Subcutaneous Panniculitic T-cell Lymphoma

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Subcutaneous panniculitic T-cell lymphoma(SPTCL) is a rare subtype of peripheral T-cell lymphoma that clinically and histologically mimics benign panniculitis. SPTCL is characterized by subcutaneous nodules on the extremities and trunk. It has a tendency to occur mainly in female adults with eosinophilia, pruritus or hemophagocytic syndromes. Histopathologically, typical lesions of SPTCL show moderate to dense lymphocytic infiltrates in the subcutaneous fat, primarily involving the lobules. Early lesions may show only focal lymphocytic atypia: later lesions display karyorrhexis, necrosis and cytophagia.

A 34-year-old woman presented with multiple, recurrent, tender subcutaneous nodules on the abdomen and extremities which she had had for 13 years. There was no hepatosplenomegaly or lymphadenopathy. Skin biopsy specimens revealed atypical small and large lymphocytic infiltrations in the subcutaneous tissue. Occasionally, histiocytes contained erythrocytes and lymphocytes in their cytoplasm. Immunohistochemical staining showed positive reactions to CD45RO and CD43. Negative reactions were seen to CD20, Leu-7 and lysozyme antigen. On the basis of the clinical & histological findings, we established the diagnosis of SPTCL. (Ann Dermatol 10:(3) 179~184, 1998).

Key Words : Subcutaneous panniculitic T-cell lymphoma

Postthymic peripheral T-cell lymphomas are a heterogeneous group of malignant lymphoreticular neoplasms that share a T-cell phenotypic origin[1,2,3]. They may occur as distinct clinicopathological entities such as mycosis fungoides, adult T-cell leukemia/lymphoma, and angiocentric immunoproliferative lesions. Gonzalez et al[4] recently characterized subcutaneous T-cell lymphoma as another distinct peripheral T-cell lymphoma. This disorder primarily involves the subcutaneous tissue and may have an aggressive clinical course. These tumors have since been incorporated as a provisional entity in the recently proposed Revised European-American Classification of Lymphoid Neoplasms and have been renamed as subcutaneous panniculitic T-cell lymphoma(SPTCL)[5].

Herein, we report a case of subcutaneous panniculitic T-cell lymphoma with a protracted course.

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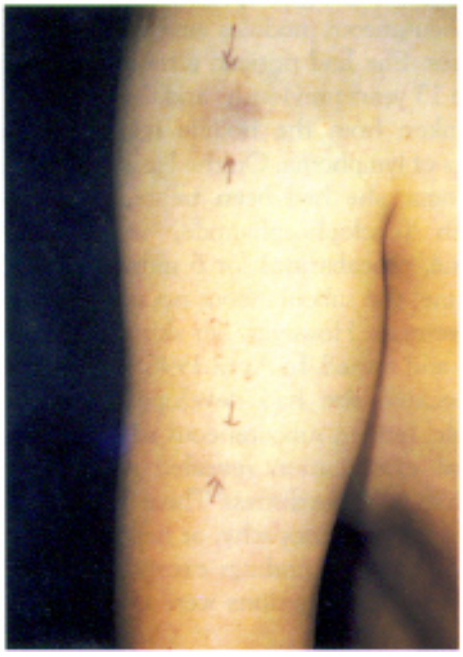
CASE REPORT

A 34-year-old women presented to us with multiple subcutaneous nodules on her trunk and extremities. She had noticed a tender subcutaneous nodule 13 years previously, and a skin biopsy specimen taken from the nodule revealed suspicious features of lymphoma. On the basis of a diagnosis of lymphoma, she had been treated with a COPP regimen (cyclophosphamide, vincristine, prednisolone, procabazine) for 6 months in 1983. At that time, the subcutaneous nodules showed some improvement. However, her skin lesions has been waxed and waned. In April 1996, she was hospitalized because she had developed variable sized, multiple, tender, subcutaneous nodules (Fig. 1). A physical examination revealed a well-developed woman in no acute distress. There were no objective signs of lymphadenopathy, or hepatosplenomegaly and no abnormal findings except the skin lesion. Laboratory investigations were undertaken to ex-

clude the possibility of an underlying systemic disease or immunological abnormalities. Her hemoglobin was 12.0 gm/dℓ, hematocrit was 38.9 %, and the platelet count was 380×10^9/L. Analysis of serum showed the following results: AST, 36 U/L (normal, 0 to 40 U/L); ALT, 41 U/L (normal, 0 to 40 U/L); and alkaline phosphatase, 77 U/L (normal, 39 to 117 U/L). BUN and creatinine levels were within normal limits. Coagulation studies revealed normal results. EKG, radiographs of the chest, and abdominal sonograpy were all normal. A bone marrow aspiration showed a normocellular marrow without any abnormality. Other data including IgA, IgE, IgG, IgM, ANCA and anti-platelet antibodies were within normal limits or negative.

