Kikuchi Fujimoto Disease: A Series of Three Cases

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Abstract

Introduction: Kikuchi-Fujimoto disease (KFD) is a rare self-limited disorder manifested by painful cervical lymphadenopathies commonly associated with fever and night sweats. This is a series of three female patients presenting with fever and lymphadenopathies diagnosed with KFD.

Case: The first case is a 34-year-old female admitted due to fever of 10 days associated with lymphadenopathies and joint pains. Excision biopsy done showed necrotizing histiocytic lymphadenitis consistent with KFD. Other laboratories showed hypocomplementemia, positive ANA and anti-dsDNA. Patient was discharged improved with low dose oral corticosteroid and hydroxychloroquine. The second case is a 53-year-old female with fever, lymphadenopathies, polyarthritis and morning stiffness. Biopsy of the cervical lymph node was done showing KFD and lupus serologies (ANA 1:640 speckled, anti-dsDNA and anti-Smith) revealed positive results as well. Patient was then diagnosed with SLE and was started on low dose oral corticosteroid and hydroxychloroquine which resulted to resolution of fever and gradual resolution of lymph nodes on out-patient follow up. The last case is a 45-year-old female admitted due to persistent fever, painful lymphadenopathies and headache. Serological work-up including autoantibody tests for SLE were all unremarkable but showed associated iron deficiency anemia. Biopsy of the cervical lymph node showed Kikuchi's disease. Patient was discharged with oral methylprednisolone.

Conclusion: The rarity of KFD makes defining an autoimmune etiology a challenge to clinicians. Careful disease course follow up is then recommended for patients who initially lack parameters for SLE diagnosis.

Keywords: Kikuchi-Fujimoto disease, cervical lymphadenopahy, SLE

Introduction

Kikuchi-Fujimoto disease (KFD) is a rare self-limited disorder manifested by painful cervical lymphadenopathies commonly associated with fever and night sweats.[1] It is more common in young adults less than 30 years of age with female predominance. Kikuchi first described the disease in 1972 in Japan. Fujimoto and colleagues independently described KFD in the same year.[2]

Case

The first case is a 34-year-old female admitted due to fever, arthritis, palatal ulcers and palpable masses on her neck and axilla. Initial laboratories revealed elevated ESR (47 mm/hr), CRP (12 mg/L) and LDH (405 U/L). Complete blood count showed normochromic, normocytic anemia (hemoglobin: 11.1 g/dl) with slightly decreased WBC count (4990 mm3). Excision biopsy done on the cervical lymph node showing well circumscribed paracortical lesions with necrotizing changes were all consistent with necrotizing histiocytic lymphadenitis as seen in KFD (Figure 1).

Laboratories requested showed marked hypocomplementemia (34 mg/dl), positive ANA (1:160 speckled pattern) and anti-dsDNA (23.3 U/mL). Having met the diagnosis for systemic lupus erythematosus (SLE)(arthritis, mucosal ulcers, positive ANA, positive anti-dsDNA, hypocomplementemia), patient was started with low dose oral corticosteroid and hydroxychloroquine.

The second case is a 53-year-old female who consulted as outpatient due to fever, lymphadenopathies, polyarthritis and morning stiffness. Patient underwent excision biopsy of cervical lymph node showing KFD. Patient later developed fever, alopecia and oral ulcers. Initial laboratories revealed normochromic, normocytic anemia (hemoglobin: 11.6 g/dl), elevated ESR (61 mm/hr) and CRP, normal complement levels and positive lupus serologies (ANA 1:640 speckled, positive anti-dsDNA and anti-smith). Patient was also diagnosed with lupus.

The last case is a 45-year-old female admitted due to persistent fever, painful lymphadenopathies and headache.

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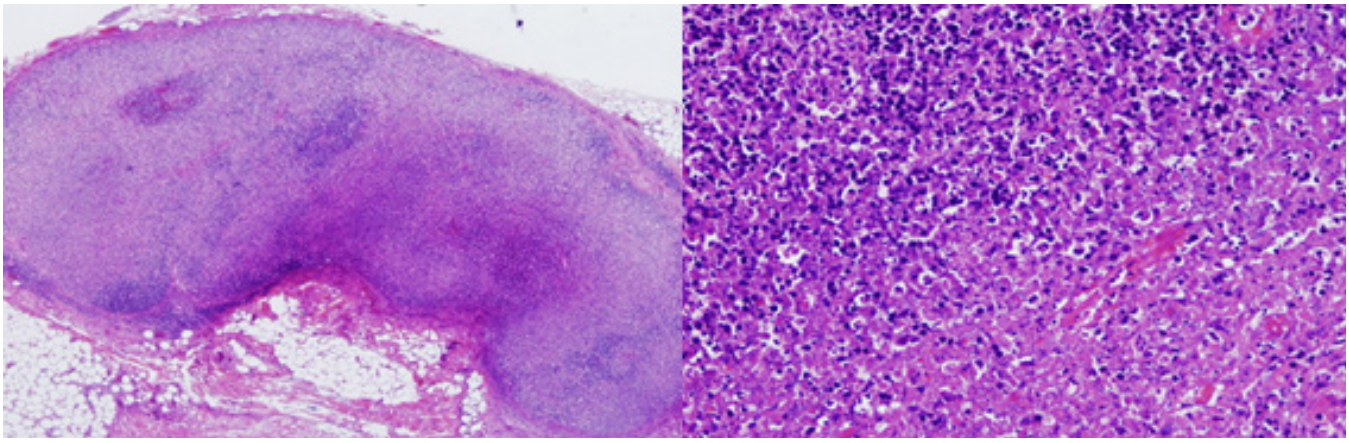

