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Kimura's disease: a neoplasm mimicking, a rare benign form of chronic inflammatory disorder



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ABSTRACT

Background: Kimura's Disease (KD) is a benign, rare form of chronic inflammatory disease of unknown origin, almost exclusively found in Asian males in their second to fourth decades of life. This rare condition is mostly present as soft tissue mass consists of multiple painless solitary subcutaneous nodules mostly localized in the head and neck region, with coexisting lymph node enlargement and eosinophilia. This case study aims to describe Kimura's Disease (KD) characteristics and give an insight into the role of Computed Tomography (CT) scan in identifying KD and its imaging characteristics.

Case Presentation: We reported a case of an Asian man with a history of 18 years left-sided painless facial mass, gradually increase in size with no history of hoarseness, epistaxis, previous facial mass or

malignancy, and familial malignancy. CT scan findings showed an inhomogeneous contrast enhancement soft tissue mass located on the left parotid-submandibular region with multiple neck lymphadenopathy and left parotid gland involvement. Eosinophilia was found persistently in the laboratory outcomes, and this mass had been confirmed with histological findings consistent with KD features.

Conclusion: Recognizing the characteristics of KD and the imaging findings on Ultrasound and CT-scan as accessible and first-line diagnostic tools, might help in facilitating the diagnosis, making a decision and sparing the patient from unnecessary and harmful procedures.

Keywords: Soft Tissue Mass, Chronic Inflammatory Disorder, Kimura's Disease, CT Scan.

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INTRODUCTION

Kimura's Disease (KD) was first described in 1937 in China by Kim and Szeto as an 'eosinophilic hyperplastic granuloma', and then Kimura et al. reported its definitive histological criteria in 1948.^{1,2} KD is a benign, rare form chronic inflammatory disorder with angiolymphatic proliferation with unknown etiology affecting subcutaneous tissues.³

KD mainly occurs in young Asian males, with a female to male ratio of 1:3 and occurs in the 2nd to 3rd decades of life.¹ KD is mainly presented as asymmetric painless solitary or multiple subcutaneous nodules, predominantly in the head and neck region with coexisting lymph node enlargement in 30-40% of the cases.^{2,3} Typical areas for the nodules are submandibular, popliteal and preauricular regions, parotid glands, oral cavity,

and larynx.⁴ In laboratory examination findings, a consistent increase in IgE levels and high eosinophil counts are almost always present.⁵

This case study aims to evaluate Kimura's disease as a neoplasm mimicking, a rare benign form of the chronic inflammatory disorder, by using Computed Tomography (CT) scan and determine its imaging characteristics.

CASE REPORTS

A 55-years old man comes to our hospital complaining of painless non-discharging swelling in the left parotid region, which gradually increased in size over these 18 years. He didn't complain of any focal symptoms like functional compromise, constitutional symptoms or pruritus. He had no previous chronic medical illness or history of malignancy or familial

malignancy. No history of any concurrent autoimmune or renal disease, no history of hoarseness and epistaxis.

Physical examinations showed that the size of the mass was approximately 20x10 cm, with an indistinct border, mass was immobile and non-exudative with palpable firm lymphadenopathy on the left neck with a size of approximately 2x1 cm. The rest physical examinations of the head and neck region, including the eye, nose, ears and throat, were normal. Physical examinations of the chest, abdomen and extremities were also within normal limits (Figure 1).

We did two laboratory investigations with 9 days intervals (December 11th and 20th 2018). Investigations included complete blood count (CBC), renal and liver function tests, albumin, coagulation test, blood glucose, and electrolytes. The

CBC showed persistent eosinophilia and the others were within normal limits (Table 1).

USG examination of the neck revealed a large soft tissue mass on the left parotid region with multiple enlarged and inflamed lymph nodes on the left submandibular, left submental, left supraclavicular, left parotid, and left neck regions. The largest

lymph node size measured was 2x1 cm (Figure 2). CT scan of the midface and neck, with axial, sagittal, and coronal reconstruction, was taken with and without contrast. CT scan showed a solid heterogeneous with indistinct border mass, which was non-homogeneously enhanced with contrast in the left zygoma until the left submandibular region. This

mass had a necrotic area within it. There were scattered benign-looking lymph nodes visualized, as well as multiple lymph node enlargement of the neck. No evidence of bone destruction and spreading towards adjacent tissues. Other organs in the midface and neck region were within normal limits (Figure 3).

Fine needle aspiration biopsy (FNAB) from the zygoma region was performed and showed an atypical lymphoid proliferation finding. One month after the FNAB, an excisional biopsy was performed and showed multiple lymphoid follicles with enlarged germinativum centrum with the wide spreading of peri-follicle eosinophil cells, which highly suggestive of Kimura's disease (Figure 4).



