Short communication

Crystalline keratopathy due to kappa chains in a monoclonal gammapathy


Servicio de Oftalmología, Hospital Esperit Sant, Santa Coloma de Gramenet, Barcelona, Spain

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ABSTRACT

Case report: The following case shows corneal crystal formation in a patient in whom the systemic work-up led to the diagnosis of a monoclonal gammapathy with increased monoclonal immunoglobulin G (IgG). We present the corneal signs and subsequent hematological investigations undertaken to establish this important association.

Discussion: Systemic work-up of a patient with corneal deposits showed a monoclonal gammapathy with increased monoclonal immunoglobulin (IgG-type kappa). Corneal crystals, a rare, but significant, clinical finding, may be the initial presentation in a patient with monoclonal gammapathy.

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Queratopatía cristalina por cadenas kappa en gammapatía monoclonal

RESUMEN

Caso clínico: Se muestra una queratopatía cristalina en un paciente cuyo estudio sistémico permitió el diagnóstico de una gammapatía monoclonal por cadenas kappa de inmunoglobulina G (IgG). Se presentan los signos corneales y la investigación diagnóstica que se llevó a cabo para establecer esta importante asociación.

Discusión: La investigación sistemática de un paciente con depósitos corneales constató una gammapatía monoclonal IgG-kappa. Los cristales corneales pueden ser la manifestación inicial en un paciente con gammapatía monoclonal, un hallazgo clínico poco frecuente aunque muy significativo.

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* Corresponding author.
E-mail address: jcarlosmesa@mixmail.com (J.C. Mesa-Gutiérrez).

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Introduction

Monoclonal gammopathy is a rare cause of crystalline keratopathy, although the possibility of a lymphatic proliferation disorder must be considered in a patient who does not match the clinical pattern of other crystalline keratopathies (Table 1). Crystals of deposits in the corneal epithelium or stroma and give rise to variable symptoms.\(^1\)\(^2\) It is advisable to obtain full clinical records and physical examination as well as referring the patient to the hematologist for adequate diagnostic and treatment.

This paper presents a patient with crystalline keratopathy where systemic assessment and kidney and hematological study enabled the diagnostic of IgG-kappa monoclonal gammopathy.

Clinical case

This case study reports the case of a patient, aged 54, who visited the practice for nonspecific visual disorders in July 2008. No relevant systemic or familiar antecedents, although at the ophthalmological level the patient had undergone bilateral phacoemulsification in 2004. In both eyes the corrected visual acuity (VA) was of 1 and intraocular pressure of 16 mmHg. Biomicroscopy revealed small diffuse yellowish crystals in the corneal stroma (Figs. 1–3). No inflammatory signs were observed in the anterior chamber and the ocular fundus was normal. Due to the crystalline appearance of said deposits, the diagnostic considered corneal dystrophy (lattice dystrophy, Schnyder dystrophy and Bietti dystrophy), cystinosis dystrophy and blood dyscrasia. Serum and leukocyte cysteine levels were normal. Proteinogram evidenced overall proteins increase (10.9 g/dl) and IgG kappa chain increase (5690 mg/dl). Overall proteins in urine amounted to 1200 mg/24h (normal 0–150 mg). Urine electrophoresis exhibited IgG kappa monoclonal strip and free Kappa light chains (Bence-Jones proteinuria). The hematological and biochemical examination did not reveal altered parameters. Bone marrow aspiration revealed 70% of plasmatic cells. A diagnostic of IgG-kappa monoclonal gammopathy with IgG corneal deposits was concluded.

After the diagnostic, the patient was treated with cyclophosphamide and prednisone (8 cycles) due to kidney function deterioration without an objective response being obtained. In September 2009 kidney function was observed to deteriorate again, whereupon autogenic transplant was performed with melphalan and infusion of hematopoietic CD34+ 1.8 × 10^6/kg) progenitors, obtaining partial response. In December 2010 the monoclonal component was observed to develop.

Fig. 1 – Tiny, diffusely distributed whitish crystals.

Fig. 2 – Crystalline deposits in anterior and posterior corneal stroma.

Fig. 3 – Crystalline deposits distributed from limbus to limbus in anterior and posterior corneal stroma.
Table 1 – Differential diagnostic of crystalline keratopathy.

