JAMA Ophthalmology Clinical Challenge

Episodic Upper Eyelid Edema in an African American Patient

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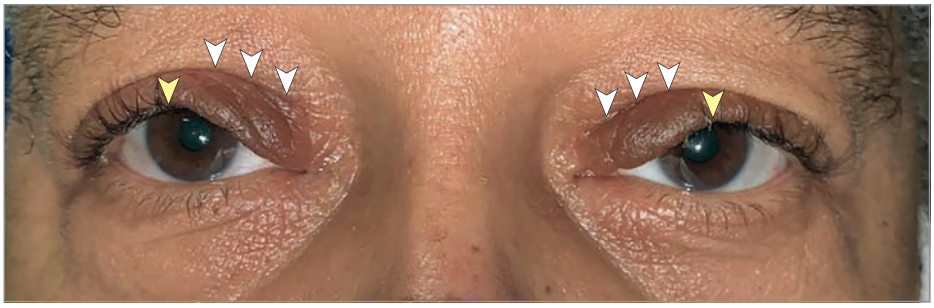

Figure 1. External photograph showing diffusely thickened and ecchymotic-appearing skin of the medial upper eyelids (white arrowheads) without palpable nodules. There is a clearly defined border between the normal eyelid margin temporally and where the redundant abnormal tissue obscures this margin medially (yellow arrowheads).

An African American patient in their early 60s with a medical history significant for recent diagnosis of monoclonal gammopathy of unknown significance (MGUS) and prostate cancer was referred to the oculoplastic service for evaluation of intermittent, bilateral swelling and pain of their medial upper eyelids only for the past 2 years. They denied pruritus. Episodes occurred every few months and lasted for a few weeks at a time, with no obvious triggers. The patient denied other ocular symptoms and had no other skin findings. Their examination was notable for mild upper eyelid spongy edema with hyperpigmented, ecchymotic-appearing redundant skin overhanging the eyelid margins (**Figure 1**). There were no palpable nodules, and there was no lymphadenopathy. Review of systems was negative for fatigue, generalized muscle weakness, or neurologic deficits.

WHAT WOULD YOU DO NEXT?

A. Biopsy the eyelid skin

B. Obtain computed tomography of the orbits

C. Start a course of topical corticosteroids

D. Order thyroid serologies

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Diagnosis

Cutaneous amyloidosis

What to Do Next

A. Biopsy the eyelid skin

Discussion

The differential diagnosis for noninfectious eyelid swelling includes autoimmune blepharochalasis, sarcoidosis, thyroid-associated ophthalmopathy, lupus erythematosus, dacryoadenitis, or idiopathic orbital inflammation. Other possible diagnoses include hereditary angioedema, atopic dermatitis, periocular rosacea, eczema, and localized cutis laxa.

Given the lack of orbital signs such as proptosis or extraocular motility restriction, imaging is unnecessary (option B). Empirical topical corticosteroids (option C) may provide symptomatic relief but can mask an underlying etiology. Because this patient had no clinical signs of thyroid ophthalmopathy, serologies (option D) are unnecessary.

Based on this patient's history of MGUS, there was suspicion for an underlying systemic process and biopsy was undertaken (option A). The association of MGUS with cutaneous amyloidosis is exceedingly rare[1]; however, MGUS is a suspected precursor of multiple myeloma and light-chain amyloidosis, which are both associated with cutaneous disease.[2,3] Hematoxylin-eosin stain showed deposition of amorphous eosinophilic material in the dermis, which was positive for Congo red stain with birefringence, consistent with amyloid (**Figure 2**). Subsequent systemic workup by the hematology service was negative.

Periocular amyloidosis is a rare disease characterized by extracellular deposition of proteinaceous insoluble fibrils in the conjunctiva, eyelid, or in the orbit.[4] When such deposition is unrelated to systemic disease, ie, primary localized cutaneous amyloidosis (PLCA), repeated friction, scratching, and sun exposure are thought to be

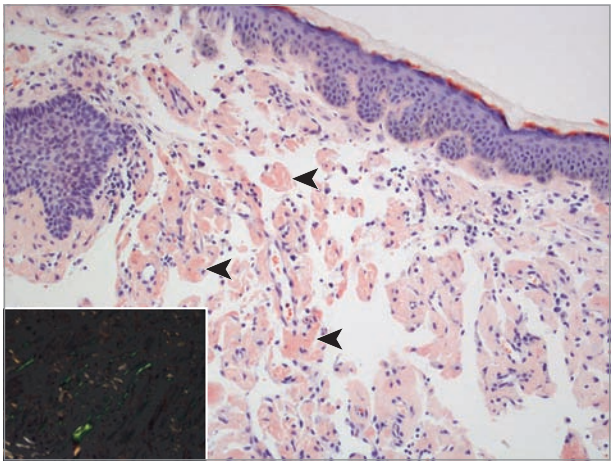

Figure 2. Amorphous eosinophilic material in the dermis stains positive for Congo red (arrowheads) and shows apple-green birefringence with polarized light, inset (Congo red, original magnification ×100).

causative.[5] Its clinical presentation varies widely, which may delay diagnosis by years. Typical findings are diffuse eyelid thickening, blepharoptosis, and recurrent subcutaneous or subconjunctival hemorrhages.[4] Deeper orbital disease can manifest with subjective pressure sensation, proptosis, and extraocular motility restriction.[4] Orbital imaging is not diagnostic but can be helpful in localizing the disease. Ultimately, tissue biopsy with pathognomonic red-green dichroism after Congo red staining and viewing in intense unidirectional polarized light is required.[5]

Once the diagnosis is confirmed, systemic workup for amyloidosis or plasma cell dyscrasia is required as 15% to 50% of patients have or will develop systemic disease.[6] Because amyloid deposition occurs in a cumulative, progressive fashion culminating in organ failure and death, early detection and intervention are key and may improve outcomes.[3,6] It is not known whether periocular amyloidosis has a higher or lower rate of systemic involvement.

Given the relative rarity of this presentation, there is no treatment consensus. Cutaneous periocular disease is commonly observed, but en bloc resection, surgical debulking, and radiation have also been reported.[4,7] Unlike PLCA, where chronic itch-scratch cycle drives disease pathogenesis, periocular disease has not been associated with pruritus.[4,7] However, if pruritus is present, every effort should be made to control it with topical or systemic immunomodulators, as breaking the itch-scratch cycle can halt progression.[8] Unfortunately, pruritus is often refractory to medical therapies including corticosteroids, topical tacrolimus, phototherapy, laser therapy, oral retinoids, cyclosporine, cyclophosphamide, and thalidomide. Recently, there have been limited case reports suggesting a good response to Janus kinase inhibitors.[8] For deeper space-occupying lesions in the orbit, debulking may be considered.[4] Rates of recurrence after treatment may be as high as 21%.[4]

Although there are no reported data in the literature regarding racial predilection of cutaneous amyloidosis, many of its identifying clinical features are derived from experiences with White skin.[2,4-7,9] Behera et al[10] have previously shown in a South Asian population that certain "classic" dermoscopic features may not be present in dark-pigmented skin. This report of primary cutaneous amyloidosis in an African American patient adds to the small existing body of knowledge regarding this disease presentation in dark-pigmented skin.

ARTICLE INFORMATION

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