Figure 1. Patient's physical examination

Table 1. The evaluation of Complete Blood Count (CBC) examination during the study period with persistent eosinophilia

Parameter	Complete Blood Count (CBC) Examination		Reference Range
	11/12/2018	20/12/2018	
WBC (10 ³ /μL)	8.34	9.51	
Neutrophils (%)	53.69	30.02	47-80
Lymphocyte (%)	23.56	21.30	13-40
Monocyte (%)	6.43	6.61	2.00-11.00
Eosinophils (%)	15.48	41.23	0.00-5.00
Basophils (%)	0.84	0.85	0.00-2.00
Neutrophils (#)	4.48	2.86	2.50-7.50
Lymphocyte (#)	1.97	2.03	1.00-4.00
Monocyte (#)	0.54	0.63	0.10-1.20
Eosinophils (#)	1.29	3.92	0.00-0.50
Basophils (#)	0.07	0.08	0.00-0.10
MCHC (g/dL)	29.92	31.25	31-36
RDW (%)	12.24	12.47	11.60-14.80
Platelet (10 ³ /μL)	257.30	186.70	150-440
MPV (fL)	6.09	6.20	6.80-10.00
RBC (10 ⁶ /μL)	4.37	4.18	4.50-5.90
Hemoglobin (g/dL)	12.69	12.68	13.50-17.50
Hematocrit (%)	42.42	40.57	41.00-53.00
MCV (fL)	97.07	97.01	80.00-100.00
MCH (pg)	29.04	30.32	26.00-34.00

WBC: White Blood Cells; MCHC: Mean Corpuscular Hemoglobin Concentration; RDW: Red-Cell Distribution Width; MPV: Mean Platelet Volume; RBC: Red Blood Cells; MCV: Mean Corpuscular Volume; MCH: Mean Corpuscular Hemoglobin

DISCUSSION

Kimura's disease (KD), first known as eosinophilic hyperplastic lymphogranuloma, was first described by Kim and Szeto, 1937 in China. After that, this disease was named Kimura's disease after detailed histological criteria were described by Kimura et al. in 1948.¹ KD is a rare chronic inflammatory disorder of unknown origin that mainly affects the subcutaneous tissue and lymph nodes occur in young Asian male patients.¹ KD has a male preponderance, with a male to female ratio of 3:1, and mainly occurs in the second and third decades of life.^{5,6} KD predominantly manifests as a unilateral painless subcutaneous mass in the head and neck region, commonly affecting lymph nodes and major salivary glands.^{1,6} Typical areas for KD nodules are parotid, submandibular, preauricular, larynx, oral cavity and popliteal regions and may present in other localizations like orbits, lacrimal glands, eyelids, forearm, kidneys, and groins.⁴

Mostly KD is endemic in parts of Asia such as China, Indonesia, Japan, etc.⁷ Although it had also been reported in America and Europe, which was for a time been called angio-lymphoid hyperplasia with eosinophilia (ALHE), the permanent population was Asian. There were only around 300 cases reported all over the world.^{5,8} This rare disease onset is insidious, and the manifestations are enlarging nodular masses in the head and neck regions, most frequently infra

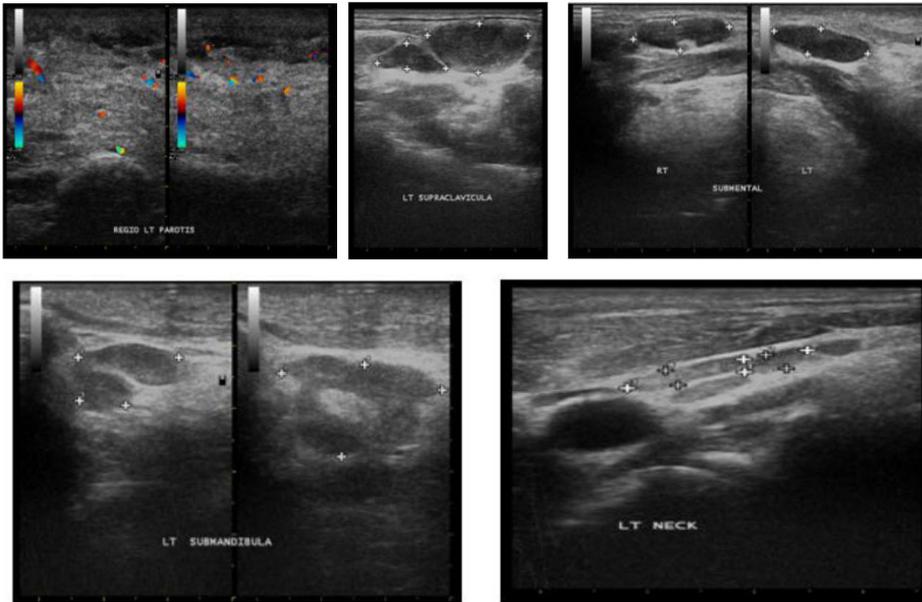


Figure 2. USG examination, a large left parotid soft tissue mass with multiple lymphadenopathies on the left submental, submandibular, supraclavicular, parotid, and neck regions.

