Kikuchi-Fujimoto disease mimicking hematological malignancy: a case report

Hakan Yarkıcı1, Faruk Elyiğit1, Ahmet Peker1, Dudu Solakoğlu Kahraman2, Nilgün Erbil2, Harun Akar1

1Department of Internal Medicine, University of Health Sciences, Tepecik Training and Research Hospital, İzmir, Turkey
2Department of Clinic of Pathology, University of Health Sciences, Tepecik Training and Research Hospital, İzmir, Turkey

ABSTRACT
Kikuchi-Fujimoto disease or histiocytic necrotizing lymphadenitis is a benign histopathological condition and a rare cause of lymphadenopathies. This disease which is seen in women around the age of 30 in the far east countries is generally presented with lymphadenopathy, fever, weight loss, and myalgia symptoms. In this article, we would like to present a case of Kikuchi-Fujimoto disease in the histopathology of the lymph node excision, which was examined in terms of lymphadenopathy.

Keywords: Kikuchi-Fujimoto disease, histiocytic necrotizing lymphadenitis, benign, lymphadenopathy

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Kikuchi-Fujimoto disease (KFD) was initially described in Japan. This disease is also known as histiocytic necrotizing lymphadenitis and the underlying pathogenesis of this disease is unclear. This disease which is seen in women around the age of 30 is generally presented with lymphadenopathy, fever, weight loss, and myalgia. In addition, it also affects men and it has wide age limits. It manifests with diffuse lymphadenopathy, especially in the head and neck region. Mediastinal lymphadenopathy, hepatosplenomegaly can also be seen in some patients. Rarely, skin lesions such as diffuse erythema and urticaria can be seen in the body. There is no specific laboratory test used to diagnose Kikuchi-Fujimoto disease. Increases in erythrocyte sedimentation rate and C-reactive protein (CRP) levels and mild leucopenia can be seen in these cases. Lactate dehydrogenase (LDH) levels and anti-nuclear antibody (ANA) titers may increase in complicated patients [1]. It is important to distinguish between infectious, rheumatologic, and malignant conditions as they are in differential diagnosis. In differential diagnosis, lymphoma, adenocarcinoma metastasis, tuberculosis, toxoplasmosis, cat scratch disease, human immun deficiency virus disease (HIV), parvovirus and systemic lupus erythematosus (SLE) should be considered [2]. The exact diagnosis of the disease is made by lymph node biopsy. We wanted to present a case of Kikuchi-Fujimoto disease, which was diagnosed via lymph node excision.

CASE PRESENTATION
An immigrant 25-year-old male patient with no known history of a disease was hospitalized in our Internal Medicine Clinic to investigate fatigue and high fever ongoing 15 days, weight loss of 8 kg in the
last 3 months, and mediastinal mass etiology on chest X-ray. He hadn’t a history of hematological disease, tuberculosis, contact with a case of tuberculosis and history of bite or contact with wild animals. On physical examination, his blood pressure was 120/80 mm Hg, pulse was 85/min, temperature was 36.5°C. Physical examination was normal except for the presence of lymphadenopathies in the bilateral neck, cervical and supravacular regions. Laboratory values showed that white blood cell count was 3300/μL, hemoglobin:11.8 g/dL, thrombocyte count: 313,000/μL, urea: 23 mg/dL, creatinine: 0.9 mg/dL, AST: 23 u/L, lactate dehydrogenase: 347 u/L, total bilirubin: 0.4 mg/dL, direct bilirubin: 0.02 mg/dL, albumin: 3.7 g/dL, sodium: 136 mmol/L, potassium: 4.14 mmol/L and calcium 9.9 mg/dL. The erythrocyte sedimentation rate was 42 mm/h and CRP was 4.2 mg/dl. HIV, antinuclear antibody, anti-ds DNA, rheumatoid factor, Ebstein-Barr virus (EBV) and cytomegalovirus (CMV) tests were negative. Computed tomography of the thorax revealed conglomerated mediastinal lymphadenopathies reaching 9×6 cm in size and lymphadenopathies in the left paracardiac areas. Ultrasonography of the neck showed a large number of heterogeneous lymph nodes, which lost their hilar echogenicity, with a size of 45×22 mm in bilateral supraclavicular region. Excision of the right supraclavicular lymph node was performed in the patient whose bone marrow biopsy examination was normal. Patchy fibrinoid necrosis with nuclear fragments in the lymph node, lymphohistiocytic infiltration (Figure 1), caryorectic nuclear debris in necrosis, surrounding histiocytes, lymphocytes and eosinophils (Figure 2) were observed in the biopsy. The biopsy was reported as subacute necrotizing lymphadenitis (Kikuchi-Fujimoto disease). After the diagnosis, the patient's supportive treatment continued. Outpatient controls were planned and he was discharged. Spontaneous regression in lymphadenopathy dimensions and clinical improvement was observed at 6 months follow-up.