A skin biopsy specimen was taken from a subcutaneous nodule of the abdomen. The main infiltrate was present in the subcutaneous tissue, simulating panniculitis (Fig. 2). The infiltrate consisted of small, medium and large lymphoid cells with a markedly irregular nuclear contour and densely clumped chromatin. Occasional cells contained prominent nucleoli. A high mitotic activity with pronounced karyorrhexis was present. Occasional histiocytes contained erythrocytes and lymphocytes in their cytoplasm (Fig. 3). However, the lesions were not angiocentric. On immunohistochemical staining, the neoplastic cells stained positive to CD45(Dako, Denmark), CD45RO(Dako, Denmark) and CD43(Dako, Denmark) but not to CD20(Dako, Denmark), Leu-7(Becton Dickinson, U.S.A.) or lysozyme antigen(Dako, Denmark) (Fig. 4). We did not perform an in situ hybridization study for EBV. Systemic chemotherapy was initiated promptly with vincristine in May 1996. Because she developed anorexia and nausea which was thought to be due to vincristine, the drug was changed to prednisone in June 1996. After the chemotherapy, there was a slight clinical improvement of the cutaneous lesions. To date, she is alive and well, and her subcutaneous nodules waxed and waned.



DISCUSSION

SPTCL is a distinctive type of T-cell lymphoma involving the subcutaneous tissue with an aggressive clinical course and a tendency to be associated with a hemophagocytic syndrome[4,6].

Four cases of SPTCL have been reported since 1995 in Korea[7-9]. These patients were relatively young, with an average age of 42 years (range, 30 to 63 years), and all female. All patients had subcutaneous nodules affecting the extremities or the trunk. The initial diagnosis was a benign or lupus panniculitis in the three cases. Most of these patients were treated with chemotherapy, but two cases died (Table 1).

Clinically, the patients of SPTCL were relatively young, and more commonly female[1,7,10]. All patients had subcutaneous nodules or plaques affecting the extremities or the trunk, with associated constitutional symptoms and fever[7,8,11]. The initial diagnosis was frequently a panniculitis, such as erythema

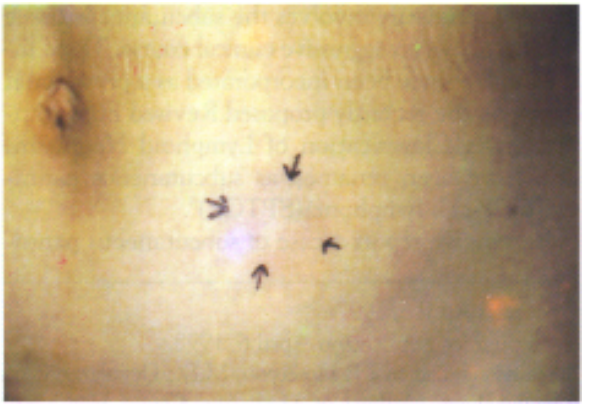


Fig. 1. Numerous, indurative purpuric subcutaneous nodules on the upper extremity(A) and abdomen(B).

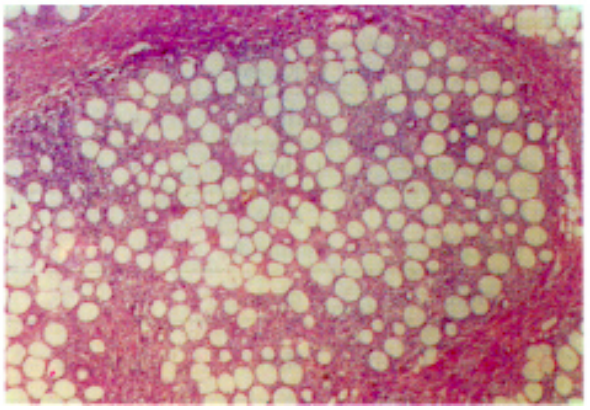


Fig. 2. Involvement of lobule and septum of subcutaneous tissue with atypical lymphoid cells. (H&E stain, ×40).

