Case Report

Potential for misdiagnosis in a rare entity: A case report of kimura's disease

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Abstract

Kimura disease (KD) is a rare form of chronic inflammatory disorder involving subcutaneous tissue, predominantly in the head and neck region and frequently associated with regional lymphadenopathy and/or salivary gland involvement. Cytologically, the varied spectrum of findings in KD range from nonspecific lymphadenitis to features simulating many other lesions. Imaging is often not diagnostic as they give nonspecific variable appearance, though CT and MRI are helpful in delineating the extent of disease. Differentials to be excluded on histopathological examination are angiolymphoid hyperplasia with eosinophilia, Hodgkin's lymphoma, angioimmunoblastic T-cell lymphoma, Langerhan's cell histiocytosis and parasitic lymphadenitis. Due to variable involvement of multiple lymph nodes, salivary glands and subcutaneous tissue, a multimodal line of investigation is usually required. However, there are several pitfalls and final diagnosis requires an excision biopsy and histopathological examination. We present a case of a 42 year old male patient with involvement of subcutaneous tissue, lymph nodes as well as salivary gland. Imaging and cytologic examination were suggestive of vascular lesion and reactive lymphadenitis respectively. Final diagnosis was reached only after histopathologic examination.

Key Words: Eosinophils, lymphadenitis, histopathology, cytopathology.

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CASE REPORT

A 42 year old male patient presented with multiple subcutaneous nodules in the head and neck region which gradually increased in size over past 6 months. There was no pain in the swellings. Patient did not have any fever, pruritus or any systemic symptoms. On examination, the largest nodule measuring approximately 4 cm in diameter was present over the right upper eyelid which caused difficulty in opening the eye. The other nodules were present in bilateral preauricular, right submandibular and left postauricular region, measured from 3.5 to 2 cm in diameter approximately and were asymptomatic. They were well-defined and soft in consistency and non-tender. There was no axillary or inguinal lymphadenopathy. Both general and systemic examinations were unremarkable. A clinical diagnosis of neurofibroma was kept and the patient was advised Fine needle aspiration cytology (FNAC) and CECT- Head. A routine hemogram of the patient showed eosinophilia with an Absolute Eosinophil Count of 2100/cumm. CECT- head was suggestive of a vascular lesion, possibly an Arteriovenous malformation. An MRI head was done at this stage for a definitive diagnosis. MRI showed these lesions to be in subcutaneous plane. No Intracranial or intraorbital lesions were seen. (Fig 1) However, no conclusive diagnosis was reached. On FNAC, multiple aspirations from all the swellings revealed only lymphoid tissue with few lymphohistiocytic clusters suggestive of a chronic

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inflammatory process. Only occasional eosinophils were seen in the smears. (Fig 2) Excision of the right eyelid mass was performed. Grossly, the excised mass was grey white, firm, measuring 3*2*1 cm, with an attached elliptical part of skin measuring 0.8*0.5 cm. Histopathological examination of the mass showed unremarkable epidermis and dermis. Subcutaneous tissue showed several lobulated masses composed of multiplelymphoid follicles with prominent germinal center. A thin capsule of compressed fibrocollagenous tissue was seen surrounding the lesion. Extensive infiltration of eosinophils was noted in the interfollicular region as well as within the follicles. Multiple capillary channels and deposits of pink proteinateous material in were noted in the germinal centres in addition to germinal centre hyperplasia. Several eosinophilic abscesses were also seen in the interfollicular areas and periphery of the lymphoid follicles. (Fig 3) Based on these features and clinical presentation, a diagnosis of KD was made. Serum IgE levels were done and found to be 950UI/ml (normal range=150-300UI/ml), which supported the diagnosis. Since the other swellings were asymptomatic and due to patients unwillingness to undergo surgery, a course of steroid was prescribed and the patient was kept under follow up.

