Unusual Superficial Variant of Granular Corneal Dystrophy With Amyloid Deposition

Superficial granular corneal dystrophy (SGCD) is a variant of GCD that is restricted to involvement of the Bowman layer and the superficial corneal stroma.1,2 Superficial and classic GCD result from mutations in the human transforming growth factor β–induced gene (BIGH3) on human chromosome 5 (5q31).3,4 We report an unusual case of a patient with SGCD in which the typical deposits of GCD were associated with amyloid and in which the 2 commonly affected exons (4 and 12) of the BIGH3 gene were not mutated.

Report of a Case. A 40-year-old woman from northern India sought care because of gradual decreasing vision in both eyes during the preceding 25 years. On examination, her visual acuity was 1/60 OU. Slit-lamp biomicroscopy revealed bilateral dense opacities in the superficial portion of the corneal stroma, with clear areas between the deposits (Figure 1A and B). The deposits were most marked centrally, with a peripheral rim of clear cornea.

Although it was not possible to examine any of the other family members, the patient stated that her parents had good vision, and she was not aware of any similar problems in any of her relatives. There was no history of consanguinity. The patient had no children.

The patient underwent a superficial lamellar keratectomy of the left eye, followed by smoothing with an excimer laser scanning beam. At 5 months postoperatively, the left cornea was clear, with scattered radial white dots and a 6/60 best-corrected visual acuity (Figure 2). The fundus appeared normal. A similar surgical procedure was performed on the right eye. The patient failed to return for any further examinations.

A histopathologic examination of both superficial keratectomy specimens revealed fairly confluent serpentine and granular eosinophilic deposits located in close proximity to the epithelium. The deposits involved the superficial corneal stroma and replaced most of the Bowman layer (Figure 3). These areas stained red with Masson trichrome (Figure 3), but did not have an affinity for alcian blue, colloidal iron, or immunoglobulins. There was focal staining of the deposits with Congo red, which showed apple-green birefringence under polarized light (Figure 4A and B).

A transmission electron microscopic examination of both specimens revealed electron-dense, rod-shaped structures, frequently with apertures characteristic of GCD, that involved the Bowman layer and the superficial stroma (Figure 5). In both specimens, these structures were locally adjacent to clusters of 10- to 11-nm-diameter filaments characteristic of amyloid (Figure 5).

DNA was isolated from paraffin-embedded corneal tissue using a tissue kit (DNeasy; QIAGEN Inc, Valencia, Calif). Exons 4 and 12 (the codons for amino acids 124 and 555, respectively) of the BIGH3 gene were amplified by the polymerase chain reaction using the primers described by Munier and associates.3 The polymerase chain reaction products were purified on an agarose gel and then with a gel extraction kit (QIAGEN Inc). DNA sequencing in a forward and reverse direction was performed using a DNA sequencer (ABI 377XL DNA Sequencer; PE Applied Biosystems, Foster City, Calif) and terminator cycle sequencing reagents (dRhodamine/BigDye; PE Applied Biosystems). Denaturing high-performance liquid chromatographic analysis for mutations was per...
formed (WAVE system; Transgenomic, Inc, Omaha, Neb). Excellent sequence data for exons 4 and 12 of the \( \text{BIGH3} \) gene disclosed no mutations.

**Comment.** Our patient is noteworthy because of the association of her SGCD with amyloid. To our knowledge, only 2 other published cases\(^1,5\) describe amyloid with superficial granules.

