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Case Report

Bilateral granular dystrophy: A clinicopathogenetic correlation after alcohol assisted debridement with phototherapeutic keratectomy

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and genetic basis, thereby giving a complete insight into each dystrophy, and has also enabled easy adaptation to advances in understanding from the continued discovery of new genes and mutations. Herein, we report two siblings who were clinically diagnosed with a rare variant of granular dystrophy i.e. superficial variety, confirmed histopathologically from debrided epithelia using an innovative procedure i.e. alcohol assisted phototherapeutic keratectomy (PTK). To the best of our knowledge, such an innovative method to confirm the diagnosis has not been mentioned in literature. Genetic analysis was also done, thereby enabling a clinicopathogenetic correlation, considering the newer classification of corneal dystrophies.

Introduction

Bilateral corneal dystrophy includes a group of genetically determined, non-inflammatory corneal diseases, which result in loss of corneal transparency and visual impairment.¹ Earlier, the classification of corneal dystrophy was solely anatomically based. However, the newer classification system based on recommendations of the International Committee for Classification of the Corneal Dystrophies (IC3D)² has incorporated clinical findings, pathological characteristics

Case Report

Case 1: the 42-year-old elder sibling had painless progressive diminution of vision in both eyes since childhood. His preoperative visual acuity was 20/400 with −7.5D Sph in both eyes.

Case 2: the 39-year-old younger sibling presented with a similar complaint. His preoperative visual acuity was 20/100 with −4.5D Sph in both eyes.

Slit lamp examination (Fig. 1) on diffuse and optical section showed bilateral, multiple, grayish-white, discrete,

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Fig. 1 – Preoperative slit lamp photograph (A & B): multiple, grayish-white, discrete, breadcrumb to ring shaped opacities predominantly in the anterior stroma, with clear corneal periphery.

breadcrumb to ring shaped opacities predominantly in the anterior stroma, with clear corneal periphery in both siblings. Anterior segment OCT revealed normal corneal thickness. Based on the above findings, clinically, a diagnosis of bilateral granular dystrophy was made.

Considering corneal involvement predominantly in the anterior stroma, both siblings were subjected to alcohol assisted debridement with phototherapeutic keratectomy. In this procedure, a cleavage was achieved between basement membrane and epithelium with the help of 20% alcohol for 60 s duration. Following this, the epithelial sheet was gently peeled off and excise ablation was carried out to remove stromal lesion up to a depth of 100 microns level. The ablation

Table 2 – Pachymetry reading.

	Total (μm)	After flap (μm)	After ablation (μm)
Case 1			
Right eye	608	552	495
Left eye	596	543	492
Case 2			
Right eye	541	505	452

parameters are given in Table 2. It is these debrided epithelia that were sent for histopathological examination. Blood samples were collected and sent for genetic analysis. Post-operatively, there was marked improvement in vision, as highlighted in Table 1. The cornea was relatively clear, except for a few deep seated opacities (Fig. 2).

On histopathological evaluation (Fig. 3), amorphous eosinophilic deposits were seen underlying the epithelium on H&E staining. This amorphous deposit stained a brilliant red with Masson trichrome, thereby confirming the diagnosis of GCD.

Genetically, through polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) analysis followed by sequencing of exon 12, it was found that both siblings have Arg555Trp mutation in the TGFBI gene. This mutation was heterozygous in nature as shown on gel electrophoresis (Fig. 4).

Fig. 2 – Postoperative slit lamp photograph (A & B).

Table 1 – Demographic details.

	Pre op vision	Post op vision (at 2 months)	Hyperopic shift
Case 1			
Right eye	20/400 with –7.5DS	20/30 with –7DS	+0.5DS
Left eye	20/400 with –7.5DS	20/30 with –7DS	+0.5DS
Case 2			
Right eye	20/100 with –4.5DS	20/25 with –4DS	+0.5DS

Fig. 3 – Histopathological photographs with H&E and Massons trichrome stains (A & B).

Fig. 4 – Gel electrophoresis photograph showing heterozygous mutation at 12 (4).

Discussion

Granular dystrophy was first described by Groenouw in 1890. Using the IC3D classification, it is TGFBI corneal dystrophy representing Category I (C1), which means a well-defined corneal dystrophy, in which the gene has been mapped and identified, and for which specific mutations are known.² It is point mutation in TGFBI gene (hotspots are at codons for Arg124 and Arg555 residues in exons 4 & 12 respectively) which leads to deposition of abnormal keratoepithelin³ in anterior stroma. In our case series, heterozygous Arg555Trp mutation found in exon 12, was confirmatory for GCD type I.

It is characteristic of non-collagenous protein to stain a brilliant red with Masson trichrome whereas collagenous protein i.e. stromal lamellar fibers stain blue with it.

Various surgical options are available depending on depth of lesions. For more deeper involvement, deep anterior lamellar keratoplasty,⁴ penetrating keratoplasty with⁵ and without⁶ femtosecond laser have been described. However, since our patients manifest as a superficial variant of granular dystrophy type I, alcohol assisted phototherapeutic keratectomy was opted for to remove central epithelium *in toto* for histopathological analysis, followed by phototherapeutic keratectomy to remove deposits from anterior stroma. Following alcohol assisted epithelial debridement; it was found that most of the granular deposits adhered to the epithelium that had stained eosinophilic with H&E stain and brilliant red with Masson trichrome. This method provides an innovative way of confirming a dystrophy through histopathological analysis of the debrided tissue. To our knowledge, this has not been described in literature.

Following PTK, a marked improvement in vision was observed, which is similar to an earlier study.⁷ A hyperopic shift of +0.5D was observed in our case series, whereas earlier studies^{8,9} have quoted it as +2.25D and +1D respectively. This difference could be attributed to a varying depth of ablation.

Recurrence is known to occur after PTK.^{8,9} Inoue et al¹⁰ have found that the mutation pattern determines the recurrence after PTK i.e. heterozygous mutation has less severe recurrence and they can have prolonged recurrence-free interval. In conclusion, herein we have made an attempt to confirm a rare variant of granular dystrophy histopathologically through an innovative method i.e. alcohol assisted debridement combined with PTK, and establish IC3D based diagnosis through clinicopathogenetic correlation.

Conflicts of interest

All authors have none to declare.

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