



Case report

Late onset corneal haze after corneal cross-linking for progressive keratoconus



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ARTICLE INFO

Keywords:

Corneal haze
Corneal crosslinking
Keratoconus

ABSTRACT

Purpose: To present the case of a patient that underwent corneal crosslinking for progressive keratoconus and 18 months later revealed clinically significant corneal stromal haze.

Observations: A 20-year-old male presented with progressive visual loss OU for the past few years. His corrected distance visual acuity (CDVA) OD was 20/30 (−2.75 −1.75 @55) and OS 20/30 (−0.50 −1.75@110). Corneal topography revealed keratoconus OU and the patient underwent corneal crosslinking according to the Dresden Protocol. The postoperative regimen included combined tobramycin and dexamethasone qid along with lubrication until epithelium healed and then fluorometholone qid with weekly tapering. At 3 months postoperatively, his topography was stable and his corrected distance visual acuity (CDVA) was 20/25 OU. On slit lamp examination, only clinically insignificant stromal haze was observed. At 18 months postoperatively, the patient reported vision deterioration. On examination his CDVA was 20/25 in right eye, and 20/40 in his left eye. Deep stromal haze was revealed in his central cornea, more dense in his left eye. Corneal topography was stable and the CDVA loss was attributed to the notable deep stromal haze. The patient was treated with dexamethasone qid with biweekly tapering. 18 months after corneal crosslinking, the patient demonstrated clinically significant stromal haze, most prominent OS. He was treated with dexamethasone qid. One month later his CDVA OS gradually improved to 20/25, and stromal haze was still noted but less dense.

Conclusions and importance: Late-onset deep corneal haze is a possible complication of corneal crosslinking in keratoconic patients.

1. Introduction

Corneal Cross-linking (CXL) is becoming an increasingly popular technique for the treatment of corneal ectatic disorders.^{1–4} However, although the technique has been proven to be effective, the stabilization of cornea ectasia, occurring after CXL, is accompanied by changes in microscopic structure and properties of the cornea.^{5–8}

According to corneal confocal microscopy studies, there is an immediate keratocyte desertion after CXL, followed by repopulation by activated keratocytes as early as 2 months postoperatively.^{9,10} It is possible that these activated keratocytes contribute to the development of CXL-associated corneal haze. Other factors that may contribute to CXL-associated corneal haze include stromal swelling pressure changes,¹¹ proteoglycan-collagen interactions,¹² and glycosaminoglycan hydration.¹³ Greenstein et al. studied the natural history of corneal haze after CXL and found that corneal haze has a peak at 1 month after CXL, reaches a plateau between 1 and 3 months, begins to clear 3–6 months after the procedure, and continues to decrease

between 6 months and 1-year post-CXL.⁵

Herein, we report a case of late-onset deep corneal haze, which developed 18 months after CXL in a young patient with keratoconus and significantly affected vision. The case was documented with corneal confocal microscopy and treated successfully with topical steroids.

2. Case report

A 20-year old male presented to our clinic with progressive visual loss OU for the past few years. The patient had no past medical history. His previous ophthalmic history included use of spectacles for myopia and astigmatism bilaterally.

His corrected distance visual acuity (CDVA) at presentation was 20/30 (manifest refraction, MR: −2.75 −1.75 @55) in the right eye and 20/30 (MR: −0.50 −1.75@110) in the left eye. Slit lamp examination of anterior and posterior segment revealed no remarkable findings. Corneal topography and pachymetry revealed keratoconus bilaterally (Fig. 1).

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<https://doi.org/10.1016/j.ajoc.2019.02.008>

Received 28 September 2018; Received in revised form 23 January 2019; Accepted 19 February 2019

