Case report

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Epithelial downgrowth leading to graft rejection after penetrating keratoplasty

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Abstract

Purpose: To report a case of epithelial downgrowth after penetrating keratoplasty.

Case description: A 58-year-old man presented with graft rejection in his three-month-old, repeat penetrating keratoplasty. Examination revealed centripetal opacification of the posterior cornea due to deep epithelization. He had new retro-corneal membranes and anterior uveitis. Specular microscopy and anterior segment optical coherence tomography were performed, and a clinical diagnosis of epithelial downgrowth was made. The patient had intracameral injections with 5-fluorouracil (5FU) and achieved resolution of intraocular findings after treatment.

Conclusions: Epithelial downgrowth is an uncommon complication of penetrating keratoplasty. It affects the patients' visual acuity and graft survival. Clinical observation is preferred in severe cases due to the high risk of intraocular damage; intracameral 5FU promises to be a good option in these cases.

Keywords

epithelial downgrowth, retro-corneal membranes, corneal transplant, intracameral chemotherapy

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Introduction

Epithelial downgrowth (ED) is a rare but severe complication observed after penetrating ocular trauma, refractive, and intraocular surgery.[1] This entity threatens the visual acuity of the patient. In severe cases, the invasion of epithelial cells in the anterior chamber can grow deep into the iris surface, generating corneal decompensation, corectopia, ectropion uveae, or even secondary glaucoma.

Mackenzie first described this pathology as a translucent cyst in the anterior chamber of a post-traumatic patient and has been reported with an incidence of 0.076–0.12% in extracapsular cataract extraction and 0.25% in penetrating corneal transplant. Few cases have been reported after endothelial keratoplasty in the last decade.[2] Zhang and Suh reported that 15%–20% of failed Descemet stripping automated-endothelial keratoplasty (DSAEK) grafts were related to ED.[3,4]

The pathophysiology is unclear, and several theories have been proposed. The most accepted states that non-keratinized epithelial cells are introduced to the cornea through surgical or traumatic wounds. Others suggest that eccentric trephination of the donor tissue may attach to the graft or that the host epithelial cells adhere to the folded lenticule and are introduced in lamellar surgery.[3]

ED was classified by Chen et al.[1] into three primary forms: epithelial pearls, cysts, and diffuse sheets of epithelium, the latter being the most common and aggressive form. Epithelial cells can deposit in every layer of the cornea; lamellar location is the most common and most aggressive one and can lead to secondary glaucoma and corneal decompensation. Patients with ED can present with

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decreased vision, pain, tearing, and photophobia. We present a case of ED after a corneal transplant, with atypical findings such as retro-corneal membranes and anterior uveitis.

Case presentation

A 58-year-old male is referred by the glaucoma service to the cornea department with a corneal transplant rejection diagnosis on the left eye. Past surgical history was notable for corneal transplant in both eyes due to keratoconus 30 years ago.

The patient had ocular trauma OS (left eye) requiring vitrectomy, iridoplasty, cataract extraction, and scleral fixated intraocular lens done 12 months prior to presentation, followed by a second penetrating keratoplasty done three months before presentation. After ocular trauma, he had a complicated course, presented recurrent anterior uveitis with intraocular pressure peaks, which needed transscleral photocoagulation.

On presentation, visual acuity was 20/50 OD (right eye) and 20/800 OS. Slit-lamp examination revealed deep epithelization of the graft producing a centripetal opacification of the cornea (Figure 1(a)) and retro-corneal membranes, not described in the previous visits. Intraocular pressure continued to be high, and new 3 + cell was seen. Gonioscopy revealed inferior, nasal and superior synechiae; the pupil was fixed in mydriasis. An endothelial cell count and high-resolution anterior segment ocular coherence tomography (HR-OCT) were done. (Figure 1(b) and (c)) The endothelial cell count was 2817, but areas of missing endothelial cells were seen on specular imaging. HR-OCT revealed subepithelial hyperreflectivity and a thickened hyperreflective membrane in the corneal endothelium.

A diagnosis of ED was made. The patient underwent treatment with 500 mcg of intracameral 5-Fluorouracil (5FU); he was also on steroid drops, glaucoma drops, and oral prednisone. An improvement in intraocular inflammation was noted; four months later we applied a second

