



Case report

Alternaria keratitis after corneal crosslinking

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ABSTRACT

Purpose: To report a case of fungal keratitis after corneal collagen crosslinking (CXL) surgery.

Observations: We report a case of fungal keratitis after CXL for post-refractive surgery ectasia. The patient presented 12 days after surgery with a corneal ulcer that was culture positive for *Alternaria* species of fungus. She subsequently developed a bacterial superinfection. The keratitis resolved with medical therapy, although the patient required a penetrating keratoplasty (PKP) due to central corneal scarring.

Conclusions and Importance: To our knowledge, this is the first case of fungal keratitis as a complication after CXL in the United States and the first case of *Alternaria* infection after CXL using the Dresden protocol. Infectious keratitis is a rare but serious complication of CXL, and we suggest continued innovation of operative techniques that may reduce the risk of infectious keratitis.

1. Introduction

Corneal ectasia, or thinning with anterior bulging of the cornea, is a rare but well known complication of laser in situ keratomileusis (LASIK) resulting in progressive irregular astigmatism and decrease in visual acuity. Post-LASIK ectasia is linked to reduced biomechanical stability of the cornea.¹ Corneal CXL is a procedure to delay progression of ectasia by increasing corneal rigidity. Introduced by Wollensak et al., in 2003, CXL uses riboflavin and ultraviolet-A (UV-A) to induce covalent bond formation between collagen fibrils in the cornea.² It has since been used worldwide to treat keratoconus and related disorders like pellucid marginal degeneration, as well as ectasia arising post-refractive surgery. There are also reports of CXL demonstrating benefit in treatment of cases of microbial keratitis.³ CXL was approved by the Food and Drug Administration in April 2016 and is gaining widespread use in the U.S.

2. Case report

An otherwise healthy 57-year-old woman was referred to the Truhsen Eye Institute (TEI) at the University of Nebraska Medical Center for persistent corneal ulcer and anterior chamber hypopyon due to post-CXL fungal keratitis not resolving with topical antifungal therapy. The patient underwent CXL of the right eye (OD) using the Dresden protocol³ by the referring provider 48 days prior to treat post-refractive ectasia. A bandage contact lens (BCL) was placed post-operatively and routine postoperative topical drops were initiated

including prednisolone acetate 1%, gatifloxacin 0.5% and bromfenac 0.07%. Her preoperative best corrected visual acuity (BCVA) using rigid contact lenses was 20/30–2 OD using a Snellen eye chart. The patient presented back to the provider on postoperative day (POD) 1 with a central epithelial defect and her BCL still in place. The BCL was removed without complication on POD 5. On POD 12, the patient complained of blurry vision, photophobia, redness and soreness in the treated eye. A corneal infiltrate was noted (Fig. 1), and topical cefazolin 50 mg/mL and tobramycin 10 mg/mL were started. Cultures were obtained POD 13. On POD 20, due to increasing central infiltrate density, she was started empirically on natamycin 5% and voriconazole eye drops for possible fungal keratitis. Culture results with sensitivities were finalized POD 32 and demonstrated *Alternaria* species of fungus. Natamycin and voriconazole were stopped, and itraconazole and amphotericin B eye drops were started based on antifungal susceptibility testing. Her fungal infiltrate showed significant improvement by POD 46. However, increasing corneal opacification and persistence of her hypopyon led to referral to TEI.

Upon referral on POD 48, best uncorrected visual acuity (UCVA) in the right eye was counting fingers at one inch. Examination of the right eye revealed a 5.0 mm × 4.0 mm corneal ulcer with infiltrate, feathery edges and filamentary extension superiorly into mid-deep stroma. The eye also had 2+ injection of the conjunctiva and a 10% hypopyon in the anterior chamber. The patient was instructed to continue the itraconazole and amphotericin B. She was also started on 200 mg oral voriconazole twice daily, as well as moxifloxacin eye drops every 2 h for possible bacterial superinfection. Subsequent corneal culture was

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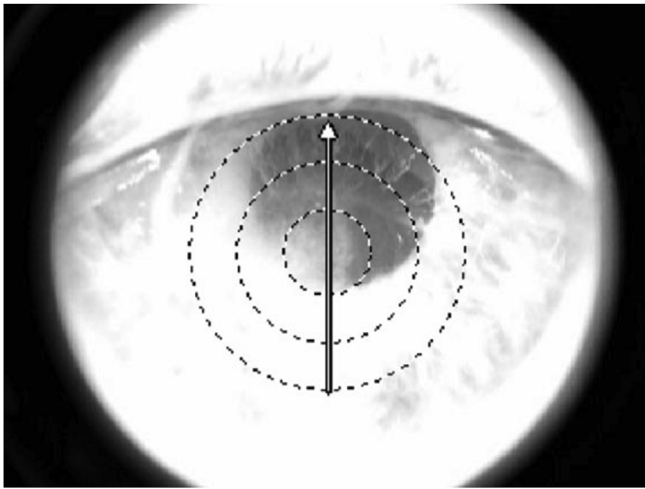


Fig. 1. Corneal infiltrate on POD 12. The photo shows infiltrate in the inferotemporal quadrant of the right eye.

positive for pan-sensitive *Staphylococcus haemolyticus*.

