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A Rare Case of Kikuchi-Fujimoto Disease in a Young Female Patient

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABD 1 Le Hoan
AE 1 Le Minh Hang
BD 2 Le Tuan Linh
EF 2 Thieu Thi Tra My
C 3 Tran Ngoc Minh
DF 3 Dang Duc Thinh
ABDE 2 Nguyen Ngoc Cuong

1 Department of Respiratory Medicine, Hanoi Medical University Hospital, Hanoi, Vietnam
2 Diagnostic Imaging and Interventional Radiology Center, Hanoi Medical University Hospital, Hanoi, Vietnam
3 Department of Pathology, Hanoi Medical University Hospital, Hanoi, Vietnam

Corresponding Author: Nguyen Ngoc Cuong, e-mail: cuoncdha@hmuh.vn
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Patient: Female, 25-year-old
Final Diagnosis: Kikuchi-Fujimoto disease
Symptoms: Neck pain • palpable mass neck
Medication: —
Clinical Procedure: —
Specialty: Pathology • Pulmonology • Radiology

Objective: Rare disease

Background: Kikuchi-Fujimoto disease (KFD) is a rare benign and usually local lymphadenopathy that typically occurs in young women. Patients with it usually have non-specific symptoms, such as fever in the afternoon, cervical lymphadenitis, and weight loss. Posterior cervical lymphadenopathy is the most common manifestation of KFD. The symptoms often last for a few weeks and then resolve spontaneously. The cause of KFD is unknown; however, it is considered to be related to some infectious agents, as well as several autoimmune diseases. Because of the non-specific symptoms and the rarity of KFD, the cervical lymphadenopathy associated with it can be misdiagnosed as coming from a more common condition. Making a correct diagnosis requires histology of the affected lymph nodes.

Case Report: Here, we describe the case of a 25-year-old Vietnamese woman who presented with mild fever in the afternoons and enlarged cervical lymph nodes with no local sign of inflammation. She was initially believed to have tubercular lymphadenitis because of her symptoms and the high prevalence of tuberculosis in Vietnam. However, she had no respiratory symptoms and tested negative on QuantiFERON-TB Gold. Pathology from the patient's lymph node specimen showed an abnormal inflammatory reaction in the tissue. Her lesions were suspected to have been caused by KFD and she was treated successfully with nonsteroidal anti-inflammatory drug (NSAID) therapy.

Conclusions: KFD is a benign disease that manifests with common symptoms. The diagnosis is based on biopsy of a specimen and pathology results. No treatment is required in patients who have no symptoms. Patients with symptoms usually respond well to a short course of NSAID therapy.

Keywords: Lymphadenitis • Neck Pain • Tuberculosis, Lymph Node

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/933377

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Background

Kikuchi-Fujimoto disease (KFD) is a rare, benign, and self-limited lymphadenopathy [1]. This disease was first described by Kikuchi and Fujimoto in Japan in 1972 [2,3]. The exact incidence rate is unknown. A statistical analysis by Kim et al [4] showed that worldwide, 733 patients were diagnosed with KJD between 2001 and 2012. It mainly affects Asians between ages 20 and 35 years and has a female predominance, with a ratio of 2: 1 [5]. KFD typically manifests with cervical lymphadenopathy. The clinical presentation is non-specific and it can be misdiagnosed as tuberculosis (TB), lymphoma, or a metastatic tumor. Here, we report on a case of KFD in a 25-year-old Asian woman who was misdiagnosed with TB lymphadenitis. The diagnosis of KFD was confirmed with histopathology and the patient recovered completely after treatment.

Case Report

A 25-year-old Vietnamese woman was admitted to the hospital because she had been experiencing mild fever in the afternoons and swelling in her right neck for several weeks. She had no history of allergy, travel, or medical conditions. She reported not having a cat or being bitten or scratched by one. She had no cough, dyspnea, chest pain, headache, or weight loss. She had no contact with anyone who had TB, either at home or in her workplace.

