

Subcutaneous T-Cell Lymphoma. A Clinical and Histopathologic Study of An Additional Case

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SUMMARY A case of a 62-year-old woman with recurrent subcutaneous nodules, fever and pancytopenia diagnosed as subcutaneous T-cell lymphoma is presented. Incision biopsy revealed lobular panniculitis with an inflammatory infiltrate of atypical T lymphocytes. She was treated with 7 courses of CHOP with transient remission, and she died after 17 months of disease from fatal hemorrhagic complications due to the hemophagocytic syndrome.

KEY WORDS subcutaneous T-cell lymphoma; panniculitis; hemophagocytic syndrome

Introduction

Peripheral T-cell lymphoma primarily involving subcutaneous adipose tissue and mimicking panniculitis with general complications is rarely diagnosed. This entity was fully described in 1991 by Gonzales *et al.* (1), and has been referred to as subcutaneous T-cell lymphoma (SCTCL) in EORTC (2) and WHO (3) classifications. SCTCL is very often misdiagnosed as panniculitis or erythema nodosum in their early stages. The clinical course may be benign, but in most cases it is aggressive and fatal with general symptoms and complications (1).

We describe an additional case of SCTCL in a female patient.

Case report

A previously healthy 62-year-old woman was admitted to the Department of Dermatology, Wroclaw University Hospital in August 2001 with a

4-month history of recurrent, multiple, painful, subcutaneous, only partly ulcerated red nodules on the extremities and abdominal region (Fig. 1). The lesions were resolving with small hyperpigmented depressions or with scars. There were chills, fever up to 40 °C, and sore throat at the time of new nodule eruption. The diagnosis of erythema nodosum was made and the patient was treated with antibiotics and anti-inflammatory agents (aspirin and indomethacin) with no success.

Examination at the hospital revealed tender, matted nodes in her lower legs. The liver and spleen were not enlarged and there was no lymphadenopathy. Chest x-ray and ultrasound of the abdomen were negative. Bone marrow biopsy findings showed no evidence of lymphoma.

Laboratory evaluation showed moderate anemia (Hb 10.2 g/dL, Htc 33.0%, erythrocytes $4.1 \times 10^6 / L$) with decreased iron level (35 g/dL, normal



Figure 1. Subcutaneous T-cell lymphoma. Erythematous indurated nodules on the lower extremities.

50-175), hypoproteinemia (45 g/L, normal 60-80 g/L) and higher D-dimer level (1.5 g/ml, normal, <0.5 g/ml). Laboratory studies including differential cell count, ESR, rheumatoid factor, ANA, anti EBV antibodies, urinalysis and liver function tests were normal or negative.

Biopsy specimens from subcutaneous nodules of her lower legs were interpreted as characteristic of lymphoma (SCTCL).

Steroid therapy (prednisone 1 mg/kg/daily) was introduced. After one month the results were poor and systemic chemotherapy with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) was initiated. She received seven monthly cycles of CHOP. Marked clinical regression of subcutaneous nodules was noted after 2 cycles of chemotherapy. Her lymphoma remained in clinical remission as of September 2002. In this month fever (39 °C) developed without evidence of infection. Laboratory findings revealed leukopenia ($3.0 \times 10^3 / L$), thrombocytopenia ($131 \times 10^3 / L$), anemia (Hb 9.1 g/dL, Hct 29.0%, erythrocytes $3.0 \times 10^6 / L$). Fibrinogen decreased to 0.5 g/L (normal 1.8-3.5 g/L), and D-dimer increased to 11.2 g/ml (normal <0.5 g/ml). Very high levels of liver enzymes (aspartate aminotransferase 160 U/L, -glutamyltransferase 950 U/l) and total bilirubin (4.4 mg/dL) were also recorded.

The treatment with steroids and cyclosporin A in high doses did not help her. Generalized ecchymoses developed and she died from hemorrhagic complications 2 weeks of the last exacerbation and 17 months of the first symptom onset. Autopsy was not performed.

Histology

Histologic examination showed proliferation of pleomorphic lymphoid cells infiltrating lower parts of the dermis and especially the subcutis. The subcutaneous tissue was infiltrated in a lace-like pattern. Often a rimming around individual adipocytes was observed (Fig. 2). Small- to medium-sized neoplastic cells with irregular hyperchromatic nuclei and inconspicuous nucleoli predominated. Occasionally large and anaplastic cells were seen. Prominent karyorrhexis and foci of necrosis were observed.

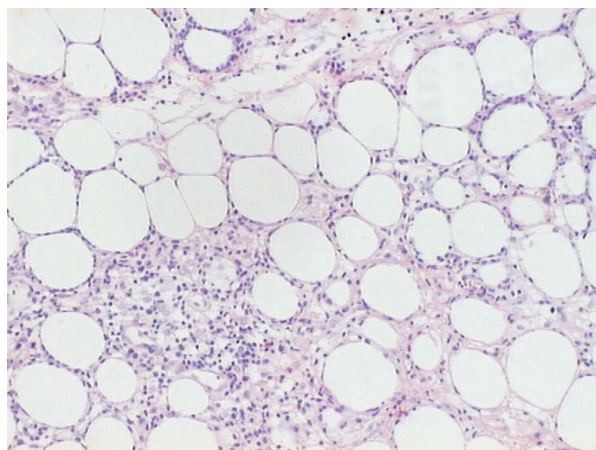


Figure 2. Dense lymphocytic infiltrate involving the subcutaneous tissue. Characteristic rimming of the fat cells by atypical lymphocytes. HE $\times 100$.

