Kikuchi-Fujimoto Disease as a Differential Diagnosis for Cervical Lymphadenopathy in India: A Case Report and Review of Literature

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Abstract Cervical Lymphadenopathy has a large list of differential diagnosis. In India, Tuberculosis and Malignant Neoplasms are the most common specific causes for cervical lymph node enlargement. Kikuchi–Fujimoto Disease (KFD), is an uncommon but increasingly reported cause, especially in Asia. Awareness of this condition amongst physicians leads to an accurate diagnosis without the need for expensive and often potentially harmful investigations. The disease is self limiting and responds well to symptomatic treatment.

Keywords Histiocytic necrotizing lymphadenitis · Kikuchi disease · Lymphadenitis

Introduction

Kikuchi–Fujimoto disease is a self limiting illness characterized by tender cervical lymphadenopathy and fever, more frequently reported in Asia. Though it is an uncommon cause for cervical lymphadenopathy, the clinician should be aware of this condition as a potential differential for cervical lymph node enlargement. This allows accurate diagnosis and avoids expensive and potentially harmful investigations and anxiety for the patient.

Case Report

A twenty-five years old South Indian lady presented to the outpatient department with a painful swelling in the left

side of neck of two weeks duration. She gave history of fever on and off but no other constitutional symptoms. On examination, she had a tender, lymph nodal mass in the left level IIA, IIB [1], measuring 3 cm, and multiple smaller discrete lymph nodes in level V [1]. She did not have any other site of significantly enlarged lymph nodes. Thyroid gland was not palpable. Oral cavity and indirect laryngoscope examination, blood biochemistry, hematology and chest X-ray were normal. Fine needle aspiration cytology (FNAC) was suggestive of reactive lymphadenitis. She was given a course of oral cephalosporin antibiotic, analgesics and was reviewed at the end of a week. There was no change in the symptoms or size of the lymph nodal mass. Ultrasound did not reveal suppuration in the nodes. Contrast CT of the neck suggested cervical lymphadenopathy in the previously described stations without any calcification or necrosis.

Left cervical lymph node excision biopsy was done. Light microscopy (Fig. 1) showed large areas of necrosis with nuclear debris surrounded by large histiocytes. Granulomas were absent and Acid Fast Bacilli (AFB) stains were negative. A diagnosis of Kikuchi–Fujimoto disease was made, and patient was treated symptomatically with Ofloxacin and NSAIDS. The disease resolved in four weeks and patient was completely symptom free when reviewed after three months.

Discussion

Kikuchi and Fujimoto first described independently in 1972 a form of necrotizing lymphadenitis which has now come to be known as Kikuchi–Fujimoto disease (KFD) [2, 3]. The disease has been reported worldwide with a higher prevalence among Asians. Affected patients are often young

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Fig. 1 Light Microscope appearance of Kikuchi-Fujimoto Disease

adults usually under 40 years of age. There is a strong female preponderance reported, but recent evidence from Eastern countries suggests a female to male ratio closer to 1:1 [4]. The etiology remains a mystery, though a viral origin is strongly suspected based on the clinical manifestation of the disease. The viral agents implicated based on immunological tests include Epstein Barr virus (EBV), Human Herpes virus (HHV) 6 and 8, Parvovirus B19 [5, 6].

The classical clinical manifestation includes tender unilateral cervical lymphadenopathy involving predominantly the posterior triangle and the nodes may vary in size between 0.5 and 4 cm. Generalized lymphadenopathy, though reported, is uncommon. Usually the patient has associated low grade fever and upper respiratory symptoms [4]. Extranodal involvement including skin, bone marrow and liver dysfunction have been reported but are uncommon.

CT and MRI appearances are variable and there are no characteristic findings that can be diagnostic of KFD. Both modalities pick up enlarged nodes with necrosis that may mimic, metastatic carcinomas, lymphomas or tuberculosis [7]. Cytological features on FNAC include, polymorphous lymphoid population with abundant karyorrhectic debris and histiocytes, many of which show a small size and eccentrically placed, crescent nuclei. When all these features are present with classical clinical presentation, then a confident diagnosis of KFD is possible. In all other situations, excision biopsy of the lymph node is mandatory for diagnosis. The diagnostic accuracy of FNAC for KFD has been estimated to be 56.3% [8].

The characteristic histopathologic features of KFD include irregular paracortical areas of coagulative necrosis with abundant karyorrhectic debris, with large numbers of different types of histiocytes at the margin of the necrotic areas. Karyorrhectic foci are formed by different cellular types, predominantly histiocytes and plasmacytoid monocytes, but also immunoblasts, small and large lymphocytes. Atypia in the reactive immunoblastic component is not

uncommon and can be mistaken for a lymphoma. Various types of histiocytes can be observed, including crescentic histiocytes, foamy histiocytes and tangible body macrophages. There usually areas of paracortical hyperplasia. Neutrophils are characteristically absent and plasma cells are absent or scarce. The minimum diagnostic criterion and the earliest features are the presence of paracortical clusters of plasmacytoid monocytes with interspersed karyorrhexis and crescentic histiocytes [9]. The immunophenotype of KFD consists of a predominance of T cells, with very few B cells. There is a predominance of CD8 cells over CD4 cells [4].

The histological differential diagnosis includes lymphadenopathy associated with Systemic Lupus erythematosus (SLE), Herpes Simplex associated lymphadenopathy, malignant lymphoma, Plasmacytoid T cell leukemia, metastatic adenocarcinoma, infectious lymphadenitis and Kawasaki disease [4]. In a study of 1724 lymph node biopsy specimens from adult patients from India, Mohan et al. [10] reported that 35.6% had non specific lymphadenitis, 31.3% had tuberculous lymphadenitis, 25.9% had malignancy and <1% were diagnosed with Kikuchi-Fujimoto disease.

The clinical course of KFD is self limiting and lasts 1–4 months. Fatal cases have been reported but are rare. Some advocate the use of steroids in patients with more severe form of disease [11]. There have also been reports of good response to ciprofloxacin [12], minocycline, chloroquine and hydroxychloroquine. In most situations however the disease responds with symptomatic treatment of pain and fever with analgesics and antipyretics.

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