High hyperopic shift after collagen crosslinking in a patient with pellucid marginal degeneration

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We report a 24-year-old patient with bilateral pellucid marginal degeneration (PMD) who had the collagen crosslinking (CXL) procedure in both eyes. Corneal stromal haze developed in the left eye 3 years postoperatively and induced a +5.75 D hyperopic shift in the cornea. No improvement of vision, refraction, or keratometry occurred in response to topical betamethasone eyedrops. We concluded that unpredicted complications can occur after CXL and that patients with PMD need longer follow-up after the CXL procedure.

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Pellucid marginal degeneration (PMD), often confused with keratoconus, is a rare bilateral corneal ectatic disorder.1 Pellucid marginal degeneration is characterized by a noninflammatory inferior peripheral band of thinning extending from the 5 o’clock to the 7 o’clock positions.2 Patients present with a decrease in visual acuity due to high irregular or against-the-rule astigmatism.3 Although PMD is sometimes considered a variant of keratoconus histopathologically, there are some differences; marked corneal steepening is located more inferiorly, above a narrow band of corneal stromal thinning concentric to the inferior limbus.4 Intrastromal corneal rings, thermo cauterization, and various types of keratoplasty are surgical approaches to improve the irregular corneal conditions; none reliably achieve an optimum visual result.3

Corneal collagen crosslinking (CXL) is a new treatment intended to halt the progression of keratectasia, keratoconus, and PMD.5 Corneal CXL increases the biomechanical stability of the cornea using ultraviolet-A (UVA) light and riboflavin.6 The corrected distance visual acuity (CDVA), spherical and cylindrical refraction, as well as quantitative descriptors of the cornea in topographic imaging improve after CXL.7

Several studies have reported that maximum keratometry (Kmax), a key topographic indicator of the success of CXL, decreases up to 4.34 diopters (D) after the procedure.5 Although it is suggested that CXL is safe, several short-term and long-term complications—postoperative infectious keratitis, corneal haze, endothelial damage, peripheral sterile infiltrate, herpes reactivation, and treatment failure—have been reported.8 Haze and stromal hyperdensity are the only known direct complications of the CXL procedure.5 Haze formation after CXL may be the result of keratocyte repopulation9 and dense extracellular matrix formation in the corneal stroma.10 Postoperative corneal haze appears to occur in more advanced keratoconus with lower mean corneal thickness and a higher keratometry value of the apex.11

In this report, we describe a case of PMD with a preoperative spherical equivalent of −0.25 D, central corneal thickness of 506 μm, and Kmax of 46.6 D that developed corneal stromal haze and a 5.75 D hyperopic shift 3 years after CXL.

CASE REPORT

A 24-year-old man had bilateral PMD. He had lost 2 lines of CDVA (Snellen acuity chart) in both eyes over the previous year. Slitlamp microscopy showed no corneal opacities. The preoperative CDVA was 20/200 in the right eye and 20/60 in the left eye. The manifest refraction was +0.50 −3.50 × 77 and +0.25 −1.00 × 96, respectively, and the central corneal thickness measured with scanning-slit anterior topography (Orbscan II, Bausch & Lomb), 483 μm and 506 μm,
respectively. The preoperative scanning-slit topography (Orbscan II) (Figure 1) showed against-the-rule astigmatism and a lobster-claw pattern in the right eye and inferior steepening in the left eye. Simulated keratometry analysis showed a $K_{\text{max}}$ of 47.4 D in the right eye and 44.6 D in the left eye.

The standard CXL procedure was performed in both eyes. A 9.0 mm diameter irradiation area was decentered inferiorly, preserving an untreated surface area 1.0 mm from the limbus. Riboflavin 0.1% in 20.0% dextran was administered topically every 2 minutes for 30 minutes. Slitlamp examination was used to confirm riboflavin absorption throughout the corneal stroma and anterior chamber. The cornea was then exposed to UVA 365 nm light for 30 minutes at an irradiance of 3.0 mW/cm$^2$ and 5.0 cm from the cornea. During UVA exposure, isotonic riboflavin was administered every 2 minutes. A bandage soft contact lens was used during the epithelial regrowth period. Chloramphenicol and betamethasone 0.1% eyedrops were administered 4 times a day for 1 week and then 4 times a day for 2 weeks. No side effect was observed during reepithelialization and the early follow-up period.

