Bilateral Lacrimal Gland Involvement With Kimura Disease in an African American Male

Kimura disease (KD) is an inflammatory condition that classically manifests as painless subcutaneous nodules of the head and neck in young Asian males. Histologically, it is characterized by lymphoid follicles with germinal centers, distinguished by an eosinophilic infiltrate and varying degrees of fibrosis. This makes the diagnosis of KD challenging as these histological features may overlap that of idiopathic orbital inflammation or angiolymphoid hyperplasia with eosinophilia (ALHE). We discuss a unique case of KD with bilateral orbital involvement in an African American male. Based on our English-language MEDLINE literature search, to our knowledge, this seems to be the first clearly documented case of KD with simultaneous bilateral lacrimal gland involvement. This case is particularly intriguing as it occurred in a non-Asian patient.

Report of a Case. A 24-year-old urban African American man was seen with bilateral upper eyelid swelling, discomfort, and intermittent vertical diplopia of 1 year's duration. His medical history was noncontributory. Ophthalmic examination revealed bilateral upper eyelid edema and a palpable mass in the anterosuperior temporal aspect of both orbits (Figure 1). No lymphadenopathy of the head and neck was appreciated. A computed tomographic scan showed bilateral lacrimal gland enlargement without adjacent bony erosion (Figure 2). Workup disclosed normal findings on a chest radiograph and for serum urea nitrogen, serum creatinine, and antinuclear body, antineutrophil cytoplasmic antibody, rapid plasma reagent, and purified protein derivative (tuberculin). However, a complete blood cell count revealed a high eosinophil distribution of 24% (reference range, 0%-6%). An excisional biopsy via anterior orbitotomy (Figure 3) demonstrated lacrimal gland atrophy, fibrosis, lymphoid hyperplasia, and prominent eosinophilic infiltrate (Figure 4). There was no evidence of vasculitis or prominent vascular endothelial cell proliferation. The results of flow cytometric analyses were normal and special stains for parasites were negative. The patient was given the provisional diagnosis of idiopathic orbital inflammation and was treated with prednisone, 60 mg/d. His eyelid edema and discomfort were improved at the 1-month follow-up, but the treatment with prednisone was discontinued because of the patient's constitutional complaints. A follow-up computed tomographic scan showed a slight decrease in the size of the lacrimal glands.

Nine months after the initial manifestation, the patient had a tender, right submandibular mass measuring 3 cm in width. On physical examination, an additional 1-cm-wide mass was palpated in the left side of the

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the neck, suggesting lymphadenopathy. An incisional biopsy specimen showed lymphoid proliferation with germinal centers, periductal fibrosis, and eosinophilic infiltrate, similar to that of his lacrimal gland with the addition of eosinophilic abscesses. A complete blood cell count continued to show an elevated eosinophilic distribution of 23%. A serum IgE level showed hypergamma-globulinemia of 973 IU/mL (reference range, <91 IU/mL). The combination of a neck mass with classic KD histopathological features almost identical to that of his lacrimal gland, persistent peripheral eosinophilia, and elevated IgE levels without any signs of allergic or other systemic process established the diagnosis of KD. The patient was treated with cyclosporine, 100 mg twice daily, for 1 month and prednisone, 10 mg/d, for 6 months and demonstrated moderate improvement of swelling and pain at the last follow-up visit.

**Comment.** Kimura disease is an inflammatory process whose characteristics may overlap those of ALHE, also known as “epithelioid hemangioma.” Despite confusion in the earlier literature, they are considered 2 distinct clinicopathological diagnoses with different epidemiological, clinical, and histopathological characteristics.

Kimura disease almost exclusively affects young Asian males, ranging in age from 2 through 59 years. In contrast, ALHE predominates in the West, particularly affecting white women in early to middle adult life. Kimura disease typically manifests as firm subcutaneous nodules that commonly involve the periauricular, parotid, or submandibular regions. Regional lymphadenopathy and salivary gland involvement is common. Angiolymphoid hyperplasia with eosinophilia develops as smaller red papules or plaques, also of the head and neck usually without lymphadenopathy or salivary gland involvement. Systemically, many patients with KD have elevated IgE levels, with reports demonstrating up to a 98% incidence of eosinophilia in KD vs 24% in ALHE. Kimura disease has been reported to be associated with asthma, tuberculosis, nephrotic syndrome, and Loeffler syndrome. Angiolymphoid hyperplasia with eosinophilia may have a benign neoplastic origin or represent a secondary reaction to inflammation or other insult such as AIDS, trauma, infection, pregnancy, or hormonal imbalance.

Authors have reviewed recent cases of KD and ALHE and better defined their histological characteristics. Kimura disease is identified by follicular lymphoid hyperplasia with germinal centers embedded in a fibrocollagenous stroma. Capillary proliferation is not characteristic of KD, but if present, the blood vessels are thin walled and lined by flat endothelial cells. Eosinophilic infiltrate is typical and eosinophilic abscesses are common. The defining feature of ALHE is an abnormal proliferation of vascular endothelial cells that are plump, atypical, cobblestone-like, or histiocytoid. An inflammatory infiltrate is also characteristic of ALHE but usually contains fewer eosinophils than that of KD.

According to the 2002 review by Yeung and Ma, 43 cases of KD involving the orbit, lacrimal gland, eyelid, conjunctiva, or chorioretina, have been identified, predominantly in Asian patients. Patients with orbital KD may have exophthalmos, eyelid swelling, a palpable mass, ocular dysmotility, ptosis, tearing, pruritis, pain, or headache. The superior orbit has been found to be the most common location of disease. How-
ever, only 8 reported orbital cases had bilateral involvement, with none of these clearly documenting bilateral lacrimal gland involvement. Our patient’s initial manifestation involving bilateral lacrimal gland enlargement and inflammatory signs led us to initially pursue a workup for conditions such as syphilis, sarcoidosis, tuberculosis, and Wegener granulomatosis. Other possible considerations in the differential included Hodgkin or non-Hodgkin lymphoma, pyogenic granuloma, eosinophilic granuloma, parasitic infection, benign papillary endothelial hyperplasia, Kaposi sarcoma, angiosarcoma, retrobulbar optic nerve meningioma or glioma, recurrent choroidal melanoma, and metastases, which were excluded by clinical and histological evaluation.1,7 The rarity of KD in this setting, especially in a non-Asian patient led us to consider a diagnosis of exclusion, orbital pseudotumor (ie, idiopathic orbital inflammation), which can manifest in a similar manner. Idiopathic orbital inflammation is histopathologically diverse and an eosinophilic infiltrate can also be seen.3 However, the subsequent occurrence of a lesion with similar histopathological features in our patient’s neck, a more typical location for KD, in combination with persistent peripheral eosinophilia and elevated IgE levels, helped establish the diagnosis of KD. Angiolymphoid hyperplasia with eosinophilia was ruled out because vascular proliferation of endothelial cells was not a predominant feature of the specimen.

In summary, we report a unique case of KD demonstrating bilateral lacrimal gland involvement in a non-Asian patient. Since this disease may involve the orbit and possibly have systemic involvement, it is important that physicians be aware of this unusual manifestation.

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