

Kikuchi-Fujimoto disease: A rare case of pyrexia of unknown origin

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ABSTRACT

A young male was referred to a clinician for a complaint of fever of short duration with non-specific joint pain and treated for 1 week but after some time again presented with the same complaints with severe epigastric tenderness and vomiting. There was no past medical history before this episode. When cervical lymph node biopsy was performed gave us the diagnosis of histiocytic necrotizing lymphadenitis (Kikuchi-Fujimoto disease). A rare form of necrotizing lymphadenitis is an uncommon, benign, self-limiting disorder of obscure etiology. It affects mostly young adults of both genders. Clinically, it presents with fever and lymphadenopathy of a firm to rubbery consistency frequently involving cervical lymph nodes while weight loss, splenomegaly, and leukopenia in severely ill patients.

Key words: Cervical lymphadenopathy, Histiocytic necrotizing lymphadenitis, Lymphoma, Pyrexia of unknown origin, Sjogren's disease

Kikuchi-Fujimoto disease (KFD), a rare form of necrotizing lymphadenitis, is a self-limiting disorder of unknown Etiology. Initially described in young Japanese women [1], KFD was first reported in 1972 almost simultaneously by Kikuchi and Fujimoto as a lymphadenitis with focal proliferation of reticular cells accompanied by numerous histiocytes and extensive nuclear debris. KFD is a rare benign cause of fever and lymphadenopathy usually involving cervical lymph nodes. The disease has been reported worldwide in both genders across ethnic and age groups. The onset of KFD could be intense or sub-acute and can last up to weeks and, in some cases, even months. Unilateral or bilateral cervical tender lymphadenopathy associated with low-grade fever typically occurs in the posterior cervical triangle. The disease can cause generalized lymphadenopathy [2,3], though it is pretty rare. A low-grade fever may be reported in 50% of KFD patients, along with respiratory symptoms such as cough and headache. Less frequent symptoms of KFD include skin rash, weight loss, nausea, vomiting, sore throat, and night sweats. Apart from fever and tender cervical lymphadenopathy [2], leukopenia has been detected in 50% of KFD patients. Atypical lymphocytes, similar to those identified in Epstein-Barr virus (EBV) infection, are seen in peripheral blood studies. Extranodal involvement is relatively infrequent in KFD. Splenomegaly and hepatomegaly can also occur in a few cases. The bone marrow and nervous system involvement have also been reported among a few KFD patients.


CASE REPORT

A 21-year-old boy complained of fever, joint pain, and abdominal pain for the last 1 week.

Ultrasonography of the abdomen and X-ray chest PA view was normal. Blood cultures were sent; which came negative. Surprisingly, the fever subsided with 7-day treatment of empirical antibiotics in the form of third-generation cephalosporin considering clinical enteric fever. But again after 3 days, the fever started, and this time, it was with severe vomiting with epigastric pain.

Tenderness was present on per abdominal examination. Routine blood investigations showed C-reactive protein was 167 and erythrocyte sedimentation rate was 72. Due to the raised levels of acute phase reactants, further investigations were carried out. Contrast-enhanced computed tomography thorax with abdomen was done which shows multiple cervical, thoracic, and abdominal lymphadenopathy. These nodes were small to medium in size.

After all investigations and treatment, fever and epigastric pain did not subside; an excisional biopsy of the cervical lymph node was performed which showed the following picture of histiocytic necrotic lymph nodes. Cervical and abdominal lymphadenopathy showed subcentimeter nodes in the bilateral axillae which were insignificant, and multiple small mildly enlarged lymph nodes in the right iliac fossa along mesenteric and right iliac vessels without evidence of obvious internal necrosis or calcification suggestive of infective or inflammatory pathology (Fig. 1). Necrotic histiocytic lymph nodes showed residual lymphoid tissue and widespread necrosis showing characteristic crescent-shaped histiocytes. Furthermore, there were abundant histiocytes, apoptotic debris, and the lack of neutrophils (Fig. 2).

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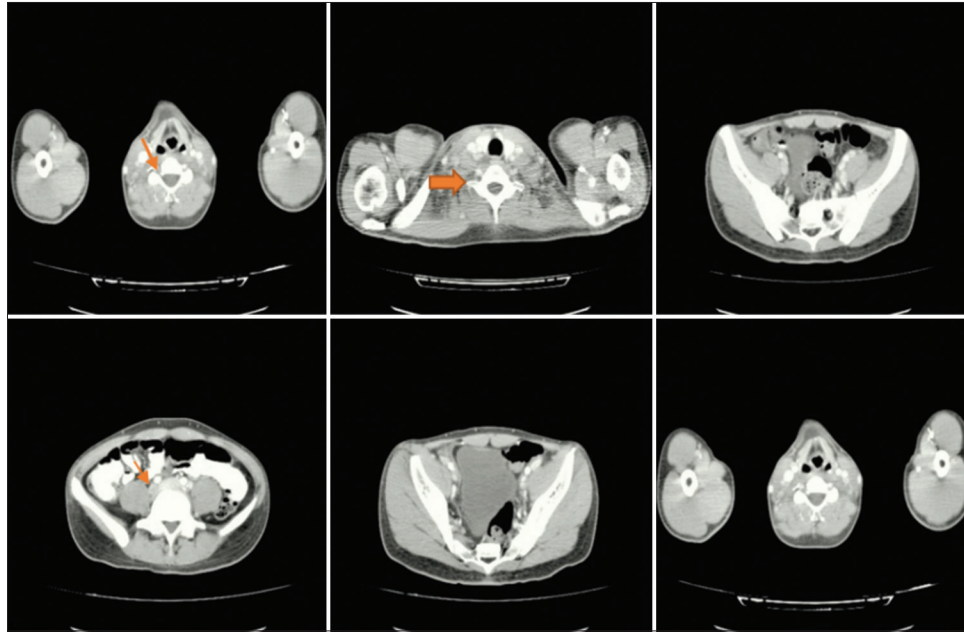


