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Case Report

Kikuchi's Disease in Systemic Lupus Erythematosus : an Independent or Dependent Event ?

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Summary **The authors describe necrotizing histiocytic lymphadenitis (Kikuchi's disease) in association with systemic lupus erythematosus (SLE). To our knowledge this is the first case report where SLE preceded Kikuchi's disease. Whether Kikuchi's disease is an independent event or directly connected with SLE is discussed.**

Key words: **Histiocytic Necrotizing Lymphadenitis, Lymphadenopathy, Systemic Lupus Erythematosus.**

INTRODUCTION

Kikuchi's disease or histiocytic necrotizing lymphadenitis was first described by Kikuchi and Fujimoto et al. (1,2) as a cause of benign lymph node enlargement and is well known in the eastern hemisphere but only recently in Europe and North America (3).

It usually affects the cervical lymph nodes, particularly in young women and subsides spontaneously within weeks or a few months with no recurrences. The most common clinical symptoms are adenopathy alone or adenopathy with fever. Sometimes the lymph nodes are tender, the erythrocyte sedimentation rate (ESR) is elevated and leukopenia and an increase of hepatic transaminases can be present (4,5).

Histology is characterized by a patchy necrotizing process localized mainly in the paracortical areas of the lymph nodes with karyorrhectic debris, a mononuclear cell infiltrate and an absence of neutrophils and plasma cells (6). The cause of the disease remains uncertain, although recently some authors proposed that Kikuchi's disease may reflect a self-limited autoimmune condition induced by virus-infected transformed lymphocytes (7).

Lymphadenopathy is present in approximately 60% of patients with SLE (8). It is usually detected in the cervical, axillary and inguinal areas and is nontender, soft, and discrete. Histological findings of enlarged lymph node in SLE usually show areas of necrosis, hematoxylin bodies with numerous granulocytes and plasma cells, but in some cases it may be indistinguishable from Kikuchi's lymphadenitis (6).

We describe a case of a young woman suffering from SLE who developed Kikuchi's disease. The aetiological and chronological relationship between Kikuchi's disease and SLE are discussed.

CASE REPORT

A 22-year-old Italian woman was affected with SLE. Her principal symptoms were: fever, arthritis, "butterfly" rash on the face and gran mal convulsions. Laboratory studies confirmed the diagnosis : positive LE cells, antinuclear antibodies (ANA) 1/2560 (speckled pattern) with positivity for anti-Sm antibodies. The rheumatoid factor and VDRL were negative. Magnetic resonance imaging of the brain showed an area of vasculitis in the parieto-lateral region of the right cerebral hemisphere.

The disease was well controlled by the administration of 25 mg/die of prednisone when she presented a daily fever of up to 40°C, malaise and enlarged tender lymph nodes varying in size from 1-2 cm in the right latero-cervical region. No hepatosplenomegaly or other lymphadenopathy was noted.

She was hospitalized and the only laboratory abnormalities were : a moderately increased ESR (38 mm/h Westergren), leukopenia (2800/mm^3) with a normal differential count and an increase of serum glutamic oxalacetic transaminase (3× normal value) and serum glu-

