

Erase the haze: Resolution of Immediate Corneal Stromal Haze Following CXL: A Case Report

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Abstract: Corneal collagen cross-linking (CXL) is a standard treatment to halt the progression of keratoconus. While generally safe, early postoperative complications such as stromal haze can significantly affect visual outcomes. We report a case of immediate-onset stromal haze developing one month after accelerated CXL in a 16-year-old male with keratoconus. The patient underwent uneventful CXL in the left eye, following which he developed significant central stromal haze accompanied by corneal flattening. Initiation of aggressive topical corticosteroid therapy with 1% prednisolone acetate resulted in a marked reduction in haze, with corresponding clinical improvement. This case underscores the importance of close postoperative monitoring and highlights the efficacy of early, intensive corticosteroid therapy in managing acute stromal haze following CXL. Timely intervention may optimize visual recovery and minimize long-term sequelae. Further studies are warranted to establish standardized treatment protocols for such early complications.

Keywords: Corneal collagen cross-linking, Keratoconus, Stromal haze, Corticosteroids

1. Introduction

Keratoconus is a non-inflammatory, progressive ectatic disorder characterized by corneal thinning, irregular astigmatism, and visual impairment (1). Corneal collagen cross-linking (CXL) has become the standard intervention to halt the progression of keratoconus by enhancing the biomechanical strength of the cornea through the induction of covalent bonds between collagen fibers (2,3). Although generally considered safe and effective, CXL may be associated with early postoperative complications, including corneal stromal haze, which can impact visual outcomes (4). The incidence and severity of stromal haze can vary depending on factors such as treatment protocol (standard vs. accelerated), patient age, and healing response. In this report, we present a case of significant corneal stromal haze developing one month after accelerated CXL in a young patient, which was successfully managed with intensive topical corticosteroid therapy.

2. Case Presentation

A 16-year-old otherwise healthy male presented with a one-year history of painless, progressive diminution of vision in both eyes, accompanied by frequent spectacle prescription changes. He also reported habitual eye rubbing. On examination, uncorrected distance visual acuity (UDVA) was 5/60 in both eyes, improving to 6/9 with correction. Slit-lamp examination showed prominent papillae on the upper tarsal conjunctiva of both eyes, along with a steep cornea and presence of a Fleischer's ring, suggestive of keratoconus. Corneal tomography using a Scheimpflug imaging system (Pentacam Oculyzer; Oculus Optikgeräte GmbH, Heidelberg, Germany) showed thinnest corneal thickness

(TCT) of 486 μm (right eye) and 497 μm (left eye) with keratometry readings of K1 45.0 D, K2 46.0 D in the right eye, and K1 45.1 D, K2 46.9 D in the left eye. Based on clinical and topographic findings, a diagnosis of stage 1 keratoconus was made, and the patient was scheduled for corneal collagen cross-linking (CXL), starting with the left eye.

The left eye underwent uneventful accelerated CXL (9 mW/cm² for 10 minutes, total energy 5.4 J/cm²) under sterile conditions. Postoperatively, the patient was started on moxifloxacin 0.5% eye drops six times daily. At the one-week follow-up, dense stromal edema with Descemet's membrane folds was observed. Following confirmation of complete epithelial healing, loteprednol etabonate 0.5% eye drops were initiated four times daily, and the patient was re-evaluated after five days. A reduction in stromal edema was noted; however, there was significant central corneal stromal haze (Figure 1A), accompanied by corneal flattening and decreased uncorrected distance visual acuity (UDVA) of 3/60. These findings were corroborated by Pentacam tomography and anterior segment optical coherence tomography (AS-OCT). The treatment regimen was then escalated to intensive topical corticosteroid therapy with prednisolone acetate 1% four times daily in a weekly taper, along with sodium hyaluronate 0.1% four times daily.

Subsequent follow-up revealed marked improvement (Figure 1B). Serial clinical exams, Pentacam, and AS-OCT scans (Figure 2) showed progressive resolution of stromal haze. At six months postoperatively, UDVA improved to 6/36, and corrected distance visual acuity (CDVA) was 6/6p. A faint anterior stromal scar remained, which had nearly resolved by the end of one year.

