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Case Report

Spheroidal Degeneration in Two Siblings: Clinical and Histopathological Features

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Abstract

Spheroidal corneal degeneration is predominantly seen in advanced age and hereditary predisposition to this disorder is very rare. This report describes the occurrence of bilateral band-shaped spheroidal corneal degeneration in two siblings.

Keywords: Spheroidal degeneration of the cornea and conjunctiva, band-shaped amber-colored spherules, familial predisposition, *in vivo* confocal microscopy

Introduction

Spheroidal degeneration is a slowly progressive corneal and conjunctival disorder that occurs mostly in the interpalpebral region with homogenous, band-shaped, translucent, yellow-golden globular deposits.[1,2] As corneal spherules corresponding to this clinical entity have been described under 20 different names, spheroidal degeneration is regarded as a very rare disorder in the world literature.[3] In reality, however, spheroidal degeneration is a common occurrence. Hereditary cases of this disorder are extremely rare and the pattern of inheritance is not clear.[4,5] Here, we report two cases of familial spheroidal degeneration.

Case Reports

Case 1

A 45-year-old Turkish man was evaluated for bilateral progressive loss of vision over the past 25 years. His family history was significant in that one of his sisters was diagnosed with similar corneal lesions in both eyes. His parents were not related and he had no previous history of any ocular or systemic inflammatory diseases.

Best corrected visual acuity was 20/100 in the right eye and counting fingers at 10 cm in the left eye. The ocular adnexa were normal. Slit-lamp examination revealed dilated bulbar conjunctival vasculature in both eyes and pinguecula in his left interpalpebral bulbar conjunctiva. Evaluation of both corneas revealed the presence of irregular epithelium overlying multiple amber-colored globules in the superficial stroma (Figure 1A, B). The surrounding stroma appeared hazy. Corneal thickness was measured as 1,090 µm and 1,095 µm in the right and left eyes, respectively. Although the posterior segment structures could not be visualized due to the presence of corneal lesions, ocular ultrasonography revealed attached retinas with clear vitreous. Intraocular pressures were within normal limits. The patient underwent incisional biopsy of the corneal lesions in his left eye.

Histopathology: The corneal specimen was stained with hematoxylin and eosin (H&E) (Figure 1C). On microscopic examination, the epithelium appeared normal and Bowman's layer contained small deposits that stained basophilic.

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Confocal microscopy: The patient's corneal characteristics were evaluated using an *in vivo* laser confocal microscope, the Heidelberg Retinal Tomograph II, Rostock Cornea Module (Heidelberg Engineering GmgH, Dossenheim, Germany). A condensation of hyperreflective large globules, like hyaline accumulations, was noticed in the superficial layers of the central cornea as a consequence of protein denaturation (Figure 1D).

Case 2

The 35-year-old sister of the patient described above had bilateral progressive loss of vision and lacrimation since childhood. No ocular trauma or systemic or ocular inflammatory disorders were reported. Best corrected visual acuities were 20/125 in each eye. The ocular adnexa were normal. Biomicroscopically, band-shaped amber-colored anterior stromal globules were present in the interpalpebral cornea. The overlying epithelium appeared to be intact (Figure 2A, B). The anterior chamber was of normal depth and quiet, the iris showed normal architecture, and both eyes had moderate nuclear sclerosis. On ophthalmoscopic examination, both retinas appeared hazy due to the presence of the corneal lesions. Intraocular pressures were within normal limits. The patient underwent incisional biopsy of the corneal lesions in her right eye.

Histopathology: The corneal specimen was stained with Verhoeff-van Gieson for elastin (Figure 2C). The corneal stroma was free of deposits, but the superficial stroma lacked the normal parallel arrangement secondary to increased amount and thickness of elastic fibers as observed with Verhoeff-van Gieson staining.

Confocal microscopy: An accumulation of punctiform hyperreflective deposits was observed in confocal microscopy (Figure 2D).

Discussion

The clinical picture of spheroidal degeneration of the cornea and conjunctiva has three typical forms. Primary corneal spheroidal degeneration consists of superficial solitary or clustered spherules adjacent to the limbus, is seen especially in advanced age, is almost always bilateral, and can also be detected in normal eyes. Secondary corneal spheroidal degeneration involves single, grouped, or a solid plaque of spherules that occurs more frequently in eyes with a unilateral corneal pathology, often located in the deep stroma of the central cornea. The conjunctival type consists of conjunctival golden spherules associated with either of the corneal types and often with pinguecula, which is common in older ages.[1,2,3] However, the distinction between these forms is not sufficiently clear, and in many cases more than one form can be seen at the same time.[3]

In our report, we revealed familial band-shaped spheroidal changes with both conjunctival and corneal involvement in a family. The first patient had corneal spheroidal lesions in both eyes with intact epithelium in the subepithelium, Bowman's membrane, and superficial stroma (Figure 1A, B). In the second patient, the globules were smaller, vision was better in both eyes, and the opacity was identical in location (Figure 2A, B). Bilateral involvement and location of the spherules might indicate the diagnosis of primary corneal form. However, lesions had appeared prior to the age of 30 years. In case 1, the central plaque

