

Kikuchi-fujimoto disease: histopathological and clinical review of a caseBelma Pehlivan¹, Muammer Karagoz², Şeyda Belli¹, Fatma Tokat³, Yesim Saglican³**Abstract**

Kikuchi-Fujimoto disease (KFD) or histiocytic necrotizing lymphadenitis is an idiopathic, benign, self-limited, rare disease. This disease is mostly encountered in Asia and in young adult. Cervical lymph node involvement is the most common symptom. In addition, fever, fatigue, increase in erythrocyte sedimentation rate, and leukocytopenia may also occur. A specific diagnosis and treatment for this disease has not been defined. The diagnosis of this disease however can be diagnosed with excision of lymph node and histopathological examination. KFD can often resolve spontaneously. If there is no spontaneous regression, oral corticosteroid therapy can be applied. In this case report, we were referred a rare case of Kikuchi-Fujimoto disease, presented with the cervical lymphadenopathy, increased erythrocyte sedimentation rate, and fever.

Keywords: Kikuchi-Fujimoto disease (KFD), histiocytic necrotizing lymphadenitis, cervical lymph node

Introduction

Kikuchi-Fujimoto disease (KFH) or histiocytic necrotizing lymphadenitis (HNL) is a rare, benign self-limited disease with unknown etiology [1, 2]. The disease was first described in 1972 by Fujimoto and Kikuchi [3]. The disease is most common in late 20s and early 30s among Asian women [3]. It commonly presents with posterior cervical lymphadenopathy, fever and night sweats [2, 4]. It typically has a benign course and 1-6 months after the diagnosis, it usually resolves spontaneously [3]. Microscopically, lymph node demonstrates par cortical coagulation necrosis, focal histiocytic proliferation, and karyorrhexis. There is currently no specific treatment for the disease [2].

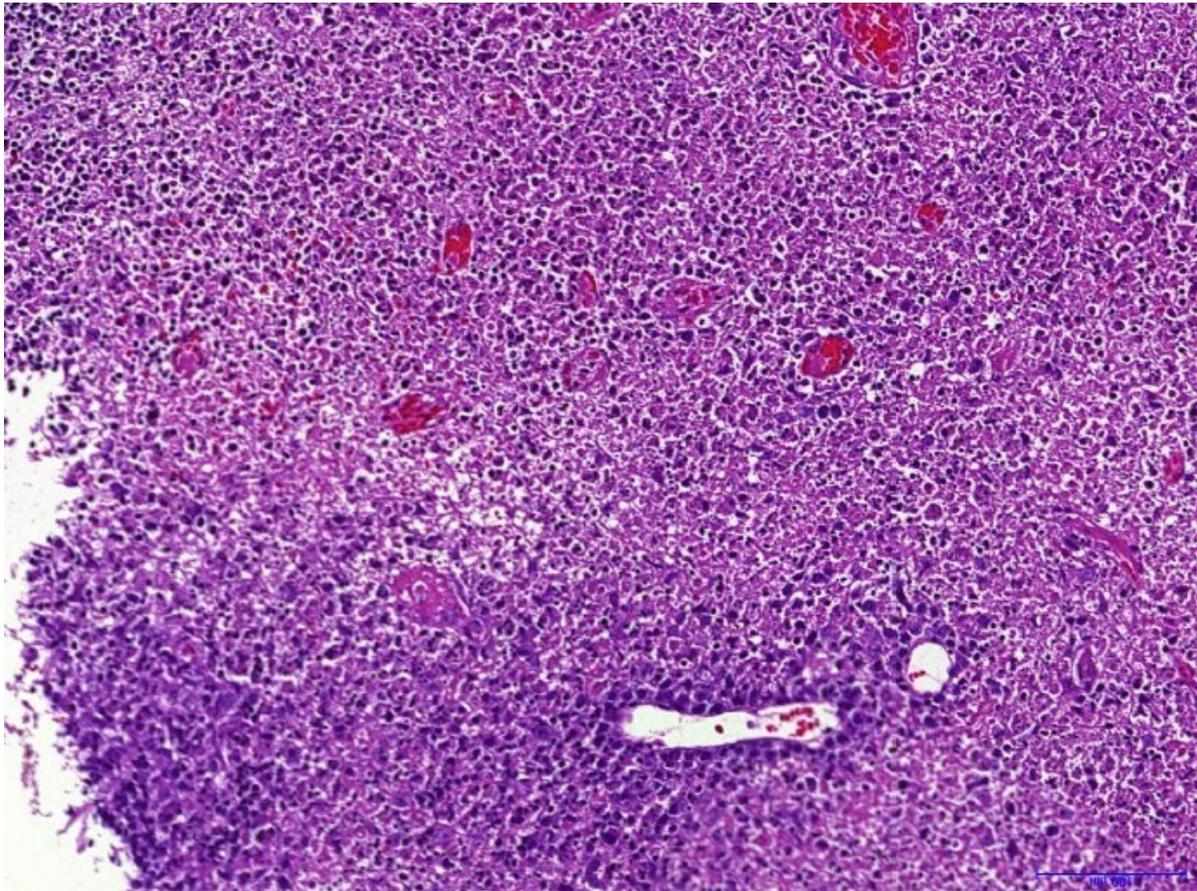
In this report, we discussed a 21 year old woman with Kikuchi-Fujimoto disease (KFD) who had had painful cervical lymphadenopathy and fever for 3 months, and resolved under treatment with prednisolone

