Cloudy corneas as an initial presentation of multiple myeloma

Priyanka Sharma1
Haifa A Madi1
Richard Bonshek2
Stephen J Morgan1

1Sunderland Eye Infirmary, Sunderland, UK; 2National Specialist Ophthalmic Pathology Service, Department of Histopathology, Manchester Royal Infirmary, Manchester, UK

Summary: We report a case of previously unsuspected myeloma, presenting with cornea verticillata due to intracorneal paraprotein deposition.

History: An 85-year-old female presented via her optician with a 4-month history of cloudy vision. She had undergone an uneventful bilateral phacoemulsification surgery 7 years earlier. Extensive spiraling corneal epithelial opacification was noted on slit-lamp examination. On further investigation, she was found to have a previously unsuspected low-grade multiple myeloma. We established the nature of the corneal deposits with corneal epithelial biopsy histopathology and electron microscopy. It is very rare for multiple myeloma to present in this fashion. Ophthalmologists should be aware that such a presentation may rarely be due to systemic multiple myeloma.

Keywords: corneal crystals, multiple myeloma, crystalline keratopathy, vortex keratopathy

Introduction

Corneal deposits of various types have been described in multiple myeloma, monoclonal gammopathy, and essential cryoglobulinemia.1,2 There are only a very few case reports of corneal immunoglobulin (Ig) deposition. We present one such case in which there was intraepithelial deposition of corneal IgG-kappa. In addition, it is noteworthy that the presentation to the ophthalmologist was the presenting complaint leading to the diagnosis of myeloma.

Case report

An 85-year-old lady with bilateral cloudy corneas was referred to ophthalmology as an outpatient from her optometrist. She gave a 3–4 month history of cloudy vision, mainly in her right eye. She had undergone an uneventful bilateral phacoemulsification surgery 7 years earlier.

Her visual acuity at presentation was 6/7.5 OU. On examination, she had marked grayish intraepithelial corneal opacities in a pattern of hazy spiraling lines in both eyes (Figure 1). The corneal stroma and endothelium had normal appearance; there was no evidence of corneal edema. Specular microscopy was not possible. The anterior chamber depth and contents, intraocular lenses, posterior capsule, and fundus examination were normal.

She had a past medical history of ischemic heart disease and osteopenia. Her current medications were aspirin, simvastatin, lisinopril, codeine, and paracetamol.

Systemic investigation revealed a raised serum IgG with a kappa paraprotein band (12.4 g/L) on serum protein electrophoresis (Figure 2). The erythrocyte sedimentation...
rate was raised (49 mm/hour), and there was a mild kidney impairment with raised urea (8.1 mmol/L) and raised creatinine (118 µmol/L). The random blood glucose, electrolytes, liver function, lipid profile, and calcium profile were normal. Urinary Bence Jones proteins were elevated. There was no evidence of Fabry disease as the lysosomal enzymes were all found to be normal.

She was referred to the Department of Haematology, Sunderland Royal Hospital, Sunderland, UK, and a bone marrow biopsy was carried out that showed increased plasma cells (11%) with pink staining crystals in the cytoplasm. Free crystals were also seen. These findings were consistent with multiple myeloma.

A corneal epithelial biopsy was undertaken and subjected to further laboratory analysis. Immunohistochemistry of the corneal biopsy showed excessive amounts of kappa light chain staining, relative to lambda light chain staining. On transmission electron microscopy, there was evidence of intraepithelial intracellular and extracellular geometrically irregular hexagonal electron dense particles (Figure 3). These are typically found in crystalline keratopathy due to gammopathy. There was an absence of immunotactoid, a paraprotein also commonly present in these cases, but not detected in our case.

The patient was commenced on systemic chemotherapy with cyclophosphamide and dexamethasone. Six months later, there was significant improvement in corneal clarity (Figure 4).

**Discussion**

Corneal epithelial disturbance in a spiraling pattern is variously known as cornea verticillata, vortex keratopathy, and hurricane keratopathy. Well-recognized causes include: Fabry disease; the drugs (amiodarone, chloroquine, hydroxychloroquine, indomethacin, chlorpromazine, tamoxifen, meperidine); toxicity of topical medications; and ocular surface failure secondary to chemical and thermal burns, conjunctival malignancy, and cicatrizating conjunctivitis.

In myeloma, an intracorneal accumulation of Ig is well-described. Patients may be asymptomatic or complain of decreased vision, irritation, photophobia, and erosions. The corneal deposition can be crystalline, amorphous, or a combination.

Other ocular surface manifestations of multiple myeloma include repeated subconjunctival hemorrhages, peripheral
ulcerative keratitis, prominent corneal nerves, and band keratopathy.

Our patient turned out to have intracorneal crystal deposition, although the crystals were too small to be seen on slit-lamp examination. Other causes of intracorneal crystal deposition include cystinosis, Schnyder crystalline corneal dystrophy, Bietti crystalline corneoretinal dystrophy, tyrosinemia, gout, and topical medications (fluoroquinolone).

The pathophysiology of intracorneal crystal formation in multiple myeloma remains enigmatic. One theory is that the deposits result from elevated Ig levels in the tears and aqueous humor; another is that they enter the cornea from the limbal blood vessels; and a third is that the keratocytes themselves synthesize the precipitated Ig. Henderson et al discuss that some of the reasons for Ig deposition are: 1) an inherent propensity of some Ig or kappa light chains to crystallize; and 2) local factors in the cornea that may promote deposition, such as temperature, pH, water content, and extracellular matrix deposition. The immunoglobulin substances have been found in serum, tears, urine, aqueous humor, cornea (subepithelial, intraepithelial, bone marrow).

This case is unusual because it is rare to have corneal deposition in multiple myeloma. It is even rarer for it to be the presenting complaint to an ophthalmologist. On searching the literature, we have found a total of 27 case reports of corneal Ig deposition in multiple myeloma. Of these, 17 were crystalline, four were amorphous, two were hyaline, one was granular, and no tissue was obtained in three. This suggests that the corneal Ig distribution in multiple myeloma is frequently crystalline. Ig deposits can be both intracellular and extracellular. Another distinct pattern of involvement is an immunotactoid pattern. Stirling et al showed ultrastructural images of tubular paracristalline structure of corneal immunoglobulin deposition which were later termed as “immunotactoid keratopathy” by Garibaldi. Garibaldi proposed the use of term “immunotactoid keratopathy” to describe corneal Ig deposits in tubular, electron-dense, crystallloid deposits with central lucent core on electron microscopy (they reported two such cases with Ig kappa deposits).

Ig-kappa deposition in the cornea was seen in eleven cases of multiple myeloma, although IgG gamma globulin was deposited in three corneas, and IgG lambda was deposited in three cases – with IgG-kappa and lambda in one case, IgD in one case, and IgA in one case. The type of Ig deposited in the cornea was not clarified in seven cases. This suggests that Ig deposition in the cornea is most frequent in the kappa variety of multiple myeloma.
of material/Ig deposited. We did not have access to confocal microscopy at our center.

Our case is, therefore, the first published case of vortex keratopathy in multiple myeloma with corneal deposition of Ig confirmed by corneal epithelial biopsy.

It is very rare for multiple myeloma to present in this fashion. There are several causes of intracorneal crystalline deposits, and the differentiation is impossible clinically, but laboratory studies – specifically a serum protein electrophoresis – will help detect any unsuspected multiple myeloma. Ophthalmologists should be aware that such a presentation may rarely be due to systemic multiple myeloma.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**


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