

Familial Case of Keratoconus With Corneal Granular Dystrophy

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Abstract: A family with keratoconus combined with corneal granular dystrophy is reported. The patients are a mother and her two sons. The mother and her elder son have both keratoconus and corneal granular dystrophy; the younger son has keratoconus. Thus, the keratoconus in this family is thought to be of autosomal dominant inheritance. These familial cases suggest that the gene loci for both diseases localize in proximity or have a close relationship. **Jpn J Ophthalmol 1998;42:385-388** © 1998 Japanese Ophthalmological Society

Key Words: Autosomal dominant inheritance, corneal granular dystrophy, familial case, gene locus, keratoconus.

Introduction

Keratoconus is reported to be an inherited disease¹⁻⁴ or associated with other systemic^{5,6} or ocular diseases.^{7,8} Corneal granular dystrophy is a well-known autosomal dominant disorder.⁹ Several keratoconus cases combined with granular dystrophy have been reported^{10,11}; all were sporadic cases. So far as we know, familial cases of the combined diseases have not been reported. We report a family with these diseases.

Case Reports

Case 1, 15 years old, had complained of blurred vision in both eyes for 1 year. He did not have any systemic diseases. His parents had not intermarried. Other family members have keratoconus and granular dystrophy, as shown in Figure 1. We could not get patient cooperation to investigate relatives other than those shown in the figure. The ocular findings at our first examination were as follows. His visual acuity was 0.09 (0.1x-0.75 cyl-0.5 Ax90) for the right eye and 0.5 (1.2x-0.5 cyl-0.5 Ax90) for the left. His

intraocular pressure was 10 mmHg for the right eye and 11 mmHg for the left. There were no particular findings in the anterior chamber, lens, and ocular fundus. Both corneas showed steep deformity in the paracentral area of the inferior cornea, as shown in Figure 2. The right cornea developed Fleischer's ring and keratoconus line, but the left showed no remarkable change except its cone shape. Both corneas developed many small, round, granular pattern opacities with clear margin. The opacity was similar in both eyes. There was no vascularization from the limbus, as can be seen in Figure 3. The corneal topography for both eyes showed a typical keratoconus pattern (Figure 4A). His added vision with contact lenses was 0.9 for the right eye and 1.2 for the left.

Case 2, the 43-year-old mother of Case 1, had noticed bilateral deterioration in vision and corneal opacity since the age of 15. We examined her suspecting granular dystrophy after the examination of her son, case 1. Her vision was 0.7 (n.c.) for the right eye and 0.1 (n.c.) for the left. A slitlamp examination revealed keratoconus, but we could not observe Fleischer's ring or keratoconus line. Her right cornea developed a white granular opacity with clear margin in the anterior half of the stroma. The left cornea developed an opacity with a christmas-tree pattern in addition to a granular opacity similar to the one observed in her right cornea in the anterior half of

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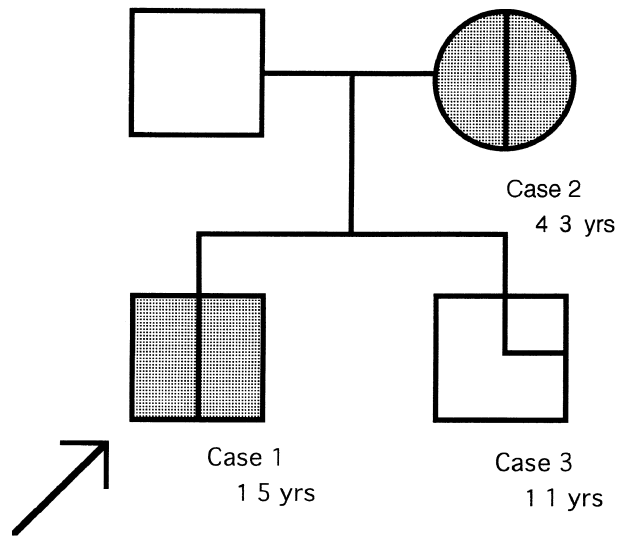


Figure 1. Family tree. Square: male, circle: female, shading: granular dystrophy, bisecting line: keratoconus, square within a square: early stage of keratoconus.

the stroma, as shown in Figure 5. Neither cornea showed vascularization from the limbus. Corneal topography demonstrated a typical keratoconus pattern, as shown in Figure 4B. There were no particular findings in the anterior chamber, lens, and fundus.

