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CASE REPORT

Anterior Uveitis after Collagen Cross-linking for Keratoconus

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ABSTRACT

This report describes a case of severe intraocular inflammation followed after CXL with UVA and riboflavin treatment for progressive keratoconus.

Keywords: Anterior uveitis, Collagen Cross-linking, Keratoconus.

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INTRODUCTION

Corneal collagen cross-linking (CXL) using ultraviolet-A (UVA) light and riboflavin has become a common treatment to halt the progression of keratoconus.[1] Treatment effect is theorized to be obtained through increasing covalent bindings between collagen molecules in the anterior corneal stroma. This process is mediated by free radicals generated by photosensitization of riboflavin by UVA light.[1,2] Both photochemically induced free radicals and UVA irradiation can potentially damage intraocular structures including corneal endothelial cells and human retina.[3-6] Collagen cross-linking treatment may be applied to the cornea with or without removing corneal epithelium, so called epi-on and epi-off techniques and studies are underway trying to evaluate which technique is more effective.[7] The de-epithelization itself has potential complications related to denuded stroma and prolonged healing process.

Several previous reports described complications related CXL treatment in keratoconic patients. Infections keratitis reported include herpetic, amoeba and bacterial pathogens. Bacteria involved species, such as *Pseudomonas, Streptococcus, Staphylococcus*, *Escherichia coli*.[8-13] Recently, corneal melting after CXL that eventually required penetrating keratoplasty because of perforation has been reported.[14]

We report a case of severe intraocular inflammation followed after CXL with UVA and riboflavin treatment for progressive keratoconus.

CASE REPORT

A 25-year-old female presented to the Yonge Eglinton Laser Centre, Toronto, Canada, with progressive keratoconus in both eyes. She has been diagnosed with keratoconus (KC) 2 years prior to her initial presentation and reported subjective decline in visual acuity. Consecutive tomographic maps showed progression of KC in both eyes. Through the follow-up period of 5 months, uncorrected visual acuity (UCVA) in her right eye declined from 20/30 to 20/40 with progressive thinning and increase in keratometry values (Figs 1A to C). During the same period, UCVA in her left eye decreased from 20/60 to 20/300 with increase in keratometry values (Figs 2A and B).

Decision was taken to proceed with CXL treatment organizational unit (OU) combined with Intacs (Addition Technology Inc.) in OS.

The treatment protocol was as following:

Under aseptic conditions using topical preoperative anesthesia with proparacaine hydrochloride 0.5% (Alcaine, Alcon Laboratories, Inc, Fort Worth, Texas, USA) the patient underwent 6.5 mm diameter 50 micron depth phototherapeutic keratoplasty OU followed by an 8 mm diameter area epithelial removal assisted by application of 50% alcohol in BSS for 5 seconds. Then, the left eye underwent Intralase (Abbott Laboratories Inc., Abbott Park, Illinois, USA) assisted insertion of Intacs. Then, single-use isotonic eye drops of riboflavin 0.1% in 20% dextran solution (Habers Pharmacy, Toronto, ON, Canada) were instilled every 2 minutes for 30 minutes in both eyes. Corneal CXL was performed by using the Institute of Refractive and Ophthalmic Surgery (IROC) UV-X 2000 system (IROC AG, Zurich, Switzerland) for a 10 minutes UVA irradiation duration at 9 mW/cm^2. At the

