



ORIGINAL ARTICLE

Kikuchi's disease (KD); mimicking malignant lymphoma: A rare cause of cervical lymphadenopathy.

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ABSTRACT... Objective: The aim of this study is to present six cases of cervical lymphadenopathy, diagnosed as Kikuchi's disease and raise the index of suspicion for this disease. **Study Design:** Case Series. **Setting:** Histopathology and Otolaryngology/Head & Neck Surgery Department at Rehman Medical Institute (RMI) Peshawar. **Period:** July 2016 to March 2021. **Material & Methods:** Records of patients for cases diagnosed as "histiocytic necrotising lymphadenitis" were retrieved, their corresponding patient files accessed from the archive, and case notes analyzed. **Results:** In this series, a total of six cases of Kikuchi's disease are presented. A female predominance is evident from the present data (2:1 female to male ratio). All patients presented with palpable lymph nodes in the neck, predominantly on the left (66.7%). Majority (66.7%) presented with neuralgic pain (on/off). Only one patient did not show weight loss and night sweating, the remaining had all the symptoms. All of the patients recovered spontaneously within 6 months (range 2 to 6 months) with symptomatic treatment for neuralgic pain. **Conclusion:** Kikuchi's disease should be kept in the differential diagnosis in young females with persistent neck masses, palpable lymph nodes and suspicious fine needle aspiration cytology (FNAC).

Key words: Biopsy, Histiocytic Necrotizing Lymphadenitis, Kikuchi Disease, Lymph Nodes, Otolaryngology.

INTRODUCTION

Histiocytic necrotizing lymphadenitis or Kikuchi's disease (KD) was first described in 1972 by Dr Masahiro Kikuchi and Fujimoto in the Japanese literature.^{1,2} It is an increasingly recognised, self-limiting cervical lymphadenitis of unknown origin predominantly affecting young women under the age of 30, with men having a wider range of presentation ages.³

The classical presentation is a unilateral painful posterior neck lymphadenopathy, fever, in a young adult, usually female. Less commonly it also involves axillary and abdominal lymph nodes. Parotid gland and spleen enlargement with skin rashes is also reported.⁴ The exact cause of KD is still not known but autoimmune and infections are considered as a possible aetiology. The Gold Standard for the diagnosis of KD is lymph node biopsy with histological and microscopic confirmation of paracortical necrosis

and histiocytic infiltration. The serological test like antinuclear antibodies (ANAs), anti-double strand antibodies, rheumatoid factor are usually negative in patients with KD. The association between KD and systemic lupus erythematosus (SLE) is mentioned in certain literature.⁵ Lymphadenopathy due to SLE is clinically and histologically similar to KD but the manifestations are different as reported by Chua SH, et.al.⁶

Any patient presenting with persistent neck lymph nodes, especially if young females, with high temperature, high or normal Erythrocyte sedimentation rate (ESR)/C-reactive Protein (CRP) and a suspicious fine needle aspiration cytology (FNAC) report should undergo excision biopsy to rule out KD.

The aim of this study is to present six cases of cervical lymphadenopathy, diagnosed as Kikuchi's disease and raise the index of suspicion

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for this disease.

MATERIAL & METHODS

This study was conducted at the Histopathology Department and Department of Otolaryngology/ Head & Neck Surgery of a Tertiary Care Hospital of Peshawar. A manual search through the histopathology department archives from July 2016 till March 2021 for cases diagnosed as "histiocytic necrotising lymphadenitis" was conducted which resulted in six cases. Pathologist reviewed the slides again and diagnosis were re-confirmed. Patient records were retrieved, case notes analysed, and relevant data collected.

Illustrative Case

A 19-year-old female, presented to ENT outpatient department with right sided palpable neck lymph nodes, on/off pain in the right side of neck, night sweats, and weight loss for the past 5 months. Prior to this, she was otherwise in good health apart from hospitalization for typhoid fever two years ago. There was no family history for any disease. Clinical exam shows a firm, non-tender, palpable lymph nodes on the right neck, mobile, no erythema, edema or brawny induration seen.

The patient had a routine complete blood count (Hemoglobin (Hb): 11.5gm/dcl White Blood Cell Count (WBC): 8.9/mcl Platelets: 335,000/mm³, CRP (2.5mg/L raised) and ANCA (Negative). A chest X-ray was also done which showed cervical lymphadenopathy. Ultrasound of the neck showed multiple lymph nodes, up to 3cm in size and loss of fatty hilum. Fine Needle Aspiration Cytology (FNAC) was done for her which yielded, high cellularity with polymorphous population of lymphocytes. An excision biopsy was advised and subsequently performed. The sections showed extensive area of necrosis with multiple macrophages. No granuloma or malignancy was noted. The patient was labelled as a case of histiocytic necrotising lymphadenitis or Kikuchi's disease.

