A Case of Subcutaneous Panniculitic T-cell Lymphoma

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We herein report a case of subcutaneous panniculitic T-cell lymphoma which occurred in a 48-year-old Korean woman. Her disease presented as multiple subcutaneous nodules on the arms, legs, and abdomen, with systemic symptoms and signs. From the results of immunophenotypic studies, we suggest her disease may originate from cytotoxic T-lymphocytes.

The patient had a protracted course of multiple dark-red-colored subcutaneous nodules on both arms, legs, and abdomen for 1 year, often with fever, chills, and malaise. Histopathologic findings for the subcutaneous nodule in the lower abdomen revealed diffuse infiltration of atypical lymphocytes in the subcutis, with extensive fat necrosis and karyorrhexis and a bean-bag cell appearance with engulfed lymphocytes in some histiocytes. The immunophenotypic studies showed a cytotoxic T-lymphocyte profile, i. e., LCA+, lysozyme+, UCHL1+, CD8+, CD20-, CD30-, and CD56-. In situ hybridization studies for the Epstein-Barr virus genome resulted in a negative finding. A lymphadenopathy was found in the right upper paratracheal area on the chest CT associated with pancytopenia and abnormal LFT findings. She received high-dose chemotherapy with autologous blood stem cell transplantation, but died after 6 months. (Ann Dermatol 12(4) 275~279, 2000).

Key Words : Subcutaneous panniculitic T-cell lymphoma, Cutaneous T-cell lymphoma

Subcutaneous panniculitic T-cell lymphoma (SPTCL) is an uncommon form of cutaneous lymphoma localized in the subcutis with clinical features mimicking lobular panniculitis[1]. Recently, SPTCL has been included as a provisional entity in the Revised European-American Lymphoma classification (REAL) and the European Organization for Research and Treatment of Cancer (EORTC) classification for primary cutaneous lymphomas[2,3], and detailed studies of its origin in immunogenesis are in progress.

SPTCL usually presents with multiple subcutaneous tumors or plaques involving the extremities or trunk and is associated with fever, malaise, fatigue, myalgia, chills, and weight loss[4]. These constitutional symptoms develop in a frequently occurring systemic hemophagocytic syndrome (HPS); however, systemic dissemination of lymphoma usually does not occur[1]. Most patients with SPTCL follow an aggressive clinical course with short-term survival, and death usually results from systemic HPS[1,4], except some patients in an indolent course with recurrent, self-healing lesions[5].

Six cases of SPTCL have been reported since 1995 in Korea[6-10]. These patients were young with an average age of 42 years (range 30 to 63 years), and were all female. The results of immunohistochemical staining are summarized in Table 1. Most of these patients were treated with chemotherapy, and two of them died.

Recently, some authors emphasized SPTCL should be classified as a clonal, cytotoxic T-cell lymphoma, mostly expressing TIA-1, perforin, and CD8+ without the Epstein-Barr virus (EBV) genome[11,12]. We report a case of SPTCL that has characteristic clinicopathological features and a

Received January 3, 2000.
Accepted for publication June 20, 2000.
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cytotoxic T-lymphocyte immunophenotype.

CASE REPORT

A 48-year-old woman was admitted to Dong-A University Hospital in July 1998, with numerous, tender subcutaneous nodules and plaques on the abdomen and both upper and lower extremities (Fig. 1). She had noticed a tender subcutaneous plaque on the left upper arm 1 year before, and subsequently multiple subcutaneous plaques developed in various sizes on both upper and lower extremities, abdomen, and neck, associated with fever, chills, and malaise. She had suffered from protracted fever and chills and recurrent crops of those painful indurative nodules during the last year in spite of symptomatic treatments such as nonsteroidal anti-inflammatory drugs and herb drugs.

Initial CBC profiles revealed a mild pancytopenia and also a finding of elevated liver enzymes was noted. Chest CT revealed lymphadenopathy on the right upper paratracheal area. The histopathologic findings on biopsy specimens from the left arm and abdominal region initially showed a lobular panniculitis infiltrated with lymphoid cells and macrophages. But the subsequently biopsied specimen from the larger lesion showed diffuse infiltration of small to medium-sized atypical lymphoid cells with pleomorphic nuclei and clear cytoplasm in the subcutis. Numerous mitotic figures with extensive karyorrhexis and fat necrosis were also found. Some histiocytes were large and contained one or more engulfed lymphocytes, with a bean-bag cell appearance. However, there was no evidence of angioinvasion or epidermotropism (Fig. 2). Immunohistochemical studies revealed positivity for the LCA, lysozyme, UCHL-1, and CD8 antigens, but negative for the CD20, CD30, and CD56 antigen (Fig. 3). In situ hybridization for the EBV resulted in negative findings. She transferred to the hemato-oncology department for a combination chemotherapy of cyclophosphamide, adriamycin, vincristine, and prednisone (CHOP) and an autologous blood stem cell transplantation, but died of sepsis after 6 months.