Six months postoperatively, the CDVA improved to 20/25 and 20/20 in the right eye and left eye, respectively, and the manifest refraction changed to $+1.00 -2.50 \times 70$ and $+1.00 -1.50 \times 90$, respectively. The patient did not attend postoperative visits from 6 months to 3 years, when he returned with a complaint of blurred vision in the left eye. The CDVA had remained stable in the right eye (20/25) but had dropped to 20/100 in the left eye, and the manifest refraction had changed to $+0.50 -1.50 \times 70$ and $+6.50 -2.00 \times 70$, respectively. Alterations in the CDVA and manifest refraction after CXL are shown in Table 1.

Slitlamp examination showed corneal stromal haze with a dust-like appearance extending from the subepithelial area to 90% stromal depth. A corneal slitlamp photograph is shown in Figure 2. Evaluation of the left eye refraction showed that a $+5.75 \text{ D}$ hyperopic shift had developed. The postoperative corneal changes were evaluated using rotating Scheimpflug topography (Pentacam, Oculus, Inc.) (Figure 3). There was inferior paracentral flattening in the right eye and an oblate pattern with severe central flattening in the left eye. The anterior surface $K_{\text{max}}$ changed to 41.5 D in the right eye and 34.8 D in the left eye. Topical betamethasone 0.1% 4 times a day was prescribed for 4 months with intraocular pressure monitoring; however, no improvement in vision, refraction, and keratometry occurred.

Table 1. Visual acuity and manifest refraction changes after the CXL procedure.

| Variable             | Preoperative | 6 Months | 3 Years |
|----------------------|--------------|----------|---------|
| CDVA                 |              |          |         |
| Right eye            | 20/200       | 20/25    | 20/25   |
| Left eye             | 20/60        | 20/20    | 20/100  |
| Manifest refraction  |              |          |         |
| Right eye            | +0.50 $-3.50 \times 77$ | +0.10 $-2.50 \times 70$ | +0.50 $-1.50 \times 70$ |
| Left eye             | +0.25 $-1.00 \times 96$ | +1.0 $-1.5 \times 90$ | +6.50 $-2.00 \times 77$ |

CDVA = corrected distance visual acuity; CXL = collagen crosslinking
DISCUSSION

Corneal CXL improves visual acuity, mean K values, and definable measures of corneal topography regularity. The mean amount of myopia that is usually corrected by CXL is 1.4 to 2.01 D. However, Hoyer et al. report a 4.34 D decrease in K max after CXL in a 12- to 36-month follow-up. In this report, our patient showed improvement in CDVA from 20/200 to 20/25 in the right eye and from 20/60 to 20/20 in the left eye 6 months after CXL. However, the left eye CDVA dropped to 20/100 due to corneal stromal haze at the 3-year follow-up examination. Post-CXL corneal stromal haze induced a +5.75 D hyperopic shift in the cornea.

Corneal haze and stromal hyperdensity are the only known direct complications of the CXL procedure. Patients with a K max greater than 58.0 D, who are older than 35 years, and have a CDVA better than 20/25 are at higher risk for decreased vision after CXL. Raiskup et al. reported a 9% incidence of post-CXL corneal haze in keratoconus, with increased risk in patients with lower corneal thickness and higher corneal curvature. However, Lim et al. observed that corneal haze also occurs in patients with mild forms of keratoconus and concluded that factors other than severity play a role in the formation of corneal haze. In this report, our patient developed corneal stromal haze and decreased vision, although he did not have any of the mentioned risk factors, such as low corneal thickness and high corneal curvature.

We believe this is the first report of a high hyperopic shift and severe corneal haze after the CXL procedure in a patient with PMD. It has been reported that corneal haze responded gradually to corticosteroid treatment over a few months; however, the corneal haze in our patient did not improve after 4 months of topical treatment with betamethasone eyedrops. We concluded that although CXL is a relatively safe procedure, unpredictable complications can occur postoperatively. It is advisable to inform patients with PMD or keratoconus about the possible complications of the CXL procedure.

Figure 2. Slitlamp photography of the cornea 3 years after CXL shows stromal haze with a dust-like appearance extending from the subepithelial area to 90% stromal depth.

Figure 3. Rotating Scheimpflug topography of the cornea 3 years after CXL shows inferior paracentral flattening in the right eye and an oblate pattern with severe central flattening in the left eye.
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