Bilateral Orbital Kimura's Disease in a Young Asian Man

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A 16-year-old Asian man adolescent presented with bilateral eyelid swelling with multiple palpable mass lesions, which waned after treatment with corticosteroids but waxed after medications were discontinued, for about 1 year. He was otherwise healthy except that bilateral postauricular lymphadenopathy had developed for about 9 years. Laboratory study revealed peripheral eosinophilia with an elevated IgE level. The tumor masses of the left orbit were completely excised through an incision similar to that used in blepharoplasty, which gave good cosmetic results. Postoperative computed tomography scan showed no residual tumor mass in the left orbit but contralateral homogeneous soft-tissue mass lesions around the lacrimal gland and extending deep into the orbit, between the superior and lateral rectus muscles. Pathology reported numerous lymphoid follicles with active germinal centers and extensive lymphocyte and eosinophil infiltration, which characterize Kimura's disease (KD). The tumor mass in the right orbit was also excised during a second elective surgery 10 days later. No evidence of recurrence was noted after follow-up for 7 months. KD of the orbit is rare and usually occurs in middle-aged to elderly Asian men but can also be present in young adolescent. Complete excision with simultaneous blepharoplasty gives satisfactory cosmetic results. *(Chang Gung Med J 2002;25:45-50)*

Key words: orbital Kimura's disease, angiolymphoid hyperplasia with eosinophilia.

Kimura's disease (KD) is an inflammatory disease characterized by recurrent subcutaneous mass lesions predominantly in the head and neck region of young oriental males.[1] Peripheral blood eosinophilia with an elevated IgE level is a common finding. Involvement of the orbit and ocular adnexa, especially bilaterally, by KD is rare.[1-7] Patients with orbital KD are usually older (30-50 years) than the typically teenaged KD patient.[1-4,6,8] Orbital KD may cause a devastating visual outcome if not properly treated although it is a benign lesion.[2] We present a case of bilateral orbital KD in a 16-year-old adolescent who was successfully treated with surgery.

CASE REPORT

A 16-year-old Asian male adolescent presented with bilateral eyelid swelling for about 1 year. Multiple firm, painless mass lesions were readily palpable under the skin of both eyelids. He complained that he always looked sleepy and conspicuous because of his severely puffy and edematous eyelids, although, they did caused no significant visual disturbance. Other ocular examinations including anterior and posterior segments of both eyes were unremarkable except for refractive errors

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(myopic astigmatism). Intraocular pressure was within the normal level. No exophthalmos was noted. He came to our ophthalmic clinics and requested surgery for cosmetic reasons.

He was otherwise healthy except for having bilateral, symmetric masses on both sides of the postauricular areas for about 9 years. The masses increased in size in the first 2 years and then remained stationary. No mass lesion was palpable in the parotid or submandibular region. No systemic disease was identified. He received medical treatment including antiviral agents (ganciclovir and acyclovir) and interferon at several other hospitals but they were not effective. High-resolution computed tomography (CT) of the temporal bones revealed normal external ears and internal auditory canals on both sides except for the bilateral postauricular masses, which resembled lymph node enlargement. Under the impression of lymphadenopathy of unknown cause, he received right-side postauricular lymph node excisional biopsy 1 year ago. Pathology showed fibrosis, many lymphoid follicles with prominent germinal centers, many high endothelial venules, and numerous eosinophils. Eosinophilic microabscesses were seen. Complete blood count showed white blood cells of 10,600/mm^3, while differential count of eosinophils reached 45%.

In the past year, he received trials with short-term oral corticosteroids (prednisolone 10 mg t.i.d. for 2 weeks which was then slowly tapered off) several times. The bilateral eyelid swelling improved, and postauricular lymph nodes shrank to some extent. They returned to their original sizes when the corticosteroid was discontinued. His eosinophil counts continually fluctuated between 45% and 60%, and IgE levels were around 5000 IU/ml.

