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Case Report

Kimura's Disease: A Case Report and Review of Literatures

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ABSTRACT

Kimura's disease (KD) is a chronic inflammatory disorder primarily seen in male Asians during the second and third decades of life. Clinically, it presents as solitary or multiple subcutaneous nodules, predominantly in the head and neck region, typically in the pre auricular region, forehead, and scalp. The etiology of Kimura disease is still unknown. This disorder should be suspected when the clinical triad of painless unilateral cervical adenopathy, hypereosinophilia, and hyper-IgE is present. We report a case of KD with multiple subcutaneous nodules in the parotid, submandibular and posterior auricular regions, hypereosinophilia and hyper IgE levels.

Keywords: **Kimura Disease, Case Report**

Introduction

Kimura's disease (KD) is a rare chronic benign disorder (1)**,** usually affecting young men of Asian race but is rare in western countries (2). Kimura's disease is usually seen in young adults, with most patients being 20-40 years of age. Men are affected more commonly than women, with a 3:1 ratio (3).

The major physical manifestation of the disorder is slowly enlarging subcutaneous masses, often in the head and neck area and usually in association with peripheral blood and tissue eosinophilia, in combination with markedly increased serum IgE concentrations (1, 4, 5).

The etiology of KD is still unknown but may be due to impairment or interference with immune regulation, atopic reaction to a persistent antigenic stimulus by arthropod bites, virus, and neoplasm. The most interesting hypothesis suggests *Candida* acting as a source of persistent antigenemia, although neither hyphae nor spores have been isolated (3). The pathologic findings of the disease are hyperplasia of lymphoid follicles and prominent vascular endothelium in the lymph node. "Peripheral eosinophilia and the presence of eosinophils in the inflammatory infiltrate suggest that KD might be a kind of hypersensitivity

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reaction" (Wikipedia). It seems that, T-helper 2 (Th2) lymphocytes might play a role in this reaction (3).The main differential diagnoses for Kimura's disease includes Hodgkin's lymphoma, follicular lymphoma, eosinophilic granuloma, Mikulicz's disease, acute myelogenous leukemia with eosinophilia, angioimmunoblastic lymphadenopathy, and angiolymphoid hyperplasia with eosinophilia (6). Kimura's disease lesions may be similar to the neoplasms in the head and neck region, that pathology is mandatory for rule out.

Except for angiolymphoid hyperplasia with eosinophilia, the clinical and histopathological features of other diseases easily distinguish them from KD (6). Although KD has long been described as a distinct entity since the original report by Kimura (6-9)**,** it is often confused with angiolymphoid hyperplasia with eosinophilia (ALHE) in many reports (10-13), however there are some differences in clinical and pathologic manifestations. The clinical course of Kimura's disease is benign but renal disease is commonly coexisting, with an incidence of 10% to 60% while 10% to 12% of patients may be affected by nephrotic syndrome, which is responsive to steroids (6).

For treatment, three different therapeutic options exist. Excision of the tumor may be effective if the entire lesion can be removed; but recurrence is common. Other therapeutic options are local irradiation, but it is generally not advised. Systemic and intralesional corticosteroids may reduce the size of the lesion, but the tumor tends to recur.

Case report

A 45-year-old male from the Zarand City of Kerman Province presented with a pruritic posterior auricular mass of 22 years duration, since military service. The lesion had been excised 12 years ago after a recurrence in a previous surgery region. The original pathology report was not available. One year ago in the same posterior auricular and submandibular areas, large subcutaneous painless masses developed (Fig. 1). Other than pruritus, no other specific symptoms were present. Physical examination revealed multiple firm rounds to oval masses in the left submandibular and right posterior auricular regions measuring up to 6×4×1.5cm. A parotid tumor was suspected clinically. With impression of parotid tumor, the patient underwent for surgical excision and the mass was surgically excised.

