

Failed Deep Anterior Lamellar Keratoplasty in Avellino Stromal Dystrophy: A Case Report and Review of Literature

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Abstract

Corneal dystrophy (CD) has an autosomal dominant inheritance pattern. A female 45 years of age presented with both eyes dimension of vision in the recent past without any associated ocular pathology. Examination revealed an Avellino's stromal CD. Multiple white dots about 0.5 mm in diameter, studding the stroma not involving the endothelium, spread over central 8 mm with an interdigitating network of filaments. Deep anterior lamellar keratoplasty (DALK) on the table showed the filaments were anchored to the endothelium not allowing a separation though anterior segment optical coherence tomography and histopathology showed they are neatly separated from it. We are publishing this case to highlight the need for a good corneal endothelial count in the donor cornea and the need to keep the option of penetrating keratoplasty in a Avellino stromal dystrophy though DALK is the first choice of management.

Key words: Avellino dystrophy, Corneal dystrophy, Deep anterior lamellar keratoplasty, Keratoplasty

INTRODUCTION

Corneal dystrophy (CD) is defined as bilateral and symmetric primary corneal disease, without previous associated ocular inflammation. Most cases of CD have an autosomal dominant inheritance pattern, starting at the first decades of life, with a stable or slowly progressive course. CDs are classified according to the involved corneal layer (Table 1).

Avellino CD was first described by Folberg *et al.* (1988). It exhibits features of both granular and lattice dystrophy. It is inherited in an autosomal dominant fashion and related to the transforming growth factor beta-induced gene (TGFβ1), locus 5q31.¹ Biomicroscopically, granular deposits are more superficial and as the disease progresses, a snowflake appearance deeper in the stroma can be noted. The linear refractile deposits tend to be deeper than the

granular deposits, but with progression these lines coalesce with the round opacities.² First signs of the disease can be seen as early as 3 years of age in homozygotic cases, but most common during puberty or early adulthood.³ Visual acuity deteriorates as the central visual axis becomes affected, and corneal erosions can result in episodes of pain. Homozygotes can have a more rapid course comparing with heterozygotes patients. Visual rehabilitation is achieved by corneal transplantation usually lamellar.

CASE REPORT

Female 45 years old presented with complaints of gradual progressive diminution of vision since 10 years of age. She was unable to do her routine activities in the past 3-4 months necessitating a visit to the eye doctor. There was no contributory history in the form of trauma, inflammation, or any surgical procedure in the past. The patient did not have any systemic illness negating any metabolic disorders. Family members did not have any similar visual problem.

On examination, the ocular findings in both eyes were similar. Best corrected visual acuity 6/60 due to opacity

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Table 1: Type of CD

CD categorized by corneal layer
Epithelial and subepithelial dystrophies
EBMD
ERED
SMCD
Meesmann's CD
Lisch epithelial CD
Gelatinous drop-like CD
Bowman's layer dystrophies
Reis-Bucklers' CD
Thiel-Benke CD
Grayson-Wilbrandt CD
Stromal dystrophies
Lattice (Type I, II, III, and IV)
Granular (Groenouw type, Avellino dystrophy)
Macular (Type I and II)
SCCD
Congenital stromal CD
Fleck's CD
Posterior amorphous CD
Central cloudy dystrophy of Francois
Pre-Descemet's CD
Descemet and endothelial dystrophies
Fuch's endothelial CD (early onset and late onset)
Posterior polymorphous dystrophy
Congenital hereditary endothelial dystrophy
X-linked endothelial dystrophy

CD: Corneal dystrophy, EBMD: Epithelial basement membrane dystrophy, ERED: Epithelial recurrent erosion dystrophy, SMCD: Subepithelial mucinous corneal dystrophy, SCCD: Schnyder's corneal crystalline dystrophy

involving the optical axis. Ocular adnexa, conjunctiva, and sclera were normal. The cornea was normal in size and shape. Multiple white dots about 0.5 mm in diameter eroding out of the epithelium, studding the stroma not involving the endothelium, spread over 8 mm area, with the interdigitating network of filaments. No vascularization, pigmentation, or degeneration (Figures 1 and 2). The corneal sensations were present. The rest of anterior segment and posterior segment were within normal limit (Table 2).

