

CASE REPORT

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Kikuchi's Disease: A Rare Cause of Fever and Lymphadenopathy

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Abstract: Kikuchi's disease is a benign condition that occurs in women. A young woman presented to the hospital with fevers and cervical lymphadenopathy. Infectious work-up was negative except for streptococcus pharyngitis. Imaging studies revealed the presence of diffuse cervical and axillary lymphadenopathy. The fevers persisted and she underwent excisional cervical lymph node biopsy that revealed histiocytic necrotizing lymphadenitis corresponding to a benign diagnosis of Kikuchi's disease. Three months later, the patient was afebrile and there was complete resolution of the cervical lymphadenopathy.

Keywords: Kikuchi's disease, cervical lymphadenopathy, Kikuchi Fujimoto disease, Histiocytic necrotizing lymphadenitis

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Introduction

Kikuchi's disease is a rare and benign condition described in young women. It is characterized by cervical lymphadenopathy and fever and is often mistaken for more serious conditions. We describe a case of a young woman who presented with fever, malaise and diffuse cervical lymphadenopathy.

Case Presentation

A 29-year-old healthy woman presented to the emergency department with complaints of fever, chills and malaise for one week. She had been taking ibuprofen at home with no relief. She also noticed swelling in her neck bilaterally. There was no history of recent travel, sick contacts or exposure to people with tuberculosis. She denied dysuria, cough, diarrhea, shortness of breath, chest pain, menorrhagia, night sweats or weight loss. She has been in a monogamous relationship for many years. There was no family history of lymphoma, leukemia, systemic lupus erythematosus, rheumatoid arthritis or any other rheumatologic disorders. She did not take any prescription or herbal medications. Social history was negative. Vital signs in the emergency department revealed a temperature of 103.2 F and a pulse of 113. Physical exam was normal except for bilateral anterior and posterior cervical, pre and post-auricular, submandibular, submental and right axillary lymphadenopathy. Initial laboratory studies revealed white blood cell count-3000 th/mm³, hemoglobin-8.8 g/dL, platelets-273 th/mm³ and mean corpuscular volume-66.2 mcm³. Chest x-ray was normal. Subsequently, she was admitted to the inpatient floor with persistent fevers and lymphadenopathy. Further laboratory studies revealed anemia of chronic disease. Hemolytic work-up was negative. Hemoglobin electrophoresis revealed no evidence of β thalassemia. HIV, EBV monospot, Toxoplasma, and CMV serologies were negative. The patient continued to experience high fevers with rapidly increasing diffuse lymphadenopathy and further laboratory testing was ordered. Peripheral blood flow cytometry revealed no monoclonal B cell population that was identified and no evidence of paroxysmal nocturnal hemoglobinuria. The throat culture revealed β hemolytic streptococcus and she was prescribed penicillin. CT scans of the chest, and abdomen/pelvis with intravenous contrast revealed enlarged bilateral axillary

lymphadenopathy measuring up to 2.7 cm in largest dimensions. CT scan of the neck with intravenous contrast showed diffuse enhancing lymphadenopathy involving all neck levels, soft tissues and axillae bilaterally. Surgery consultation was obtained for the consideration of an excision lymph node biopsy. Further laboratory studies revealed an elevated IgG level. Antinuclear antibody and anti-double stranded DNA testing were negative. β 2 microglobulin level was elevated. Angiotensin-converting enzyme level was normal. She underwent excisional lymph node biopsy of the left cervical lymph node and was discharged home with instructions to take acetaminophen if she had recurrent fevers. The pathology report of the lymph node revealed lymphoid tissue with extensive geographic necrosis (necrotizing histiocytic inflammation) suggestive of Kikuchi's disease (Fig. 1). There was no evidence of infection in the lymph node specimen. The patient was informed of the diagnosis and told to return to the outpatient clinic for follow-up evaluation.

One month later, the patient presented to the outpatient clinic. The fevers had resolved and the lymph nodes had markedly reduced in size to less than a centimeter clinically. The hemoglobin was improving. She had further work-up to search for an identifiable cause of her condition. Serologic testing for human herpes virus 6, human herpes virus 8, and respiratory virus panel were negative except for an elevated parvovirus IgG level. Repeat HIV testing was also negative. She was also referred to the rheumatology clinic because she began experiencing morning stiffness. On a three month follow-up visit, she continued to

