CASE REPORT

# Sterile corneal infiltrates after simultaneous photorefractive keratectomy and corneal crosslinking

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We report 3 eyes with corneal sterile infiltration after simultaneous photorefractive keratectomy (PRK) and corneal crosslinking (CXL). Case 1 (2 eyes) was a 23-year-old woman who requested refractive surgery for myopic astigmatism in both eyes. Because the thinnest location was less than 500 µm and there was inferior steepening in the left eye, simultaneous PRK and CXL were performed. One day postoperatively, the right eye showed infiltrates at the deepithelialized ablated cornea. Treatment was started with moxifloxacin 0.5% hourly and fluorometholone 0.1% 5 times a day. After 4 days, the epithelium healed with central corneal opacification. In Case 2, the postoperative condition was similar to that in Case 1; however, the treatment was moxifloxacin 0.5% 5 times a day and prednisolone hourly. After 5 days, the infiltrates disappeared and the center of the cornea was clear. Sterile corneal infiltrates are uncommon complications after simultaneous PRK and CXL. Early topical steroid treatment might prevent central corneal scar formation.

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Although the technology combining corneal crosslinking (CXL) with photorefractive surgeries has many advantages, these types of procedures have not yet been widely performed in clinical practice. This can be explained by a number of undesired side effects of CXL related to the adding effect of corneal exposure to ultraviolet (UV) radiation.[1–3] It was assumed that combined application of prophylactic CXL and transepithelial photorefractive keratectomy (PRK) would have a positive effect on refractive outcomes and posterior corneal elevations.[4]

Several complications of CXL have been reported. These include haze,[5] infectious and sterile keratitis,[5–8] corneal melting,[9] and diffuse lamellar keratitis.[10] We report 2 cases of sterile corneal infiltrates after combined PRK with accelerated CXL.

## CASE REPORTS

### Case 1

A 23-year-old woman desired refractive surgery for myopic astigmatism error in both eyes. The uncorrected distance visual acuity (UDVA) in the left eye was 6/120 with a refraction of −3.50 −1.75 @ 110 corrected to 6/12. The thinnest location was less than 500 µm in the left eye, which showed inferior steepening. Thus, the decision was made to perform simultaneous PRK and CXL.

Under strict sterile conditions using topical anesthesia, transepithelial PRK was performed using an excimer laser (Visx Star S4 IR, Abbott Medical Optics, Inc.). Then, mitomycin-C 0.02% was applied to the ablated corneal surface for 20 seconds; this was followed by a thorough wash with a balanced salt solution. The patient was then treated with riboflavin 0.1% with hydroxypropyl methylcellulose (Vibex Rapid, Avedro, Inc.) applied to the corneal surface and spread with an irrigating cannula for 1.5 minutes. After the soaking, the corneal surface was washed thoroughly with a balanced salt solution. An unltraviolet-A (UVA) beam (wavelength, 365 nm) 9.0 mm in diameter was applied to the cornea in a continuous fashion in a uniform circular pattern using the CXL device (Avedro, Inc.). The UVA exposure was performed for 90 seconds at a power of 30 mW/cm$^2$ (total dose 2.7 J/cm$^2$).

At the end of the procedure, topical gatifloxacin 0.50% eyedrops were instilled and a bandage soft contact lens was fitted. Postoperatively, gatifloxacin 0.50% and fluorometholone 0.1% eyedrops were prescribed 5 times daily.

One day postoperatively, slitlamp examination of the right eye showed infiltrates at the deepithelialized ablated cornea extending outside the thickened whitish margin of area of ablation. There was no blepharospasm or ciliary injection. Corneal scraping was performed, and the specimen was sent for Gram and Giemsa staining; the results were negative. Bacterial and viral cultures were performed, and treatment was started while waiting for the results of the culture, which were also negative.

Treatment was started in the form of broad-spectrum topical antibiotic moxifloxacin 0.5% hourly with topical steroid therapy in the form of fluorometholone 0.1% eyedrops 5 times daily. The follow-up was done daily for the fear of imminent infection. After 4 days of this treatment, the epithelium started to heal, with dense opacification at the area of ablation (Figure 1). On follow-up, the area of opacification regressed with time, leaving a central rounded scar that necessitated penetrating keratoplasty.

### Case 2

A 36-year-old woman sought refractive surgery for myopic astigmatism in both eyes. The UDVA was 6/60 with a refraction

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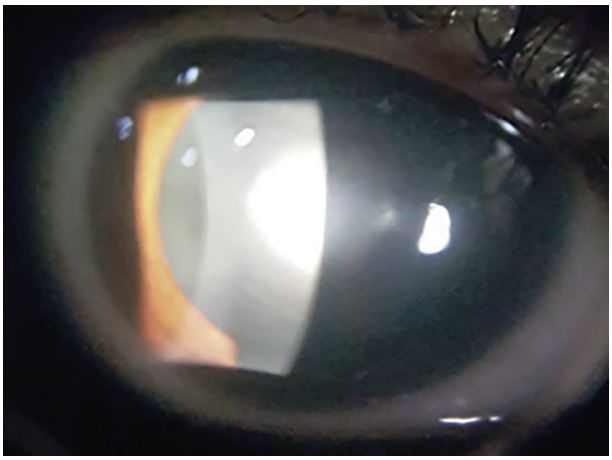