Case

A twenty-one year old female patient applied to our outpatient clinic with painful neck mass and fever, which had first appeared 3 months earlier. She was a non-smoker with no past-medical history of chronic diseases (e.g. diabetes, hypertension, etc.). She had multiple painful

conglomerate palpable masses on her neck at levels of C2, C3, C4 and C5, of which the largest one had a diameter of 1.5 cm. At the same time, patient had a low grade fever. A prior fine needle aspiration biopsy performed in an outside facility was non-diagnostic. The patient had no symptoms regarding respiratory system. She had no other complaints including fatigue, night sweats, skin rash, significant weight loss, and decrease in appetite. Past-medical and family histories were insignificant for tuberculosis or anti-tuberculosis medication use. The mass had been recently noticed by the patient.

Her pulse was 98 beats/minute, respiratory rate was 20 breaths/minute, axillary temperature was 37.8 °C, and arterial blood pressure was 110/65 mmHg. Neck examination showed multiple masses on the left side at zones 2, 3, 4, and 5, which were painful, mobile, ovoid, rubbery, conglomerate masses with 2.5 cm in greatest dimension. She also had left supraclavicular lymphedema. Swelling was not fixed to the skin or subcutaneous tissues and the mass did not have fluctuation, fistulization or change in color of overlying skin. Patient had normal nasopharynx, oropharynx and larynx with no signs of pathologies. Respiratory system and other systems were normal on examination. The patient was not icteric and had no hepatosplenomegaly.



Picture 1: Necrosis, abundant karyorrhectic debris, distributed fibrin deposits and mononuclear cells

The patient had normal complete blood count and blood chemistry. Erythrocyte sedimentation rate was 49 mm/hour. Mantoux test was negative (induration was 5 cm/72 hours). The levels of anti-HIV, anti-Ebstein Barr virus (EBV), anti-cytomegalovirus (CMV), anti-Toxoplasma gondii and anti-Bartonella henselae titers were all negative. The levels of C-reactive protein (CRP), antinuclear antibodies (ANA), and angiotensin converting enzyme (ACE) were normal.

