

Case Report

Unexplained Fatigue in an Otherwise Healthy Man Linked to Kikuchi-Fujimoto Disease, A Case Report

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ABSTRACT

Kikuchi histiocytic necrotizing lymphadenitis is a benign and self-limited illness usually characterized by cervical lymphadenopathy and fever. We present a case of a 42-year male who complained of extreme fatigue for 2 weeks. On laboratory workup, he had leucopenia and thrombocytopenia with normal peripheral blood and bone marrow examination. The radiological investigation revealed multiple enlarged lymph nodes in the left axilla and left supraclavicular region. The subsequent excisional biopsy of the axillary node clinched the diagnosis of Kikuchi-Fujimoto disease. The patient was completely recovered and laboratory parameters were normal with supportive treatment. Kikuchi-Fujimoto disease should be considered in patients with unexplained fatigue with lymphadenopathy and early biopsy prevents unnecessary investigations as well as potentially harmful treatments.

Keywords: Kikuchi-Fujimoto disease; Lymphadenopathy; Unexplained fatigue

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INTRODUCTION

Kikuchi-Fujimoto disease (KFD) is a rare benign inflammatory disorder of unknown etiology. Typical clinical features include fever, anterior cervical lymphadenopathy, and night sweats. The hallmark histopathological finding is necrotizing lymphadenitis with the absence of neutrophils.¹ It is common in Asia and the affected individuals are mostly younger females.¹⁻³ The exact cause of KFD is unknown but viral or autoimmune etiology has been reported.⁴ The role of Epstein-Barr virus (EBV), as well as other viruses, in the pathogenesis of KFD remains controversial. The incidence of Human leukocyte antigen (HLA) class II genes, DPA1*01, and DPB1*0202 alleles is higher in patients with KFD than in healthy control subjects.⁵ These genes are extremely rare among Caucasians but common in Asian people.⁵ In a

study that described 244 patients with KFD, the most common signs and symptoms seen were lymphadenopathy in 100%, fever in 35%, rash in 10%, arthritis in 7%, fatigue in 7%, and hepatosplenomegaly in 3% of cases.⁶

Thus, KFD may rarely present with nonspecific symptoms like weakness and lymphadenitis in sites other than the cervical region. This is often confused with several other conditions like tuberculosis, EBV infection, Human Immunodeficiency (HIV) virus, Systemic lupus erythematosus (SLE), and malignancy. Here, we present a case of an adult male who complained of weakness that was unexplained and received numerous laboratory investigations before the final diagnosis of KFD was made.

CASE REPORT

A 42 years male visited the medical outpatient department with complaints of fatigue and extreme weakness of the lower leg bilaterally for two weeks. The patient also complained of low-grade fever. No significant finding on general and systemic examination was noted. His laboratory investigation revealed leucopenia and thrombocytopenia. Total count was 2,300/mm³ [N:48 L:38 M:8 E:6 B:0], hemoglobin was 15.5 gm/dl and platelet count was 72,000/ mm³. Organ function tests (liver, kidney, and thyroid) were all within normal limits. C-reactive protein (CRP) was increased to 13.6mg/L (<6.0) and erythrocyte sedimentation rate (ESR) was increased to 23 mm/hour (0-12 mm/hour). Dengue IgG/IgM antibody was negative. Malaria parasite antigen was negative. Serum lactate dehydrogenase, 8 am cortisol level and creatinine phosphokinase were normal. Peripheral blood smear revealed cytopenia. Vitamin B₁₂, folic acid, and serum iron were also normal. Bone marrow aspiration demonstrated markedly hypercellular marrow showing no abnormal cells, parasites, or granulomas. HIV and viral hepatitis screening were negative. The patient was not taking any herbal preparations and had not any recent travel history. He did not have any specific complaints besides weakness. Tuberculosis was ruled out. Work up for systemic lupus erythematosus and other autoimmune diseases were negative. Investigation for EBV capsid antigen and nuclear antigen and cytomegalovirus were negative. All these investigations were done because the patient had a progressive increasing weakness, and leukopenia with thrombocytopenia was deteriorating. Throughout these periods of investigations, the patient was being managed with prophylactic antibiotics.

