

Microbial Keratitis Following Corneal Collagen Cross Linking: A Case Series

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Abstract:

Microbial keratitis in Keratoconus patients after corneal collagen cross linking: a case series Corneal collagen cross linking (C3R) has emerged as an effective treatment in patients with Keratoconus. Although a safe procedure, complications, including infections have been known to occur which may adversely impact the post-operative outcomes in these patients. A retrospective analysis of one year data revealed three patients with microbial keratitis. One patient had undergone hypotonic C3R and remaining had isotonic C3R. Corneal scraping for Gram and KOH staining and BCL culture and sensitivity were done. One of the three patients was culture positive for *Pseudomonas* species while the other two showed clinical signs of bacterial keratitis. All three patients responded well to medical treatment with an average 2 lines drop in visual acuity. One of the three patient had Vernal keratoconjunctivitis which might have been a risk factor. Infections following C3R can occur due to epithelial debridement, placement of BCL over steep corneas, eye rubbing and pre-existing ocular infections. Hence careful watch during the initial post-operative period is essential to avoid unwarranted outcomes.

Key Words: Corneal collagen cross-linking; Microbial Keratitis; Keratoconus.

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I. Introduction

Keratoconus is a progressive, non-inflammatory, usually bilateral though often asymmetric ectatic disease of the cornea, generally affecting children and young adults and may eventually lead to severe visual impairment. However, newer modalities have, today, revolutionized the management of Keratoconus. One among these is Corneal Collagen Cross Linking.

Corneal Collagen Cross Linking with Riboflavin (C3R) using Ultraviolet-A (UV-A) helps increase the mechanical rigidity of the cornea, thus delaying the progression of Keratoconus. While usually safe and effective with few complications, microbial keratitis following C3R has been reported and is known to be caused by a variety of etiological agents.

We report a series of three cases of bacterial keratitis following C3R.

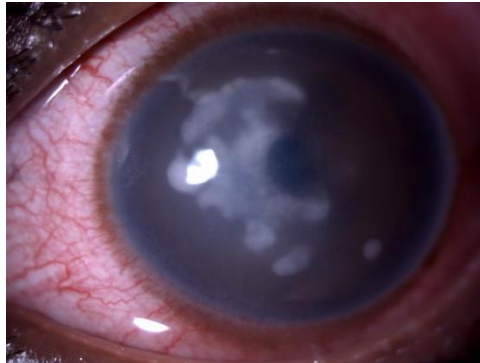
II. Case report

Case 1

A 20-year-old male presented with complaints of decreased vision in the left eye. Visual acuity was 6/9 in the right eye and 6/60 in the left eye improving to 6/6 and 6/36 respectively. Retinoscopy showed a scissor reflex in the left eye. Slit lamp examination of both eyes showed conjunctival and limbal papillae with Vogt striae and Fleischer ring in the left eye. Pentacam showed corneal thinning in the right eye and was diagnostic of Keratoconus in the left eye. The patient was diagnosed with Vernal Keratoconjunctivitis in both eyes and Keratoconus in the left eye. He was advised Accelerated Isotonic Corneal Collagen Cross Linking (C3R) in the left eye.

The procedure was uneventful. Bandage contact lens (BCL) was applied over the left eye and the patient was started on a post-operative regimen of Moxifloxacin 0.5% eye drops once every two hours (Vigamox) and HPMC 0.4% eye drops four times daily (Tears naturale, Alcon, India). Examination on the first, second and third post-operative days were within normal limits. On the fourth post-operative day, slit lamp examination of the left eye showed corneal stromal infiltrate in the anterior two thirds with Descemet membrane folds, clinically suggestive of bacterial keratitis. BCL was in situ. Corneal scraping for Gram stain, KOH mount, culture on blood agar and potato dextrose agar was performed, all of which were negative. BCL culture showed no growth.

