

CASE REPORT

Kimura's disease - An unusual presentation involving subcutaneous tissue, parotid gland and lymph node

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ABSTRACT

Kimura's disease is a rare chronic inflammatory condition of uncertain etiology which has an affinity for the Asian population. It primarily involves the head and neck region, presenting as deep subcutaneous masses and is often accompanied by regional lymphadenopathy and salivary gland involvement. Peripheral blood eosinophilia and elevated serum immunoglobulin E (IgE) levels are characteristic features and the microscopic picture reveals lymphoid proliferation with eosinophilic infiltration. For years, Kimura's disease was believed to be identical to or part of the same disease spectrum as angiolymphoid hyperplasia with eosinophilia (ALHE). Recent reports, however, have confirmed that the two are, in fact, separate entities. We report a case of Kimura's disease in a 22-year-old Indian male who presented with a subcutaneous mass, parotid enlargement and lymphadenopathy. The clinical presentation was suggestive of Kimura's disease and microscopic examination following biopsy of the lesion allowed us to make a definitive diagnosis.

Key words: Angiolymphoid hyperplasia with eosinophilia, Kimura disease, lymphadenopathy, parotid gland

INTRODUCTION

Kimura's disease is a chronic inflammatory condition of uncertain etiology. First described by Kimm and Szeto in 1937 as 'eosinophilic hyperplastic lymphogranuloma',^[1] it gained prominence as Kimura's disease following a report by Kimura and coworkers in 1948, which elaborated on an 'unusual granulation combined with hyperplastic changes in lymphoid tissue'.^[2] Kimura's disease primarily involves the head and neck region, presenting as deep, subcutaneous masses in the preauricular region, forehead or scalp.^[3] Regional lymphadenopathy and salivary gland involvement are frequently seen, along with peripheral blood eosinophilia and strikingly elevated serum immunoglobulin E (IgE) levels.^[4] The disease is endemic in Asians, but occurs sporadically in other racial groups and shows a distinct male predilection.^[3,5]

Our case was distinctive with respect to the fact that it displayed clear involvement of all three possible areas of predilection:

The subcutaneous tissue, salivary gland (parotid in this case) and lymph nodes.

CASE REPORT

A 22-year-old male patient presented to our dental clinics with bilateral facial swelling. The swelling on the left was larger, painful and appeared consequent to trauma 7 years prior to presentation. Initially small and diffuse, it progressively increased over time to its present size. The mass on the right had been present for a year and was asymptomatic. The patient did not report any increase in the size of the swelling at mealtime, reduction in salivary flow or pus discharge. There was no history of weight loss, low grade fever or night sweating. The dental history did not include any incidence of tooth-related pain or space infection. Medical, surgical and family histories were noncontributory. There were no symptoms suggestive of facial nerve involvement.

Physical examination revealed a 4 × 5 cm firm, nontender, subcutaneous mass in the region of the left parotid gland, overlying the left masseter muscle and extending from the zygomatic arch to the lower border of the mandible. The overlying skin was normal with respect to both color and temperature and facial nerve function was unaffected. The swelling on the right side had similar clinical characteristics but was 2 × 2.5 cm in size, located 3 cm from the corner of the mouth and well ahead of the anterior border of the

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ramus [Figure 1]. Bilateral submandibular and upper cervical lymph nodes were palpable. There was no axillary or inguinal lymphadenopathy and the liver and spleen were not enlarged.

Laboratory studies revealed hemoglobin concentration of 155 g/L, white cell count $8 \times 10^9/L$ and an absolute eosinophil count of $1.5 \times 10^9/L$ (reference range: $0.0-0.4 \times 10^9/L$). The IgE serum level was not determined.

A computed tomography (CT) scan disclosed enlarged superficial and deep lobes of the left parotid gland, a well-defined lesion measuring 3.3×2.4 cm in the right buccal space and enlarged level IB, level III and level V lymph nodes [Figures 2 and 3]. Fine needle aspiration cytology (FNAC) from the left parotid swelling and lymph nodes, as well as from the right cheek gave the impression of chronic nonspecific lymphadenitis and myoepithelial sialadenitis. Based on the CT and FNAC findings, an incisional biopsy from the right cheek swelling and image guided biopsy from the left parotid lesion was advised.