To support our clinical finding, we ordered anterior segment optical coherence tomography of both eyes. There was deep stromal involvement sparing the descemet's membrane (DM) and the endothelium (Figure 3). For visual rehabilitation, a decision to do deep anterior lamellar keratoplasty (DALK) was taken as the stromal involvement spared the descemets and the endothelium. Routine investigation for anesthesia fitness was taken and tissue arranged with a good endothelial count of 2450 cells/cumm. This was done in contingency to an inadvertent conversion to penetrating keratoplasty (PKP). On the table, Big bubble technique was done after lamellar dissection of 300 μ of the central 8 mm of the corneal tissue. A central cruciate incision over the central cornea over an iris repository was done to prevent an inadvertent corneal perforation. During the lamellar dissection to

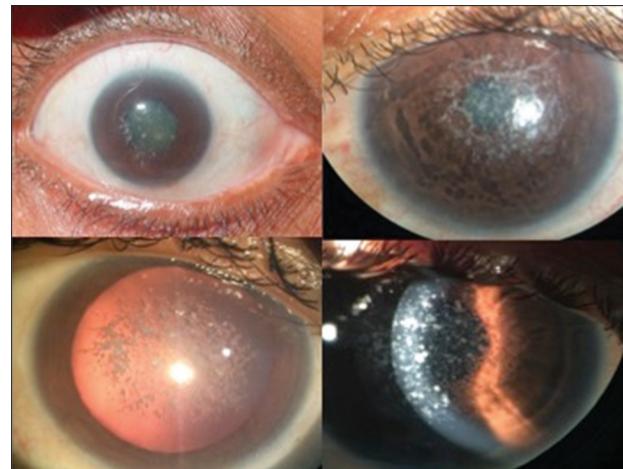


Figure 1: Right eye stromal corneal dystrophy external and slitlamp view

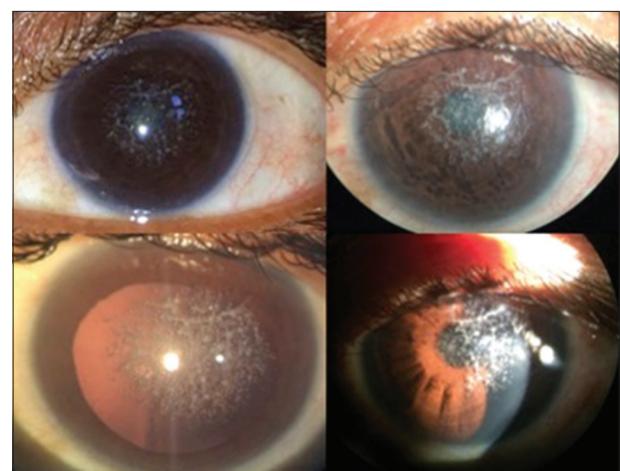


Figure 2: Left eye stromal corneal dystrophy external and slitlamp view

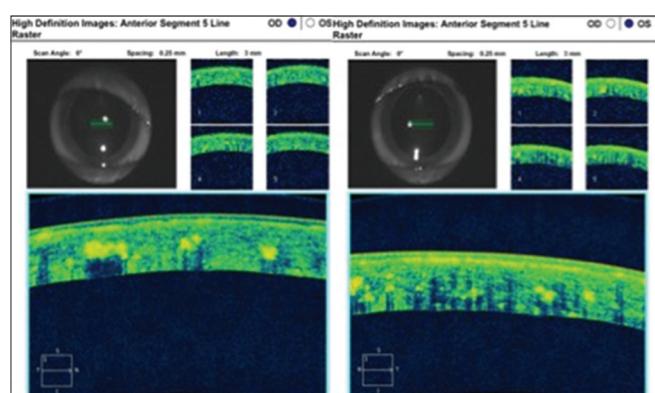


Figure 3: BE anterior segment optical coherence tomography showing stromal corneal dystrophy

the periphery, it was noticed that the filaments in the stroma were deeply embedded into the descemets and the endothelium making it difficult to find the plane between the stroma and descemets. The descemets

Table 2: Ocular findings in both eyes

Ocular Examination	Right eye	Left eye
BCVA	6/36	6/60
Retinoscopy	+1.25±1.25	+1.0±1.0
Ocular adnexa	Normal	
Cornea	Normal size shape. Multiple white dots about 0.5 mm in diameter eroding out of the epithelium, studding the stroma not involving the endothelium, spread over 8 mm area, with interdigitating network of filaments. No vascularization, pigmentation or degeneration.	
	Corneal sensation WNL.	
Anterior chamber	Normal in depth. No KPs, flares, and cells	
Iris/pupil	CPN/CCRTL	CPN/CCRTL
Lens	No evidence of cataract	
EOM	Free and full	Free and full
Dil. fundus examination	Media: Clear Disc: 0.3 C/D ratio, with normal neuroretinal rim Vessels normal A V ratio; Macula: Normal FR: +	
Gonioscopy	Open angles in both eyes	
IOP on applanation	17 mm of Hg	16 mm of Hg