The patient's vital signs were a respiratory rate of 17 breaths/min, temperature of 38°C, blood pressure of 130/70 mmHg, and a heart rate of 90 beats/min. Physical examination revealed multiple soft, tender masses on the right side of her neck, which measured approximately 2 cm in diameter; no changes were evident in the skin overlying them.The patient's oral cavity, ears, nose, and throat, and thyroid gland were examined first because acute cervical lymphadenopathy in those areas is common with an infection, but no lesion was found. Cardiovascular, neurologic, and respiratory testing was normal. The patient's abdomen was soft with normal bowel sounds.

Results from laboratory tests (complete blood count, creatinine, electrolytes, C-reactive protein, and erythrocyte sedimentation rate) were normal. An ultrasound of the patient's neck showed enlarged right supraclavicular lymph nodes (**Figure 1**) but no lesions in the thyroid or parotid glands. Because she was Vietnamese, the patient was at risk for TB, although she reported having no contacts with anyone with the disease. Because she had prolonged, mild fever in the afternoons for several weeks before being admitted to the hospital and had abnormal cervical lymph nodes, we initially diagnosed her with TB lymphadenitis. However, a chest X-ray was normal (**Figure 2**) and a QuantiFERON-TB Gold (QFT-G) test was negative, making the TB lymphadenitis diagnosis less likely.

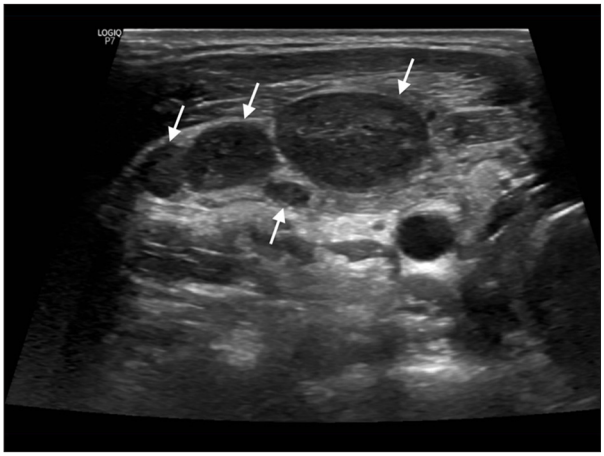

Figure 1. An ultrasound of the patient on admission revealed multiple lymph nodes on the right side of her neck (arrows). The largest one measured 2 cm along its short axis. Although some of the lymph nodes were enlarged and hypoechoic, they were well-circumscribed.

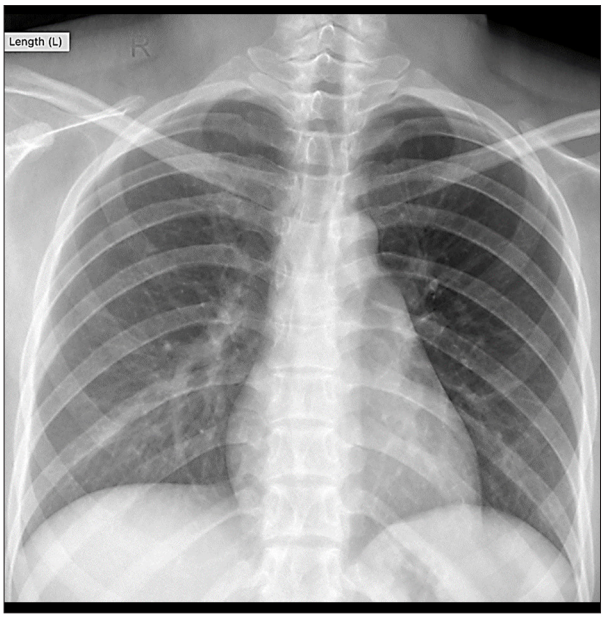

Figure 2. Chest X-ray showing a normal appearance.