**Figure 1.** Dense area of corneal scar at the area of ablation.

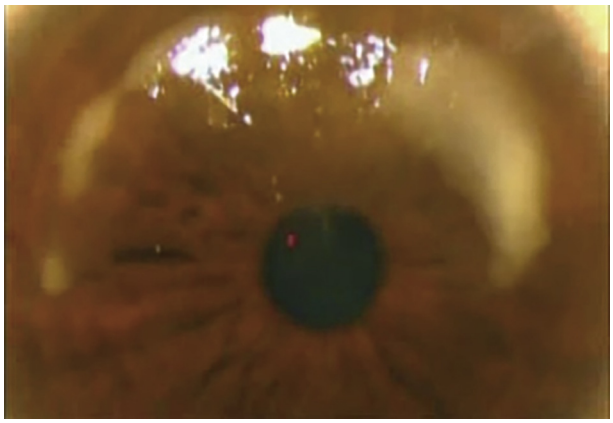

**Figure 2.** Thickened white masses at the margin of area of ablation with infiltrates at the ablated area.

of −1.00 −3.75 @ 98 in the right eye and −3.00 −1.25 @ 90 in the left eye. The corrected distance visual acuity (CDVA) was 6/10 in both eyes. Posterior elevation was noted on examination with a rotating Scheimpflug camera (Pentacam, Oculus Optikgeräte GmbH). Thus, the decision was made to perform simultaneous PRK and CXL.

Under strict sterile conditions using topical anesthesia, transepithelial PRK with accelerated CXL in the same session were performed. One day postoperatively, slitlamp examination of both eyes showed thickened white masses at the margin of the area of ablation with infiltrates at the ablated area (Figure 2); there was no blepharospasm or ciliary injection. Corneal scraping was performed, and the specimen was sent for Gram and Giemsa staining; the result was negative. Bacterial and viral cultures were done, and treatment was started while waiting for the results of the culture, which were also negative.

Treatment was commenced in the form of broad-spectrum topical antibiotic moxifloxacin 0.5% 5 times daily with frequent topical steroid therapy in the form of prednisolone eyedrops hourly. The follow-up was performed daily for fear of imminent infection. After 5 days, the epithelium started to heal, with regression of the infiltrates and a faint island of opacification at the margin of the ablation area. The center of the cornea was then clear (Figure 3).

## DISCUSSION

Corneal crosslinking with riboflavin and UVA is a safe and effective surgical procedure for cases of keratoconus with few reported complications.[11] The 2 common protocols for CXL are standard and the accelerated. In accelerated CXL, a high-energy setting (up to an irradiance of 30 mW/cm) is used versus an irradiance of 3 mW/cm for standard CXL, shortening the treatment duration from 30 minutes to as few as 3 to 10 minutes while maintaining the total radiant exposure (5.4 J/cm).[12] Several recent studies[13–16] have compared the 2 protocols. All agreed that accelerated protocols, in particular 9 mW/cm$^2$, might be a safe and effective alternative to standard CXL in stabilizing corneal ectatic disease. Also, they concluded that a larger population and a longer follow-up period are needed.

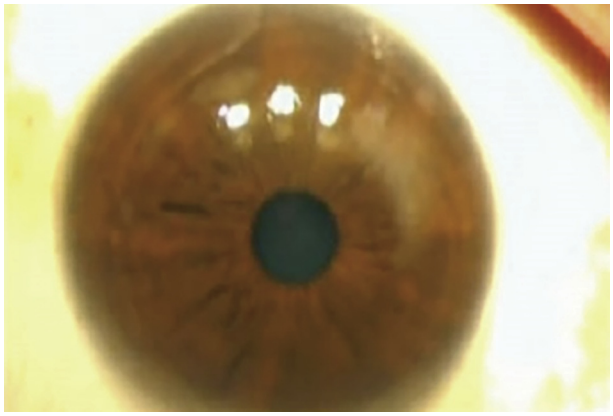

**Figure 3.** Faint island of opacification at the margin of ablation area with clear central cornea.

However, CXL is not a completely safe technique. Several case reports and original studies report complications ranging from insignificant stromal haze to sight-threatening haze and infectious keratitis and noninfectious corneal melting.[1,2] Sterile corneal infiltrates are an uncommon complication after CXL, although they have been reported.[17,18]

Also, corneal infiltrates after PRK have also been reported, and they can be infectious and sterile and can affect vision.[19] Peripheral sterile corneal infiltrates have been reported after PRK.[20,21]

Güell et al.[22] reported a visually significant deep stromal scar that occurred 5 months after uneventful combined CXL and PRK in a case of forme fruste keratoconus.

Because of the negative results of staining and cultures in our 2 cases, sterile keratitis was the only explanation for what occurred. Theories for possible etiologies of sterile keratitis include changes in immune responses to the crosslinked proteins[17] and enhanced cell-mediated immunity to staphylococcal antigen deposition in areas of static tear film pooling beneath the bandage contact lens.[6] Contact lens–induced hypoxia can also lead to sterile corneal infiltrates.[21,23]

In Case 1, we used a usual dose of mild topical steroids and the infiltration left a dense scar. However in Case 2, we used a more potent and more frequent dose of topical steroids and the cornea ended up having a clear center.

In conclusion, sterile corneal infiltrates are an uncommon complication after simultaneous PRK with accelerated CXL. Infection should be excluded by staining and cultures combined with clinical correlation. Early topical steroid

treatment might save the cornea from inevitable central scar formation.

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