Subcutaneous Panniculitis-like T-Cell Lymphoma with a Transformation to Lupus Erythematosus Panniculitis: A Case Report

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Abstract
Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare primary cutaneous lymphoma characterized by infiltration of the subcutaneous tissue by neoplastic cytotoxic T cells mimicking panniculitis. There is a strong association between SPTCL and lupus erythematosus panniculitis (LEP). However, patients who were diagnosed with LEP with a preceding diagnosis of SPTCL have been scarcely reported. We herein reported a 21-year-old Thai woman presenting to a dermatology clinic for evaluation of a 1-month history of a painful mass on the right buttock and bilateral upper eyelid swelling. A subcutaneous mass which was 5 by 2 cm in diameter, tender, firm, and fixed with a smooth surface was palpated over the upper outer quadrant of her right gluteal area. After a diagnosis of SPTCL had been made based on the histological and immunohistochemical studies, treatment with oral dexamethasone and ciclosporin A was initially started. Because of intolerance to adverse reactions of dexamethasone, only ciclosporin A was given. Improvement was not achieved at 6-month follow-up. She then underwent the re-incisional biopsy at the same gluteal area and the histological features were consistent with LEP. After hydroxychloroquine was given, the lesion resolved within 3 months, and no recurrence was detected during the following 6-month follow-up. We emphasize that long-term follow-up of patients with SPTCL is required. Additionally, in case of poor response to the given treatment, a repeat skin biopsy should be considered in order to determine the proper management.

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Introduction

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare primary cutaneous lymphoma characterized by infiltration of the subcutaneous tissue by neoplastic cytotoxic T cells mimicking panniculitis [1, 2]. An incidence rate in the USA was reported to be 0.1 per 1 million person-years (0.6% of all cutaneous lymphoma) [3]. In Asian populations, previous studies revealed that its incidence varied between 2.3 and 11.0% of all cutaneous lymphoma [4, 5]. The median age of diagnosis was 36 years [6]. Clinical manifestations include solitary or multiple nodules or subcutaneous plaques with a diameter varying from 0.5 to 2.0 cm, primarily on the extremities and trunk. Constitutional symptoms such as fever, fatigue, and weight loss may be present [7]. Moreover, eyelid erythema and swelling, like in our case, is noted as the initial manifestation of SPTCL [8, 9]. In contrast, ulceration, lymph node and bone marrow involvement rarely occur [10, 11]. Despite a strong association between SPTCL and lupus erythematosus panniculitis (LEP), patients diagnosed with LEP with a preceding diagnosis of SPTCL have been scarcely reported. We herein present a rare case with a histological transformation of SPTCL to LEP.

