

Pregnancy-related exacerbation of iatrogenic keratectasia despite corneal collagen crosslinking

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Iatrogenic keratectasia after laser in situ keratomileusis (LASIK) represents a serious complication of refractive laser surgery. We describe a woman who developed bilateral iatrogenic keratectasia during her first pregnancy 26 months after LASIK. Corneal collagen crosslinking (CCL) with riboflavin and ultraviolet-A was performed in March 2005 (right eye) and April 2005 (left eye). This treatment stopped the progression and even caused the keratometric steepness to regress over a postoperative follow-up of 22 months, as demonstrated by preoperative and postoperative corneal topographies and maximum K-readings. During the patient's second pregnancy, the keratectasia exacerbated. To our knowledge, this is the first case showing exacerbation of keratectasia despite CCL and, as the exacerbation occurred only during pregnancy, suggesting that hormonal changes might affect corneal biomechanical stability.

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Laser in situ keratomileusis (LASIK) of the cornea for the correction of myopia is the most frequently performed procedure in ophthalmology. Unfortunately, under certain circumstances, the cornea does not remain biomechanically stable postoperatively and shows signs of iatrogenic keratectasia.^{1,2} Similar to those in keratoconus, the signs include progressive corneal thinning and bulging, an increase in astigmatism, severe corneal scarring, and, ultimately, loss of vision.³ Randleman et al.^{3,4} recently summarized the risk factors for the induction of this potentially devastating complication: abnormal preoperative topographies, age, high corrections, and thin residual stroma. A subgroup of patients showed no preoperative reason for the development of keratectasia. Thus, unknown factors might be involved in the pathogenesis of this complication.

CASE REPORT

A 33-year-old woman had bilateral LASIK in Mexico in 2000 for myopia of -5.5 -0.5×0 in the right eye and -5.25 -0.75×165 in the left eye. Preoperatively, the best spectacle-

corrected visual acuity (BSCVA) was 20/20 in both eyes. According to the surgeon's notes, the preoperative examinations showed no signs of preexisting corneal abnormalities. Laser in situ keratomileusis was performed using a Visx Star S2 excimer laser system at a repetition rate of 10 Hz. The total ablation depth was 68 μm in the right eye and 62 μm in the left eye. Surgery was uneventful in both eyes. However, there is no information available on the flap creation process or on estimated flap thickness and preoperative corneal thickness. After LASIK, the uncorrected visual acuity was 20/20 bilaterally with normal topographies. Ultrasound corneal pachymetry (DGH-5100e, DGH Technology, Inc.) showed a central corneal thickness of 410 μm in the right cornea and 400 μm in the left cornea. Corneal parameters remained stable in the examinations over the following 2 years.

In January 2003, the patient began her first pregnancy. In the seventh gestational month (July 2003), she noted a significant decrease in visual acuity in the right eye, coupled with glare and halos under mesopic conditions. She did not consult an ophthalmologist at that time. The next examination was performed in October 2004, when iatrogenic keratectasia was diagnosed. At that time, the BSCVA was 20/25 with -1.0 -3.5×75 in the right eye and 20/30 with -2.0 -2.5×140 in the left eye. Corneal thickness as measured by ultrasound pachymetry was 437 μm and 412 μm , respectively.

At the time of the patient's first examination at our practice in January 2005, the BSCVA was 20/63 with -3.5 -4.0×90 in the right eye and 20/50 with -5.0 -4.5×140 in the left eye. With pinhole, this improved to 20/25 and 20/30, respectively. Corneal topography showed bilateral iatrogenic keratectasia, and optical pachymetry (Pentacam, Oculus Instruments) showed a minimum corneal thickness of 370 μm in the right eye and 360 μm in the left eye.

During the following 4 months (January to April 2005), corneal topographical analyses revealed distinct bilateral progression of keratectasia (Figure 1, A). Corneal collagen crosslinking was performed in both eyes and during the

