# Kikuchi-Fujimoto disease: Need for awareness among paediatricians

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## Introduction

Kikuchi-Fujimoto Disease (KFD) or histiocytic necrotizing lymphadenitis is considered an idiopathic, enigmatic, self-limited syndrome. Patients commonly present with cervical lymphadenopathy and fever. There are few cases reported in the paediatric age group. Most times it is misdiagnosed as tuberculosis (TB). We report a 7 year old girl who was referred as a case of suspected TB which was later diagnosed as KFD.

## Case report

A 7 year old girl presented with high grade intermittent fever for 10 days. There was no history of rash over body or joint pain. She had a history of idiopathic thrombocytopenic purpura (ITP) 2 years back. There was no other significant family history and no history of contact with TB. She had received antibiotics for 7 days. Clinical examination revealed an enlarged 2cm x 2cm cervical lymph node on the right side. The rest of the systemic examination was normal. There was no hepatosplenomegaly. She was referred as a suspected case of tubercular lymphadenitis.

The total leucocyte count was 4.8 x $10^9$/L and the platelet count 191 x $10^9$/L. Her erythrocyte sedimentation rate was 24 mm in the first hour and her C-reactive protein was 1.2 mg/dl (normal <0.5 mg/dl). Her Mantoux test was negative. Her procalcitonin level was 1.2µg/L (normal <0.2µg/L). Her peripheral blood picture showed normal counts with normal differentials and reactive lymphocytes. Repeated blood cultures were normal and the chest x-ray was normal. Her anti-nuclear antibody (ANA) was weakly positive. Antibiotics were continued in view of the elevated procalcitonin level. Cervical lymph node biopsy showed irregular central and para-cortical necrosis with karyorrhectic foci formed predominantly by histiocytes and plasmacytoid monocytes (Figures 1 and 2) confirming KFD. Antibiotics were stopped later and after two weeks patient became asymptomatic. We did not use steroids.

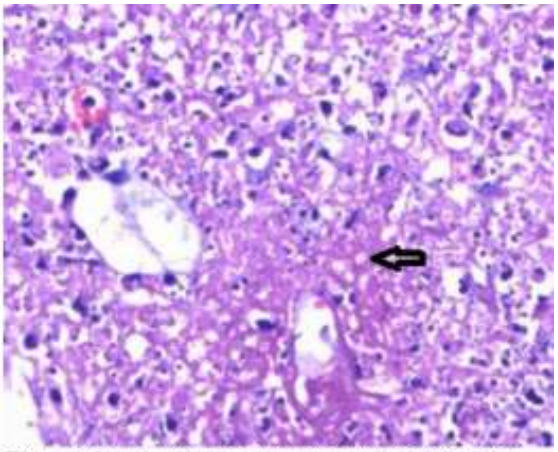

**Figure 1:** ***Lymph node biopsy low power microscopic picture showing foci of necrosis, karyorrhectic debris (shown by arrow) and histiocytes***

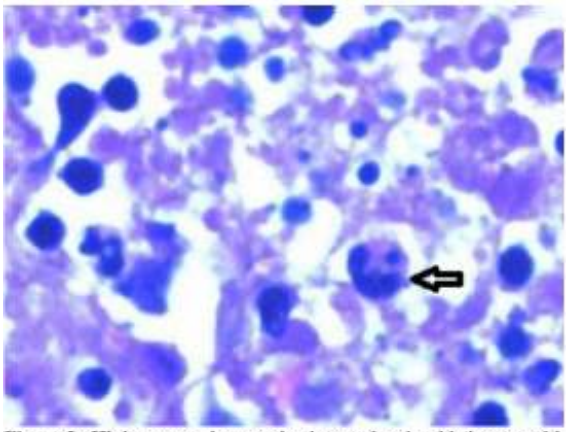

**Figure 2:** ***High power microscopic picture showing histiocytes with crescent-shaped nuclei and phagocytosed debris (shown by arrow)***

## Discussion

KFD was first described in 1972[1]. The aetiology remains unknown although an immune triggered mechanism by viral infections like Epstein-Bar virus, human T cell leukaemia virus type 1, parvovirus, cytomegalovirus and parainfluenza virus has been suspected[2]. Most studies mention female predominance in KFD (1.4 to 3:1)[3] but a few studies mention male dominance[4]. The common age group is early twenties with a few cases reported in the paediatric age group[5].

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In a review by Kucukardali Y *et al* of 244 cases, common symptoms reported were fever (35%), fatigue (7%) and joint pain (7%)[3]. In the same review, common findings reported were lymphadenopathy (100%), erythematous rashes (10%), arthritis (5%), hepatosplenomegaly (3%), leucopenia (43%), atypical lymphocytes (25%), high erythrocyte sedimentation rate (40%) and anaemia (23%)[3]. In a study of 79 patients by Kuo TT *et al.* there was 100% cervical node involvement[6]. In a study by Dorfman RF *et al.* of 108 patients over fifteen years of age, 83 patients had lymphadenopathy localized to one site, usually cervical and particularly posterior cervical with 3 patients having bilateral cervical adenopathy[7]. Lymph nodes are usually of size 1-2 cm and rarely larger up to 7 cm[6].

Diagnosis of KFD is invariably made on lymph node biopsy. On histopathology, there are two stages depending on disease progression: proliferative phase and necrotizing phase. Proliferative phase shows follicular hyperplasia and paracortical expansion by lymphocytes, T and B cell blasts, plasmacytoid monocytes and histiocytes with numerous apoptosis in the background whereas necrotizing phase show necrosis without a neutrophilic infiltrate with abundance of histiocytes[7]. The histiocytes often have crescentic nuclei and contain phagocytosed debris. Immuno-histochemical stains show CD68-positive plasmacytoid monocytes and histiocytes with predominantly CD8-positive T lymphocytes[8]. The absence of neutrophils in the necrotizing phase is helpful in distinguishing this condition from systemic lupus erythematosus (SLE) and drug-induced lymphadenopathy. KFD is considered a benign self-limited disease lasting over a few weeks and hence treatment is only symptomatic. One report of recurrent KFD mentions use of hydroxychloroquine[9]. Recurrence can occur in 3-4% of cases[10].

KFD is often misdiagnosed as tubercular lymphadenitis and started on anti-tubercular treatment[11,12]. As it is a self-limiting disease, patient gets cured in few weeks and it may be misinterpreted as a response to anti-tubercular medicines. We feel that KFD is an iceberg phenomenon with many cases in community which are misdiagnosed or not reported in literature. Some reports also mentions KFD being misdiagnosed as lymphoma and started on cytotoxic drugs[7].

One intriguing thing with KFD is its close association with SLE even some reporting KFD as unusual manifestation of SLE. Differentiation between SLE and KFD is also difficult as some histologic features overlap with SLE. In some patients with KFD, SLE follows after few years. KFD is reported in 4% to 13% SLE patients[2]. Thus, KFD patients need to be followed up for the development of SLE. Our patient had a previous history of ITP and her ANA was weakly positive which strongly points to autoimmune nature of the disease. Whether KFD should be considered one of the earlier manifestation of SLE or it should be considered a separate entity is a matter of research and debate.

In conclusion, KFD should be suspected in young paediatric patients with prolonged fever and cervical lymphadenopathy and they should be followed up for years for development of SLE. More awareness among the pediatricians is required to diagnose and report this disease. We also hope to get the answer to the question whether KFD should be considered a separate entity or a "forme fruste" of SLE.

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