SHORT COMMUNICATION

Subcutaneous Panniculitis-like T-cell Lymphoma with Secondary Haemophagocytic Lymphohistiocytosis Arising at Widespread Tattoo Sites: A Case Report

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Submitted Sept 19, 2025. Accepted after revision Nov 19, 2025
Published Feb 3, 2026. DOI: 10.2340/actadv.v106.adv-2025-0036 Acta Derm Venereol 2026; 106: adv-2025-0036.

Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a lymphoma of cytotoxic T-cell origin that infiltrates the subcutaneous adipose tissue (1). The clinical manifestations are chiefly subcutaneous nodules or indurated plaques on the trunk and extremities, with the occasional involvement of sites such as the mesentery, breast or upper eyelid (2, 3). Lymph node or bone marrow involvement is generally absent (4). Approximately half of patients exhibit nonspecific systemic symptoms, including weight loss, low-grade fever and malaise, whereas the other patients present with only localized symptoms (4). The 5-year overall survival is about 80%, although haemophagocytic lymphohistiocytosis (HLH) is recognized as a predictor of poor prognosis (5).

We treated an SPTCL patient who had widespread tattoos, with multiple subcutaneous nodules beneath tattooed skin, making histopathologic identification difficult. Targeted incisional skin biopsies guided by computed tomography (CT), findings did not establish a definitive diagnosis. However, a complete excisional biopsy of a lesion selected on the basis of positron emission tomography (PET)–CT findings allowed a diagnosis of SPTCL (6). The patient further developed HLH and exhibited panniculitis involving intra-abdominal and retroperitoneal fat, resulting in a rapidly progressive clinical course. We report this case in view of its unusual presentation and aggressive course.

CASE REPORT

A 44-year-old man presented to the Department of Internal Medicine with a 2-week history of persistent fever accompanied by chills and night sweats and was admitted for evaluation of fever of unknown origin (**Fig. 1A**). Laboratory tests revealed elevated serum ferritin (2,264 ng/mL) and lactate dehydrogenase (LDH) (590 U/L). Unenhanced and contrast-enhanced CT demonstrated hepatosplenomegaly and atrophy of the abdominal and subcutaneous adipose tissue (Fig. 1B). Blood cultures were negative. Bone marrow aspiration showed no evidence of malignancy. At the initial examination, a total of 9 firm subcutaneous nodules of varying sizes were palpable without heat sensation or tenderness on the trunk and extremities (Fig. 1C–M), 8 of them within tattooed areas. Nine 4-mm punch biopsies were obtained from subcutaneous nodules on the abdomen and thigh, and the histopathological features suggested SPTCL. Prednisolone (PSL) at 30 mg/day (0.4 mg/kg/day) was initiated, and the fever subsided. However, the fever recurred when the PSL was tapered to

Fig. 1. Cutaneous features and imaging findings for the present patient. (A) Extensive multicoloured tattoos involving the chest and back, as well as the proximal portions of all 4 extremities. (B) Computed tomography shows increased attenuation/stranding of the subcutaneous tissue and peritoneal fat (arrows). (C–K) Locations of the 9 subcutaneous nodules (arrowheads). (L) PET–CT at relapse. Orange arrowheads indicate extracutaneous lesions; red arrowheads indicate cutaneous lesions; an arrow marks the cutaneous lesion with the greatest uptake, from which an excisional biopsy was performed.

