Older-age onset of Kimura's disease

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***Abstract*:** A 60-year-old man was admitted to our hospital with bilateral post auricular masses, first noticed 1 year earlier. Blood tests showed eosinophilia and high immunoglobulin E (IgE) levels, and cervical computed tomography showed 10-mm soft tissue masses with scattered lymphadenopathy. The tumors showed intermediate and high signal intensity on T1- and T2-weighted cervical magnetic resonance imaging, respectively. After mass resection, the tumors were diagnosed as Kimura's disease (KD). Generally, KD affects young men; however, even in older patients, KD should be included as a differential diagnosis for head and neck tumors in patients with eosinophilia and high IgE.

Keywords: eosinophilia, high immunoglobulin E, Kimura's disease, older patients

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Introduction

Kimura's disease (KD) is a rare, chronic inflammatory disorder associated with eosinophilia and high immunoglobulin E (IgE).[1] KD occurs mainly in young Asian men,[1] but has also been reported in patients older than 60 years.[2–17] Typically, KD presents with slowly enlarging, painless, subcutaneous masses in the head and neck, with occasional pruritus of the overlying skin.[1] When a mass is found in the head and neck of an older patient, a malignant tumor is generally suspected. The diagnosis of KD is based mainly on characteristic pathological features, which include florid germinal center hyperplasia, extensive eosinophilic infiltrates, and proliferation of the postcapillary venules.[18] However, the pathological features are not pathognomonic for KD, and a number of malignant conditions, such as Hodgkin's disease and T-cell lymphoma, can closely mimic these findings.[19,20] Unusual presentations of KD might cause diagnostic difficulty or be misdiagnosed as malignancy, if the clinical suspicion is insufficiently high; therefore, tissue biopsy is required for diagnosis.

We present details of a patient with older-age onset of KD, which was inconsistent with the classical description. This case underscores the importance of a high clinical suspicion for an underlying malignant diagnosis if a patient shows clinical progression.

Case

A 60-year-old Japanese man presented with a 1-year history of non-painful bilateral postauricular subcutaneous masses without signs of inflammation. The patient had no history of fever, night sweats, weight loss, or appetite loss. On clinical examination, bilateral 1×1-cm swellings were found behind his ears. The masses did not feel warm, and they were firm, fixed to the skin, and non-tender. Satellite nodes were not palpable.

Blood tests showed eosinophilia (33%; reference range, 0–5%) and an IgE level of 4837.3 IU/ml (reference range, <170 U/ml). Biochemical parameters, including plasma glucose, serum urea, creatinine, and liver function tests, were within the respective normal ranges. Computed tomography showed 10-mm soft tissue masses with scattered lymphadenopathy in bilateral postauricular regions (Figure 1A). Isointense signals were observed on T1-weighted magnetic resonance images (Figure 1B), and high-intensity signals were observed on T2-weighted images and

