Kikuchi-Fujimoto Disease (Histiocytic Necrotizing lymphadenitis): From a Wrong Diagnosis to the Right Disease

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Abstract

Kikuchi-Fujimoto disease (KFD), also known as histiocytic necrotizing lymphadenitis, is a self-limiting, benign, and rare systemic lymphadenitis with unknown etiology. The cardinal symptoms are fever, lymphadenopathy and night sweat; consequently, it is first necessary to rule out infectious, lymphoproliferative, and connective tissue diseases such as systemic lupus erythematosus. Histology can allow diagnosis by demonstrating necrotizing histiocyte lymphadenitis. Disease, which has no specific treatment, self-limits itself in 1 to 6 months clinically. However, non-steroid anti-inflammatory agents can be given for symptomatic treatment and there are reports using corticosteroids and antibiotics in complicated cases. This article concerns a 23 years-old female who was diagnosed of a wrong disease but later had the right Kikuchi-Fujimoto disease diagnosis and was treated with anti-inflammatory agents.

Keywords: Kikuchi-fujimoto disease; Biopsy; Cervical adenopathy; Anti-inflammatory agents; Systemic lupus erythematosus; Lymphadenopathy

Introduction

Histiocytic necrotizing lymphadenitis, the so-called Kikuchi-Fujimoto disease, was first described in 1972 by two independent Japanese pathologists, Kikuchi and Fujimoto [1-3] is a rare disease affecting mainly young women. The presenting symptoms are high fever and painful cervical adenopathy, with pathological findings of histiocytic necrotizing lymphadenitis [1,2,4]. Several authors have reported cases with lymphadenopathy in an atypical location, and such cases are difficult to differentiate from malignant lymphoma [5-8]. A biopsy is necessary to arrive at a final histological diagnosis. In patients presenting with cervical adenopathy, the differential diagnosis can be broad. Here, we present the case of a young woman with KFD and review the significant features of this syndrome.

Case Report

A 23-year-old woman presented to our out patient clinic with generalized pain, tender left cervical adenopathy, and loss of appetite, night sweats, and fever to 37.5°C. Her recent history indicated progressive painful bilateral neck adenopathy for about two weeks.

She has not been remarkable medical history and not travelled abroad. Her laboratory data showed a normal white cell count (5300/μL) and slight elevation of lactase dehydrogenase (250; normal 120-240 IU/L) and CRP (1.04; normal under 0.50 mg/dL). Physical examination showed painful cervical lymph nodes. Laboratory studies were negative for toxoplasmosis, hepatitis B, hepatitis C, HIV, CMV, VDRL, and Brucella agglutination, while EBV-IgM showed a borderline positive result. Anti-dsDNA was in normal limits, while ANA, RF, angiotensin-converting enzyme and PPD were negative.

Routine biochemical analysis, coagulation tests, and urine analysis were in normal limits. Peripheral smear showed a relative lymphocytosis.

CT-neck showed bilateral cervical, submandibular, and left supraclavicular lymphadenopathy, while CT-thorax and abdomen showed no pathologic findings and cardiac ultrasonographic studies also revealed no abnormalities.

Whole body 18F-2-deoxyfluoro-D-glucose (FDG) positron emission tomography (PET-CT) was performed, which showed high maximum standardized uptake values (max SUV 13.5 to 21.1) in the left cervical posterior and supraclavicular lymphadenopathy. Late-phase augmentation of SUV in PET-CT suggested malignant lymphoma (Figures 1 and 2).

Keywords:

- Kikuchi-fujimoto disease
- Biopsy
- Cervical adenopathy
- Anti-inflammatory agents
- Systemic lupus erythematosus
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She had earlier presented to a local otolaryngology clinic and was given broad-spectrum antibiotics for possible lymphadenitis and developed weight loss, and ultimately a biopsy was performed. In this biopsy pathologic examination was T Lymphoblastic Lymphoma. So before the treatment we planned a bone marrow biopsy. The pathologic result of this biopsy was normal. So we decided to consult the lymph node biopsy to another pathologist and the pathologic examination showed diffuse necrosis with no definite malignancy. Although the morphologic findings showed necrotizing lymphadenitis suggestive of KFD (Figure 3).

With the potential diagnosis of KFD, nonsteroidal anti-inflammatory drug (NSAID) therapy with meloxicam and diclofenac was given. One month's later physical examination and laboratory measurements were within normal limits and the patient is well. The patient is currently not receiving any treatment after 3 months of follow-up and is undergoing further assessment for possible connective tissue disorder Nowadays the patients is well.

Discussion

KFD is a syndrome of unknown etiology. It is generally associated with fever, sweats, and progressive painful adenopathy, primarily in the cervical region. The disease is rare, and most reports are from the Asian countries, especially Japan. Most patients are under the age of 30, with a female-to-male ratio of 4:1 [3,4,9].

There are many speculations as to etiology with both viral and autoimmune processes suspected. Human Herpes Virus 6, Human Herpes Virus 8, Parvovirus B-19, and Epstein - Barr virus have all been implicated. The presentation is generally acute, with progression over a 2-3 week period. In this time frame, painful cervical adenopathy dominates, with generalized lymphadenopathy uncommon [9] and fever sometimes exceeds 40°C. Other symptoms include night sweats, upper respiratory complaints, and weight loss. Laboratory analyses generally reveal leucopenia with a relative lymphocytosis.

The diagnosis depends on examination of an excisional biopsy with characteristic histopathologic findings of KFD, including paracortical areas of coagulates necrosis with abundant karyorrhectic debris, distortion of the nodal architecture, and large numbers of histiocytes at the margins of necrotic areas [3,4,9]. Although uncommon, the diagnosis of KFD should be considered in a differential diagnosis that includes tuberculosis, connective tissue diseases such as SLE, or lymphoproliferative disorders. Indefinite clinical follow up of KFD has been suggested for emergence of SLE or other connective tissue disorders.

The process is typically limited from one to six months [3,4,9], with recurrence reported in 3-4% of patients [10]. Lymphadenopathy can resolve spontaneously. Following definitive diagnosis, the essentials of treatment include analgesia, antipyretics, and NSAID therapy.

In some recent cases manifesting lymphadenopathies in atypical sites, PET-CT tended to be performed to differentiate benign from malignant lymphoma but most cases required surgical biopsy for a final diagnosis [5].

PET-CT is a convenient tool widely used now to investigate the location of malignancy foci [11]. This method utilizes the feature of amplified glucose activity and glycolysis in malignant cells [12]. However, benign lesions, some inflammation [13] and sarcoidosis [14] also demonstrate increased FDG uptake as in malignant lesions, and it is not possible to distinguish malignant from benign disease by SUV at a single time point. New advanced PET-CT technology examines early- and late-phase SUV, and increased late phase compared to early-phase SUV is expected to suggest malignant [15]. In the present case, PET-CT also showed late phase SUV augmentation. This finding suggested malignant lymphoma affecting on the left cervical posterior and supraclavicular lymphadenopathy [16], and surgical excision of the lymph node was necessary to make a definitive diagnosis.

In several reports of Kikuchi-Fujimoto disease showing high late SUV on PET-CT, surgical biopsies of lymph node were necessary for differentiation from malignant lymphoma. In the present case, physical examination, routine laboratory data and radiographs showed no specific abnormalities, and the patient had no chest-related symptoms.

Conclusion

This case is a rare case and not a series of cases. It shows that right pathology is necessary for the consequently diagnosis.

References


