

Kimura's Disease in Malay Patients

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SUMMARY

Kimura's Disease (KD) is an uncommon, chronic inflammatory disorder of unknown etiology which is endemic in Orientals. It is characterized by painless, large solitary or multiple nodules in subcutis of head and neck region or the major salivary glands, associated with regional lymphadenopathy, blood eosinophilia and elevated IgE levels. Its treatment ranging from conservative observation in asymptomatic patient to surgical resection of the mass, corticotherapy and irradiation therapy for the symptomatic ones.

KEY WORDS:

Kimura's Disease, Orientals, Head and Neck, Nodules, Lymphadenopathy

INTRODUCTION

Kimura's disease (KD) was first described in China by Szeto in 1937 and later reported by Kimura in Japan in 1948¹. The etiology of KD is still unknown and once thought to be a disease that affected only Orientals, but it also occurs sporadically in Caucasians. The affected age varies from 10 to 76 years, but most cases occur in the second and third decades of life. Males (about 80 – 87 percent) are affected more than female¹. Clinically, it consists of painless large solitary or multiple nodules in the subcutis of the head and neck mainly in the preauricular and submandibular region. It is also accompanied by satellite adenopathies and/or increase volume of the salivary glands (mainly the parotid and submandibular glands) and this frequently being misdiagnosed as salivary gland tumor².

CASE 1

A 27-year old Malay gentleman from Seremban presented in the year 1998 with a bilateral postauricular swellings for fifteen years which gradually increased in size, painless and non-discharging. The swellings remained unchanged in size for the past two years with no constitutional symptoms such as fever, fatigue or weight loss. Physical examination revealed bilateral postauricular swellings measuring eight by eight cm of the right and six by six cm of the left swelling which were soft, non-tender, mobile, non-pulsatile but with vague borders. Multiple palpable cervical lymphadenopathy of varying sizes were felt. Ear, nose, oropharynx, nasopharynx, larynx and other systemic examinations were unremarkable. There was no cranial nerve involvement.

The differential blood count revealed blood eosinophilia of 26% with raised erythrocyte sedimentation rate (ESR) of 30

mm/1 hour (normal: 0 – 15 mm/1 hour). The chest radiography was normal. A computed tomography (CT) scan of the neck revealed an enhancing mass on both sides of the neck which varies in density of subcutaneous fat plane. The fossa of Rossenmullers and both parapharyngeal spaces appeared normal.

The histopathological examination showed an extensive lymphoid infiltrate with formation of numerous lymphoid follicles and prominent germinal centers with large amount of eosinophils, plasma cells and mast cells with eosinophilic microabscesses (Fig.1). The adjacent lymph nodes showed markedly hyperplastic follicles with reactive germinal centers and diffusely infiltrated by eosinophils (Fig.2). No evidence of malignancy seen. The features were consistent with Kimura's disease.

CASE 2

A 53 year old Malay man presented with a gradually increasing left sided neck mass for many years which was painless and non-discharging. He was from Seremban and presented to the Otorhinolaryngology (ORL) specialist clinic in the year 2002. Besides the left neck mass other examinations were unremarkable. There was relative eosinophilia of 12% with normal chest radiography. The ESR was 10mm/1 hour. CT scan revealed an enhancing mass with uncleared subcutaneous fat plane between the mass and the left sternocleidomastoid muscle. Both fossa of Rossenmuller were normal. The histopathological examination of the excised mass showed features which were suggestive of Kimura's disease.

CASE 3

A 29 year old Malay man was referred from a health clinic for two isolated painless masses in the right pre- and post-auricular areas for three years and two years respectively. He was from Seremban and presented to the Otorhinolaryngology (ORL) specialist clinic in the year 2003. On physical examination, both masses were firm, mobile and non-tender with normal overlying skin. No other lymphadenopathy was noted. Ear, nose, throat, nasopharynx, oropharynx, larynx and scalp examinations were normal. Other systemic examinations were unremarkable. His blood count showed leucocytosis with mild eosinophilia of 7%. The ESR was within normal range. CT scan revealed an enhancing lesion of the right parotid gland that extended down to the right external auditory meatus. Multiple small cervical lymphadenopathy were noted. The histopathological examination of the excised mass showed features which were suggestive of Kimura's disease.

