Kikuchi's Disease and Systemic Lupus Erythematosus in A Saudi Child

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Kikuchi's disease, or histiocytic necrotizing lymphadenitis, is a disorder initially described in Japan[1] and now recognized worldwide.[2-10] This disease entity manifests clinically with localized cervical lymphadenopathy, occasionally tender to palpation. Some patients exhibit weight loss, fever, splenomegaly,[3] leukopenia,[11] and high sedimentation rate.[8] The disease particularly affects young women, in a ratio of 4:1.[2,12] The youngest patient reported was 11 years old.[2] The disease usually resolves spontaneously in one to four months.[13]

Histologically, the lymph nodes show localized proliferation of histiocytes and reticulum cells associated with abundant nuclear debris and marked tissue necrosis.[2,3] Systemic lupus erythematosus (SLE) is the most difficult differential diagnosis histologically[2,11] and clinically, and the inability to distinguish between these two diseases may lead to development of a progressive and serious disorder.[2,6,7,14] This report describes the case of a child who developed a florid case of SLE, presenting initially as Kikuchi's disease.

Case Report

A 10-year-old Saudi boy presented with fever, anorexia, loss of weight and joint pain over a period of one month. There was a history of raw milk ingestion. One week prior to admission, swelling was observed on the right side of the neck, which progressively increased in size. Physical examination showed an enlarged lymph node in the right cervical posterior triangle, measuring 3x3 cm, tender and mobile. There was no other significant lymphadenopathy.

Investigations revealed lymphopenia (0.7×10^9/L) and anemia, Hb 67 g/L, ESR 20 mm/hr, urea 4.5 mmol/L, and creatinine 58 μmol/L. Urinalysis, WBC <10, protein 30 mg/dL, and tuberculin skin test (5 units) were all normal. Toxoplasma and brucella serology were negative. Chest x-ray showed prominent right paramediastinal shadow. CT scan of the chest and abdomen showed para-aortic lymphadenopathy. Bone marrow aspiration and biopsy were normal. Cervical lymph node biopsy (Figures 1A and 1B) showed fibrous thickening of the capsule. The subcapsular sinus in some areas was expanded and filled with individually necrotic cells mixed with foamy histiocytes, many of which contained nuclear debris. Another area with individually necrotic cells and phagocytic histiocytes showed sprinkling and atypical plasmacytoid cells with prominent nucleoli. No Sternberg-Reed cells were seen, and three to four well-formed multinucleated giant cells were also present. The special stains for micro-organisms (PAS, Gram, ZN, Warthin Starry) were all negative, with overall impression of histiocytic necrotizing lymphadenitis.

The diagnosis of Kikuchi's disease was made based on the clinical and histological presentations. There was spontaneous improvement clinically and the patient was discharged.

Two months later, the patient developed symptoms similar to the initial presentation, with an ESR of 75 mm/hr. Four months after the initial presentation, he was re-admitted because of severe joint pain, persistent fever and hypertension. There was significant proteinuria and hematuria, hemoglobin was 71 g/L, ESR 72 mm/hr, serum urea 10.6 mmol/L, creatinine 148 μmol/L, antinuclear antibody titer (ANA) 1:2560, anti-double-stranded DNA was 1200 IU/mL (0-100), C_3 30 mg/dL (88-199 mg/dL), C_4 8 mg/dL (12-40 mg/dL). Renal biopsy was done and showed diffuse proliferative glomerulonephritis (class IV lupus nephritis) (Figure 2).

A diagnosis of SLE with lupus nephritis was made. The patient was started on prednisolone 2 mg/kg/day and IV cyclophosphamide 0.5 g/m^2 on a monthly basis. Two months later, he was completely well, with no proteinuria, ESR 35 mm/hr, serum urea 6.2 mmol/L and creatinine of 75 μmol/L. ANA, anti-double-stranded DNA, C_3 and C_4 levels were normal.

Discussion

On clinical grounds, Kikuchi's disease (KD) is known as a benign self-limiting disease. The patients with this disease are characteristically young women with cervical adenopathy which may be tender and associated in some cases with fever and leukopenia. It resolves spontaneously within two to three months.[1] Our patient represents the youngest male child presenting with KD, whose symptoms of fever and arthralgia subsided spontaneously to present after a few months with systemic lupus erythematosus.

