CASE REPORT

Late corneal acute hydrops in ineffective accelerated transepithelial corneal crosslinking in a patient with keratoconus

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A 20-year-old man with a very thin cornea developed acute hydrops with corneal thinning after accelerated transepithelial corneal crosslinking (CXL) for keratoconus. Because the corneal thinning and deformation were progressing, accelerated transepithelial CXL was performed in the right eye. However, corneal thinning still progressed after the procedure. After 3.5 years, blurred vision occurred suddenly and acute hydrops was diagnosed. With a pressure eye patch and ofloxacin ointment, the acute hydrops resolved 2 months after the onset. Corneal thickness and topographic change should be monitored carefully after accelerated transepithelial CXL, especially in patients with thin corneas.

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Corneal crosslinking (CXL) is an established method to halt the progression of corneal ectatic diseases such as keratoconus through photopolymerization of corneal collagen fibrils by ultraviolet-A (UVA) radiation combined with riboflavin. The standard CXL protocol involves delivery of 370 nm UVA radiation 1 cm from the cornea for 30 minutes (3 mW/cm²; total energy 5.4 J/cm²) after removal of the corneal epithelium and application of riboflavin. Transepithelial (epithelium-on [epi-on]) CXL was proposed in 2010 by Leccisotti and Islam to reduce postoperative complications such as infections, corneal haze, and corneal edema. More recently, an accelerated CXL method was established after development of a high-power UVA device. Accelerated transepithelial CXL is a combination of the previous techniques with the advantages of fewer complications and a shorter surgical time; it also controls progression of keratoconus.

Acute hydrops is a complication of keratoconus in which corneal stromal edema and acute visual disturbance are caused by leakage of aqueous humor through a break in Descemet membrane. The estimated incidence of acute hydrops among keratoconus patients is reported to be 1.43 per 1000. However, acute hydrops is rare after CXL and our literature search identified only 2 case reports; in both cases, the acute hydrops occurred after epithelium-off (epi-off) CXL.

We report a case in which the patient was diagnosed with keratoconus with a very thin cornea. Epi-on accelerated CXL was performed but failed to halt the progression of keratoconus. As a result, the patient developed late acute hydrops.

CASE REPORT

A 20-year-old man was referred to the University of Tokyo Hospital. Grade 4 keratoconus in the right eye was diagnosed according to the Amsler-Krumeich classification. At the first visit, corrected distance visual acuity (CDVA) with spectacles was 20/20. Anterior segment optical coherence tomography (AS-OCT) with an SS-2000 and CASIA2 (Tomey Corp.) showed that the thinnest corneal thickness, steep keratometry (K), flat K, average K, and maximum K were 389 μm, 57.8 diopters (D), 54.1 D, 55.9 D, and 63.4 D, respectively. After a 6-month follow-up, the thinnest corneal thickness decreased to 358 μm and the steep K increased to 63.6 D, showing the progression of the keratoconus.

Because the cornea was too thin for standard epi-off CXL, accelerated transepithelial CXL was performed. After application of riboflavin 0.25% with hydroxypropyl methylcellulose and benzalkonium chloride (ParaCel, Avedro, Inc.) for 4 minutes and riboflavin 0.22% (VIBEK S XTRA, Avedro, Inc.) for 6 minutes, the corneal thickness was measured. The intraoperative corneal thickness before UVA irradiation was 380 μm, which is within the institution’s safe limit. Hence, the procedure was continued with application of UVA irradiation of 30 mW/mm² for 3 minutes using a XKL system (Avedro, Inc.). The procedure was uneventful.

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The depth of the demarcation line from epithelium measured by AS-OCT was 153 μm 2 weeks after the accelerated transepithelial CXL procedure. During the postoperative follow-up, the maximum K was lower from the baseline, the average K and thinnest corneal thickness indicated gradual deterioration, which indicated that the procedure failed to halt progression of the keratoconus (Figure 1, A to C). Figure 1, D, shows the CDVA with contact lenses and the CDVA with spectacles over time.

Three years after the procedure, the contact lens CDVA, thinnest corneal thickness, steep K, flat K, average K, and maximum K were 20/50, 255 μm, 67.0 D, 60.0 D, 63.8 D, and 68.0 D, respectively (Figure 2, A). The patient suddenly developed blurred vision 3.5 years after the procedure after sleeping face down. The patient stated that he might have rubbed his right eye hard while sleeping. Slitlamp examination and AS-OCT showed corneal stromal edema with rupture and detachment of Descemet membrane. Accordingly, acute hydrops of the right eye was diagnosed (Figure 2, B). The patient was treated with a pressure eye patch and ofloxacin 0.3% ointment. By 2 months after the onset of acute hydrops, the Descemet membrane detachment and corneal stromal edema had resolved (Figure 2, C). Although corneal stromal opacity persisted, the CDVA with a hard contact lens improved from 20/50 before the onset of hydrops to 20/20 after its resolution. The cornea was flatter after the development of hydrops (mean K from 63.8 to 55.9 D and maximum K from 68.0 D to 59.9 D before and 3 weeks after onset of hydrops, respectively).

DISCUSSION

Our literature search of PubMed from 2002 (using the terms corneal crosslinking, CXL, corneal CXL, acute corneal hydrops, and acute hydrops) identified only 2 case reports of acute hydrops after CXL (Table 1). One report was of a 15-year-old boy with keratoconus and allergic conjunctivitis who had uneventful intrastromal corneal ring segment implantation and standard CXL. Three years later, acute hydrops and exacerbation of allergic conjunctivitis occurred. Because the acute hydrops never resolved and corneal edema persisted, penetrating keratoplasty was performed.
especially epi-on CXL in eyes with a very thin cornea. In the case of the 15-year-old boy, corneal thinning progressed, as in the current case. Thus, topography and corneal thickness must be carefully monitored in management of keratoconus, even after a CXL procedure.