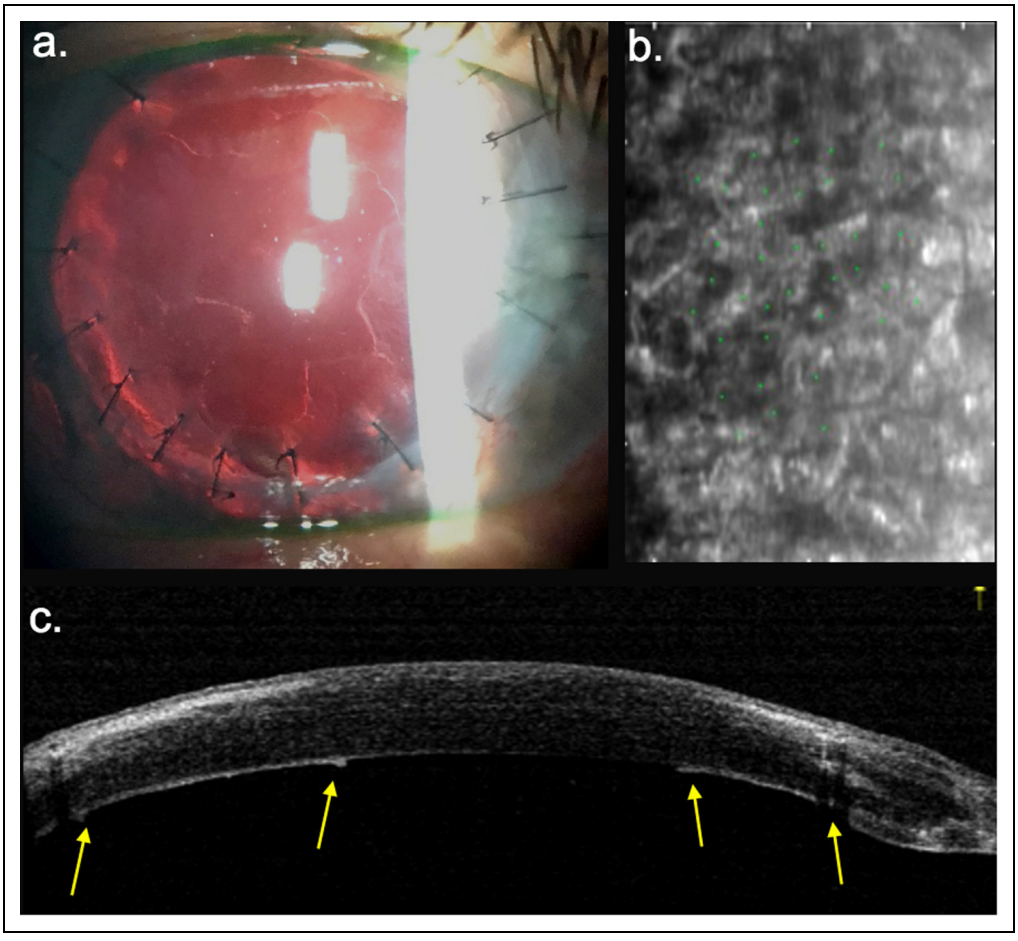

Figure 1. (a) slit-lamp photograph of the left eye, denoting a centripetal posterior opacity of deep epithelization in the corneal graft. (b) Specular microscopy OS, showing an amorphous pattern of endothelial cells with hyperreflective nuclei, possible epithelial cells. (c) Anterior segment OCT of the left eye, denoting a subepithelial hyperreflectivity and thickened hyperreflective endothelium (yellow arrows).

