

Kimura's disease—an unusual cause of lymphadenopathy in children

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Abstract Kimura's disease is a rare inflammatory disorder of unknown cause primarily seen in young Asian males. The disease is characterized by a triad of painless subcutaneous masses in the head or neck region, blood and tissue eosinophilia, and markedly elevated serum immunoglobulin E levels. We describe a 3-year-old Indian boy with Kimura's disease who presented with generalized lymphadenopathy. The diagnosis was based on the characteristic histopathologic findings after surgical excision in conjunction with peripheral eosinophilia and elevated serum immunoglobulin E levels.

Keywords Elevated immunoglobulin E level · Kimura's disease · Lymphadenopathy · Peripheral eosinophilia

Introduction

Kimura's disease is a chronic inflammatory condition characterized by a triad of painless subcutaneous masses in the head or neck region, blood and tissue eosinophilia, and markedly elevated serum immunoglobulin E levels.

Kimura's disease was first reported by Chinese authors Kimm and Szeto in 1937 [1], and besides its eponym, has been variously known as epithelioid hemangioma, atypical pyogenic granuloma, and cutaneous eosinophilic lymphofolliculosis. The original description was made by Kimura

et al in Japan in 1948 [2], and since that time, there have been a slowly increasing number of reports. While most cases have originated in China, Japan, or Southeast Asia, there has been sporadic case reports from Europe and America, and by late 1994, there had been some 120 cases described in the world literature. The disease is most prevalent in Asians, uncommon in whites, and rare in blacks. It has been suggested that the common factor is a degree of Asian ancestry [1].

Clinically, the subcutaneous soft tissue masses occur predominantly in the head and neck and often involve the parotid glands. Approximately 67 to 100% of patients develop regional lymphadenopathy, and in longstanding disease, this may become generalized [3]. Patients may complain of local or generalized pruritus and subacute or chronic dermatitis. There may be proteinuria, and laboratory investigations will invariably reveal peripheral eosinophilia and increased serum immunoglobulin (Ig)E.

We describe a 3-year-old Indian boy with Kimura's disease who presented with generalized lymphadenopathy. The diagnosis was based on the characteristic histopathologic findings after lymph node biopsy in conjunction with peripheral eosinophilia and elevated serum immunoglobulin E levels.

Case report

A 3-year-old boy from Hyderabad presented with complaints of swelling in the neck, axilla, and groin since one and half years duration. The family doctor had noticed the cervical swelling initially and treated the boy as a case of glandular tuberculosis with anti-tuberculous treatment for 1 year. Over the next few months, the parents noticed new swellings in the axilla and groin.

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Since the last 6 months, his parents noticed recurrent episodes of rashes in both lower limbs, which were erythematous maculo-papular, and pruritic and disappeared within 2–3 days. Along with rashes, the patient had swelling in the ankle and knees.

Examination revealed a cheerful child with generalized lymphadenopathy. The patient had maculo-papular rashes in both lower limbs, along with inflammatory arthritis involving knees and ankles. Both these features disappeared within 2 days during the hospital stay.

Blood investigation showed microcytic hypochromic anemia with eosinophilia (Hemoglobin, 9 g%, absolute eosinophil count 1,100 cells per microliter). Computed tomography had shown small lymph nodes in mediastinum and porta hepatis.

An excision biopsy was performed which revealed a dense inflammatory infiltrate and fibrosis. The infiltrate was characterized by lymphoid tissues with germinal centers and numerous eosinophils with eosinophilic micro abscess formation. A prominent proliferation of small venule-sized vessels was noted. There was no evidence of malignancy, and no organisms were noted. The Immunoglobulin E concentration was increased at 625 µg/l (normal 30–280). Serological tests for human immunodeficiency virus, *Toxoplasma gondii*, rubella, cytomegalovirus, filariasis, *Trichinella spiralis*, *Toxocara canis* and *catis*, and *Trypanosoma cruzi* were negative.

Discussion

Kimura's disease is now recognized as a benign cause of painless localized lymphadenopathy in Asians, especially boys of Chinese and Japanese origin [2–6]. Although the disease can become apparent at any age, most cases have been reported in the second and third decades of life. The clinical triad of subcutaneous nodules found in the head or neck, prominent peripheral eosinophilia, and highly increased IgE concentrations, particularly when seen in an Asian boy, is highly suggestive of Kimura's disease. Pathologically, nodular lesions usually affect the lymph nodes, although occasionally, skin or salivary tissues are affected [2, 3]. Normal tissue architecture is usually preserved, but follicular hypertrophy of lymphatic tissue with infiltration of lymphocytes, histiocytes, and large numbers of eosinophils is typical. Germinal centers may be necrotic, with central eosinophilic abscesses [2, 3].

The pathophysiology of Kimura's disease is not understood at this time, but may relate to a disturbance in the normal rate of production of eosinophils and IgE, currently believed to be a product of an interaction between types 1 and 2 (Th1 and Th2) T helper cells. Such a derangement could result in excessive elaboration of eosinophilotropic

cytokines such as interleukin 4 [7]. Patients with Kimura's disease have been shown to have high levels of circulating eosinophilic cationic protein and major basic protein, with heavy concentrations of IgE in their tissues [2]. Allergic or parasitic etiologies for Kimura's disease have been actively sought, but not identified.

The clinical course of Kimura's disease is usually benign. The subcutaneous masses are usually found in the head and neck region, sometimes affecting the parotid or minor salivary glands [4]. Infrequently, axillary, inguinal, or epitrochlear nodes may be affected [4]. Untreated, these masses tend to slowly enlarge and may eventually become disfiguring, as in our patient. In the long term, patients seem to do well, although about 10% may develop a steroid responsive nephrotic syndrome [5].

Three major therapeutic options exist for Kimura's disease. Resection of the tumor mass may be effective in permanently eradicating the mass if the entire lesion can be removed, but regrowth is common [2, 3, 6]. Local irradiation has also been shown to be effective in shrinking lesions, but is generally not advocated in younger patients [5, 6]. Finally, systemic and intralesional corticosteroids have been shown to reduce the size of the lesion, but the tumor tends to recur when these drugs are discontinued [6, 8]. In selected patients, it may be advisable to take a conservative approach, treating only if the mass continues to grow or causes significant deformity.

The differential diagnosis for Kimura's disease includes such entities as eosinophilic granuloma, Mikulicz's disease, acute non-lymphocytic leukemia, Hodgkin's disease, follicular lymphoma, angioimmunoblastic lymphadenopathy, and angiolymphoid hyperplasia with eosinophilia. Except for angiolymphoid hyperplasia with eosinophilia, the clinical and histological feature of these diseases easily distinguishes them from Kimura's disease. Angiolymphoid hyperplasia with eosinophilia is a chronic benign disorder associated with cutaneous nodules heavily infiltrated with eosinophils. It is found in older, mostly female patients, however, and lesions tend to be small and intracutaneous, rather than subcutaneous as in Kimura's disease [9]. IgE concentrations are usually not increased in angiolymphoid hyperplasia with eosinophilia, and there is often no peripheral eosinophilia [9].

Disclosure None

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