IOP: Intraocular pressure, BCVA: Best corrected visual acuity, KP: Keratic precipitates

and the endothelial residual layer were cut with corneal scissor and donor graft full thickness was replaced on the recipient 8 mm corneal defect bed. It is thus mandatory not to separate the anterior and posterior lamellae before the recipient dissection is completed (Figure 4). On table decision to convert to PKP was taken as dissection was not possible. 2450 cells/cumm would prognosticate a good success rate of this PKP (Figure 5). It thus becomes mandatory to have a good endothelial count in case of doing a DALK just to prevent a disaster in case of conversion to PKP. Histopathological (HP) examination of the excised corneal tissue showed hyaline degeneration of collagen and fusiform shaped amyloid deposits confirming a dual granular and lattice stromal dystrophy pointing toward Avellinos' CD (Figure 6).

DISCUSSION

Corneal stromal dystrophies are grossly classified into a lattice, granular and macular depending on the age of presentation, vision deprivation, and clinical characteristics. You may have isolated presentation or combination of any two (Table 3). In our patient, we had features of granular as well as lattice confirming Avellino CD.⁴ For close to 100 years, this entity was considered a mild variety of granular CD (Groenouw Type I). Bucklers, as early as 1938, described a large family with illustrative pictures of this phenotype. 50 years later, Weidle published the same patients and subdivided granular dystrophy according to



Figure 4: Left eye intra operative conversion of deep anterior lamellar keratoplasty to penetrating keratoplasty due to inability to separate the layers



Figure 5: Left eye post-operative clear graft



Figure 6: Histopathology showing granular deposite extremely close indenting the endothelium

subtle differences of clinical appearance. In 1988, Folberg *et al.* described the histopathology of deposition of both amyloid and hyaline deposits in these patients. In 1992, the clinical findings of these patients were published. Avellino, which is the Italian district of the progenitor of the pedigree, became the popular name.^{1,3} It is an autosomal dominant disease. Mutation of TGFβ1, or keratoepithelin

Table 3: Types of corneal stromal dystrophy and its characteristics

Characteristics	Lattice	Granular	Macular
Genetics	Autosomal dominant	Autosomal dominant	Autosomal recessive
Onset	1 st decade of life	Early adolescence	1 st decade
Vision	Early reduction with obvious clouding	Good until middle age	Reduced by 30-40 years, FC by 50 years
Symptoms	Severe recurrent erosions	Minimal inflammation and irritation	Mild recurrent erosions
Opacities	Grayish "pipe cleaner" linear, branching, threads; dots and flakes; distinct borders	Grayish opaque granules; bread crumbs; sharp borders	Grayish opaque spots; indistinct borders
Intervening stroma	Relatively clear	Clear	Diffusely clear
Distribution of Opacities	Entire cornea with dots; linear opacities central; periphery usually clear;	Axial only; periphery clear	Entire cornea; but most dense centrally
Histopathology	Progress to central disciform by middle age Large hyaline lesions with scattered fibrillar material; also subepithelial	Discrete, hyaline, granulated	Diffuse, granular, nonhyaline, Asso with keratocytes
Defect	Structural protein: Primary amyloidosis of cornea	Structural proteins: Hyaline degeneration of collagen	Metabolic: Defective acid mucopolysaccharide metabolism

gene in human chromosome 5 (5q31) is the key pathogenic process. Corneal trauma activates TGF β 1 and then it overproduces TGF β 1p, which is the main component of the corneal opacity (Table 4).

