Complications After CXL

The possible causes of keratitis after corneal collagen crosslinking in four patients are examined.

BY JÉRÔME C. VRYGHEM, MD; AND CARINA KOPPEN, MD

In 2003, corneal collagen crosslinking (CXL) was introduced as a treatment to reinforce corneal structural properties and halt keratoconus progression. In the first report on long-term results of CXL for keratoconus,[1] investigators identified CXL as an effective therapeutic option for progressive keratoconus and documented long-term stabilization following the procedure; however, the study included a low number of patients with 3 years or more of follow-up. Only in the past 3 years have reports on complications of CXL appeared.[2-6] Complications reported include sterile infiltrates, stromal scars, delayed epithelial healing, and bacterial keratitis. In September 2009, we reported four cases of severe keratitis after standard CXL treatment for keratoconus.[7] This article summarizes the findings we presented in that article and discusses potential causes for keratitis after CXL.

METHODS AND RESULTS

Four patients with progressive keratoconus from two independent centers in Beligum were treated with ultraviolet-A (UV-A) CXL; riboflavin was used as a photosensitizer (Figures 1 and 2). The epithelium was removed over the central 8 to 9 mm of the cornea. Riboflavin 0.1% in dextran 20% was instilled every 2 minutes for 30 minutes before UV-A exposure. The UV-X light source (Iroc AG, Zürich, Switzerland), calibrated at 3 mW/cm^2, was applied for 30 minutes, and instillation was continued every 2 minutes. At the end of the treatment, a bandage lens was applied and a combination of topical antibiotics and/or antiinflamatory drops was initiated.

After CXL treatments, these four patients presented with symptoms of inflammation, such as pain, redness, and decreased visual acuity. Other signs included ciliary flush, iritis with keratic precipitates, corneal edema, and infiltration. We administered high-dose topical or subconjunctival corticosteroids, which led to rapid initial improvement of symptoms and signs. The herpes virus could not be detected on the ocular surface or in the anterior chamber tap of one patient. In two eyes, there was a persistent decrease in BCVA.

Figure 1. Four days after CXL in one patient described here.

POTENTIAL CAUSES

It is not yet clear why these four cases of severe keratitis occurred after CXL treatment. Several hypotheses have been suggested, but no single hypothesis would explain all four cases described above.

One hypothesis suggests that these complications were related to the patients' particular health conditions. For example, of the four cases, two of the patients had allergies. We determined that allergies were an unlikely culprit; however, as one patient presenting with severe

TAKE-HOME MESSAGE

- Reported complications of CXL include sterile infiltrates, stromal scars, delayed epithelial healing, and bacterial keratitis.
- Surgeons must discuss the risks of keratitis and loss of BCVA associated with CXL during the informed consent process.

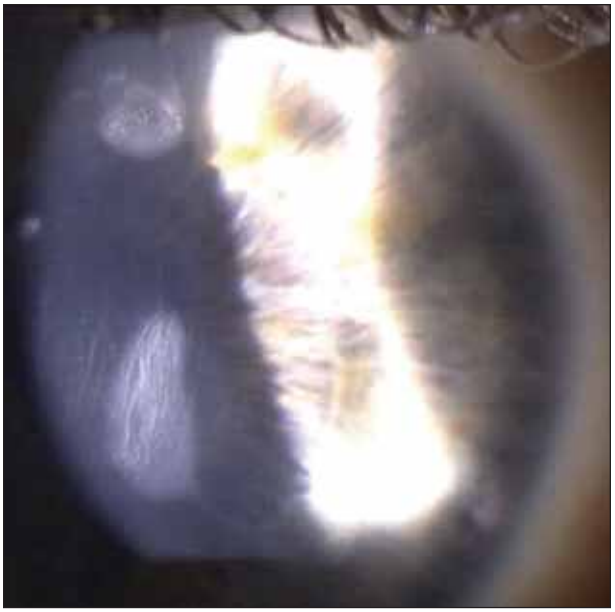

Figure 2. Six weeks after CXL in the same patient.

allergies underwent CXL in the fellow eye with an uneventful postoperative course.

Topical NSAIDs for ophthalmic use have been associated with inflammatory exacerbation, especially in cases of corneal hypoxia.[8] It is highly unlikely that this situation is applicable to all the cases in our study, as drops were used only in cases three and four; cases one and two did not require topical nonsteroidal antiinflammatory drugs. Additionally, the bandage lenses were made of highly oxygen-permeable silicone hydrogel materials, so hypoxia was not likely to occur under these lenses.

Removing the epithelium with ethanol in refractive surgery is a well-accepted method. In cases two through four, the epithelium was removed with ethanol 20% for 20 seconds. It is possible that the use of alcohol might modulate the response to the CXL treatment. However, in case one, the epithelium was removed manually with an Amoils epithelial scrubber (Innovative Excimer Solutions, Toronto, Ontario, Canada).

Another hypothesis is that an overdose of UV-A irradiation was administered. The power of the light source was set at 3 mW/cm^2; this setting is checked with an ultraviolet meter (PeakTech 5085; Heinz-Günter Lau GmbH, Ahrensburg, Germany) before every treatment. The irradiation time is limited to 30 minutes, and the standard radiant exposure of 5.4 J/cm^2 was not exceeded.