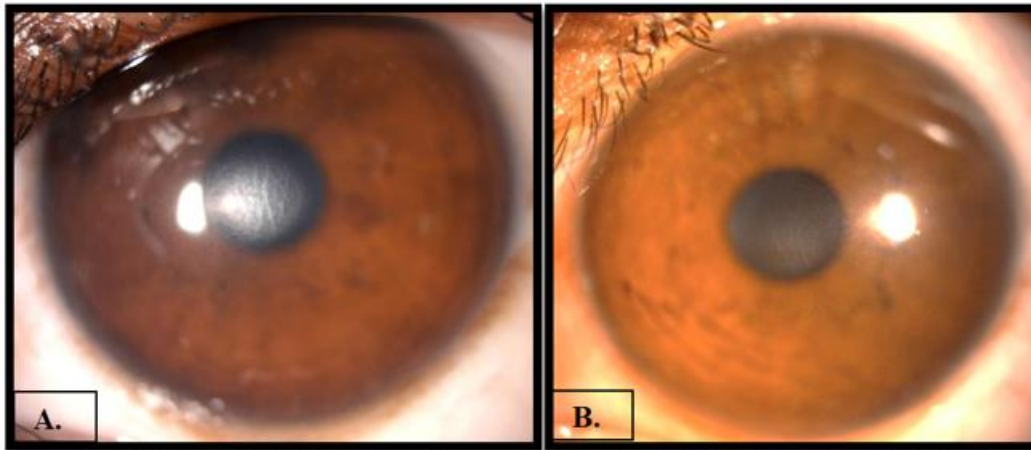
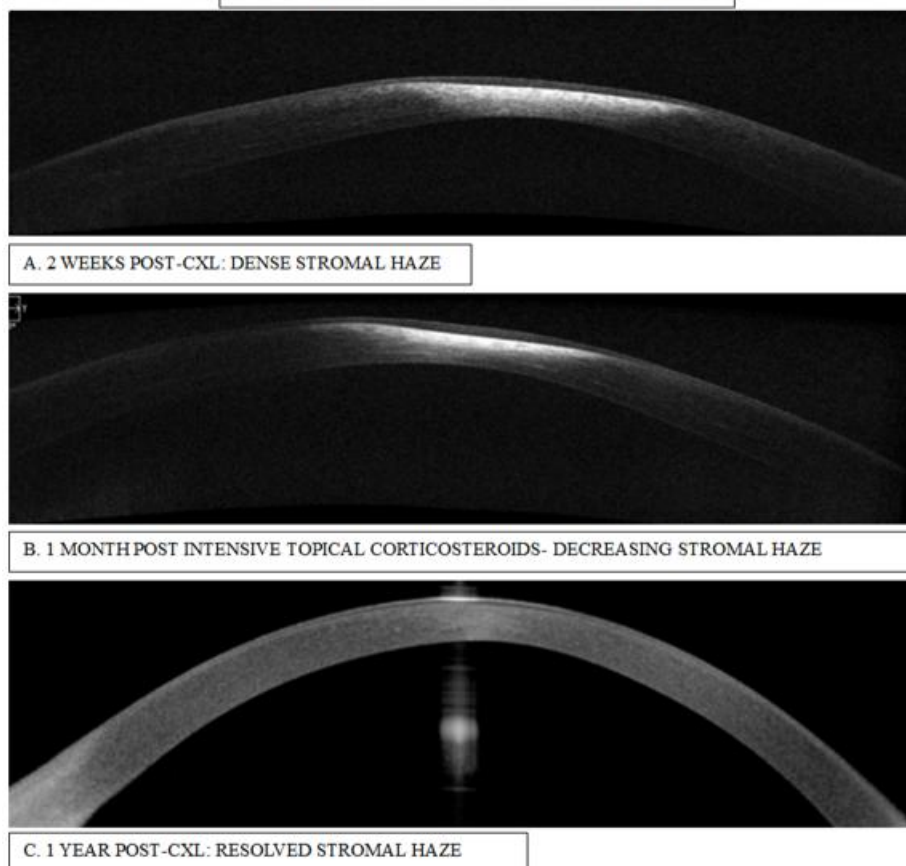


Figure 1 A. POST-CXL 2 WEEKS - DENSE SIGNIFICANT CENTRAL STOMAL HAZE; B: 6 MONTHS POST-CXL (5 MONTHS POST INTENSIVE TOPICAL CORTICOSTEROIDS) - SIGNIFICANT REDUCTION OF STOMAL HAZE

FIGURE 2: SERIAL AS-OCT IMAGES (LEFT EYE)



3. Discussion

Corneal collagen cross-linking (CXL) is a widely accepted procedure to stabilize progressive keratoconus by strengthening the corneal stroma. Although considered safe, postoperative stromal haze is a recognized complication, with a peak incidence at 1 month and a typical resolution by 12 months in most patients (4,5). However, in some cases, especially among younger patients and those undergoing accelerated protocols, the haze may be unusually dense and persistent, leading to significant visual impairment (6,7). The pathogenesis of post-CXL haze includes keratocyte apoptosis, collagen fiber remodeling, and extracellular matrix changes that increase corneal light scatter (8,9). Factors such as epithelial removal, inflammation, and

subclinical ocular surface disease may exacerbate the risk (10). Confocal microscopy and densitometry studies have shown that the anterior 300 μm of the stroma is predominantly affected, and haze formation correlates with increased reflectivity in this region (11,12). In the present case, a 16-year-old male developed dense central stromal haze two weeks after accelerated CXL, resulting in reduced visual acuity. Initiation of aggressive topical corticosteroid therapy (1% prednisolone acetate) led to a rapid and substantial resolution of the haze, with near-complete visual recovery by six months.

