Subepithelial Corneal Immunoglobulin Deposition as a Manifestation of Multiple Myeloma: A Case Report and Literature Review

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Clinical Practice Points

- Crystalline deposition in the cornea can be an early manifestation of paraproteinemia, which may parallel disease activity.
- Local treatment with superficial keratectomy or penetrating keratoplasty provides symptomatic but only transient improvement.
- Treatment of systemic disease often leads to resolution of corneal involvement.

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Introduction

Multiple myeloma (MM) and other paraproteinemias may rarely cause subepithelial crystalline deposition disease in the cornea.[1-3] These deposits have been shown to be immunoglobulins, usually IgG, although rare cases of other immunoglobulins have been reported.[4,5] There are limited reports in the literature regarding the treatment and prognosis of patients with subepithelial corneal crystals. We report the diagnosis and treatment of a patient whose presenting manifestation of symptomatic MM was blurry vision with corneal involvement secondary to paraprotein-associated subepithelial corneal crystalline deposits.

Case Report

A 63-year-old male with a history of age-related macular degeneration was seen by his primary care physician for progressively worsening blurry vision associated with a gritty sensation. On referral to an ophthalmologist, he was noted to have visual acuity of 20/60 bilaterally, vision of 20/200 in the presence of glare, and significant amounts of subepithelial corneal crystals in both corneas (Fig. 1). He was subsequently referred to a hematologist/oncologist for workup of a plasma cell dyscrasia.

His initial laboratory results revealed the following: serum electrophoresis showed an M spike of 1.35 g/dL; quantitative immunoglobulin levels of IgG—1778 mg/dL; IgA—56 mg/dL, and IgM—15 mg/dL; and normal creatinine and hemoglobin concentrations. A bone marrow aspirate showed a kappa-light-chain–restricted plasma cell population with < 5% marrow plasmacytosis and a normal metaphase karyotype. A metastatic skeletal survey was negative. He was diagnosed with monoclonal gammopathy of undetermined significance (MGUS) and was followed at 6-month intervals without therapeutic intervention. For his visual complaints, he twice underwent superficial keratectomy, but the subepithelial corneal crystals returned within 3 months after each procedure.

Two years after the initial MGUS diagnosis, he was referred to the Myeloma Division at the John Theurer Cancer Center at Hackensack University Medical Center. A repeated bone marrow aspiration was performed and showed 20% to 30% marrow plasmacytosis. His skeletal survey result remained negative, and the M spike on serum electrophoresis was 1.48 g/dL; there was no evidence of renal impairment, anemia, or hypercalcemia (no CRAB [hypercalcemia, renal insufficiency, anemia or bone lesions]). Although he did not meet the classic CRAB criteria for treatment of his MM, the recurrent subepithelial corneal immunoglobulin deposition was considered a manifestation of active MM requiring therapeutic intervention.

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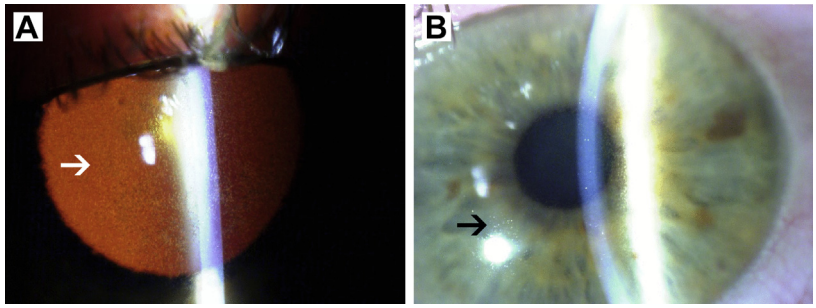
Figure 1 (A) Right Eye at Presentation With Significant Corneal Crystals (Arrow) Seen Clearly on Retroillumination at the Slit Lamp. (B) Slit-Lamp View Showing Corneal Crystals (Arrow) Throughout Cornea Before Treatment. They Were Affecting the Patient's Vision



The patient was treated with oral lenalidomide (25 mg on days 1-21) and oral low-dose dexamethasone (40 mg on days 1, 8, 15, and 22 on a 28-day cycle) for 4 cycles. He responded to this induction regimen with an improvement in his M-protein level from 1.35 g/dL to 0.19 g/dL. To further consolidate his response, he underwent stem cell mobilization followed by high-dose melphalan (200 mg/m^2) with autologous stem cell transplantation. At his 3-month posttransplantation evaluation, he was noted to have a partial remission with a decrease in his M protein to 0.16 g/dL. However, he had clearing of his subepithelial corneal immunoglobulin deposition (Fig. 2). Two years after transplantation, his MM remains in biochemical complete remission, and he has not had recurrence of his crystalline deposits.

Discussion

Paraproteinemias, including MGUS, Waldenstrom macroglobulinemia, amyloidosis, and MM may be associated with a variety of ophthalmic conditions, including corneal deposits, conjunctival deposits, proptosis, diplopia, lid ecchymosis, scleritis, episcleritis, and retinopathy associated with hyperviscosity.[3,6,7] Our patient's presenting sign of MM was symptomatic bilateral corneal crystalline deposits. Although many patients have minimal visual impairment and do not require intervention, those with significant visual symptoms have been treated with several modalities, including superficial keratectomy,[8] penetrating keratoplasty,[9] and systemic therapy.[4,5,8-13] Table 1 presents a summary of cases reported in the literature.

One of the initial cases of corneal involvement of immunoglobulin deposition was described by Firkin et al regarding a 69-year-old male who was diagnosed with IgG lambda MM after complaining of glare in his vision and was found to have bilateral golden corneal crystals.[10] Treatment with vincristine, melphalan, and prednisolone resulted in improvement of both paraprotein levels and corneal deposits. Years later, Hill et al reported a 46-year-old woman with IgG lambda disseminated myeloma with corneal deposits. Despite treatment with irradiation of upper and lower body halves, paraprotein levels and corneal deposits remained unchanged.[11] Chong et al described a 52-year-old woman presenting initially with vortex keratopathy and diagnosed with IgG-kappa MM.[12] After undergoing unspecified chemotherapy, this patient had mild improvement in stroma deposits but persistent blurry vision.

Shuttleworth at al described a 64-year-old man found to have pancorneal epithelial crystalline keratopathy with IgG-kappa MM. Epithelial debridement provided improvement of visual symptoms for several weeks only before recurrence. He was being treated with

Figure 2 (A) Right Eye Seen After Being Treated for Multiple Myeloma. There is Complete Resolution of the Corneal Crystals as Seen Here on Retroillumination (Arrow). An Intraocular Lens can be Seen Centered Within the Capsular Bag. (B) Slit-Lamp Image Showing Clear Cornea With Resolution of Corneal Crystals (Arrow) After Systemic Treatment for Multiple Myeloma