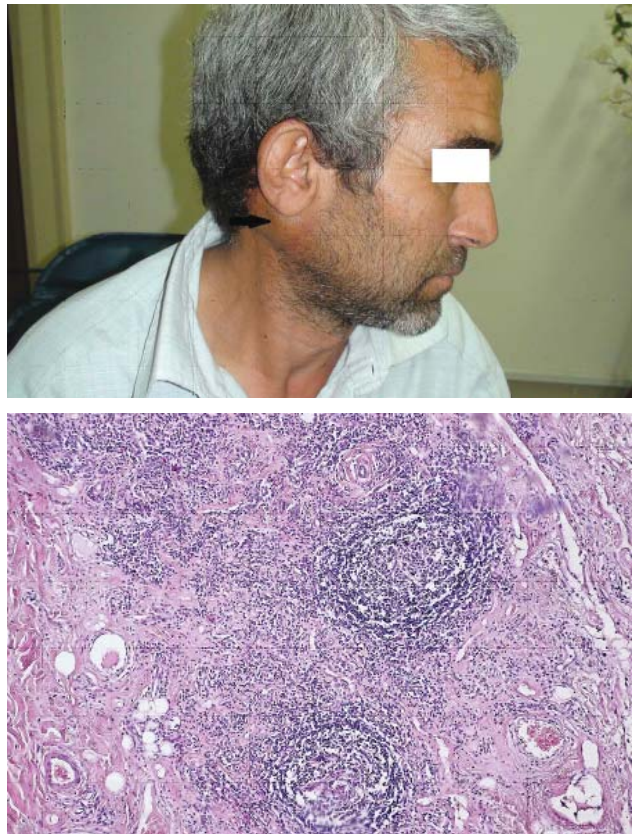

Fig. 1- A-45 year old man with a 22-year history of a slow growing posterior auricular and submandibular mass. B-Reactive follicular hyperplasia with prominent germinal center formation in a subcutaneous region. (Hematoxylin-eosin stain; magnification ×100)

Routine laboratory tests including complete blood counts (CBC), fasting blood sugar (FBS), urea, creatinine, urinanalysis and coagulation tests were all within normal limits, except for a 23% peripheral eosinophilia.

After pathologic evaluation was suspicious for KD, serum IgE levels were measured. These

were elevated at greater than 100 IU/ml (normal level <100IU/ml).

The specimen designated "lymph nodes and parotid tumor" consisted of four variable sized, firm, creamy, elastic nodules measuring from 1.2 to 6 cm in greatest dimension. Overlying skin was also present.

Histologic examination of mass revealed prominent lymphocytic and eosinophilic infiltration of the subcutaneous soft tissue with follicular hyperplasia (Fig. 1D). Eosinophilic infiltration and scattered eosinphilic micro-abscesses separated by numerous prominent thin walled vessels and fibrous bundles were present. The endothelial cells were flat with no vacuolization (Fig. 2A). In some areas typical polykaryocytic giant cells were also seen (Fig. 2B).

On following up, the patient reported a recurrent mass in the right submadibular area of the neck. Further information is not available.

