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Unmasking Kimura Disease: A Hidden Challenge in Head and Neck Health

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Abstract

Introduction: Kimura Disease (KD), also known as eosinophilic lymphogranuloma, is an uncommon chronic inflammatory condition of unknown origin. It is primarily seen in Asian males, though rare in Indians, presenting as subcutaneous nodules especially in the head and neck with coexisting lymphadenopathy, major salivary gland hypertrophy and peripheral eosinophilia. Diagnosis is challenging as it needs to be differentiated from hypersensitivity, drug reactions, infections and through its characteristic histologic features. The disease is benign but prone to recurrence.

Case Details: We present a case of a 36-year-old Indian male with lymphadenopathy, parotid enlargement and peripheral eosinophilia. Reactive lymphoid hyperplasia with eosinophilic predominance was interpreted on fine needle aspiration cytology. However, the patient decided not to have any further intervention. He presented 2 years later with gradually progressing neck swelling and biopsy of the lesion followed by histopathological examination allowed us to make a definitive diagnosis.

Conclusion: The rarity and uncommon presentation of KD pose a diagnostic challenge. It can often be mistaken for malignancy prompting unnecessary investigations and thus, should be considered in the differential diagnosis of salivary gland swellings with non-specific lymphadenitis and eosinophilia to provide early diagnosis and timely management of patient.

Keywords: Eosinophilia, Kimura disease, Lymphadenopathy, Parotid.

Introduction

Kimura disease (KD), also known as eosinophilic lymphogranuloma, is a rare, chronic inflammatory disorder with an uncertain cause. Initially described by Kimm and Szeto in 1937 as "eosinophilic hyperplastic lymphogranuloma," the condition became widely known as Kimura disease after Kimura and his colleagues published a detailed report in 1948, highlighting

"unusual granulation combined with hyperplastic changes in lymphoid tissue". KD mainly affects the head and neck area, typically presenting as deep, subcutaneous masses. Regional lymph nodes and salivary gland involvement are common in KD. There is also peripheral blood eosinophilia and increased IgE levels. The disease is most common among Asian males [1].

While it can resemble a neoplastic condition, but early accurate diagnosis can prevent unnecessary invasive diagnostic procedures [2]. The etiology of the disease is still largely unclear, though allergic reactions and alterations in the immune system are suggested as key factors in its development. Other possible triggers maybe arthropod bites or infections like parasites, Candida [3].

Initially thought to be related to angiolymphoid hyperplasia with eosinophilia (ALHE), KD is now recognized as a distinct condition [4]. Diagnosis is challenging as it needs to be differentiated from hypersensitivity, drug reactions, infections and tumours through its characteristic histologic features. Malignant transformation has not been reported. Treatment remains debated; however, options often include systemic corticosteroids, cyclophosphamide, surgical excision, and local radiation [4].

Our case is peculiar as it involved three predisposing sites: subcutaneous tissue, major salivary gland and lymph nodes.

Patient Presentation: We present a case of 36-year-old Indian male with lymphadenopathy, parotid enlargement and peripheral eosinophilia. Reactive lymphoid hyperplasia with eosinophilic predominance was interpreted on fine needle aspiration cytology. However, the patient decided not to have any further intervention. He presented 2 years later with gradually progressing neck swelling and biopsy of the lesion followed by histopathological examination allowed us to make a definitive diagnosis.

Gross Findings: Right Superficial parotidectomy specimen with separately sent right level IIA, IIB, III, IV lymph nodes were received along with excised skin margin. External surface of parotid was unremarkable. Cut surface showed an ill- defined grey-brown lesion measuring 8 x 4.2 x 1 cm.

Microscopy: Grid sections studied from the lesion in parotid showed involvement of intraparotid lymph node having preserved nodal architecture with proliferation of enlarged but well-spaced secondary lymphoid follicles that maintained the normal zoning pattern of follicle centre cells. The interfollicular areas were expanded by numerous eosinophils and accompanied by small lymphocytes and immunoblasts. The paracortex also showed vascular proliferation. At places, there was formation of eosinophilic microabscesses and some of the follicle centres were also infiltrated by eosinophils. Occasional germinal centres showed polykaryocytes. Areas of extensive fibrosis were also observed. The adjacent salivary gland parenchyma was compressed and pushed towards periphery by involved intraparotid node.

The overlying skin showed mild eosinophilic infiltrate in dermis. The deep lesional stroma had increased eosinophils forming microabscesses admixed with lymphocytes & congested blood vessels. All the lymph nodes sent exhibited an inflammatory milieu comprising markedly increased eosinophils admixed with lymphocytes. The excised skin margin showed foreign body giant cell reaction with surrounding eosinophil deposits in dermis and mild perivascular lymphocytic infiltration. All the above morphological features favoured KD.