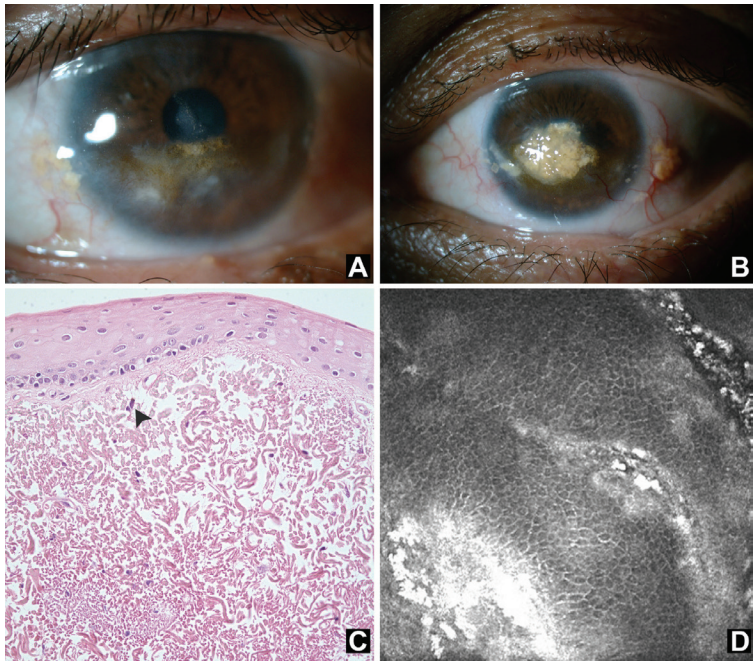

Figure 1. Clinical and histopathological characteristics of patient 1. Grade III keratopathy with spherical deposits in the central cornea.[6] The epithelium had a normal appearance on a microscopic examination. Note the subepithelial vascular invasion from the temporal and inferonasal limbus to the area of opacification (A, right eye). Grade IV keratopathy with a central plaque elevating the corneal epithelium, and pinguecula formation[6] (B, left eye). Hematoxylin and eosin (H&E) stained cornea specimen, X400. The arrow indicates basophilic stained deposits (C, left eye). *In vivo* confocal microscopy shows large hyperreflective globular deposits in the superficial layers of the central cornea (D, left eye)

was considered to be the secondary corneal form. However, the patients lacked significant signs of trauma or inflammatory diseases. The presence of pinguecula and conjunctival spherules suggested the conjunctival form. However, the patients suffered devastating corneal complications.

Based on the characteristics mentioned above, we concluded that the two siblings did not comply with the forms described.[1] With the increasing number of familial presentations, we hope that familial spheroidal degeneration might be included in the classification.

According to Johnson et al.[6], spheroidal degeneration is categorized into four grades (Grade I-IV). In our patients' right eyes, the spherules affected vision by progressing from the corneal periphery to the central zone, while the epithelium was not damaged, consistent with grade III keratopathy (Figure 1A, 2A). In the left eyes, the epithelium was raised by deposits, consistent with grade IV keratopathy, even though there were areas of clear cornea in the periphery (Figure 1B, 2B).

All forms of spheroidal degeneration are pathologically identical in both light and electron microscopy.[2] The epithelium and its basement membrane remain unaffected unless advanced degeneration is present, whereas Bowman's membrane is often disrupted. Hida et al.[5] observed changes in epithelial thickness and noted that the epithelium which was raised by spherical deposits was noticeably thinner in some areas. The spheroids, which contain proteins and are positively stained with Verhoeff's elastic stain, are characteristically found beneath the epithelium, in Bowman's layer and the superficial corneal stroma.[7] In this report, it was noted that the epithelium was not affected in the H&E-stained sections and that Bowman's membrane contained small basophilic deposits. These aggregates exhibited a positive reaction with the Verhoeff-van Gieson stain, giving the deposits a black and dark olive green appearance, and the superficial stroma lost its normal parallel pattern due to the increased amount and thickness of the elastic fibers. These hyaline corneal deposits are frequently observed in a variety of chronic ocular and corneal disorders, and as a result of exposure to climatic extremes.

Any cases of keratopathy associated with interpalpebral deposition should be considered in the differential diagnosis. Climatic conditions play a major role in climatic proteoglycan stromal keratopathy. The appearance of gray corneal opacification, central flattening, and proteoglycan accumulation differentiate it from spheroidal degeneration.[8] Mild calcific band keratopathy, in which calcium salts accumulate, differs from secondary corneal spheroidal degeneration by having a systemic or ocular inflammatory disease in the etiology.[9] Salzmann's nodular degeneration is bluish-white to grayish-yellow round lesions. Ocular surface inflammation is common. The presence of eosinophilic deposits and early destruction of epithelium can be seen in any part of the cornea, not only the interpalpebral region.

Confocal microscopy enables the clinician to evaluate microstructural corneal changes with a noninvasive approach.[11] In both of our patients, the golden spherules were observed as hyperreflective globules under the confocal microscope. These hyperreflective globules were well correlated with the histopathological specimens.