Figure 1: Clinical image of the patient showing bilateral swelling in the parotid region

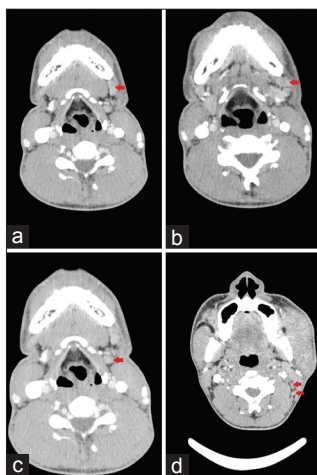


Figure 3: Radiographic image of contrast enhanced axial CT scans showing enlargement of following lymph nodes (red arrows), (a) Left level IB, (b) Left level II, (c) Left level III, (d) Left level V

Histopathological study of the specimen demonstrated lymphoid tissue with reactive follicular hyperplasia. Within the germinal centers, deposits of eosinophilic proteinaceous material and areas of folliculolysis were seen. The interfollicular infiltrate was rich in eosinophils with admixed lymphocytes and plasma cells. Numerous thin-walled vessels were present, often grouped in small foci; their endothelial lining was flattened with no epithelioid or vacuolated cells [Figure 4].

Surgical excision of the right subcutaneous mass and superficial parotidectomy for the left parotid swelling with selective neck dissection was performed. Postoperative recovery was good with no signs of facial nerve injury. However, after the patient was discharged from the hospital, he was lost to follow-up; hence presence or absence of recurrence could not be assessed.



Figure 2: Radiographic image of contrast-enhanced coronal computed tomography scan showing enlarged left parotid gland and well-defined irregular soft tissue enhancing lesion in right buccal space and subcutaneous tissue

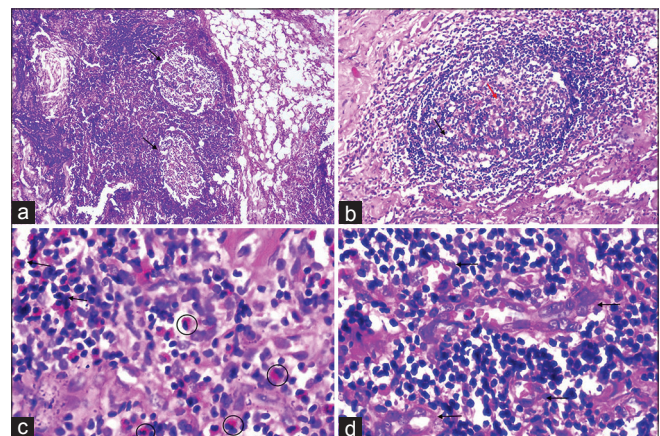


Figure 4: Histopathological image shows (a) Lymphoid tissue with reactive follicular hyperplasia (arrows; H&E stain, $\times 100$); (b) Germinal centers with deposits of eosinophilic proteinaceous material (red arrows) and areas of folliculolysis (black arrows; H&E stain, $\times 200$); (c) Intense eosinophilic infiltration (circles) with formation of eosinophilic microabscesses (arrows; H&E stain, $\times 400$); (d) Numerous thin-walled vessels with flattened endothelial lining and absence of epithelioid or vacuolated cells (arrows; H&E stain, $\times 400$)

DISCUSSION

The archetypal patient of Kimura's disease is male, with the mean age of affected individuals being 31-years- in one case series.^[5] Vast majority of cases originate from Asia.^[6] The other countries where it is common are Japan, China, Vietnam, Philippines and occasionally the Indian subcontinent.^[7] However, numerous reports have verified that the disease occasionally occurs in other ethnic groups^[5] and such cases cannot be clinically or histologically differentiated from those presenting in patients from Asia.

Microscopically, 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. 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. Immunohistochemistry reveals the presence of IgE reticular network in germinal centers and IgE coated non-degranulated mast cells.^[8]

Laboratory findings that lend credence to the diagnosis of Kimura's disease are blood eosinophilia and elevated serum IgE levels. It has been speculated that the degree of blood eosinophilia may be correlated with the size of the lesion, which might be used to measure the disease activity.^[6]