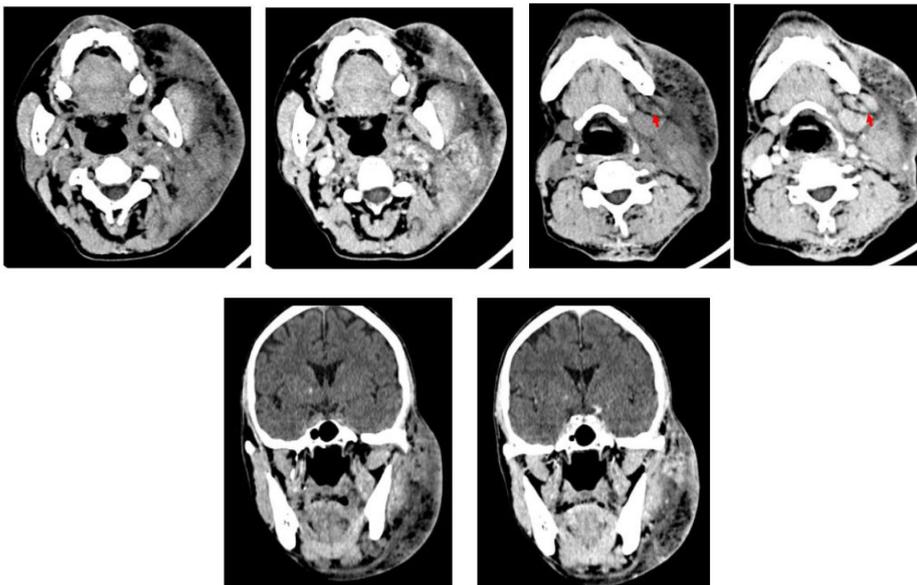


Figure 3. Head and neck CT scan, solid heterogeneous indistinct border mass which was non-homogeneously enhanced with contrast in the left zygoma until the left submandibular region. There were scattered benign-looking lymph nodes visualized, as well as multiple lymphadenopathies (red arrow).

or retroauricular, which may simulate a neoplasm.⁸

Etiology of KD is idiopathic, despite the presence of increased eosinophils, serum IgE, tumor necrosis factor (TNF α), interleukin IL-13, IL-5, IL-4, and mast cells levels in peripheral blood count and also in the lesion's tissue biopsy,

still no specific antigens have been identified in patients with KD.⁹ There were many possible risk factors postulated by scientists in KD, including allergic reaction, parasite infection, autoimmunity or even neoplasm. Another study finding had also suggested that overgrowth of the CD4+ Th2 and Th2 cytokines might have

an important role in KD.⁵

In histopathological examinations, KD will form germinal and follicle centers with lymphoid infiltration and accompanied by plasma cells, mast cells, and particularly enormous amounts of eosinophils.⁹ Lymph nodes may enlarge from 1 to 4 cm in diameter and frequently adherent to one another, show markedly hyperplastic follicles with reactive germinal centers and a well-defined peripheral mantle. Cytopathology of FNAB examinations from the lymph nodes may produce smears composed of dissociated and clustered endothelial cells, eosinophils, lymphocytes, and giant cells.^{8,9}

Because of its rarity and confined epidemiological distribution, there's limited radiological literature on this disease. When dealing with lymph node enlargement cases, the first imaging modality must be neck and salivary glands ultrasound. Ultrasound findings of KD Lymph nodes are solid round/oval-shaped lesions which are hypoechoic in the submandibular and parotid region with normal surrounding soft tissues.⁴

KD might show typical patterns of arrangement, distributions and enhancement with contrast media on CT scan.¹⁰ Mostly, KD lesions might be seen in the proximity of major salivary glands. On scanning, subcutaneous masses with lymph node enlargement were the typical findings. The density of the lesions might vary from iso-dense to hyperdense, and on CT with IV contrast media, enhancement patterns of the lesions will vary from low intensity to high intensity and from homogenous to heterogeneous.^{6,10}

