Systemic lupus erythematosus presenting with generalized lymphadenopathy A case report

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Systemic lupus erythematosus (SLE) is an immune complex disease with many different clinical presentations. Here we report a 13-year-old female patient presenting with generalized lymphadenopathy, who meanwhile developed butterflly rash and pericarditis. The diagnosis of SLE was based on the clinical features, positive antinuclear antibody, and positive antibodies to dsDNA. The patient had an active disease and developed renal involvement, despite steroid therapy. The patient's clinical presentation, course and response to therapy are detailed, and the literature on lupus lymphadenitis is reviewed.

Key words: lymphadenopathy, systemic lupus erythematosus.

Systemic lupus erythematosus (SLE) is a challenging autoimmune disease of interest to general pediatricians because the wide variety of its manifestations necessitates its inclusion in the differential diagnosis for children and adolescents presenting with many different complaints[1]. SLE is an episodic, multisystem, autoimmune disease characterized by the widespread inflammation of blood vessels and connective tissues and by the presence of antinuclear antibodies (ANAs), especially antibodies to native (double-stranded) deoxyribonucleic acid (nDNA)[2]. Its clinical manifestations are extremely variable, and its natural history is unpredictable. The diagnosis of SLE is a clinical one and is supported by specific laboratory abnormalities[1,2]. No single clinical, laboratory or pathologic finding is sufficient to establish the diagnosis of SLE[3]. It remains a diagnosis of exclusion, requiring a combination of findings from a limited set of possible features. The American College of Rheumatology (ACR) has published 11 criteria for the diagnosis of definite SLE[4]. About half of chíldren with SLE have localized or generalized lymphadenopathy (LAP)[1,2,5,6]. Here we report a case presenting with generalized LAP who was diagnosed as SLE, and we review the relevant literature.

Case Report

A 13-year old girl was admitted with the complaints of cervical, axillary, and inguinal masses, periorbital swelling and erythema. Four months previously, periorbital swelling and erythema were noticed and she was evaluated as an outpatient in our hospital: compelete blood count, urinalysis and biochemistry were normal. Her complaints recurred, and cervical, axilary and inguinal masses appeared 15 days before admission.

There was no history of malignancy or autoimmune disease in the family.

Physical examination revealed mild periorbital edema, and blood pressure of 110/80 mmHg. Occipital, bilateral posterior cervical, bilateral axillary and bilateral inguinal multiple LAP (1.5 x 2 cm) were remarkable. Her liver and spleen were palpable 2 cm and 1 cm, respectively, below the costal margins on the midclavicular line. The remainder of the examination was normal.

Laboratory investigations revealed a Hb value of 11.1 g/dl, leukocyte count of 12,000/mm^3 with 60% neutrophils and 40% lymphocytes, platelet count of 194,000/mm^3 and erythrocyte sedimentation rate of 80 mm/h. Urinalysis, renal

and liver function tests, and coagulation tests were within normal limits. Chest roentgenogram was normal, cervical ultrasonography revealed multiple conglomerates of LAP without necrotic pattern. Abdominal ultrasonography disclosed hepatosplenomegaly. Echocardiography displayed pericardial effusion. Microbiological tests were negative for a pathogen microorganism. Salmonella and Brucella aglutination tests were negative. The serological tests were negative for Epstein-Barr virus, cytomegalovirus and toxoplasma.

The patient was first evaluated for the diffential diagnosis of generalized LAP. Infectious diseases like typhoid fever and brucellosis were eliminated by negative serological tests and culture results.

She developed malar rash on the second day of hospitalization. When she was evaluated for the diagnosis of SLE, ANA was positive, anti-dsDNA was 170 IU/ml (0-7), anti-Sm (+) C3 38.5 mg/dl (50-90), C4 25 mg/dl (10-40), direct Coombs' (-), anti-thrombocyte antibody (-), VDRL (-), and IgG 2920 mg/dl (800-1700). Four of the 11 criteria of ACR were fulfilled (malar rash, pericarditis, ANA positivity, anti-dsDNA antibodies and anti-Sm nuclear antigen antibodies), and the patient was diagnosed as SLE.