The presence of lymph node enlargement indicated reactive lymphadenopathy, nodal metastasis and lymphoma as the possible differential diagnoses. Reactive lymphadenopathy was excluded based on the characteristic histologic picture with prominent eosinophilia and vascularization, nodal metastasis due to lack of tumor cells and lymphoma due to the presence of a mixed cell population. The presence of parotid masses required Mikulicz's disease, infective parotitis, salivary gland tumors like Warthin's, mumps and Sjogren's syndrome to be excluded. The absence of epimyoeplithelial islands and presence of eosinophils on histopathological examination allowed us to exclude Mikulicz disease,^[9] while the duration and clinical features excluded infective parotitis and mumps. The lack of diagnostic histologic features and the absence of concurrent xerostomia and xerophthalmia excluded salivary neoplasms and Sjogren's, respectively. Moreover, the microscopic picture of lymphoid proliferation and eosinophilia gave rise to a differential diagnosis of Hodgkin's lymphoma, angioimmunoblastic T-cell lymphoma, Langerhan's cell histiocytosis and parasitic lymphadenitis. However, the absence of classic Reed-Sternberg cells

and/or its variants, atypical lymphocytes, Langerhans cells and parasitic remnants aided in separating our case from the aforementioned entities.^[5]

However, the lesion that bears the closest resemblance to Kimura's disease, to the extent that the two were once considered the same entity, is angiolymphoid hyperplasia with eosinophilia (ALHE). Ever since ALHE was described in 1969, the misapprehension that ALHE and Kimura's disease were identical, or at least two ends of the same disease spectrum, has been perpetuated by the similarities between the two conditions;^[10] 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.^[4,5]

A path-breaking study by Rosai *et al.* (1979)^[11] eventually clarified this misconception, and Kimura's disease and ALHE were established as two distinct entities. Currently, Kimura's disease is believed to be a chronic, allergic inflammatory process^[12] of unknown origin; whereas, ALHE is considered a benign vascular proliferative disorder.^[4] Kimura's disease is predominantly seen in young Asian males and manifests as single or multiple, asymptomatic large masses in the subcutaneous tissue or salivary glands. Regional lymphadenopathy, peripheral blood eosinophilia and elevated serum IgE levels are commonly seen and the lesions are of shorter duration.^[13] On the contrary, ALHE principally affects women in the 3rd-4th decades and has no racial predilection.^[4] It typically presents as multiple erythematous to brown dermal papules or nodules accompanied by tenderness and pruritus. Regional lymphadenopathy, peripheral blood eosinophilia, and increased serum IgE levels are rare and the lesions usually occur with a longer duration. The tendency towards renal involvement and nephrotic syndrome is also restricted to patients of Kimura's disease and is not observed in ALHE.^[14]

The microscopic picture of Kimura's disease consists of lymphoid proliferation with prominent germinal centers and immense eosinophilic infiltrates, which may lead to folliculolysis and aggregation of eosinophils to form microabscesses.^[12] In ALHE, however, lymphoid infiltration is mild to moderate,^[15] 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.^[10] The vascular component is prominent, and consists of 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.^[4] In contrast, the blood vessels in Kimura's disease are thin walled with flattened endothelial cells. The classic "epithelioid" or "histiocytoid" cells of ALHE are not seen.^[12] Fibrosis, a frequent feature in Kimura's disease, is absent in ALHE.^[10]

Our patient was an Asian male in his 2nd decade with a subcutaneous mass in the parotid region. There was regional lymphadenopathy and peripheral blood eosinophilia, and the lesion had been present for the past 7 years. Histopathologically, there were multiple lymphoid follicles with eosinophilic infiltrates and folliculolysis. The blood vessels had flattened endothelial cells and “histiocytoid” cells were absent. These features guided us toward a definitive diagnosis of Kimura's disease. A Pub Med search was carried out using the title ‘Kimura's disease’ and cases where the diagnosis was ‘ALHE’ or ‘epithelioid hemangioma’ were excluded. We found that, to date, 19 cases of Kimura's disease have been reported in the Indian population, with our case being the 20th. Out of these, in three cases only lymph nodes were involved,^[7,16,17] in one the parotid gland alone was involved,^[18] and in six cases the disease affected the subcutaneous tissue.^[19-24] There were five instances of simultaneous involvement of parotid gland and lymph nodes.^[25-29] Details of the other cases were inaccessible.

