Hiroshima J. Med. Sci.
Vol.44, No.1, 13～16, March, 1995
HIJM 44–3

Cytophagic Histiocytic Panniculitis in Systemic Lupus Erythematosus

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ABSTRACT

This paper presents a case of cytophagic histiocytic panniculitis in a Japanese woman, who had systemic lupus erythematosus complicated with Hashimoto's thyroiditis and lupus nephritis from the age of 12. The patient had painful multiple purplish subcutaneous nodules on the face, trunk and extremities, high fever and liver dysfunction without coagulopathy. The histological features of the skin nodules were extensive histiocyte and/or macrophage infiltration often with leuko- and/or erythrophagocytosis in the subcutaneous fat tissue.

Key words: *Cytophagic histiocytic panniculitis, SLE*

Cytophagic histiocytic panniculitis (CHP) is the term proposed by Winkelmann[11)] for panniculitis with proliferation of histiocytes and/or macrophages and often with leuko- and/or erythrophagocytosis. The patients may have high fever, pancytopenia, liver dysfunction and recurrent subcutaneous nodules. The authors encountered a case of CHP with sicca symptoms and lupus nephritis[10)] and proposed that systemic lupus erythematosus (SLE), Sjögren's syndrome and related disorders may involve increased risk of CHP. A case of CHP in systemic lupus erythematosus is presented in the following.

CASE REPORT

In October of 1985, a 12-year-old Japanese girl, previously seen for thyroid goiter at a local hospital, with T3 uptake, 16.1% (normal, 35.0–49.0%); T4, 1.5 μg/dl (4.6–12.2 μg/dl); TSH (thyroid stimulating hormone), 239.3 μU/ml (0.30–4.00 μU/ml); titers of thyroid test, ×25,600 (<×100); titers of microsome test, ×102,400 (<×100), was diagnosed as a case of Hashimoto's thyroiditis and treated with systemic thyroxine. By March 1986, general fatigue, high fever over 39°C, a butterfly-like rash on the face and Raynaud's phenomenon were noted. At the time of admission to our pediatric clinic, physical examination showed decreased platelets, hyperglobulinemia, high titers of antinuclear antibodies (ANA) of ×320 (homogeneous type); high titers of anti-DNA antibodies and low serum complement levels. The patient had continuous urinary protein; a kidney biopsy specimen indicated diffuse proliferation of the mesangial cells, characteristic of diffuse proliferative lupus nephritis (Fig. 1). Direct immunofluorescent staining of the specimen indicated IgG, IgA, IgM, and C1q granular deposits in mesangial areas. Based on clinical and histological findings, a diagnosis of systemic lupus erythematosus (SLE) was initially made. Systemic corticosteroid therapy was subsequently carried out.

In September 1987, the patient at age 14, previously treated with prednisolone at 15 mg/day and cyclophosphamide at 25 mg/day, developed high fever, and several painful purplish subcutaneous nodules on the face, trunk and extremities (Fig. 2) were noted. The same symptoms persisted. Laboratory data showed GOT, 47 IU/L; GPT, 19 IU/L; LDH, 1,400 IU/L. A biopsy specimen of a subcutaneous nodular lesion from the left arm showed liquefaction degeneration of the basal layer, and lymphohistiocytic cell infiltration without phagocytic features in the subcutaneous fat tissue, both characteristic of lobular panniculitis (Fig. 3a, b). Her condition was diagnosed as LE profundus. Systemic methyl-prednisolone pulse therapy with 1,000 mg/day was conducted for 3 days. Within one month, her general condition and laboratory data showed remarkable improvement and the skin nodules had disappeared. On resuming low doses of prednisolone at 25 to 10 mg/day and cyclophosphamide at 25 to 15 mg/day, the initial symptoms reappeared.

In February of 1989, the patient again developed high spike fever, swelling of both cheeks (Fig. 4a) and subcutaneous, erythematous nodules on the face, trunk and extremities (Fig. 4b).

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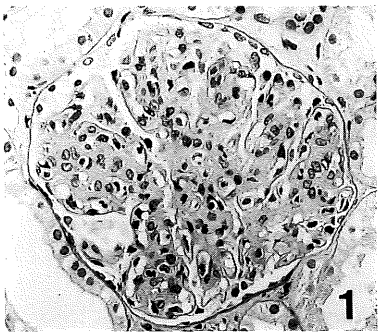

