans Vis Sci Tech*. 2021;10(4):18.
8. Moloney G, Petsoglou C, Ball M, et al. Descemetorhexis without grafting for Fuchs endothelial dystrophy—supplementation with topical ripasudil. *Cornea*. 2017;36(6):642-648.
9. Kruse FE, Giessl A, Zenkel M, Tourtas T, Schlötzer-Schrehardt U. Differential effects of ROCK inhibitors ripasudil and netarsudil on corneal endothelial and epithelial cells. *Invest Ophthalmol Vis Sci*. 2023;64(8):657.
10. Hatou S, Yamada M, Mochizuki H, Shiraishi A, Joko T, Nishida T. The effects of dexamethasone on the Na,K-ATPase activity and pump function of corneal endothelial cells. *Curr Eye Res*. 2009;34(5):347-354.
11. Guerra FP, Anshu A, Price MO, Price FW. Endothelial keratoplasty: fellow eyes comparison of Descemet stripping automated endothelial keratoplasty and Descemet membrane endothelial keratoplasty. *Cornea*. 2011;30(12):1382-1386.
12. Semler-Collery A, Bloch F, Hayek G, Goetz C, Perone JM. Comparison of triple-DMEK to pseudophakic-DMEK: a cohort study of 95 eyes. *PLoS One*. 2022;17(5):e0267940.
13. Chaurasia S, Price FW, Gunderson L, Price MO. Descemet's membrane endothelial keratoplasty: clinical results of single versus triple procedures (combined with cataract surgery). *Ophthalmology*. 2014;121(2):454-458.
14. Shahnazaryan D, Sese AH, Hollick EJ. Endothelial cell loss after Descemet's membrane endothelial keratoplasty for Fuchs' endothelial dystrophy: DMEK compared to triple DMEK. *Am J Ophthalmol*. 2020;218:1-6.
15. Iovieno A, Neri A, Soldani AM, Adani C, Fontana L. Descemetorhexis without graft placement for the treatment of Fuchs endothelial dystrophy: preliminary results and review of the literature. *Cornea*. 2017;36(6):637-641.
16. Moloney G, Garcerant Congote D, Himschall N, et al. Descemet stripping only supplemented with topical ripasudil for Fuchs endothelial dystrophy 12-month outcomes of the Sydney Eye Hospital study. *Cornea*. 2021;40(3):320-326.
17. Spinozzi D, Miron A, Bruinsma M, et al. New developments in corneal endothelial cell replacement. *Acta Ophthalmol*. 2021;99(7):712-729.

SARAH L. BELL, OD
- Optometrist, Mid-Atlantic Cornea Consultants, York, Pennsylvania
- sarahbell@midatlanticcornea.com
- Financial disclosure: None

ALYSSA CALTA, OD
- Optometrist, Brumm Eye Center, Omaha, Nebraska
- Financial disclosure: None