The clinical and histological features of Kimura's disease and ALHE are compared in Table 1.^[4,6,12]

Theories abound regarding the origin of Kimura's disease, but its exact pathogenesis 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.^[4] 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.^[3,5] *Candida albicans*^[12] has chiefly been postulated as the antigen responsible, although some researchers have also speculated Epstein-Barr virus, human herpes virus-8, and parasitic infection as potential causes.^[6] Studies have also shown that the high IgE and lymphoid follicle production seen in Kimura's disease may be triggered by the proliferation of CD4+ T cells, specifically the CD4 T-helper 2 (Th2) cells and resultant overproduction of their cytokines, such as granulocyte macrophage colony-stimulating factor, tumor necrosis factor- α , IL-4, IL-5, eotaxin, and RANTES (regulated on activation, normal T cell expressed and secreted).^[3] Additionally, disease development and recurrence may be attributed to a clonal T-cell population.^[4] The immune reaction that is believed to be the root of Kimura's disease also predisposes the patient to allergic conditions like asthma, chronic urticaria, pruritis and rhinitis.^[3] Moreover, up to 60% of these patients exhibit renal involvement manifesting as proteinuria and nephrotic syndrome,^[7] which necessitates a thorough physical evaluation following diagnosis.

In asymptomatic cases, conservative observation is often adequate as lesions occasionally undergo spontaneous resolution. Surgical excision is considered the first line of treatment in symptomatic cases,^[3] but it should be kept in mind that Kimura's disease has a tendency to recur. Our patient had cosmetically disfiguring bilateral swelling with associated pain,

Table 1: A comparison of the clinical and histological features of Kimura's disease with ALHE

Characteristics	Kimura's disease	Angiolymphoid hyperplasia with eosinophilia
Clinical features		
Sex	Female predominance (70%)	Male predominance (85%)
Age	Young adulthood	Young to middle age
Race	More common in Asians	Occurs in all races
Location	Head and neck	Head and neck
Presentation	Localized subcutaneous mass	Dermal papules or nodules
Number	Single or multiple	Usually multiple
Size	Average 3 cm	Average 1 cm
Lymph node involvement	Common	Rare
Salivary gland involvement	Common	Rare
Peripheral eosinophilia	Almost invariably present	Rare (20%)
Serum immunoglobulin E (IgE) level	Elevated	Normal
Renal involvement	Occasional (21%)	Rare
Recurrence rate	30%	15-40%
Histopathological features		
Depth	Subcutaneous, muscle	Cutaneous, subcutaneous
Vascular proliferation	Some degree of vascular proliferation	Florid vascular proliferation
Lymphoid follicles	Always found	May be present
Eosinophils	Abundant	Sparse to abundant
Eosinophilic abscesses	Present	Not seen
Endothelium	Flattened	Cuboidal to dome shaped: “Histiocytoid”
Fibrosis	Present	Absent

ALHE: Angiolymphoid hyperplasia with eosinophilia

hence surgery was considered the treatment of choice. Topical and systemic corticosteroids have also been effective and in patients resistant to steroids, radiation therapy has been used.^[6]