During hospitalization she developed purpuric rash and arthralgia. The patient was started on 60 mg prednisone daily, and in a few days pericardial effusion and LAP resolved, complement levels returned to normal and anti-dsDNA antibody titer decreased. At the end of six weeks, the prednisone dose was tapered by 5 mg at two-week intervals to a minimum dose sufficient to maintain clinical and serological remission. Parallel to the tapering of the prednisone dose, C3 and C4 levels decreased again. Although the patient was asymptomatic, complement levels were continuously low. In a short time proteinuria (0.7 g/m^2/d) had amenorrhea developed. Urinalysis showed erythrocyte casts and 2 + proteinuria, and the patient was referred to a center for renal biopsy. Later it was learned that her renal biopsy revealed Grade 3 SLE nephritis, and she was treated with cyclophosphamide pulses.

Discussion

Generalized LAP is defined as LAP involving two or more noncontiguous lymph node regions. Bacterial, viral, and protozoal infections; connective tissue disorders; hypersensitivity states; lymphoproliferative disorders; neoplastic diseases; storage diseases and granulomatous diseases should be taken into consideration in the differential diagnosis of generalized LAP[7]. In the case of a problem in diagnosis, excisional lymph node biopsy is indicated. No infectious etiology could be found in our patient. During her saty in our hospital, she developed butterfuly rash, and the laboratory findings revealed the diagnosis of SLE. It is known that about half of children with SLE have localized or generalized LAP[1,2,5,6]. Occasionally this may be extreme, suggesting a diagnosis of Hodgkin's disease, a malignancy that rarely has been reported in association with childhood SLE[8]. In recent series from the literature, the prevalence of LAP is 12 to 59 percent of patients with SLE[9].

Bhalla et al.[10] reported 14 SLE cases with Hodgkin's disease; mediastinal LAP was found in 58 percent of the cases, and retroperitoneal LAP in 17 percent. They concluded that a feature of LAP due to SLE was their peripheral localization. It is generally accepted that mediastinal and abdominal lymph nodes are always pathologic, if enlarged[7]. Our case also had only peripheral LAP; neither a mediastinal nor abdominal LAP was found. Bhalla et al.[10] also called attention to severe itching that was found in 63 percent of SLE patients with Hodgkin's disease; only 2.8 percent of SLE cases had itching. Eisner et al.[9] described the most commonly involved nodal groups in SLE as cervical (43%), mesenteric (21%), axillary (18%) and inguinal (17%).

The description of the lymph node pathology in SLE is paracortical foci of necrosis and infiltration by histiocytes, lymphocytes, plasma cells and immunoblasts; the hematoxylin body, an amorphic aggregate of basophilic material, is pathognomonic of lupus adenitis[2,9]. The necrotizing lymphadenitis of SLE was found to be similar pathologically to Kikuchi-Fujimoto disease, which is a distinctive, self-limited form of necrotizing lymphadenitis[9,11].

Chandrasekaran et al.[12] analyzed 59 children with SLE whose initial manifestations were fever (67%), arthritis (61%), skin rash (59%) and LAP (27.1%). The cumulative clinical features observed were arthritis (86.6%), fever (79.8%),skin rash (69.4%), LAP (61%) and hepatosplenomegaly (39.9%). On the other

hand, Cassidy et al.[13] evaluated the initial and cumulative manifestations of 58 children with SLE, and LAP were not mentioned.

In a report of 28 SLE patients, anti-Sm antibody was found in 30 percent of cases, particularly in those patients with LAP and fever[14]. Antibodies to Sm are closely linked to SLE, found roughly in two-thirds of patients with active SLE[1]. But in a study of 22 children with SLE, anti-Sm was found to be present in only 14 percent[2]. Antibodies to Sm antigen complex, in the absence of other autoantibody activity, have been related to central nervous system (CNS) disease[16,17]. Our patient had positive anti-Sm antibody but did not have CNS symptoms.

In a previous report by Shapira et al.[18], LAP was present in 26 percent of of 90 patients. Patients with LAP had significantly more constitutional symptoms of fatigue, fever and weight loss, more cutaneous symptoms and signs, a higher rate of hepatomegaly and splenomegaly, increased anti-dsDNA antibodies and decreased complement levels. Although disease activity index was higher among patients with LAP, there was no difference in renal or CNS involvement between patients with LAP and those without LAP. Our case also had a fulminant course with renal involvement.

In conclusion, arthritis and skin lesions are the most frequent and wellknown manifestations of SLE, but SLE should also be considered in patients presenting with generalized LAP.

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