A rare case of Kikuchi-Fujimoto disease

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Abstract

Kikuchi-Fujimoto disease, characterized by histiocytic necrotizing lymphadenitis, closely mimics tuberculosis, and lymphoma are two most common etiologies of cervical lymphadenitis. It is a rare, benign, and self-limited disease. Viral infections or autoimmunity are hypothesized as its etiology, but no causal relationship is definitely established till date. No specific treatment is available, only supportive treatment is given. Here, we represent a rare case of Kikuchi's disease in a 29-year-old male patient who presented to us with right-sided posterior cervical lymphadenopathy with low-grade fever for three months.

Key words: *Excision biopsy, histiocytic necrotizing lymphadenitis, karyorrhectic debris, Kikuchi-Fujimoto disease, paracortical necrosis, self-limited disease*

INTRODUCTION

Kikuchi-Fujimoto disease (KFD) is an extremely uncommon, benign, and self-limited disease. It is also known as histiocytic necrotizing lymphadenitis, and characterized by tender lymphadenopathy in young females, occasionally associated with low-grade fever and night sweats. It was first described by Kikuchi in 1972 in Japan, and also by Fujimoto *et al.* in the same year.[1,2] Etiology of this disease is unknown. Microscopically, it is characterized by lymphadenitis with paracortical coagulative necrosis, focal proliferation of histiocytes, and extensive karyorrhexis. There is no specific treatment for KFD. Here, we report a rare case of Kikuchi's disease in a 29-year-old male patient, presented with posterior cervical lymphadenopathy for three months with spontaneous recovery on symptomatic treatment.

CASE REPORT

A 29-year-old non-smoker, normotensive, non-diabetic, male patient presented with two painless, round swellings in right side of the neck for three months with low-grade fever. Initial sizes of the swellings were 2 × 3 cm, and 2 × 2 cm respectively, and their sizes were not increased. There were no respiratory symptoms. Other symptoms like night sweats, fatigue, skin rash, significant weight loss, and anorexia were absent. There was no past history or family history of tuberculosis or intake of antitubercular drugs. There was no history of similar swellings in recent or remote past. On general survey, his pulse rate was 96 beats/minute, respiratory rate 16 breaths/minute, axillary temperature was 99°F, and blood pressure was 110/70 mmHg. Examination of neck revealed two, non-tender, rounded swellings in posterior triangle of right side. Swellings were mobile, discrete, not fixed to underlying structures or overlying skin, and firm in consistency with lobulated surface. Sizes of the swellings were 2 × 3 cm, and 2 × 2 cm respectively, and margins were discrete, not palpable inferiorly. Transillumination test and fluctuation test were negative. There was no color change or discharging sinus on overlying skin. Examination of respiratory and other system revealed no abnormality.

Complete hemogram and blood biochemistry were normal. Chest radiograph, posteroanterior view revealed no abnormality. Ultrasound of whole abdomen was normal. Anti HIV-1/2 antibodies were non-reactive. Mantoux test (5 TU) was negative (induration of 6 cm at 72 hours). The patient was advised tablet co-amoxiclav-625 mg three times daily for seven days. As there was no improvement, fine needle aspiration cytology of cervical lymph node was done, which revealed reactive lymphoid hyperplasia only, no granuloma or malignant cell was found. Finally, excision biopsy of the cervical lymph node was done to establish the diagnosis, and histopathological examination of biopsy specimen showed lymphoid follicles with germinal centers, paracortical coagulative necrosis containing karyorrhectic foci, suggestive of Kikuchi's disease. The necrotic focis are surrounded by reactive histiocytes, lymphocytes, and occasionally by plasma cells. Ziehl Neelsen stain revealed no acid fast bacilli [Figure 1]. Immunohistochemistry revealed predominance of CD8+ T lymphocytes and histiocytes in the karyorrhectic foci expressed positivity for CD 68 antigen. Serum anti-nuclear antibody and

anti-dsDNA antibody was negative. So, our final diagnosis was Kikuchi's disease. As it is a self-limited disease entity, no active treatment was given further; the complete recovery was documented on follow up after one month.

DISCUSSION

KFD is characterized by histiocytic necrotizing lymphadenitis of unknown etiology, mainly involves cervical lymph nodes in females with a male-female ratio of 1:4.[3] The disease is mostly prevalent in Asiatic population, especially in Japanese.[4] It is predominantly seen in young adults of second and third decades. Cervical lymph nodes are predominantly involved, i.e., in around 80% cases, and most commonly in the posterior triangle.[5] Enlarged lymph nodes may be tender, and associated with low-grade fever, upper respiratory symptoms, or less commonly with arthralgia, skin rashes, fatigue, malaise, weight loss, anorexia, night sweats, diarrhea, nausea, vomiting, chest or abdominal pain, and hepatosplenomegaly.

