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Internal Medicine

INCESSANT FEVER AND LYMPHADENOPATHY: A CASE REPORT OF KIKUCHI-FUJIMOTO DISEASE

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ABSTRACT Kikuchi–Fujimoto illness, also known as histiocytic necrotizing lymphadenitis, is a very uncommon idiopathic, self-limiting condition, mainly affecting young females. It has been linked to autoimmune diseases, the most notable of which is systemic lupus erythematosus. This entity has been associated with systemic lupus erythematosus (SLE) on rare occasions, and its diagnosis might occur before, after, or concurrently with SLE. The histological examination of lymph nodes is used to make the diagnosis. We present a case of Kikuchi Fujimoto Disease (KFD).

KEYWORDS : Kikuchi Fujimoto Disease, Histiocytic necrotizing lymphadenitis, Systemic Lupus Erythematosus

Introduction:

Histiocytic necrotizing lymphadenitis or Kikuchi Fujimoto Disease (KFD) was first documented in Japan by Kikuchi and Fujimoto et al. In 1972.[1] Although it is common in young Asian women, it has been well documented in other continents as well. In addition to sporadic cases, familial Kikuchi disease has been recorded rarely in the literature.[2] In terms of clinical presentation, the disease frequently resembles tuberculous lymphadenitis, lymphoma, lymphadenopathies found in connective disorders like SLE, Still's disease, and rheumatoid arthritis; and bacterial or viral infections such as infectious mononucleosis, cat scratch disease, herpes simplex, toxoplasmosis, HIV, and other benign and/or malignant diseases.[3,4] The most frequent occurrence is unilateral involvement of the posterior cervical group. Fever, mesenteric and axillary lymphadenopathy, splenomegaly, cutaneous rash, parotid gland enlargement, myalgias, arthralgias, bone marrow haemophagocytosis, aseptic meningitis, and interstitial lung disease are some of the less common findings.[3,5]

Case report:

In November 2015, Mrs. T, a 21-year-old lady from West Bengal, with no known co-morbidities presented with a history of high grade, on and off fever (T max 102.1°F) for the past 40 days, associated with vague abdominal discomfort and headache. There was a history of easy fatigability and myalgia but there was no history of weight loss, night sweats, or joint pain. She was evaluated in a nearby hospital and was started on standard Antitubercular therapy (ATT).

On arrival at our hospital, she was conscious, orientated with a Heart Rate of 106/min, Blood pressure of 114/70 mmHg, and Respiratory Rate of 18/min. She was febrile with a temperature being 102°F. The physical examination was notable for cervical lymphadenopathy. Systemic examination was unremarkable.

Her basic investigations were given in Table 1. Abdominal sonography was notable for mesenteric lymphadenopathy. 2D ECHO showed no regional wall motion abnormalities with an EF of 68%. There was no evidence of vegetation. Her plasma LDH was 1190 U/L, serum ferritin levels were 4100 ng/mL. The direct Antiglobulin test was 2+. Her reticulocyte counts were normal and peripheral blood smear showed a normocytic, normochromic picture with leucopenia with a few reactive cells.

Her Vasculitis work-up including ANA, Anti-DS DNA, ANCA, RA Factor, and Anti CCP were negative. Serum protein electrophoresis did not reveal any M band. Her bone marrow studies were notable for trilineage hematopoiesis with no notable abnormal cells. Blood and urine cultures were negative. Whole-body PET CT scan was notable for prominent, bilateral level II cervical lymphadenopathy with mesenteric lymphadenopathy.

An Infectious disease specialist, a hematologist, and a General surgeon were also involved in her care. A cervical lymph node excisional biopsy was obtained and it showed Karyorrhectic debris with some necrosis and histiocytic infiltration. A focus of follicular hyperplasia, sinus histiocytes, and plasmacytosis was also noted, which was fitting into the diagnosis of Kikuchi- Fujimoto Disease (Figure 1 and 2). Her empirical ATT was stopped and she was started on Naproxen, a Non-steroidal anti-inflammatory drug. Her symptoms were better and she was following up regularly.

She presented to the Out-Patient Department again in June 2019, with high-grade fever, generalized fatigability, and constipation. Her physical examination was notable for bilateral cervical lymphadenopathy with a fever of 103°F. Basic investigations were notable for anemia (7.3 g/dL), mild leucopenia (3.8* 10^3 /mm^3), and elevated ESR (123 mm/hr). Liver function tests, renal function tests, and urine routine were within normal limits. Repeat bone marrow biopsy also did not reveal any significant abnormalities. Since Kikuchi-Fujimoto Disease patients are prone to the development of Lupus, a repeat vasculitis evaluation including ANA, Anti-DS DNA, ANCA, and ENA was done and it was negative. Her blood culture reports were negative. She was treated again with NSAIDS and her symptoms improved.

