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Case Report

A case report on Kikuchi disease

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ABSTRACT

Kikuchi-Fujimoto disease (KFD), or histiocytic necrotizing lymphadenitis, is a benign and self-limited disease that mainly affects young women. Patients present with localized lymphadenopathy, fever, and leukopenia in up to half of the cases. KFD can occur in association with systemic lupus erythematosus. We present the case of a patient with KFD and systemic lupus erythematosus. A 38 years old female presented with right sided cervical lymphadenopathy, fever and a rash on the face, with a loss of apetite and generalized body weakness. After a series of investigations to rule out other conditions like tuberculosis, a diagnosis of kikuchi disease was made based on the biopsy report. There was a strong suspiscion of SLE as well pertaining to the facial rash. An ANA profile was done which strongly indicated SLE as well. The patient was started on steroids and other systematic treatment and recovered gradually. With its shared clinical features, Kikuchi-Fujimoto disease can be mistaken for other forms of lymphadenitis. A combined use of medical imaging and laboratory tests is the effective way to avoid misdiagnosis.

Keywords: Kikuchi-Fujimoto (KFD), Necrotizing lymphadenitis, Systemic lupus erythematosus (SLE), ANA profile, Perinodal

INTRODUCTION

KFD, or histiocytic necrotizing lymphadenitis, was originally reported in 1972 in Japan. It has been reported in several countries since then. It occurs most commonly in young women.[1] Kikuchi-Fujimoto disease (KFD), or histiocytic necrotizing lymphadenitis, is a benign and self-limited disease that mainly affects young women. Patients present with localizeded lymphadenopathy, fever, and leukopenia in up to half of the cases. It is associated with fever and leukopenia in up to 50% of patients.[3] KFD can occur in association with systemic lupus erythematosus.

The characteristic histology of KFD is single or multiple areas within the lymph node that contain necrosis and histiocytic cellular infiltrate. The capsule of the node may be invaded, and perinodal inflammation is common.[4] No effective treatment has been established for KFD. It is a benign, self-limited disease that resolves in 1 to 4 months. Patients should be monitored, however, since they may subsequently develop SLE or, in unusual circumstances, develop a recurrence of KFD. Recurrences of the latter are uncommon.[7]

CASE REPORT

A 38 years old female presented with right sided cervical lymphadenopathy, fever and a rash on the face, with a loss of apetite and generalized body weakness. After a series of investigations to rule out other conditions like tuberculosis, a diagnosis of Kikuchi disease was made based on the biopsy report.

There was a strong suspiscion of SLE as well pertaining to the facial rash. An ANA profile was done which strongly indicated SLE as well. The patient was started

on steroids and other systematic treatment and recovered gradually.

Figure 1: PT with KFD and SLE.

Figure 2: Picture showing the cervical lymphnodal swelling.

Figure 3: Picture showing the SLE rash.

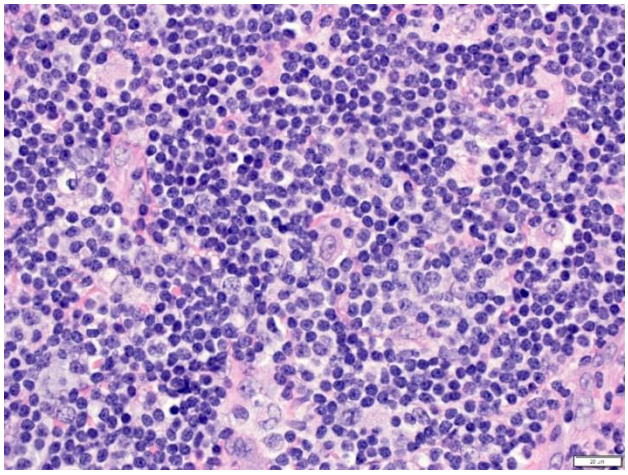

Figure 4: Hitopathology slide.

