Kikuchi Fujimoto Disease with Unusual Features

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Abstract
An uncommon case of Kikuchi Fujimoto disease with unusual associated serologic-autoimmune abnormalities and aseptic meningitis is reported for its rarity.

INTRODUCTION
Kikuchi Fujimoto disease (KFD) was originally described in 1972.1 It presents with painful or painless lymph node enlargement, most commonly in the posterior cervical triangle but can be in the anterior cervical triangle or the supraclavicular, mediastinal, inguinal or peritoneal or retroperitoneal regions, along with arthralgia, myalgia, rash and hepatosplenomegaly. Some patients have neutropenia or anaemia, or both, and a slight elevation of the ESR.

It is a disorder of unknown cause, but there may not be just one cause for this disease.2 It may be instigated by an infectious, physical, or chemical agent but evidence of a bacterial, fungal, viral, protozoal infection is negative. The onset is acute, it is more common in females, the females to males ratio is 4:1 and it can be recurrent in 5% of cases.

The association of KFD and systemic lupus erythematosus (SLE) is interesting but only few such cases are reported.3

CASE REPORT
A 17 years female patient was treated elsewhere in May 1998, Dec. 1998 and Apr. 1999 for episodes of high grade fever, and headache lasting ~ 20 days. In May 1999 she was diagnosed as having appendicitis and was operated. Soon thereafter she lost 15 kg weight, developed bilateral cervical lymphadenopathy and headache. Her complete blood count was normal, ESR 75 mm/hr, widal titre was O 1:160, H 1:180, TB IgG, IgM antibodies, brucella, HIV, anti-streptolysin antibodies were negative. Anti -nuclear antibodies, antidualle stranded DNA antibodies were weakly +ve, rheumatoid factor was +ve, IgM anti-cardiolipin antibodies were +ve. X-ray chest, abdominal ultrasonography was normal, 2D echocardiography showed mitral valve prolapse.

The brain CT scan was normal. She developed generalized tonic and clonic convulsions three hours after the scan. EEG was suggestive of encephalopathy with a few seizure potentials. CSF was clear, protein 150 mg/dl, glucose 50 mg/dl, WBC 3/mm³. She was treated with phenytoin and anti tuberculous treatment : streptomycin, INH, rifampin and ethambutol for three months, INH, rifampin and ethambutol for six months further and with steroids, which were tapered off over four months.

She was well for nearly two years till May 2001, when she presented at PDHNH to one of us (AS) with fever, headache, right sided tender cervical lymphadenopathy. Kernig’s sign was +ve, fundoscopy was normal. Complete blood count was normal, ESR 78 mm/hr, platelets 3.5 lacs/mm³, anti-nuclear antibodies was +ve 1:40, anti-double stranded DNA antibodies was +ve 1:10, anti-neutrophilic cytoplasmic antibodies were negative. Mantoux test, HIV, TORCH, Paul Bunnel antibodies were -ve, blood culture was negative. Head CT scan (plain) was normal, she developed generalized tonic, clonic convulsions during the procedure. CSF was clear, no clot, Pandy’s test was positive. Glucose was 54 mg/dl with a parallel blood glucose of 140 mg/dl, proteins 160 mg/dl, chloride 121 meq/l, RBC 4/mm³, WBC 19/mm³, L 96%, P 3%, M 1%. Gram’s and ZN stain, bacterial culture were -ve.

An excision biopsy of cervical nodes was done which showed extensive necrosis with karyorrhectic debris. No granulomas, giant cells, atypical lymphoid cells or Reed Sternberg cells were seen. Immunostaining showed a large number of histiocytes (myeloid/histiocytic antigen +ve). Occassional T cells (UCHL 1 +ve) were seen. No acid fast bacilli were seen on ZN staining. These features are suggestive of histiocytic necrotizing lymphadenitis or Kikuchi Fujimoto disease (KFD). She was started on anti-tuberculous treatment with INH, rifampin, ethambutol and pyrazinamide and prednisolone 1 mg/kg, because of the possibility of tuberculous meningitis and autoimmune disease. Phenytoin was continued. The patient showed a dramatic response, fever and toxicity subsided in 24 hours. CSF polymerase chain reaction for mycobacterium tuberculosis and TB Bactec culture of lymph node material was negative. Anti-tuberculou
treatment was withdrawn and steroids were tapered rapidly. At follow up three months later she had no symptoms or abnormal findings. She, however needs a close follow up for development of the clinical features of systemic lupus erythematosus in future.

**Disscussion**

Kikuchi Fujimoto disease is a hyperimmune reaction of T cells which triggers cellular degeneration of necrosis. The resulting nuclear dust or karyorrhectic debris is phagocytosed and degraded by histiocytes which are plasmacytoid mononuclears that stain with macrophage reagents. The immunophenotype of the histiocytes is identical. There is an early predominance of CD8, later of CD4 cells. The necrotic appearance is caused by apoptosis induced by the Fas-Fas ligand system. Hematoxylin bodies, and encrustation of blood vessel walls with nuclear dust (Azzopardi phenomenon) are seen with those cases of Kikuchi Fujimoto disease that are associated SLE. It has been suggested that it may be a forme fruste of SLE.

The unusual features in this case are:

1. Presence of serologic autoimmune abnormalities like anti-nuclear antibodies, anti-double stranded DNA antibodies, rheumatoid factor and anti-cardiolipin antibodies. Some cases of Kikuchi Fujimoto disease described in the literature do have such serologic abnormalities and autoimmune phenomena.
2. The association of Kikuchi Fujimoto disease and systemic lupus erythematosus (SLE) is interesting and there is some clinical and histologic overlap between the two diseases, but only a few such cases are reported. One patient of SLE subsequently developed Kikuchi Fujimoto disease, three patients with SLE and antibodies to parovirus B19 developed Kikuchi Fujimoto disease.
3. Aseptic meningitis in kikuchi fujimoto disease is described in the literature but is rare. Two cases are reported in the Japanese literature and one from India.
4. The illness in May 1999 was similar to the present one and so this case represents a case of recurrent Kikuchi Fujimoto disease, as in 5% of cases.

The case is reported to highlight that an excision biopsy of the nodes is important because the differential diagnosis of fever and cervical lymphadenopathy includes Kikuchi Fujimoto disease along with any other infective, immunologic and neoplastic causes.

**References**