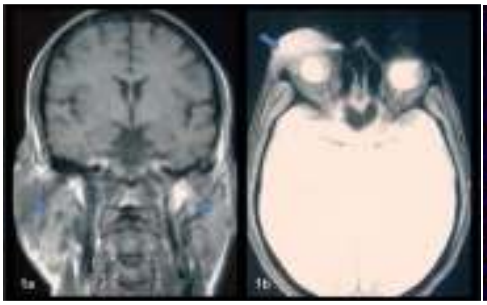

Figure 1:

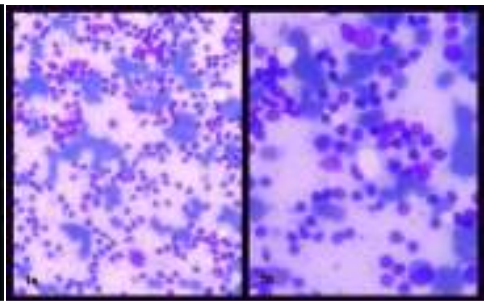

Figure 2:

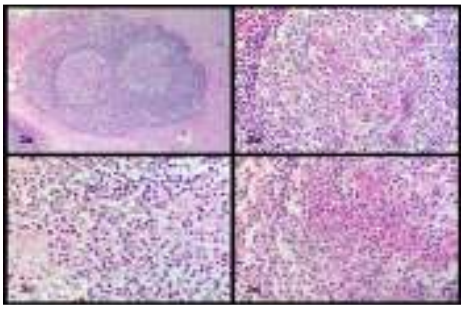

Figure 3:

Figure 1: MRI head. Fig 1a. Bilateral preauricular soft tissue swelling. (arrowheads) Fig. 1b. Eyelid swelling (arrow). All swellings are in subcutaneous plane.

Figure 2: FNAC of eyelid mass (MGG). Smears show reactive population of lymphoid cells with few histiocytes. No eosinophil is seen. Fig 2a. 100x Fig 2b. (400X)

Figure 3: Excision biopsy of the eyelid mass(H and E).Fig 3a. Reactive lymphoid follicles with prominent germinal centre. (100X) Fig 3b. Hyperplastic germinal centre with infiltration of eosinophils. (400X) Fig 3c. Admixture of lymphoid cells and eosinophils (400X) Fig 3d. Proteinaceous deposits in germinal centre. (400x)

DISCUSSION

KD is a rare form of chronic inflammatory disorder involving subcutaneous tissue, regionally mphadenopathy and/or salivary gland, commonly in the head and neck region. This condition has a predilection formales of Asian descent.[1,2] It was first described by Kimm and Szeto in 1937 as 'eosinophilic hyperplastic lymphogranuloma'.[3] However, it gained prominence as Kimura's disease following a report by Kimura *et al* in 1948, which described an 'unusual granulation combined with hyperplastic changes in lymphoid tissue'.[4] Diagnosis is usually based on multimodal investigations. Imaging is often not diagnostic as they give nonspecific variable appearance, though CT and MRI are helpful in delineating the extent of disease.[5,6] Cytologically, the varied spectrum of findings in KD range from nonspecific lymphadenitis to features simulating many other lesions. Characteristic FNAC findings in KD are polymorphous population of lymphocytes and significant number of eosinophils. Warthin Finkeldey type of giant cells, epithelioid granulomas, and necrosis may also be seen.[7-11] However, not all cases show these features. Presence of