Figure 1. A. Microscopically, the affected nodes show focal, well-circumscribed paracortical lesions. B. Higher power view showing the boundary between an area of karyorrhexis/ pyknosis and an area of karyolysis. There are abundant karyorrhectic debris, scattered fibrin deposits, and collections of mononuclear cells (mostly plasmacytoid dendritic cells and activated T cells). No plasma cells and neutrophils were seen.

There were no other systemic signs and symptoms consistent with an autoimmune condition. Serologies for SLE were negative. Biopsy of the cervical lymph node showed KFD. Patient was discharged with oral methylprednisolone.

Discussion

In patients presenting with lymphadenopathies, the primary disease entities that should be considered are infections and malignancy. Important differentials include Tuberculosis, considering the endemicity in the country, and lymphoid malignancy which may present similarly. Lymphadenopathies seen In SLE show aggregates of degenerated nuclear debris (hematoxylin bodies) and aggregates of degenerated nuclear material present in the walls of blood vessels (Azzopardi phenomenon). There is also prominent reactive follicular hyperplasia, abundant plasma cells in SLE lymphadenitis.[3]

Laboratory findings seen KFD include anemia, elevated lactate dehydrogenase levels, liver function tests and erythrocyte sedimentation rate. Mild leucopenia is present in 20%- 58% of patients which may be attributed to cytokine induced mechanisms. Atypical lymphocytes can be seen in up to 25% of patients with KFD.[1] Hutchinson on his paper on histopathologic findings of KFD describes three evolving phases of the disease- proliferative, necrotizing and xanthomatous phase.[3]

In the cases cited, two of the patients presenting with KFD were diagnosed with systemic lupus erythematosus. Goldblatt in his paper on the discussion of KFD and SLE in 2008, postulated that the association may be supported by electron microscopic studies showing tubular reticular structures in the cytoplasm of stimulated lymphocytes and histiocytes which are also noted with the endothelial cells and lymphocytes of SLE patients.[4] Having a number of overlapping clinical features, differentiating KFD and lupus lymphadenitis may be tedious. Clinicians may however be guided by several key points in the diagnosis of each disease entity; 1, KFD which is characterized by lymphadenopathies, fever and other systemic features has less of extra-nodal involvement upon presentation and 2, Lupus lymphadenitis, which has been reported in between 12% and 59%of patients with SLE, in contrast to KFD, is rarely the presenting feature of Lupus. Still, the most reliable way to differentiate the two entities is by careful clinical examination and correlation with lymph node histopathology.[4]

Kikuchi Fujimoto Disease typically affects women although it has been described in both genders and a variety of ethnic backgrounds. Lymphadenopathies, which are present in 59% of cases, range from 0.5 to 4.0 cm in size are described as tender and painful. Extranodal involvement is uncommon but well documented. Skin lesions, more common in the face or upper body, may be present as erythematous plaques, papules, indurated lesions and ulcers. Upper respiratory infections have also been described. Less common symptoms include fatigue, joint pain, nausea, vomiting and sore throat.[3]

A study published in Clinical Rheumatology compared the clinical and laboratory data of 244 patients reported in 181 publications. Of the 244 cases, 33% were male and 77% were female, with mean age of 25. Most cases were reported in Taiwan (36%), USA (6.6%) and Spain (6.3%). Fever (35%) and lymphadenopathies (100%) were the most frequent symptom and physical finding.[5] KFD associated with autoimmune disease was also reported in the case of a 43 year old with eight-year history of Overlap Syndrome (Scleroderma and SLE) with features consistent with the cases in this publication.[6] Aside from a presumptive aberrant autoimmune reaction, an infectious etiology was also suspected to be a possible inciting event in the pathogenesis of KFD as supported by the presence of peripheral blood

abnormalities suggestive of mononucleosis-like viral infection.[7]

The disease course of KFD is typically self-limited. Lymphadenopathies run a benign course and appear to resolve spontaneously one to six months after definite diagnosis. A recurrence rate of 3-4% has been reported. A local treatment guideline is lacking. The treatment plan includes use of analgesics, antipyretics and nonsteroidal anti-inflammatory drugs to alleviate lymph node tenderness and fever. The use of corticosteroids has been recommended in severe extranodal or generalized KFD but is of uncertain efficacy.[1] In this case series, corticosteroids were used as first line with good outcomes.

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