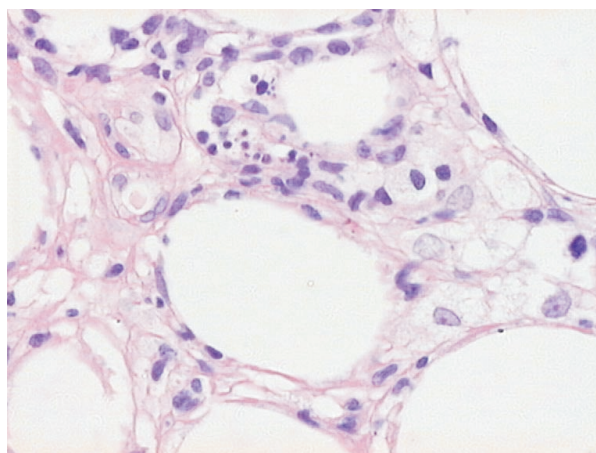


Figure 3. Lymphoma cells population interspersed with histiocytes (ABC $\times 200$)

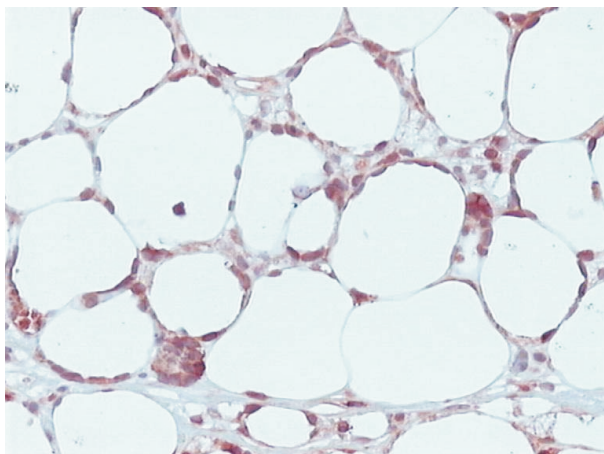


Figure 4. Lymphocytes express the T-cell antigen CD3 (ABC $\times 200$)

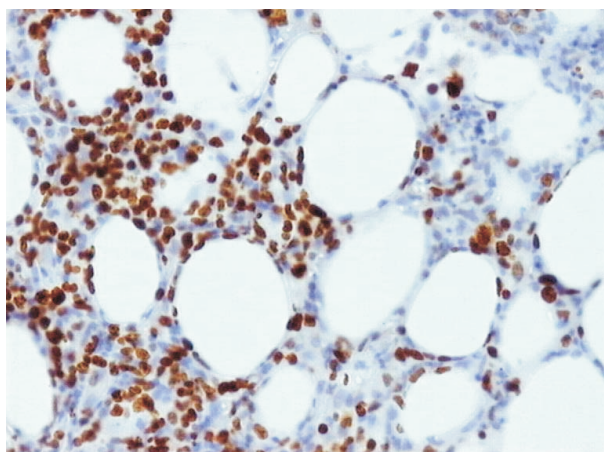


Figure 5. Important proliferative activity (Ki-67) (ABC $\times 200$)

The lymphoma cell population included interspersed histiocytes with phagocytic activity (Fig. 3).

Immunohistochemistry showed positivity for T-lineage markers (CD3+, CD43+) and cytotoxic marker (TIA-1) (Fig. 4). The lymphoma cells were CD4-/CD8+. The CD56 was negative. A pronounced proliferative activity (Ki-67 expression) was observed (Fig. 5).

Discussion

Subcutaneous T-cell lymphoma (SCTCL) is a distinctive form of peripheral lymphoma occurring worldwide and representing far less than 1% of all non-Hodgkin's lymphomas (4). SCTCL is characterized by aggressive natural history and poor prognosis. Its median survival is less than 3 years (5),

however, a subset of patients follow a chronic, indolent course (6).

SCTCL presents with subcutaneous infiltrations on the legs, less commonly on the lower parts of the trunk, mostly in young adults. Fatigue, fever, and weight loss usually accompany the onset of florid hemophagocytic syndrome, which indicates fatal prognosis.

Histologic studies show lobular infiltrations by atypical lymphoides with necrosis in the subcutaneous fat tissue. Karyorrhexis is very prominent and found in every case. Immunophenotyping reveals lymphoma of T-cell lineage, positive for CD45 and CD45Ro antibodies and negative for CD20 antibody.

We do not know which factors in SCTCL trigger the hemophagocytic syndrome and why they are or are not present in particular cases of lymphoma. It is conceivable that stimulated T lymphocytes release lymphokines (PIF, Phagocytosis Inducing Factor), which recruit histiocytes phagocytizing erythrocytes, platelets and lymphocytes (7). We ought to know that this syndrome may also occur in many other disorders such as viral infections (8), or in renal transplantation (9).

There is no established treatment protocol in the reported cases of SCTCL. Most patients received aggressive chemotherapy with CHOP for several months (10). Some patients are treated with fludarabine (11), cyclosporin A (12) or radiotherapy and autologous stem cell transplantation (13).

It is impossible to compare the value of different modes of therapy because of the very individual course of the disease.

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