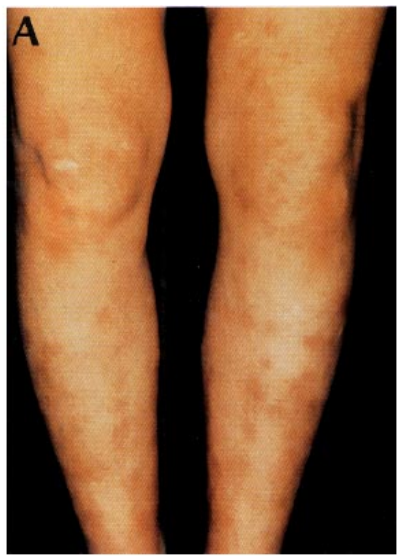
Table 1. Reported Cases of SPTCL in Korea.

No	Age/Sex	Result of Staining	Therapy and Outcome	Reference
1	30/F	+; CD3, LCA -; CD8	supportive died	6
2	45/F	+; LCA, UCHL1, lysozyme -; CD20	prednisone alive	7
3	30/F	+; CD45, UCHL1, -; CD20	BACOP*, CHOP† alive	8
4	63/F	+; CD45, UCHL1 -; CD20	CHOP died	8
5	34/F	+; CD45, UCHL1, CD43, EBV -; CD20, Leu7, lysozyme	vincristine, prednisone alive	9
6	41/F	+; CD3, LCA, UCHL1, CD67, EBV -; CD20, CD30	prednisone alive	10
※	48/F	+; LCA, UCHL1, lysozyme, CD8 -; CD20, CD30, CD56, EBV	CHOP, ASCT ‡ died	our case

BACOP* : bleomycin, adriamycin, cyclophosphamide, vincristine, prednisone
CHOP† : cyclophosphamide, adriamycin, vincristine, prednisone
ASCT ‡ : autologous stem cell transplantation

DISCUSSION

SPTCL is a distinct type of cutaneous T cell lymphoma with a quite rare occurrence and is characterized by subcutaneous nodules, systemic signs and symptoms, and an aggressive clinical course with death due to a HPS[1]. Recent studies



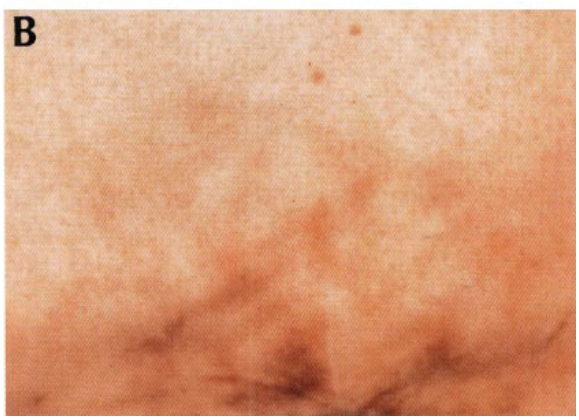


Fig. 1. Multiple red-colored subcutaneous nodules and plaques on the lower extremities (A) and abdomen (B).

have further defined the immunophenotypic profile in SPTCL, elucidating the nature of apoptosis often seen in this entity[12]. The neoplastic cells uniformly express a CD8+ cytotoxic T-cell phenotype with perforin and the granular proteins granzyme and TIA-1. These proteins mediate cytotoxicity and apoptosis by T cells and NK cells, and therefore may be responsible for the apoptotic nature of these lesions[12-14].

SPTCL represents a distinct clinicopathologic entity of clonal, EBV negative, cytotoxic T-cell lymphomas[12]. The SPTCLs may be derived from either $\alpha\beta$ T cells or $\gamma\delta$ T cells. Our case seems to derive from $\alpha\beta$ T cells, which show a CD56-, and CD8+. However, many of the reported cases of $\gamma\delta$ T cell lymphoma have been positive for CD56 and

