

### **Kikuchi Fujimoto Disease: A Case Report with Literature Review**

#### **Abstract:**

Kikuchi-Fujimoto disease (KFD), also referred to as histiocytic necrotizing lymphadenitis, is an uncommon entity, usually benign, self-limiting disease characterised by fever and regional lymphadenopathy of unexplained aetiology. The patients also exhibit features of mild fever and night sweats. There is an increase in reported cases of KFD, particularly in Asia. It is important to recognize this condition because it may be confused for systemic lupus erythematosus (SLE), tuberculosis or lymphoma. The knowledge of this condition among clinicians and pathologists can help to avoid misdiagnosis and inappropriate treatment. It must be considered among the differential diagnoses of cervical lymphadenopathy. Here, we present a case of 20-year-old male who came to the hospital with complaints of mild fever, chills, fatigue and cervical lymphadenopathy. After radiological investigations an excisional biopsy of the cervical lymph node was done and the diagnosis of KFD was confirmed. Due to the paucity of cases in literature, reporting this case may help shed light on this rare disease.

**Key-words:** Kikuchi Fujimoto Disease, histiocytic necrotizing lymphadenitis, cervical lymphadenopathy, fever

**Introduction:**

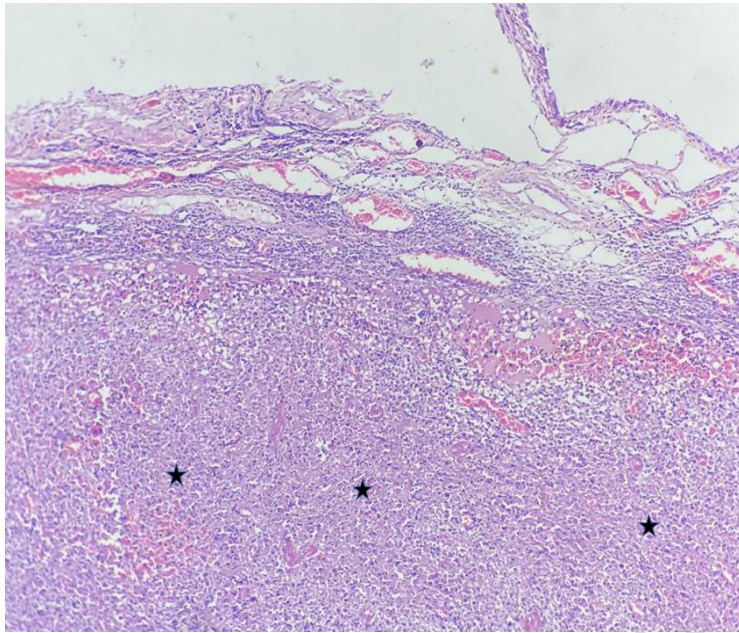
Kikuchi-Fujimoto disease (KFD) is an uncommon, self-limiting disease characterised by fever and regional lymphadenopathy with a startlingly close resemblance to some of the more serious diseases. The condition was named after the scientists who first identified it in Japan in 1972, Kikuchi and Fujimoto. The clinical course is variable and of mild to moderate severity with no confirmed aetiology. The cause is hypothesized to be viral, autoimmune or genetic. Though the distribution of cases is worldwide, there seems to be an increased occurrence in Asian females, usually in their third decade.<sup>[1]</sup> Patients usually present with persistent fever, tender cervical lymphadenopathy and elevated inflammatory markers. Due to the varied, non-specific clinical presentation of this entity, it is easily mistaken for other conditions with a 40% rate of misdiagnosis.<sup>[2]</sup>

**Case Report:**

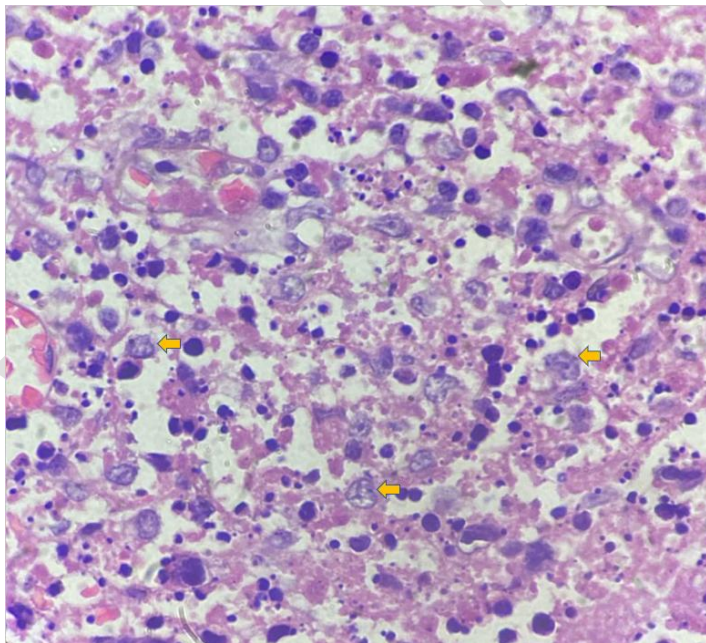
A 20-year-old male presented to the hospital with complaints of mild fever, chills, fatigue and palpable localized left sided neck swelling for a duration of about 2 weeks. The fever was on and off which was associated with malaise. The patient had suffered from rat fever 5 years ago. There was no history of tuberculosis in the family. He was taking paracetamol once a day to control fever. No history of significant weight loss, headache or insomnia.

