Medium-Term Failure of Descemet's Stripping Only and Fuchs' Dystrophy With Pancorneal Guttae

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Purpose: The purpose of this study was to report the medium-term outcome of our index case of Descemet stripping only (DSO) in the clinical setting of Fuchs endothelial corneal dystrophy with pancorneal guttae.

Methods: This was a retrospective case report.

Results: A 44-year-old woman with bilateral Fuchs endothelial corneal dystrophy was referred for consideration of DSO. At initial slit-lamp examination, widespread guttae were observed with no clear zone visible. Confocal microscopic examination also failed to isolate a population of undisturbed endothelial cells. DSO with supplemental ripasudil was performed with corneal clearance achieved at 2.5 months. A stable result was obtained for 18 months with a subsequent slow decline in vision and return of diurnal fluctuation. At 3.5 years after DSO, DMEK was performed with resolution of symptoms.

Conclusions: Medium-term failure in this clinical setting is further evidence that DSO is likely best offered to patients with central guttae but a clear corneal periphery, indicative of a healthy cell reservoir.

Key Words: Descemet stripping only, Fuchs dystrophy, confocal microscopy, limbus-to-limbus guttae

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The surgical removal of Descemet membrane without placement of graft material has grown in acceptance as a therapeutic option for Fuchs endothelial corneal dystrophy (FECD). Its first recorded description was by Louis Paufique decades ago, but a renaissance has occurred in recent years.[1–3] The original acronym introduced was descemetorhexis without endothelial keratoplasty (DWEK) with Descemet stripping only (DSO) also later suggested.[4–6] With increased dissemination and refinement of surgical technique, we are as a community approaching a better understanding of where this surgical option fits into the algorithms for FECD treatment. One point of contention has been what surface area of guttae represents the upper limit of offering this procedure. Similarly, what population of endothelial cells is required in the peripheral reservoir to allow healing by migration. Early in our surgical journey with DSO, we performed this operation on a young patient with limbus-to-limbus guttae. We report here the medium-term outcome of this procedure in this clinical setting.

CASE REPORT

A 44-year-old woman was referred with FECD and visual symptoms. She complained of diurnal visual fluctuation, generalized blur, and photophobia preventing night driving. Her symptoms were beginning to intrude on normal functioning as a mother and work as a photographer. She had been prescribed hypertonic saline and was finding this of limited benefit in relieving symptoms. Owing to a family member's mixed experience with an endothelial graft elsewhere, she was highly motivated to explore her candidacy for nongraft options for FECD.

Baseline examination revealed best spectacle–corrected vision (BCVA) of between 20/60 and 20/40 in each eye, depending on morning or afternoon assessment. Central corneal pachymetry measured by optical coherence tomography (Cirrus 4000; Carl Zeiss, Germany) was 634 μm in the right eye (OD) and 643 μm in the left eye (OS). Slit-lamp examination revealed guttae from limbus to limbus in all meridians, with focal microcystic edema observed in the inferior right cornea at 1 early morning assessment.

In vivo white light confocal microscopy (Confoscan 3; NIDEK Technologies, Padova, Italy) revealed no areas of endothelial mosaic uninterrupted by gutta formation (Figs. 1A–D). Based on this assessment, the patient was excluded from research trials into FECD that were active at the time. To further understand the severity of her disease, sputum samples were collected to confirm the presence and severity of a transcription factor-4 repeat expansion (Oragene; DNAGenotek, Ottawa, ON, Canada). These revealed 11 cytosine, thymine, and guanine triplet repeats at 1 allele but 107 at the other. Owing to the patient's strong motivation to trial DSO, we acquiesced to surgery