Unlike most reports that document mild or late-onset haze, this case features early-onset, dense, visually significant haze responding dramatically to intensive topical therapy. To the

best of our knowledge, it is among the first such cases reported from South India, specifically Coimbatore, Tamil Nadu. While Peponis et al. reported steroid-responsive late-onset haze (13), and Sayegh et al. described favorable outcomes in milder cases (14), early dense haze managed successfully with aggressive steroids remains sparsely documented. This underscores the importance of close postoperative monitoring and early therapeutic intervention, particularly in pediatric keratoconus, where inflammatory healing may be exaggerated.

4. Conclusion

This case highlights that aggressive topical corticosteroid therapy can effectively reverse early-onset dense anterior stromal haze following accelerated CXL, resulting in notable visual improvement. The prompt response to high-dose prednisolone acetate supports the hypothesis that early inflammatory haze is steroid-responsive. Given the limited number of case reports in literature detailing such a response, further reporting is warranted to establish evidence-based guidelines. Importantly, regular postoperative monitoring remains essential to detect and manage complications early, particularly in young, high-risk patients undergoing accelerated protocols.

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References

- [1] Rabinowitz YS. Keratoconus. *Surv Ophthalmol*. 1998;42(4):297–319.
- [2] Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol*. 2003;135(5):620–627.
- [3] Hersh PS, Stulting RD, Muller D, Durrie DS, Rajpal RK. United States multicenter clinical trial of corneal collagen crosslinking for keratoconus treatment. *Ophthalmology*. 2017;124(9):1259–1270.
- [4] Greenstein SA, Fry KL, Hersh PS. Natural history of corneal haze after collagen crosslinking for keratoconus and corneal ectasia: Scheimpflug and biomicroscopic analysis. *J Cataract Refract Surg*. 2010;36(12):2105–2114.
- [5] J. Lai M, Greenstein SA, Gelles JD, Hersh PS. Corneal Haze After Transepithelial Collagen Cross-linking for Keratoconus: A Scheimpflug Densitometry Analysis. *Cornea*. 2020 Sep;39(9):1117–21.
- [6] Evangelista CB, Hatch KM. Corneal Collagen Cross-Linking Complications. *Semin Ophthalmol*. 2018 Jan 2;33(1):29–35.
- [7] Badawi AE. Corneal haze and densitometry in keratoconus after collagen cross-linking by three different protocols. *J Curr Ophthalmol*. 2021;33(4):422–430.
- [8] Mazzotta C, Hafezi F, Kymionis G, Caragiuli S, Jacob S, Traversi C, et al. In Vivo Confocal Microscopy after Corneal Collagen Crosslinking. *Ocul Surf*. 2015 Oct;13(4):298–314.
- [9] Lim LS. Late-Onset Deep Stromal Scarring After Riboflavin–UV-A Corneal Collagen Cross-Linking for Mild Keratoconus. *Arch Ophthalmol*. 2011 Mar 14;129(3):360.
- [10] Natarajan R, Giridhar D. Corneal scarring after epithelium-off collagen cross-linking. *Indian J Ophthalmol*. 2025 Jan;73(1):28–34.
- [11] Raiskup F, Hoyer A, Spoerl E. Permanent Corneal Haze after Riboflavin–UVA-induced Cross-Linking in Keratoconus. *J Refract Surg [Internet]*. 2009 Sep [cited 2025 May 15];25(S3). Available from: <https://journals.healio.com/doi/10.3928/1081597X-20090813-12>
- [12] Dhawan S, Rao K, Natrajan S. Complications of Corneal Collagen Cross-Linking. *J Ophthalmol*. 2011; 2011:1–5.
- [13] Peponis VG, Rosenberg T, Vajpayee RB, et al. Late-onset corneal haze after corneal cross-linking for progressive keratoconus. *Int Med Case Rep J*. 2015; 8: 135–139.
- [14] Sayegh KH, Sammouh FK, Ayash JG, El Chakik GF, Haddam MS, Warrak EL. Corneal Haze Secondary to Corneal Collagen Cross-linking in Keratoconus Patients: Treatment and Outcomes. *Middle East Afr J Ophthalmol*. 2022 Oct;29(4):186–9.