In general, epi-on transepithelial CXL is more forgiving in eyes with thinner corneas because corneal epithelium debridement is unnecessary. On the other hand, a previous report found that the penetration of riboflavin into the corneal stroma was limited in the epi-on method because the epithelium is left in situ. In our case, the cornea was not thick enough for epi-off CXL; thus, the accelerated transepithelial CXL procedure was selected. However, despite the development of various techniques to improve the penetration of riboflavin solutions, in our case a shallow demarcation line was observed after accelerated transepithelial CXL. This implies that the accelerated transepithelial CXL procedure affected the collagen of the corneal shallow stromal layer only and not the deeper stromal layer. Thus, the procedure failed to halt deterioration of the keratoconus and the gradual progression of corneal thinning. Corneal stromal thickness is regarded as an anatomic predictive factor of acute hydrops. Therefore, continuous corneal thinning after accelerated transepithelial CXL might increase the probability of acute hydrops occurrence.

Eye rubbing is also known to be a risk factor for acute hydrops. This is presumably because eye rubbing is associated with elevation of intraocular pressure, which is thought to be associated with the mechanism of acute hydrops and corneal perforation. Hence, in the current case, eye rubbing and the patient’s posture during sleeping (sleeping on his front) might have increased the intraocular pressure, leading to acute hydrops.

In conclusion, we present a patient with keratoconus in whom epi-on accelerated transepithelial CXL failed to prevent corneal thinning and acute hydrops resulting from the progression of keratoconus. We believe this is the first reported case of acute hydrops after this procedure. Fortunately, corneal flattening after hydrops improved the patient’s CDVA. Even so, changes in corneal thickness and topography should be carefully monitored after CXL, especially epi-on CXL in eyes with a very thin cornea.

Table 1. Reports of acute hydrops after CXL for keratoconus.

| Study* | Case | Method | Condition | Outcome |
|--------|------|--------|-----------|---------|
| Antonios6 (2016) | 15-year-old male | Epi-off CXL + ICRS | Acute hydrops from allergic conjunctivitis | No resolution; keratoplasty required |
| Stock7 (2017) | 26-year-old female | Epi-off CXL | Acute hydrops during pregnancy after CXL | Resolution in 8 days |
| Current (2019) | 20-year-old male | Epi-on CXL | Acute hydrops after eye rubbing | Resolution in 2 months |

CXL = corneal crosslinking; Epi-off = epithelium-off; ICRS = intracorneal ring segment
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REFERENCES

1. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen cross-linking for the treatment of keratoconus. Am J Ophthalmol 2003; 135:620–627.
2. Lecicotti A, Islam T. Transepithelial corneal collagen cross-linking in keratoconus. J Refract Surg 2010; 26:942–948.
3. Wernli J, Schurnacher S, Spoerl E, Mrochen M. The efficacy of corneal cross-linking shows a sudden decrease with very high intensity UV light and short treatment time. Invest Ophthalmol Vis Sci 2013; 54:1176–1180.
4. Axioujuewu W, Usui T, Myia T, Toyono T, Sakisaka T, Yamagami S. Accelerated transepithelial corneal cross-linking for progressive keratoconus: a prospective study of 12 months. Br J Ophthalmol 2017; 101:1244–1249.
5. Barsam A, Petruszkin H, Brennan N, Bunce C, Xing W, Foot B, Tufts S. Acute corneal hydrops in keratoconus: a national prospective study of incidence and management. Eye 2015; 29:469–474.
6. Antonios R, Dirani A, Fadlallah A, Chelala E, Hamadeh A, Jarade E. Acute corneal hydrops 3 years after intra-corneal ring segments and corneal collagen cross-linking. Middle East Afr J Ophthalmol 2016; 23:156–159.
7. Stock RA, Thurné T, Bonamigo EL. Acute corneal hydrops during pregnancy with spontaneous resolution after corneal cross-linking for keratoconus: a case report. J Med Case Rep 2017; 11:53.
8. Krumreich JH, Daniel J, Leibend-Epikeratophakie und Tiefe Lamelläre Keratoplastik zur Stadiengerechten chirurgischen Behandlung des Keratoconus (KK) l–III (Live-epikeratophakia and deep lamellar keratoplasty for stage-related treatment of keratoconus). Klin Monbl Augenheilkd 1997; 211:94–100.
9. Biaocchi S, Mazzotta C, Cerretani D, Caporossi T, Caporossi A. Corneal crosslinking: riboflavin concentration in corneal stroma exposed with and without epithelium. J Cataract Refract Surg 2009; 35:893–899.
10. Raiškūp F, Pinét R, Spoerl E. Riboflavin osmolar modification for tranepithelial corneal cross-linking. Curr Eye Res 2012; 37:234–238.
11. Fuentes E, Sandali O, El Sanharawi M, Basli E, Hamiche T, Goemaere I, Borderie V, Bouharmoux N, Laroche L. Anatomic predictive factors of acute corneal hydrops in keratoconus: an optical coherence tomography study. Ophthalmology 2015; 122:1653–1659.
12. Fan Gaskin JC, Good WR, Jordan CA, Patel DV, McGhee CNJ. The Auckland keratoconus study: identifying predictors of acute corneal hydrops in keratoconus. Clin Exp Optom 2013; 96:208–213.
13. McMonnies CW. Management of chronic habits of abnormal eye rubbing. Contact Lens Anterior Eye 2008; 31:95–102.
14. McMonnies CW. Mechanisms for acute corneal hydrops and perforation. Eye Contact Lens 2014; 40:257–264.

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