Immunologic perspective on the denuded stromal “gutter” after Descemet membrane endothelial keratoplasty

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We present the case of an 87-year-old woman with Fuchs endothelial dystrophy who had successful Descemet membrane endothelial keratoplasty (DMEK) surgery with a standardized DMEK technique, including overstripping of the recipient descemetorhexis by 0.5 mm. Twenty-one months after surgery, the patient presented with mildly progressive vision loss and scant keratic precipitates. A few endothelial deposits were on the previously denuded gutter, which was now covered with endothelial ingrowth, but no deposits were present on the peripheral recipient Descemet membrane. Treatment with topical corticosteroids resulted in a rapid and full resolution of the keratic precipitates. Visual acuity and central corneal thickness were not significantly affected, but endothelial cell counts showed a modest decline of 19% 2 years after surgery (5 months after the rejection episode) compared with the 1-year measurements.

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We incorporated a descemetorhexis that is 0.5 mm larger in diameter than the donor graft into our standardized Descemet membrane endothelial keratoplasty (DMEK) technique after Tourtas et al. showed that rebubble rates were lower in recipients with no overlap between the recipient and donor. In addition to helping us achieve a low rebubble rate, this practice has allowed us to observe how the denuded gutter between the recipient and donor Descemet membranes behaves over time (Figure 1).

The stromal gutter has a distinct clinical course from the rest of the cornea because it is without an endothelium for at least the first few weeks after DMEK surgery and is frequently the site of residual edema.

Over the ensuing 1 to 2 months, the peripheral ring of stromal and epithelial edema slowly resolves as endothelial cells migrate to cover the bare stroma.

The exact physiology of the gutter’s spontaneous clearance is uncertain. Postulates have been proposed, but there is no definitive evidence to indicate whether endothelial cells migrate from the recipient or from the donor to fill in the denuded stroma after DMEK surgery. We present a case of DMEK graft rejection that provides further data to support the postulate that peripheral denuded stroma clears because of endothelial migration from the donor onto the recipient.

CASE REPORT

An 87-year-old woman with Fuchs endothelial dystrophy had uneventful DMEK surgery using our standard technique, including overstripping the recipient stromal bed with an 8.0 mm descemetorhexis and implanting a 7.5 mm graft. The postoperative course was uneventful, with the corrected distance visual acuity (CDVA) improving from 20/50 preoperatively to 20/25 by postoperative month 6. Prednisolone acetate 1.0% was stopped at 1 year after a gradual taper from 6 times per day.

Twenty-one months after surgery, the patient presented with complaints of slowly progressive blurry vision and a corresponding reduction in CDVA to 20/30. Slitlamp biomicroscopy revealed a mild episode of graft rejection.

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The conjunctiva and sclera were not inflamed, the corneal epithelium was smooth, and there was a scant collection of fine keratic precipitates on the DMEK graft (Figure 2). Keratic precipitates were completely absent from the peripheral recipient Descemet membrane, and there were 3 keratic precipitates on the temporal gutter between the graft and recipient Descemet membranes (Figure 3). Otherwise, there was no stromal edema and no Khodadoust line, the anterior chamber showed 1 cell, the iris was normal, a posterior chamber intraocular lens was present, and the posterior segment showed no abnormalities other than mild age-related mottling of the retinal pigment epithelium. The central corneal thickness (CCT) was essentially unchanged, measuring 576 μm compared with 579 μm 3 months earlier.

Intensive topical prednisolone acetate 1.0% was administered every hour followed by a gradual taper to once daily. The keratic precipitates and anterior chamber inflammation resolved completely within 4 weeks. The CDVA returned to 20/25. The endothelial cell count (ECC) declined from 2105 cells/mm², measured 9 months before the rejection episode at the 1-year postoperative visit, to 1706 cells/mm², measured 5 months after the episode at the 2-year postoperative visit (19% cell loss). The CCT decreased by about 10 μm to 567 μm, where it has remained.

**DISCUSSION**

This is the third reported DMEK patient who presented with keratic precipitates on the stromal gutter but no precipitates on the recipient Descemet membrane. Hos et al. were the first to report this phenomenon in 2 men who received DMEK transplants for Fuchs endothelial dystrophy and followed a clinical course very similar to that in our case. Based on the premise that keratic precipitates indicate an in situ immune reaction against the allograft, the authors postulated that their observations provided “the first direct evidence of the donor origin of repopulating corneal endothelial cells” filling in the “naked” gutter after DMEK.

Whether donor endothelium migrates onto the recipient or recipient endothelium migrates onto the donor after endothelial keratoplasty remains debatable. Our case report and the 2 cases reported by...
Hos et al. support the former hypothesis, as does confocal microscopy analysis of the stromal gutter by Jakobi et al. However, there is also convincing evidence for the latter hypothesis. The strongest is perhaps the case reported by Ziaei et al., which exhibited spontaneous centripetal ingrowth of peripheral endothelium after Descemet stripping without endothelial transplantation.

Although reassuring from a surgeon’s perspective, reports of spontaneous corneal clearance despite incomplete DMEK attachments do not convincingly favor one postulate over the other. This is because endothelial ingrowth could emanate from the donor or the recipient or from both. Even in extreme cases of DMEK detachment, as in Descemet membrane endothelial transfer, the confounding nature of donor tissue being in the anterior chamber is still true.

We believe that our case report in conjunction with the 2 cases reported by Hos et al. provides reasonable evidence to support the hypothesis that migration is from the donor onto the recipient. It is possible that the location of the endothelial deposits on the stromal gutter was purely by chance. However, the relative paucity of keratic precipitates on the recipient cornea and the temporal rather than inferior location of the precipitates argue in favor of an immunologic mechanism. It is also possible that an in situ immune response occurred against donor endothelial cells that had admixed with recipient cells to form a heterogeneous population over the gutter. Such a scenario could yield the clinical observations noted in our case as well as in the cases reported by Hos et al. If it indeed existed, to what degree an admixed population of endothelial cells comprised donor cells versus recipient cells could in theory depend on several factors, including the relative health of the 2 populations of endothelial cells and the size of the denuded gutter.

Another noteworthy aspect of this case is the mild clinical presentation—one line of vision loss and sparse keratic precipitates in an essentially white and quiet eye—and the relative ease with which the rejection episode was extinguished—a few weeks of prednisolone acetate 1.0% with subsequent return of vision. This is consistent with what Price et al. found in their large DMEK series.

In summary, this case report provides further evidence in support of previous findings suggesting that donor endothelial cells play a roll in repopulating the denuded stromal gutter. If donor endothelial cells migrate from the DMEK graft onto the recipient cornea, and even if they admix with recipient cells, the tendency may have important implications for long-term central ECCs. For the DMEK surgeon, the ultimate implication may be deciding how much larger to make the descemotorhexis than the graft, knowing that a subpopulation of cells will migrate off the graft but that graft–donor overlap may raise the risk for a rebubble in the immediate postoperative period. It could also mean that surgeons will have to consider whether to implant larger grafts in eyes with severe endothelial cell loss. Further research is needed to better understand the nature of donor endothelial migration after DMEK.

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