

## Severe focal stromal degeneration up to Descemet membrane after corneal collagen cross-linking

G V Prabhakar, N Panickar, J K Reddy,  
S K Sivasubramaniam, A Singh

Corneal collagen cross-linking (CXL) is an effective treatment for arresting progression in keratoconus cases. It is considered safe despite a few complications that have been recorded earlier. In this case series, we report a rare and late complication caused due to severe stromal thinning up to Descemet's membrane in three patients who underwent CXL 3 to 6 years back for keratoconus. Deep anterior lamellar keratoplasty (DALK) was then done for the affected eye with good outcomes. This case series highlights the possible late effects of UVA irradiation post CXL.

**Key words:** Collagen cross-linking, descemetocele, keratoconus, stromal thinning, ultraviolet A irradiation

Corneal collagen cross-linking (CXL), first introduced by Wollensack *et al.*,<sup>[1]</sup> is currently considered as a standard treatment for arresting progression in keratoconus patients. It strengthens the corneal collagen by forming chemical bonds, both within and between the collagen fibrils, thus enhancing the biomechanical and biochemical stability of the corneal collagen.<sup>[2]</sup> CXL involves photoactivation of riboflavin by exposure to ultraviolet A (UVA) which then increases the collagen cross-linking.

CXL has proved to be an effective treatment for most cases. However, besides the transient reversible side effects, some cases with complications such as corneal haze and scarring, reduced uncorrected and best spectacle-corrected visual acuity (BSCVA), infectious and noninfectious stromal melting, and treatment failure with the progression of ectasia have been reported.<sup>[3]</sup> In this case series, we highlight a rather rare complication of CXL noted in three patients who came to our centre 3 to 6 years post CXL (done under Dresden protocol),<sup>[1]</sup> with clinical findings of severe corneal thinning in the treated eye.

Access this article online	
Quick Response Code:	Website: www.ijjo.in
	DOI: 10.4103/ijjo.IJO_475_19

Department of Cornea and Refractive Surgery, Sankara Eye Hospital, Coimbatore, Tamil Nadu, India

**Correspondence to:** Dr. G V Prabhakar, Department of Cornea and Refractive Surgery Sankara Eye Hospital, Sathy Road, Coimbatore - 641 035, Tamil Nadu, India. E-mail: prabhakar.mbbs@gmail.com

Received: 14-Mar-2019

Revision: 23-Apr-2019

Accepted: 24-Sep-2019

Published: 19-Dec-2019

## Case Reports

### Case 1

A 17-year-old female, presented with defective vision in the left eye (OS) for 4 months. There was no history of associated pain or photophobia. The patient was a known case of keratoconus with a history of CXL done under Dresden protocol in the left eye 4 years back.

Preoperative pachymetry values are RE- 456 microns, LE- 420 microns as per old records. On evaluation, the best-corrected visual acuity (BCVA) in the right eye was 20/80 and left eye was 20/200. On slit-lamp biomicroscopy, OS central corneal haze with a localized area of stromal thinning up to Descemet's membrane measuring 3 × 3 mm was noted [Fig. 1]. Fluorescein dye showed pooling over the thinned area of cornea. There were no signs of anterior chamber inflammation. Keratometry (OS) showed mean K1 = 48.23D and K2 = 49.73D. Lens was clear and posterior segment was within normal limits. The specular count was 3214 cells/mm<sup>2</sup>. In view of the severe stromal thinning, deep anterior lamellar keratoplasty (DALK) was done for the same eye [Fig. 2]. On evaluation, the right eye was within normal limits.

### Case 2

A 22-year-old male approached with complaint of defective vision in the right eye (OD) for 6 months, with past history of CXL done in the right eye 3 years back for keratoconus. The patient had no history of associated pain or photophobia. BCVA in the right eye was recorded as 20/63. Preoperative pachymetry was RE -412 microns, LE - 515 microns. On slit-lamp examination, corneal thinning up to Descemet's membrane was seen in central cornea (area 3 × 3 mm) with surrounding stromal haze, [Fig. 3] with corresponding optical coherence tomography (OCT) findings [Fig. 4]. The pooling of fluorescein dye was seen over the descemetocele. Anterior chamber showed no signs of inflammation. Posterior segment was within normal limits. Mean K1 = 38.4D and K2 = 50.1 D were recorded. The specular count was 3110 cells/mm<sup>2</sup>. DALK was advised for the same eye.

