Kimura's Disease: Report of a Case & Review of Literature

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Abstract Kimura's disease is an uncommon allergic disorder of unknown etiology affecting sporadic populations. A male patient in his third decade presented with a swelling in his left facial region. His investigations showed a raised eosinophil count. The lesion was excised surgically. He was put on a short term steroid therapy. Biopsy revealed it as Kimura's disease. Subsequent follow-ups have been satisfactory with no recurrences.

Keywords Kimura · Eosinophilia · Angiolymphoid hyperplasia

Introduction

Though it is conventional to think of common diseases first while treating lesions of jaw bone, often one is surprised to come across unusual lesions for which one is not prepared.

Kimura's disease is such an uncommon chronic inflammatory disorder of unknown etiology involving subcutaneous tissue, predominantly in the head and neck region. This condition has a predilection for males of Asian descent and may clinically simulate a neoplasm. Kimura disease is sometimes confused with Angiolymphoid hyperplasia with eosinophilia, which occurs in the superficial skin of the head and neck region. Kimura disease has been described more often in Asians, but it does occur in non-Asians with a similar clinic-pathologic presentation. It has characteristic histological features that are important to

recognize and can be used to differentiate it from hypersensitivity and drug reactions and infections.

Case-Report

A 39 year old Asian male had reported to the Department of Oral and Maxillofacial Surgery with the chief complaint of a soft mass in his left lower facial region present since 2 years. The onset of the swelling was gradual without any obvious cause. It was initially small in size but later increased. Located over the left cheek region (Fig. 1) measuring about 5×5 sq cms approximately, it had a smooth surface with indistinct edges and had remained asymptomatic all the way through. Clinically it was non-tender with a uniformly soft consistency and no fixity. The patient became aware of the swelling when it did not subside even after the extraction of a carious tooth in the vicinity. The swelling frequently increased and decreased in size. Increase in size was more related to exposure to cold (Due to frequent night duties necessitated by the patient's job). Swellings of similar kind could not be found elsewhere. There was no functional impairment of any kind. The patient's history revealed that he was allergic to cold and sea food and had an episode of typhoid and associated eosinophilia. A differential count of blood showed eosinophil count with a high value (16 %). He had frequent sinusitis problem. Cervical lymph nodes were not palpable and other routine physical examinations did not reveal any abnormalities. Fine Needle Aspiration Cytology (FNAC) was performed and diagnosis given was lympho-epithelial lesion. The swelling was excised surgically through an intra-oral approach. There was significant bleeding encountered during the excision and curettage procedure which was controlled with diathermy and

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Fig. 1 Marked swelling over the left facial region

pressure pack. The excised specimen was sent for histopathological examination. Post-surgery he was put on a short-term steroid therapy [Oral Prednisolone (Wysolone) 1 mg/kg/day]. The histopathological report gave the diagnosis as Kimura's disease. Subsequently, quantitative estimation of IgE was performed and the value was found to be 3222.20 IU/mL, way above the normal parameters (reference range: 0.00–158.00). This finding of elevated IgE along with chronic eosinophilia was significant in confirming the diagnosis as Kimura's disease. The patient was called for a regular follow-up for a period of 1 year. 3 months after the intervention, the IgE level dropped down to 280 IU and the Eosinophil count had decreased to 6 %. There has been no recurrence of the disease to date.

Discussion

Kimura's disease is a benign, rare, chronic inflammatory disorder of unknown etiology affecting mainly the middle-aged Asian people. However, sporadic cases have been also found in the non-Asian population. It was first described in 1937 by Kim and Szeto (China) as "Eosinophilic Hyperplastic Lymphogranuloma" [6]. Kimura et al. in 1948 reported it in literature titled "On the unusual granulation combined with hyperplastic changes of lymphatic tissue" after which this entity became widely known as Kimura's disease [7].

Kimura's disease usually involves the deep subcutaneous tissue and lymph nodes of the head and neck region. The clinical presentation is characterized by triad of painless unilateral cervical lymphadenopathy, eosinophilia

and markedly elevated serum IgE levels. It presents with painless subcutaneous masses in the head and neck region. It usually involves preauricular, axillary and inguinal lymph nodes, parotid and submandibular glands with unusual sites being auricle, scalp, orbit, nerves and spermatic cord. It is a benign condition with self-limiting course. Renal involvement in the disease characterized by proteinuria (12–16 %) may be seen [2].

The most common histologic features of Kimura disease include preserved nodal architecture, follicular hyperplasia (Fig. 2) with reactive germinal centers; well-formed mantle zones; eosinophilic infiltrates involving the interfollicular areas, sinusoidal areas, perinodal soft tissue and subcutaneous tissue; and proliferation of postcapillary venules [3]. Other findings include proteinaceous deposits in germinal centers, vascularization of germinal centers, necrosis of germinal centers, polykaryocytes (Warthin-Finkeldey type

Fig. 2 Histo-pathological picture showing follicular hyperplasia

Fig. 3 Histo-pathological picture showing eosinophilic micro-abscesses

Fig. 4 Histo-pathological picture showing folliculolysis (residual follicle) [Black arrow] by eosinophils [White arrow]

giant cells), eosinophils in germinal centers, eosinophilic folliculolysis (Fig. 4), eosinophilic micro-abscesses (Fig. 3), postcapillary venule proliferation, stromal sclerosis, perivenular sclerosis, rare giant cells (Warthin-Finkeldey type giant cells), or small eosinophilic granulomas. Sclerosis of variable degrees is often observed. Immunohistochemical staining with IgE shows a characteristic reticular staining pattern of germinal centers [3].

