Brief Report

Spontaneous regression of epithelial downgrowth from clear corneal phacoemulsification wound

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ABSTRACT

Purpose: To report a case of spontaneous regression of optical coherence tomography (OCT) and confocal microscopy-supported epithelial downgrowth associated with clear corneal phacoemulsification wound.

Observations: A 66-year-old Caucasian male presented two years after phacoemulsification in the left eye with an enlarging cornea endothelial lesion in that eye. His early post-operative course had been complicated by corneal edema and iris transillumination defects. The patient presented to our clinic with a large geographic sheet of epithelial downgrowth and iris synechiae to the temporal clear corneal wound. His vision was correctable to 20/25 in his left eye. Anterior segment OCT showed a hyperreflective layer on the posterior cornea with an abrupt transition that corresponded to the clinical transition zone of the epithelial downgrowth. Confocal microscopy showed polygonal cells with hyperreflective nuclei suggestive of epithelial cells in the area of the lesion with a transition to a normal endothelial cell mosaic. Given the lack of glaucoma or inflammation and the relatively good vision, the plan was made to closely monitor for progression with the anticipation that he may require aggressive surgery. Over course of subsequent follow-up visits at three, seven and ten months; the endothelial lesion receded significantly. Confocal imaging in the area of the previously affected cornea showed essentially normal morphology with an endothelial cell count of 1664 cells/mm2.

Conclusions and importance: Epithelial downgrowth may spontaneously regress. Though the mechanism is yet understood, contact inhibition of movement may play a role. Despite this finding, epithelial downgrowth is typically a devastating process requiring aggressive treatment.

1. Introduction

Epithelial downgrowth is a rare, destructive complication of intraocular surgery or penetrating trauma, with the majority of cases developing post-cataract extraction. The cumulative incidence of epithelial downgrowth after cataract extraction in one 30-year review was 0.12%, however only 0.08% in the latter decade.1 The declining incidence in recent years may be related to improved microsurgical instrumentation and techniques, such as sutureless small incision clear-corneal approaches. Despite this, there have been several reports of epithelial downgrowth after clear corneal cataract surgery.2–4 Delayed or inadequate wound closure, wound fistulas, iris or vitreous incarceration, suture track leaks, or intraocular implantation of epithelial cells via instruments or penetrating objects increase the risk for epithelial invasion into the anterior chamber.2 When downgrowth does develop the course is typically progressive with a poor prognosis.

Previously described treatment options include a local or complete (en bloc) resection of all involved tissues with possible cryotherapy or intraocular injection of antimetabolites. Radiation also has been used with suboptimal results due to local side effects. The use of endoscopic photocoagulation has been reported as an option in the cystic growth pattern of epithelial downgrowth. Finally, enucleation is an unfortunate but sometimes unavoidable option reserved for end-stage, refractory disease. The most common cause for enucleation is severe secondary glaucoma.

Although typically progressive in nature, we report an unusual case of epithelial downgrowth after cataract surgery that developed and spontaneously regressed over a 3 year period without intervention.

2. Materials and methods

A retrospective chart review was performed.

3. Case report

A 66-year-old Caucasian male presented to the Cleveland Clinic Cole

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Eye Institute cornea service for a second opinion regarding a left corneal lesion. His ocular history includes phacoemulsification of the left eye with temporal clear corneal wound two years prior in June 2014. His course was complicated by early post-operative corneal edema. He was evaluated five weeks after initial surgery for persistent corneal edema by a corneal specialist who considered Descemet's membrane endothelial keratoplasty (DMEK) and started prednisolone acetate 1% drops twice daily. Uncorrected visual acuity (UCVA) at the time of the evaluation was 20/70. On follow-up in September 2014, the uncorrected vision had improved to 20/20 and the corneal edema was noted to have resolved, though there was a question of a Descemet's membrane "tear" noted temporally. Given the improvement in both the vision and corneal edema, steroid drops were discontinued and observation was recommended.