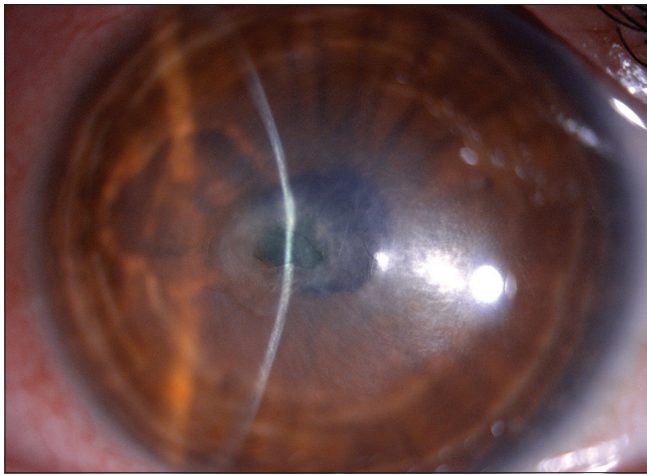
### Case 3

A 21-year-old male came to our hospital with defective vision (OD) for 4 months. The patient gave a history of CXL in the right eye 6 years back. Preoperative pachymetry was RE- 410 microns, LE- 510. He had a known case of keratoconus. On presentation, recorded BCVA was 20/200. Slit-lamp examination showed severe stromal thinning up to Descemet's membrane measuring 2 × 3 mm in the affected eye involving the central corneal area [Fig. 5]. Fluorescein stain pooling was seen over the bare Descemet's membrane. Specular was 3200 cells/mm<sup>2</sup>. Posterior segment was within normal limits. Mean K1 = 42.03D

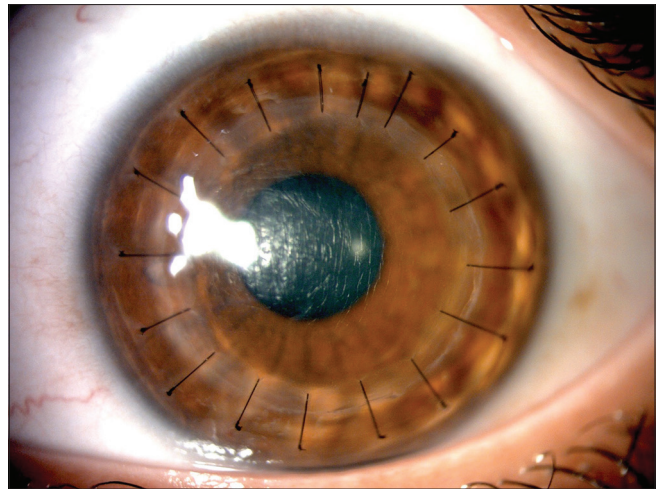
This is an open access journal, and articles are distributed under the terms of the Creative Commons Attribution-NonCommercial-ShareAlike 4.0 License, which allows others to remix, tweak, and build upon the work non-commercially, as long as appropriate credit is given and the new creations are licensed under the identical terms.

**For reprints contact:** reprints@medknow.com

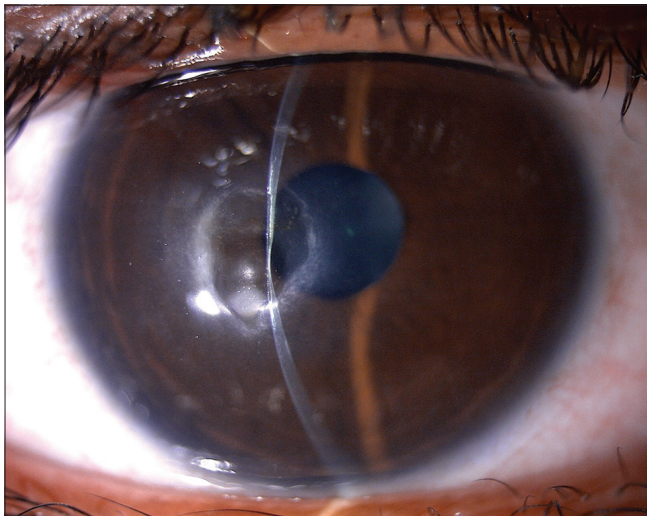
**Cite this article as:** Prabhakar GV, Panickar N, Reddy JK, Sivasubramaniam SK, Singh A. Severe focal stromal degeneration up to Descemet membrane after corneal collagen cross-linking. Indian J Ophthalmol 2020;68:224-6.



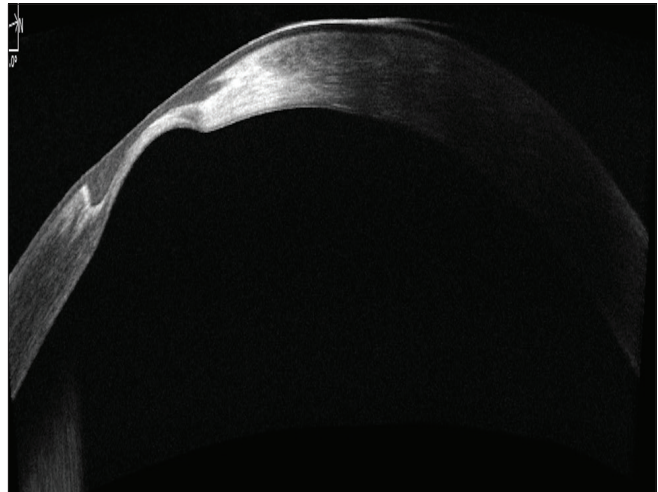
**Figure 1:** Slit-lamp biomicroscopy image (OS) of case 1 showing central corneal haze with a localized area of stromal thinning stroma with bare Descemet's membrane