To screen the patient for systemic lupus erythematosus (SLE), antinuclear antibody and anti-dsDNA tests were performed, all of which were negative. Epstein-Barr virus (EBV) and cytomegalovirus (CMV) also can cause cervical lymphadenopathy, but CMV immunoglobulin M (IgM) and EBV IgM tests were negative.

We then performed noninvasive imaging, including whole-body magnetic resonance imaging (MRI) and a thoracic-abdominal computed tomography (CT) scan, to rule out lymph node metastasis. The MRI showed only abnormal cervical lymph nodes (**Figure 3**). No abnormalities were seen on the thoracic-abdominal

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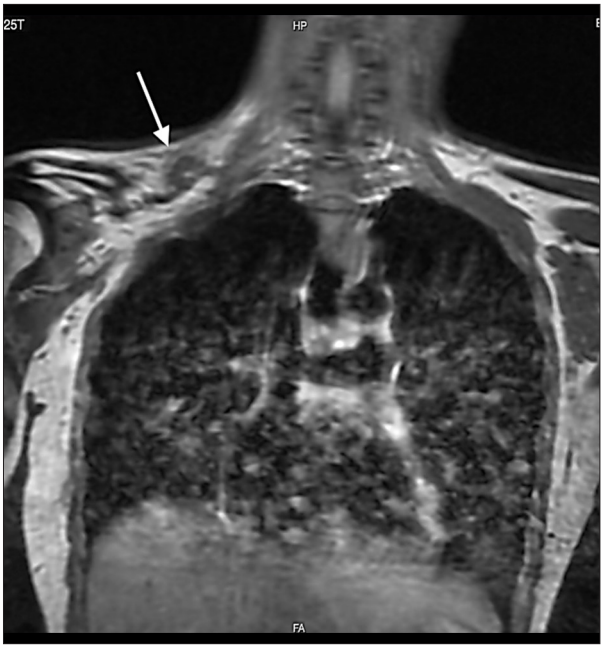

Figure 3. Cervical thoracic magnetic resonance imaging. On a T1-weighted coronal image, right supraclavicular lymph nodes were visible (arrow). Note the fatty stranding around the lymph node, which indicates an inflammatory reaction in that area.

CT scan. A percutaneous ultrasound-guided biopsy of the patient's supraclavicular lymph node was then performed. The histopathology showed paracortical lymph node expansion with patchy, well-circumscribed areas of necrosis with nuclear debris and no neutrophils. Given the results, we suspected that the patient had KFD (**Figure 4**). She was treated with meloxicam 15 mg per day and her symptoms abated within 2 weeks. A subsequent ultrasound showed that the NSAID therapy had resolved the abnormal supraclavicular lymph nodes in her neck.

Discussion

KFD or histiocytic necrotizing lymphadenitis is an uncommon cause of lymphadenopathy [1]. It mostly occurs in patients in Asia and rarely in the United States [1]. The exact incidence of KFD remains unclear because this disease is easily mistaken for other causes of lymphadenopathy. A review by Kucukardali et al [6] in 2007 identified 330 cases of KFD since 1991. A report by Feder et al [7] in 2014 revealed that 10 cases had been reported in the United States. The etiology and pathogenesis of KFD remain unclear; however, infectious agents and an autoimmune response are considered the 2 main causes [8]. Infections that have been proposed as possible etiologic agents of KFD include EBV, varicella-zoster virus, human herpesviruses 6, 7, and 8, parvovirus B19, paramyxovirus, parainfluenza virus, rubella, and human T-lymphotropic virus type 1 [4]. An association also has been found between autoimmune conditions and KFD, especially SLE [1].