In October of 2014, the patient presented to an optometrist for refraction at which time the vision was still correctable to 20/20 but the presence of a large "endothelial defect" was noted in the temporal one-third of the cornea. The iris was noted to have transillumination defects between 4 and 5 o'clock although no synechiae were documented. Sixteen months later, the patient returned to the same optometrist for a routine examination with the complaint of slowly progressive blurriness in the left eye. Vision was still correctable to 20/25, however there was an increase in size and prominence of the previously noted temporal endothelial lesion. The patient was again examined by the optometrist in August of 2016, at which time he documented the presence of new temporal peripheral anterior iris synechiae and corneal edema.

The patient was referred back to the initial cornea specialist in August 2016 for an "enlarging endothelial lesion." His UCVA at the time was 20/40. The presumptive diagnosis was pseudophakic bullous keratopathy, possibly due to a Descemet membrane tear, and the patient was scheduled for DMEK. Prior to surgery, the patient presented for a second opinion at the Cole Eye Institute in September 2016.

At our initial evaluation, the left eye had an UCVA of 20/40 and his best-corrected visual acuity (BCVA) was 20/25 with manifest refractive astigmatism of 1.50 diopters. Intraocular pressure was 9 mmHg in the left eye. Examination of the right eye was unremarkable except for the presence of a moderate nuclear sclerotic cataract and normal appearing corneal endothelium. Slit lamp examination of the left eye revealed a geographic pattern of translucent, faint gray membrane on the posterior corneal surface that was contiguous with an area of temporal peripheral anterior synechiae. This synechia was directly underlying the clear corneal incision from his prior cataract surgery (Fig. 1A–C). The anterior chamber was quiet. The temporal iris was atrophic with transillumination defects, however the remainder of the iris appeared normal with mild ovalization of the pupil toward the area of synechiae. The intraocular lens was well-positioned in the capsular bag with an intact posterior capsule.

Anterior segment OCT revealed a distinct hyperreflective layer along the posterior corneal surface that corresponded with the clinical endothelial lesion (Fig. 2A). The hyperreflective layer was contiguous with the internal aspect of the temporal clear corneal wound (Fig. 2B). Subsequent confocal microscopy at the margin of the defect demonstrated the presence of normal endothelial cells adjacent to polygonal cells with hyperreflective nuclei, a pattern suggestive of epithelial morphology (Fig. 3).

Given the clinical findings and results of the diagnostic imaging, a diagnosis of epithelial downgrowth was made. Based on his visual acuity, normal intraocular pressure (IOP), and the lack of significant anterior segment inflammation or patient discomfort, the decision was made to observe closely with the expectation that aggressive surgery could be required should the condition progress.

Three months later, the patient returned for follow-up. UCVA in the left eye had improved to 20/25. Intraocular pressure was 12 mmHg. Surprisingly, the endothelial lesion had receded significantly, localized "islands" now visible in the area of previous contiguous involvement (Fig. 1D). Observation was again recommended and the lesion continued to regress on subsequent visits. At his seven month visit (Fig. 1E), his vision had improved to 20/20 uncorrected. As the lesion regressed, slit lamp examination revealed a normal-appearing cornea, including Descemet's membrane (Fig. 1F). Confocal microscopy of the central, previously affected, cornea revealed an endothelial cell count of 1664 cells/mm² with essentially normal morphology.

The area of temporal peripheral iris synechiae remained unchanged, as did the mild ovalization of the pupil.

4. Discussion

We present a case of spontaneous regression of sheet-like epithelial downgrowth in the anterior chamber. There have been prior reports of spontaneous resolution of epithelial downgrowth, or ingrowth, within a LASIK flap interface. Zhang et al. described a case in which the patient presented 23 months after uneventful microkeratome LASIK. The patient refused surgical intervention and the ingrowth was noted to expand over the first three months then gradually decrease over the next three months until complete resolution. Lin et al. described a case of a woman with a largely displaced LASIK flap on the first postoperative day and a subsequent finding of epithelial ingrowth at her one month postoperative visit with one area developing a dense sheet. Twenty months after her surgery there was spontaneous resolution of the ingrowth.