The case was then discussed with other medical and surgical faculties. The contrast CT -scan of the chest and abdomen was done that revealed multiple enlarged lymph nodes in the left axilla and left the supraclavicular region with the largest 18×12 mm in size. Then, an excisional biopsy of six lymph nodes from the left axillary and supraclavicular area was done which showed several aggregates of histiocytes in the interfollicular area. A single necrotic focus with apoptotic debris devoid of neutrophils was seen in the largest node. No fungal elements were seen. Molecular genetic assay in tissue biopsy specimen for identification of resistance to rifampicin was not detected. No organisms were isolated after 48 hours of incubation of the lymph node. The immunohistochemistry study did not reveal any abnormality. The diagnosis of KFD was made based on the finding of a lymph node biopsy. The patient was then managed with paracetamol and multivitamins. He was advised to have complete bed rest and high-energy diets. On follow-up, after two weeks patient had no complaints and his blood counts were in the normal range. Informed consent was taken from the patient for publication of this case report.

DISCUSSION

KFD may present with nonspecific symptoms like weakness and viral flu-like prodrome, so several diseases such as tuberculosis, EBV infection, HIV, SLE, and malignancy should be considered in the differential diagnosis. Work out for EBV, CMV, HIV, SLE,

tuberculosis and hematological malignancy was negative in our case. Around 25–58% of patients experience leukopenia and 2–5% of patients experience leukocytosis in KFD.⁷ In the index case leukopenia and thrombocytopenia were seen and the severity increased day by day. The total leucocyte count was 2100/ mm³ and the total platelet count was 45,000/ mm³ when it reached its lowest value.

Histopathological findings in KFD include partially preserved nodal architecture with the expansion of the paracortex by patchy areas of fibrinoid necrosis with marked apoptosis and nuclear debris, surrounded by aggregates of histiocytes with crescentic nuclei, activated T-lymphocytes (immunoblasts), and characteristic absence of neutrophils and eosinophils.^{4,7} In the index case, excisional biopsy of the left axillary node demonstrated reactive and lymphoid follicles with a single necrotic focus with apoptosis, devoid of neutrophils. In KFD, CD30 positive cytotoxic T cells are abundant around necrotic areas which help to differentiate it from SLE.⁸ In immunohistochemistry, few immunoblasts around the necrotic area were positive for CD30 in this case.

Since the disease is a self-limited, only symptomatic treatment to relieve distressing complaints should be used like analgesics, antipyretics, and rest. The patient, in this case, was managed with supportive measures. KFD spontaneously resolves within 1–4 months; however, 3–4% of patients will experience recurrent episodes of KFD.⁹ Reoccurrence has been recorded after a period of 2-10 years of initial presentation.¹⁰

Various atypical presentation or association of KFD has been reported such as high levels of circulating Epstein-Barr viral DNA¹¹, lymphocytic meningitis,¹² autoimmune hemolytic anemia,¹³ Corona virus disease-19,¹⁴ relapsing polychondritis,¹⁵ acute appendicitis,¹⁶ periportal and retroperitoneal lymphadenopathy,¹⁷ fever of unknown origin,¹⁸ and acute renal failure.¹⁹ The consequence of various nonspecific clinical presentations of KFD is a broader differential diagnosis. Thus, it is easily mistaken for lymphoma, tuberculosis, viral diseases, and autoimmune diseases. The index case also suffered a wide range of investigations and tolerated unnecessary antibiotics treatment and hospital stay. Proper physical examination for identification of any enlarged lymph nodes and early biopsy in suspected cases prevents unnecessary investigations as well as iatrogenic effects.

CONCLUSIONS

KFD although is rare, should be considered in the differential diagnosis of chronic fatigue and lymphadenopathy in otherwise normal cases. An early biopsy in suspected cases prevents unnecessary investigations as well as potentially harmful treatments. Scientific reporting of Kikuchi-Fujimoto disease may lead to more recognition by healthcare providers and the prevention of unnecessary investigations.

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