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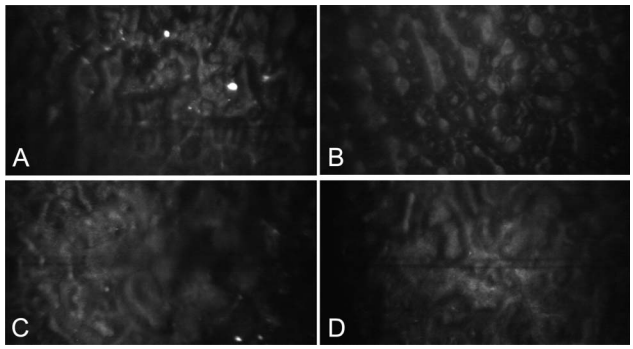

FIGURE 1. In vivo confocal microscopic images of central (A, B) and superior peripheral (C, D) endothelial cell populations in our patient. A normal endothelial mosaic is not discernible because of the presence of confluent guttae.

provided she was accepting of the possible need for an endothelial graft and the possible side effects of topical rho-kinase inhibitor. Individual application was made for the use of ripasudil under the Australian Therapeutic Goods Administration guidelines. A negative pregnancy test was obtained, and abstinence was advised. Individual consent for DSO/DWEK was obtained, and salvage Descemet membrane endothelial keratoplasty (DMEK) tissue was organized should the cornea fail to clear. Surgery was performed uneventfully, and 5 mm of Descemet membrane was stripped. Postoperative drops included topical ripasudil 0.4% 6 times daily and dexamethasone 0.1% 4 times daily (qid), chloramphenicol qid, ketorolac 0.5% qid, and 5% hypertonic saline qid. Drops commenced on day 1, the morning after surgery. At 2 weeks, ripasudil was reduced to qid, and at 1 month, all other drops were ceased. Corneal clearance was achieved at 2 months and 16 days, with ripasudil reduced to twice daily (bid) and continued for a further 2 months.

On corneal clearance, her BCVA improved to 20/20 with resolution of photophobia in the treated eye (Fig. 2). For 18 months, the corneal clearance appeared stable, and the patient was satisfied with the procedure. After this time point, clearance became increasingly unstable with a slow return of diurnal fluctuation. By 3.5 years after surgery, BCVA had declined to preoperative levels of 20/40, with increasing diurnal fluctuation and microcystic edema. The patient's symptoms became intrusive again, and right DMEK was performed (Figs. 3A–D), with intraoperative optical coherence tomography confirmation of orientation (Figs. 3E, F). At week 1, BCVA had returned to 20/20 with resolution of visual symptoms (Figs. 4A, B). She underwent primary DMEK in her left eye 2 months after her right DMEK. The central cell count was 1890 cell/mm^2 OD and 1847 cells/mm^2 OS at the end of 6 months (Figs. 5A, B).

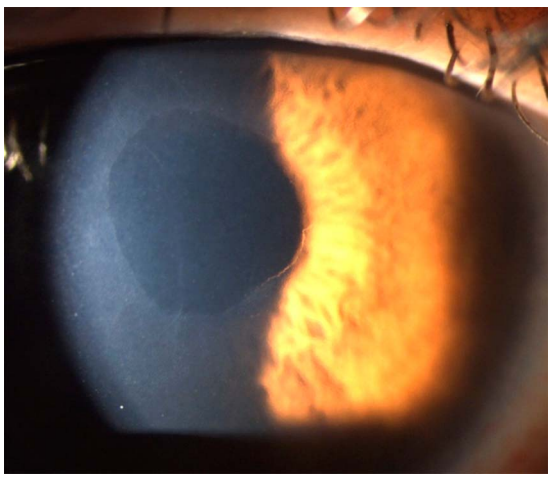

FIGURE 2. Slit-lamp image of the right eye 3 months after DSO. Note relative clarity of central zone and widespread "beaten metal" appearance of nonstripped endothelium.

DISCUSSION

FECD is a highly heterogenous disease. The assumption that medium-term failure in our case excludes all similar phenotypes from receiving DWEK/DSO may not be true. The use of the slit-lamp finding of pancorneal guttae as a measure of equivalence between patients may also be misguided.