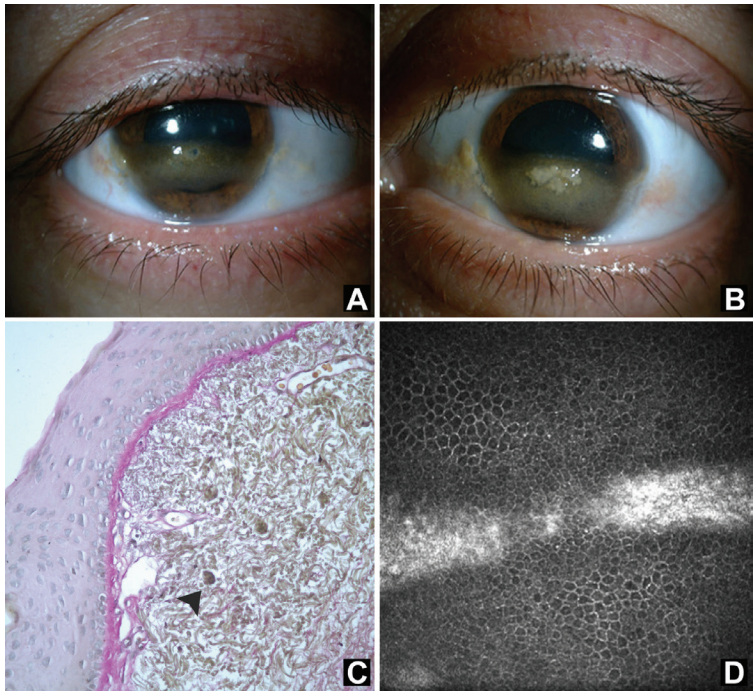

Figure 2. Clinical and histopathological characteristics of patient 2. Grade III keratopathy, characterized by band-shaped transparent amber-colored corneal spherules.[6] Note the spherules adjacent to the limbus (A, right eye). Grade IV keratopathy identified by band-shaped corneal deposits and clusters of punctiform spherules[6] (B, left eye). Cornea specimen stained with Verhoeff-van Gieson, X400. The superficial stroma lacks normal parallel arrangement. Note the bluish discoloration of the stroma. The arrow indicates dark olive green stained deposits (C, right eye). *In vivo* confocal microscopy shows punctiform hyperreflective deposits (D, right eye)

Advancing age and exposure to environmental factors or underlying ocular pathology have a major role in the etiology of spheroidal degeneration. These environmental factors include low humidity, very low temperatures, very high temperatures, microtrauma from wind blowing snow or ice particles and solar radiation from ultraviolet (UV) wavelengths. Chronic exposure to UV radiation is considered to be the primary causative factor in spheroidal degeneration. The patients in the present report were living in the province of Adana, which is the southern part of Turkey (35° 18' 49.4496'' E). It has a dry-hot summer subtropical climate. In Adana, the highest annual average temperature in summer is 40 degrees Celsius and the average daylight duration is 10 hours.[12] The average annual solar radiation in the southern part of Turkey is above 4.6 $kWhm^{-2}$.[13] In fact, chronic UV exposure may be a causative factor in our cases due to the region in which our patients live. However, in the present report our patients were rather young and had no history of preexisting ocular diseases. Although chronic exposure to UV is thought to be a causative factor, the assessment of conjunctival and corneal spheroidal degeneration with early onset in two members of the same family led us to presume a familial form of spheroidal degeneration. There are a few cases of spheroidal degeneration thought to be familial in the literature.[4,5] The limitation here is that the genetic transmission of spheroidal degeneration was not supported by concrete evidence. Spheroidal degeneration was detected in only two individuals in the same family, both in our cases and in other presumed familial cases presented in the literature. It is therefore difficult to determine the inheritance pattern of the spheroidal degeneration. With our current knowledge, it would be more accurate to interpret that there may be a familial predisposition to corneal and conjunctival microtraumas in these cases.

There is no single medical approach for treatment. In mild cases, lubrication of the ocular surface, protection from UV exposure, and appropriate ascorbic acid intake are advised. In moderate keratopathy, superficial or photorefractive keratectomy are performed.[14] In advanced cases, penetrating keratoplasty may be recommended. However, the recurrence rate is unknown.

Contrary to the relatively more common sporadic spheroidal degeneration, familial cases are bilateral, more affected by the environment, and typically symptomatic in the first decade.

In conclusion, spheroidal degeneration of the cornea and conjunctiva has mostly been reported in older subjects and most researchers did not recognize a familial tendency. This report describes bilateral band-shaped spheroidal corneal degeneration in two young siblings, which is extremely rare.

Ethics

Informed Consent: Obtained.

Peer-review: Internally and externally peer reviewed.

Authorship Contributions

Concept: M.İ., Design: M.İ., D.Y., M.C.M., M.O., Data Collection or Processing: M.İ., D.Y., M.C.M., M.O., Analysis or Interpretation: M.İ., D.Y., M.C.M., M.O., F.S., Ö.T.I., Literature Search: D.Y., Writing: D.Y., M.C.M, M.İ.

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