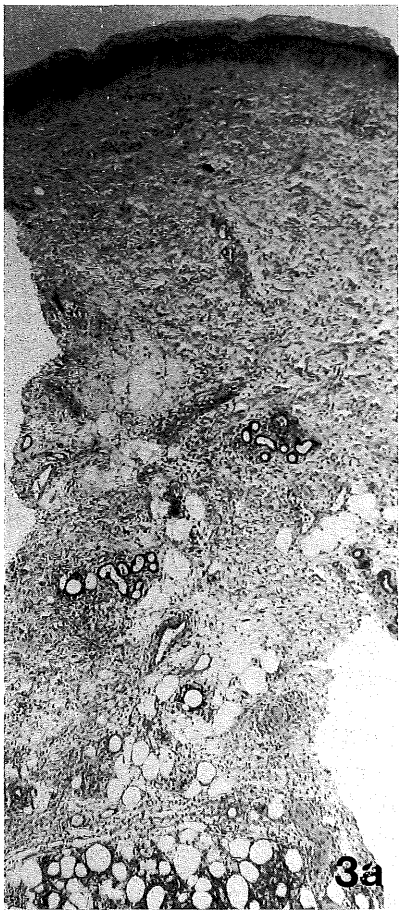

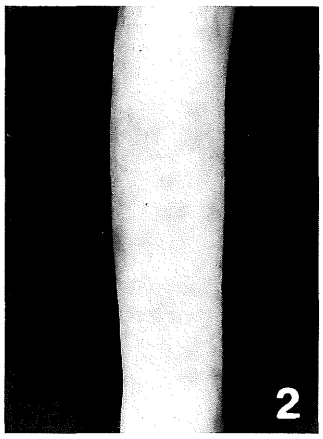

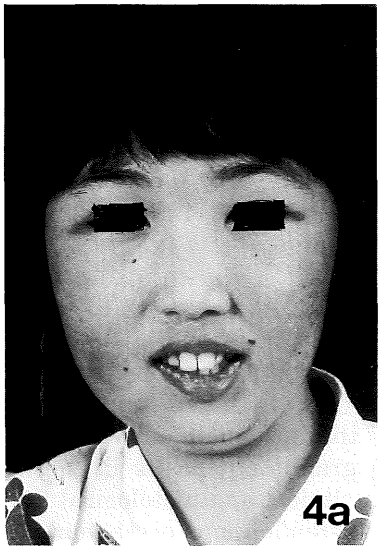

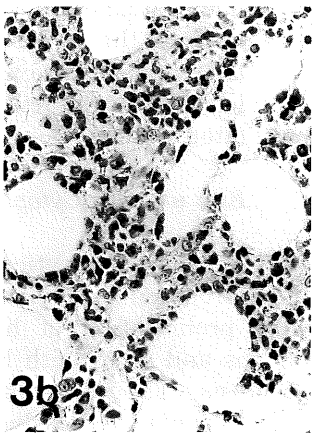

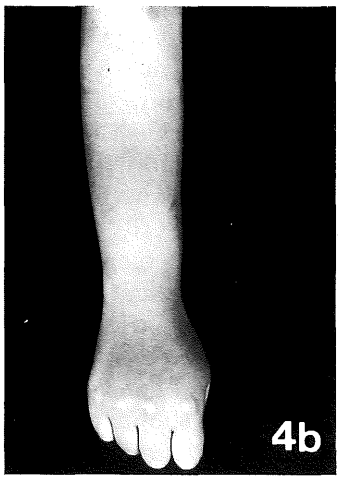

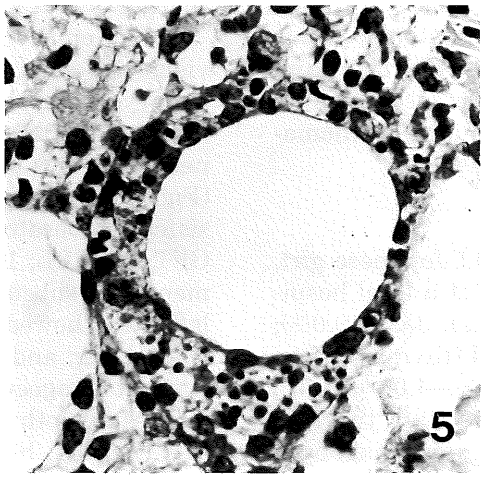

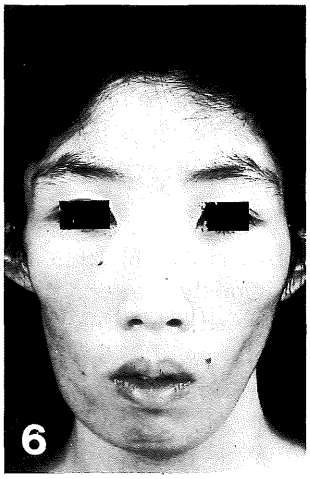

Fig. 1. Biopsy specimen of kidney showing diffuse proliferation of mesangial cells and the characteristics of diffuse proliferative lupus nephritis.
Fig. 2. Subcutaneous nodules on the arms in 1987.
Fig. 3a. Biopsy specimens of subcutaneous nodular lesions showing the features of lobular panniculitis (hematoxylin & eosin, ×20).
Fig. 3b. Photograph at high magnification (hematoxylin & eosin, ×100) showing infiltrating histiocytes without phagocytic cells.
Fig. 4a. Swelling of both cheeks and subcutaneous nodules on the face.
Fig. 4b. Subcutaneous nodules on the arms in 1989.
Fig. 5. Photograph at high power magnification showing infiltrating histiocytes mixed with phagocytic cells in the subcutaneous fat tissue (hematoxylin & eosin, ×200).
Fig. 6. Atrophy of subcutaneous fat in the patient's cheeks in 1991.