Case Report

A 21-year-old woman presented to a dermatology clinic for evaluation of a 1-month history of a painful mass on the right buttoc and bilateral upper eyelid swelling. She denied a history of recurrent high-grade fever, general fatigue, anorexia, or significant weight loss. Other organ-specific symptoms were not present. Her comorbidities included beta thalassemia trait and obesity. On physical examination, the temperature was 37.0°C, the blood pressure was 130/85 mm Hg, the heart rate was 90 beats per minute, and the respiratory rate was 18 breaths per minute. A subcutaneous mass which was 5 by 2 cm in diameter, tender, firm, and fixed with a smooth surface was palpated over the upper outer quadrant of her right gluteal area. Bilateral upper eyelids were erythematous, non-tender, and swollen. No palpable cervical, supraclavicular, infradavicular, axillary, or inguinal lymphadenopathy was noted. The remainder of the examination was normal. Ultrasonography of the right gluteal area revealed increased echogenicity and thickness of the subcutaneous fat, measuring 5 by 4 by 2 cm without any collection. A complete blood count revealed a leukocyte count of 6,700 cells/mm³ with neutrophil predominance (62%), a hemoglobin of 11.3 g/dL, and a platelet count of 255,000 cells/mm³. Her serum creatinine and liver function tests were normal. Under local anesthesia, a biopsy was performed and the tissue sample was submitted for histological evaluation. Histological findings demonstrated nodular and diffuse inflammatory cell infiltrates in the dermis and subcutaneous tissue. The cellular infiltrate composed of lymphocytes, plasma cells, extravasated erythrocytes, and histiocytes with abundant foamy or pale cytoplasm (Fig. 1a and b). Erythrocytes and lymphocytes were phagocytized by some of these histiocytes. Immunohistochemical studies revealed that the lymphoid cells were predominantly positive for BF1, CD3, CD5, CD7, CD8, and CD20; focally positive for granzyme B; but negative for CD30, CD56, and EBV. The proliferative index marker (Ki67) showed variable positive ranging from 5 to 20%. Additional blood investigations were done to evaluate associated conditions and severity of disease: lactate dehydrogenase 101 U/L (normal range, 125–220 U/L), ferritin of 62.8 ng/mL (normal range, 15.0–150.0 ng/mL), fibrinogen level of 157.0 mg/dL (normal range, 200.0–400.0 mg/dL), creatinine kinase of 22 U/L (normal range, 29–168 U/L), and negative antinuclear antibodies. Based on the clinical picture, histology and immunohistochemical studies, the diagnosis of SPTCL (α/β T-cell subtype) without hemophagocytic lymphohistiocytosis was made. Additionally, genetic testing was performed and it demonstrated a heterozygous
missense variant of *BLM* gene (c.2293G>A, p.Val765Ile). Treatment with dexamethasone (40 mg/day) and ciclosporin A (200 mg/day) was started orally. Her lesions on bilateral eyelids resolved completely within 2 weeks; however, she developed generalized myalgia and a burning sensation in the epigastric area. Since then, dexamethasone was suspended and she was treated with only ciclosporin A at the same dose. She tolerated the therapy well. The follow-up visits were scheduled every month to monitor clinical responses and adverse events. The subcutaneous lesion gradually decreased in size with softer consistency, and no new lesion was noted. At the follow-up visit after 7 months of receiving the medications, the lesion turned out to be about the same size and tender. She then underwent magnetic resonance imaging of the right hip to distinguish among possible conditions including unresolving SPTCL, concomitant LEP, and post-biopsy scars. It revealed a mass-like area, measuring 3 by 6 by 4 cm, with increased signal infiltrating the subcutaneous tissue in the right posterior buttock region. A few right femoral nodes were identified, measuring up to 1 cm in size. The incisional biopsy was re-performed in the right gluteal area where it was previously diagnosed as SPTCL. The histological findings revealed diffuse inflammatory cell infiltration of lymphocytes, plasma cells, and a few multinucleated giant cells with hyalinizing fat necrosis in subcutaneous tissue (Fig. 2a and b). There was no evidence of atypical histiocytes with hemophagocytosis. These findings were consistent with LEP. Ciclosporin was discontinued and hydroxychloroquine (200 mg/day) was administered. The lesion resolved within 3 months and no recurrence was detected during the following 6-month follow-up.

**Discussion**

The diagnosis of SPTCL in our case was confirmed by histopathology and immunohistochemical studies. The most challenging and significant differential diagnosis for SPTCL is with LEP since the diseases are clinically indistinguishable [12]. Although histologic findings of SPTCL bear a remarkable resemblance to LEP, it is essential to distinguish SPTCL from LEP since treatment strategies and prognoses differ between conditions. Useful histologic features supporting for the diagnosis of SPTCL include (1) protrusion of neoplastic lymphocytes into the interior of the adipocyte, (2) erythrophagocytosis by histiocytes, and (3) low density