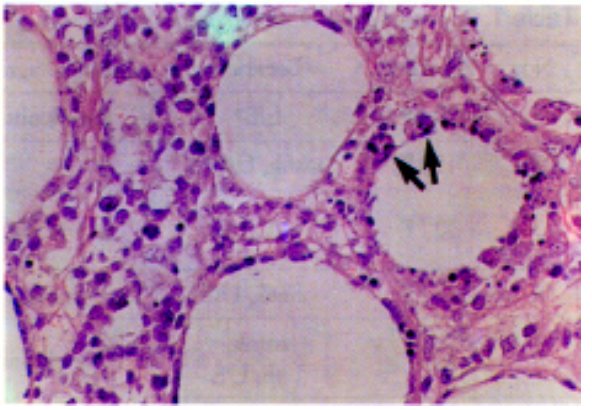


Fig. 3. Small to medium sized atypical lymphoid cells had varing nuclear irregularities. Karyorrhexis and large histiocytic engulfing erythrocyte or small lymphocyte (arrows) were also present. (H&E stain, ×400).

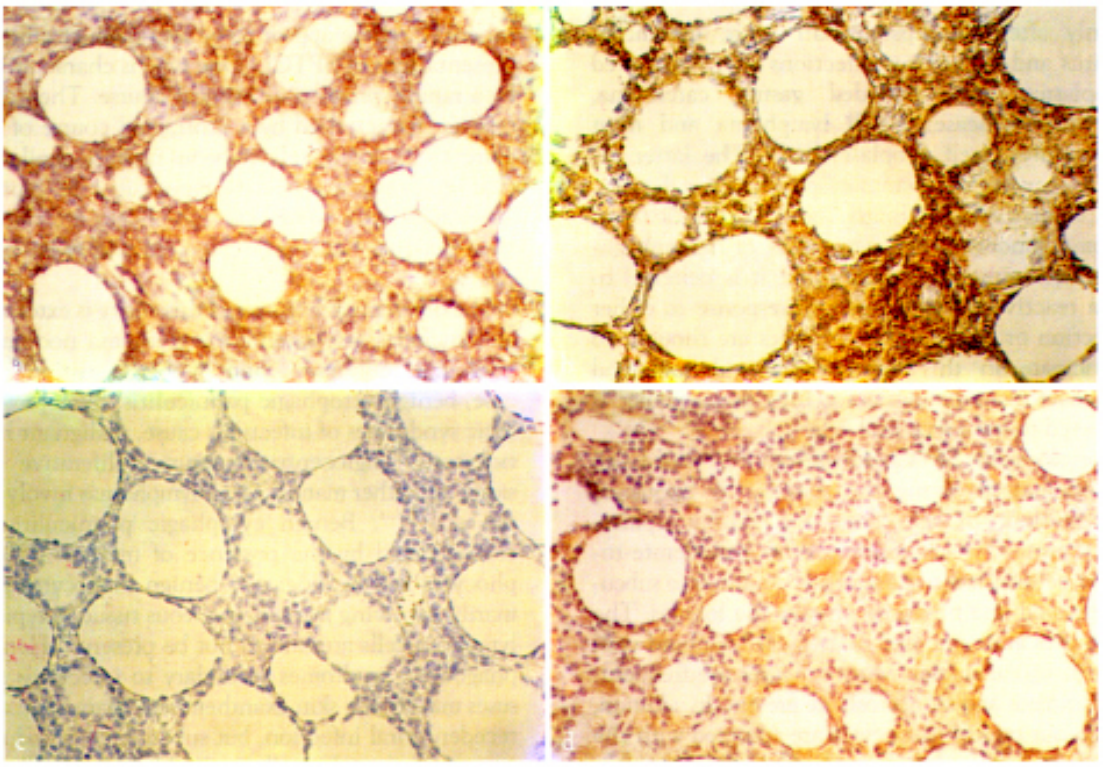


Fig. 4. Immunohistochemical findings of the skin lesion (×200). The neoplastic cells positive stained with CD45 (a) and CD45RO (b) but not with CD20 (c) and Lysozyme antigen (d).

nodosum or Weber-Christian disease, or a lymphoproliferative process, such as lymphomatoid granulomatosis[1,10]. Constitutional symptoms were often chronic and mild in the initial stages but later became severe[1,4,9,12].