Case 3, the 11-year-old younger brother of Case 1, also had complained of blurred vision since an early age, 9 years. He had no systemic disorders. He was examined suspecting granular dystrophy after the examination of his sibling. His vision was 0.5 (1.0x-2.0 cyl-1.0 Ax80) for the right eye and 0.4 (1.5x-1.25 cyl-0.75 Ax 110) for the left. A slit-lamp examination revealed neither keratoconus nor corneal opacity. However, corneal topography showed an

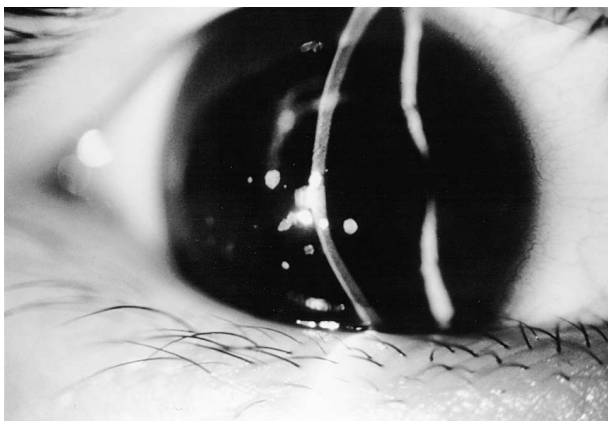


Figure 2. Slit-lamp photography in Case 1 shows steep deformity in paracentral area.

early stage of keratoconus (Figure 4C). There were no particular findings in intraocular pressure, anterior chamber, lens, and fundus.

Discussion

As far as we know, there are only two reports regarding patients with keratoconus associated with corneal granular dystrophy.^{10,11} They were not familial cases but sporadic cases. Yoshida et al¹¹ estimated the pathogenesis of the keratoconus to be secondary and due to the tissue degeneration caused by granular dystrophy. Koomoto et al¹⁰ concluded that the two diseases had occurred coincidentally. Our case is the first familial case with both diseases. We speculate that there are three possibilities for the pathogenesis of the combination of these two diseases. The first is secondary keratoconus due to granular dystrophy. The second is that the two diseases occurred coincidentally in the members of one family. The third is that a genetic factor played a role in the simultaneous development of both diseases. Secondary keratoconus is not probable because of the corneal findings showing no vascularization and an irregular conus pattern that is typically seen in secondary keratoconus.⁶ Furthermore, Case 3 has shown only keratoconus without granular dystrophy, so far. The combination of both diseases in the same eye is so rare that coincidental development of both diseases in the same family is improbable and not logical. Therefore, we thought that a genetic factor is involved in the present cases. The involvement of genetic factors has been reported in keratoconus, however, its hereditary pattern was not identified. Hammerstein^{12,13} reported autosomal dominant and X linked recessive patterns in keratoconus. Waardenburg et al¹⁴ thought an autosomal recessive inheritance due to the consanguinity in their case. Hallermann and Wilson¹⁵ thought a multiple gene involvement, because keratoconus shows sexual deviation and occasional complication with other disorders. Tanabe et al⁴ speculated that keratoconus may have multiple gene involvement based on estimated analysis. According to the literature, frequency of familial keratoconus ranges from 10-20% in Europe.¹³ Only a few families with keratoconus have been reported in Japan.¹⁻⁴ There are only two families, including the present case, in 239 patients with keratoconus in our clinic. We could not get approval to examine other family members of the present case. We can speculate autosomal dominant inheritance based on the involvement pattern in this case. Corneal granular dystrophy is identified as an autosomal

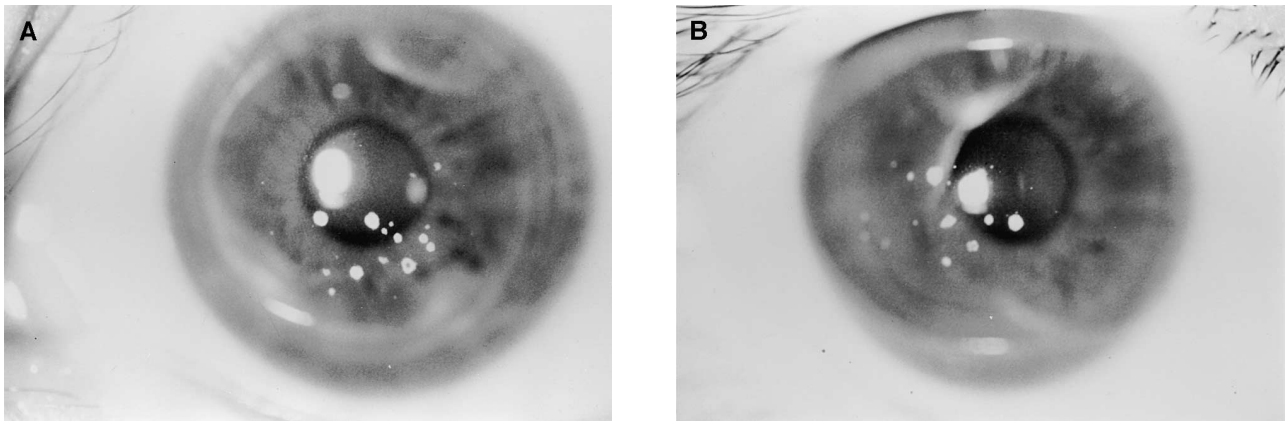


Figure 3. Typical granular deposits are observed in corneas of right (A) and left (B) eyes of Case 1.

dominant disease. In addition, Stone et al¹⁶ revealed three autosomal dominant corneal dystrophies mapped to chromosome 5q, and Munier et al¹⁷ established a common molecular origin for the 5q31-linked corneal dystrophies. The present cases are also comparable with the above inherited pattern be-

tween the mother and elder brother. If the keratoconus in this case is inherited in the same pattern as granular dystrophy, it makes us think that the gene loci of the two diseases localize in proximity or have some linkage. Granular dystrophy occurs mostly in the teens and develops with age.⁹ If the difference in