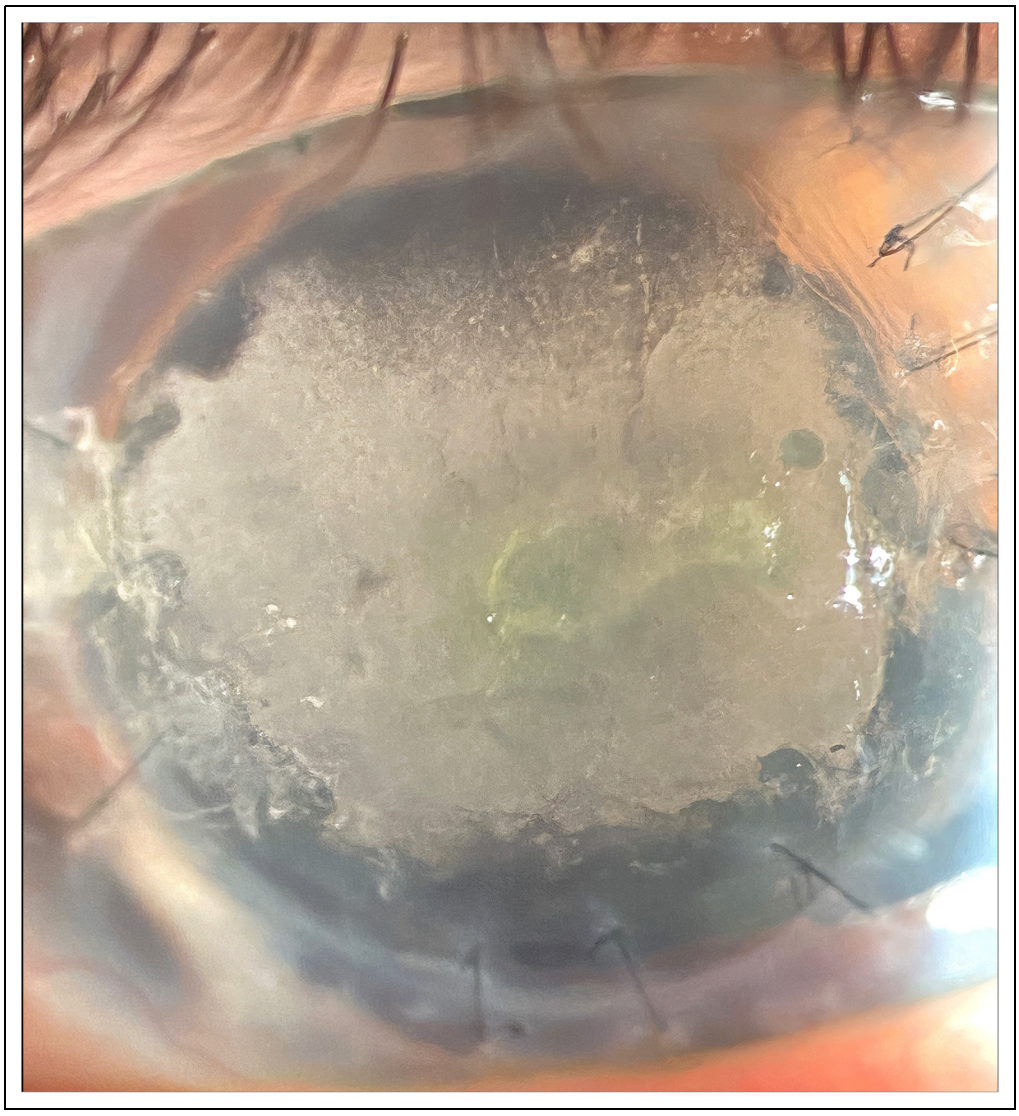

Figure 2. Slit-lamp photograph of the left eye, denoting new superficial band keratopathy and resolution of epithelial downgrowth.

dose of intracameral 5FU. Complete resolution of ED, retro-corneal membranes, and uveitis, and new band keratopathy was noted one month following the second dose of 5FU (Figure 2). The patient is scheduled for a third transplant OS.

Conclusions

The incidence of ED is challenging to determine, given the rarity of this complication. In a major review by Chen and Pineda[1] the most common event leading to ED was cataract surgery, followed by penetrating trauma and penetrating keratoplasty. Estimates are that ED occurs in up to 0.25% of patients who undergo aphakic penetrating keratoplasty.[5] In our case, it is unclear if the ED happened secondary to ocular trauma or repeat keratoplasty. The presence of this prior to the second keratoplasty might explain secondary glaucoma and repeat inflammation. Usually, the diagnosis is made weeks or months after the inciting event. Diagnosis of this condition can be challenging because the presenting symptoms and signs may be non-specific. Some clinical findings in these patients are retro corneal membranes, increased intraocular pressure, wound leak, and corneal edema. Our patient presented with retro-corneal membranes soon after deep epithelization was noted. We hypothesize that this might be due to the endotheliitis caused by epithelial implantation that translates into an exacerbated intraocular inflammatory response that led to anterior uveitis and the adherence of these fibrous membranes in the posterior cornea.

Treatment options of ED may vary depending on the form and progression of the disease. Various therapeutic interventions have been attempted to treat ED with

limited success. Regarding the diffuse sheet of epithelium form of ED, many approaches were suggested in cases where vision is affected. These modalities include direct surgical excision, surgical excision followed by cryotherapy of involved structures, radiation therapy, and, in some cases, clinical observation.[6] Most of these have been abandoned because of ocular damage and a high rate of enucleation. Because surgical intervention results in the destruction of intraocular structures, some clinicians have used antimetabolites such as 5- fluorouracil. This pyrimidine analog interferes with DNA and RNA synthesis, it has been used with varying degrees of success and complication rates.[7–9] Despite the various uses of 5FU in intraocular surgery, there is no consensus on the safest intraocular dose. 5FU is ineffective at halting ED proliferation at low doses, whereas higher doses induce corneal endothelial cell damage and endothelial decompensation.[8,10] Dosage was based on the protocol described by Lai and Haller[7] where 500mcgs were injected in the anterior chamber followed by a second injection at 2 weeks. After no toxicity was induced in our case, a second dose was given spaced out in time. This turned out to be effective in treating ED and the associated findings, but at that point, the graft had already failed, and the patient requires a third transplant. Regardless, we consider this step is essential to ensure no future recurrences of ED in the new graft. We acknowledge that endothelial microscopy measurements could have been influenced by the transparency of the corneal tissue and by the fallacy in capturing images; this is a limitation in our case report. Manual measurements are ideal in abnormal corneas, but this has to be requested to the technician before the exam, and its operator dependent.

This case highlights the severe course of ED in a transplant patient, leading to decreased visual acuity and graft rejection. Early treatment with 5FU may be beneficial for these patients. Further studies with larger cohorts are needed to determine the best dosage of intracameral 5FU to treat this pathology.

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Patient consent

Written informed consent for information and images to be published was provided by the patient.

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