

An Unusual Form of Avellino Dystrophy after Laser in situ keratomileusis: A Late Onset or Recurrence?

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Abstract

Purpose: To report an unusual manifestation of a corneal deposit of Avellino corneal dystrophy (ACD) after bilateral, simultaneous laser in situ keratomileusis (LASIK).

Methods: A 36-year-old Korean woman who underwent uncomplicated, bilateral LASIK and repeated phototherapeutic keratectomy (PTK) in her left eye due to corneal opacities, showed numerous, fine, white opacities with central corneal stromal haze in the left eye, which was the typical manifestation of the recurrent form of ACD. However, in the right eye, several discrete white opacities were deposited in the central anterior stroma, which was a morphologic feature of the natural course of ACD.

Results: The heterozygous R124H (CGC→CAC) mutation of the *BIGH3* gene was found in her genomic DNA extraction.

Conclusion: Further studies should be focused on what is responsible for the differences of the onset period and the shapes of the deposits in patients with ACD.

Keywords: Avellino corneal dystrophy; Laser in situ keratomileusis; Phototherapeutic keratectomy

Introduction

Granular dystrophy type II (Avellino corneal dystrophy, ACD) is an autosomal dominant corneal stromal disease that shares features of both granular and lattice corneal dystrophies. This disorder is caused by a R124 mutation in the *TGFBI* gene, which is activated by transforming growth factor (TGF)- β [1-4].

Recent studies have shown that laser in situ keratomileusis (LASIK) aggravates corneal deposits in patients with exacerbated ACD and so LASIK should be avoided in these patients [5-8]. All of the exacerbated corneal deposit of ACD after LASIK in the literature showed multiple, fine, extensive opacities in the anterior stroma, and they were mainly concentrated in the LASIK flap interface with or without diffuse central corneal stromal haze. The manifestations of the recurrent, or secondary form of ACD is significantly different from the natural-onset, or primary form for the morphological features.

We report here on an unusual manifestation of a corneal deposit of ACD after bilateral, simultaneous LASIK.

Case Report

A 36-year-old Korean woman reported blurred vision of both eyes for 6 years. She underwent uncomplicated, bilateral LASIK that was performed elsewhere 8 years ago in other clinic. Decreased visual acuity occurred 24 months after LASIK surgery, and two additional phototherapeutic keratectomy (PTK) procedures were done in her left eyes at the same clinic. Preoperatively, the spherical equivalent manifest refraction was -3.50 diopter in the right eye and -3.00 diopter in the left eye, yielding 20/20 best spectacle-corrected visual acuity (BSCVA) in both eyes. The central corneal thickness was 550 μ m on the right eye and 535 μ m on the left eye, and the intraocular pressure was 18mmHg in both eyes. According to retrospective chart review of the clinic, anterior corneal segment examination showed a clear corneal surface with no deposit. Uncomplicated LASIK surgery was performed and the uncorrected visual acuity was remained 20/20.

Twenty four months after the surgery, the patient reported glare and visual discomfort, and especially in the left eye. Her BSCVA was 20/20 in both eyes and the ophthalmologist found a few white granules on the anterior stroma, and this was worse in the left eye. The surgeon performed PTK two times at 2 and 4 years after the previous LASIK in the left eye to remove the corneal deposit. The visual disturbance was improved immediately after the PTK; however, the corneal deposits were exacerbated after a few months. The patient was referred to our clinic for consultation.

On her first visit, the manifest refraction was +1.00 -1.75 x 170 OD and +1.25 -1.00 x 50 OS, yielding 20/20 BSCVA in both eyes. Slit-lamp examination showed numerous, fine, white opacities with central corneal stromal haze in the left eye, which was the typical manifestation of the recurrent form of ACD after LASIK. However, in the right eye, several discrete white opacities were deposited in the central anterior stroma, which was a morphologic feature of the natural course of ACD. There was no signs of inflammation, edema or thinning, and no other ocular abnormalities were noted. A pedigree analysis and slit-lamp examination of her parents and siblings showed no family history of corneal dystrophy.

After informed consent was obtained, genomic DNA was extracted from the peripheral leukocytes of the patient and the heterozygous R124H (CGC→CAC) mutation of the *BIGH3* gene was found.