The patient was treated with Moxifloxacin 0.5% eye drops once every hour, (Vigamox, Alcon, India), Moxifloxacin 0.5% eye ointment twice daily (4-Quin, Entod, India), Tobramycin 0.3% once every two hours (Toba, Sun, India), Homatropine 2% w/v twice daily (Homide, Warren, India). Subsequent follow up examinations showed a healing infiltrate which later healed with scarring with final visual acuity restored being 6/60 improving to 6/18 in the left eye.



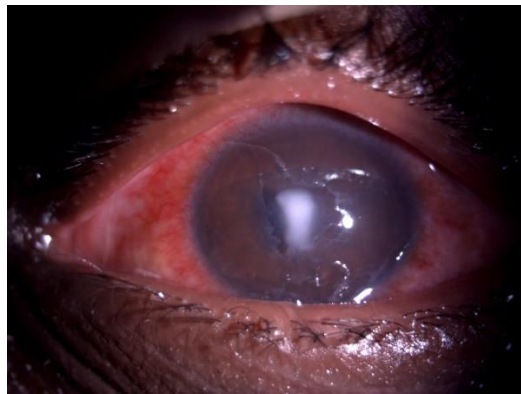
Post Operative Day 3 image of the left eye showing corneal infiltrate with satellite lesions

Case 2

An 11-year-old male presented with progressively decreasing vision in both eyes. Visual acuity at presentation was 6/60 in both eyes improving to 6/12. Slit lamp examination of the right eye showed Vogt striae and Fleischer ring. Left eye was normal. Pentacam was diagnostic of Keratoconus in both eyes. The patient underwent Standard Isotonic C3R in the right eye which was uneventful.

Seven months later, the patient was advised Standard Isotonic C3R in the left eye. The procedure was uneventful and BCL was applied. The patient was prescribed Moxifloxacin 0.5% eye drops once every two hours (Vigamox) and HPMC 0.4% eye drops four times daily (Tears naturale, Alcon, India) after the procedure. Examination on the first and second post-operative days was normal. On the third post-operative day, slit lamp examination of the left eye showed a patchy stromal infiltrate with cellular reaction, with a progressive border and multiple satellite lesions. Corneal scraping done for Gram stain, KOH mount and blood agar culture yielded no results. BCL culture was positive for *Pseudomonas* spp.

The patient was started on Chloramphenicol 4mg/ml with Polymyxin B 5000 IU eye drops once every hour (Ocupol, Centaur, India), Chloramphenicol 10mg/g with Polymyxin B 10000 IU eye ointment twice daily (Ocupol, Centaur, India), Amikacin 1% w/v once every hour (Aminogen, Jawa, India), Gatifloxacin 0.5% w/v once every hour (Gatilox HS, Sun, India) and Homatropine 2mg% twice daily (Homide, Warren, India). Subsequent visits showed healing of the nasal and later temporal margins of the infiltrate with minimal central active infiltrate, which later healed with scarring. Final best corrected visual acuity (BCVA) in the right was 6/18 and left eye 6/36.



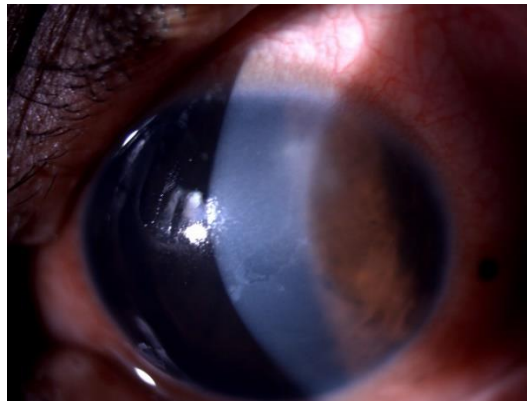
Post Operative Day 4 image of the left eye showing corneal infiltrate with a healing epithelial defect

Case 3

A 14-year-old male, known case of Keratoconus and Vernal Keratoconjunctivitis in both eyes presented with a visual acuity in the right eye of 6/36 improving to 6/12 and in the left eye 6/18 improving to 6/9. Retinoscopy showed a scissor reflex in both eyes. Slit lamp examination of both eyes showed a steep cornea. Pentacam findings were diagnostic of Keratoconus in both eyes.