Discussion: The exact cause and development of KD remains unclear. Potential contributing factors include allergic reactions, infections and autoimmune responses with abnormal immune activation. Evidence such as elevated levels of eosinophils in the blood, increased serum IgE and the accumulation of mast cells points towards an atopic component. [4,5] Despite ongoing investigations into allergic or parasitic causes, no definitive evidence has been found to support relevant theories.[6]

KD predominantly affects males and is mostly observed during the second and third decades of life. It is particularly prevalent in Asia [7]. The condition usually presents as subcutaneous masses or lymphadenopathy, predominantly in the head and neck area, and occasionally affects other regions such as the axillary, periauricular, inguinal, or epitrochlear nodes. However, it typically has a benign and self-limiting clinical course. [8]

A meagre 40 cases of KD involving the parotid gland are reported in the literature and most instances of the disease are isolated to other regions.[5] In some cases, it can involve the kidneys, with nephrotic syndrome being the most common renal complication and proteinuria may be observed in 12-16% of patients with renal involvement. [2]

Microscopically, KD is characterized by three components: cellular i.e. increased eosinophilic infiltration and follicular hyperplasia, fibrocollagenous and vascular i.e. proliferation of post-capillary venules [9]. Distinctive features that are pathognomonic include sclerosis, increased vascularization, proteinaceous deposits within germinal centers, micro-abscesses, and the presence of polykaryocytes of the Warthin-Finkeldey type. [10]

Laboratory findings supporting the diagnosis of KD include blood eosinophilia and elevated serum IgE levels. These abnormalities are consistent with the atopic features often associated with the condition.[4] Radiographic imaging techniques such as ultrasound (USG), computed tomography (CT), and magnetic resonance imaging (MRI) are valuable for assessing salivary gland involvement and identifying abnormal lymph nodes in Kimura's Disease. [3,11] Although these imaging modalities can aid in the evaluation of lesions, their radiographic features are not specific enough to make a definitive diagnosis. Only a histopathological examination of an excisional biopsy specimen from the lesion aids to establish a definite diagnosis. [2]

Differential diagnoses for a parotid gland condition resembling KD include Mikulicz disease, angiolymphoid hyperplasia with eosinophilia, Kikuchi disease, tuberculosis, acquired immunodeficiency syndrome, infectious parotitis, salivary gland tumors, and Sjögren’s syndrome. For lymphoid proliferation accompanied by eosinophilia, a differential diagnoses of Hodgkin’s lymphoma, Langerhans cell histiocytosis, and parasitic lymphadenitis might be considered.[3]

The absence of classic Reed-Sternberg cells and their variants, atypical lymphocytes, Langerhans cells, and parasitic remnants helped distinguish our case. The absence of epimyoepithelial islands and the presence of eosinophils on microscopy exclude Mikulicz disease. Additionally, the duration of symptoms and clinical features ruled out infective parotitis and mumps. The lack of distinctive histologic features excluded salivary neoplasms, while the absence of concurrent xerostomia and xerophthalmia ruled out Sjögren’s syndrome. Kikuchi disease is marked by painful cervical lymphadenopathy, fever, leukopenia, and elevated

erythrocyte sedimentation rate along with morphological features including paracortical necrotic foci, histiocytic infiltrate with karyorrhectic debris, proliferation of histiocytes and immunoblasts, and absence of granulocytes.[4]

The lesion most closely resembling Kimura's disease, to the extent that they were once considered the same entity, is angiolymphoid hyperplasia with eosinophilia [1]. Female predominance in third to fourth decades, no racial predilection, absent fibrosis, eosinophilic microabscesses and folliculolysis, and prominent florid proliferation of blood vessels with characteristic endothelial lining of plump, low cuboidal epithelioid or histiocytoid cells are the differentiating features. There is no standardized approach to managing KD and three primary therapeutic strategies are often utilized. Complete removal of the lesion is often the preferred method, but local recurrence can sometimes be managed with additional surgical interventions.[12] Local irradiation may be employed for cases that are recurrent, persistent, or resistant to surgery and medication. Systemic and intralesional corticosteroids are commonly used and can reduce lesion size; however, recurrence is likely after discontinuation. Hence, treatment plans should be specifically tailored as per individual patient needs. [2,13]

Because of rarity of KD, many clinicians and pathologists are unfamiliar with its characteristic findings, thus leading to improper diagnosis and treatment.[14] In our case, the patient presented with peripheral blood eosinophilia and swelling involving three sites: subcutaneous tissue, the parotid gland, and cervical lymph nodes.