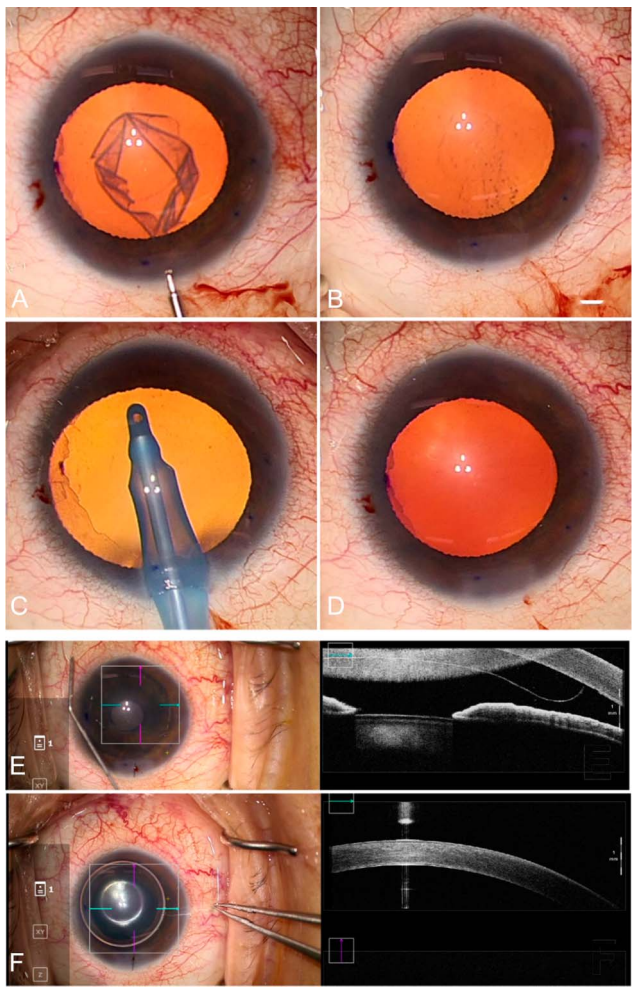

FIGURE 3. Intraoperative still photographs of DMEK in the same patient. A, Stripped zone is widened and "donut" of Descemet membrane removed, (B) residual endothelial debris remains in the central stripped zone, (C) irrigation and aspiration with a silicone-tipped sleeve to clear central debris and cells, (D) clear cornea now obtained, (E) correct graft orientation confirmed with intraoperative OCT (Carl Zeiss, Germany), and (F) hyperfill of air to secure graft position. OCT, optical coherence tomography.

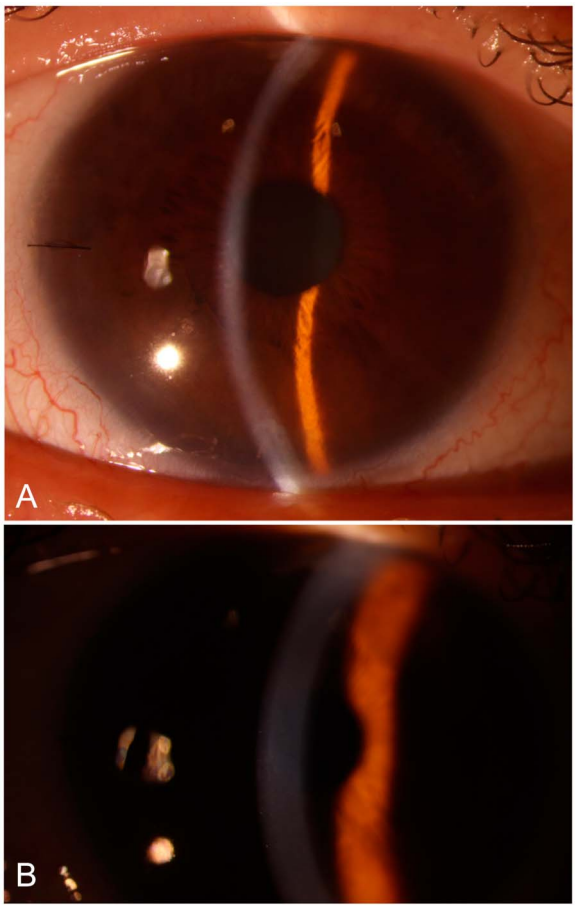

FIGURE 4. Slit-lamp images of the patient day 4 after DMEK. A, Magnification at ×10 demonstrating clear cornea and well-positioned graft and (B) ×16 magnification demonstrating no discernible interface haze or debris.

