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CASE REPORT

KIMURA DISEASE: A RARE ENTITY.

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Abstract

Kimura disease (KD) is a chronic inflammatory condition with a benign course, commonly affecting the head and neck region. The underlying aetiology is still uncertain. The prevalence of this condition is unknown. It has been reported sporadically especially in Asian region predominantly in young males. We report a 48-year-old Malay man who presented with progressive swelling over the right cheek which responded well to corticosteroid and leflunomide.
Key words: Kimura disease, corticosteroids, leflunomide.

Introduction

Kimura disease (KD) is a benign, chronic inflammatory condition of unknown aetiology affecting young Asian men [1, 2], first reported in China in 1937.[3] It commonly presents with painless solitary swelling which may cause disfigurement in the head and neck regions. Autoimmune dysregulation has been postulated in its pathogenesis and the presence of peripheral eosinophilia and inflammatory infiltrate may well suggest hypersensitivity reaction being part of the process. [4, 5, 6, 7] Surgical removal, cytotoxic drugs and radiation therapy are among the recommended treatment for KD with an excellent prognosis, although relapses can occur post-surgically. We present a case of chronic KD who did not respond to corticosteroid alone but eventually regressed with the addition of leflunomide (arava).

Case report

A 48-years old Malay gentleman presented to the Rheumatology clinic, Hospital Taiping with a progressive painless swelling on his right cheek for the past six years. The swelling became itchy if he was sweating or ate seafood especially squids. He did not experience any constitutional symptoms and none of his family members had similar problem. He was a non-smoker and worked in an electronics factory where he had daily exposure to soldering.

On clinical examination, there was a pedunculated swelling at his right cheek, measuring 8cm x 4cm x 4cm (Figure 1). There was no overlying skin changes or discoloration, ulcer or discharge. The swelling was smooth, non-tender, firm, warm, non-fluctuate, non-pulsatile, fixed to the skin, with limited mobility. Cervical lymph nodes were not palpable. Other systemic examinations were unremarkable.

Laboratory assessment showed mild leucocytosis of 14.8µ/L. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were raised, 15.8 mg/L (0-5 mg/L) and 30 mm/hr (2 to 6 mm/hr) respectively. Screening of Hepatitis B, Hepatitis C and Human immunodeficiency virus (HIV) were negative. The diagnosis of Kimura disease was based on the histopathological finding from a biopsy done in 2016 which showed diffuse eosinophilic infiltration partially to completely diminish the lymph node parenchymal architecture with areas of depletion of germinal centres. Prominent capillary hyperplasia with prominent endothelial cells and areas of folliculosis with marked apoptosis were seen

He was started with oral leflunomide 20mg every alternate day in combination with his previous medication, oral prednisolone 30mg daily. He responded well after 1 month treatment with regression of the swelling (Figure 2).

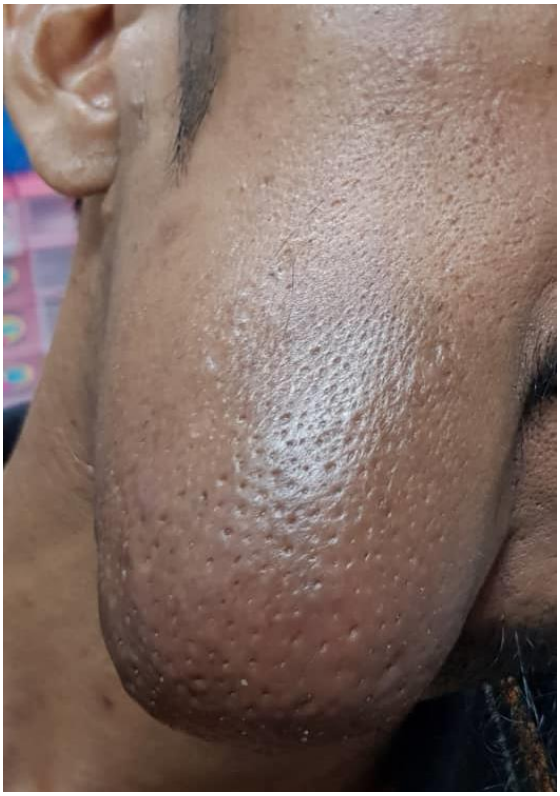

Figure 1. Pedunculated mass over the right parotid area a month prior to treatment.