A final hypothesis suggests that greater irradiance of

(Continued on page 72)

CONFERENCE CALENDAR

June 2010
World Ophthalmology Congress
June 5 to 9
Berlin
Web site: www.woc2010.de
E-mail: pco@woc2010.org or pco@woc2010.de

Joint Congress of SOE and AAO
June 4 to 7
Geneva, Switzerland
Web site: www.soe2011.org
Phone: +46 8 459 6600
Fax: +46 8 661 9125
E-mail: soe2011@congrex.com

July 2010
The 12th National Congress and 35th Annual Scientific Meeting of the Indonesian Ophthalmologist Association
July 23 to 26
Semarang, Indonesia

September 2010
XXVIII Congress of the ESCRS
September 4 to 8
Paris
Web site: www.escrs.org
Phone: +353 1 209 1100
Fax: +353 1 209 1112
E-mail: escrs@escrs.org

The 25th Congress of the Asia-Pacific Academy of Ophthalmology in combination with the 15th National Congress of the Chinese Ophthalmological Society
September 16 to 20
Beijing
Web site: www.apao2010beijing.org

October 2010
The American Academy of Ophthalmology
October 16 to 19
Chicago
Web site: www.aao.org/annual_meeting
Phone: +1 415 447 0320
Fax: +1 415 561 8576
E-mail: meetings@aao.org

December 2010
The Second Biannual Cornea Scientific Meeting
December 1 to 2
Kyoto, Japan
Web site: www.asiacorneasociety.org

September 2011
The XVIX Congress of the ESCRS
September 17 to 20
Vienna, Austria
Web site: www.escrs.org
Phone: +353 1 209 1100
E-mail: escrs@escrs.org

October 2011
The American Academy of Ophthalmology
October 22 to 25
Orlando, Florida
Web site: www.aao.org/annual_meeting
Phone: +1 415 447 0320
Fax: +1 415 561 8576
E-mail: meetings@aao.org ■

(Continued from page 23)

the cornea could be caused unintentionally by poor focusing of the light source on the cornea. A simple experiment with the UV-X crosslinking device confirmed that moving the ultraviolet meter up and down out of the treatment plane under the light source produced irradiance values of less than 3 mW/cm^2. This suggests that it is not possible to cause an overdose using this UV-A light source.

CONCLUSION

It is only in recent years that isolated complications after CXL have been discussed in the literature. Although we have identified potential causes for the cases of keratitis in our study, we have not yet identified a primary cause.

Because CXL is gradually becoming the standard treatment procedure for progressive keratoconus, evaluation of short- and long-term side effects and complications is essential. We recommend that surgeons discuss the risks of keratitis and loss of BCVA associated with CXL with patients during the informed consent process. ■

Carina Koppen, MD, is a member of the Department of Ophthalmology, Antwerp University Hospital, Belgium. She states that she has no financial interest in the products or companies mentioned. Dr. Koppen may reached at tel: +32 476 41 47 34; fax: +32 3 825 19 26; e-mail: carina.koppen@uza.be.

Jérôme C. Vryghem, MD, is the Medical Director of Brussels Eye Doctors, Brussels, Belgium. Dr. Vryghem states that he has no financial interest in the products or companies mentioned. He is a member of the CRST Europe *Editorial Board. Dr. Vryghem may be reached at e-mail: info@vryghem.be.*

1. Raiskup-Wolf F, Hoyer A, Spoerl E, Pillunat LE. Collagen crosslinking with riboflavin and ultraviolet-A light in keratoconus: long-term results. *J Cataract Refract Surg.* 2008;34:796-801.
2. Kymionis GD, Bouzoukis DI, Diakonis VF, Portaliou DM, Pallikaris AI, Yoo SH. Diffuse lamellar keratitis after corneal crosslinking in a patient with post-laser in situ keratomileusis corneal ectasia. *J Cataract Refract Surg.* 2007;33:2135-2137.
3. Kymionis GD, Portaliou DM, Bouzoukis DI, et al. Herpetic keratitis with iritis after corneal crosslinking with ribofl avin and ultraviolet A for keratoconus. *J Cataract Refract Surg.* 2007;33:1982-1984.
4. Herrmann CI, Hammer T, Duncker GI. Haze formation (corneal scarring) after cross-linking therapy in keratoconus [in German]. *Ophthalmologe.* 2008;105:485-487.
5. Mazzotta C, Balestrazzi A, Baiocchi S, Traversi C, Caporossi A. Stromal haze after combined riboflavin-UVA corneal collagen cross-linking in keratoconus: in vivo confocal microscopic evaluation. *Clin Experiment Ophthalmol.* 2007;35:580-582.
6. Eberwein P, Auw-Hädrich C, Birnbaum F, Maier PC, Reinhard T. Corneal melting after cross-linking and deep lamellar keratoplasty in a keratoconus patient. *Klin Monatsbl Augenheilkd.* 2008;225:96-98.
7. Koppen C, Vryghem JC, Gobin L, et al. Keratitis and corneal scarring after UVA/riboflavin cross-linking for keratoconus. *J Refract Surg.* 2009;25(9):S819-23.
8. Gaynes BI, Fiscella R. Topical nonsteroidal anti-inflammatory drugs for ophthalmic use: a safety review. *Drug Saf.* 2002;25:233-250.