Excisional biopsy through an incision like that usual in blepharoplasty was performed on his left eyelid. The eyelid masses, wrapping around the lacrimal gland, were multiple and extended deep into the orbit (Fig. 1). We carefully separated them carefully from the lacrimal gland in order to prevent any injury to lacrimal gland. Finally, all the mass lesions were isolated and completely excised. The wound was closed with the method as in surgery for blepharoplasty. Because the masses enteral more deeply into the orbit than we had previously expected, postoperative orbit CT scan was performed, but no residual mass was found in his left orbit (Fig. 2). On the right side orbit, CT scan showed homogeneous, soft-tissue-density masses, which could not be distinguished from the adjacent lacrimal gland, extending deep into the orbit, between the superior and lateral rectus muscles. All extraocular rectus muscles were normal in size, and the retrobulbar area was clear. Histopathology reported the left side mass lesions to

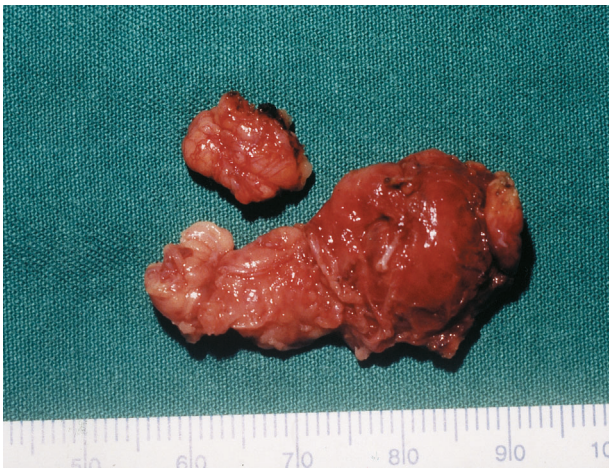

Fig. 1 Excisional biopsy through an incision like that used in blepharoplasty, performed on the left eyelid, showing solid appearance of the lesion (total tumor size: 4 × 2 × 2 cm).

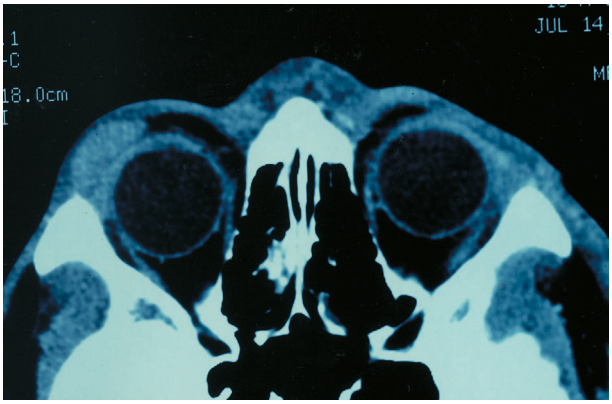

Fig. 2 Postoperative orbital CT scan. The scan was performed, and no residual mass was found in his left orbit, but in the right-side orbit, a homogeneous soft-tissue-density mass, which could not be distinguished from the adjacent lacrimal gland, extended deep into the orbit, between the superior and lateral rectus muscles.

be numerous lymphoid follicles with active germinal centers and with extensive lymphocyte and eosinophil infiltration (Fig. 3). Fibrosis of the tissue and vascular proliferation of capillaries were also identified. Ten days later, orbital tumor excision was performed on his right orbit using the same method as on the left side (Fig. 4). The patient was followed up for 7 months, and there was no evidence of recurrence. He was satisfied with the results of surgery.

