CASE REPORT

Sterile Corneal Perforation Following Corneal Collagen Cross-linking in a Patient with Down Syndrome

Jacob D Grodsky[1], Sean Edelstein[2]

Abstract

Aim and objective: To report a case of a patient with Down syndrome (DS) and keratoconus who experienced acute hydrops in one eye as well as sterile perforation requiring emergent tectonic penetrating keratoplasty following epithelium-off corneal collagen cross-linking (CXL) in the fellow eye.

Background: Keratoconus is a progressive, bilateral, corneal ectasia in which there is stromal thinning and apical protrusion of the cornea resulting in irregular astigmatism. This condition has been shown to have a disproportionately high association with DS. We describe a unique case that highlights this potentially rapidly progressive disease and its manifestations.

Case description: An 18-year-old male with history of DS presented with bilateral floppy eyelid syndrome and corneal ectasia as well as acute hydrops of the right eye (OD).

Medical management included 5% sodium chloride drops, prophylactic antibiotic ointment, and counseling against eye rubbing and to wear a Fox shield when sleeping. Worsening hydrops OD prompted intracameral injection of 20% SF_6 gas which hastened resolution of edema within 3 weeks. Residual severe corneal scarring, however, limited visual improvement to light perception. Meanwhile, progressive ectasia of the left eye (OS) prompted epithelium-off CXL procedure. Sterile corneal perforation was noted 4 days following uneventful surgery, necessitating emergency tectonic penetrating keratoplasty and temporary tarsorrhaphy.

Conclusion: This case illustrates that patients with DS and keratoconus are at especially high risk for rapidly progressive disease and for surgery-related complications.

Clinical significance: Patients with keratoconus, especially younger patients that can experience rapid progression, need to be closely monitored with early intervention but can still experience uncommon complications. Similar at-risk patients may be considered instead for investigational non-FDA-approved epithelium-on cross-linking, which should intuitively be associated with a lower risk of corneal perforation.

Keywords: Acute hydrops, Corneal collagen cross-linking, Corneal collagen cross-linking complications, Down syndrome, Keratoconus, Perforation.

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Background

Keratoconus is a progressive, bilateral, corneal ectasia in which there is stromal thinning and apical protrusion of the cornea resulting in irregular astigmatism. Pathogenesis theories associated with keratoconus include degradation of collagen content in the cornea, keratocyte apoptosis and decreased keratocyte cell density, oxidative stress, and altered enzyme activity including increased levels of proinflammatory cytokines IL-6 and TNF-α.[1]

Case Description

An 18-year-old African American male with Down syndrome (DS) presented with blurry vision, pain, increased tearing, and redness of the right eye (RE). Past medical history was significant for hypothyroidism, obstructive sleep apnea without current use of continuous positive airway pressure, asthma, seasonal allergies, and congenital heart disease with history of surgical repair of ventricular septal defect. Past ocular history included strabismus surgery to correct esotropia. Floppy eyelids and allergic facies were noted bilaterally. Figure 1 illustrates corneal ectasia with central hydrops RE, which progressed to affect over 80% of the cornea at follow-up and residual corneal scar formation with resolution of the hydrops following intracameral injection of 20% SF_6 gas.