Granular corneal dystrophy is an autosomal dominant inherited disorder characterized by discrete white opacities in the axial region of the corneal stroma.\(^2,8\) Although these lesions initially appear in the first or second decade of life, because the intervening stroma remains clear, the visual acuity is usually fairly good until the fourth or fifth decade of life. Histopathologically, GCD is characterized by granular eosinophilic deposits that are scattered throughout the stroma and the Bowman layer. These deposits stain bright red with Masson trichrome and stain negatively for glycosaminoglycans.\(^6\) Ultrastructurally, these deposits consist of electron-dense rod-shaped bodies that often contain apertures, which give the deposits a moth-eaten appearance.\(^7\) The corneal accumulations result from an extracellular deposition of a mutated protein encoded by the \( \text{BIGH3} \) gene.\(^7-9\) The most common form of GCD (type I) results from an Arg555Trp mutation in the \( \text{BIGH3} \) gene.\(^4\) In patients with SGCD (also known as GCD type III, true Reis-Bücklers corneal dystrophy, and corneal dystrophy of the Bowman layer and superficial stroma [CDB] type I), the typical rod-shaped deposits of GCD accumulate mainly in the Bowman layer and immediately beneath the corneal epithelium.\(^4\) This variant of GCD is caused by an Arg124Leu mutation in the \( \text{BIGH3} \) gene. Another type of GCD (GCD type II, Avellino corneal dystrophy, or combined lattice corneal dystrophy–GCD) has deposits of stromal amyloid.\(^4\) All examples of GCD type II that have been studied with molecular genetic techniques have had an Arg124His mutation in the \( \text{BIGH3} \) gene.

**Figure 2.** Five months postoperatively, the left cornea is clear, with scattered radial white dots that may represent residual or recurrent deposits.

**Figure 3.** Serpentine and granular red deposits in the superficial corneal stroma with replacement of the Bowman layer (Masson trichrome, original magnification \( \times 625 \)).

**Figure 4.** A, Focal congophilic corneal stromal deposits (Congo red, original magnification \( \times 250 \)). B, Focal apple-green birefringence (arrows) under polarized light in the congophilic areas (Congo red, original magnification \( \times 250 \)).
Compared with patients with classic GCD, those with the superficial variants have more opacities, leading to an earlier age of decreased visual acuity, generally during the second decade of life, and therein an earlier need for surgical intervention. Our patient claimed that her vision began to diminish when she was a teenager. The distinction between the superficial and classic forms of GCD has important clinical therapeutic implications because the superficial variants can be managed successfully by a superficial keratectomy, as in our patient, or by excimer laser phototherapeutic keratectomy; however, recurrences can occur and there are limits to the amount of acceptable corneal thinning.

Superficial GCD represents 1 of 2 well-characterized dystrophies that involve the Bowman layer. Ultrastructurally, the other dystrophy (Thiel-Behnke dystrophy) can be readily distinguished from SGCD because of the presence of subepithelial “curly” fibers. Because of the confusing nomenclature, the term CDB has been proposed for both of these dystrophies: CDB type I for SGCD and CDB type II for Thiel-Behnke dystrophy.

Our failure to detect a mutation in exon 4 or 12 of the BIGH3 gene indicates that either this gene is not responsible for this case of SGCD and for the amyloid in our patient or a different part of the gene is mutated. Regardless of which of these 2 possibilities is true, the present case indicates that SGCD with amyloid deposition can occur without a mutation in either of the 2 exons in the BIGH3 gene that are known to be hot spots for mutations.

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This study was supported in part by research grant R01 EY 12712 from the National Eye Institute, Bethesda, Md.

We thank the Duke University Medical Center DNA Analysis Facility, Durham, for performing DNA sequencing and denaturing high-performance liquid chromatography.

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Endophthalmitis Caused by Mycobacterium chelonae abscessus After Intravitreal Injection of Triamcinolone

Several authors have recently reported successful treatment of diabetic macular edema resistant to conventional laser photocoagulation with the injection of long-acting intravitreal corticosteroids. Endophthalmitis after intravitreal injection is unusual. We report a case of Mycobacterium chelonae abscessus endophthalmitis occurring 1 month after the injection of intravitreal triamcinolone acetonide (Kenalog 40; Bristol-Myers Squibb Co, Princeton, NJ) to treat persistent diabetic macular edema.

Report of a Case. A 62-year-old man with a history of non–insulin dependent diabetes mellitus developed clinically significant macular edema. He underwent multiple sessions of focal grid argon laser photocoagulation to the edematous areas of the macula. Despite these sessions of focal grid macular laser photocoagulation, clinical examina-