Figure 1: Cervical and abdominal lymphadenopathy (subcentimeter nodes in the bilateral axillae which were insignificant, and multiple small mildly enlarged lymph nodes in the right iliac fossa along mesenteric and right iliac vessels without evidence of obvious internal necrosis or calcification suggestive of infective or inflammatory pathology)

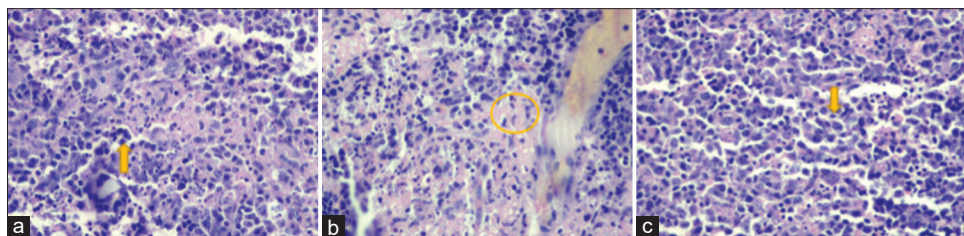


Figure 2: Necrotic histiocytic lymph nodes. (a) Low power view of lymph node with residual lymphoid tissue and widespread necrosis. (b) Medium power view of necrosis with abundant histiocytes, apoptotic debris, and lack of neutrophils. (c) High power view of necrosis showing characteristic crescent-shaped histiocytes

DISCUSSION

Clinically, as compared to adults, children are more prone to severe and protracted fever and have a higher risk of lymph node necrosis. Although the pathogenesis of KFD is not well known, a preceding viral infection or an autoimmune process are the two most common theories. Disease characteristics suggesting a viral etiology include inadequate antibiotic response and histopathological features representing a viral response; however, no association exists between KFD and a specific virus.

The disease is often linked to an autoimmune [1,2,4], resulting in an overactive T-cell-mediated immune response. It is sometimes related to *Yersinia enterocolitica* and *Toxoplasma Gondii* infections. Additionally, EBV and cytomegalovirus (CMV) may be considered in the pathogenesis of KFD. Other differentials of KFD include cat scratch disease and AIDS.

KFD typically takes a subacute course, evolving over multiple weeks. Physical examination and laboratory findings in KFD are wide-ranging and variable. The two most common findings are tender posterior cervical lymphadenopathy and fevers. However,

lymph node involvement can encompass other regions or be generalized. Low-grade fever and localized lymphadenopathy of KFD might be mistaken for tuberculosis. It serves as the most prevalent preliminary diagnosis for any long-term non-tender lymphadenopathy. Both illnesses also cause nocturnal sweats and weight loss. Fine-needle aspiration cytology is less invasive and cost-effective and the diagnostic time is quicker but its accuracy is only 50% [5]. However, on observing atypical clinical symptoms, it is recommended to perform a histological assessment of the affected lymph nodes for diagnosis. Based on the foregoing discussion, a viral or unknown infectious pathogen triggers an inflammatory response and causes KFD.

No specific treatment is available for KFD as it typically follows a self-limited course with spontaneous resolution occurring within 1–4 months. Supportive management is the mainstay of treatment involving antipyretics and analgesics to alleviate symptoms. For patients who have a co-diagnosis of KFD and other autoimmune diseases (with SLE being the most common), appropriate treatment for the secondary autoimmune disorder is required. This may involve using agents such as corticosteroids and hydroxychloroquine [6,7].

CONCLUSION

The various manifestations of KFD create significant diagnostic and therapeutic challenges. Lymph node biopsy is best for diagnosing KFD. Investigations should be continued until the primary etiology of the disease is found. Many clinical studies showed that KFD could occur due to an immune response to underlying autoimmune diseases, viral diseases, or bacterial infections like tuberculosis. Therefore, the diseases associated with KFD also need to be studied. Information sharing will help determine the etiology, prognosis, pathophysiology, and definitive treatment over the long term.

REFERENCES

1. Vithoosan S, Karunaratna T, Shanjeeban P, Piranavan P, Matthias T, Gamlaksha D, *et al.* Kikuchi-Fujimoto disease associated with systemic lupus erythematosus complicated with hemophagocytic lymphohistiocytosis: A case report. *J Med Case Rep* 2019;13:173.
2. Harrison J, Sukumaran S, Vijayan V. Systemic lupus erythematosus

lymphadenopathy presenting as Kikuchi-Fujimoto disease in an adolescent. *Cureus* 2023;15:e35304.

3. Gurung S, Pariyar RS, Karki S, Gautam A, Sapkota H. Kikuchi-Fujimoto disease in a 20-year-old female: A case report. *Ann Med Surg (Lond)* 2023;85:1894-6.
4. Al-Allaf AW, Yahia YM. Kikuchi-Fujimoto disease associated with Sjögren's syndrome: A case report. *Eur J Case Rep Intern Med* 2018;5:000856.
5. Cunha BA, Mickail N, Durie N, Pherez FM, Strollo S. Fever of unknown origin (FUO) caused by Kikuchi's disease mimicking lymphoma. *Heart Lung* 2009;38:450-6.
6. Mahajan T, Merriman RC, Stone MJ. Kikuchi-Fujimoto disease (histiocytic necrotizing lymphadenitis): Report of a case with other autoimmune manifestations. *Proc (Bayl Univ Med Cent)* 2007;20:149-51.
7. Masab M, Surmachevska N, Farooq H. Kikuchi disease. In: *StatPearls*. Treasure Island, FL: StatPearls Publishing; 2022.

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