Nevertheless, this case represents the first medium-term failure of DSO from our clinic and is likely instructive.

Surgical factors associated with success or failure of DWEK are increasingly well defined. Early studies of Descemet stripping demonstrated increased rates of successful clearance once the stripped zone was reduced to 4 to 5 mm.[7–11] Avoidance of stromal trauma seems critical in creating a microenvironment suitable for endothelial migration.[2,9,12] Patient factors relevant to success are suspected, but specific parameters remain poorly defined.[2,9,12,13] Younger age, a clear corneal periphery on slit-lamp examination, and a healthy peripheral endothelial cell reservoir if measurable are all desired.

It is not yet known with certainty whether we are required to limit this surgery to patients with guttae present only within the central 4 to 5 mm zone. There are patients at an intermediate amount of guttae beyond 4 to 5 mm (but not pancorneal) who may still benefit. Our current clinical practice is to offer DWEK/DSO to patients with a healthy peripheral cell reserve on confocal scan, limit the stripped zone to 4 to 5 mm, and not remove any remaining guttae outside this area if present. In nongraft techniques for FECD, we still, after several years of study, have not clearly linked either chance of corneal clearance

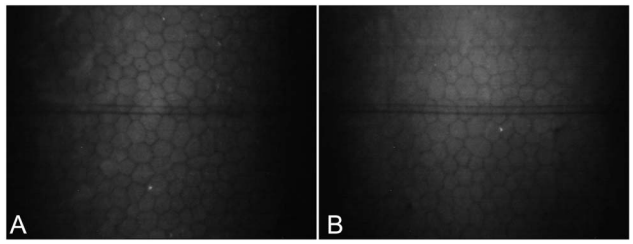

FIGURE 5. Central cell counts after DMEK in the same patient. A, The right eye showing a good population of endothelial cells with a healthy mosaic pattern, and (B) the left eye showing similar features of healthy endothelial cells.

or longevity of stable corneal clearance with "cutoff" numerical values, pachymetry, cell count, or guttae surface area.

In what we term "Fuchs dystrophy," a variety of genotypes have been found to produce a similar phenotype.[14–19] The most common mutation (trinucleotide repeat expansion within transcription factor-4) may create a variable disease burden depending on the repeat expansion size and consequent mRNA "load."[18] In this case, genetic testing was undertaken to possibly arbitrate between a graft or nongraft option, with admittedly little evidence base, but extreme normal or abnormal possibly tipping judgment. The finding of 1 essentially normal allele and 1 highly expanded allele helped little in the decision-making process. In the end, DWEK was undertaken because of the patient's young age, strong desire to avoid a graft, and our recent positive experience with ROCKi in other patients.[2,10]

It is important to note that in the absence of any stromal scarring or haze, DMEK performed years later can have good outcomes after DWEK, with a clear interface. This is an important point of reassurance for patients contemplating the procedure. The shorter duration of benefit in our patient may suggest this procedure has a role in patients who themselves have limited life expectancy. This would be a rare circumstance; however, as with advanced age, the necessary endothelial reserve will be depleted, and in terminal conditions in younger patients, the visual benefit may not be a priority.

We recently reported good medium-term outcomes from DSO/DWEK in the setting of central guttae removal.[11] As algorithms for DSO continue to be refined, this case proves instructive that the longevity of this procedure without a healthy peripheral cell reserve may be limited. It could be argued that 3 years of functional vision in a phakic patient is still a useful amount of time to achieve without a transplant. Nevertheless, our case illustrates the caution and careful communication required in this clinical setting.

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