Neurological Manifestations in a Patient of Kikuchi’s Disease

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Abstract

Kikuchi’s disease is a rare condition that mainly presents in young females along with lymphadenitis. Involvement of the nervous system is rare. We report a young female who presented with fever, headache, vomiting, lymphadenopathy and neurological manifestations in the form of aseptic meningitis, ataxia and paraparesis. Since the disease can be mistaken clinically and histologically for SLE, lymphoma and tuberculosis it is important to differentiate it from these conditions. Also our case emphasizes the importance of recognising this disorder in diagnosing patients with meningitis.

Introduction

Kikuchi-Fujumoto disease was first described by Kikuchi in 1972 in Japan. Fujimoto and colleagues independently described it in the same year. Also known as histiocytic necrotising lymphadenitis, it is an uncommon, idiopathic, generally self-limiting cause of lymphadenitis.¹

No specific cause of Kikuchi’s disease has been found. Some kind of viral or post viral aetiology has been proposed. It has also been linked to SLE.¹ The course is benign, spontaneous resolution usually occurs within 2-3 weeks.²

Case Report

A 16 year old girl presented with one week history of fever, frontal headache, instability while walking, weakness of both lower limbs, photophobia, abdominal pain, loose motions, vomiting and rash over forearms. There was no history of weight loss, past history or contact with tuberculosis.

On examination she had temperature of 102 oF, tachycardia, bilateral cervical lymphadenopathy involving submandibular and posterior auricular lymph nodes, measuring 2 x 3 cms which were firm, tender and mobile and left axillary lymph nodes measuring 2 x 2 cms. There was a maculopapular rash over both forearms. Systemic examination revealed a non tender liver palpable 1 cm below subcostal margin.

Neurological examination showed grade 3 power in both lower limbs with exaggerated deep tendon reflexes and extensor plantars. Power in upper limbs was normal. There was no sensory deficit or bladder involvement. Patient had bilateral cerebellar signs in upper limbs with tremor and past pointing. There was also nystagmus bilaterally and truncal ataxia. Nuchal rigidity was present.

Laboratory investigations revealed haemoglobin of 11 g%, total WBC count of 4500 cells/cmm - stabs 16%, polymorphs 71%, lymphocytes 11%, monocytes 2% - and platelet count of 1.5 lakh cells/cmm. ESR was 22 mm at end of 1st hour, CRP was positive. CSF examination revealed aseptic meningitis with absence of cells, protein 86 mg%, sugar 62 mg%. CSF culture was sterile, CSF ADA was negative, CSF PCR for TB was negative. Plain and post contrast brain scan was normal. MRI of brain was normal. Abdominal ultrasonography showed multiple para-aortic and mesenteric lymphadenopathy. Sputum examination for AFB smear was negative. Liver function tests showed normal bilirubin with elevated aspartate aminotransferase of 143 U/L. Renal function tests were normal. Mantoux test was negative. Serological tests for leptospirosis and typhoid were negative. HBsAg was negative, HIV ELISA was negative. Routine urine examination was...
unremarkable and culture sterile. ANA and dsDNA were negative. ECG showed sinus tachycardia, chest X-ray was normal. FNAC cervical lymph node was suggestive of reactive hyperplasia.

The patient was started on injection mannitol, ceftriaxone 2 g iv 12 hourly and injection Acyclovir 10 mg/kg body weight 8 hourly with the possibility of viral encephalomyelitis with cerebellitis in mind. A submandibular lymph node biopsy showed effaced architecture with large areas of coagulative necrosis and histiocytes speckled with karyorrhectic debris and absence of granuloma suggestive of histiocytic necrotising lymphadenitis consistent with Kikuchi’s disease. Antibiotics and antivirals were withheld. Patient was treated symptomatically for fever. Headache and fever subsided in 10 days and cerebellar signs and power in both lower limbs improved in 2 weeks. Rash subsided in 2 weeks. Lymph nodes regressed by 4 weeks. Figures 1 and 2 show the histologic picture of Kikuchi’s disease.

Discussion

Kikuchi’s disease has a higher prevalence among the Japanese and other Asiatic individuals affecting women more than men in a ratio of 3:1 although recent reports suggest the ratio to be 1:1. It typically affects young adults (mean age- 20-30 years).3

Clinically it presents mainly as a relatively acute onset of lymphadenopathy with fever and a flu-like prodrome.3 Cervical nodes are affected in about 80% of cases and are usually painless or mildly tender, firm and mobile, and tend to be 2-3 cms in diameter, although masses of multiple nodes may reach 6 cms.3

Less common symptoms include arthralgia, skin rashes, weakness and night sweats, weight loss, diarrhoea, anorexia, chills, nausea and vomiting. Chest and abdominal pain seen in our patient have
also been noted. Some patients may also have hepatosplenomegaly.

