Corneal Cupremia in Multiple Myeloma: A Clinicopathologic Correlation

We describe the study of an eye from a patient with corneal cupremia secondary to multiple myeloma. An intercurrent episode of mucormycosis necessitated removal of this individual’s eye, enabling this unique study.

Report of a Case. A 71-year-old white woman with an 8-year history of refractory multiple myeloma had blurred vision. Her best-corrected visual acuity was 20/30 OU. In both eyes, the cornea manifested a remarkable golden-brown, metallic sheen that on slitlamp examination was determined to be at the level of the Descemet membrane (Figure 1). The remainder of her examination disclosed no abnormalities. Several months later, the patient’s vision rapidly decreased and she was diagnosed with mucormycosis of the orbit and sinus. Despite aggressive sinus and orbit debridement as well as the use of antifungal agents, the patient required exenteration. The exenteration specimen provided a unique opportunity to study her eye.

Light microscopy demonstrated slightly granular, tan pigmentation of the anterior portion of the Descemet membrane in the central cornea. Copper-specific staining with rubeanic acid showed highly positive staining of the central cornea, primarily in the anterior Descemet membrane with some additional granular staining of the posterior Descemet membrane (Figure 2). Similar stains of the midperipheral and peripheral cornea revealed that copper was absent from these regions. No copper deposition was noted in the lens capsule as has been previously reported.1-6

Comment. Deposition of copper in ocular tissues has been reported in the context of multiple myeloma,1-3 IgG monoclonal gammopathy associated with pulmonary carcinoma,4 and benign monoclonal gammopathy of undetermined significance.5 The unifying factor in these conditions appears to be the presence of IgG light chains that bind copper with an unusually high affinity. Both k and l light chains have been reported to bind copper. Patients with these conditions have markedly elevated serum copper levels and normal to slightly elevated serum ceruloplasmin levels (in contrast to the low ceruloplasmin levels found in Wilson disease). Copper deposits have been reported in the cornea at the level of the Descemet membrane, within the anterior and posterior lens capsule, and within the trabecular meshwork.1-3,5

In multiple myeloma, the copper deposition is central and tends to spare the limbal region. The central cornea manifests a remarkable iridescent sheen secondary to fine, metallic particles at the level of the Descemet membrane. The diffuse central sheen may be supplemented by a radial pattern of spokes but is universally reported to stop within 2 to 3 mm of the limbus.

Various theories attempt to explain why copper is deposited centrally in monoclonal gammopathy and peripherally in Wilson disease. It has been hypothesized that the corneal copper is derived from the limbal circulation in Wilson disease, whereas in multiple myeloma the deposition is secondary to elevated levels of copper in the aqueous humor.1

Figure 1. Slitlamp image of the patient’s left eye, demonstrating a golden-brown sheen at the level of the Descemet membrane secondary to corneal copper deposition.

Figure 2. Copper-specific staining of the central cornea highlights the areas of copper deposition. Deposits were seen primarily in the anterior portion of the Descemet membrane, with a small amount of staining in the posterior Descemet membrane as well (rubeanic acid, original magnification x100).
Interestingly, monoclonal IgG and IgG light chains appear to bind copper in these disease states but are not known to do so in vitro. In at least 1 case, the copper-carrying protein was sequenced in an attempt to determine whether it shared the N-terminal Asp-Ala-His amino acid sequence known to bind copper in albumin, but no such sequence was found. Sequences as simple as Gly-His are capable of binding copper under certain circumstances, especially if they are repeated, rendering it difficult to determine the location of a potential binding site based on sequence alone. Myeloma protein is known to accumulate in the eye as an amyloid, and although individual myeloma proteins do not appear to bind copper, closely packed myeloma proteins may be able to do so.

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Poliosis as a Manifestation of Conjunctival Melanoma

Acquired poliosis of the eyelashes is usually seen in conjunction with benign conditions. However, its appearance should prompt a careful examination to rule out malignant neoplasia. We report a case of conjunctival melanoma with eyelid poliosis.

Report of a Case. A 71-year-old woman with a history of primary-acquired melanosis with atypia and recurrent anaplastic conjunctival melanoma of the right eye (Figure 1A) had a 2-month history of ocular pain and growth of 3 pigmented conjunctival lesions. A patch of white eyelashes on the lateral aspect of the right upper eyelid was noted adjacent to the pigmented palpebral conjunctival lesion (Figure 1C and D). The eyelid appeared thickened and inflamed. No other abnormality in the eyelid architecture was noted, and there was no vitiligo or intraocular inflammation. Previous examinations revealed no evidence of tumor recurrence and normal eyelash pigmentation (Figure 1B). The primary melanoma had been resected 4 years prior. At the time of excision, cryotherapy was used on the bulbar conjunctiva but not on the palpebral conjunctiva. The patient denied any topical medication use including prostaglandins or chemotherapeutic agents. Findings from histological examination of the area immediately adjacent to the poliosis revealed a conjunctival melanoma. There was no histological evidence of inflammatory cell infiltration or destruction of the hair follicle (Figure 2).

Comment. The term poliosis is used to describe a localized area of hair depigmentation. In the skin, it has been described in association with lesions such as intradermal nevi, giant congenital nevi, and halo nevi. Acquired poliosis of the eyelashes has been described in several ophthalmic conditions, including blepharitis, sarcoidosis, sympathetic ophthalmia, herpes zoster, Vogt-Koyanagi-Harada syndrome, vitiligo, tuberous sclerosis, following irradiation, and with topical administration of prostaglandin F2a analogues. Although poliosis of the eyelid is usually associated with benign eyelid conditions, in this case it developed in conjunction with conjunctival melanoma. Poliosis associated with malignant neoplasms has only once been reported with malignant melanoma of the scalp. To our knowledge, there have been no prior reports of poliosis in association with conjunctival melanoma.

The pathogenesis of poliosis is not known. It has been suggested that it may be related to an inflammatory destruction of the melanocytes in the hair follicle, apoptosis of the follicular melanocytes, or a targeted autoimmune response. Perhaps the malignant cells initiate an immune response that cross reacts with the normal follicular melanocytes. In other conditions where poliosis is present, selective antibodies against melanocytes have been found. The poliosis in our case developed next to areas of atypical melanocytic proliferation, but there was no evidence of a dense inflammatory response around the hair follicle. Acquired poliosis of the eyelashes is an important clinical sign, and it should prompt careful examination of the tarsal conjunctiva for suspicious pigmented lesions.

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