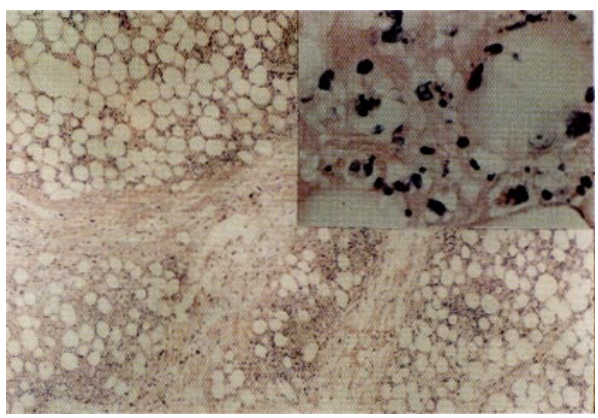
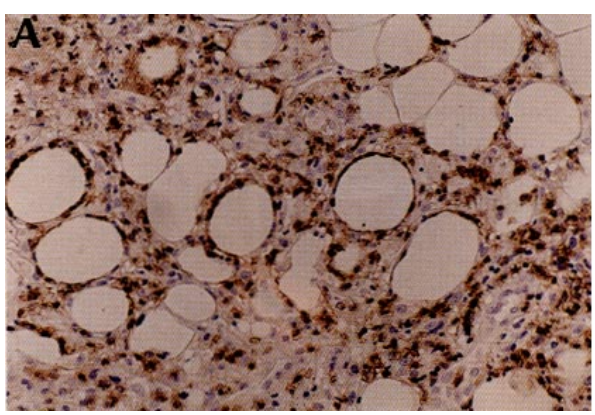


Fig. 2. Diffuse infiltration of atypical lymphocytes in the subcutis (H&E, ×40), with extensive fat necrosis, karyorrhexis, and a bean-bag cell appearance with engulfed lymphocytes in some histiocytes (inset) (H&E, ×400).



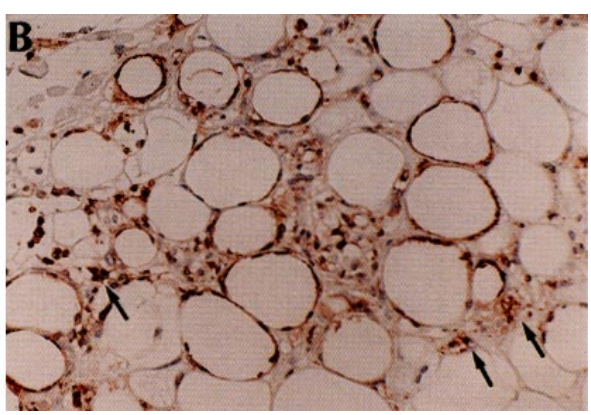


Fig. 3. The atypical lymphocytes stained positive to CD8 antigen (×100) (A), and the phagocytic cells stained positive to lysozyme antigen (arrows) (×100) (B).

negative for CD4 and CD8. Salhany et al. suggest that $\gamma\delta$ SPTCL may be associated more commonly with aggressive diseases, systemic HPS, and clinically significant cytopenia than $\alpha\beta$ SPTCL[11]. However, some SPTCL cases without expression of CD56 have a poor prognosis, as in our case, despite aggressive chemotherapy[11]. Therefore, further studies are needed to determine the prognostic value of these variables and to determine whether clinically significant differences exist between $\alpha\beta$ and $\gamma\delta$ subtypes.

A HPS is a frequent complication of SPTCL[1,5,15]. Patients have fever, pancytopenia, elevated liver enzyme, and lymphadenopathy of the right upper paratracheal area on CT scan. The HPS is most readily diagnosed in bone marrow aspirate smears in which macrophages containing phagocytosed erythrocytes and occasionally platelets may be observed. This usually precipitates a fulminant downhill clinical course, and it is the cause of death in the majority of patients with SPTCL. Dissemination to lymph nodes and other organs is uncommon and usually occurs late in the clinical course. Our patient had fever, pancytopenia, elevated liver enzyme, and lymphadenopathy, which perhaps led to death. The cause of the HPS seems related to cytokine production by the malignant cells. Interferon γ and granulocyte-monocyte colony-stimulating factors have been identified[13].

SPTCL is one of the processes previously described as histiocytic cytophagic panniculitis[16]. It had been believed that histiocytic cytophagic panniculitis was a malignant histiocytic proliferation. Although macrophages may be numerous in these lesions, the malignant cells have a mature T-cell phenotype. Evidence for EBV has been absent[13].

Natural killer/T-cell lymphoma involving the subcutis presents the most difficult differential diagnosis for SPTCL because SPTCL and NK/T-cell lymphoma have similar features in clinical, histopathological, and immunophenotypic aspects, e.g. initial presentation as multiple subcutaneous nodules, lobular panniculitis-like histologic patterns with admixtures of pleomorphic lymphocytes, and expression of T-cell-associated antigens[1,4,17,18]. Cutaneous NK cell/T-cell lymphomas tend to be centered in the dermis with extension into the subcutis, resulting in angiocentric, angiodestructive lesions with coagulation necrosis, mostly with a phenotype and genotype for NK cell lineage and positivity for EBV genome[17]. Conversely, SPTCLs generally are confined to the subcutis with occasional spillover into the deep dermis and are EBV-, clonal T-cell neoplasms[1,4,19].

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