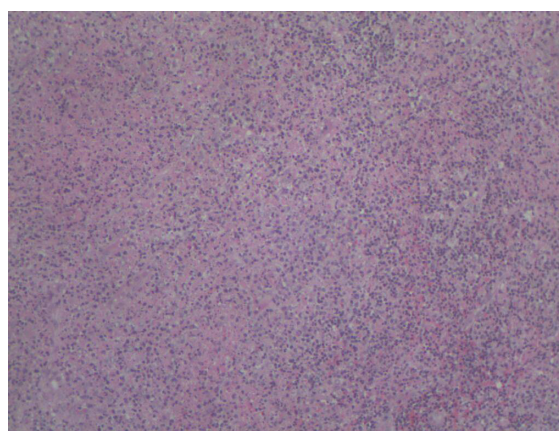


Figure 1. Low magnification view showing necrotizing histiocytic inflammation

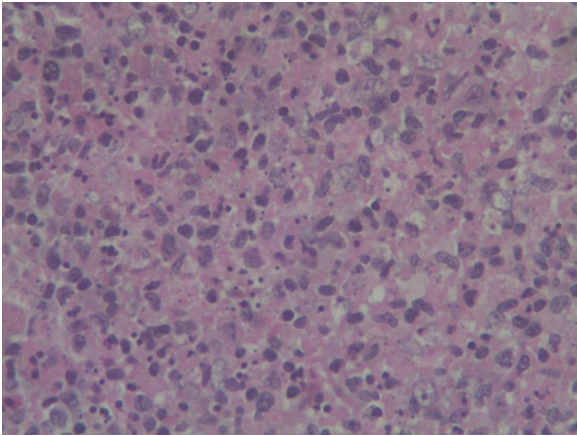


Figure 2. Oil immersion view showing histiocytes and plasmacytoid monocytes

be afebrile and the lymphadenopathy and microcytic anemia had resolved. Although the microcytic anemia had resolved, she was recommended to undergo a colonoscopy and upper endoscopy to evaluate the etiology of the microcytic anemia. Laboratory testing done in the rheumatology clinic revealed no evidence of any rheumatologic conditions.

Discussion

Kikuchi's disease also referred to as Kikuchi-Fujimoto disease and Kikuchi's histiocytic necrotizing lymphadenitis is a rare and benign condition that has been mainly described in women younger than 40 years of age. It has been described in all ethnic groups. Although it mainly affects woman, it has also been described in men. It can mimic serious conditions like lymphoproliferative disorders and tuberculosis lymphadenitis. There have only been a few case reports described in the literature.

The pathogenesis of Kikuchi's disease is not clear. It is believed that there is an immune response of the T cells and histiocytes to an inciting agent. Numerous pathogens have been described including Epstein Barr virus,¹ human herpes virus 6 and 8,² human immunodeficiency virus, toxoplasma, yersenia enterocolitica, parvovirus,³ parainfluenza and paramyxoviruses. It is thought that cellular destruction is due to apoptotic cell death that is mediated by CD8 T lymphocytes.⁴

Kikuchi's disease usually presents with fever and cervical lymphadenopathy in a young healthy woman. Fever is the most prominent symptom and can persist for a week. Patients can also present with systemic

signs and symptoms such as night sweats, weight loss, diarrhea, rash, and arthritis. Lymphadenopathy is present universally in all the patients. Rash that is similar to drug-induced lupus or rubella can be seen in some patients.⁵ Lymphadenopathy is usually localized and involves the cervical lymph nodes but there may be involvement of the axillary, mediastinal, iliac, intrapancreatic, retrocrural, peripancreatic and celiac nodes. The nodes are firm, smooth, mobile and about 1–2 cm in size and patients may often experience pain associated with nodal enlargement. Neurological symptoms such as ataxia, tremors and aseptic meningitis have also been described in some patients.^{6,7} Anemia, leukopenia, elevated immunoglobulin levels, and elevated erythrocyte sedimentation rate can be seen in the laboratory studies.¹ Bone marrow examination can reveal an increase in macrophages without atypical cells.⁸ Antinuclear antibodies and rheumatoid factor are generally negative. However some patients diagnosed with Kikuchi's disease can develop autoimmune disorders.⁹

Differential diagnoses for Kikuchi's disease include lymphoma, tuberculous adenitis, lymphogranuloma venereum and Kawasaki disease. CT scans of the neck and chest will show diffuse enhancing lymphadenopathy. Lymph node biopsy is the definitive way to make the diagnosis of Kikuchi's disease. Biopsy should be done to exclude serious disorders like lymphoma. Patients have been misdiagnosed as having lymphoma and have been treated with chemotherapy.⁹ The histology of the lymph node in Kikuchi's disease is unique and can be differentiated from other infectious causes of lymphadenopathy except in systemic lupus erythematosus.⁹ Necrotic foci can be seen on gross examination. Paracortical foci with histiocytic infiltrate are seen on microscopic examination. The histological appearance of the lymph node can vary according to progression of the disease. The proliferative phase can show the presence of follicular hyperplasia with T and B blast cells that can be confused for lymphoma. The necrotizing phase can show necrosis with histiocytes. Immunohistochemical stains will be positive for CD68 plasmacytoid monocytes and histiocytes with predominantly CD8 T lymphocytes.

There is no effective treatment for Kikuchi's disease. The signs and symptoms typically resolve in



one to four months. High dose glucocorticoids with intravenous immunoglobulin have been shown to have some benefit in severe symptoms.¹⁰ Kikuchi's disease is self-limited but the patients should be followed for a few years since recurrence is common and some of the patients can develop systemic lupus erythematosus.

Conclusion

Although Kikuchi's disease is a rare entity, we should consider it in the differential diagnosis when a young woman presents with fever and cervical lymphadenopathy. Accurate diagnosis of this condition is essential in preventing unnecessary emotional and mental distress associated with labeling a patient as having a more serious condition such as lymphoma or systemic lupus erythematosus.

Disclosures

Author(s) have provided signed confirmations to the publisher of their compliance with all applicable legal and ethical obligations in respect to declaration of conflicts of interest, funding, authorship and contributorship, and compliance with ethical requirements in respect to treatment of human and animal test subjects. If this article contains identifiable human subject(s) author(s) were required to supply signed patient consent prior to publication. Author(s) have confirmed that the published article is unique and not under consideration nor published by any other publication and that they have consent to reproduce any copyrighted material. The peer reviewers declared no conflicts of interest.

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