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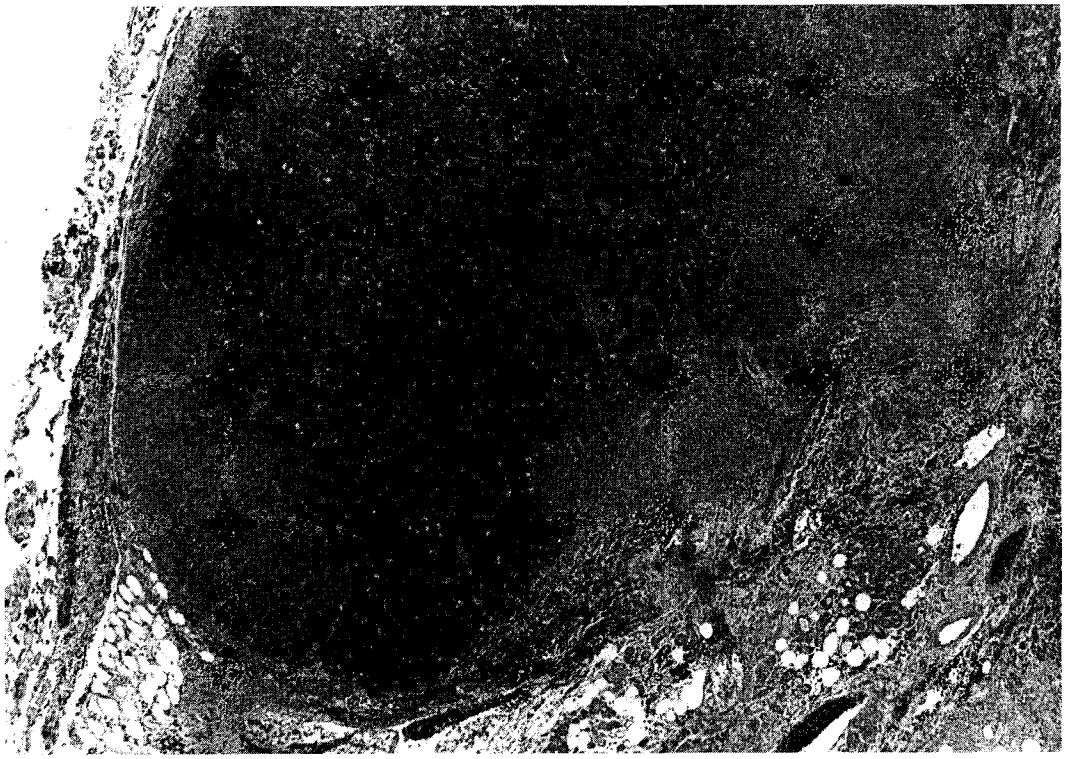

Fig. 1: Lymph node with several well-circumscribed paracortical necrotizing process and with residual structures (germinal centers, sinuses, expanded paracortex with mottled patterns). (Hematoxylin-eosin, × 25). These features were compatible with necrotizing lymphadenitis.

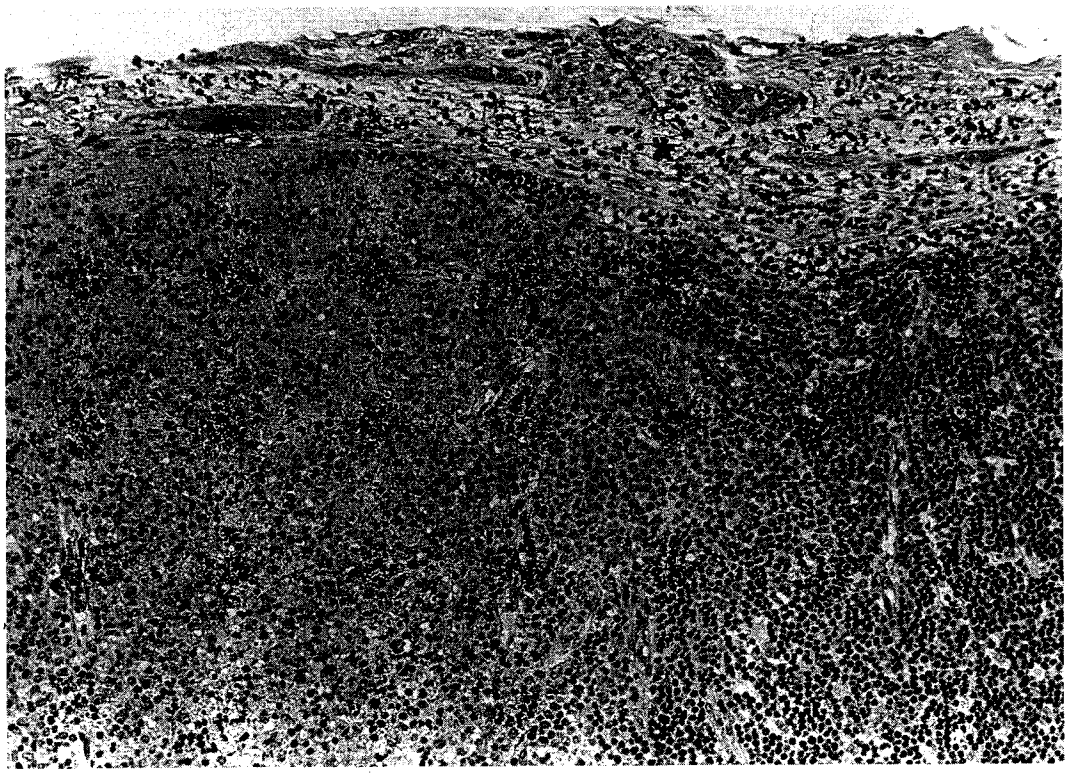

Fig. 2: Focal well-circumscribed sub-capsular necrotizing process characterized by karyorrhectic nuclear debris, histiocytes, large lymphoid cells. Intact lymph node capsule. (Hematoxylin-eosin, X 100).

