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CASE REPORT / OLGU SUNUMU

Kikuchi-Fujimoto Disease in a Patient with Mediastinal Lymphadenopathy

Mediastinal Lenfadenopati ile Seyreden Bir Kikuchi Fujimoto Olgusu

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Abstract

Kikuchi-Fujimoto disease is a benign self-limited syndrome with distinct histopathologic characteristics. Clinical symptoms include cervical lymphadenopathy with tenderness, fever of medium grade, night sweats, nausea, vomiting, and a sore throat. It is a rare disease worldwide. Diagnosis is based on histopathologic findings from an excisional lymph node biopsy. We present the case of a 37-year-old male patient with a fever of 15 days' duration. Clinical examination revealed no other pathologic signs except for oral aphthous lesions and a fever of unknown origin. The patient's fever did not resolve after 15 days' follow-up, and the results of computed tomographic study of the thorax revealed several sites of mediastinal lymphadenopathy. The diagnosis of Kikuchi-Fujimoto disease (histiocytic necrotising lymphadenitis) was based on the results of pathologic examination of the biopsy specimen. The patient's signs and symptoms resolved without antibiotic therapy. This case report of a patient with a fever of unknown origin is presented because of the rare involvement of mediastinal lymphadenopathy without cervical lymphadenopathy. Kikuchi-Fujimoto disease should be considered in the differential diagnosis of the patient who presents with fever and mediastinal lymphadenopathy.

KEY WORDS: Fever, Kikuchi-Fujimoto disease, mediastinal lymphadenopathy

Özet

Kikuchi-Fujimoto hastalığı etyolojisi belli olmayan iyi seyirli, kendiliğinden düzelebilen ve kendine özgü histopatolojik görünümü olan bir hastalıktır. Klinikte bölgesel servikal lenfadenopati, hassasiyet, orta derecede ateş, gece terlemesi, bulantı, kusma ve boğaz ağrısı ile seyreder. Dünya çapında son derece nadir bir hastalıktır. Tanısı eksizyonel lenf nodu biyopsisi ve histopatolojik bulgular ile konur. Olgumuz, 37 yaşında erkek 15 gündür devam eden ateş nedeniyle başvurdu. Fizik muayenesinde oral aftöz lezyonlar ve ateş dışında patoloji saptanmadı. Takiplerinde ateşi olan hastanın bilgisayarlı toraks tomografisinde mediastinal lenfadenopatiler saptandı. Lenfadenopati biyopsisi yapıldı ve patolojik incelemesinde Kikuchi-Fujimoto lenfadeniti (Histiyositik nekrotizan lenfadenit) bulundu. Antibiyotik verilmeden izlenen hastada kendiliğinden iyileşme gözlendi. Nedeni bilinmeyen ateş etyolojisi araştırılan bu hastada servikal lenfadenopati olmaksızın mediastinal lenfadenopatinin olduğu bu olgu nadir bir tutulum olması nedeniyle bildirilmiştir. Ateş ve mediastinal lenfadenopatinin olduğu olgularda da Kikuchi-Fujimoto hastalığı akla gelmelidir.

ANAHTAR SÖZCÜKLER: Ateş, Kikuchi-Fujimoto hastalığı, mediastinal lenfadenopati

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INTRODUCTION

Kikuchi-Fujimoto disease (Kikuchi's lymphadenitis, Kikuchi's disease, histiocytic necrotising lymphadenitis, subacute necrotising lymphadenitis) is a self-limited benign syndrome first described by Kikuchi and Fujimoto in 1972. Primarily a disease of young women, it is characterised by cervical lymphadenopathy that resolves spontaneously [1]. The cause of Kikuchi-Fujimoto disease has not been identified, although a viral or autoimmune origin is suspected. Many pathogens, such as Epstein-Barr virus (EBV), human herpesvirus 6 (HHV-6), human herpesvirus 8 (HHV-8), human immunodeficiency virus (HIV) and parvovirus B19, may be involved in the pathogenesis of Kikuchi-Fujimoto disease [2]. Histopathologic examination is necessary for a definitive diagnosis, but diagnostic difficulty may lead to a misdiagnosis of lymphoma or an autoimmune disease such as systemic lupus erythematosus or infectious lymphadenitis, which can result in the unnecessary use of chemotherapeutic medications and steroids [1].

Lymphadenopathy in patients with Kikuchi-Fujimoto disease usually develops in the cervical region, although peripheral lymphadenopathy at other sites and abdominal lymphadenopathy have also been reported [3]. We present a patient with Kikuchi-Fujimoto disease whose examination for a fever of unknown origin revealed only mediastinal lymphadenopathy.