Cervical ultrasonography (USG) revealed conglomerate lymphadenopathies at levels 2 and 5 on the left side of the neck, of which the largest was at level 4 with 15x9 mm in dimensions. Echogenic hilus were not clearly visualized and they were suspicious for malignancy. Bilateral parotid, submandibular and thyroid glands had normal echogenicity. Abdominal USG and chest X-ray were normal. Fine needle aspiration biopsy performed in an outer facility was consistent with reactive lymphoid hyperplasia. She received cefuroxime for 10 days at a dose of 500 mg bid and did not resolve. Excisional lymph node biopsy was planned with a preliminary diagnosis of lymphoma.

Histopathological evaluation showed apoptotic cells at sites of necrosis, together with semilunar histiocytes which had phagocytosed nuclear debris. Neutrophils were absent at sites of necrosis and other sites had immunoblastic transformed cells and focal monocytoid B cell

hyperplasia, lymphocytes, and rare histiocytic cells constituting inflammatory infiltration (Figure 1). Immunohistochemical staining showed increased proliferation (45-50%) with ki-67, positivity with CD3 and CD8, positive reaction with CD68 in histiocytic cells, and partial CD4 and CD20 reactivity in lymphocytic cells. ALK-1 and CD30 were negative. Pathological diagnosis was necrotizing histiocytic lymphadenitis (Kikuchi-Fujimoto disease) (KFD).

Prednisolone was started at a dose of 25 mg/day and gradually tapered after 2 weeks of therapy. The patient was afebrile at day 2 and free of relapse at 6 months follow-up at outpatient clinic.

Discussion

KFD is a rare disease which is relatively more common in Asia and its etiology is unclear. Most of the current reports demonstrated a female/male ratio of 1/4 while some of the current data showed equal ratios [4]. The disease is characterized by cervical lymph node involvement (i.e. especially in the posterior triangle) in young adults at second and third decades [2, 3].

There are several theories to explain its etiology which includes viral infections and autoimmune phenomenon [5]. In addition to cervical lymphadenopathy, patients might have

fever, myalgia, leukopenia, and elevated erythrocyte sedimentation rate (ESR). Some of the reports in current literature discuss liver, spleen, kidney and skin involvement [5, 6]. However, our patient did not have any additional signs or symptoms other than cervical lymph node involvement, mildly elevated ESR and subfebrile fever. The duration of symptoms were longer than 2 months and the recurrence rate was 2-3% [5]. The duration of symptoms was 3 months in our patient as well. Some patients might have panuveitis, arthritis, aseptic meningitis, amygdalitis, or atypical symptoms with pneumonia and renal failure caused by opportunistic infections [5, 7]. Current literature reported a rare association between KFD and heart failure-related death, need for transplantation, febrile syndrome, and hemophagocytic syndrome [4, 5, 7].

The diagnosis of KFD can only be made with lymph node biopsy and histopathological analysis [4, 5]. Histopathological findings of this disease include paracortical coagulative necrosis with abundant karyorrhectic debris which distorts normal architecture of the lymph node. Abundant histiocytic and plasmacytoid monocytic infiltration and relative absence of neutrophils are common at sites of necrosis. The predominant lymphocyte type at lymph nodes is T cells and they stain positively with CD8 [2]. These results are consistent with histopathological and immunohistochemical findings of our patient.

Findings on computerized tomography and USG are similar to lymphoma [4, 5]. There are no specific radiological imaging findings in KFD [5]. Our preliminary diagnosis after ultrasonography was lymphoma and we confirmed the diagnosis only after histopathological analysis.

Differential diagnosis of this disease includes infectious agents including EBV, CMV, tuberculosis, Herpes Simplex virus (HSV), and HIV; and systemic lupus (SLE) [4, 7].

KFD has an excellent prognosis with minimal risk of death and it has a benign course. Early diagnosis of this disease is important to distinguish it from lymphoma and other diseases in order to avoid expensive and excessive diagnostic tests. Pathologists and clinicians should have a high index of suspicion to avoid wrong diagnosis. We aimed to increase awareness on this rare disease by presenting this case.

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