To our knowledge, our case is the second described in the literature of spontaneous resolution of epithelial downgrowth invading the anterior chamber. Previously, Fan et al. describe a case of spontaneous regression of a retrocorneal epithelial downgrowth sheet in a patient two years after argon laser photocoagulation of an iris implantation cyst. They authors postulate that the corneal endothelial cells were locally damaged and unable to inhibit proliferation. They believe the normal, undamaged endothelial cells not only impeded the progression via contact inhibition but eventually migrated and displaced the invading epithelial cells leading to regression. In addition, they felt the continued progression of the epithelial downgrowth observed over the iris supported the hypothesis since there would be no expected contact inhibition at play on the iris surface.

In comparison to the aforementioned case report, our case includes OCT and confocal microscopy imaging, as well as high resolution slit lamp photography. Confocal microscopy has been shown to be a useful, reliable tool to characterize epithelial downgrowth. In addition to the typical epithelial appearance of polygonal cells with hyperreflective nuclei, there are areas of ill-defined cellular features likely representing apoptotic cells that seem to correlate with areas of spontaneous epithelial regression.

Regarding the phenomenon of contact inhibition of movement, it was first described in vitro by Abercrombie and Heaysman in 1954. Yanoff et al. showed that in full thickness human corneal buttons placed in culture the epithelial cell layer and endothelial layer both demonstrate migration up until the point of contact with each other. In human cornea organ culture, five of the seven corneal buttons studied demonstrated epithelial-endothelial contact inhibition. The epithelium was uninhibited on the remaining two corneal buttons, presumably due to the presence of corneal guttata on both buttons. Yanoff also noted that corneal status post superior extracapsular wounds had a propensity for epithelial downgrowth to involve the superior two-thirds (typically the site of intraoperative endothelial cell trauma) and sparing the inferior one-third.

Bourne and Brubaker, reported on a case of a patient with near complete regression of partial corneal involvement in iridocorneal endothelial syndrome (ICE). This is noteworthy as ICE features abnormal, migratory, epithelial-like endothelium in the involved cornea. Three subjects were followed over ten years, and in one subject the abnormal endothelium of ICE was gradually replaced with a normal endothelial cell layer with normal cell density similar to the uninvolved fellow eye. The authors also noted that Descemet's membrane appeared normal.
after regression of the abnormal cellular layer (as in our patient) despite the initial “hammered-silver” clinical appearance. This seemed to support the notion that the endothelial layer itself and not Descemet’s membrane accounted for the posterior corneal “hammered-silver” appearance.

5. Conclusions

In summary, epithelial downgrowth is a rare, usually aggressive complication of intraocular surgery or trauma. We report an interesting and unusual case of spontaneously regressing epithelial downgrowth after clear cornea phacoemulsification. The reasons and exact

**Fig. 1.** A, B, C: Clinical photos at the time of presentation. Note the iris synechiae in the area of the old temporal clear corneal wound and the large faint, translucent gray endothelial lesion. The margins and whorled pattern (*) are best seen on retrolumination.

D, E and F: 3 months, 7 months and 10 months, respectively, after presentation. Note the gradual regression from the nasal leading edge, with formation of transient, isolated islands (arrows) and eventual complete disappearance leaving behind normal appearing cornea.

**Fig. 2.** Anterior segment optical coherence tomography.

A: Temporal hyperreflective layer deep to endothelium with abrupt transition corresponding to clinical lesion (arrow).

B: The hyperreflectivity is contiguous with the temporal synechiae (*) and clear corneal wound.

**Fig. 3.** Confocal microscopy. Towards the bottom there are large hyperreflective nuclei characteristic of epithelial cells (arrowheads). These are more posterior than the hexagonal endothelial cell mosaic seen in the top half of the image (*).
mechanism for regression in this patient are not fully understood but may be related to migration of the remaining healthy endothelial cells to displace and replace the proliferated epithelial layer. Although our case report suggests that some cases of endothelial ingrowth may regress spontaneously, aggressive and early intervention may still be necessary in most cases based on the known risk of progression to severe irreversible vision loss.

6. Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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