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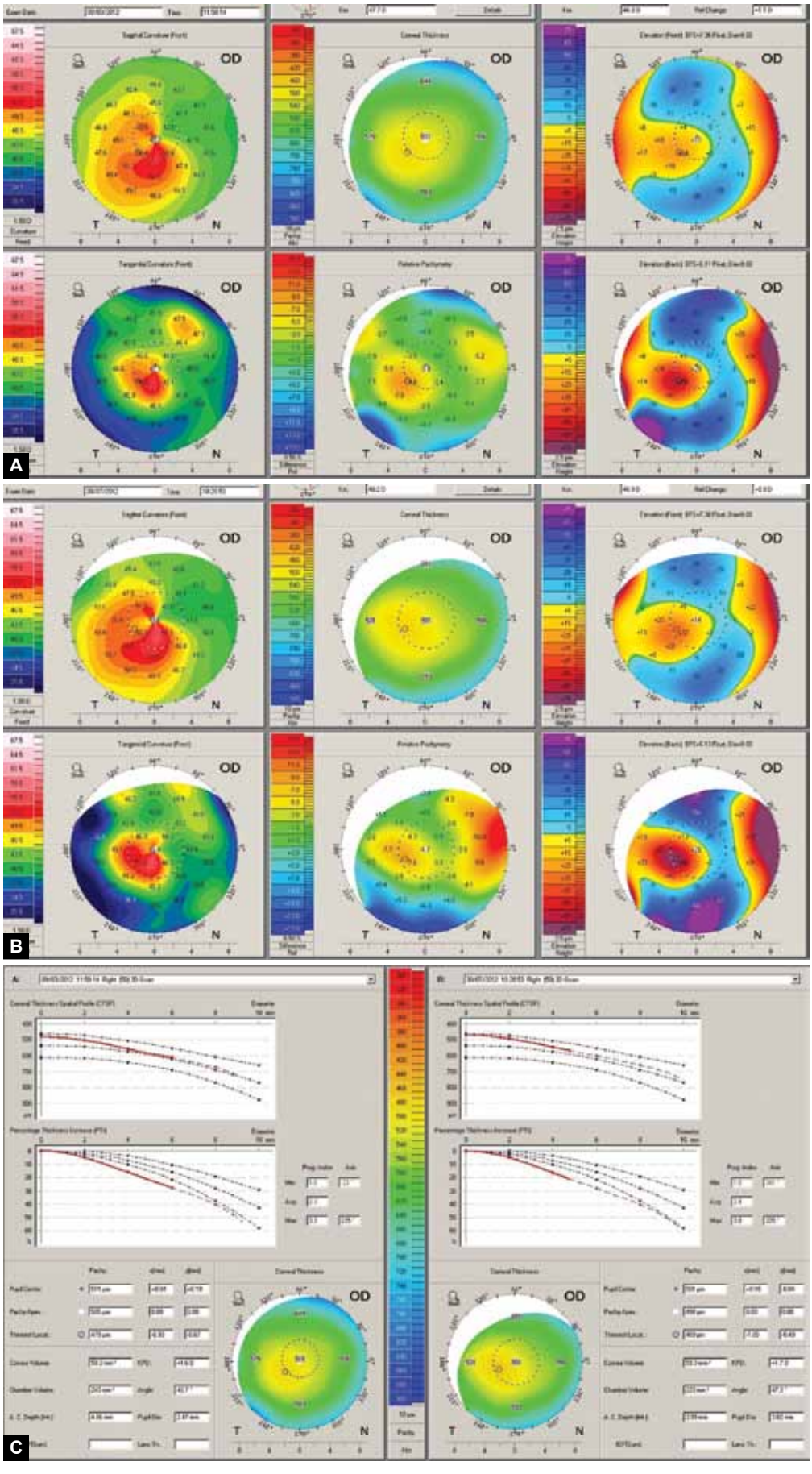
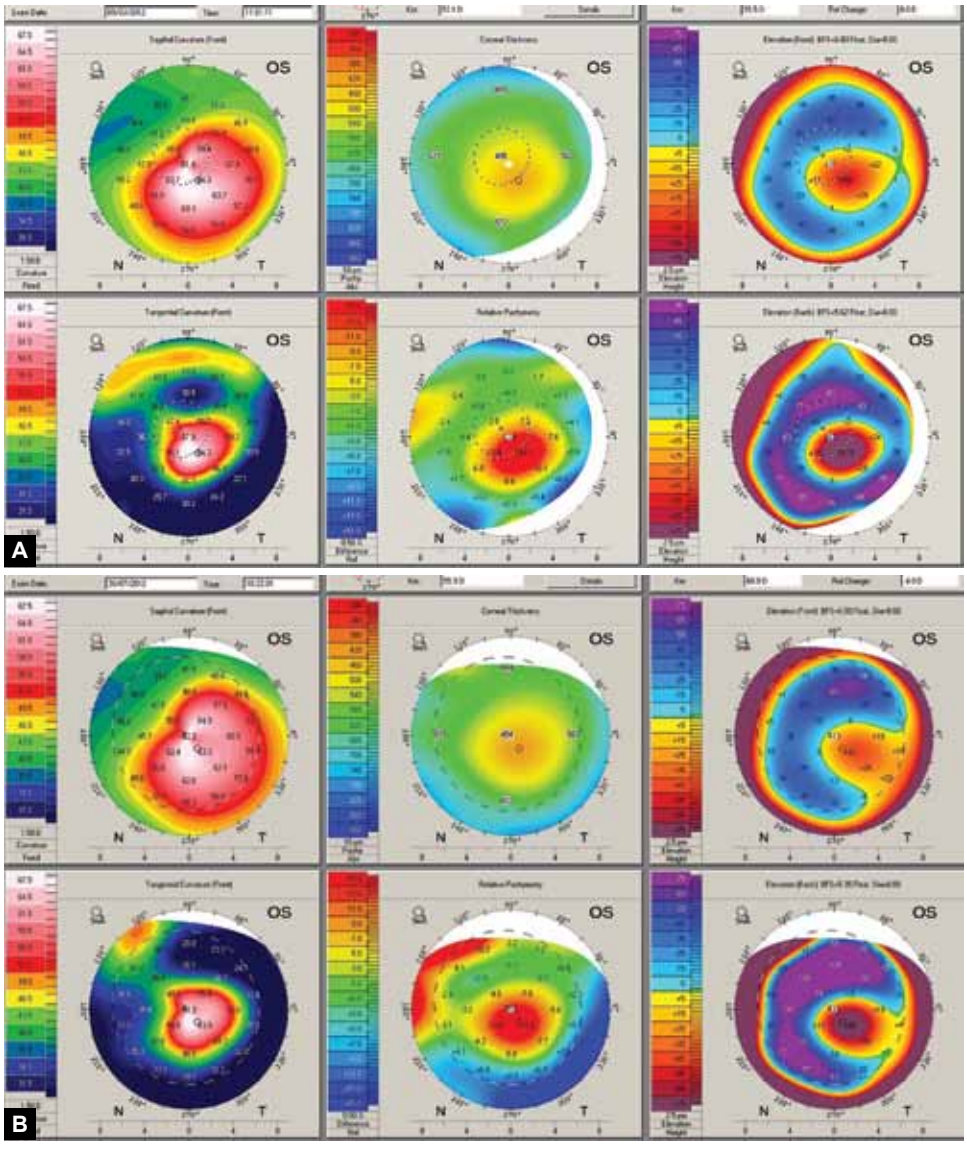