Homozygous patients have an earlier onset of presentation, as early as 3 years of age, compared with heterozygote patients, which may be diagnosed by 10 years.⁵ Initial slit lamp signs are subtle superficial stromal tiny whitish dots. In the next stage, rings or stellate-shaped snowflake stromal opacities appear between the superficial stroma and the mid stroma, also demonstrate lattice lines in the deeper cornea.⁶ Typically, these lines are located deeper than the snowflake stromal opacity. In the final stage, there is a more superficial, translucent flattened breadcrumb opacity, which may coalesce in the anterior stroma. Some patients only manifest multiple white dots with persistent epithelial erosions. By adulthood, there are larger, very dense subepithelial irregularly shaped opacities, which may become deeper with time. Vision decreases with age as the central visual axis becomes affected. Pain may accompany mild corneal erosions. It is slowly progressive though homozygotes demonstrate more rapid progression. On HP exam, corneal opacities extend from the basal epithelium to the deep stroma and individual opacities stain positive with H&E, Masson trichrome, or Congo red.² Mixed deposits of hyaline and amyloid; hyaline stains with Masson Trichrome and amyloid stains with Congo red³ (Table 5). Initial management options include lubricating drops, or autologous serum therapy, punctal plugs, bandage contact lenses \pm antibiotics for recurrent erosions. Surgical management options are phototherapeutic keratectomy, lamellar keratoplasty, DALK, and PKP. However, the recurrence is still an unsolved problem. DALK has been proposed as an excellent alternative to PKP for corneal diseases that do not affect the endothelium. In patients with epithelial and stromal CD and keratoconus, DALK

Table 4: TGF β 1 and CD

TGF β 1 (gene product of TGF β 1) is very abundant in cornea
 >30 mutations in TGF β 1 gene that result in corneal dystrophies
 68 kDa protein known as keratoepithelin
 It is secreted by corneal epithelial cells and is found in normal stroma bound to type VI collagen \rightarrow Mutations in the TGF β 1 gene protein aggregation in the cornea
 2/2 protein misfolding
 TGF β 1 induced protein accumulates as insoluble products in various forms.

The severity, clinicopathologic variations, age of onset, and location of deposits all depend in the type of amino acid alterations in the protein

CD: Corneal dystrophy, TGF β 1: Transforming growth factor beta-induced gene

Table 5: Staining pattern

Staines	Lattice	Granular	Macular	Avellino
PAS	+		+	+
Trichrome masson	+	+		+
Congo red (under polarization)	+			+
Alcian blue			+	

PAS: Periodic acid schiff

preserves native endothelium and reduces host immune system reaction and graft rejection. Current surgical techniques of DALK involve manual dissection up to near DM or injection of air, fluid, or viscoelastic into deep stroma to create a plane of separation between DM and stromal tissue.⁷ Malbrans stromal "peeling technique" technique allows dissection of deep corneal stroma in a safe and effective manner even in cases of advanced keratoconus. Intrastromal air injection to aid stromal resection was first described by Archila in 1985. Price and Chau described "air lamellar keratoplasty" using similar technique with deeper dissection and lyophilized full thickness donor tissue for replacement.⁸ Sugita and Kondo described technique of hydro-delamination of posterior stromal fibers with an injection of saline using 27-gauge cannula, which was performed after the removal of anterior

three quarters depth of recipient tissue.^{8,9} The DM was exposed in the central 5 mm zone prior to the placement of full thickness donor tissue. A similar technique using viscoelastic instead of saline, i.e., “visco-delamination” was described by Morris *et al.* Melles described a technique of planned depth lamellar dissection in DALK. This involves injection of air into the anterior chamber following which an incision is made in the peripheral corneal stroma, observing the reflex of the sharp tip against the convex mirror from air endothelium interface. Anwar and Teichmann described the “big bubble” technique, wherein air injection was performed into the deep stromal tissue to achieve separation of DM from the corneal stroma. Manual DALK techniques have been described which allow deep dissection down to near DM levels.¹⁰ These are useful in cases where big bubble is not achieved following air injection, or there is scarring process involving the DM for which air injection is contraindicated.¹⁰

Major indications for conversion of DALK to PKP include macropunctations and extensive DM deposition. The rate of conversion from DALK to PKP was about 2.96%. Other studies have reported 0-14% conversion rate.⁸ A study by Unal *et al.* in 2013 had 94.6% cases of stromal dystrophy successfully treated with DALK out of which 35.3% had a recurrence.

CONCLUSION/SUMMARY

An attempt was made to perform a DALK in this case primarily for its benefits of early rehabilitation and reduced chances of graft rejection. No disruption of the

anterior chamber refuting peripheral anterior synechiae and secondary glaucoma. Reduced number of sutures, even 8 or 12 is adequate preventing vascularization and infiltration. Sutures can be done away if tissue glue with placement sutures are used. However, the fibrillar strands binding the posterior stroma to descemet and endothelium in optical axis make it mandatory to do a PKP for better visual recovery inspite of enhanced risk of rejection.

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