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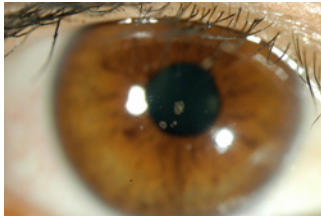


Figure 1: Slit-lamp photograph of granular deposits of anterior stroma in Avellino corneal dystrophy. The right eye shows discrete stromal opacities with intervening clear stroma and sparing of the periphery.

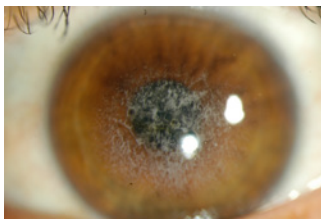


Figure 2: The left eye shows confluent and ground-glass like opacities sparing of the periphery.

Prednisolone acetate 0.12% and ofloxacin 0.3% were used four times daily in both eyes for 2 months without any improvement. The corneal deposits of both eyes showed no progression or improvement on the slit-lamp examination, and the patient's symptoms were stationary without any changes. The BSCVA remained 20/20 during the 1 year follow-up period and the patient was recommended to undergo further observation.

Discussion

Recurrence of ACD has been observed after excimer laser corneal surgery, including laser epithelial keratomileusis (LASEK) [9], LASIK [5-8] and PTK [10,11]. To treat ACD, PTK, lamellar keratoplasty, deep lamellar keratoplasty, and penetrating keratoplasty (PKP) were used, however, the recurrence remains unsolved [12-14]. In the recurrent or secondary form of ACD, the opacities are diffuse, confluent and fine whitish opacities rather than the larger, discrete white deposits that are the typical manifestation of natural-onset or primary heterozygous ACD in the absence of corneal surgery. In our patient, the left eye showed a typical recurrent feature, but the right eye showed a typical natural-onset feature. One would raise a question that there is possibilities that the surgeon who examined the patient before LASIK was not aware of the minimal evidences of ACD, which we could not identify because the prior laser surgeries were operated in other clinic. If we assume that these lesions were the aggravated form of ACD after LASIK, then the left eye still showed an unprecedented characteristic. On the contrary, if we assume that the corneal deposits developed irrespective of the corneal surgery, then the age of onset would be in her early thirties. Considering that the heterozygous ACD usually appears during the first or second decade of life⁴, our case has a very rare and unusual period of onset.

ACD was originally described in patients with ancestry traced to Northern Italy, and specifically around the region of Avellino [15], but more recently, ACD has been reported in other parts of the world. Until the mid 1990's, the diagnosis of ACD was obtained mainly from the morphological findings. Due the development of gene analysis, it is widely accepted that the diagnosis of Avellino dystrophy should be

genetically confirmed. However, the pathogenesis of ACD is unclear, except for the mutation in codon 124 of the BIGH3 gene (histidine replacing arginine), and this codes for the resultant TGF β - induced cell adhesion protein keratoepithelin (68 Kda), which is responsible for the disease progression. The mechanism for the worsening of ACD after LASIK remains elusive. TGF β is a well known cytokine associated with BIGH3 protein and any insult to the cornea could be related to an increased TGF β production and the resultant BIGH3 protein deposit. In our patient, a serial PTK induced a more prominent expression of TGF β in the keratocytes in the left eye as compared to that of the right eye, which underwent LASIK only when we assumed that the ACD of both eyes was a recurrent form.

The prevailing theory is that the stimulation of the mutated keratoepithelin protein in ACD corneas by LASIK seems to be independent of TGF β [7]. Generally, the recurrence of ACD after LASIK is more severe than that after PRK or PTK. However, the epithelial basement membrane and Bowman's layer remained intact after LASIK surgery, and there was a minimal increase in TGF β in the first few months and this became undetectable after only a few months. When we look at our patient from this point of view, we could conclude that the right eye showed the primary form of ACD in the natural course, and only the left eye showed the recurrent form of ACD after PTK. The morphological manifestation of the left eye was similar to the majority of the previously reported cases of recurrence after PTK.

