KIKUCHI DISEASE WITH ASSOCIATED SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

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ABSTRACT

This case report describes a 28 year old male patient presenting with low-grad fever, symmetrical polyarthritis, rash on palms, neck and trunk, oral ulcers and cervical, axillary and hilar lymphadenopathy. Other systemic examination was unremarkable. Patient was diagnosed as Kikuchi-Fujimoto's disease on the basis of lymph node histopathology, which showed the pathognomonic "Acute Histiocytic Necrotizing Lymphadenitis". Concurrently diagnosis of systemic lupus erythematosus (SLE) was also made because of the presence of five out of eleven criteria for the diagnosis of SLE. The five criteria which were present in this patient were oral ulcers, arthritis, proteinuria of 1295 mg/24 hrs, positive Antinuclear Antibody and positive anti-double stranded DNA.

Key words: *Kikiuchi-Fujimoto's disease, Systemic Lupus Erythematosus, Acute Histiocytic Necrotizing Lymphadenitis, Antinuclear antibody, Anti-double stranded DNA.*

INTRODUCTION

Kikuchi disease, defined as acute histiocytic necrotizing lymphadenitis, is an uncommon, idiopathic, generally self-limited cause of lymphadenitis. Kikuchi first described the disease in 1972 in Japan.

It was originally described in young women of Asian origin. It is usually characterized by cervical lymphadenopathy and fever. It usually settles by itself in 1-6 months. It is diagnosed by doing the histopathology of the involved lymph node, which shows the pathognomonic histiocytic necroitizing lymphadenitis. The cause of Kikuchi disease is unknown, although infectious and autoimmune etiologies have been proposed. The most favored theory proposes that Kikuchi disease results when one or more unidentified agents trigger a self-limited autoimmune process. Several viral candidates have been proposed, including cytomegalovirus, Epstein-Barr virus, human herpes virus, varicella-zoster virus, parainfluenza virus, parvovirus B19, and paramyxovirus[1].

Kikuchi disease has been reported in association with a number of autoimmune and infectious diseases including infrequent co-existence with Systemic Lupus Erythematosus (SLE). Differentiation between Kikuchi disease and SLE is imperative because of significant differences in treatment and prognosis. SLE may precede, coincide with or develop after the presentation of Kikuchi's disease[2].

CASE REPORT

A 28 years old male presented with six months history of low-grade intermittent fever usually in the evening associated with sweating. Fever almost always responded to Paracetamol and Ibuprofen. Three months after developing fever he gradually developed joint pains and swelling of wrists, small joints of the hands and knees symmetrically, with morning stiffness of more than one hour. Later on he developed oral ulcers and rash on the trunk and palms of the hand. In his past history he was never admitted for any medical or surgical reasons. He used to take on and off NSAIDs for fever and joint pains. On physical examination he was pale, weak and anxious with pulse rate 95/min, regular and normal volume. His Blood Pressure was 105/60 with no postural drop temperature at the time of admission was 100 °F. Nails showed dystrophic

changes with infarcts in the nail beds and maculopapular rashes on the palms and trunk. The affected joints were swollen, red, warm and painful. Mobility of the joints was hampered due to pain. There was bilateral axillary lymphadenopathy, and cervical lymphadenopathy. Patient had thin, sparse scalp hair. Other systemic examination was normal.

Investigations revealed Hb of 9.9 gram%; WBC count 10,100/mm³ (N=85%,L=15%); platelets 270 x 10^3 /µL; ESR 50mm/1st hr; blood urea 37 mg% and serum creatinine of 0.73 mg% . Serum electrolytes performed and showed Na? 135 meq/L; K? 4.13 meq/L and Cl? 106.5 meq/L. Serum LDH 254 U/L, Prothrombin time was 14 seconds against 13 seconds of control; activated Partial Thromboplastin Time was 37 seconds against 35 seconds of control. Urinalysis revealed 8-10 pus cells, 0-1 RBCs, Albumin +1, Granular casts +3, 24hrs urinary Proteins 1295 mg/24 hrs. Complement levels were sent which showed low C3 and C4; C3 0.33 gram % (normal range 0.88-2.01 gram %); C4 0.05 (normal range 0.16-0.47 gram %), Rheumatoid factor was Positive; Antinuclear antibody Positive; anti-double stranded DNA positive; VDRL negative serum ferreitin 380 ng/dl (normal range 20-400 ng/dl); Hepatitis B surface antigen and Anti-HCV antibodies both were non-reactive. ECG, echocardiography and ultrasound of abdomen and pelvis were normal. Chest x-ray showed bilateral hilar Lymphadenopathy. Biopsy of cervical lymph node was done and the histopathology report showed “Cortex has variable sized follicles with germinal centers. Paracortical area shows large confluent eosinophilic areas having histiocytes and plasma cells, karyorrhectic and eosinophilic debris. No neutrophils are seen. Diagnosis is Kikuchi-Fujimoto disease because of the pathognomonic acute histiocytic necrotizing lymphadenitis”.