General examination revealed palpable cervical lymphadenopathy on both sides and in the right axilla. The swelling was mildly tender, mobile, firm and non-matted. In no other sites of significant lymphadenopathy were found. Liver and spleen were not palpable. Oral cavity and nasopharynx were normal. Other systemic examination was unremarkable. Biochemical investigations and complete blood count were non-contributory. Mantoux test came out negative and chest x-ray was normal. Hence, ruling out the possibility of tuberculous lymphadenitis. CT chest showed enlarged carinal and mediastinal lymph nodes with normal lung fields. Anti-nuclear antibody (ANA) anti-double-stranded DNA (dsDNA) antibody were negative which excluded Systemic Lupus Erythematosus (SLE). Ultrasonography (USG) of the neck showed enlarged left cervical lymph node (Level III) with a size of 1.5 x 2 cm. A lymph node biopsy was advised. The patient reported only after about 3 weeks and at that time, the right cervical lymph node had become visibly enlarged with the same characteristics. The cervical lymph node biopsy on the right side was done which then revealed effaced architecture (Fig.1) with focus of necrosis characterised by karyorrhectic debris (Fig.2), rimmed by monocytoïd lymphocytes suggestive of acute necrotizing lymphadenitis. This gave a probable diagnosis of Kikuchi-Fujimoto Disease

(KFD). During this one month, the lymph nodes of the left side had regressed and ultimately disappeared. After a follow-up 2 weeks later, the patient remained afebrile and in good health.



**Fig.1 Effaced Lymph nodal architecture showing sub-capsular dilated sinusoids and large areas of necrosis (highlighted as stars)**



**Fig.2 High power field showing necrotic areas with karyorrhectic debris and histiocytoid cells with crescent shaped nucleus (yellow arrow marks)**

### **Discussion:**

Kikuchi-Fujimoto disease (KFD) is a rare lymphohistiocytic disorder which has been reported worldwide with increased cases in Asia. Between 1972 and 2014, a total of 733 cases have been reported worldwide in literature.<sup>[3]</sup> Various theories have been put forth regarding the etiopathogenesis of KFD. Initially, it was hypothesized that it was caused by eating raw fish but this was disproved later.<sup>[4]</sup> Viral aetiology was proposed based on the immunological tests. Epstein Barr virus (EBV), Human Herpes Virus (HHV) 6 and 8, and Parvovirus B19 are among the viral agents involved.<sup>[5]</sup> Autoimmune mechanisms have also been proven to play a role in the etiology, especially SLE which is the most common associated condition.<sup>[6]</sup> Oshima *et al* described apoptotic Fas and perforin pathways which were responsible for inducing necrotising lesions.<sup>[7]</sup>

The clinical features of KFD encompasses a wide range of non-specific signs and symptoms. According to Kucukardali *et al*, who had assessed 244 cases, lymphadenopathy was found in 100% of the cases, erythematous rashes in 10% and hepatosplenomegaly in 3% of the cases.<sup>[8]</sup> Skin is the most common organ to be involved in extranodal presentation.<sup>[9]</sup> Haematological investigations have revealed various findings including lymphocytosis, leukopenia, neutropenia, thrombocytopenia and anemia. However, the most common finding seems to be elevated Erythrocyte Sedimentation Rate (ESR).<sup>[6]</sup> Magnetic resonance imaging (MRI) and Computed tomography (CT) reveal non specific lymph node enlargement which may mimic tuberculosis, lymphoma or metastatic carcinoma.<sup>[10]</sup> No clear diagnostic criteria have been established for the identification of KFD. Excisional biopsy of lymph node is the only reliable means to reach a provisional diagnosis as done in the present case. Bennie *et al* suggested the classification histopathological changes into 3 types: proliferative, necrotizing and xanthomatous types.<sup>[11]</sup> Our case showed necrotizing type. Immunohistochemical staining may reveal myeloperoxidase (MPO), CD68, and CD4 expression in histiocytes, which is typical of KFD.<sup>[12]</sup>

Treatment protocols for KFD are yet to be developed, but recommendations are solely focused on symptomatic therapy and individualised expert advice. KFD is mostly self-limiting, which is why we chose not to actively treat the patient but to manage just the symptoms. It rarely requires specific treatment and usually subsides within 1-4 months. Glucocorticoids and hydroxychloroquine have been used in complicated cases.<sup>[3]</sup> It is important to recognize KFD so that time-consuming and expensive investigations for infections and lymphoproliferative diseases can be avoided.

### **Conclusion:**

Although KFD has been described almost 50 years ago, there are many questions regarding the condition that remain an enigma. Thus, there is a dire requirement of case reports and studies regarding aetiology and pathogenesis of this condition. Despite its rarity, KFD should be considered in the differential diagnosis of lymph node enlargement because its path and care vary significantly from those of tuberculosis, lymphoma and SLE.

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