Available online 26 February 2019

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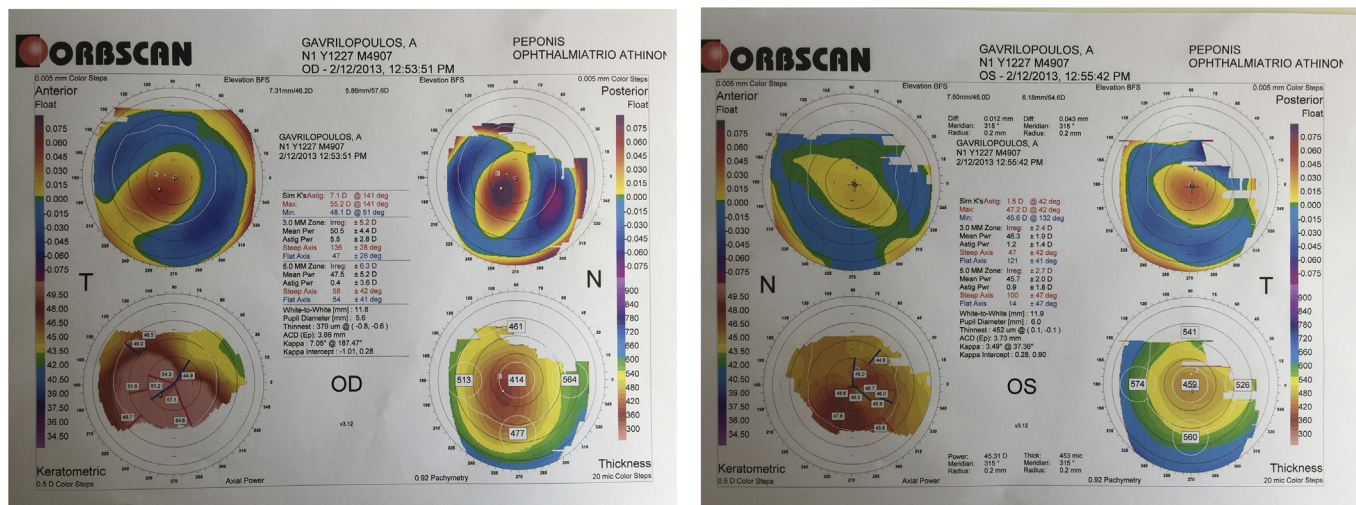


Fig. 1. Corneal topography. Keratoconus bilaterally.

Taking into consideration the young age of the patient and the self-reported visual acuity decline over the past years, we decided to perform CXL, in order to halt the progression of keratoconus. The procedure was uncomplicated. It was performed according to the Dresden Protocol bilaterally.⁷

The postoperative regimen included combined tobramycin and dexamethasone qid along with lubricant eye drops until epithelium healed and then fluorometholone qid with weekly tapering. At 3 and 6 months postoperatively, his topography was stable and his corrected distance visual acuity (CDVA) was 20/25 OU. On slit lamp examination, only trace stromal haze was observed.

At 18 months postoperatively, the patient reported vision deterioration. On examination his CDVA was 20/25 in right eye, and 20/40 in his left eye. Deep stromal haze was observed in his central cornea, more prominent in his left eye. Corneal topography was stable and the CDVA loss was attributed to the notable deep haze (Fig. 2). Corneal confocal microscopy revealed activated keratocytes and linear hyperreflective structures in the posterior stroma (Fig. 3).

The patient was treated with dexamethasone qid with biweekly tapering. One month later his CDVA OS gradually improved to 20/25, and stromal haze was still noted but less dense (Fig. 4).

3. Discussion

In this report we present a case of a young patient, who developed visually significant stromal haze after CXL in the late postoperative

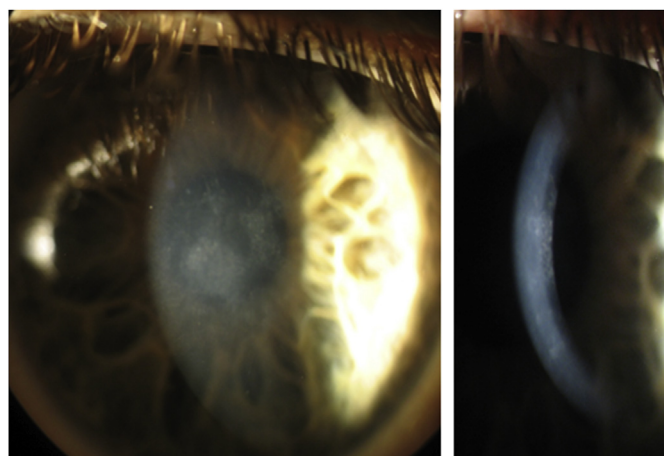


Fig. 2. Slit-lamp photos of the left eye. Deep stromal haze.

period. Contrary to our case, early onset clinically non-significant corneal haze is very common after CXL and considered by some authors to be part of the natural history of the condition after the procedure.^{7,14}

In a study by Greenstein et al., haze was measured by both Scheimpflug densitometry and slit-lamp assessment and it was found to increase postoperatively. The rise peaked at 1 month and reached its plateau between 1 and 3 months. Consequently, between 3 and 6 months, the cornea began to clear and there was a significant decrease in CXL-associated corneal haze. From 6 months to 1 year postoperatively, there continued to be a decrease in haze measurements.⁵ A few other studies also revealed a similar clinical appearance of post-CXL haze, however, nearly all cases of this corneal haze were clinically insignificant.^{7,15,16}

As far as late-onset corneal haze after CXL, Omary R et al. reported a case of a clinically significant corneal haze that appeared 11 months after CXL and persisted with only slow and incomplete clearing with topical steroid treatment.¹⁴ In our patient, clinically significant corneal haze appeared in the late postoperative period, 18 months after CXL, and treated successfully with topical steroids.