On the basis of biopsy report, clinical features and laboratory investigation the diagnosis of Kikuchi disease with concurrent systemic lupus erythematosus was made. He was started on prednisone at 1mg/kg/day. On follow up after 6 weeks he was free of constitutional symptoms and there was no active arthritis, rash was still present and lymphadenopathy had resolved except for 2 non-significant lymph nodes in the left axilla. He was tolerating steroids generally well except slight cushingoid face as compared to previous photograph and mild on and off epigastric pain. In an attempt to withdraw steroid he was started on azathioprine at 50mg t.i.d. and tapering dose of prednisone and was asked to come for follow up after 6 weeks when the dose of prednisone reaches 10mg/day. We also addressed his gastritis and photosensitivity by starting him on ranitidine 150mg b.d. and to use sunscreen while going out. After 6 weeks he was tolerating the low dose of steroid well and has improved symptomatically. His routine blood workup which included blood complete, Liver function tests U&E and urinalysis were normal. He is now using azathioprine 50md t.i.d. with alternate day prednisone 10 mg. He was referred to nephrologist for renal assessment and is currently being investigated for renal involvement.

DISCUSSION

Kikuchi's disease is a characterized by fever (30-50%), and cervical lymphadenopathy (100%) constitutional symptoms and rash[3,4], as in our patient. In contrast to our patient, generalized lymphadenoapthy is very rare. Extranoadal sites like joints, liver, spleen, thyroid and meninges may also occur. Lymph node histology shows pathognomonic acute histiocytic necrotizing lymphadenitis and can be mistaken for lymphoma or systemic lupus erythematosus especially when the biopsy shows proliferative phase (see below). Our patient's biopsy showed the necrotizing phase which helped us to diagnose kikuchi.

While initially described in young women, Kikuchi's syndrome clearly also occurs in men, as in our case. The ratio of affected males to females in three series was 1:4, 1:1.6, and 1:1.26, respectively[3]. Most patients are less than 40 years of age, but this condition has been reported in patients ranging in age from 6 to 80 years, most of whom were previously well[5]. Most cases have been reported from East Asia, with fewer cases from Europe and America.

The diagnosis of Kikuchi's disease is made by lymph node biopsy[3], which shows “Acute histiocytic necrotizing lymphadenitis”. Three histologic phases of Kikuchi disease are being described[6].

A. Proliferative phase: follicular hyperplasia, paracortical expansion by lymphocytes, T and B cell blasts, plasmacytoid monocytes and histiocytes (presence of numerous blast cells may confuse with lymphoma, EBV, or HSV infection)

B. Necrotizing phase: necrosis without a neutrophilic infiltrate; progressive dominance of histiocytes as major cell type. So our patient was in the necrotizing phase as there was histiocytic necrosis on biopsy with the absence of any foamy cells (see below).

C. Xanthomatous ("foamy cell") phase: The recovery phase with resolution of necrosis.

The diagnosis of Kikuchi disease is more

likely than lymphoma[7] if, there is incomplete architectural effacement with patent sinuses; Presence of numerous reactive histiocytes; relatively low mitotic rates; Absence of Reed-Sternberg (RS) cells. Absence of RS cells and low mitotic figures and preserved nodal architecture efficiently excludes lymphoma in our patient. Similarly: Kikuchi disease and SLE[7] have similar histopathologic appearances. Kikuchi disease is suggested by the absence of Hematoxylin bodies, Plasma cells; Neutrophil. The biopsy of our patient shows no neutrophil thereby excluding SLE adenitis.

Kikuchi disease is generally a self-limited disease with a favorable prognosis. Lymphadenopathy usually resolves within 1-6 months after onset, although it may persist longer. Our patient's lumphadenopathy resolved in 10 weeks with treatment. About 3% of patients experience recurrence[7]. Four deaths have been reported. Three patients died during the acute phase of generalized Kikuchi disease. One patient died from cardiac failure; another from the effects of hepatic and pulmonary involvement; and a third, from an acute lupus-like syndrome. A fourth patient died from severe infection in a patient with Kikuchi disease and concurrent SLE[8]. In our patient his kikuchi disease has resolved but due to the presence of SLE he is still placed in a bad prognosis group, because he is male and also he is at increased risk of developing infection (both due to immunosuppressant therapy and the disease itself) and cardiac complications.

Treatment of Kikuchi disease is generally supportive. Nonsteroidal anti-inflammatory drugs (NSAIDs) may be used to alleviate lymph node tenderness and fever. The use of corticosteroids and immunosuppressants has been used successfully in severe extranodal or generalized Kikuchi disease[9, 10]. In our patient due to debilitating constitutional symptoms and concomitant SLE the need of hight dose steroid and latter azathioprine was necessary.

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