This case was presented in the 32nd Turkish Congress of Microbiology (September 12-16, 2006, Antalya).
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CASE PRESENTATION

A 37-year-old male patient presented with complaints of alternating chills and fever that peaked at 38.5ºC, both of which had persisted for 15 days. During the 10 days before he presented to our clinic, oral aphthous lesions had also developed. He denied weight loss and had not experienced night sweats, arthralgia, myalgia, or any type of skin rash. Oral clarithromycin 500 mg b.d. had been prescribed by his personal physician five days earlier but the fever did not resolve as a result of this treatment. Physical examination revealed an axillary temperature of 36.6ºC, a pulse rate of 84 bpm and a blood pressure of 110/60 mm Hg. There was no peripheral lymphadenopathy. Examination of other organ systems did not yield any abnormality except for oral aphthous lesions. The patient was admitted to hospital so that the cause of his fever of unknown origin could be determined. During his hospital stay, his febrile episodes peaked at 38ºC. Laboratory examinations yielded the following results, all of which were within normal limits: white blood cell count 4900/mm^3; haemoglobin 13.8 g/dL; haematocrit 39%; platelets 225000/mm^3; and sedimentation rate 9 mm/h. The results of a peripheral blood smear showed 66% polymorphonuclear leukocytes, 14% lymphocytes, 10% monocytes, and 10% eosinophils. The result of analysis of a smear for malaria was negative, and the patient's biochemical test results were as follows: CRP 23 mg/L (reference range, 0-10 mg/L); RF 31 IU/mL (reference range, 0-20 IU/mL) ALT 45 U/L (reference range, 0-41 U/L) and LDH 367 U/L (reference range, 100-210 U/L). The results of serological tests for the following entities were negative: Cytomegalovirus, Epstein-Barr virus, rubella, Toxoplasma, Herpes simplex (human herpesvirus types 1 and 2), Parvovirus B19, HBsAg, anti-HBcIgM, anti-HAVIgM, anti-HCV, anti-HIV, Brucella, Gruber-Widal reaction, antinuclear antibody, anti-dsDNA, pANCA, cANCA, anti-SS-A, anti-SS-B, and a PPD test. Findings from a PA radiographic study of the thorax and abdominal ultrasonography were within normal limits, and blood cultures drawn during the patient's febrile period were found to be negative. Thoracoabdominal computed tomographic evaluations were performed to determine the cause of the fever of unknown origin. Several enlarged paratracheal and prevascular lymph nodes, the largest of which was 22×15 mm, were detected in the thorax. There was no abdominal lymphadenopathy. A mediastinal lymph node was excised via mediastinoscopy, and its histopathologic examination revealed a distorted lymph node structure due to focal areas of necrosis. The number of CD68 stained histiocytes was increased around the necrotic areas. There were no neutrophils, and the necrotic areas were filled with karyorrhectic debris (Figure 1). These findings confirmed the diagnosis of Kikuchi-Fujimoto disease. The patient was discharged after his fever spontaneously decreased, and a schedule of follow-up visits was recommended. He received no antibiotic treatment after his discharge from hospital, and he did not experience a fever or any other symptom during the follow-up period. A computed tomographic scan of the thorax performed six months later showed that the largest of his mediastinal prevascular, paratracheal, and aortopulmonary lymph nodes was 10×5 mm, which, when compared with the results of the previous study, indicated a spontaneous reduction in size (Figure 2). At the time of writing, nine months after the conclusion of the follow-up period, the patient is still asymptomatic. The written consent of the patient allows publishing of his data.

DISCUSSION

Kikuchi-Fujimoto disease usually produces a clinical picture characterised by cervical lymphadenopathy and fever, especially in young women. Lack of awareness of the disease may contribute to its rarity [1]. Although it is common in women younger than 30 years of age, cases have been reported in all age groups. The disease is characterised by multiple tender lymphadenopathies, which resist antibiotic treatment and result in hyperaemia of the skin overlying the involved lymph nodes. Fever, headache, nausea, vomiting, malaise, weight loss, arthralgia, and splenomegaly may also occur. Slight neutropenia and lymphocytosis develop in 50% of patients with Kikuchi-Fujimoto disease. Extranodal involvement has also been described, and skin manifestations, such papulopustular lesions, may be observed [2,4]. Because it can cause cervical lymphadenopathy, Kikuchi-Fujimoto disease must be included in the differential diagnosis of patients with suspected tuberculosis, systemic lupus erythematosus, malignant lymphoma, sarcoidosis, Kawasaki disease, toxoplasmosis, infectious mononucleosis, infection caused by *Yersinia*, or cat scratch disease [2].

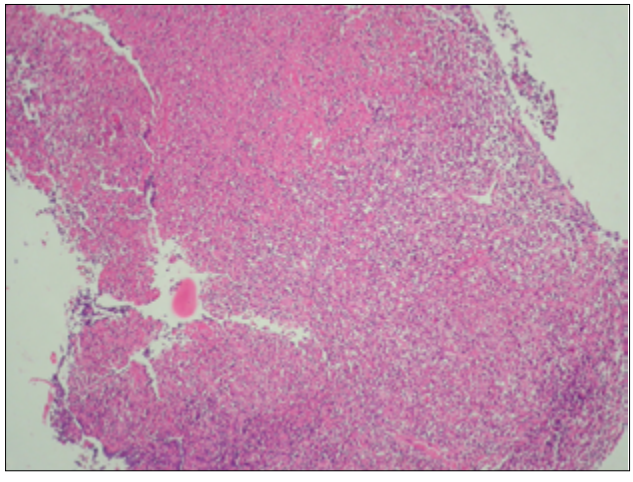

Figure 1. Diffuse necrotic area is observed in the upper part of the lymph node
(hematoxylin-eosin stain, original magnification ×10)