According to a study by Koppen et al., clinically significant corneal haze appears in about 8.6% of eyes after CXL,¹⁵ and it may persist for over a year after treatment.¹⁶ Authors suggest that advanced keratoconus should be considered at higher risk of haze development after CXL due to low corneal thickness and high corneal curvature.¹⁷

The haze after CXL differs from the haze after PRK in stromal depth. Whereas haze after PRK is strictly subepithelial, haze after CXL extends into the stroma, on average equal to an absolute depth of 300 μm. Additionally, clinical characteristics of haze differ between procedures, since haze after CXL is compiled by hyper-reflective structures and dust-like changes in the mid-stroma, whereas haze after PRK has a more reticulated subepithelial appearance.³ The haze may be associated with the depth of CXL into the stroma as well as the amount of keratocyte loss.^{13,18,19} Typically, late permanent scarring should be differentiated from the early postoperative temporary haze which is often paracentral and compatible with good visual results.⁴ It may not be actually related to CXL itself but rather to the ongoing disease process and corneal remodeling.¹⁶

In conclusion, this case demonstrates that late-onset, clinically significant, deep corneal haze is a possible complication of CXL in patients with keratoconus. A few cases have been described after PRK and lasek,²⁰ but to our knowledge, there is only one other case report that presented this complication after CXL in a patient with keratoconus. More evidence-based research is needed in order to clarify and confirm the mechanism of such late-onset corneal haze.

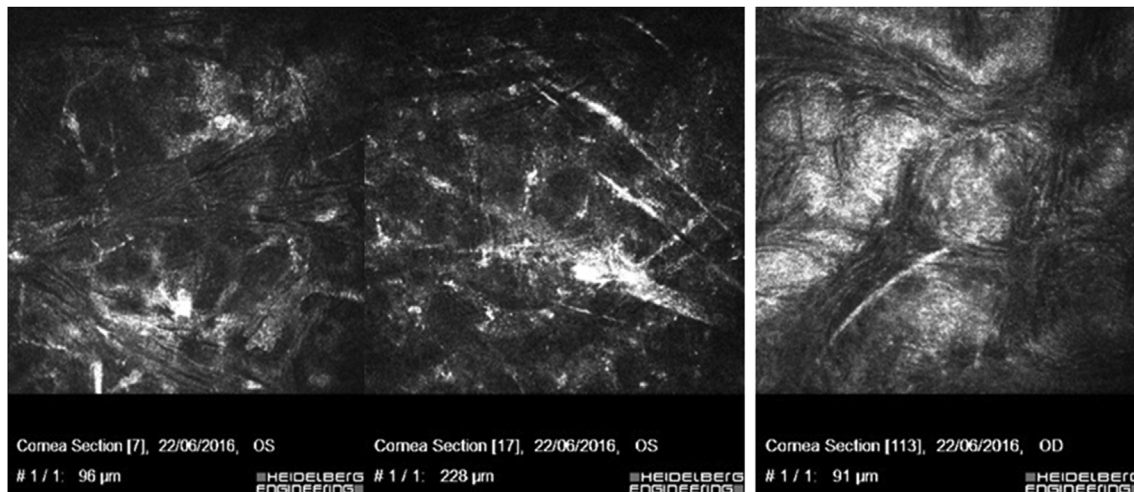


Fig. 3. Corneal confocal microscopy. Activated keratocytes and linear hyperreflective structures in the posterior stroma.

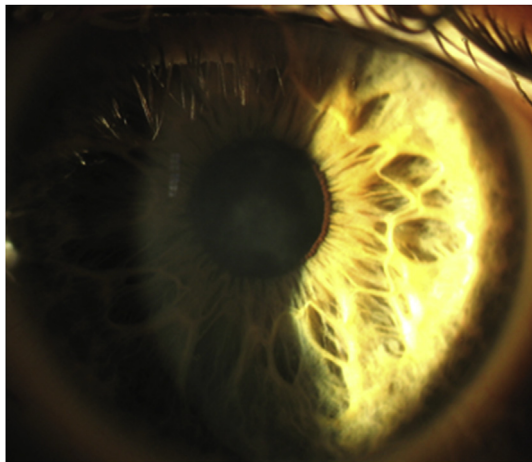


Fig. 4. Slit-lamp photos of left eye after treatment. Stromal haze but less dense.

Acknowledgements and disclosures

Funding: No funding or grant support

Conflicts of interest: The following authors have no financial disclosures: V.P, L.K., I.C., G.K., E.P.

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

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.ajoc.2019.02.008>.

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