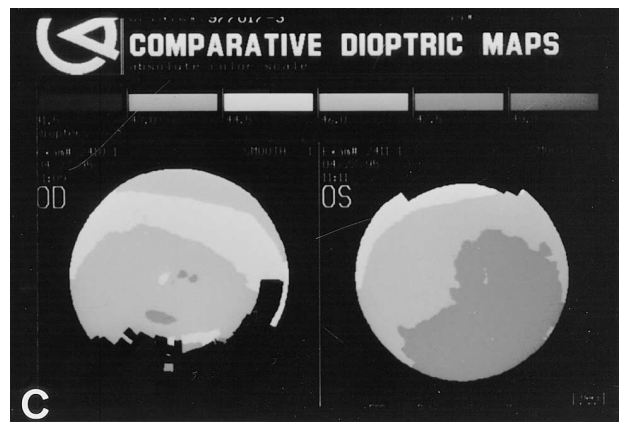
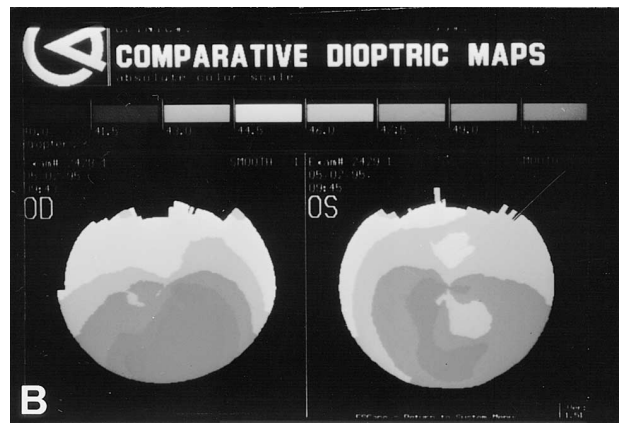
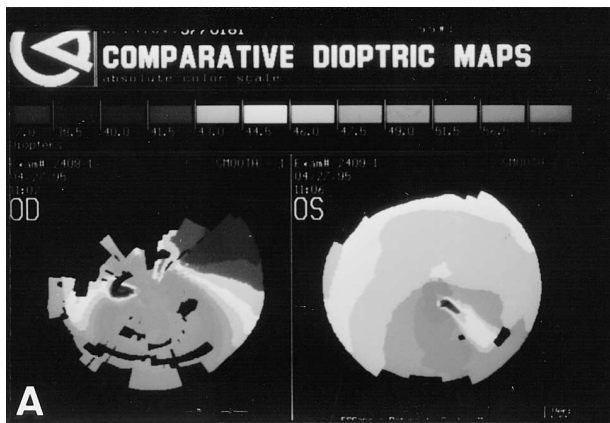


Figure 4. Corneal topography shows typical keratoconus pattern. (A) Case 1 (elder son), (B) Case 2 (mother), (C) Case 3 (younger son).

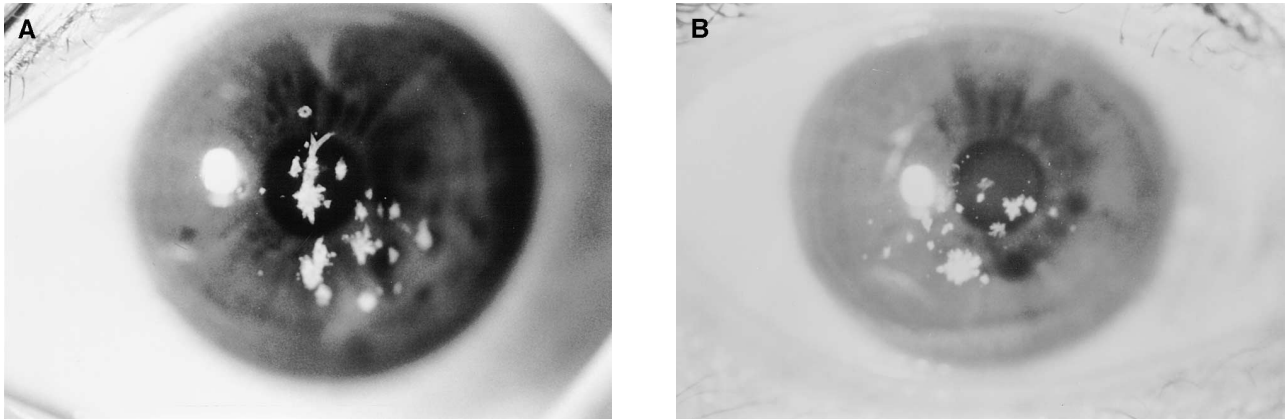


Figure 5. Typical granular deposits are observed in corneas of right (A) and left (B) eyes of Case 2.

grade of corneal opacity is due to the age difference in these patients, then the younger brother will develop granular dystrophy as he ages. Follow-up examinations are necessary and gene analysis can help clarify the pathogenesis of these diseases.

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