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

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Introduction

Multiple myeloma (MM) and other paraproteinemias may rarely cause subepithelial crystalline deposition disease in the cornea. These deposits have been shown to be immunoglobulins, usually IgG, although rare cases of other immunoglobulins have been reported. 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.

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.
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/m²) 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. 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, penetrating keratoplasty, and systemic therapy.

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. 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. Chong et al described a 52-year-old woman presenting initially with vortex keratopathy and diagnosed with IgG-kappa MM. After undergoing unspecified chemotherapy, this patient had mild improvement in stroma deposits but persistent blurry vision.

Shuttleworth et al described a 64-year-old man found to have panconal 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...
ABCMani (Adriamycin [doxorubicin], BCNU [carmustine], cyclophosphamide, and melphalan) for 7 cycles and CIDEX (CCNU [lomustine], idarubicin, and dexamethasone) for 6 cycles, in addition to regular epithelial debridement every 2 to 3 months. After discontinuation of CIDEX because of renal deterioration, he was treated with thalidomide and dexamethasone, which provided complete resolution of crystalline keratopathy within 7 months.

There are several case reports of MM with corneal deposition in which patients were treated with autologous stem cell transplantation. Font et al reported “systemic chemotherapy” as treatment for a 52-year-old man with deep stromal corneal crystals. Despite initial improvement, the crystals recurred. The patient later received high-dose therapy with autologous stem cell transplantation without resolution of stromal opacities. It was not until therapy with pulsed dexamethasone and corneal transplantation that he experienced durable improvement. In another case, bilateral subepithelial corneal inﬁltrates at the level of the Descemet membrane were described by Edmunds et al. After being diagnosed with IgD-kappa MM, the patient was treated with cyclophosphamide, dexamethasone, and thalidomide. It was not until subsequent autologous stem cell transplantation that the patient achieved neuroophthalmic resolution of symptoms. Hsueh et al described a 62-year-old woman with IgA-kappa MM and bilateral diffuse stromal white crystalline deposits treated with melphalan and prednisone. She did not achieve remission of her MM or resolution of the corneal crystals.

The manifestation of corneal crystals in the setting of MGUS may be associated with an accelerated progression into MM. Chou et al described a case of a 51-year-old man with crystalline deposits who had MGUS for at least 3 years before being diagnosed with MM. Our patient was found to have subepithelial corneal crystals and was diagnosed with MGUS at least 2 years before progressing to MM. Given the paucity of well-described cases, however, it remains difﬁcult to speculate whether corneal crystals in MGUS are a poor prognostic indicator.

**Conclusion**

Corneal crystalline immunoglobulin deposition is a rare clinical manifestation of paraproteinaemia. The differential diagnosis includes corneal dystrophies, cystinosis, and gout. The presenting symptom of ocular involvement for this patient’s MM is a very rare entity. In this case, systemic treatment of the underlying MM with lenalidomide and dexamethasone followed by autologous stem cell transplantation resulted in resolution of the subepithelial corneal crystalline deposition. Based on the few reported cases (Table 1), the highest likelihood of success is with systemic chemotherapeutic treatment of the underlying plasma cell dyscrasia rather than surgical intervention, which provides only transient improvement.

**Disclosure**

The authors have stated that they have no conﬂicts of interest.

**References**

Corneal Manifestations in Multiple Myeloma