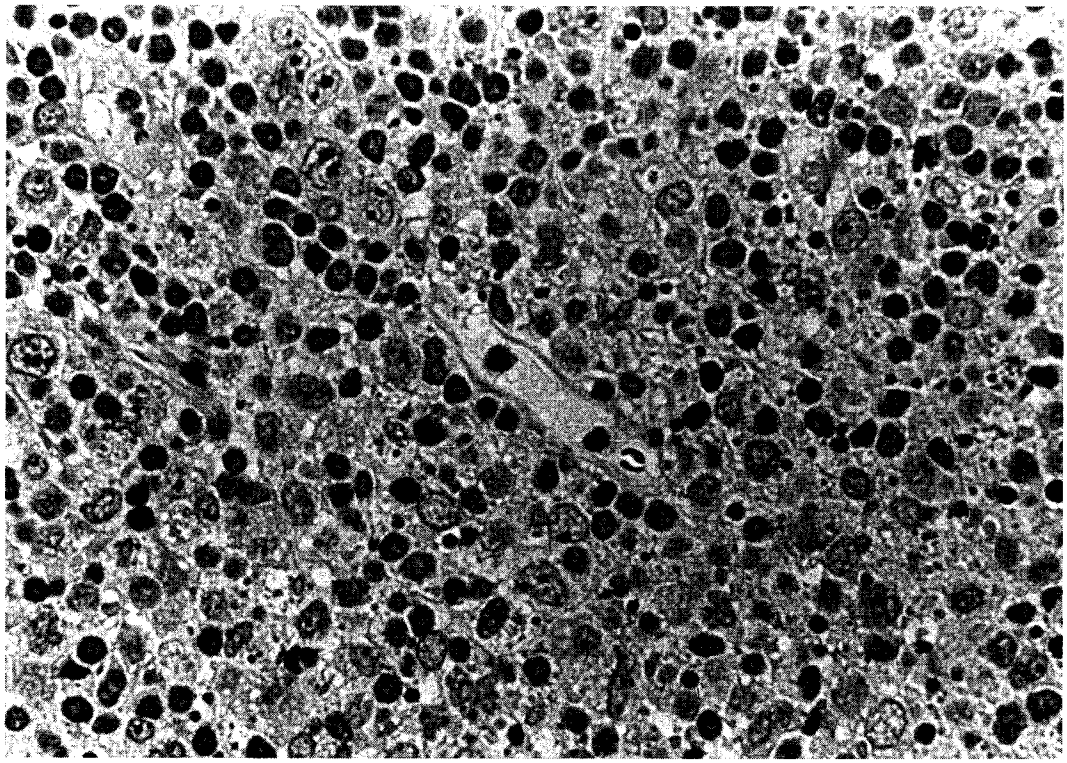

Fig. 3: Area of incomplete necrosis with small vessels, karyorrhectic nuclear debris, histiocytes, large lymphoid cells, small lymphocytes. Absence of granulocytes and plasma cells. (Hematoxylin-eosin, X 250).

tamic pyruvic transaminase (3.2× normal value). C3 was 72 mg% (normal 70-150) and C4 was 14.5 mg% (normal 13-30). IgG and IgM serological tests for hepatitis A, hepatitis B and hepatitis C were negative. Toxoplasma and cytomegalovirus IgM and IgG titres and the serological test for mononucleosis were negative. All blood, urine and throat bacterial cultures showed no growth. Bone marrow aspirate and biopsy and serum protein electrophoresis were unremarkable. Chest radiography, chest computed tomography (CT) and abdominal CT revealed no abnormalities.