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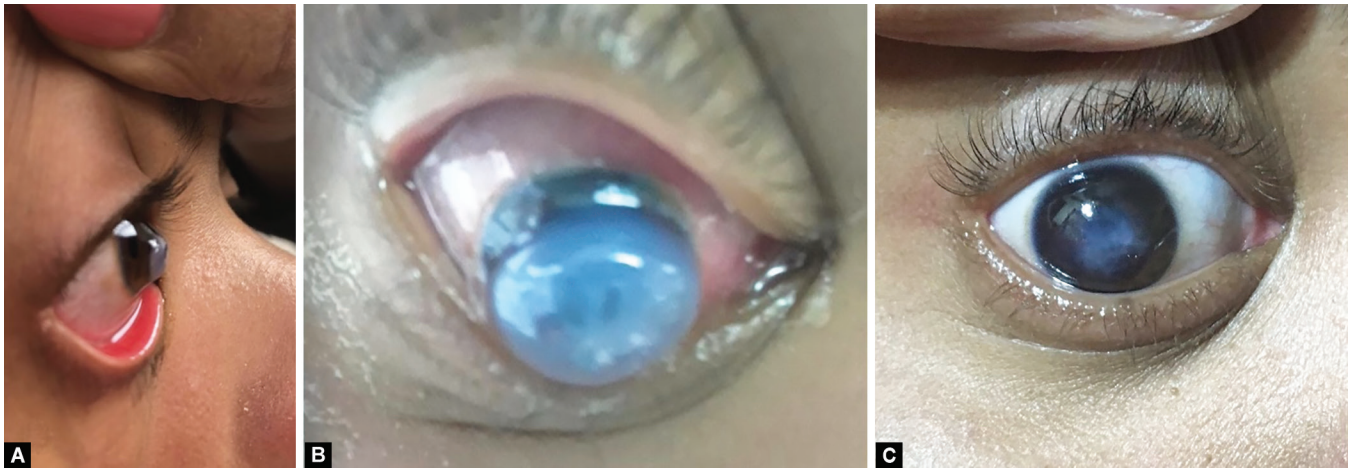
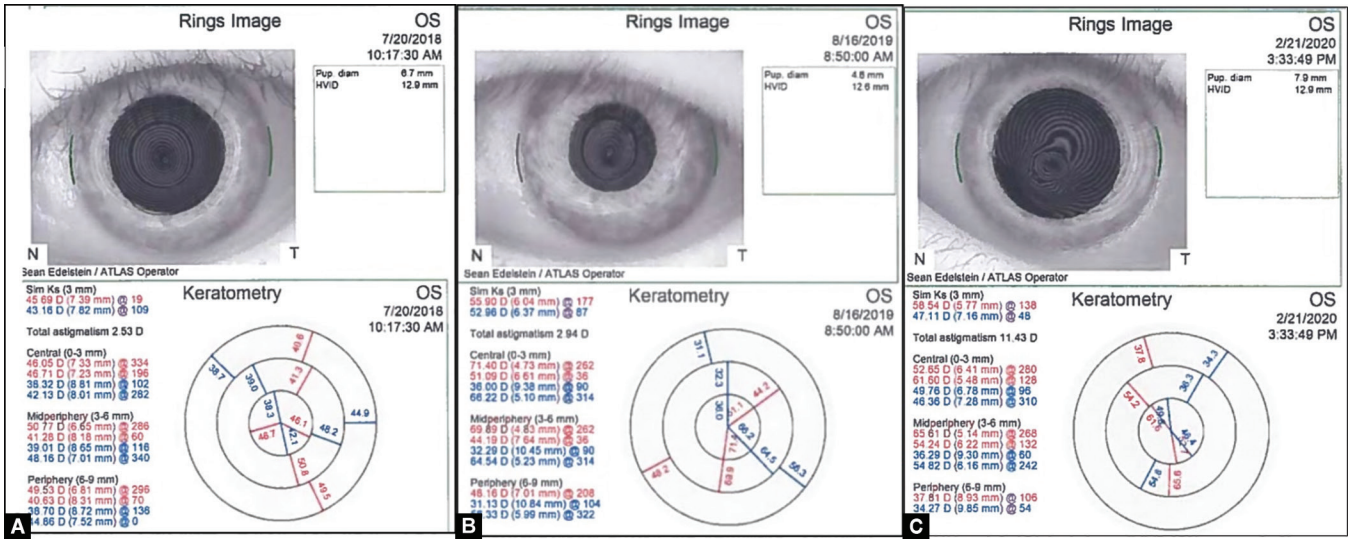
Uncorrected visual acuity (UCVA) was light perception at presentation and was unchanged following resolution of the hydrops. In the interim, the contralateral left eye (LE) had progressively deteriorated from UCVA of 20/60 to 20/100 and without corneal scarring noted on exam; Placido ring corneal topography SimK and Kmax values worsened from 45/43D and 50.8D, respectively, at baseline to 58/47 and 65D several months later (Fig. 2).

Therefore, epithelium-off corneal collagen cross-linking (CXL) treatment was performed in LE utilizing local anesthesia. Ultrasound pachymetry confirmed residual corneal thickness to be 451 µm prior to initiation of UVA treatment. Postoperative eyedrop regimen included moxifloxacin and prednisolone acetate 1% four times daily,

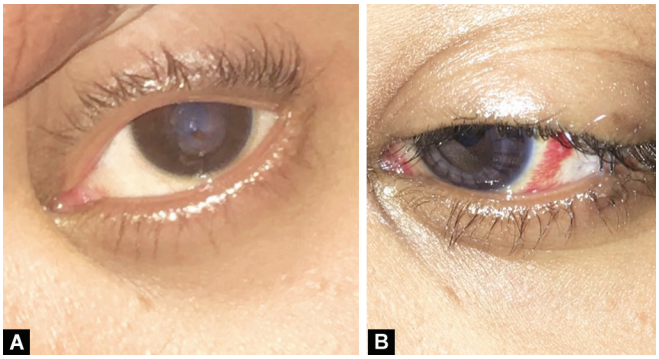


Figs 1A to C: External photographs of the right eye: (A) Acute hydrops affecting the central one-third of the cornea; (B) Progression to involve 80% of the cornea (10 days later); (C) Resolution of hydrops with residual corneal scarring following intracameral SF_6 injection