Although involvement of the nervous system is rare, aseptic meningitis, acute cerebellar ataxia, acute brachial neuritis and brainstem encephalitis have been reported to complicate the disease. To our knowledge paraspinus has not yet been reported. Acute cerebellar symptoms are very rare. A case has been reported wherein a patient presented with kinetic tremor and gait ataxia preceding clinical lymphadenopathy in Kikuchi’s disease. Brain and spinal MRI done in this patient showed no structural abnormality.

Routine laboratory tests may be normal except for an elevated ESR and C-reactive protein and a low WBC count. Fine needle aspiration cytology only has a limited role in establishing the diagnosis with the overall accuracy estimated at 56%. Diagnosis is based on histopathological findings of a lymph node biopsy, the pathologic hallmark of which is paracortical necrotic foci, which are devoid of neutrophils and surrounded by plasmacytoid monocytes, immunoblasts and crescenteric histiocytes. The coagulative necrosis and abundant karyorrhectic debris can distort the nodal architecture. The immune phenotype of Kikuchi’s disease is primarily composed of mature CD8 positive and CD4 positive T-lymphocytes. The histiocytes express histiocyte associated antigens such as lysozyme, myeloperoxidase and CD68.

Kikuchi’s disease has to be included in the differential diagnosis of lymph node enlargement such as SLE associated lymphadenitis, malignant lymphoma, tuberculosis, herpes simplex lymphadenitis, plasmacytoid T cell leukaemia, Kawasaki’s disease, nodal colonisation by acute myeloid leukaemia, infectious mononucleosis, sarcoidosis and metastatic adenocarcinoma. SLE associated lymphadenitis is characterised by prominent foci of necrosis resembling Kikuchi’s disease. However, serologic tests like ANA and dsDNA are positive in SLE and histologically it is characterised by the presence of haematoxylin bodies, the Azzopardi phenomenon (i.e. encrustation of blood vessel walls with nuclear material), paucity of cytotoxic T cells and large number of plasma cells in nodal tissue.

Kikuchi’s disease is differentiated from malignant lymphoma by incomplete architectural effacement with patent sinuses, presence of numerous reactive histiocytes, relatively low mitotic rates and absence of Reed-Sternberg cells. Immunohistochemical staining shows that the cells in Kikuchi’s disease are negative for CD3 and CD20 and they are positive for CD68. Positive immunostaining results by monoclonal antibody Ki-M1P are seen in Kikuchi’s disease but not in lymphoma.

Histologically it differs from tuberculosis by the classic biopsy features and the absence of caseating granulomas. Herpes simplex associated lymphadenitis may also have the characteristic histiocytic infiltrates and necrotic debris as in Kikuchi’s disease. However, the infiltrate is less striking, neutrophils are often present, the histiocytes are myeloperoxidase negative and the diagnosis is confirmed by the presence of viral inclusions. Plasmacytoid T cell leukaemia seen mainly in elderly males presents with lymphadenopathy, hepatosplenomegaly and weight loss. The lymph nodes display T zone expansion by plasmacytoid–like cells which do not express myeloperoxidase. They may later develop acute or chronic myelomonocytic leukaemia. Infectious mononucleosis is diagnosed on the basis of characteristic clinical, haematological and serological findings. Kikuchi’s disease may be mistaken for metastatic carcinoma since the histiocytes seen may resemble signet-ring carcinoma cells. However, the cells in metastatic carcinoma are characterised by atypical nuclei and contain mucin rather than cellular debris.

Table 1 summarises the clues to the differential diagnosis of Kikuchi’s disease.

Treatment for Kikuchi’s disease is usually supportive using NSAIDs to alleviate lymph node tenderness and fever. Our patient was treated symptomatically and improved. Corticosteroids have been recommended for severe forms of the disease.

The disease runs a benign course and is usually self-limiting, resolving in several weeks to months. It has a recurrence rate of 3-4%. In some patients, SLE may occur few years later.

**Conclusion**

Although Kikuchi’s disease is self-limiting, the systemic symptoms such as fever can be very distressing to the patient. Clinicians and pathologists should be aware of this condition especially when dealing with a young female patient with fever and cervical lymphadenopathy. The possibility of aseptic meningitis should be considered in patients of Kikuchi’s disease who complain of severe systemic symptoms such as fever and headache during the course of the illness. Also Kikuchi’s disease should be suspected in meningitis of unknown aetiology. Early recognition of Kikuchi’s disease can minimise potentially harmful and unnecessary evaluation and thus prevent misdiagnosis and inappropriate treatment.

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References