DISCUSSION

KFD, or histiocytic necrotizing lymphadenitis, was originally reported in 1972 in Japan. It has been reported in several countries since then. It occurs most commonly in young women.[1] with localized lymphadenopathy, most commonly in the cervical region.[2] It is associated with fever and leukopenia in up to 50% of patients.[3]

The differential diagnosis of fever and cervical lymphadenopathy is broad and often leads to an extensive workup. Our patient was tested for tuberculosis, Epstein-Barr virus, cytomegalovirus, HIV, toxoplasmosis, and syphilis. In addition, she had a bone marrow examination to check for lymphoma. All of these studies were negative or normal. Lymph node biopsy results did facilitate the diagnosis. The characteristic histology of KFD is single or multiple areas within the lymph node that contain necrosis and histiocytic cellular infiltrate. The capsule of the node may be invaded, and perinodal inflammation is common.[4] Cultures and stains for organisms are negative.

KFD is known to occur in conjunction with SLE.[5] Some experts even suggest that KFD is one unusual presentation of SLE. Santana et al did a Medline/LILACS (Latin American and Caribbean Health Sciences) search in 2003 and found 35 reported cases in which KFD and SLE occurred together. In the majority of the cases, SLE was diagnosed either after or at the same time as the KFD.[6] In the case of our patient, SLE was diagnosed about the same time as her second episode of KFD. It is interesting to note, however, that during her first episode, she did present with arthralgias. It is not known whether SLE serologies were checked at that time.

No effective treatment has been established for KFD. It is a benign, self-limited disease that resolves in 1 to 4 months. Patients should be monitored, however, since they may subsequently develop SLE or, in unusual circumstances, develop a recurrence of KFD. Recurrences of the latter are uncommon.[7]

In cases in which KFD is diagnosed after or at the same time as SLE, corticosteroids are often used for treatment, often along with hydroxychloroquine.[8-10] After treatment with prednisone, our patient received hydroxychloroquine once SLE was diagnosed. She did very well. Her symptoms resolved within 1 month of starting the treatment, and she has not relapsed since.

The etiology of KFD is unknown. Certain causative organisms have been proposed. These include Epstein-Barr virus, human T-cell leukemia virus type 1, human herpesvirus type 6, B19 parvovirus, cytomegalovirus, *Brucella*, *Yersinia enterocolitica*, and parainfluenza virus.[11] An autoimmune mechanism has also been proposed because KFD is seen in conjunction with SLE. One theory involves molecular mimicry, in which infectious agents that closely resemble a host peptide affect the ability of T cells to detect self from nonself.[12] An example of this is the cross-reaction between *Borrelia burgdorferi* antigen and a peptide from human lymphocyte function–associated antigen 1 that leads to the chronic arthritis seen in lyme disease.[13] Another theory regarding autoimmunity is that apoptotic cells are the source of the autoantigens of SLE. Apoptotic cells express many of the nuclear autoantigens of SLE on their surface. In patients with defective clearance of these cells (i.e., complement deficiency), these cells may become a nidus for autoimmune disease.[14]

Relapsing polychondritis, a disorder of cartilage and connective tissue, is another problem that the patients developed. Patients most commonly present with unilateral or bilateral ear inflammation with sparing of the noncartilaginous parts of the ear.[15] The next most common presentation is joint involvement, followed by nasal and ocular involvement.[16] Relapsing polychondritis is also thought to have an autoimmune etiology, with autoantibodies attacking the patient's cartilage.[17]

Complement levels may play a role in the constellation of diseases seen in our patient. The complement system is a set of proteins that aids in phagocytosis, chemotaxis, opsonization, and the clearance of immune complexes. There are three different paths in the complement system: the classic pathway, the alternative pathway, and the mannose-binding lectin pathway.[18] Each pathway is activated differently. The classic pathway is activated by binding to immune complexes.[19] C4 is an important component of the classic pathway, and so a deficiency in it results in defective immune-complex clear. Allotyping had demonstrated two “null” alleles at her C4 locus. C4 is involved in the early part of the classical complement pathway. Homozygous complement deficiency, especially of the early components of the classical pathway, has been strongly associated with the development of some autoimmune disorders, in particular SLE.[20]

We believe that low C4 levels in our patient perhaps contributed to impaired clearance of immune complexes and may have predisposed her to SLE, KFD (which may have been an unusual presentation of her SLE), and perhaps even to relapsing polychondritis. After her initial treatment with low-dose prednisone and hydroxychloroquine, she gradually became asymptomatic and has done well for the last several years.

CONCLUSION

With its shared clinical features, Kikuchi-Fujimoto disease can be mistaken for other forms of lymphadenitis. A combined use of medical imaging and laboratory tests is the effective way to avoid misdiagnosis.

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