<table>
<thead>
<tr>
<th>Etiology</th>
<th>History/clinic</th>
<th>Biomicroscopy</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infectious</td>
<td>De novo</td>
<td>Tree-shaped deposits in the cornea</td>
<td>Antibiotic therapy</td>
</tr>
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<td></td>
<td>Recent refractive surgery</td>
<td></td>
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<tr>
<td>Schnyder dystrophy</td>
<td>Personal or familiar hypercholesterolemia history</td>
<td>Subepithelial central and mid-periphery cholesterol crystals; corneal arch; diminished corneal sensitivity</td>
<td>Observation in asymptomatic cases</td>
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<tr>
<td></td>
<td>Photophobia</td>
<td></td>
<td>Treat hyperlipidemia</td>
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<td></td>
<td></td>
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<td>Phototherapeutic keratectomy in symptomatic cases</td>
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<tr>
<td>Bietti dystrophy</td>
<td>Progressive night blindness</td>
<td>Whitish-yellowish crystals in mid periphery; yellowish retinal crystals</td>
<td>No treatment</td>
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<td></td>
<td>Campimetric loss</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>Photophobia</td>
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<td></td>
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<tr>
<td>Cystinosis</td>
<td>Nephropathy (polyuria/polydipsia)</td>
<td>Polychromatic cystine crystals in conjunctiva and stroma.</td>
<td>Cysteamine drops for corneal deposits</td>
</tr>
<tr>
<td></td>
<td>Photophobia</td>
<td>Cystine crystals in chamber angle</td>
<td>Oral cysteamine for the systemic form</td>
</tr>
<tr>
<td>Lymph-proliferative disorders</td>
<td>Nonspecific ocular symptoms</td>
<td>Corneal deposits in epithelium or stroma</td>
<td>Refer to hematologist</td>
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<td></td>
<td>Bone pains</td>
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<td>Drugs</td>
<td>Recent use of fluoroquinolones</td>
<td>Diffuse crystalline deposits in cornea</td>
<td>Suspend drug</td>
</tr>
<tr>
<td></td>
<td>Photophobia</td>
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</tr>
</tbody>
</table>

Together with kidney insufficiency worsening, beginning treatment with lenalidomide and prednisone. Corneal deposits did not change with the various treatments (Figs. 4 and 5).

Discussion

Crystalline keratopathy is an important clinical entity which can be secondary to a broad range of causes, from topical medication to systemic diseases. Once the diagnostic has been established it is important to adequately research the etiology and implement appropriate treatment.\textsuperscript{1,2}

Infrequently, crystalline keratopathy can be secondary to monoclonal gammopathy. With the exception of

Fig. 4 – Thin diffuse deposits in the corneal stroma and cornea verticillata in the inferior third.

Fig. 5 – Crystalline deposits did not change with different treatments.
Waldenström macroglobulinemia, crystals are made up of light IgG chains (usually kappa and exceptionally lambda). Ultrastructural studies demonstrate crystalloid deposits in keratocytes of the stroma, epithelium, limbar vascular endothelium and lens.\textsuperscript{1,2} The reason for such infrequent crystallization in this entity is not known although the structure, chemical proteins and concentration of paraproteins, as well as the local medium properties, are all critical. Concentration would be the most important factor because crystals tend to disappear with diminished parprotein concentration. However, considering the rare expression of these sedimentations, the chemical properties and the tertiary structure of said paraproteins would be critical.\textsuperscript{4}

Corneal pathology is rare in monoclonal gammopathy. Bourne demonstrated only one case of crystalline sedimentation in the cornea in 100 patients with monoclonal gammopathy.\textsuperscript{1} More superficial crystals produce more symptoms (diminished VA, photophobia, tearing). However, in most cases these crystals do not produce any symptoms at all.

In monoclonal gammopathy, IgG is the immunoglobulin that is produced in 70\% of cases. The progression of a benign monoclonal gammopathy to multiple myeloma, macroglobulinemia, amyloidosis or lymphoma is observed in 18\% of patients. This potential malignization calls for a full hematological examination with bone marrow biopsy as well as serum and urine electrophoresis.\textsuperscript{1}

In conclusion, this case demonstrates the important association between ocular signs and underlying systemic diseases. Even though corneal deposits are an infrequent expression of monoclonal gammopathy, etiological diagnostic is important for adequately treating the patient as well as for vital prognostic. Even in the absence of systemic symptoms, systemic assessment is a requirement, including serum and urine electrophoresis.

Corneal crystals can be the initial expression of monoclonal gammopathy, a rare but significant clinical finding.\textsuperscript{1,3}

**Conflict of interests**

No conflict of interests has been declared by the authors.

**References**