Hemophagocytic syndrome frequently occurs in association with infection or neoplasm. Hemophagocytic syndrome has been reported most com-

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Table 1. Reported cases of subcutaneous panniculitic T-cell lymphoma in Korea

No	Age/Sex	Location	Initial Diagnosis	Therapy	Outcome	Reference
1	30 / F	L/E*	panniculitis	supportive	died	7
2	45 / F	trunk, U/E**	-	prednisone	alive	8
3	30 / F	U/E, L/E	panniculitis	BACOP# CHOP##	alive remmision	9
4	63 / F	cheek, U/E	lupus panniculitis	CHOP	died	9
*	34 / F	trunk, U/E, L/E	lymphoma	vincristine prednisone	alive	our case

L/E* : lower extremity
U/E** : upper extremity
BACOP# : bleomycin, adriamycin, cyclophosphamide, vincristine, prednisone
CHOP## : cyclophosphamide, adriamycin, vincristine, prednisone

monly after the Epstein-Barr virus, cytomegalovirus and adenovirus infections[10,13,14]. Associated neoplasms have included gastric carcinoma, Hodgkin's disease, B-cell lymphoma and most commonly T-cell neoplasms[4,10,14,15]. The latter include benign angioimmunoproliferative lesions, lymphoblastic lymphoma, and Lenner's lymphoma, among others. The cause of hemophagocytic syndrome is unknown, but it is believed to be a reactive T-cell process in response to either infection or lymphoma. Cytokines are thought to participate in this immune dysregulation, and phagocytosis-inducing factor(PIF) in particular is believed to have a central role[4,6].

Histologically, SPTCL differs from the other T-cell lymphomas involving the skin by its lipotropic predilection. SPTCL does not exhibit epidermotropism. Typical lesions show a moderate-to-dense cellular infiltration largely confined to subcutaneous fat and primarily involve the lobules. The infiltrates are composed of atypical lymphoid cells with irregular nuclei. Mitotic figures are frequent. Karyorrhexis and fat necrosis are present. In addition, numerous typical histiocytes are admixed with the lymphoid cells and show marked hemophagocytosis of white blood cells, nuclear fragments, and red blood cells[1,4,6,9,10]. In our case, subcutaneous nodules occured at the extremities and the trunk of a young female. Typical histopathological findings of SPTCL were revealed. The absence of hemophagocytic syndrome lead to the appearance of a protracted course. On the basis of the experience of others[1,4,7-9], there appear to be two distinct clinical presentations of SPTCL. One type is characterized by a rapidly progressive clinical course. The other type is characterized by a protracted course of recurrent self-healing subcutaneous nodules, similar to that of our patient. In both types, after the typical features of lymphoma and cytophagia are noted, most patients have an accelerated and often fatal course[1,4,6].

The differential diagnosis of this entity is extensive and includes assessments for erythema nodosum, erythema induratum, and Weber-Christian disease, benign cytophagic panniculitis, hemophagocytic syndromes of infectious cause, malignant histiocytosis, angiocentric immunoproliferative lesions, and other mature T-cell lymphomas involving the skin[4,7,8,16]. Benign cytophagic panniculitis is characterized by the presence of mature T lymphocytes and cytologically benign histiocytes primarily involving the subcutaneous tissue. Atypical lymphoid cells are said to not be present[16]. Hemophagocytic syndromes secondary to infectious casuses may have a skin exanthem secondary to an antecedent viral infection, but subcutaneous nodules composed of cytologically atypical lymphoid cells are absent[4,8,16]. In malignant histiocytosis, in contrast to SPTCL in which malignant cells are found only in the skin, the malignant cells systemically involve the entire reticuloendothelial system and the nuclei of the macrophages are not cytologically atypical[4,16]. Angiocentric immunoproliferative lesions(AILs) are characterized by marked angio-

centricity, angiodestruction, and necrosis often accompanying the most atypical lesions. Histologically, the distinction between AILs involving the skin and SPTCL is difficult. However, AILs commonly involve multiple organ systems in addition to the skin. Vessel involvement is primary and necrosis would be extensive in association with a latent EB virus[4,7,11,13].

Previous investigators using PCR-based methods have suggested that EBV may be linked to the pathogenesis of cytophagic histocytic panniculitis[13]. However, an in situ hybridization study of 11 cases of SPTCL by Medeiros LJ[17], et al were negative for EBV RNA. The reasons for the discrepancy are probably related to the methods used[18]. The PCR-based method amplifies EBV genomes that may be found in both non-neoplastic and neoplastic cells. In contrast, in situ hybridization methods can be used to specifically assess the tumor cells.

Multiagent chemotherapy for treatment is recommended, but the outcome was fatal in the majority of cases despite aggressive treatment with chemotherapy, systemic glucocorticoids, and radiotherapy[1,4,10,11,18]. Death was caused by complications of the hemophagocytic syndrome in most patients[1,4,6], one death was due to pneumonia and cardiac failure[12]. In some patients, however, a survival time between 26 and 60 months has been reported[4]. No prognostic factor has been determined. The presence of a systemic hemophagocytic syndrome, however, should be considered as a sign of a poor prognosis[1,4,6,10]. Our patient was treated with prednisone because of a side effects from vincristin.