The hypopyon resolved with medical treatment POD 62, and the patient had a BCL inserted on POD 67 due to persistent epithelial defect. Due to central corneal scarring and persistent poor vision otherwise without hope of recovery, PKP was performed 92 days post-CXL. Corneal button pathology was negative for fungal or bacterial elements. At one-month postoperative follow-up, the epithelial defect was closed, and the patient had an UCVA of 20/400 in the right eye. At 11 months post-PKP and 14 months post-CXL, her BCVA was 20/25 with a scleral contact lens OD.

3. Discussion

Infectious keratitis is a rare complication of corneal CXL, with previously reported rates as low as 0.0017%,⁴ and post-CXL fungal keratitis is especially rare. Previously reported infections after CXL using the Dresden protocol include the bacteria *Staphylococcus epidermidis*,⁵ *S. aureus*,⁶ *Escherichia coli*⁷ and *Pseudomonas aeruginosa*,⁸ the herpes virus,⁹ *Acanthamoeba*¹⁰ and the fungi *Fusarium*¹¹ and *Microsporidia*.¹² The *Fusarium* and *Microsporidia* cases occurred in Spain and India, respectively. To our knowledge, this is the first case of fungal keratitis as a complication after CXL in the United States and the first case of *Alternaria* infection after CXL using the Dresden protocol. Maharana et al.¹³ recently reported three cases of fungal keratitis at a tertiary center in India following accelerated CXL, a protocol that delivers higher power UV-A radiation over a shorter duration than the Dresden protocol. These cases included one case of *Alternaria* keratitis, one case of coagulase-negative *Staphylococcus* and *Aspergillus fumigatus* co-infection and one case of *S. aureus* and *Mucor* co-infection. Notably, the patient with *Alternaria* keratitis presented three days after aCXL with an ulcer that progressed to corneal perforation despite medical therapy and required PKP. All three cases were pediatric patients, and the study authors hypothesized that young age could be a risk factor for post-CXL infection in developing countries due to poor compliance and postoperative care.

4. Conclusions

In a systematic review, Hsiao et al. identified preexisting corneal disease or previous ocular surgery to be a risk factor for *Alternaria* keratitis.¹⁴ The factors that place our patient at higher risk for this

infection include prior refractive surgery, corneal ectasia, a post-operative epithelial defect that is routine in the Dresden protocol, and standard use of postoperative topical steroid. Of note, our patient was compliant with her post-operative drop regimen and was noted to have good ocular hygiene. Fungal keratitis should be on the differential for an otherwise healthy patient who presents with a corneal infiltrate after CXL. Infectious keratitis is a rare but serious complication of CXL, and we suggest continued innovation of operative techniques that may reduce the risk of infectious keratitis.

Patient consent

The patient consented to publication of the case orally. This report does not contain any personal information that could lead to the identification of the patient.

Authorship

All authors attest that they meet the current ICMJE criteria for authorship.

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Declaration of competing interest

None of the authors have any financial disclosures related to this submission.

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References

- Bohac M, Koncarevic M, Pasalic A, et al. Incidence and clinical characteristics of post LASIK ectasia: a review of over 30,000 LASIK cases. *Semin Ophthalmol.* 2018;33:869–877.
- 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.
- Papaioannou L, Milligkos M, Papatthanassiou M. Corneal collagen cross-linking for infectious keratitis: a systematic review and meta-analysis. *Cornea.* 2016;35:62–71.
- Shetty R, Kaweri L, Nuijts RM, Nagaraja H, Arora V, Kumar R. Profile of microbial keratitis after corneal collagen cross-linking. *BioMed Res Int.* 2014;2014 340509.
- Pérez-Santonja JJ, Artola A, Javaloy J, Alió' JL. Microbial keratitis after corneal collagen crosslinking. *J Cataract Refract Surg.* 2009;35 1138–1114.
- Rana M, Lau A, Aralikatti A, Shah S. Severe microbial keratitis and associated perforation after corneal crosslinking for keratoconus. *Contact Lens Anterior Eye.* 2015;38:134–137.
- Pollhammer M, Cursiefen C. Bacterial keratitis early after corneal crosslinking with riboflavin and ultraviolet-A. *J Cataract Refract Surg.* 2009;35:588–589.
- Sharma N, Maharana P, Singh G, Titiyal JS. Pseudomonas keratitis after collagen crosslinking for keratoconus: case report and review of literature. *J Cataract Refract Surg.* 2010;36:517–520.
- Kymionis GD, Portaliou DM, Bouzoukis DI, et al. Herpetic keratitis with iritis after corneal crosslinking with riboflavin and ultraviolet A for keratoconus. *J Cataract Refract Surg.* 2007;33:1982–1984.
- Rama P, Di Matteo F, Matuska S, Paganoni G, Spinelli A. Acanthamoeba keratitis with perforation after corneal crosslinking and bandage contact lens use. *J Cataract Refract Surg.* 2009;35:788–791.
- Garcia-Delpech S, Díaz-Llopis M, Udaondo P, Salom D. Fusarium keratitis 3 weeks after healed corneal cross-linking. *J Refract Surg.* 2010;26:994–995.
- Gautam VJ, Jhanji V, Satpathy G, Khokhar S, Agarwal T. Microsporidial keratitis after collagen cross-linking. *Ocul Immunol Inflamm.* 2013;21:495–497.
- Maharana PK, Sahay P, Sujeeth M, et al. Microbial keratitis after accelerated corneal cross-linking in keratoconus. *Cornea.* 2018;37:162–167.
- Hsiao CH, Yeh LK, Chen HC, et al. Clinical characteristics of *Alternaria* keratitis. *J Ophthalmol.* 2014;2014 536985.