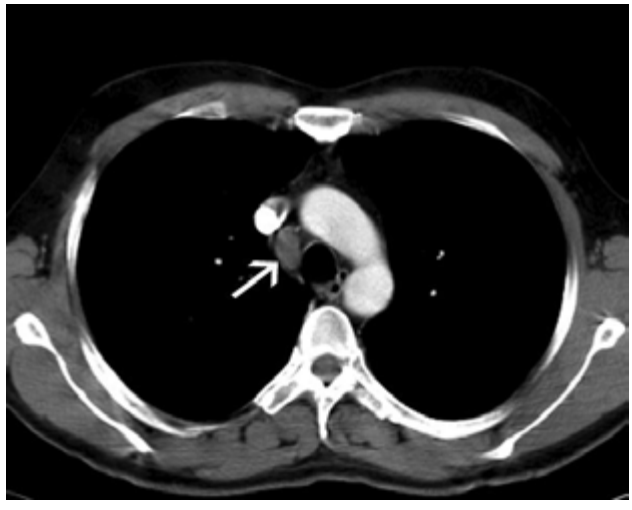

Figure 2. The first computed tomographic study of the patient's thorax shows mediastinal lymphadenopathy

Kikuchi-Fujimoto disease was not initially considered in the differential diagnosis of the patient described in this report, who presented with nonspecific complaints. Fever, which is usually low grade, is the main symptom in 30% to 50% of patients with Kikuchi-Fujimoto disease [2,5]. The fever may continue undiminished for a week, and occasionally persists for a month or longer [6]. In our patient, the fever did not exceed 38.5°C and persisted for two months, as it has in similar cases in the literature. Oral aphthous lesions, which have been reported in 1% of patients with Kikuchi-Fujimoto disease, and fever were the major physical findings in our patient [7].

Lymphadenopathy is present in virtually all patients with Kikuchi-Fujimoto disease. Usually, cervical lymph nodes are involved. In one study, cervical lymphadenopathy was identified in 79% of patients with Kikuchi-Fujimoto disease, axillary and cervical lymphadenopathy in 8%, isolated axillary lymphadenopathy in 5%, and generalised lymphadenopathy in 5%. Inguinal, mesenteric, and cutaneous lymph node involvement is relatively rare [7]. There was no cervical or axillary lymphadenopathy in our patient, but computed tomographic study revealed several enlarged paratracheal and prevascular lymph nodes, the largest of which was 22×15 mm in size. To our knowledge, mediastinal lymphadenopathy has only been reported in some cases of patients with Kikuchi-Fujimoto disease. To illustrate, one previously reported case was that of a young woman with mediastinal involvement and recurrent disease, and another was that of a patient with Kikuchi-Fujimoto disease, mediastinal lymphadenopathy caused by infection with Entamoeba histolytica, and axillary and cervical lymphadenopathy [8,9]. The third case was that of a patient with Kikuchi-Fujimoto disease and mediastinal lymphadenopathy without cervical lymphadenopathy as in our case [10].

There is no specific treatment for Kikuchi-Fujimoto disease, which is benign and usually resolves spontaneously. Recurrence develops in 3% to 4% of patients [2]. The lymphadenopathy caused by Kikuchi-Fujimoto disease usually resolves in several weeks or months. Analgesic, antipyretic, and nonsteroidal anti-inflammatory drugs may be administered to decrease fever and relieve tenderness of the lymph nodes. Corticosteroids are recommended for patients with severe extranodal involvement or generalised Kikuchi-Fujimoto disease [2]. Treatment with analgesic medications, nonsteroidal anti-inflammatory drugs, or steroids was not administered to our patient because of his favourable condition. Both his fever and his lymphadenopathy resolved during the follow-up period.

When geographical distribution is considered in the investigation of fever of unknown origin, Kikuchi-Fujimoto disease (of which fever is a classic sign) frequently occurs in Japan as necrotising lymphadenitis [7]. However, Kikuchi-Fujimoto disease should also be considered in the investigation of fever of unknown origin in regions in which the disease is relatively uncommon.

In conclusion, Kikuchi-Fujimoto disease was not considered in the differential diagnosis of our patient, who presented with nonspecific symptoms and findings. Kikuchi-Fujimoto is usually a disease of young women, in whom it causes cervical lymphadenopathy and fever [2,5]. Our case was a male patient without cervical lymphadenopathy. Mediastinal lymphadenopathy was detected by computed tomographic studies of the thorax, which were performed to determine the cause of his persistent fever. We suggest that Kikuchi-Fujimoto disease should be considered in patients with a fever of unknown origin and mediastinal lymphadenopathy.

Informed Consent: Written informed consent was obtained from patient who participated in this case.

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