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**Fig. 1.** a Histologic findings of a diffuse cellular infiltrate involving both septa and lobules within the subcutis and protrusion of neoplastic lymphocytes into the interior of the adipocyte with relative sparing of the overlying dermis and epidermis (original magnification, ×100, hematoxylin-eosin). b Cells show peripheral alignment (rimming) around adipocytes and some histiocytes show phagocytosis of red blood cells and lymphocytes (original magnification, ×400, hematoxylin-eosin).
The mechanisms by which SPTCL induces or promotes LEP remain poorly understood. There was evidence that these two entities shared the same CXCR3 pathway [20]. CXCR3 and CXCR9, as markers for this pathway, appeared more abundantly expressed in SPTCL than in LEP. This pathway is involved in the recruitment of T cells in inflammatory lesions, chemotactic migration, and angiostasis, causing the development of autoimmune diseases including rheumatoid arthritis and systemic lupus erythematosus [21]. However, further studies are required on the exact etiology and pathogenesis of changes involved in this disease to establish a potential therapeutic intervention.

An association between SPTCL and a loss-of-function mutation in HAVCR2 has been well described [22–24]. In our case, we instead identified BLM heterozygous mutation. BLM gene is involved in the regulation of DNA replication, recombination, and both homologous and non-homologous pathways of double-strand break repair [25]. The absence of a functional BLM protein causes chromosome instability and an increased risk for cancer – particularly lymphoma, acute myelogenous leukemia, squamous cell skin cancer, and gastrointestinal tract cancer [26, 27]. This mutation has not been described in cases with SPTCL. However, DNA
repair function of BLM gene is especially important for the development and maturation of the T and B cells, so BLM deficiency affects the development, maintenance, and function of T and B lymphocytes [28, 29]. Moreover, several studies have reported that BLM heterozygous mutation is sufficient to increase the risk of developing cancer [30–34]. Therefore, heterozygous carriers of BLM mutation may promote clinical phenotypes that have an increased risk of SPTCL.

The strengths of the study include, first, a rarity of the disease with a transformation into the same cutaneous lesion and, second, a scarcely reported BLM gene in patients with subcutaneous panniculitis-like T cell. We herein emphasize that long-term follow-up of patients with subcutaneous panniculitis-like T cell is required. In case of poor response to the given treatment, a repeat skin biopsy should be considered in order to determine the proper management. In addition, further multicenter studies are needed to confirm the association between subcutaneous panniculitis-like T cell and BLM gene.

Because of the rarity of the disease, no standard treatment modality has yet been established. Treatment options are categorized into immunosuppressives (corticosteroids alone or in combination with ciclosporin A or methotrexate) and chemotherapy (cyclophosphamide, doxorubicin, vincristine, and prednisone) [11, 35, 36]. Several studies demonstrated cases with SPTCL achieved complete remission after given ciclosporin A alone or combined with steroids as the first-line therapy [37–43]. Our patient achieved response after given the therapy. However, the remaining subcutaneous lesion later turned into LEP. Because LEP responds to treatment with antimalarials [44, 45], our patient’s lesion resolved in 3 months. No recurrence was detected during the following 6-month follow-up. We followed the CARE checklist for reporting this case report (online suppl. File S1; for all online suppl. material, see www.karger.com/doi/10.1159/000527530).

**Conclusion**

SPTCL is a rare slow-growing type of lymphoma that mainly affects the skin. There is a strong association between SPTCL and LEP. However, its risk factors and shared pathogenesis have not been well established. Long-term follow-up of patients with SPTCL is required.

**Statement of Ethics**

This study was approved by the Walailak Ethics Committee (WUEC-22-256-01). The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki. Written informed consent was obtained from the patient for publication of this case presentation and any accompanying images.

**Conflict of Interest Statement**

The authors have no conflicts of interest to declare.

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Author Contributions

Weeratian Tawanwongsri: conceptualization, data collection, and writing-original draft preparation. Jirapan Thongsroy: writing-review, and editing. All the authors have provided final approval for the version to be published, agreed on the journal to which the article has been submitted, and agreed to be accountable for all aspects of the work.

Data Availability Statement data-

All data underlying the results are available as part of the article and its online supplementary material files; no additional source data are required. Further inquiries can be directed to the corresponding author Weeratian Tawanwongsri.

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