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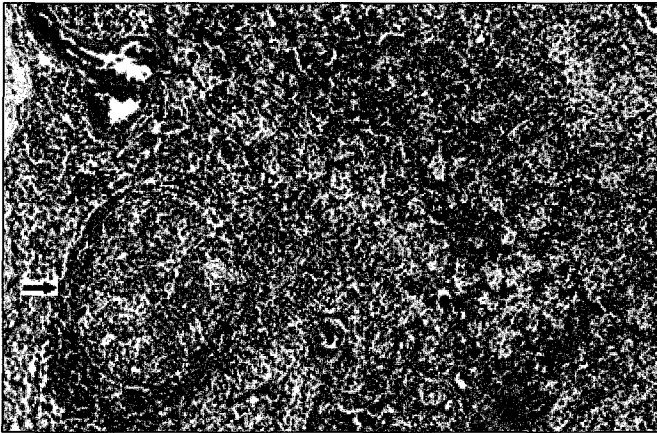


Fig. 1: Low power view of the lymph node showing germinal centre formation (arrow) with adjacent prominent capillaries.

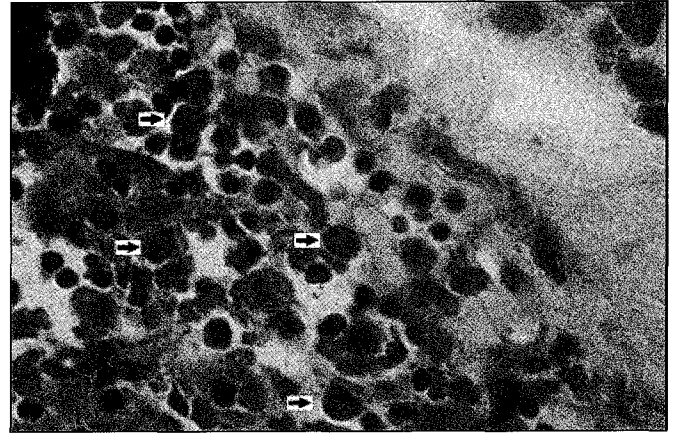


Fig. 2: A higher power view of the area adjacent to the germinal centre showing many eosinophils (arrows). None of the blood vessels show prominent endothelial lining.

In all the three cases, surgical excision was done and the patients were started on oral steroid therapy which was tapered down accordingly to the minimal dose to prevent recurrence. Follow-up period ranged from eight months to one and a half years. In the third case, the patient defaulted treatment and follow-up. He turned up eight months after treatment with relapse and was managed again with oral steroid therapy. Otherwise all the three patients didn't show any recurrence on follow-up.

DISCUSSION

The optimal treatment of KD is not well defined in the literature. At initial presentation, surgical biopsy is the most frequent diagnostic procedure, and excision may be curative. However, recurrence is common³. Complete surgical removal of a head and neck lesion may be difficult given the subsequent facial reconstruction needed and the danger of neurologic deficit such as facial nerve injury in parotidectomy⁴. Complete excision is not always possible due to the extremely diffuse nature of the disease². There have also been reports of recurrence in 15 to 40% of cases even after apparently adequate surgical excision and excisional biopsies, but this may be because of the poor delineation of the borders of KD, suggesting that adjunctive frozen sections may be useful, especially in re-excision recurrence³. Other therapeutic options including radiation, systemic corticosteroids, cyclosporine A and pentoxifylline, have all been tried with variable responses³.

The etiology and the pathogenesis of Kimura disease are unknown. The disease is classified as a benign reactive process. Allergic reactions, infections, and autoimmune reactions with an aberrant immune reaction have been suggested⁴. 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. Molecular diagnostic studies for immunoglobulin heavy-chain and T-cell receptor gene rearrangement in two studies support a reactive nature. Due to the above postulated pathogenesis, additional medical therapy including regional or systemic steroid therapy, cytotoxic therapy and radiation has been utilized. Oral steroid have been

the mainstay of therapy for subcutaneous plaque or nodule of KD even though steroid withdrawal can result in lesion recurrence⁵. Steroid therapy is useful to shrink the KD tumor in preparation before surgery. It is also indicated in frequent relapses or cases complicated by nephrotic syndrome. Patients are started on high dose of oral steroid and the dose is tapered to the minimal dose that will suppress the recurrence. Steroid withdrawal can result in lesion recurrence. Long term steroid treatment can have many side effects that limit its use.

Considering the benign nature of KD, radiation should be reserved as a second line treatment. Hareyama *et al*⁵ noted a marked response in tumour size at the completion of radiotherapy in 20 patients that had residual or recurrent KD. Irradiation was given through a single field with dosages ranging from 20 to 30 Gy regardless of tumour size and achieved local control in 74% of lesions.

In conclusion, Kimura's disease is a rare indolent benign disorder with a clinical presentation that mimics a number of other benign inflammatory and neoplastic conditions of the head and neck, and therefore poses a diagnostic challenge to clinicians. As the diagnosis is based on histopathology, surgical excision is the first line treatment. Nevertheless, this may be difficult at times since parotid gland is involved and the facial nerve may be at risk, and for this oral corticosteroid would be the treatment of choice.

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