REFERENCES

1. Kimm HT, Szeto C. Eosinophilic hyperplastic lymphogranuloma, comparison with Mikulicz's disease. *Chin Med J* 1937;23:699-700.
2. Kimura T, Yoshimura S, Ishikawa E. On the unusual granulation combined with hyperplastic changes of lymphatic tissue. *Trans Soc Pathol Jpn* 1948;37:179-80.
3. Meningaud JP, Pitak-Arnop P, Fouret P, Bertrand JC. Kimura's disease of the parotid region: Report of 2 cases and review of the literature. *J Oral Maxillofac Surg* 2007;65:134-40.
4. Chong WS, Thomas A, Goh CL. Kimura's disease and angiolymphoid hyperplasia with eosinophilia: Two disease entities in the same patient: Case report and review of the literature. *Int J Dermatol* 2006;45:139-45.
5. Chen H, Thompson LD, Aguilera NS, Abbondanzo SL. Kimura disease: A clinicopathologic study of 21 cases. *Am J Surg Pathol* 2004;28:505-13.
6. Dik VK, van der Wiel BA, Vasmel WL. Kimura's disease of the parotid glands and multiple cervical lymph nodes. *Neth J Med* 2010;68:175-7.
7. Sud K, Saha T, Das A, Kakkar N, Jha V, Kohli HS, et al. Kimura's disease and minimal-change nephrotic syndrome. *Nephrol Dial Transplant* 1996;11:1349-51.
8. Hui PK, Chan JK, Ng CS, Kung IT, Gwi E. Lymphadenopathy of Kimura's disease. *Am J Surg Pathol* 1989;13:177-86.
9. Lin P, Medeiros LJ. Hematopoietic lesions. In: Gnepp DR, editor. *Diagnostic Surgical Pathology of the Head and Neck*. 2nd ed. Philadelphia: Saunders Elsevier; 2001. p. 942-3.
10. Seregard S. Angiolymphoid hyperplasia with eosinophilia should not be confused with Kimura's disease. *Acta Ophthalmol Scand* 2001;79:91-3.
11. Rosai J, Gold J, Landy R. The histiocytoid hemangiomas. A unifying concept embracing several previously described entities of skin, soft tissue, large vessels, bone, and heart. *Hum Pathol* 1979;10:707-30.
12. Armstrong WB, Allison G, Pena F, Kim JK. Kimura's disease: Two case reports and a literature review. *Ann Otol Rhinol Laryngol* 1998;107:1066-71.
13. Jani A, Coulson M. Kimura's disease: A typical case of a rare disorder. *West J Med* 1997;166:142-4.
14. Ramchandani PL, Sabesan T, Hussein K. Angiolymphoid hyperplasia with eosinophilia masquerading as Kimura disease. *Br J Oral Maxillofac Surg* 2005;43:249-52.
15. Chun SI, Ji HG. Kimura's disease and angiolymphoid hyperplasia with eosinophilia: Clinical and histopathologic differences. *J Am Acad Dermatol* 1992;27:954-8.
16. Thomas J, Jayachandran NV, Chandrasekhara PK, Rajasekhar L, Narsimulu G. Kimura's disease--an unusual cause of lymphadenopathy in children. *Clin Rheumatol* 2008;27:675-7.
17. Kumar V, Salini, Haridas S. Kimura's disease: An uncommon cause of lymphadenopathy. *Indian J Med Pediatr Oncol* 2010;31:89-90.
18. Kumar S, Iyengar KR, Gopalakrishnan S, Ratnakar S. Kimura's disease: Rare cause of head and neck swelling. *Indian J Otolaryngol Head Neck Surg* 2004;56:291-2.
19. Kini U, Shariff S. Cytopathology of Kimura's disease. *Indian J Pathol Microbiol* 1998;41:473-7.
20. Ranka SR, Rajput A, Kantharia CV. Kimura's disease. *Indian J Otolaryngol Head Neck Surg* 2004;56:43-5.
21. Shenoy VV, Joshi SR, Kotwal VS, Shedge RT, Ramraje NN, Lanjewar DN. Recurrent Kimura's disease: Excellent response to cyclosporine. *J Assoc Physicians India* 2006;54:153-5.
22. Varshney MV, Kumar A, Khan SA, Yadav CS. Kimura disease of extremity: Unusual manifestation in a long bone. *Joint Bone Spine* 2008;75:492-4.
23. Prasad BK, Deviprasad R. Kimura's disease: An unusual case of neck mass. *Indian J Otolaryngol Head Neck Surg* 2008;60:353-5.
24. Lee JK, Almousa R, Thamboo TP, Amrith S. Kimura disease of the eyelid in an Indian man. *Clin Experiment Ophthalmol* 2009;37:412-4.
25. Dave B, Desai S, Ramadwar M. Kimura disease with proliferative squamous metaplasia: An unusual finding and a potential diagnostic pitfall. *Indian J Pathol Microbiol* 2007;50:771-3.
26. Saini A, Singh V, Chandra J, Dutta AK. Kimura's disease: An unusual glandular involvement with blood and tissue eosinophilia. *Indian J Pediatr* 2009;76:647-8.
27. Chintamani, Sugandhi N, Khandelwal R, Tandon M, Jain S, Narayan N, et al. Kimura's disease masquerading as parotid malignancy. *JRSM Short Rep* 2010;1:41.
28. Baidya DK, Chhabra A, Raj R. Anesthetic management of a patient with Kimura's disease for superficial parotidectomy. *J Anaesthesiol Clin Pharmacol* 2011;27:383-5.
29. Nehru VI, Abrol R, Vaiphei K, Singh P. Kimura's disease-report of a case masquerading as a parotid tumor. *Indian J Otolaryngol Head Neck Surg* 2000;52:302-4.

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