Conclusion

KD in the parotid gland is extremely rare and should be considered when a parotid swelling is accompanied by lymph node and neck swelling, especially if laboratory tests show peripheral blood eosinophilia. This diagnosis is particularly important for middle-aged Asian males. Although diagnosing KD can be challenging, a thorough clinical history combined with histopathological examination is crucial for accurate diagnosis, as other investigations might not be definitive. A precise histopathological assessment can help avoid unnecessary invasive tests and procedures and assist in formulating an effective treatment plan while differentiating it from mimics. Correct diagnosis ensures the patient undergoes simpler procedures with favourable outcomes.

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Legend Figures

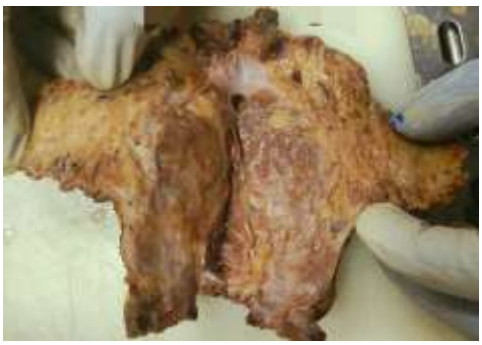

Figure 1: Cut Surface of Parotid showing lesion.

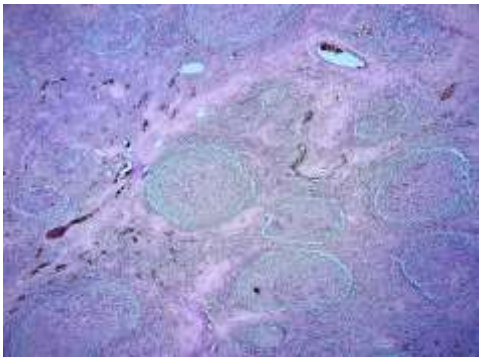

Figure 2: Lymph node with reactive follicular hyperplasia.(H&E,x100)

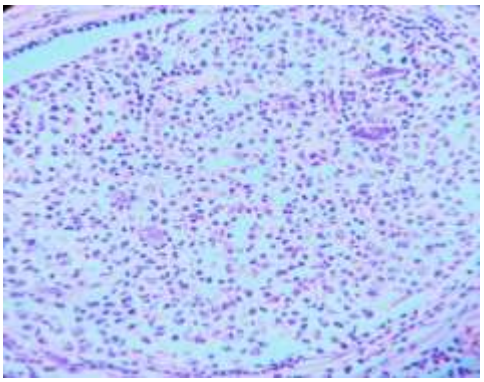

Figure 3: Germinal centers with areas of folliculolysis and eosinophilic proteinaceous material.(H&E,x400)

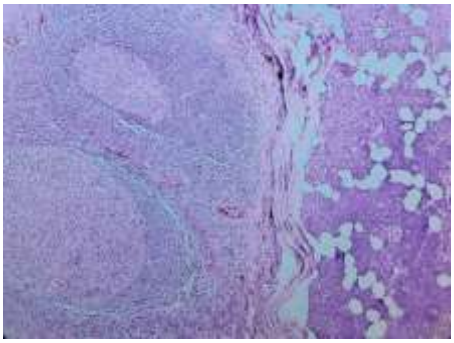

Figure 4: Lymphoid nodules with variable hyalinization including parotid gland.(H&E,x400)

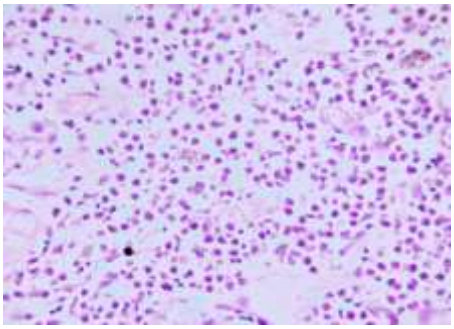

Figure 5: Intense eosinophilic infiltration with formation of eosinophilic microabscesses.(H&E,x400)

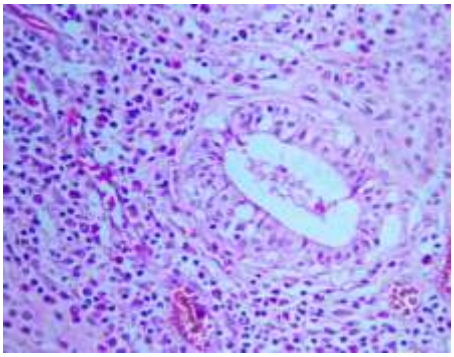

Figure 6: Salivary gland duct with eosinophils in the lumen.(H&E,x400)