Standard Isotonic C3R of the left eye was uneventful and BCL was applied. Post operatively, the patient was given Inj. Cefotaxime 500mg I.V twice daily for two days (Taxim, Acme) along with Gatifloxacin 0.3% eye drops once every hour (Zymar, Allergan). Slit lamp examination on the second post-operative day revealed no BCL and hence, it was reapplied. On the third day post operatively, examination of the left eye showed a stromal cellular infiltrate with a healing epithelial defect and BCL in place. The patient was prescribed Gatifloxacin 0.3% eye drops once every hour (Zymar, Allergan) and Tobramycin 0.3% eye drops once every hour (Toba, Sun, India). Slit lamp examination of the left eye three days later showed a healed infiltrate with mild anterior stromal haze as a result of C3R and visual acuity of 6/18.

Two months later, the patient underwent Standard Isotonic C3R in the right eye which was uneventful. His final visual acuity was 6/24 improving to 6/12 in the right eye and 6/18 improving to 6/9 in the left eye.



Post Operative Day 3 image of the right eye showing corneal infiltrate

III. Discussion

The incidence of microbial keratitis following C3R is exceedingly rare, estimated at 0.0017%.¹ However, these infections can occasionally lead to sight threatening complications including corneal perforation.⁶

A variety of factors are thought to be associated with microbial keratitis following C3R including epithelial debridement, application of bandage contact lens (BCL), use of steroids, pre-existing ocular infections and associated conditions such as Vernal Keratoconjunctivitis (VKC). Most of these cases occurred around the third day after the procedure.

The etiological agents implicated in causing infections after C3R include a wide variety of microorganisms. A retrospective analysis of 2350 patients reported an incidence of four cases of Moxifloxacin Resistant Staphylococcus Aureus (MXRSA). However, all four patients were on systemic steroids for associated conditions.¹ There has been one reported case of Acanthamoeba keratitis one month after C3R, in which the patient required a Therapeutic Penetrating Keratoplasty.² A case of polymicrobial keratitis following C3R associated with the use of contact lens has also been reported. The causative organisms were found to be Streptococcus salivarius, Streptococcus oralis and Coagulase Negative Staphylococci (CoNS).⁵ Two patients had corneal perforation following C3R, one of which was caused by Methicillin Resistant Staphylococcus Aureus (MRSA). The other patient had a staphylococcal abscess. Corneal perforation was treated using gluing.⁶ Two patients with no prior history of herpetic eye disease were reported to have Herpetic keratitis on the 6th and 9th post-operative days respectively.^{7,8} Other reported cases include a case of Pseudomonas aeruginosa,⁹ Staphylococcus epidermidis³ and one case of Staphylococcus aureus keratitis following accelerated C3R.⁴

We conducted a retrospective analysis of one-year data which revealed three patients with microbial keratitis. All three patients underwent epithelium off standard isotonic C3R in one or both eyes. Strict aseptic precautions were observed during the procedure. All three patients developed an infection around the third day post operatively. Corneal scraping for Gram stain and KOH mount were done along with corneal and BCL culture and sensitivity on blood agar and potato dextrose agar media. One patient was culture positive for Pseudomonas while the remaining showed clinical signs of bacterial keratitis. Two of the patients had Vernal Keratoconjunctivitis, which may have been a contributing factor. All three patients responded well to treatment and almost completely regained pre-operative visual acuity.

IV. Conclusion

Microbial keratitis following C3R is a rare complication of the procedure. Epithelial debridement, placement of bandage contact lens (BCL) over steep corneas, pre-existing ocular infections and reactivation as well as contact lens use are thought to be risk factors associated with development of microbial keratitis

following C3R. While most cases responded well to topical and systemic antimicrobial therapy, infections following C3R can result in grave complications including corneal perforation and severe drop in visual acuity. Hence, there is a need to maintain strict asepsis intra-operatively as well as close monitoring of patients who have undergone C3R in order to institute prompt and appropriate treatment and maximise visual recovery following C3R.

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