

Kikuchi's Disease

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An 11-year-old girl presented with high grade, intermittent fever and cervical lymphadenopathy. She had multiple enlarged left cervical lymphnodes. The examination of other systems was normal. Workup for sepsis, malignancy and autoimmune disease were negative. VA-IgM for EBV was positive and histopathology of the lymph node was consistent with Kikuchi's Disease.

Keywords: Kikuchi's disease, Necrotising histiocytic lymphadenitis.

Kikuchi's disease is a rare, benign clinicopathological condition presenting with fever and lymphadenopathy. Its association with Systemic Lupus Erythematosus (SLE) makes it necessary to be aware of this condition and follow up these children. We report this child with Kikuchi's disease. Kikuchi's disease should be considered as differential diagnosis in young patients with cervical lymphadenopathy and fever of unknown origin.

Case Report

An 11-year-old girl presented with history of fever for 45 days. Fever was intermittent,

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high grade, accompanied by headache and non-productive cough. She was anorexic with a weight loss of 3 kg. Her parents had noticed swellings on the left side of her neck, which were painful and had gradually increased in size over the last 2 weeks. There was no history of vomiting, rash, arthralgia, breathlessness, mucosal bleed or contact with tuberculosis. On examination she was conscious, febrile, not toxic. She had 5 to 7 tender, enlarged left cervical lymphnodes of 2 × 1 cms size. There were no rashes or generalized lymphadenopathy. The examination of other systems was normal.

Investigations revealed hemoglobin 11.2 g/dL, TLC 2,700 cells/mm³, with a normal differential count and peripheral smear, platelet count 3.5 lacs/mm³ and ESR 29 mm/hr. Blood and urine cultures were sterile. Mantoux, Widal, Leptospirosis-IgM, HbsAg and HIV by ELISA were negative. Chest skiagram was normal and ultrasonography of the abdomen showed mild splenomegaly. Paul Bunnell test, LE cell and ANA were negative. Her complement levels (C3 and C4) were normal. Bone marrow study was normal and culture was sterile. VCA (Viral Capsid Antigen) IgM for EBV (Epstein Barr virus) was positive 18 U/mL (>12U/mL = positive). Excision biopsy of the enlarged left cervical node was done and the histopathology revealed lymphnode with essentially preserved architecture with multiple areas of histiocytic aggregates showing necrosis and karyorrhexis with few C-shaped monocytoid cells. No granulomas were seen. There were no neutrophils in the area of karyorrhexis. Sheets of foamy histiocytes amidst blood vessels were seen. The findings were consistent with necrotising histiocytic lymphadenitis *i.e.*, Kikuchi's disease.

Discussion

Kikuchi and Fujimoto independently first

reported Kikuchi-Fujimoto disease or histiocytic necrotising lymphadenitis without granulocytic infiltration in Japan in 1972. It is considered as a self-limiting benign systemic lymphadenitis, especially involving the cervical nodes of unknown cause(1). Though it has been reported worldwide, it still remains a poorly recognized clinicopathological entity and is confused with malignant lymphoma and systemic lupus erythematosus (SLE). There are only few case reports of this disease in children(2).

The etiology of Kikuchi's disease is not known. Various etiological agents like human herpes virus (HHV₆ and HHV₈), herpes simplex virus, adenovirus, parvovirus B19, cytomegalovirus, varicella zoster, dengue virus(3), bacteria such as Mycobacterium azulgai, yersinia and protozoa have been linked to the disease(1). Kikuchi's disease is included in the protean manifestations of chronic EBV infection and could be a cause in this child. Neoplastic conditions, autoimmune disorders and physiochemical agents have also been postulated. These agents are thought to stimulate a particular immune response resulting in this disease(1,4). Familial occurrence has been reported and hence a genetic predisposition has been proposed(5). The inter relationship between SLE and Kikuchi's disease, though strong is still complex. Some authors feel that Kikuchi's disease is a forme fruste of SLE. There are also reports that suggest that Kikuchi's disease may progress to SLE, hence it is mandatory to exclude SLE and follow these children for several years to ensue early diagnosis of this autoimmune disease, since the prognosis and management differ(5,6). Pathologically malignant lymphoma resembles Kikuchi's disease. Hemophagocytic syndrome is also hypothesised as a part of this disease(7). It is postulated that the plasmacytoid monocytes

play a role in the pathogenesis of Kikuchi's disease via a cell mediated cytotoxic immune response(8).

The important clinical features of Kikuchi's disease are a female predominance (M:F 1:4) with a mean age of 30 years and painless lymphadenopathy mostly in cervical region. The other reported features are fever, myalgia, sore throat, localized pain with mild leucopenia and increased LDH(1). Cutaneous lesions like facial rash, exudative erythema, erythematous papules, vasculitis, plaques and nodules are observed in 40% of cases. They manifest simultaneously or after the illness(9). Arthralgia has also been reported. The symptoms resolve spontaneously within two to three months. Biopsy of the lymphnode is diagnostic. The pathological features of the affected lymphnode are patchy or confluent area of necrosis, varying amount of nuclear debris in affected area, aggregates of histiocytes, presence of medium - large sized transformed lymphocytes (immunoblasts) and plasmacytoid T cells, absence of neutrophils and eosinophils(8). Cytoplasmic tubuloreticular structures resembling viral particles or aberrant organelle structures have been identified by electron microscopy(10). CT scan of the affected lymphnode shows hypodense centers with peripheral ring enhancement corresponding to the central necrosis. Kikuchi's disease causes diagnostic difficulties because of lack of specific signs, symptoms and serological markers. The diagnosis is based on histopathological findings, overlapping of histological features requires differentiating it from a number of infections, autoimmune and lymphoproliferative disease. SLE is the most difficult differential diagnosis, but the complete absence of neutrophils is a good clue, though this does not exclude the possibility of evolution to SLE. In the majority of cases it is a self-limiting disease, recurrence has been

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reported in 3% cases. There are reports of rapid resolution with steroids. The early recognition of this disease helps in avoiding unnecessary investigations and treatment(4).

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