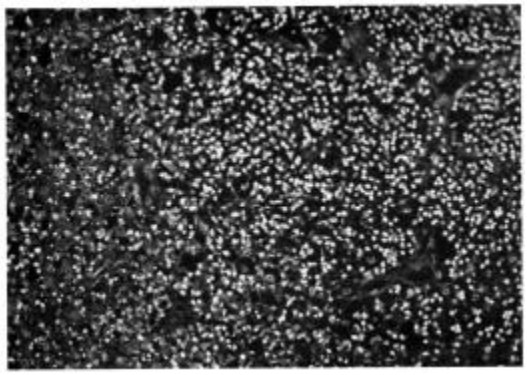

Figure 1 A. Necrotizing lymphadenitis: low-power view showing necrotic areas containing nuclear dust particles and hematoxyphilic bodies (left side of the photomicrograph) (H&E stain, 100x).

The majority of cases of KD originate from Japan, where the entity appears to be common,[11] but it is now known to have a worldwide distribution.[2] So far, 28 patients have been reported from Saudi Arabia.[6,7,9,10] The association between KD and SLE, or other autoimmune diseases, has been described in the literature,[2,6,7,14,15] where SLE appeared after the diagnosis of KD[2] or even preceded it.[8]

Histologically, the disease is characterized by coagulative necrosis, an infiltrate of histiocytic cells, varying degrees of loss of nodal architecture and an absence of polymorphs. Systemic lupus erythematosus is the most difficult differential diagnosis,[2] but the complete absence of polymorphs is a good clue.[4] In an ultrastructural study of 15 patients with subacute necrotizing lymphadenitis, a peculiar structure of unknown origin called a tubuloreticular structure was observed with high frequency within the lymph node cells of those patients. The detection of this structure in human lymph nodes is rare except in cases of SLE,[11] which may suggest that this disease reflects an SLE-like immunological event occurring in the lymph nodes. Based on these observations and the possibility raised by some authors[8,11] that Kikuchi's disease could be a common aspect of SLE or subsequent development of SLE,[2] we feel that KD as a clinical entity needs to be evaluated more seriously by clinicians, as it is a histological description which is difficult to distinguish from more serious diseases. We therefore recommend that patients with Kikuchi's disease should be closely followed for several years to ensure an early diagnosis of more serious autoimmune disease.

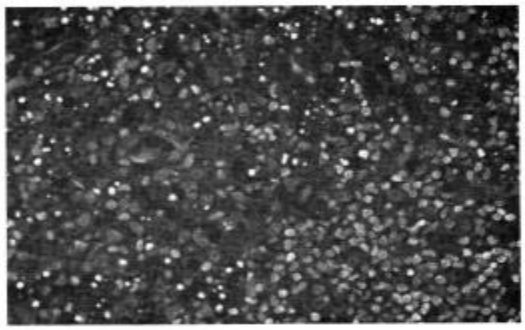

Figure 1B. Necrotizing lymphadenitis: high-power view showing a focus of necrosis with numerous nuclear particles and histiocytes. Note the complete lack of polymorph leukocytes (H&E stain, 400x).

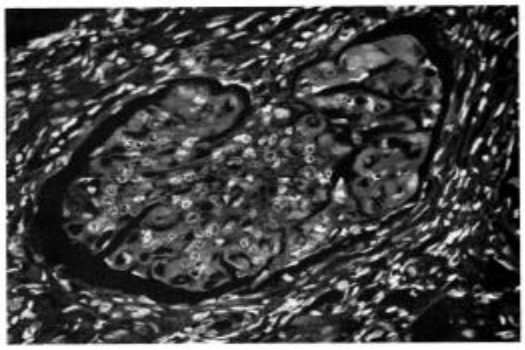

Figure 2. Lupus nephritis: WHO class IV. High-power view showing increased mesangial and endothelial cellularity with segmental necrosis (H&E stain, 400x).

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