Imaging findings of the masses found in Kimura's disease have densities that vary from iso- to hyperdense. With contrast enhanced CT, the patterns vary from mild to intense and from homogenous to heterogeneous. Though we couldn't do an MRI of the lesion, such lesions on MRI show both low and mixed or high signal intensity on T1-weighted images and low or high signal intensity on T2 weighted images.

The etiology and the pathogenesis of Kimura disease are still unknown but various suggestions have been put forward by many investigators. The disease is classified as a benign reactive process. Allergic reactions, infections, and autoimmune reactions with an aberrant immune reaction have been suggested in its etiopathogenesis [8]. A viral or parasitic trigger that may alter T-cell immunoregulation or induce an type-I hypersensitivity may result in release of eosinophilic cytokines [1, 4, 9]. The findings of increased eosinophils, mast cells, and levels of interleukin-5 and IgE suggest an abnormal T-cell stimulation to a hypersensitivity type reaction [9]. Immunohistochemical studies performed on skin, lymph nodes, and peripheral blood in Kimura's disease have shown marked proliferation of human leukocyte antigen-DR CD4 cells. Activated CD4 cells of the Th2 phenotype can release cytokines such as granulocyte macrophage colony-stimulating factor and tumor necrosis factor, interleukin IL-4 and IL-5, which in turn may precipitate the high serum IgE and marked

eosinophilia. Molecular diagnostic studies for immunoglobulin heavy chain and T-cell receptor gene rearrangement in two studies have supported a reactive nature. A case reported by Chim et al. describes a clonal T-cell receptor gamma gene rearrangement by polymerase chain reaction in an elderly man with Kimura disease. The clonal T-cell rearrangement was also confirmed by complete sequencing of the VDJ rearrangement. Specimens from previous biopsies also showed the same rearrangement by polymerase chain reaction.

Differentiating Kimura's disease from Angiolymphoid Hyperplasia with Eosinophilia (ALHE) requires a strict analysis of clinical and histologic features because the diseases are similar and were once thought to be the same disorder. Both diseases usually present with soft tissue masses in the head and neck region but in Angiolymphoid Hyperplasia with Eosinophilia, the lesions are mostly dermal or subcutaneous and not often in lymph nodes, which is a common location for Kimura's lesions. Angiolymphoid hyperplasia with eosinophilia is more typically seen in middle-aged women and Kimura's disease in younger men. In both cases, histologic examination of the lesion shows lymphocyte infiltration, numerous eosinophils, germinal center formation, and proliferative blood vessels. But most important, the vascular endothelial cells in Angiolymphoid Hyperplasia have nuclei of varied size and shape and hemosiderin deposits. Also, the endothelial lining usually is more than one cell thick. These changes are not seen in Kimura's disease. These histological changes suggest that Angiolymphoid Hyperplasia with Eosinophilia is neoplastic in origin, whereas Kimura's disease is an immune-mediated disorder [5]. In addition Meningaud et al. have described comparative features. In Kimura's disease the localization of masses is deep and subcutaneous but in ALHE it's superficial and dermal. Clinical presentation in Kimura's disease is that of nodule and in ALHE its papule. Lymphadenopathy, salivary gland involvement and hyper-eosinophilia are frequent in Kimura's disease and rare in ALHE. Serum IgE is elevated in former but normal in latter. The predominant cellular component is lymphoid infiltrate in Kimura's while it's vascular hyperplasia in ALHE.

The primary treatment for Kimura disease is surgical resection. Additional medical therapy including regional or systemic steroid therapy, cytotoxic therapy and radiation have also been utilized. Also oral retinoids, pentoxifylline, cyclosporine, azathioprine and imatinib have been used for the treatment. Imatinib may act by selectively blocking protein-tyrosine kinases [10]. Steroids when administered systemically arrests progression of the disease considerably. Cyclosporine, due to its effects on Th2 lymphocytes has been used as a therapy for Kimura's disease [11]. M A Fouda et al. [12] have tried single-pulse intra-venous

cyclophosphamide and subsequently maintained on mycophenolate mofetil (MMF) and high dose systemic steroid with a satisfactory response. Considered as an inflammatory process, the disease has an excellent prognosis, although it may recur locally and wax and wane over time. No malignancy has been reported.

Conclusion

The Diagnosis of Kimura's diseases was based on raised IgE and histopathological reports though not initially thought of while planning surgery. The treatment mainly aims to preserve function and cosmetics while keeping in view the recurrence and the sequel. This case is reported to make the surgeons aware of such rare occurrence which may be borne in mind for a complete cure. Incidence of such cases is not much documented in the literature.

Conflict of interest None declared.

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