BIGH3 mutation analysis may help to distinguish ACD from granular corneal dystrophy, yet for cases like ours, there is no other tool to differentiate the primary and the secondary forms of ACD. Hence, we should consider every possibility whether it is late onset with a natural course of ACD or it is a laser-induced recurrent form of ACD.

In summary, great care should be taken not to miss even the minimal evidence of ACD before performing LASIK. Although surface ablation procedures such as PTK have been considered effective methods for removing the opacities, the potential for recurrence and exacerbation of these deposits should be considered. Further studies should be focused on what is responsible for the differences of the onset period and the shapes of the deposits in patients with the primary and secondary forms of ACD, even though they share the same mutation on exon 4 (the R124H mutation) in the TGF β gene.

References

1. Kocak-Altintas AG, Kocak-Midillioglu I, Akarsu AN, Duman S (2001) BIGH3 gene analysis in the differential diagnosis of corneal dystrophies. *Cornea* 20: 64-68.
2. Holland EJ, Daya SM, Stone EM, Folberg R, Dobler AA, et al. (1992) Avellino corneal dystrophy. Clinical manifestations and natural history. *Ophthalmology* 99:1564-1568.
3. Konishi M, Yamada M, Nakamura Y, Mashima Y (2000) Immunohistology of kerato-epithelin in corneal stromal dystrophies associated with R124 mutations of the BIGH3 gene. *Curr Eye Res* 21: 891-896.
4. Folberg R, Alfonso E, Croxatto JO, Driezen NG, Panjwani N, et al. (1988) Clinically atypical granular corneal dystrophy with pathologic features of lattice-like amyloid deposits. A study of these families. *Ophthalmology* 95: 46-51.
5. Lee ES, Kim EK (2003) Surgical do's and don'ts of corneal dystrophies. *Curr Opin Ophthalmol* 14:186-191.
6. Kim TI, Kim T, Kim SW, Kim EK (2008) Comparison of corneal deposits after LASIK and PRK in eyes with granular corneal dystrophy type II. *J Refract Surg* 24: 392-395.
7. Awwad ST, Di Pascuale MA, Hogan RN, Forstot SL, McCulley JP, et al. (2008) Avellino corneal dystrophy worsening after laser in situ keratomileusis: further clinicopathologic observations and proposed pathogenesis. *Am J Ophthalmol* 145: 656-661.

8. Chiu EK, Lin AY, Folberg R, Saidel M (2007) Avellino dystrophy in a patient after laser-assisted in situ keratomileusis surgery manifesting as granular dystrophy. *Arch Ophthalmol* 125: 703-705.
9. Lee JH, Stulting RD, Lee DH, Lee CS, Kim WC, et al. (2008) Exacerbation of granular corneal dystrophy type II (Avellino corneal dystrophy) after LASEK. *J Refract Surg* 24: 39-45.
10. Inoue T, Watanabe H, Yamamoto S, Maeda N, Inoue Y, et al. (2002) Recurrence of corneal dystrophy resulting from an R124H Big-h3 mutation after phototherapeutic keratectomy. *Cornea* 21: 570-573.
11. Dogru M, Katakami C, Nishida T, Yamanaka A (2001) Alteration of the ocular surface with recurrence of granular/avellino corneal dystrophy after phototherapeutic keratectomy: report of five cases and literature review. *Ophthalmology* 108: 810-817.
12. Park KA, Ki CS, Chung ES, Chung TY (2007) Deep anterior lamellar keratoplasty in Korean patients with Avellino dystrophy. *Cornea* 26: 1132-1135.
13. Moon JW, Kim SW, Kim TI, Cristol SM, Chung ES, et al. (2007) Homozygous granular corneal dystrophy type II (Avellino corneal dystrophy): natural history and progression after treatment. *Cornea* 26: 1095-1100.
14. Nassaralla BA, Garbus J, McDonnell PJ (1996) Phototherapeutic keratectomy for granular and lattice corneal dystrophies at 1.5 to 4 years. *J Refract Surg* 12: 795-800.
15. Dolmetsch AM, Stockl FA, Folberg R, Gensini I, Burnier MN Jr (1996) Combined granular-lattice corneal dystrophy (Avellino) in a patient with no known Italian ancestry. *Can J Ophthalmol* 31: 29-31.