numerous eosinophils in the background of reactive lymphoid cells is the most important pointer to the diagnosis cytologically. In our case only few scattered eosinophils were seen and therefore the possibility of KD was not considered after FNAC. This could be due to selective sampling of germinal centres where eosinophilic infiltration was less. In the study of eight cases of KD by Chow *et al*, two were misdiagnosed as reactive lymphoid hyperplasia on FNAC.[12]In cases with presence of eosinophils and granulomas, a thorough search for parasites is also warranted. Histopathologically, the lesions exhibit characteristic eosinophilic lymphoid granulomas, occasionally forming eosinophilic abscesses with vascular proliferation and variable degrees of fibrosis. Hui *et al*., in 1989 classified the histological features of Kimura's disease as constant, frequent and rare.[13] The constant features include preserved nodal architecture, florid germinal center hyperplasia, eosinophilic infiltration and postcapillary venule proliferation. Frequent features comprise sclerosis, polykaryocytes, vascularization of the germinal centers, proteinaceous deposits in the germinal centers, necrosis of the germinal centers and eosinophilic abscesses. The solitary rare feature is the progressive transformation of the germinal centers. The present case showed all the constant features. In addition, vascularization of the germinal centers, proteinaceous deposits in the germinal centers and eosinophilic abscesses were noted. Granuloma formation was not seen.[13] The closest differential diagnosis of Kimura's disease is angiolymphoid hyperplasia with eosinophilia (ALHE). They were considered to be the part of the same disease process due to similarities in clinical presentation and histologic findings, namely a predilection for the head and neck region, clinical presentation as a subcutaneous mass, tendency to recur despite treatment and the presence of lymphoid infiltration with eosinophils and vascular proliferation. However, in 1979 Rosai *et al*. clarified this misconception, and Kimura's disease and ALHE were established as two distinct entities.[14]In contrast to Kimura's disease, in ALHE lymphoid infiltration is mild to moderate, the presence of lymphoid follicles is inconsistent and folliculolysis is not seen. The degree of eosinophilic infiltration is variable and eosinophilic abscesses are usually absent. There is a florid proliferation of blood vessels with a characteristic endothelial lining of plump, low cuboidal "epithelioid" or "histiocytoid" cells which have abundant, acidophilic cytoplasm with vacuolization, vesicular nuclei and display a "cobblestone" like arrangement. Vascular proliferation can be seen in the blood vessels in Kimura's disease, but they are thin walled with flattened endothelial cells. The classic "epithelioid" or "histiocytoid" cells of ALHE are not seen. Fibrosis, a frequent feature in Kimura's disease, is absent in ALHE.[2]Other differentials to be excluded on histopathological examination are Hodgkin's lymphoma, angioimmunoblastic T-cell lymphoma, Langerhan's cell histiocytosis and parasitic lymphadenitis, especially with involvement of multiple lymph nodes.[2, 14]In the present case there was no significant vascular proliferation and the vessels seen had flattened lining, thus excluding ALHE. Features of other differentials were also nut seen. Supportive investigations include blood eosinophilia and raised serum immunoglobulin E (IgE) which was seen in the present case as well. The exact pathogenesis of Kimura's disease remains uncertain. Several etiological factors have been proposed, including autoimmune, allergic, neoplastic and infective causes, although no infective agent has been isolated so far in lesions of Kimura's disease. It has been classified as a reactive immune disorder based on the presence of peripheral eosinophils, increased mast cells and increased levels of interleukin (IL)5 and IgE, which imply an abnormal T cell stimulation akin to a hypersensitivity type reaction.[1,6] In asymptomatic cases, conservative observation is often adequate as lesions occasionally undergospontaneous resolution. Surgical excision is considered the first line of treatment in symptomatic cases, but it should be kept in mind that Kimura's disease has a tendency to recur. Topical and systemic corticosteroids have also been effective and in patients resistant to steroids, radiation therapy has been used.[2] In the present case, lesions were present only in the subcutaneous tissue with sparing of salivary glands and lymph nodes. In spite of multimodal line of investigation, diagnosis was established only on histopathological examination highlighting the importance of histopathology in diagnosis of Kimura Disease. Thus, in conclusion, a high index of suspicion is required for diagnosis due to rarity of Kimura disease. In addition, due to several close differential diagnoses and pitfalls in other lines of investigations, histopathology of the lesion is always required for confirmation.

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