

## Familial Case of Keratoconus with Corneal Granular Dystrophy in a Family of Iranian Origin

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Received date: Jun 06, 2014, Accepted date: Nov 14, 2014, Published date: Nov 19, 2014

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### Abstract

**Purpose:** To report a rare case of keratoconus concurrent with granular corneal dystrophy in a family of Iranian origin.

**Methods:** Case report.

**Results:** Keratoconus combined with granular dystrophy developed bilaterally in a family from Iran. The father, mother and her elder son have both keratoconus and corneal granular dystrophy. Thus, the keratoconus in this family is thought to be of autosomal recessive inheritance. Histologic evaluation showed characteristic features of keratoconus and other corneal dystrophies were excluded. **Conclusions:** To our knowledge, this is the second reported case in the literature. The concurrence of keratoconus and granular dystrophy raises the possibility of a genetic linkage of the diseases. Moreover, the diagnosis of keratoconus in patients with granular dystrophy is important because impairment of vision might be the result of keratoconus and could be treated with contact lenses instead of keratoplasty.

**Keywords:** Autosomal recessive inheritance; Corneal granular dystrophy; Familial case; Genetic linkage; Keratoconus

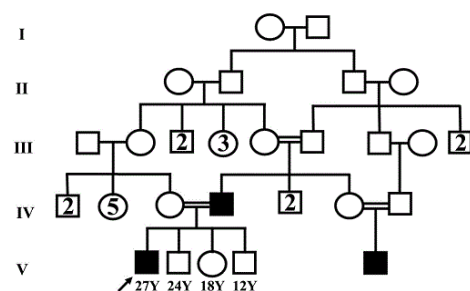
### Introduction

Keratoconus (KCN) is a bilateral, progressive and non-inflammatory disease of the cornea which often leads to high myopia and astigmatism with an estimated prevalence of approximately 1 in 2000. The Positive family history can be detected in 6-8% of patients [1]. Keratoconus is reported to be a heterogenic inherited disease [2] and eight different types of it have been described with an autosomal dominant inheritance pattern [3]. In the interim, more than a few types of granular corneal dystrophy (GCD) have been described that type 1, 2 and 3 of GCD can be caused by heterozygous mutation in the VSX1 gene. Several KCN cases combined with granular dystrophy have been reported [4,5]; all were sporadic cases. So far as we know, familial cases of the combined diseases have been reported only in one case. We report a family with these diseases.

### Case Reports

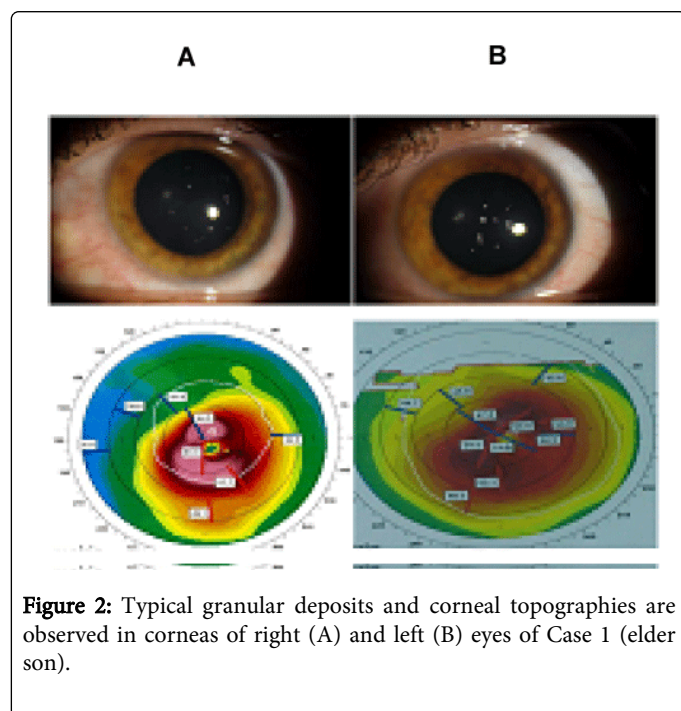
Case 1, a 27 year old male, presented with progressive bilateral visual loss for the past 9 years. The patient denied any history of systemic disease, surgery, or medications. His parents had intermarried; first cousin. There was history of a similar disease in his family as shown in (Figure 1). General physical examination was unremarkable. The ocular findings at our first examination were as follows: His best corrected vision was 0.32 (-13.00 -5.00x150) in the left eye respectively 0.5 using contact lenses and 0.63 (-4.00 -2.00x50) in the right eye respectively 0.8 using contact lenses. 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 eyes were thin and bulging. Incomplete Fleischer's rings were visible at the base of the lesions in the right cornea, but the left eye showed no remarkable change except its cone shape. Both corneas developed many small, round, granular pattern opacities with clear margin.



**Figure 1:** Family tree. Shading: combined granular dystrophy and keratoconus, a circle or a square with a number on the inside: Multiple individuals of each sex, double lines: consanguineous mating.