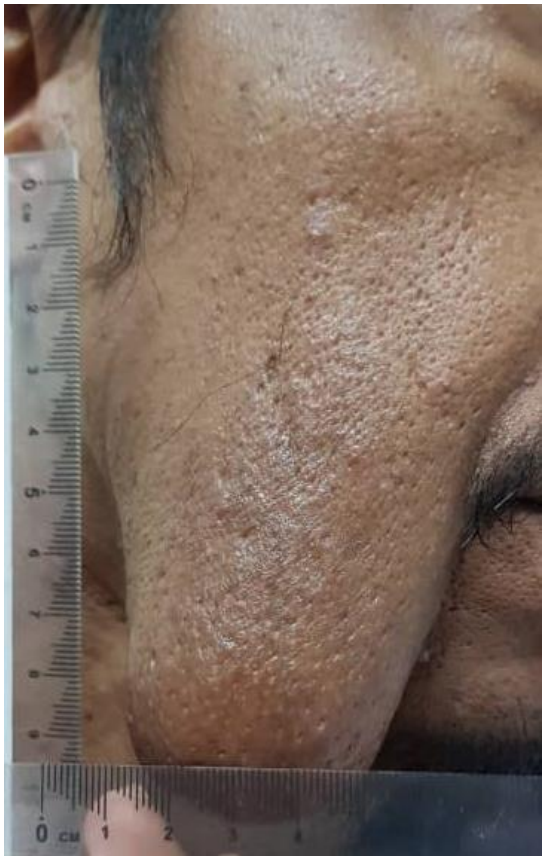

Figure 2. One month after treatment.

Discussion

First reported case of KD was in China in 1937.[3] Subsequently was named by Kimura et al in 1948 as KD following histological findings of an 'unusual granulation combined with hyperplastic changes in lymphoid tissue' surrounding the blood vessel. [8] KD commonly reported among Asian men in their second or third decades of life [1] and rarely affects children.[9] However, there are cases reported outside of Asia. Savla et. al. reported a case of KD in a young man of Arabic descent who presented with left anterior parotid gland swelling and diagnosed as KD histopathologically. [10]

The pathophysiology of KD is still unknown. It is suspected that allergic reaction and altered autoimmune dysregulation causing immunoglobulin E (IgE) mediated hypersensitivity.[5] Other triggering factors that promote the release of eosinophils and alter T-cell immunoregulation are viral, parasitic or candida infections. Various studies demonstrated the release of eosinophilic cytokines, including interleukin (IL-4 and IL-5, granulocyte macrophage-stimulating factor (GM-CSF), tumour necrosis factor-a (TNF-a), soluble IL-2 receptor, IL-5, IL-4 and IL-13. [4, 5, 6, 7]

KD predominantly occurs in the head and neck lymph nodes; however, it rarely involves axillary, inguinal lymph nodes, parotid and submandibular nodes.[11,12,13] The swelling may be indistinguishable from other conditions such as eosinophilic granuloma, Mikulicz's disease, acute lymphocytic leukaemia, Hodgkin's disease and angioimmunoblastic lymphadenopathy and angiolymphoid hyperplasia with eosinophilia. However, it has characteristic histological features. Kimura disease demonstrates IgE stain of the germinal centers [14] and is used to differentiate it from angiolymphoid hyperplasia. This test however was not done in our patient. KD's swelling usually remains unchanged or slow growing for many years without any systemic symptoms. In contrast, idiopathic hyper-eosinophilic syndrome is often accompanied by thromboembolism, persistent dry cough, pulmonary infiltrates and skin rash.[15] Renal involvement, especially nephrotic syndrome can be seen in patients with KD and is usually minimal change disease (MCD). [16, 17]

Diagnosis of KD is rather difficult and confusing. Imaging plays little role in the diagnosis as the findings on CT scan and MRI may vary. A series of case reports note the findings of multiple ill-defined enhancing lesion around the parotid gland, with associated lymphadenopathy.[18] Fine needle aspiration cytology is often used as initial test; however, it is not diagnostic. It normally shows high number of eosinophils in a background of lymphoid cells.[19] Histopathology is more definitive by showing features of

numerous lymphoid follicles, mixed inflammatory infiltrate composed of post-capillary venules and variable fibrosis. [20]

The treatment of KD depends on many factors. Observational treatment is recommended for asymptomatic cases. Surgical excision is associated with high recurrence rate despite of good prognosis.[21] The combination of surgical excision followed by post-operative low dose radiation therapy, however, results in good prognosis with low recurrences.[22] The patient discussed here had his swelling excised once and it recurred a few years after at a different site. Despite effective treatment with corticosteroids by reduction of the size of the swelling, the disease tends to recur following cessation of therapy.[5] Intralesional therapy is also used, preferable in localized disease. There are evidences of immune modulator such as cyclosporine may induce complete and partial remission. [23, 24] Our patient shows gradual improvement with leflunomide without untoward effect of the medication.

Various treatments have been used including intravenous immunoglobulin (IVIg), tyrosine kinase inhibitor imatinib, oral pentoxifylline, and trans-retinoic acid with unpromising results. IVIg has been shown to induce remission for up to 6 years follow-up of KD. [24]

Conclusion

In conclusion, KD has wide spectrum of clinical manifestations with unknown underlying pathophysiology. There is still no curative treatment, albeit combination of surgery, low dose radiation and medications including steroid prolong the remission period.

Conflict of Interest

The authors declared no conflict of interest.

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