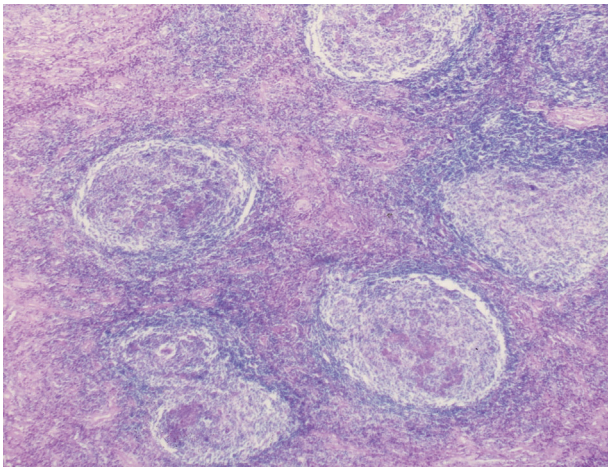

Fig. 3 Histopathology showing numerous lymphoid follicles with active germinal centers and extensive lymphocyte and eosinophil infiltration. (H&E, 400¡)

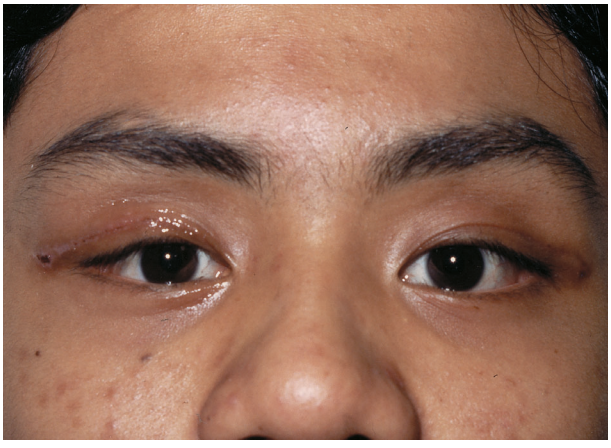

Fig. 4 Orbital tumor excision on the right orbit following left side surgery 10 days later with the same method.

DISCUSSION

The first description of this disease appeared in the Chinese literature by Kim and Szeto as eosinophilic hyperplastic lymphadenopathy in 1937, but the disorder became popularly known as KD following the report of Kimura et al. in the Japanese literature in 1948.[1,9-10] According to Amemiya, the first published case with orbital involvement was reported by Nakai in 1966.[8] In a literature search for this disease, not including ours, 42 cases (31 males and 11 females) involving the orbit, lacrimal glands, eyelids, conjunctivae and probably the chorioretina were found.[1-7] Only 7 patients were bilaterally involved. There is nosologic confusion between KD and angiolymphoid hyperplasia with eosinophilia (ALHE) in reports of the Western medical literature because the clinical and pathologic features of KD overlap significantly with those of ALHE.[1,2,5,7,8,11-15] Therefore, the actual number of orbital KD causes documented are fewer because some cases reported as orbital KD were in fact orbital ALHE in fact.[1]

In 1963, Wells and Whimster published the first case report, resembling KD, in the English literature, designating it subcutaneous angiolymphoid hyperplasia with eosinophilia in 1969.[1,10,12-13] They suggested that the 2 entities were identical or closely related, and they also concluded that the histologic variations represented changes occurring over time, with subcutaneous ALHE representing an earlier and KD a later stage in the disease process.[1] In 1971, Mehregan and Shapiro proposed the simplified term angiolymphoid hyperplasia with eosinophilia.[16] In 1982, Bostad and Pettersen reported the first case of ALHE involving the orbit.[11] Current opinion of most authorities is that the histologic features of KD sufficiently differ from those of AHLE to warrant its recognition as a distinct entity.[10,17-18] Although the exact pathogeneses of KD and ALHE remain to be determined, it is believed that KD most likely represents an allergic or autoimmune response, whereas ALHE represents a benign neoplasm of endothelial cells.[1,17] There is no evidence for the progression of lesions from the characteristic picture of ALHE to that of KD with the passage of time.[1,17]