The lesions may show a variation of signal intensity on MRI, which will vary from low to high or mixed signal intensity on T1-weighted images, and T2-weighted images may show low or high signal intensity.⁶ Gopinathan A et al. classified KD lesions into two specific morphological subtypes, first the type 1 lesions, which were homogenous enhanced nodular masses with a relatively well-defined border.¹⁰ Second, the type 2 lesions were heterogenous enhanced ill-defined masses with plaque-like configuration. The well-defined type 1 lesions and ill-defined type 2 lesions may represent a different spectrum of an inflammatory disease

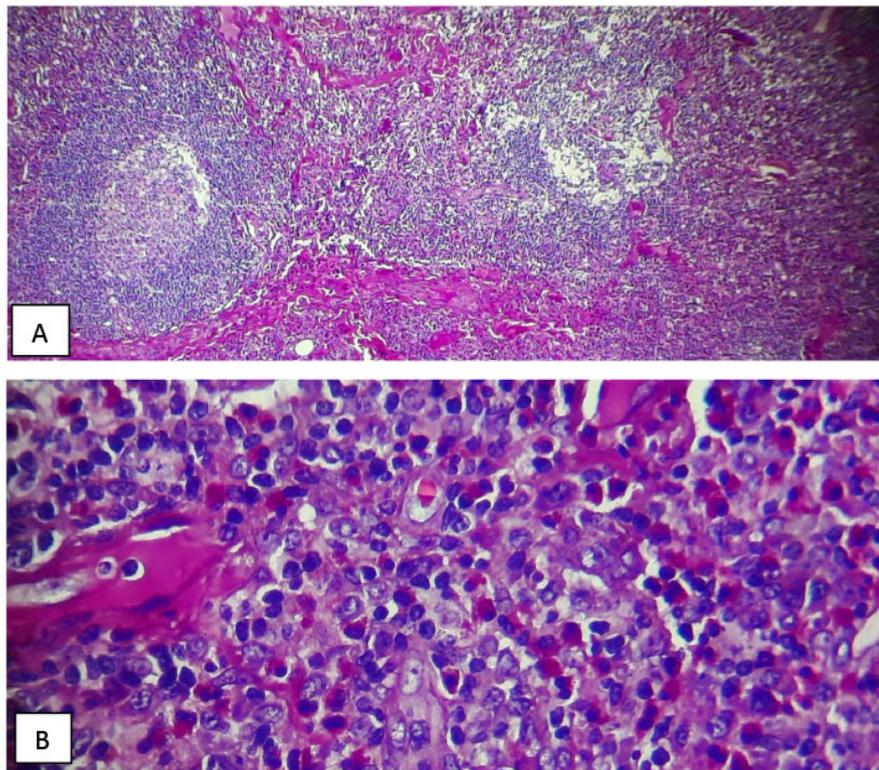


Figure 4. Excisional biopsies result from 40 times (A) and 100 times (B) magnification, multiple lymphoid follicles with enlarged germinal center with the wide spreading of peri-follicle eosinophil cells, which is highly suggestive of Kimura's Disease.

continuum. This hypothesis was supported by younger predilection in well-defined masses and older predilection in ill-defined masses. Poorly enhanced masses might have marked atrophy of underlying subcutaneous fat, reflecting the chronicity of the disease.¹⁰

Since KD is a systemic immune-mediated disease surrounding infiltrative behavior, it will be more difficult to eradicate.¹ Until now, there's no guideline for the management of KD. Many treatments and medication methods have been recommended for KD, including corticosteroids, radiotherapy, and surgical excision.^{4,5} Corticosteroids were believed to reduce lymphadenopathy's size but lack evidence in reducing the affected salivary gland size. Unfortunately, usually, these lesions might enlarge again after steroid medication was terminated.⁴

Many medications had been investigated apart from traditional therapy, including all-trans-retinoic acid, anti-allergic drugs, combined treatment with laser, oxypentoxifylline, leukotriene-

receptor blocker pranlukast and steroid, nicotine chewable tablets and vincristine. The prognosis of KD is good and this disease has no potential for malignancy changes. The course of the disease may even last decades.⁵

CONCLUSION

Recognizing the signs and symptoms of Kimura's Disease and the imaging findings on ultrasound and CT scan examinations as accessible and first-line diagnostic tools might help facilitate the diagnosis, make decisions, and spare the patient from unnecessary and harmful procedures.

CONFLICT OF INTEREST

There is no competing interest regarding the manuscript.

FUNDING

None.

AUTHOR CONTRIBUTIONS

All authors equally contribute to the study from the conceptual framework, data acquisition, evaluating the CT-scan results until reporting the outcome through publication.

ETHICAL STATEMENT

This case study has followed the publication ethics based on COPE and ICMJE guidelines as well as received informed consent from a patient prior to publication.

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