Atypical corneal subepithelial calcium deposits in a patient with sarcoidosis

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A 31-year-old Asian man with a diagnosis of sarcoidosis presented at our clinic with a complaint of blurred vision in both eyes. At the initial visit, both eyes had mild sarcoidosis-related panuveitis and a diffuse and fine corneal subepithelial opacity resembling granular dystrophy. Intraocular inflammation improved with use of steroid eyedrops, but the corneal opacity worsened, accompanied by an elevation in serum calcium levels due to the development of acute renal failure. After the serum calcium levels normalized, the corneal subepithelial opacity gradually resolved. This case involved calcium salt deposits that appeared similar to granular corneal dystrophy. The deposits improved when the serum calcium level normalized.

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CASE REPORT

A 31-year-old Asian man with a diagnosis of sarcoidosis presented at our clinic with a complaint of blurred vision in both eyes. At the initial visit, both eyes had mild sarcoidosis-related panuveitis and a diffuse and fine corneal subepithelial opacity resembling granular dystrophy. Intraocular inflammation improved with use of steroid eyedrops, but the corneal opacity worsened, accompanied by an elevation in serum calcium levels due to the development of acute renal failure. After the serum calcium levels normalized, the corneal subepithelial opacity gradually resolved. This case involved calcium salt deposits that appeared similar to granular corneal dystrophy. The deposits improved when the serum calcium level normalized.

Calcium deposition in the cornea occurs in a variety of conditions ranging from local ocular inflammation to systemic metabolic abnormalities. The most common type of corneal calcification is band keratopathy, which typically begins in the interpalpebral zones of the peripheral cornea. As the lesion grows, the deposit forms a band of chalky plaque that contains transparent small holes and sometimes clefts. The superior and inferior peripheral cornea adjacent to the limbus remain clear. Visual function is impaired when the opacity extends across the visual axis.

End-stage renal disease and systemic conditions causing hypercalcemia have been associated with calcific band keratopathy; among these, sarcoidosis is the most common cause. Of patients who have sarcoidosis with ocular involvement, 17% experience hypercalcemia but only 4% to 5% develop calcific band keratopathy.2

We report a case of sarcoidosis accompanied by hypercalcemia caused by renal dysfunction in which the corneal subepithelial calcium salt deposition was not typical of band keratopathy and regressed when the hypercalcemia improved.

CASE REPORT

A 31-year-old Asian man presented to our institute in January 2012 with blurred vision in both eyes. Sarcoidosis had been diagnosed and treated with oral steroids since 2000, but the patient had discontinued the steroids on his own at the end of 2011.

At presentation, the corrected distance visual acuity (CDVA) was 0.08 (−4.00 −1.25 × 180) in the right eye and 0.20 (−2.50 −1.00 × 180) in the left eye. Grayish-white, fine, granular subepithelial spots extending from the central cornea to the peripheral cornea were observed in both eyes. The central corneal thickness was 501 μm in the right eye and 505 μm in the left eye. Very few cells were observed in the anterior chamber and a few snowball-like opacities were observed in the vitreous in both eyes. The fundus was normal except for focal retinal degeneration in the peripheral retina of the right eye. At presentation, the patient had no systemic symptoms but on the basis of his medical history and clinical findings, mild panuveitis caused by sarcoidosis was diagnosed.

The patient was treated with steroid eyedrops (betamethasone 0.1% [Rinderon]) 4 times a day. The intraocular inflammation resolved quickly, and the CDVA recovered to 1.20 (−3.50 −2.25 × 180) in the right eye and 1.50 (−2.50 −1.00 × 180) in the left eye. However, the corneal opacities worsened (Figure 1). After written informed consent was obtained, the patient was treated with systemic corticosteroids.
obtained, to further diagnose the condition, genomic DNA was extracted from peripheral blood and amplified by polymerase chain reaction using primer pairs against all exons of the UbiA prenyltransferase domain-containing protein 1 (UBIAD1) and transforming growth factor-β–induced (TGF-β1) genes. The amplified products were treated with a mixture of exonuclease I and shrimp alkaline phosphatase (ExoSAP-IT, GE Health Care, Ltd.) to digest residual deoxyribonucleotide and primer and then were subjected to sequencing reaction followed by electrophoresis. The sequence data were analyzed using commercially available alignment software (Variant Reporter, Applied Biosystems, Inc.). Analyses of all exons of the UBIAD1 and TGF-β1 genes showed no pathological mutations, essentially excluding TGF-β1–related corneal dystrophy and Schnyder dystrophy.

In September 2012, the patient developed renal failure accompanied by hypercalcemia. The serum calcium level rose to 14.2 mg/dL and, simultaneously, the corneal opacities increased. The patient was admitted for hemodialysis and restarted on oral steroids. After 3 weeks, renal function had improved and the serum calcium level had returned to the normal range. Thereafter, the corneal subepithelial opacities gradually decreased (Figure 2).

In February 2013, a small sample (approximately 1.0 mm × 2.0 mm) of peripheral cornea was excised. The sample contained the epithelium and superficial stroma and was processed for component analysis using the KBr wafer technique. Infrared analysis showed that the sample was 67% calcium phosphate and 33% proteins.

DISCUSSION

This case involved fine granular corneal subepithelial opacities that from the clinical course and the laboratory results were assumed to be an atypical form of band keratopathy. Patients with renal failure sometimes demonstrate hypercalcemia and band keratopathy. Over 80% of severely uremic patients develop corneal and conjunctival calcific deposits. Diffuse opacification of the peripheral limbal area and interpalpebral zone is a typical conjunctival and corneal change associated with chronic renal failure.

Deposition of calcium salts on the ocular surface depends not only on the solubility product of calcium and phosphate but also on altered tissue physiology. Deposition of calcium salts on the corneal stroma and adverse effect of topical steroid phosphate preparations has been proposed. In the present case, steroid phosphate eyedrops that had been administered for a significant period from the first visit might have affected the pathogenesis of the corneal calcium deposits.

A correlation between calcium deposition on the corneal stroma and adverse effect of topical steroid phosphate preparations has been proposed. In the present case, steroid phosphate eyedrops that had been administered for a significant period from the first visit might have affected the pathogenesis of the corneal calcium deposits.

It is widely assumed that the only effective treatment for calcific band keratopathy is surgery or excimer laser therapy. Harris et al. stated that chronic hemodialysis did not influence the calcium deposits in uremic patients. However, in our case, prompt treatment of the hypercalcemia reduced the corneal opacities. In a few cases, resolution of calcific band keratopathy after correction of a high serum

Figure 1. Corneal opacities in July 2012. Grayish-white, dense, focal, poorly delineated opacities are visible in the central cornea, resembling granular corneal dystrophy.

Figure 2. Corneal opacities in April 2013. The corneal opacities in the central cornea decreased markedly with correction of the high serum calcium level. Note that the margin of opacity shows a band keratopathy–like appearance.
calcium level has been reported.\textsuperscript{8–10} Fluctuation of corneal calcium deposition along with changes in serum calcium levels and with the activity of sarcoidosis was reported in some cases. These findings may indicate that calcium salt deposition is self-limiting, at least when the lesion is diagnosed in the early stage and the elevated serum calcium level is appropriately corrected.

The present case indicates that subepithelial calcium deposition can begin not as a typical form of band keratopathy, but rather as diffuse, fine granular opacities. In such cases, we should wait for improvement of the general systemic condition while changing the ophthalmic solution to one that is less toxic to the corneal epithelium and contains no phosphate.

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