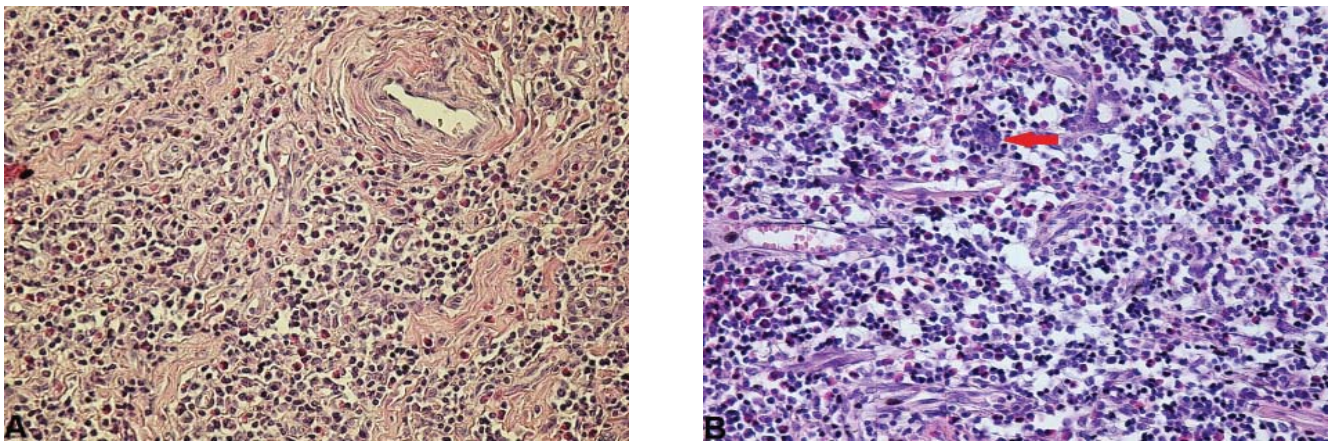

Fig. 2- A- Aggregation of lymphoid cells and eosinophils in the subcutaneous tissue, with eosinophilic micoabscess formation. The eosinophilic infiltrate is separated by fibrous bundles and numerous thin walled vessels without endothelial atypia (Hematoxylin-eosin stain; magnification ×400)
B- Typical polykaryocytic Giant cell (arrow) between thin walled vessels (Hematoxylin-eosin stain; magnification ×400.)

Discussion

Kimura's disease is a rare chronic benign disorder endemic in the Far East, often occurring in younger middle-aged males between the second and third decades of life (1). The major physical manifestation of the disorder is slowly enlarging subcutaneous masses, often in the head and neck area, particularly the preauricular and submandibular regions.

Arshad AR followed eight cases of men between 18 to 46 years with Kimura's disease from January 1987 to December 1999 with swelling in the parotid gland, ranging from 1 year to 20 years' duration and treated them with surgical excision followed by initial high-dose steroid therapy and low-dose maintenance and no recurrences (4).

The disease may present in other sites such as orbit, abdomen auxiliary or inguinal and in other age groups (16). Other often-affected sites include the oral cavity, limbs, groin, trunk, and scalp (14, 16, 17). Sorbello *et al.* reported a 33-year-old woman with abdominal mass involving ureter (2). Yip Yeung *et al.* reported a case of bilateral orbital mass with typical histopathology of Kimura's disease (17).

It is often associated with regional lymphadenopathy, usually in association with peripheral blood and tissue eosinophilia and markedly increased serum IgE concentrations (1, 4, 5). Our patient had 23% eosinophilia (about 1449 eosinophil absolute count) and IgE level >100 IU/ml. Nephrotic syndrome occurs in up to 60% of patients. Our patient had normal levels of urea and creatinine and a normal urinalysis.

The pathogenesis of the disease is unknown, however a number of theories exist. These include impairment or interference with immune regulation, atopic reaction to a persistent antigenic stimulus by arthropod bites, virus (3), and neoplasm. Many patients present with allergic conditions such as urticaria, eczema, pruritis, rhinitis, cutaneous eosinophilia, alopecia areata and vasculitis. Our patient had a history of pruritis localized to the overlying skin of involved areas.

An interesting theory is that *Candida* acts as a source of persistent antigenemia (3). Our patient had no clinical history of candidiasis but did report a history of a distant bite.

The diagnosis of KD is frequently difficult. Tissue biopsy of the involved lymph node or lesion is frequently required for a definitive histopathological diagnosis, and often proves therapeutic as well. The most frequent differential diagnoses are reactive and malignant conditions involving lymph nodes, salivary glands, and soft tissue. These include reactive lymphadenitis, Hodgkin's lymphoma, Mikulicz's disease, Castleman's disease, non-Hodgkin's lymphoma, and salivary gland tumors. A major differential diagnosis of KD is ALHA. ALHE and KD and are quite different and should be distinguished by clinical and pathologic features. Clinically in contrast to ALHA, serum IgE level is frequently elevated in KD. The main treatment is surgical excision with adequate margins. Other treatments include steroids, radiation, and immunosuppressive agents such as cyclosporine (4).

The clinical course of KD commonly involves multiple recurrences, like in our patient who had a history of two previous recurrences. Following up of patients includes monitoring for nephropathy.

Acknowledgments

The authors declare that there is no conflict of interests.

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