Delayed Onset of Lattice Corneal Dystrophy Type IIIA Due to a Novel T621P Mutation in TGFBI

To the Editor:

We recently identified a family with lattice corneal dystrophy type IIIA (LCD IIIA) associated with a novel threonine-to-proline (T621P) mutation in the transforming growth factor-beta induced (TGFBI) gene.

The 50-year-old female proband (II-2) visited our clinic because of decreased visual acuity. Slit-lamp examination disclosed thick, branching, refractile, ropy lattice lines located in both stromal corneas, which extended to the limbus radially (Figures AA-AC, available in the online version of this article). The right cornea showed a higher number of lattice lines than the left cornea. Molecular analysis involving bidirectional complete sequencing demonstrated a novel T621P mutation in exon 14 of TGFBI. After we identified this new mutation, we performed genetic and clinical examinations on 10 other family members (Severance Hospital Institutional Review Board [No. 4-2014-1046]).

The corneas of elderly affected members (I-1, II-1, and II-2) showed the LCD IIIA phenotype with asymmetry between both corneas, as reported for LCD IIIA. Three family members in their mid-twenties (III-1, III-2, and III-4) had clear corneas despite having the mutated TGFBI gene (Figure AD). This suggests that the family had a late-onset form of LCD IIIA.

The 26-year-old son of the proband (III-3), who had undergone LASIK 5 years earlier at a different facility, maintains clear corneas and showed no mutation in the recent genetic test. He was aware that his grandmother and mother had visual problems but was not aware of the genetic basis of the condition. Therefore, he did not notify the surgeon of any visual problems of the family before the LASIK procedure because he was not asked about them.

The relatively late onset of LCD IIIA is favorable for young affected individuals in that visual acuity is well preserved until advanced age. However, the III-3 family member, who is the only one having the normal gene among the four genetically examined cousins, highlights the worrying possibility of young adults harboring the mutation but having clear corneas and undergoing LASIK.

The safety of laser surgery in LCD is yet to be established.1 There are reports that LCD recurs after phototherapeutic keratectomy.2 TGFBI-related LCD IIIA might be exacerbated after refractive surgery according to reports on the exacerbation of different TGFBI-related corneal dystrophies after LASIK or LASEK.3,4 Furthermore, Weissman and Randleman5 showed that interface abnormalities occurring in granular corneal dystrophy after LASIK were improved after therapeutic amputation of the flap.

Gene tests are currently being applied to screen out common TGFBI mutations before refractive surgery. Young patients (eg, III-1, III-2, and III-4) of an affected family can be detected only when the whole TGFBI gene is sequenced. Because the whole gene sequence cannot routinely be obtained from young patients with clear corneas, it is important for the surgeon to obtain an accurate history of vision in the family before deciding to proceed with corneal refractive surgery.

REFERENCES


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Figure A. Slit-lamp photographs of the cornea of the proband, and the pedigree of the family. 

(A) The right cornea of the 50-year-old proband demonstrates multiple, radially oriented, branching lattice lines. 

(B) Refractile ropy lattice lines of the right cornea are more clearly seen on retroillumination. 

(C) Fourier domain optical coherence tomography image covering the lattice lesion of Figure A demonstrated highly reflective material in the mid-stroma. 

(D) The three-generation pedigree of the family with lattice corneal dystrophy type IIIA associated with a novel threonine-to-proline (T621P) mutation in transforming growth factor-beta induced gene. III-1, III-2, and III-4 had the T621P mutation but did not show any abnormal corneal manifestation. III-3 underwent LASIK 5 years earlier without notifying the surgeon of any vision-related family history.