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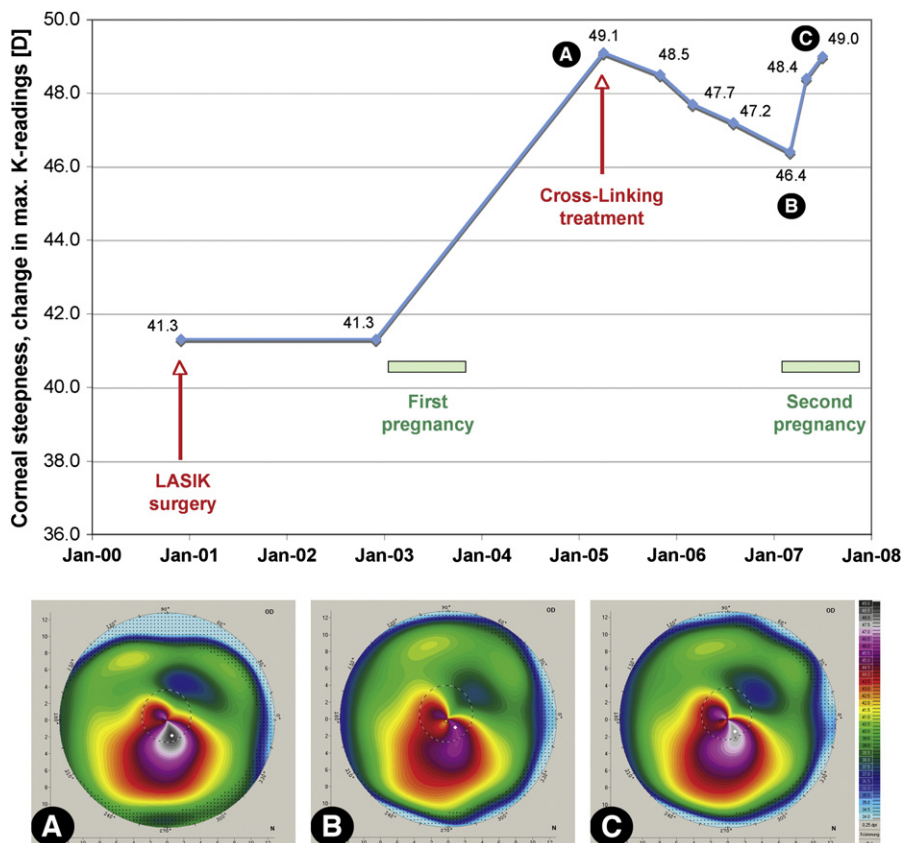


Figure 1. Time course of the exacerbation of iatrogenic keratectasia during pregnancy. Following LASIK, corneal topography remained stable for almost 3 years. *A*: During her first pregnancy, the patient noticed a distinct deterioration of vision, corresponding to LASIK-induced progressive keratectasia. *B*: The keratectasia progression not only stopped but also partially reversed up to 2 years after CCL. *C*: Iatrogenic keratectasia exacerbated again during the second pregnancy.

following 2 years, keratectasia not only remained stable but also regressed, as demonstrated by preoperative and postoperative corneal topographies and maximum K-readings and keratoconus indices (Figure 1, *B*). Concomitant with the decrease in the maximum K-readings and the regularization of central astigmatism, the BSCVA increased to 20/40 with -3.75 -2.75×85 in the right eye and 20/32 with -4.75 -2.5×145 in the left eye in October 2006. Optical pachymetry showed the expected crosslinking-induced decrease to 346 μm and 330 μm , respectively.

In January 2007, the patient began her second pregnancy and in the sixth gestational month (June 2007), she noted a sudden deterioration of vision in the right eye. Corneal topographies showed a progression of keratectasia in the right eye until the end of the second pregnancy. Maximum K-readings reached levels similar to those before CCL (Figure 1, *C*). In the left eye, the BSCVA was unchanged, and the topographies were stable.

The patient had never smoked and had no history of allergies or extensive eye rubbing. Her body mass index was between 22.2 and 25.5.

DISCUSSION

Induced keratectasia after LASIK and after photorefractive keratectomy has been widely reported in recent years. Randleman et al.⁴ have shown that the most significant risk factor for the development of iatrogenic keratectasia is preoperatively undetected abnormal topographies. Other reported cases of

induced keratectasia show no preoperative signs of corneal abnormalities. Furthermore, the postoperative time to occurrence of the first signs of keratectasia varies; in some cases, keratectasia occurred up to 36 months after LASIK.⁵ Our case shows late onset of keratectasia and is highly unusual because of the temporal accord with the patient's pregnancies.

There is growing evidence that changes in estrogen levels may play a role in LASIK-induced keratectasia: Estrogen receptors have been identified in the cornea,⁶ and exposure to estrogen reduced the biomechanical stability of the cornea in an experimental study.⁷ These data suggest that changes in estrogen levels may reduce the biomechanical stability of the cornea, which leads to the onset of iatrogenic keratectasia after LASIK. However, Randleman et al.⁴ showed a statistically significantly higher risk for men to develop iatrogenic keratectasia.

Until recently, the only therapeutic option for LASIK-induced keratectasia was keratoplasty. Recently, several groups have reported that CCL with riboflavin and ultraviolet-A can stop and even partially reverse progressive LASIK-induced keratectasia.^{8,9} In our case, CCL stabilized the ectasia and led to a partial regression of maximum K-readings over a period of 2 years. However, during the patient's

second pregnancy, the keratectasia exacerbated. One might speculate that this exacerbation was due to a "poor" or partial crosslinking effect. The actual amount of the crosslinked stroma cannot be evaluated because no tool provides direct measurement of the CCL effect. However, for several years following the first CCL treatment, the patient's topographies showed stabilization of the keratectasia. A poor cross-linking effect is therefore highly unlikely.

It is unclear why the left eye showed no progression during the second pregnancy. A possible explanation is that the residual stromal bed thickness was slightly greater than in the right eye, which developed keratectasia. In such borderline cases, minimal biomechanical differences, along with pregnancy-induced changes in estrogen levels, might determine whether a cornea develops keratectasia.

In conclusion, changes in the estrogen level during pregnancy might represent a previously unrecognized risk factor for the induction of keratectasia after LASIK surgery. To our knowledge, this is the first case to demonstrate that CCL may not be able to stabilize iatrogenic keratectasia in borderline cases.

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