Clinically, patients with orbital or ocular adnexal KD usually present with proptosis, palpable eyelid mass lesions with or without eyelid edema, and con-

junctival masses.[1] The masses, if palpebral, are firm and non-tender, and may be single or multiple. The most common location of the lesions is the orbit, with the superior orbit being the most frequent site.[1,8] Involvement of the skin of the postauricular, parotid and submandibular regions, including the salivary glands and regional lymph nodes, occurring before or simultaneousl to the orbital lesions is common.[1] Lesions may gradually enlarge and increase in number over time or spontaneously regress.[1] Many patients with KD have peripheral blood eosinophilia, whereas some of them also show elevated serum IgE levels.[1,8] Associations with nephrotic syndrome and proteinuria, asthma, tuberculosis, Loeffler syndrome, and allergy to Candida have been reported.[1] No patient with KD has been reported to develop malignancy.[1]

Histopathologically, Kimura's disease is characterized by dense fibrosis, capillary proliferation, inflammatory cell infiltration, reactive lymphoid follicles and aggregation of eosinophils.[1,17] The fibrous tissue may be densely infiltrated by blood vessels and inflammatory cells or hyalinized with a scant inflammatory infiltrate. Capillaries in KD are thought to be identical to the high endothelial venules found in reactive lymphoid tissue. Endothelial cells can be reactive or hyperplastic and are often described as plump or swollen. They do not demonstrate nuclear atypia or abundant cytoplasm and do not project into or occlude the vascular spaces. Typically, lymphoid follicles with distinct germinal centers and mixed inflammatory cell infiltration with numerous lymphocytes and eosinophils are present. Eosinophil microabscesses are common.[1,17]

ALHE is the main differential diagnosis of KD since they are now considered to be 2 distinct clinicopathologic entities. Lesions in ALHE most often appear on the face, scalp, and ears. Regional lymphadenopathy is rare. Peripheral blood eosinophilia is uncommon,[11] abnormal immunoglobulin levels are extremely unusual, and neither autoimmune phenomena nor malignant changes have been described.[1] Histologically, ALHE is characterized by proliferation of blood vessels lined with atypical endothelial cells with an infiltrate of mostly lymphocytes, histocytes, plasma cells, mast cells, and eosinophils.[1,17] Lymphoid follicles may or may not be present, and what little fibrosis is present is usually at the periphery of the lesion. The most important diagnostic feature of ALHE is the appearance of endothelial cells, variously described as plump, atypical or histocytoid. These cells project into vascular spaces or form solid cords and nests creating a resemblance to malignant vascular neoplasm.[17] Misdiagnosis of the disease to KD has not been associated with fatal outcomes because both conditions are indolent in nature and, in general, self-limiting.[1] They also have similar methods of treatment and are potentially curable with complete excision.[1]

Other situations that may mimic KD include chalazion,[19] idiopathic orbital inflammatory pseudotumor,[8] retrobulbar optic nerve meningioma or glioma,[1] orbital or conjunctival lymphoma,[5,9,15] recurrent choroidal melanoma, and metastatic orbital tumor.[13]

Therapies for ocular and adnexal KD include observation, excision, steroids, radiation, and chemotherapy alone or in combination.[1] Corticosteroids were effective in treating the lesions, but relapse tended to occur after their withdrawal.[1,8] Excision is the favored therapy, with the majority of patients followed up having a good outcome.[1,12] However, the disease continuing despite multiple surgical excisions has been reported.[2] The consequent exophthalmos and lid changes can cause lagophthalmos that results in severe visual impairment due to chronic corneal exposure.

Diagnosis without a pathology report from an excisional biopsy is difficult.[1,10,7-18] The nature of the mass lesions should be determined in order to rule out the possibility of a malignancy in some cases.[13] In other cases, debulking surgery must be performed to release optic nerve compression or exophthalmos.[1-2,8] In our case, the patient was diagnosed with KD by excisional biopsy of a postauricular lymph node with the aid of laboratory test. To our knowledge, requesting surgical treatment purely for cosmetic reasons has not been previously reported. Therefore, we discussed the details of possible treatment methods including surgery with the patient. We also explained the risks of possible surgical complications with him. During surgery, we made every effort to spare the normal lacrimal gland in order to maintain tear production. The patient felt satisfied with results of the surgery.

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