Clinically, the onset of KFD can be acute or subacute and it usually resolves spontaneously within several weeks [9]. Lymphadenopathy is observed in 100% of patients; in up to 90% of cases, it is posterior cervical, and in less than 22% of cases it is generalized [4,5]. Lymph nodes range in size from 0.5 cm to 4.0 cm [1]. Fever and tender and painful lymph nodes also are common in patients with KFD [1]. Up to 90% of them present with fever [4] ranging from 38.6°C to 40.5°C, which lasts from 1 week to 7 weeks [1]. Tender lymph nodes are present in 82% of patients with KFD [4]. Other symptoms include weight loss, nausea, vomiting, weakness, headache, night sweats, and upper respiratory symptoms [9]. The skin is the most commonly affected organ aside from lymph nodes [5]. Patients with KFD can have papules, facial palmar erythema, plaques, or nodules [1].

Results of laboratory testing for KFD are non-specific, including findings of anemia, leukopenia, leukocytosis, thrombocytopenia, and elevations in liver enzymes, lactate-dehydrogenase levels, and erythrocyte sedimentation rate [4,10]. On imaging, the lymph nodes in patients with KFD have an irregular outer rim and they are less round than is seen with lymphoma [5,11]. Ultrasound reveals a hypoechoic center with a hyperechoic rim [11]. CT shows homogeneous enhancement and no significant necrosis [10].

KFD is diagnosed based on histopathologic findings obtained from fine-needle aspiration or biopsy of the affected lymph node after other diseases have been excluded [4]. Histologic findings include preserved nodal architecture, varying degrees of coagulative necrosis in the paracortical regions with abundant karyorrhectic debris, and an absence of eosinophils or neutrophils [10]. Crescent-shaped histiocytes and plasmacytoid monocytes are normally seen surrounding necrotic areas [5]. In patients with CKD, histiocytes express CD68, myeloperoxidase, and CD4 [5].

Differential diagnosis of lymphadenopathy includes infectious agents, such as TB, toxoplasmosis, *Bartonella henselae*, HIV, and EBV; inflammation; SLE; lymphoma; and metastasis [1]. Serologic testing can suggest other causes of lymphadenopathy, such as cat-scratch disease or toxoplasmosis, and histological results can be used to exclude cancer [1].

Because KFD is self-limiting and typically resolves within a few months, observation is the most common approach to management [5,8]. NSAIDs and corticosteroids are used to treat patients who have symptoms or extranodal lymphoid organ involvement [5,8]. No guidelines exist for dosing and duration of corticosteroids in management of KFD [1,5]. In 4% of patients, KFD recurs at up to 8 years after their initial presentation [5].