Discussion:

Kikuchi–Fujimoto disease is a distinct type of self-limiting illness with an unidentified etiology that typically starts with cervical lymphadenopathy, and fever, and may also cause weight loss, nausea, vomiting, night sweats, chills, easy fatigability, and abdominal discomfort.[2] Kikuchi–Fujimoto disease was first described in 1972 by Kikuchi and Fujimoto.

The affected lymph node's histology, which shows necrotizing lymphadenitis limited to the cortical and paracortical regions, with partial or complete loss of follicular architecture, combined with significant karyorrhexis, enables the detection of KFD. Additionally, there is an increase in the number of hyperplastic histiocytes that are phagocytosing fragments of karyorrhectic nuclei and histiocytes with crescentic nuclei.[1,6]

The lymphadenitis associated with SLE, the lymphadenitis associated with herpes simplex and other microorganisms, non-Hodgkin lymphoma, plasmacytoid T-cell leukemia, Kawasaki disease, nodal colonization by acute myeloid leukemia, and even metastatic adenocarcinoma is among the conditions that make up the histologic differential diagnosis of KFD.[5]

KFD's etiology is not yet known. A hyper-immune response of the T cells and histiocytes to the infectious agents is triggered by several microorganisms, including EBV, HTLV-I, herpes human 6 viruses, Toxoplasma, parvovirus B19, CMV, Brucella, Yersinia enterocolitica, and parainfluenza virus. These microorganisms have been suggested as the disease's causative agents. None of these hypotheses, however, has been categorically demonstrated.[6]

Although liver malfunction and involvement of the skin and bone marrow, as well as extranodal locations, is rare, it has been documented in the literature. A Medline/PubMed search revealed three patterns of presentation for this association: KFD before the onset of SLE (30 percent), the concomitant presence of both illnesses (47 percent), and KFD after SLE (23 percent).[7] In addition to SLE, KFD has also been associated to various autoimmune diseases and symptoms, including pulmonary hemorrhage, cutaneous necrotizing vasculitis, polymyositis, antiphospholipid syndrome, and systemic juvenile idiopathic arthritis.

Patients with KFD have no specific treatment options. However, because the illness is self-limiting, only symptomatic treatment options should be employed to alleviate both local and systemic symptoms. Kikuchi-Fujimoto's disease is treated symptomatically with analgesics, antipyretics, NSAIDs, and, in rare cases, corticosteroids. Neurological involvement (aseptic meningitis, cerebellar ataxia), hepatic involvement with raised LDH levels, and severe lupus-like condition with positive ANA titers are all indications for corticosteroid treatment. Some authors have also suggested corticosteroid medication to reduce the length of a fever. In 1 to 4 months, spontaneous recovery takes place. Recurrence of the illness occurs in 3–4% of patients, sometimes even years after the initial episode. The development of SLE should be monitored in Kikuchi-Fujimoto's patients over a period of time, as we did in our case.[8]

It is important to recognize this condition since it can be confused with malignant lymphoma or, rarely, adenocarcinoma. Pathologists and clinicians should both be aware of this illness to avoid incorrect diagnoses and inappropriate treatments.

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Table 1: Basic investigations of the patient on admission.

Test Parameters	Patient's data	Normal Range
Complete blood count:		
Haemoglobin	7.1 (grams/deciliter)	11.5-16.5 (grams/deciliter)
Total White blood cell count	1.36* 103 /mm3	4-11 103 /mm3
Neutrophils	62%	40-80%
Lymphocytes	30%	20-40%
Monocytes	7%	02-10%
Platelet count	$248*10^3/mm^3$	150-450 103 /mm3
ESR	140	0-20 mm/hr
Liver Function tests:		
Total Bilirubin	0.3 mg/dL	0.0-1.3 mg/dL
Direct bilirubin	0.2 mg/dL	0.0-0.5 mg/dL
Indirect Bilirubin	0.1 mg/dL	0.0-1.2 mg/dL
SGOT/ AST	125 U/L	<31 U/L
SGPT/ ALT	81 U/L	<34 U/L
Alkaline Phosphatase	68 U/L	<98
Gamma Glutamyl Transpeptidase (GGTP)	94 U/L	<140 U/L
Renal Function Tes ts		
Urea	32 mg/dl	13-43 mg/dl
Creatinine	0.8 mg/dl	0.6 - 1.1 mg/dl

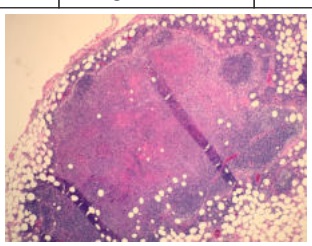

Figure 1: Kikuchi-Fujimoto disease: Showing paracortical area of coagulative necrosis (Representative H&E, magnification ×40)

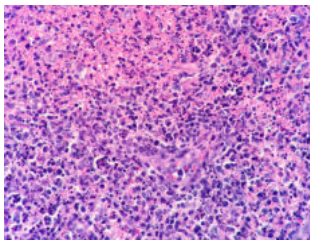

Figure 2: Karyorrhectic foci with histiocytes and some lymphoid cells (Representative H&E, magnification ×400)

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