Physical examination indicated hepatomegaly and mild splenomegaly, hyperglobulinemia, GOT,101 IU/L; GPT,109 IU/L; LDH, 880 IU/L; ANA, ×160 (homogeneous, speckled types); anti-SS-A antibody, ×16; anti-SS-B antibody, negative; anti-RNP antibody, negative; anti-Sm antibody, negative. A biopsy specimen of a subcutaneous nodular lesion from the right arm showed infiltrates of histiocytes and macrophages often with erythro- and leukophagocytosis, mingled with lymphocytic cells in the subcutaneous fat tissue (Fig. 5). The histologic diagnosis was cytophagic histiocytic panniculitis. Systemic methyl-prednisolone pulse therapy was conducted, and the patient's skin and general condition remarkably improved.

In June 1991, high fever and scattered subcutaneous nodules over the entire body surface were noted again. Atrophy of the subcutaneous fat in the cheeks also occurred (Fig. 6). Physical examination showed a white blood cell count of 3,400/mm^3 (normal, 4,000–8,500); high LDH; high serum complements; tests for HTLV–1 antibody, negative; Epstein-Barr virus VCA (viral capsid antigen) IgG, ×1,280; EA (early antigen) IgG, ×320; EBNA (nuclear antigen), ×80. Internal malignancy was absent. Histological findings for a subcutaneous biopsy specimen from the back indicated the features of CHP. Her general and skin conditions responded well to systemic corticosteroid pulse therapy.

By immunoperoxidase staining, histiocytic and phagocytic cells in all the frozen specimens for both episodes of panniculitis were shown positive for MT1 (CD43, Bio Science), OKM-1 (CD11b,Ortho), anti-lysozyme, α1-anti-chymotrypsin (Dako) and histiocyte antigen (Dako). These cells thus appeared to have the characteristics of histiocytes and/or macrophages.

DISCUSSION

Since Winkelmann[11] pointed out that cases of Weber-Christian disease reported by Mori et al[6] and others[5] were histiocytic panniculitis, other cases have occasionally been reported. Patients may display high fever, pancytopenia, liver dysfunction and recurrent subcutaneous nodules[11]. Histological features of the subcutaneous nodules are characteristic of lobular panniculitis with proliferation of histiocytes and/or macrophages and often with leuko- and/or erythrophagocytosis[11]. The present patient had no systemic coagulopathy and phagocytosis was evident only in the subcutaneous fat tissue. Crotty and Winkelmann[1] consider cases with phagocytosis in one organ only such as the panniculus, lymph nodes, or intestines, to be regional histiocytosis.

CHP is occasionally observed in patients with lymphoma/leukemia[2] and viral infection such as that from the Epstein-Barr virus[7]. The authors encountered a case of CHP with sicca symptoms and lupus nephritis[10]. SLE[8], Sjögren's syndrome[9] and/or related conditions, complicated with malignant lymphoma, have sometimes been noted, suggesting that these disorders are not always benign. We propose that these SLE-related disorders may involve increased risk of CHP and/or lymphoproliferative disorders[10]. The etiology and pathogenesis of CHP are little understood. Various explanations have been proposed for its etiology and pathogenesis such as interactions of complement on the target with specific receptors on the phagocyte surface[3].

The general condition of patients with CHP may be rather poor, but not that of patients with LE profundus[12]. Histological examination of subcutaneous nodules indicated phagocytosis, thus ruling out the possibility of LE profundus. One histological feature of LE profundus[12] is lymphocyte infiltration and occasional plasma cell and foamy histiocyte infiltration. The histology of CHP is extensive infiltration of histiocytes and/or macrophages, often with erythro- and/or leukophagocytosis, into the lobulus and/or septum of the subcutaneous fat tissue. Following the occurrence of CHP, lipoatrophic changes were noted only on the patient's face. Nevertheless, we consider this to be a secondary event following panniculitis with abnormal histiocyte infiltration. CHP may be concluded a distinct pathological disease which should not be confused with primary lipoatrophic panniculitis[4]. The relationship between CHP and LE profundus should be clarified in greater detail.

(Received November 21, 1994)
(Accepted March 6, 1995)

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