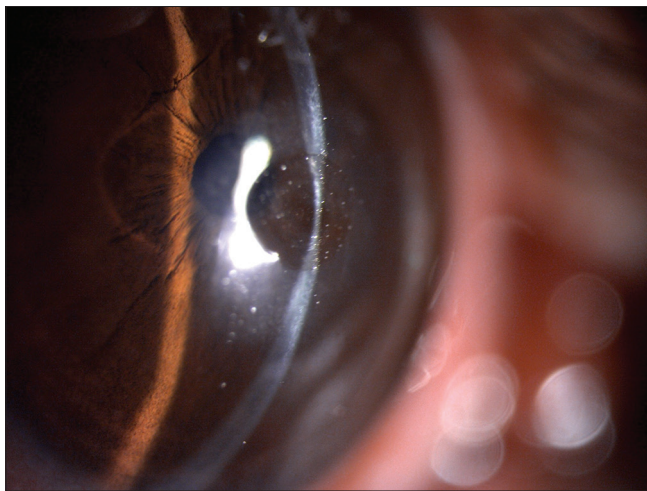
**Figure 2:** Slit-lamp biomicroscopy image (OS) of case 1 post DALK



**Figure 3:** Slit-lamp biomicroscopy image (OD) of case 2 showing severe stromal thinning in central cornea with surrounding stromal haze



**Figure 4:** OCT image (OD) of case 2 showing focal stromal thinning



**Figure 5:** Slit-lamp biomicroscopy image (OD) showing severe stromal thinning with bare Descemet's membrane in central cornea

and K2 = 45.73D were recorded. In view of the severe stromal thinning, deep anterior lamellar keratoplasty (DALK) was done for the same eye. The left eye was within normal limits.

**Discussion**

CXL is considered a gold standard treatment for progressive keratoconus. Our case series reports a rare complication and a long-term follow up highlighting deleterious effects of UV radiation. The continued effect of CXL resulting in stromal degeneration up to Descemet's membrane between 3 to 6 years post CXL can be attributed to the following hypotheses reported in literature.

Zare *et al.*,<sup>[4]</sup> conducted a study which showed that anterior and mid-stromal keratocyte density decreases greatly after CXL. Keratocyte repopulation occurs but does not complete after 6 months of the procedure. If considerable regeneration of stromal keratocytes fails to occur, it could result in stromal thinning.

The same study also demonstrated that besides the neurotrophic deficit resulting from keratoconus, CXL treatment in itself contributes to the problem by UV rays causing deeper

nerve damage. Their results indicated that nerve regeneration occurs gradually, however even after 6 months post CXL the nerve plexus was not well defined. The cases in our study also reported painless diminution of vision owing to the corneal thinning that resulted during post CXL treatment.

Lim LS *et al.*,<sup>[5]</sup> in their study showed that, UVA exposure which causes keratocyte death may show a sublethal effect in the deeper stroma which receives lower dose of radiation, resulting in fibroblastic transformation of the keratocytes with subsequent scar formation which may further decrease the supply of nutrition from aqueous to the superficial stroma.

## Conclusion

This is a first-ever case series reporting a rare complication of stromal thinning up to Descemet's membrane 3 to 6 years post CXL. This case series highlights the fact that effect of CXL continues in a long course of time and a better understanding of long-term effects of UVA irradiation is needed. Intraoperative parameters during CXL treatment such as exposure time and UVA dose play an important role in the outcomes.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other

clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Wollensak G, Spoerl E, Seiler T. Riboflavin/ultraviolet-A-induced collagen crosslinking for the treatment of keratoconus. *Am J Ophthalmol* 2003;135:620-7.
2. Spoerl E, Huhle M, Seiler T. Induction of cross-links in corneal tissue. *Exp Eye Res* 1998;66:97-103.
3. O'Brart DP. Corneal collagen cross-linking: A review. *J Optom* 2014;7:113-24.
4. Zare MA, Mazloumi M, Farajipour H, Hoseini B, Fallah MR, Mahrjerdi HZ, *et al.* Effects of corneal collagen crosslinking on confocal microscopic findings and tear indices in patients with progressive keratoconus. *Int J Prev Med* 2016;7:132.
5. Lim LS, Beuerman R, Lim L, Tan DT. Late-onset deep stromal scarring after riboflavin-uv-a corneal collagen cross-linking for mild keratoconus. *Arch Ophthalmol* 2011;129:360-71.