Cloudy corneas as an initial presentation of multiple myeloma

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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 variably known as cornea verticillata, vortex keratopathy, and hurricane keratopathy. Well-recognized causes include: Fabry disease; 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 cicatrizing 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

Figure 1 Clinical photographs of the right cornea. Notes: (A) Subepithelial deposits extending toward the corneal center by fingerlike projections; (B) at higher magnification, depicting the spiral-like pattern known as corneal verticillata.

Figure 2 Serum immunofixation electrophoresis and its graphical representation. Notes: (A) ELP, G, A, M, K, and L. The arrow indicates the position of the monoclonal protein. (B) A large spike in the gamma region is shaded in pink. Abbreviations: ELP, serum protein electrophoresis; G, immunoglobulin G; A, immunoglobulin A; M, immunoglobulin M; K, kappa light chain; L, lambda light chain.

Figure 3 Electron microscopy of the corneal biopsy specimen. Notes: (A) Numerous epithelial rod-shaped bodies (original magnification, ×7,200). (B) Epithelial rod-shaped body at higher magnification (original magnification, ×19,000). (C) Numerous intracellular hexagonal-shaped bodies (original magnification, ×19,000). (D) Intracellular hexagonal-shaped bodies at higher magnification (original magnification, ×29,000).

Figure 4 Before and after photographs of right cornea. Notes: (A) Before: cloudy cornea at baseline. (B) After: after receiving treatment for myeloma the corneal cloudiness started improving.
溃疡性角膜炎，显微角膜神经炎，和带状角膜炎。15

我们的病人是第一次出现内眼晶体沉积，尽管晶体太小不方便在裂隙灯下检查。其他原因包括鲍温氏憩室，Schnyder 晶状体性角膜营养不良，16 Bietti 晶状体性视网膜营养不良，17 tyrosinemia，18 gout，和 topical medications (fluoroquinolone)。19

内眼晶体沉积的病理生理学在多发性骨髓瘤中仍然是个谜。一种理论是，晶体沉积来自角膜中泪液和房水中，以及温度，pH，水含量，和 extracellular matrix 沉积。免疫球蛋白的物质已经发现于泪液中，尿液中，房水中的，角膜中的，耳前淋巴结中，以及眼球后膜中。20

尽管 Buerk 和 Tu25 报道一名多发性骨髓瘤患者，指出晶体沉积在 11 例中，只在 stroma 中发现，而在另外 3 例中，沉积发生在 corneal epithelium 和 stroma 中。Auran’s case 和 ours 之间有相似之处。两例患者的临床表现相似，Auran’s case 由多发性骨髓瘤引起的晶状体性角膜营养不良。在多发性骨髓瘤中，晶状体性角膜营养不良是很少见的。4 例晶状体性角膜营养不良是小瞳孔，多发性骨髓瘤有两例，5 例是 Uveitis，6 例是 gout，7 例是 tyrosinemia，8 例是 gout。25

多发性骨髓瘤的特征为角膜沉积，免疫球蛋白的分布可以影响不同的角膜层。It was reported to be deposited in: all layers of the cornea in four cases; only stromal involvement in three cases; epithelial and stromal involvement in one case; and endothelium and Descemet’s membrane involvement in one case.

 corneral deposition of immunoglobulins in multiple myeloma is rarely in a vortex pattern. Two cases of vortex keratopathy in multiple myeloma have been previously reported. Auran et al25 described a case of crystalline keratopathy in a vortex pattern in a patient with multiple myeloma. However, they did not obtain any pathological material. Their patient had already undergone bilaterial phacoemulsification 7 years previously and later developed an endocapsular hematoma that resolved without treatment. There were some similarities between Auran’s case and ours. Both cases had a clinical picture of vortex keratopathy and an Ig-kappa spike on serum electrophoresis. Auran’s case differed in that the patient had decreased vision and glare, while our patient only had decreased vision without glare or photophobia. Their patient had crystalline deposits in the epithelium and stroma, while our patient had deposition only in the epithelium.

Chong et al14 described the second case of vortex keratopathy in multiple myeloma. Their case was diagnosed with multiple myeloma 18 months after first presentation to the ophthalmologist. Again, they did not obtain a corneal biopsy. They did, however, take conjunctival specimens which stained monoclonally for IgG-kappa light chains. Conjunctival electron microscopy showed intracellular hexagonal crystalline structures – similar to our corneal biopsy picture. Their conjunctival specimen also showed some extracellular material in the form of microfibrils, which stained for kappa light chains. This was not evident in our case. Chong et al therefore assumed that the corneal crystalline vortex keratopathy was due to Ig deposition.

Buerk and Tu25 reported a patient with multiple myeloma crystalline keratopathy where confocal microscopy showed in vivo crystals in the corneal epithelium and the anterior stroma. They repeated confocal microscopy after 6 months of chemotherapy and demonstrated a decrease in the size and the number of the corneal crystals. Use of in vivo confocal microscopy was also used by Paladini et al36 in a case with bilateral crystalline corneal deposits, due to monoclonal gammopathy. Confocal microscopy has the advantage of being able to image corneal crystalline deposits in vivo and help monitor a decrease in these changes with chemotherapy more quantitatively. However, confocal microscopy is not a histological tissue test and, therefore, cannot confirm the type
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.37 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