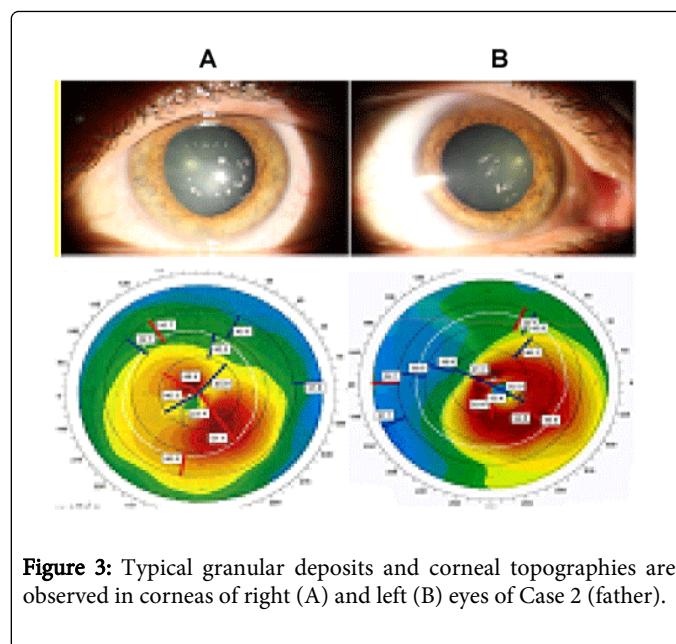
The opacity was similar in both eyes. Corneal topography (EyeSys Vision Inc., Houston, Texas, USA) for both eyes showed a characteristic pattern of KCN (Figure 2). At the age of 20, keratoconus also developed in the left eye. Due to the progressive visual loss, the patient underwent deep anterior lamellar keratoplasty (DALK) in the right eye on January 2010 and 6 months later in the left eye. The postoperative course was uneventful and there have been no episodes of rejection to date.



**Figure 2:** Typical granular deposits and corneal topographies are observed in corneas of right (A) and left (B) eyes of Case 1 (elder son).

Case 2, the 54-year-old father of Case 1, had noticed bilateral deterioration in vision and corneal opacity since the age of 19. We examined his suspecting granular dystrophy after the examination of his son, case 1. His vision was 0.8 (-2.25 -0.75x64) for the right eye and 0.4 (-4.75 -4x138) for the left. Pupillary reactions and ocular motility were normal. Slit-lamp biomicroscopy revealed keratoconus, but we could not observe Fleischer's ring or keratoconus line. His 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 his right cornea in the anterior half of the stroma, as shown in Figure 3. Corneal topography demonstrated a typical keratoconus pattern, as shown in (Figure 3). There were no particular findings in the anterior chamber, lens, and fundus.

Case 3, The 48-year-old mother of Case 1, also had complained of blurred vision since an early age; 27 years. She had no systemic disorders. She was examined suspecting granular dystrophy after the examination of her son. Her vision was 0.8 (-1 -1.25x80) for the right eye and 0.9 (-1.5-0.75x110) for the left. On slit-lamp examination, small granular corneal opacity was detected but Fleischer's rings and vogt striae were not present. Moreover, corneal topography showed no anterior keratoconus, however posterior keratoconus was confirmed by Belin-Ambrosio elevation maps of Pentacam. Intraocular pressures were 12 and 10 mmHg in the right and left eyes, respectively. There were no particular findings in intraocular pressure, anterior chamber, lens, and fundus.



**Figure 3:** Typical granular deposits and corneal topographies are observed in corneas of right (A) and left (B) eyes of Case 2 (father).

## Discussion

As far as we know, this is the second familial case and the eighth reports in the literature regarding concurrence of keratoconus and granular corneal dystrophy. Moreover, this is the first familial case reported in 2000 patients with keratoconus in our clinic that histopathologic analysis (data not shown) confirmed our clinical diagnosis and excluded other dystrophies, whose concurrence with keratoconus has also been described [1].

According to the literature, patients who had combined granular dystrophy and keratoconus, reported to be between 15 and 21 years of age [6]. Similarly our cases presented between 17 to 19 years of age.

Moreover, since it is difficult to diagnose keratoconus in early stages especially when it is associated with other diseases [6], Wollensak et al. had reported that incidence of keratoconus conjointly with granular dystrophy may be higher with granular dystrophy as a presenting diagnosis. Considering the age difference in these patients, then the other young members may develop granular dystrophy as they ages. Therefore, follow-up examinations are necessary to clarify the clinical features of this disease progression.

On the other hand, the association of keratoconus with a relatively rare disorder like granular dystrophy especially when present in two generations, suggests that there may be a genetic linkage between the two diseases, however, its hereditary pattern was not identified [5,7].

The present cases are comparable with the other inherited pattern between the father, mother and elder brother. If the keratoconus in this case is inherited in the same pattern as granular dystrophy, it makes us think that a genetic factor is involved in the present cases. The disease shown in this pedigree (Figure 1), illustrate intermarriage; first cousin in all involved cases. In addition, despite the fact that none of other family members; unaffected cases, were shown suspicious for form frust keratoconus during examination, Orbscan topography was done for them that no form fruste keratoconus was detected (data not shown). Thus, based on the involvement pattern in this case; intermarriage: first cousin in all involved cases, autosomal recessive is

the most likely pattern of inheritance in this pedigree. However, because of two healthy members of a pedigree and the existence of reduced penetrance in most of genetic disorders, an autosomal dominant pattern could not be ruled out.

Additionally, from a clinical point of view, this case shows the importance of excluding additional keratoconus in granular dystrophy because this disorder can be the main reason for the decreased vision that can often be treated with contact lenses. Moreover, due to corneal thinning secondary to additional keratoconus, keratoplasty may be delayed or even avoided and excimer laser treatment also should be applied with caution.

In summary, this study presents clinical records of three members in two generations who were affected with clinical manifestation of concurrent GCD and keratoconus with a strong family history of this disorder. Despite that, this report has not yet been defined at the molecular level. So, future molecular and genetic studies may elucidate this association.

### Acknowledgements

We would like to acknowledge the staffs of eye clinic in Bina Eye Hospital research center for their invaluable help during the entire process of this study.

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