We report herein a case of SPTCL with a benign clinical course which was different to other T-cell lymphomas of the skin because of its predominantly subcutaneous location and the presence of atypical lymphoid cells.

REFERENCES

1. Perniciaro C, Zalla MJ, White JW, Menke DM. Subcutaneous T-cell lymphoma. Report of two additional cases and further observations: Arch Dermatol 1993;129:1171-1176
2. Su IJ, Wu YC, Chen YC, Hsieh HC, Cheng AL, Wang CH, Kadin ME. Cutaneous manifestations of postthymic T cell malignancies : description of five clinicopathologic subtypes: J Am Acad Dermatol 1990;23:653-662
3. Pinkus GS, O'Hara CJ, Said JW. Peripheral/postthymic T-cell lymphomas : a spectrum of disease : clinical, pathologic, and immunologic features of 78 cases: Cancer 1990;65:971-998
4. Gonzalez CL, Medeiros LJ, Braziel RM, Jaffe ES. T-cell lymphoma involving subcutaneous tissue. A clinicopathologic entity commonly associated with hemophagocytic syndrome: Am J Surg Pathol 1991;15(1):17-27
5. Harris NL, Jaffe ES, Stein H, Banks PM, Chan JKC, Cleary ML, Delsol G, et al. A revised European-American classification of lymphoid neoplasms : A purposal from the International Lymphoma Study Group: Blood 1994;84:1361-1392
6. Avinoach I, Halevy S, Argov S, Sacks M. γ/δ T-cell lymphoma involving the subcutaneous tissue and associated with a hemophagocytic syndrome: Am J Dermatol 1994;16(4):426-433
7. Kim SW, Kim JO, Kim JW, Kim DS, Choe JY, Kim YJ. Subcutaneous panniculitic T-cell lymphoma: Ann Dermatol 1996;8:(2)158-163
8. Park WH, Lee SJ, Lee IJ, Chun SI. Cutaneous T cell lymphoma involving subcutaneous tissue: Kor J Dermatol 1995;33(1):188-192
9. Cho KH, Oh JK, Kim CW, Heo DS, Kim ST. Peripheral T-cell lymphoma involving subcutaneous tissue: Br J Dermatol 1995;132:290-295
10. Romero LS, Goltz RW, Nagi C, Shin SS, Ho AD. Subcutaneous T-cell lymphoma with associated hemophagocytic syndrome and terminal leukemic transformation: J Am Acad Dermatol 1996;34:904-910
11. Driesch PVD, Staib G, Jr MS, Sterry W. Subcutaneous T-cell lymphoma: J Am Acad Dermatol 1997;34:285-289
12. Burg G, Dummer R, Wilhelm M, Nestle F, Ott MM, Feller A, Hefner H, et al. A subcutaneous delta-positive T-cell lymphoma that produces interferon gamma: N Engl J Med 1991;325:1078-1081
13. Harada H, Iwatsuki K, Kaneko F. Detection of Epstein-Barr virus genes in malignant lymphoma with clinical and histologic features of cytophagic histiocytic panniculitis: J Am Acad Dermatol 1994;31:379-383
14. Smith KJ, Skelton HG, Yeager J, Angritt P, Wagner K, James WD, Giblin WJ, et al. Cutaneous histopathologic, immunohistochemical, and clinical manifestations in patients with hemophagocytic syndrome: Arch Dermatol 1992;128:193-200
15. Peters MS, Winkelmann RK. Cytophagic panni-

culitis and B cell lymphoma: J Am Acad Dermatol 1985;13:882-885
16. McNutt NS, Moreno A, Contreras F. Inflammatory diseases of the subcutaneous fat. In: Elder D, Elenitsas R, Jaworsky C, Johnson B, eds. Lever's histopathology of the skin. 8th ed. Philadelphia, New York : Lippincott-Raven, 1997:429-455
17. Medeiros LJ, Greiner TC, Gonzalez CL, et al. T-cell lymphoma involving subcutaneous tissue : an update: Mod Pathol 1994;7:116A(abstract) cited from ref 18
18. Monterroso V, Bujan W, Jaramillo O, Medeiros LJ . Subcutaneous tissue involvement by T-cell lymphoma. A report of 2 cases: Arch Dermatol 1996;132:1345-1350