Figs 1A to C: Pentacam keratometry maps From right eye: (A) From March 2012, (B) from July 2012 and (C) comparison of corneal-thickness spatial profile and percentage thickness increase maps



Figs 2A and B: Pentacam keratometry maps from left eye: (A) From March 2012 and (B) from July 2012

end of the procedure, a silicon-hydrogel bandage contact lenses (BCLs) were applied. Postoperatively, patient was given a combination of antibiotic and corticosteroid drops (Besivance, besifloxacin ophthalmic suspension, 0.6%, Bausch and Lomb and Lotemax, loteprednol etabonate ophthalmic suspension, 0.5%, Bausch and Lomb) four times daily.

On first postoperative day, BCVA was 20/160 OU, both eyes with bandage contact lenses in place, large central epithelial defects, Intacs in OS. Anterior chambers were deep and quiet.

Patient came back at postoperative day 5 for routine exam and planned removal of BCLs. She was complaining of an increased cloudiness and mild pain in over dose (OD).

On her examination, BCLs were found in place, removed. Uncorrected visual acuity OU was 20/200. Slit-lamp examination of OD showed conjunctival injection, small epithelial defect, central corneal haze, but no corneal stromal infiltrate. There was small (0.2 mm) hypopyon in anterior chamber. OS examination was consistent with normal healing process.

Additional investigation revealed that the cloudiness and tenderness in her right eye appeared 2 days before then and that day before these symptoms appeared the patient replaced her BCL in the right eye by herself.

Specimens were taken from the right cornea and the samples were sent for staining, culture and sensitivity microbiological studies.

Besivance and Lotemax were discontinued and treatment with fortified tobramycin 13.6 mg/ml and fortified vancomycin 25 mg/ml once hourly round the clock was initiated.

The next day UCVA was 20/200 and slit-lamp examination revealed mild improvement in conjunctival injection, cornea was diffusely hazy and no epithelial defect was present. Hypopyon decreased to barely detectable. Fortified topical antibiotic treatment was continued every 2 hours.

At the next visit, 2 days after, UCVA was improved to 20/60, very mild conjunctival injection still existed, cornea had some central haze without epithelial defect or infiltrate. Anterior chamber was deep and quiet and no hypopyon remained. Bacterial and fungal staining and cultures were all negative. Topical antibiotics were discontinued. Fluorometholone (FML) (fluorometholone 0.1%, Allergan) drops were started for three times a day for several days and then discontinued.

On patient latest follow-up, a year since CXL treatment, the findings in her right eye were as following: UCVA 20/50 and BCVA 20/30. White quiet conjunctiva, cornea with trace central haze, and deep and quiet anterior chamber.

DISCUSSION

The safety of CXL for progressing KC was assessed and reported previously.[15] Potential damage to intraocular tissue may be caused by photochemical injury or through infectious pathway.

The recommended safety criteria, however, must be observed because UV irradiation has potential to damage intraocular structures.[4-6]

Based on *in vitro* studies, Wollensak et al recommended the following safety criteria for UVA-Riboflavin CXL: corneal thickness of at least 400 μm, irradiation with 3 mW/cm^2 UVA (370 nm), and keeping the cornea constantly covered with riboflavin solution before and during UV irradiation to provide a shielding effect.[16] Applying riboflavin increases UVA absorption in the corneal stroma and reduces UVA transmission through the cornea to about 7%.[1] The endothelial damage threshold was shown to be at an irradiance of 0.35 mW/cm^2 which is approximately twice compared with the 0.18 mW/cm^2 that reaches the corneal endothelium when using the currently recommended protocol.[16,17]

Various pathogens were found responsible for infectious keratitis following CXL treatment. Such infections commonly accompanied by intraocular inflammation and hypopyon but require prolonged antibiotic treatment and usually have appropriate microbiology reports. Our case is unique in persistent hypopyon without keratitis. Fast resolution and negative microbiologic report suggest that we witnessed sterile anterior chamber reaction caused by CXL treatment.

The fact that our patient replaced BCL on her own may have put her at risk for infectious keratitis. Others reported patients' self-removal and reapplication of BCL in the immediate postoperative period being important risk factor for an infection.[13] Our patient presented anterior chamber inflammation similar to toxic anterior chamber syndrome as described after cataract removal surgeries and similar to sterile anterior reaction as described after laser refractive surgery.[18,19] Corneal trauma *per se* could also have led to inflammation. Sterile corneal epithelial defect, whatever the etiology is, may cause irydocyclitis with hypopyon mediated by increased levels of tissue plasminogen activator.[20]

Cross-linking treatment by using riboflavin as a photosensitizer causes formation of oxygen and superoxide radicals. It is plausible that these free radicals may diffuse through the corneal stroma into the anterior chamber and cause temporary inflammatory reaction. To verify this hypothesis, experimental laboratory studies may be needed.

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