The patient was counselled about the disease, acetaminophen for pain management was advised and the patient was discharged with follow-up in 1 month. Symptomatic improvement was seen in

the patient on the next visit and further follow-up after another month was advised. Spontaneous resolutions of the lymph nodes and symptoms occurred within 6 months of initial presentation. The recovery was uneventful.

RESULTS

In this series, a total of six cases of Kikuchi's disease are presented. A female predominance is evident from the present data (2:1 female to male ratio). Four of the patients were below 20 years of age while the remaining two were 30 and 39 years respectively. All patients presented with palpable lymph nodes in the neck, predominantly on the left (66.7%). Majority (66.7%) presented with neuralgic pain (on/off). Only one patient did not show weight loss and night sweating, the remaining had all the symptoms. Most of the patients had these symptoms for 3 to 6 months. Table-I shows the presenting complains.

Symptom		N (%)
Palpable Lymph Nodes	Right	1 (16.7)
	Left	4 (66.7)
	Bilateral	1 (16.7)
Neuralgic Pain (on/off) in neck		4 (66.7)
Night Sweats		5 (83.3)
Weight Loss		5 (83.3)

Table-I. Presenting complains.

None of the patients reported of fever. Ultrasound examination was done for all patients, majority of the findings were multiple lymph nodes ranging between 2cm and 3.5cm.

Fine needle aspiration cytology (FNAC) was performed on all patients which revealed high cellularity with polymorphous population of lymphocytes in four cases while two cases showed histiocytic aggregates with intermediate sized lymphoid cells. Excision biopsy was recommended on all six samples. Five excision biopsy samples yielded paracortical necrosis with starry sky pattern and foamy histiocytes (Figure-1) with one showing extensive area of necrosis and multiple macrophages (Figure-2).

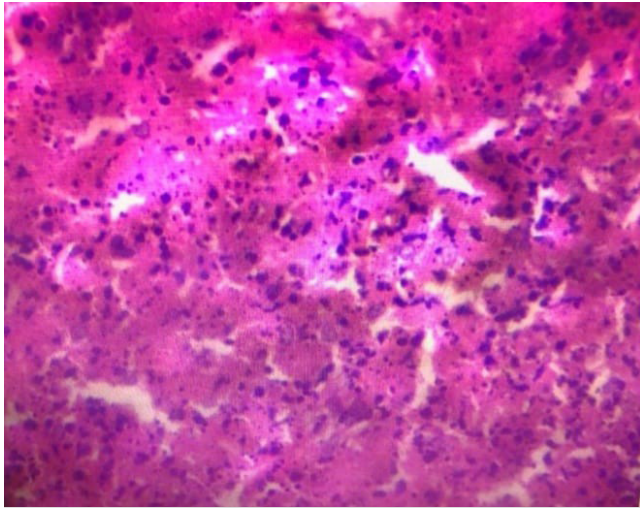


Figure-1. Paracortical necrosis with starry sky pattern, foamy histiocytes.

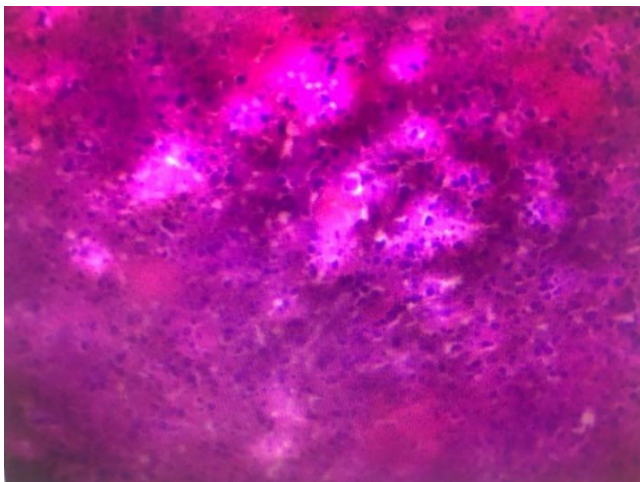


Figure-2. Histopathologic section of Kikuchi's disease.

Blood investigations did not show any characteristic findings with all samples having a normal complete blood count (CBC) and negative ANCA. Half the cases had raised C-reactive protein (CRP).

All six patients had their X-rays done which showed prominent lymph nodes. One of the patient's X-rays is shown in Figure-3.

Most of the patients did not have any significant past medical or surgical history however, one patient was asthmatic. All of the patients recovered spontaneously within 6 months (range 2 to 6 months) with symptomatic treatment for neuralgic pain.