Figs 2A to C: Placido ring corneal topography of the contralateral left eye illustrating progressive disease over a 22-month period. SimK and Kmax values increased from (A) 45/43D and 50.8D (July 20, 2018); to (B) 55/52D and 71D (August 16, 2019); to (C) to 58/47D and 65D (February 21, 2020). Significant sequential worsening in distortion of the mires is appreciated

erythromycin ophthalmic ointment at bedtime, ketorolac two times daily only if needed for pain, and frequent preservative-free artificial tears. A bandage contact lens was placed, and the eye was patched with an eye pad and a Fox shield for the first day. Instructions were given to sleep with the shield on for the first week and to avoid eye rubbing. Four days following surgery, the patient's mother called noting a bubble had formed on the operated eye (Fig. 3A) with no associated redness, pain, or drainage. Slit-lamp exam revealed no bandage contact lens, a 4-mm central perforated ulcer without stromal infiltrate, Seidel positive leak, and a shallow anterior chamber. The patient and his mother denied any postoperative eye rubbing, nor the use of topical nonsteroidal anti-inflammatory or anesthetic eye drops. Attempted glue patch was unsuccessful, and an emergency tectonic penetrating keratoplasty (Fig. 3B) with temporary tarsorrhaphy was performed that same evening. Significant improvement in vision was noted, and UCVA was 20/60 RE by the 4-month follow-up.



Figs 3A and B: External photographs of the left eye: (A) Sterile corneal perforation occurring 4 days following epithelium-off corneal collagen cross-linking; (B) Emergency tectonic corneal transplant with temporary tarsorrhaphy

Discussion

Our patient displayed several typical features associated with keratoconus, which include disease presentation around puberty with progression into the third or fourth decade of life or later, as well as a disproportionately high association with DS, atopic disease/allergies, obstructive sleep apnea, and connective tissue disorders.[1]

In addition, corneal hydrops occurs in about 3% of keratoconic eyes and results from rupture of Descemet's membrane (DM), causing subsequent stromal hydration and edema. Pneumatic descemetopexy was first described in 1987 by Zusman et al.[2] to speed up recovery, however, with questionable vision benefit. Intracameral injection of air or gas (SF_6 or C_3F_8) is used to stretch and tamponade the detached DM, thus preventing further aqueous penetration and corneal edema. Our patient experienced rapid resolution of corneal edema within 3 weeks following 20% SF_6 injection; however, significant residual corneal scarring limited vision benefit.

Progression of disease in the contralateral eye prompted recommendation for our patient to undergo epi-off CXL, a procedure first described by Wollensak et al.[3] in 2003 and receiving FDA approval in 2016 for halting progression of corneal ectatic disease.[4] The premise of this procedure is to stiffen the cornea by creating new corneal collagen cross-links following application of riboflavin (vitamin B2) drops and stromal exposure to ultraviolet a light. CXL is not recommended for patients with a corneal thickness less than 400 µm because 85–90% of the UVA radiation is absorbed in the anterior 400 µm of the cornea, thus reducing potential damage to the corneal endothelium, lens, or retina.[5] Corneal perforation is a rare complication following CXL and has been reported in 10 eyes, including 6 cases of sterile keratolysis and 4 cases of microbial keratitis.[6–10] A report in German by Faschinger et al.[9] described bilateral corneal melt in a patient with DS with baseline central corneal thickness <400 mm. Müller et al.[11] found that histological changes following CXL included possible permanent keratocyte loss or repopulation of altered keratocytes as a mechanism leading to diminished stromal remodeling and sterile melt. Similarly, we hypothesize that the etiology of corneal perforation in our case was directly related to the CXL procedure and was not bound to happen anyway due to the fact that the keratoconus affecting his LE was not severe (Ks of 58/47D and Kmax 65D), there was no corneal scarring, and the patient had adequate residual corneal thickness. In addition, no other predisposing factors were identified in our case, such as eye rubbing, infection, or NSAID and anesthetic eyedrop use. Limitations of our report included (1) no pachymetry map (tomography) measurement was available, which can more precisely identify the thinnest corneal area corresponding to the apical cone, as compared with ultrasound pachymetry, and (2) no investigation and measurement of pro-inflammatory cytokines or enzymes activity were performed on the tissue, which could provide valuable insight into the pathophysiology of corneal melt following CXL. This may be an index for future investigations.

Keratoconus may be rapidly progressive in younger patients. Therefore, close monitoring and early intervention with CXL may be prudent. Suitable CXL candidates should be educated that although the procedure is generally benign, it is not without potential significant risk and may require keratoplasty. Patients with DS may be considered at especially high risk for rapidly progressive disease and for surgery-related complications. Sterile corneal perforation is an uncommon complication after epi-off CXL.

Clinical Significance

Patients with keratoconus, especially younger patients that can experience rapid progression, need to be closely monitored with early intervention but can still experience uncommon complications. Similar at-risk patients may be considered instead for investigational non-FDA-approved epithelium-on cross-linking, which should intuitively be associated with a lower risk of corneal perforation.

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