**DISCUSSION**

Although the pathogenesis of KFD is not fully understood, it has been suggested that KFD is caused by apoptosis with hyperimmune or autoimmune mechanisms initiated by viral or other antigens [3, 4]. Viral or postviral etiologies also have been proposed. There are reports that stated the disease may be concomitant with infectious agents such as EBV, CMV, HHV-6, HIV, and toxoplasmosis and tuberculosis [1]. It has been reported in the literature that patients with SLE can subsequently develop KFD or that patients with KFD can develop SLE [5]. SLE is distinguished from KFH by the presence of hematoxylen-eosin bodies and dense plasma cells in the paracortical region in the histopathological examination [6]. In our case, the tests were negative.

![Figure 1](image1.jpg) Lymph node necrosis and lymphohistiocytic infiltration. H & E (×200)

![Figure 2](image2.jpg) Caryorectic nuclear debris in necrosis, surrounding histiocytes.
in terms of CMV, EBV and SLE. He also has a negative family history and a clinic in terms of tuberculosis. Although KFD usually involves the cervical lymph nodes, it may also involve the axillary, thoracic, abdominal, and inguinal lymph nodes [5]. Extranodal involvement has been rarely reported [7]. In our case, besides typical cervical involvement, mediastinal and paracardiac lymphadenopathy involvement was also observed. Although the disease has been reported frequently in Far Eastern countries and women [6], it is interesting that our case is Middle Eastern origin and male. For definitive diagnosis, excisional or incisional lymph node biopsy is required. The sensitivity of lymph node aspiration cytology is 55-60% and is associated with high false positive rates of diagnosis. We diagnosed the disease with excision of the right supraclavicular lymph node in our case. KFD is histopathologically characterized by focal necrotic foci, accompanied by diffuse karyorrhectic and nuclear debris, and histiocytes proliferating around them, locally with plasma cells and T lymphocytes [8]. It is differentiated from the lymphoma by the absence of cellular atypia and the absence of neutrophil leukocytes despite the presence of necrosis [6]. KFD has no specific treatment. In some cases, it is known that steroid therapy has been tested to reduce symptoms [9]. In general, KFD is a self-limited disease within 6 months. The recurrence rate of the disease was 3-4% [10]. We did not perform any specific treatment other than supportive care, and we observed clinical improvement within 6 months.

CONCLUSION

Histopathologic examination revealed a rare cause of lymphadenopathy in the benign nature of Kikuchi-Fujimoto disease, although the presence of multiple lymphadenopathies in our case suggests a possible preliminary diagnosis of hematologic malignancy on the first plan. Due to the lack of a specific diagnostic method, histopathologic examination of biopsy materials is regarded as the easiest and reliable way to achieve accurate diagnosis. Thus, early excisional biopsy in the presence of lymphadenopathy can prevent unnecessary investigations, reduce the cost of diagnosis and treatment, and can terminate the concern that the patient is malignant.

Informed consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of interest

The authors declared that there are no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

REFERENCES