During the first week in hospital, the patient's temperature was swinging in type, with daily fluctuations between 37.5°C and 40°C. In the second week, a cervical lymph node biopsy was performed. The morphologic finding showed focal well-circumscribed paracortical necrotizing process by karyorrectic nuclear debris, large lymphoid cells, hystiocytes, macrophages phagocytosing nuclear debris but no neutrophils, plasma cells or hematoxylin bodies were present. Germinal centers and mottled pattern in the paracortex were present adjacent to the lesion (Figs. 1,2,3). These features were compatible with necrotizing lymphadenitis.

In order to reduce hyperpyrexia and general malaise and shorten the duration of the disease, she was treated with 75 mg of prednisone for a week after which she was returned to the dose of 25 mg/die. Her temperature returned to normal and the lymphadenitis, transaminases and leukopenia disappeared.

DISCUSSION

On clinical grounds, Kikuchi's disease is known as a usually benign self-limiting condition and, according to Imamura (7), Kikuchi's disease may reflect a self-limited SLE-like autoimmune condition; however, the clinical outcome of these patients is not always as has been described since two of Dorfman's patients subsequently developed SLE with overt nephrotic syndrome (7). Furthermore, the chronological sequence of the two conditions can be inverted; in our case a severe arthritic and neurologic SLE had already been diagnosed and treated when a lymphadenopathy appeared.

Lymphadenopathy arising in patients with SLE may be indistinguishable from necrotizing lymphadenitis (6), but the absence of a significant number of plasma cells and the absence of irregular masses of deeply basophilic material (hematoxylin bodies) in the paracortex and vessel walls suggest Kikuchi's disease.

This is the first observation where SLE preceded Kikuchi's disease. The peculiarity of our case is to draw attention to the relationship between SLE and Kikuchi's disease and to the overall significance of histiocytic necrotizing lymphadenitis itself. The relationship between SLE and Kikuchi's disease is prompted by the following considerations: 1) Both Kikuchi's disease and SLE usually affect young women (6), 2) The morphologic features of the lymph nodes in the two conditions can sometimes be indistinguishable (6), 3) The immunohistologic study with monoclonal antibodies is similar (9).

The observation supports the hypothesis that Kikuchi's disease could be a common aspect of SLE; the appearance of Kikuchi's disease in other autoimmune disorders such as Still's disease (10) indirectly confirm this. Whether Kikuchi's disease is a complication of SLE, an independent event or directly connected with SLE has yet to be established.

REFERENCES

1. Kikuchi, M. Lymphadenitis showing focal reticulum cell hyperplasia with nuclear debris and phagocytosis. Nippon Ketsueki Gakkai Zsshi. 1972, 35, 379-380.
2. Fujimoto, Y., Kozima, Y., Yamaguchi, K. Cervical subacute necrotizing lymphadenitis. A new clinicopathological entity. Naika 1972, 20, 920-927.
3. Pileri, S., Kikuchi, M., Helbron, D., Lennert, K. Histiocytic necrotizing lymphadenitis without granulocytic infiltration. Virchows Arch 1982, 395, 257-271.
4. Kapadia, V., Robinson, B.A., Angus, H.A. Kikuchi's disease presenting as fever of unknown origin. Lancet 1989, ii, 1519.
5. Bailey, M.B., Klein, N.C., Cunha, B.A. Kikuchi's disease with liver dysfunction presenting as fever of unknown origin.
6. Dorfman, R.F., Berry, G.J. Kikuchi's histiocytic necrotizing lymphadenitis: an analysis of 108 cases with emphasis on differential diagnosis. Semin Diagn Pathol 1988, 5, 328-45.
7. Imamura, M., Ueno, H., Matsumura, A., et al. An ultrastructural study of subacute necrotizing lymphadenitis. Am J Pathol 1982, 107, 292-99.
8. Fox, R.A., Rosahn, P.D. The lymph nodes in disseminated lupus erythematosus. Am J Pathol 1943, 19, 73-79, 1943.
9. Medeiros, L.J., Kaynor, B., Harris, N.L. Lupus lymphadenitis: report of a case with immunohistologic studies on frozen section. Human Pathol 1989, 20, 295-99.
10. Ohta, A., Matsumoto, Y., Ohta, T., et al. Still's disease associated with necrotizing lymphadenitis (Kikuchi's disease): reports of 3 cases. J Rheumatol 1988, 15, 981-83.

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