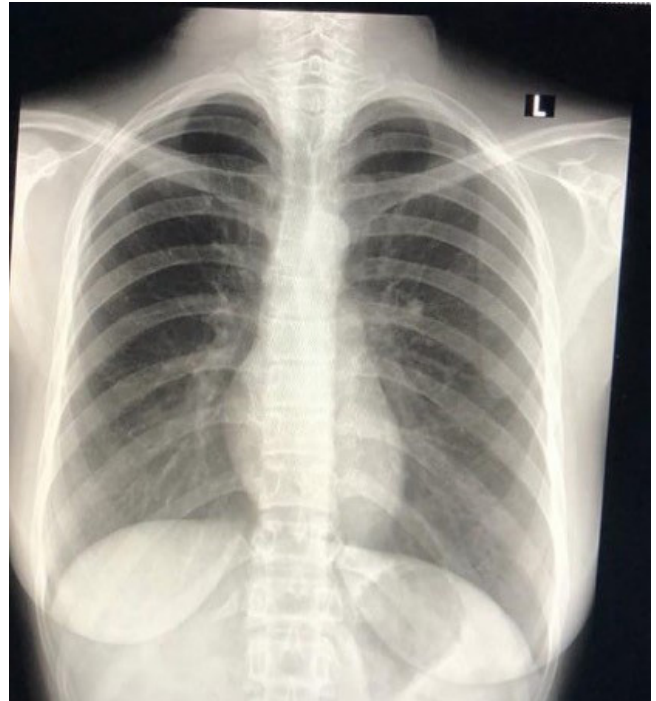


Figure-3. Cervical lymphadenopathy.

DISCUSSION

Kikuchi and Fujimoto in Japan first described Kikuchi's disease in 1972. The exact cause of Kikuchi's disease is still unknown but occurs sporadically in people with no family history of this condition, however, it is relatively benign and does not result in loss of life.⁷

A viral or post viral reaction has been proposed as its aetiology and several other infectious agents like Epstein Barr virus, Herpes simplex virus 2, cytomegalovirus (CMV), and Varicella Zoster virus have all been suggested but not confirmed till date. Other aetiological agents including HIV virus, *Yersinia enterocolitica* and silicone breast implants have also been proposed as possible aetiological agents.^{8,9}

Most patients with this disease have been reported in Asian origin. A case from India has also been reported.¹⁰ Only a few individual case reports of KD are published in Pakistan.^{9,11,12}

No diagnostic laboratory tests are available for the diagnosis of Kikuchi's disease, FNAC has been reported to be diagnostic by Hseuh EJ,

et al. in 1992 however, the disease has been misdiagnosed as lymphoma due to it and some patients have even received chemotherapy.^{13,14}

The diagnosis is usually confirmed by a lymph node biopsy, which shows the typical pathology of the disease and differentiates it from lymphoma, systemic lupus erythematosus, and other infectious lymphadenopathies. Hence, a clinician needs to keep this disease as a premium differential while diagnosis cases of neck masses/swelling. We based our diagnosis on excision biopsy of the lymph nodes, with histological features of eosinophilic necrosis, monocytes, T-immunoblast and absent neutrophils.

Clinically, the disease presents with multiple lymphadenopathies, typically in head and neck region, although it may be generalised. The affected lymph nodes are generally multiple, firm, and mildly tender and specifically one being unilateral cervical lymphadenopathy.¹⁵ Splenomegaly may be present. Other symptoms like fever, nausea, vomiting, headache, fatigue, night sweats and weight loss may be present.¹⁶ Cutaneous skin manifestations have also been reported with cases of KD.¹⁷ There was no any cutaneous lesion in all our cases.

The disease is self-limiting and benign in nature, but multiple recurrences have been reported in the same patient.¹⁸ A few fatalities like sudden heart failure and lupus like syndromes have occurred.

Some clinicians, because of its recurring nature and association with systemic lupus erythematosus recommend long-term follow up. Because of unknown its aetiology, symptomatic treatment with non-steroidal anti-inflammatory drugs is usually done. The use of steroids or other immunosuppressant drugs in selected cases to prevent fatal outcome have also been recommended.¹⁹ In other reports, oral prednisolone is shown to limit prolonged fever and other irritating symptoms lasting for more than two weeks. In the previous literature use of steroid was limited to Kikuchi's associated brachial plexus neuritis.²⁰ FNAC has high

sensitivity to identify metastatic carcinoma and melanoma in a lymph nodes. In lymphoid tumour the false negative rate is very high but FNAC with excision biopsy of lymph nodes increase the diagnostic accuracy to around 85-90%.²¹

CONCLUSION

Patients with cervical lymphadenopathy and suggested malignant lymphoma on cytology may be misdiagnosed as lymphoma and hence should have excision biopsy to confirm the diagnosis. Symptomatic treatment should be the mainstay for this benign disease, steroids and other immunosuppressant therapy should be reserved for more prolonged and aggressive forms of Kikuchi's disease.





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AUTHORSHIP AND CONTRIBUTION DECLARATION

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1	Ihsan Ullah	Conceived and designed did data collection/correction & final approval of the manuscript.	
2	M. Khizar Hayat	Editing review & final approval of the manuscript.	
3	Sanallah Khan	Data collection & manuscript writing.	
4	Nazish Khan	Data collection & manuscript writing.	
5	Chaand Bibi	Data analysis & Results generation.	chaand
6	Maham Rehman	Data analysis & Results generation.	Maham