Exacerbation of Avellino Corneal Dystrophy After LASIK in North America

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CASE REPORT

A 25-year-old white female was referred to the Cornea Service at Emory University for evaluation of decreased vision in both eyes 14 months after uneventful bilateral LASIK for a refractive error of approximately −8.00 D OU. The treating physician had observed “2 or 3 small, white, central, subepithelial opacities” in both eyes preoperatively.

Two months postoperatively, the patient complained of mild glare in both eyes when outdoors. Uncorrected visual acuity (UCVA) was 20/25 OD and 20/20 OS. Examination showed mild dry eye, but no corneal opacities were noted in the medical record. She was treated with artificial tears.

Over the next several months, the patient noted progressive loss of vision and increasing glare in both eyes. Six months postoperatively, UCVA was 20/25 OU. Numerous white, central, subepithelial opacities were now seen in both corneas, and the patient was diagnosed with mild diffuse lamellar keratitis. Loteprednol etabonate 0.2% was initially prescribed twice daily but was discontinued, and the opacities progressed.

By 1 year postoperatively, UCVA had fallen to 20/50 OD and 20/70 OS. Manifest refraction of −1.75 + 0.75 × 138 OD and −1.75 + 0.75 × 055 OS yielded visual acuities of 20/20 in each eye. Further progression of the corneal opacities in each eye prompted referral to the Cornea Service at Emory.

At this examination, UCVA was 20/60 OD and 20/70 OS, improving to 20/20 in each eye with refraction (−2.00 + 1.00 × 132 OD and −2.00 + 0.75 × 054 OS). Slit-lamp examination showed discrete corneal opacities within and posterior to the interface between the flap and stromal bed in each eye (Figs. 1–3). The opacities were white, granular in appearance, 0.1–0.3 mm in diameter, and the intervening stroma was clear. The ophthalmologic examination was otherwise unremarkable. The patient’s family history was pertinent for an undetermined corneal abnormality in her maternal grandfather and mother. Neither of these family members ever received treatment of this condition. Slit-lamp examination of the patient’s mother revealed similar corneal deposits in each eye.

Venous blood was drawn from the patient and extracted DNA sent for polymerase chain reaction testing and DNA sequencing of the BIGH3 gene. Her DNA was heterozygous for the R124H (Avellino dystrophy) mutation and negative for the R555W (granular dystrophy) mutation.

After discussion with the patient, spectacle correction was prescribed and observation of the corneal deposits was recommend. She was discouraged from pursuing LASIK enhancement. Her examination has remained stable over the ensuing 7 months.

DISCUSSION

This is the first reported case of exacerbated Avellino dystrophy after LASIK in North America or in a white patient; however, others will undoubtedly follow with the...
increasing numbers of LASIK procedures being performed. Some of these patients will be difficult to recognize preoperatively because of minimal corneal involvement.

Insight into factors that trigger phenotypic expression of stromal dystrophies is growing. Transforming growth factor beta (TGF-β) is a family of cytokines produced by epithelial cells and keratocytes that is involved in the corneal wound healing response. The activity of TGF-β increases in response to corneal injury and excimer laser surgery. TGF-β directly activates the BIGH3 gene causing overexpression of the gene product keratoepithelin. Specific mutations in this gene have been shown to cause Avellino dystrophy, along with forms of lattice dystrophy, granular dystrophy, and corneal dystrophy of Bowman’s membrane. Upregulation of TGF-β, therefore, should enhance abnormal corneal protein deposition in these dystrophies.

LASIK could exacerbate stromal dystrophies by several mechanisms. Flap creation triggers release of pro-inflammatory cytokines, including TGF-β, through epithelial and stromal cellular injury. The interface between the flap and stromal bed also likely enhances protein deposition by serving as a potential space for accumulation. Choi et al have also recently shown that ultraviolet (UV) light exposure increases TGF-β1 production in cultured human corneal fibroblasts. This discovery has potentially deleterious implications for the use of the 193 nm excimer laser in patients with mutations of the BIGH3 gene. The recurrence of stromal dystrophies after phototherapeutic keratectomy, sometimes quickly after ablation and more dense than prior to ablation, may be explained by UV exposure.

Treatment options for exacerbation of Avellino dystrophy after LASIK include observation or debridement of the flap interface. Jun et al performed flap elevation with manual debridement of the deposits on 1 patient. Although much of the interface was cleared and visual acuity improved in this patient, the deposits reaccumulated and vision declined to the pre-debridement level within 6 months. Another patient who was treated with debridement and mitomycin C has remained recurrence-free for greater than 6 months.

Inoue et al have shown that recurrence after phototherapeutic keratectomy tends to be less severe in patients with heterozygous mutations of the BIGH3 gene in Avellino dystrophy than it is in patients with homozygous mutations. This genetic determination may guide the form and timing of treatment and also provide prognostic information. These patients should avoid LASIK enhancements and environmental UV exposure. If elevation of the flap is performed for enhancement or interface debridement, mitomycin C or specific TGF-β blocking antibodies should be used.

**CONCLUSIONS**

LASIK may be contraindicated in patients with Avellino dystrophy because it can exacerbate the deposition of corneal opacities postoperatively. Preoperative evaluation of LASIK candidates should include a careful family history and corneal examination. Genetic testing is indicated in those
who may carry the genetic mutation for Avellino dystrophy, even if there are minimal or no corneal abnormalities present.

REFERENCES