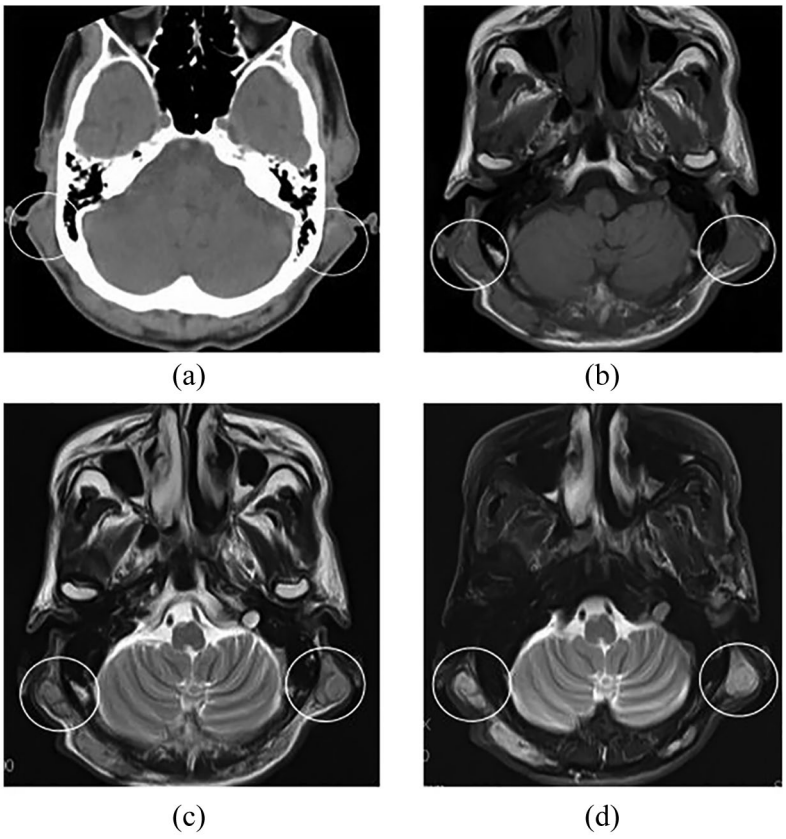

Figure 1. Bilateral cervical computed tomography images showing masses measuring approximately 10 mm in the posterior auricular areas, with scattered small lymph nodes (A). Cervical T1-weighted magnetic resonance image showing isointense signals (B) and high-intensity signals on T2-weighted (C) and T2-weighted fat-suppressed images (D).

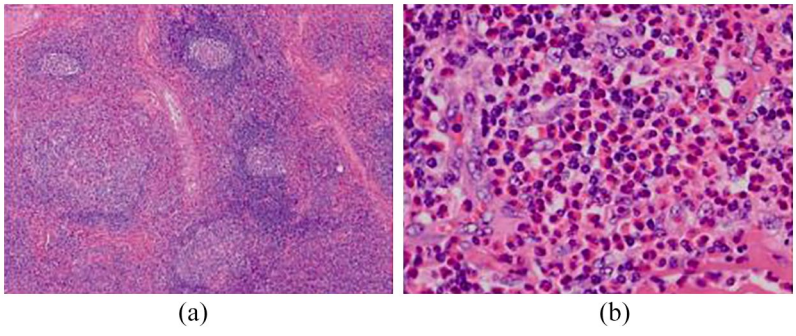

Figure 2. Large and small lymphoid follicles are prominent in the connective tissue, which consists of collagen fibers and vascularization. Eosinophilic abscesses are also seen (A). Prominent infiltration of lymphocytes, plasma cells, and eosinophils is seen among the lymphoid follicles (B).

T2-weighted fat-suppressed images (Figure 1C and D). Histopathology of the resected masses revealed germinal center hyperplasia, postcapillary venous proliferation, eosinophilic infiltration, and eosinophilic abscesses (Figure 2A and B). On the basis of these findings, the patient was diagnosed with KD. During follow up, no recurrence and no new pathologic conditions (i.e. Hodgkin's disease) were observed in the 12 months after surgery.

Discussion

We established a diagnosis of KD in a 60-year-old Japanese man according to the presence of nodular lesions in the head and neck, elevated eosinophil and IgE levels, and a highly suggestive histological appearance of eosinophilia, even though the patient's age was inconsistent with the classical description.

KD is a rare, chronic inflammatory disorder associated with eosinophilia and high IgE that occurs predominantly in young Asian men,[1] unlike in our older patient. When an older patient has a head and neck mass, it is common to first rule out a malignant disease. However, when patients have eosinophilia and increased IgE levels, medical practitioners should be aware of the clinical characteristics of KD and perform tissue biopsy and histological examination.