It is an idiopathic disease; however, association with viral infections or autoimmune diseases like systemic lupus erythematosus, mixed connective tissue disease, and Still's disease has been hypothesized in the literature, and however no causal relationship has been confirmed.[3] Epstein barr virus, Human immunodeficiency virus, Herpes simplex virus, Dengue virus, Human T lymphotrophic virus 1, Cytomegalovirus, and Parvovirus B19 have been implicated as possible etiological agents.[6] Bacteria like Toxoplasma, *Yersinia enterocolitica*, Bartonella, and Brucella are also implemented.[7] Pathogenesis of Kikuchi's disease is still not clear; however, it is thought that primary inciting agent results in activation of T lymphocytes and histiocytes. Proliferating T cells undergo apoptosis, leading to multiple paracortical areas of coagulative necrosis within the lymph nodes, which is followed by removal of nuclear debris by histiocytes.[8]

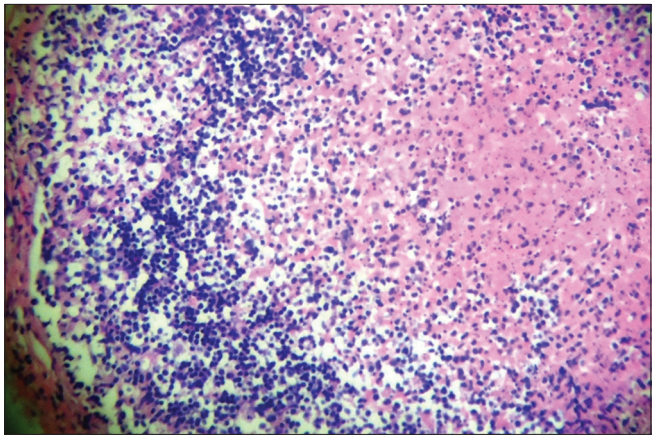

Figure 1: Microphotograph of biopsy specimen from right posterior cervical lymph nodes showing paracortical coagulative necrosis containing karyorrhectic foci, surrounded by reactive histiocytes and lymphocytes suggestive of Kikuchi's disease (H and E stain, ×40)

Complete hemogram only reveals raised erythrocyte sedimentation rate, and atypical lymphocytes are seen in 25 to 31% patients in peripheral blood.[9] C-reactive protein may be raised. Diagnostic yield of fine needle aspiration of cytology is only 56%; in most cases, the report is reactive hyperplasia of lymph nodes.[7] Hence, excision biopsy of lymph nodes is confirmatory test. Histopathologically, there are multiple paracortical areas of coagulative necrosis with abundant karyorrhectic debris, incomplete distortion of the nodal architecture, and large number of different types of histiocytes at the margin of the necrotic areas. Karyorrhexis means nuclear chromatin destruction which is dispersed as fine granules within the cytoplasm. These karyorrhectic foci are formed by CD68+ histiocytes, plasmacytoid monocytes, immunoblasts, small and large lymphocytes, mainly CD8+ T lymphocytes. Neutrophils are typically absent. Plasma cells are almost absent, which separates the disease from lupus lymphadenitis, and also anti-nuclear antibody and anti-dsDNA antibody are negative in Kikuchi's disease.[10] Based on histopathologically, Kuo described three types of Kikuchi's disease: Proliferative, necrotizing, and xanthomatous.[11] Incomplete architectural effacement with patent sinuses, presence of multiple reactive histiocytes, scarce or absent mitotic figures, and absence of Reed-Sternberg cells on microscopic examination differentiate Kikuchi's disease from Hodgkin's disease or non-Hodgkin's lymphoma.[12]

Kikuchi's disease is self-limiting disease and associated with a benign course. It usually resolves spontaneously over weeks to months. Supportive treatments like paracetamol or non-steroidal anti-inflammatory drugs are given to alleviate tender lymphadenopathy or fever. In severe cases, corticosteroids may be used. Recurrence of the disease occurs only in 3 to 4% cases.[7]

Early establishment of tissue diagnosis of enlarge lymph nodes is essential to exclude two most common etiologies like tuberculosis and lymphoma. Although Kikuchi's disease is rare, it mimics tuberculosis or lymphoma; hence, early diagnosis by excision biopsy alters the common treatment protocol and the thinking regarding prognosis.

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