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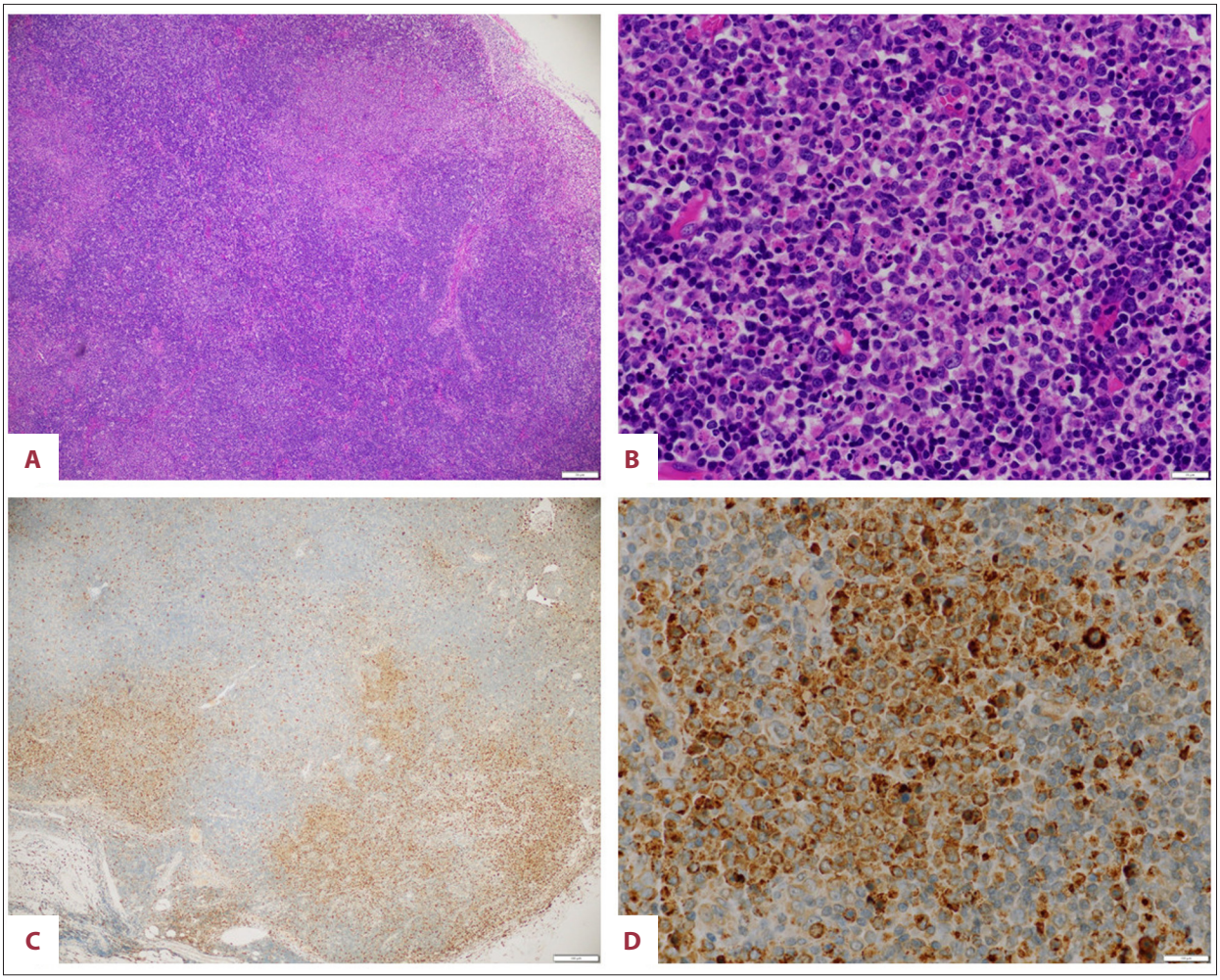

Figure 4. Microscopic view of the affected lymph node showing paracortical, fairly well-circumscribed necrotic lesions (**A**) with starry sky appearance, karyorrhexis, and phagocytic cells and plasmacytoid monocytes and (**B**) no neutrophils. Paracortical necrotic lesions were indicated by the expression of CD68 seen in the phagocytic cells at (**C**) low- and (**D**) high-power magnification.

Therefore, long-term follow-up plays an important role in assessing the recurrence rate.

The patient in the present case was young and Asian. Because she had cervical lymphadenopathy and fever in the afternoons and an ultrasound of her neck showed multiple hypoechoic lymph nodes, we considered TB lymphadenitis first in our differential diagnosis. However, the patient had no symptoms of respiratory disease, her chest X-ray was normal, and a QFT-G test was negative. CMV and EBV infection were excluded because IgM serology tests for CMV and EBV were negative. The histology of the patient's affected lymph nodes suggested the diagnosis of KFD. She recovered completely after a 2-week course of NSAID therapy. After 6 months of follow-up, she had no recognizable symptoms of SLE. A combination of clinical presentation, imaging, laboratory tests, and histopathology is necessary to exclude other diseases and to avoid misdiagnosing and mistreating KFD.

Conclusions

In conclusion, KFD is a rare, benign disease that mainly occurs in young Asian women. The clinical presentation is variable and it can mimic other diseases. The imaging features for KFD are non-specific. The diagnosis should be considered in young women who have cervical lymphadenopathy for a short time. Long-term follow-up is necessary to assess these patients for development of autoimmune disease or a recurrence of KFD.

Declaration of Figures' Authenticity

All figures submitted have been created by the authors who confirm that the images are original with no duplication and have not been previously published in whole or in part.

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