Our review of the literature describing the clinical presentation of KD showed that few patients with KD are older than 60 years of age, and that aged patients tend to be women, exhibit pruritus, and experience a long time to diagnosis compared with younger patients.[21] Our case had the general features of KD (e.g. Asian features, eosinophilia, and hyper-IgE), but similar features to those reported in our review were not seen in our aged patient.[21] Because knowledge of KD in older patients is insufficient, it is important to add the findings observed in this case to existing knowledge.[21]

The differential diagnoses are broad, and include both benign and malignant conditions such as angio-lymphoid hyperplasia with eosinophilia (ALHE), reactive lymphadenopathy, parasitic infections, drug reactions, and malignant disease (Hodgkin's disease and T-cell lymphoma).[1] ALHE occurs in older women, and vascular proliferation is more prominent, with plump endothelial cells.[22] KD and ALHE are distinguished according to their biochemical and histopathological characteristics.[23] It is important to note that malignant diseases may

mimic the characteristics of KD.[1] Cases of KD mimicking Hodgkin's disease or vice versa have been reported because of the close resemblance between the two conditions histologically and on imaging.[19] One reported patient was diagnosed with T-cell lymphoma 1 year after a diagnosis of KD.[20] In the present case, we did not perform flow cytometry or immunohistochemistry. During follow up, no recurrence and no new pathologic conditions (i.e. Hodgkin's disease) were observed in the 12 months after surgery. Although our patient was diagnosed as having KD based on the clinical presentation and histological examination, further examinations, flow cytometry, and immunohistochemical findings are considered useful for the diagnosis of KD.[1]

Hui *et al.* reported the histological characteristics of KD.[18] Some of the most common findings are listed as 'constant features': intact nodal architecture, extensive reactive lymphoid infiltrates, postcapillary venule proliferation, and infiltration with numerous eosinophils accompanied by mast cells, histiocytes, and Langerhans cells. Other, less common, features are described as 'frequent features': sclerosis, polykaryocytes, vascularization of the germinal centers, proteinaceous deposits, necrosis of the germinal centers, eosinophilic abscess, and reticular IgE deposition within germinal centers. Although the individual histological features are nonspecific, the constellation of features is highly characteristic of KD.

As in this case, computed tomography typically reveals ill-defined subcutaneous masses that are homogeneously iso-dense to hypodense without necrosis, calcification, or cystic degeneration.[24] On magnetic resonance imaging, the masses appear hypointense to isointense on T1-weighted images and hyperintense on T2-weighted images.[24] KD is difficult to distinguish from malignant lymphoma using imaging,[25] and a histological diagnosis is required.

KD is treated for cosmetic reasons or to preserve function while preventing recurrence. However, there is no consensus on the management of KD, and, in our previous report, we found no differences in treatment choice by age.[21] Several treatments for KD have been proposed, namely, surgical excision, systemic corticosteroids, immunosuppressants (cyclosporine, azathioprine, and cyclophosphamide),[26,27] and radiation.[28] Surgery is the most widely used treatment and helps to reach a definitive diagnosis, although recurrence is common.[29] Corticosteroid therapy has not shown convincing results because its effect is transient.[30,31] Radiation therapy is an alternative for recurrent KD that provides local control and prevents recurrence.[32] Other treatments are retinoids,[33] monoclonal antibodies (imatinib),[34] antiallergy drugs (cetirizine),[35] pentoxifylline,[36] photodynamic therapy,[37] and cryotherapy.[38] The wide variety of available treatments for KD might be associated with a lack of difference in treatment types according to age.

Conclusion

KD is a benign, chronic inflammatory soft tissue disorder of unknown origin, occurring predominantly in young adults, but clinicians should be aware that KD also affects older patients. KD is easily misdiagnosed because of its rarity and lack of clinical awareness of the condition. Although malignancy must be considered first when head and neck masses occur in older patients, KD should be considered in patients with concurrent eosinophilia and elevated IgE levels. Because KD may not show specific clinical or imaging features, histopathological examination is required for diagnosis.

Conflict of interest statement

The authors declare that there is no conflict of interest.

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Ethical/consent statements

The patient gave verbal informed consent, and the patient and our hospital approved the use of clinical data.

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