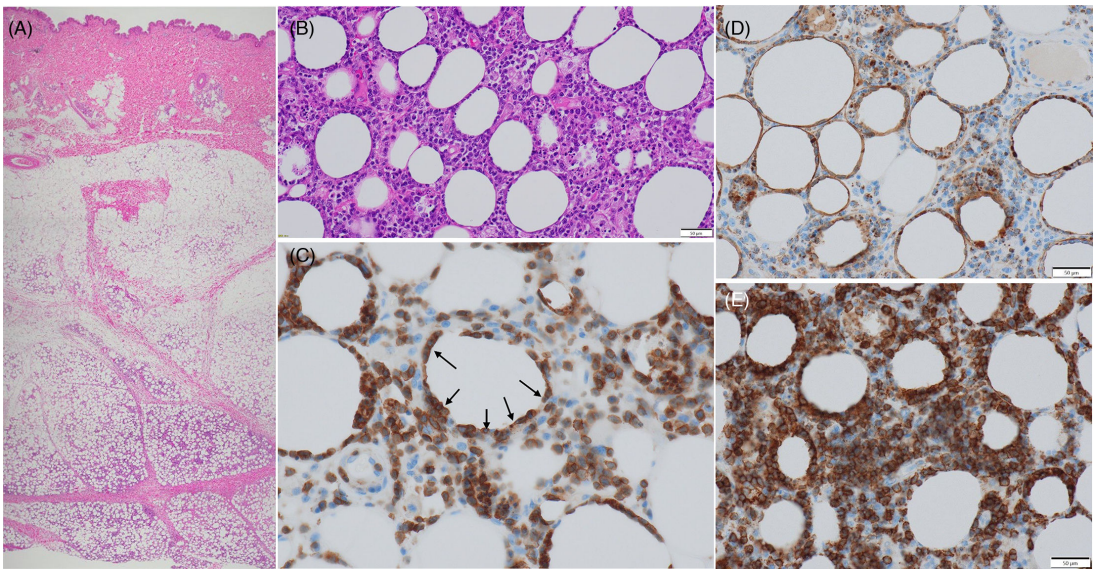

Fig. 2. Histopathological features and immunohistochemical staining of the excisional skin biopsy specimen. (A) Low-power haematoxylin and eosin (H&E) of the full-thickness excisional skin specimen (H&E, ×100). (B) The dense infiltration of atypical lymphocytes forms adipocyte rimming in the subcutaneous fat (H&E, ×100). (C) CD3 immunohistochemistry shows the rimming (arrows) of adipocytes by atypical lymphocytes (×200). (D) Granzyme B immunostaining (×100). (E) CD8 immunostaining (×100).

10 mg/day, so the dose was increased to 40 mg/day. After the subsequent reduction in the PSL dosage, a fever of 38°C or higher persisted with elevated serum LDH. CT re-evaluation at 1 month of treatment revealed ascites and worsening panniculitis-like changes in the mesenteric and retroperitoneal adipose tissue. At 2 months of treatment, PET–CT showed irregular FDG (fluorodeoxyglucose) uptake in the mesentery and retroperitoneum and in the subcutaneous tissues corresponding to the palpable nodules on the trunk and extremities (Fig. 1O). Follow-up laboratory tests showed elevated serum ferritin (1,720 ng/mL), LDH of 1,871 U/L, soluble interleukin-2 (IL-2), soluble interleukin-2 receptor (sIL-2R) of 8,910 U/mL and low fibrinogen (98 mg/dL). Given the persistent high fever and splenomegaly, the patient met the diagnostic criteria for HLH. Because of anorexia and abdominal distension, he was readmitted. Nine 4-mm punch skin biopsies were taken from the trunk and extremities. All but one were performed on tattooed skin. The selected biopsy sites were palpable indurations that corresponded to regions of increased subcutaneous fat attenuation on CT. However, the punch biopsies did not yield a definitive diagnosis. Guided by PET–CT, we performed a complete excisional biopsy of a subcutaneous nodule, including the full thickness of subcutaneous fat, from the right thigh, where the FDG uptake was greatest. This biopsy demonstrated adipocyte "rimming" by atypical lymphocytes (**Fig. 2A–C**), which were positive for CD3, Granzyme B, CD8 (Fig. 2C–E), TIA-1 and CD5, but negative for CD56. These findings were consistent with SPTCL, leading to the diagnosis of SPTCL. CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine and PSL) was started 2 weeks after readmission. Pancytopenia developed, and hepatic and renal dysfunction worsened. CT continued to show mesenteric panniculitis-like changes without improvement and worsening of hepatomegaly and ascites. The patient's condition failed to improve, and he died 4 weeks after readmission.

DISCUSSION

SPTCL clinically resembles more common dermatoses, such as erythema nodosum, erythema induratum of Bazin, tattoo granuloma, Weber–Christian disease, lupus erythematosus profundus (lupus panniculitis) (7), and cytophagic histiocytic panniculitis. This makes early diagnosis difficult. In asymptomatic patients with only cutaneous manifestations, further investigation and diagnosis may be delayed. In our patient, extensive tattoos on almost the whole body obscured the presence of the lesions. No previous studies have specifically linked tattoos to the onset of SPTCL. Concerning overall lymphoma, one twin study reported a higher lymphoma risk in identical twins with at least palm-sized tattoos than in tattoo-free identical twins (8), whereas another study reported that a tattoo-associated increase in lymphoma risk was found only for B-cell lymphomas (9). Therefore, the association between tattoos and the pathogenesis of SPTCL in the present case remains uncertain and requires further investigation.

The usefulness of PET–CT in SPTCL has begun to attract attention. As in our case, PET–CT can facilitate diagnosis by directing biopsies to the most informative site. In one series, extracutaneous lesions were detected in 5 of 11 patients who underwent

PET–CT (10), suggesting that extracutaneous lesions may be more frequent than previously appreciated. PET–CT is also considered useful for evaluating treatment response and recurrence, supporting its role not only at diagnosis but also during follow-up. Our case was further complicated by HLH, which progressed rapidly. HLH is diagnosed in the presence of pathogenic variants associated with familial HLH or when at least 5 of the following 8 criteria are fulfilled: (*i*) persistent high fever, (*ii*) splenomegaly, (*iii*) cytopenia affecting ≥2 lineages, (*iv*) hypertriglyceridaemia (fasting ≥265 mg/dL) and/or hypofibrinogenaemia (≤150 mg/dL),(*v*) haemophagocytosis in the bone marrow, spleen or lymph nodes, (*vi*) decreased or absent NK-cell activity, (*vii*) serum ferritin ≥500 ng/mL and (*viii*) sIL-2R ≥2,400 U/mL. Univariate and multivariate analyses of 324 patients with lymphoma-associated HLH (11) identified several independent adverse prognostic factors: male sex, activated partial thromboplastin time (APTT) ≥36 s, serum LDH ≥1,000 U/L and C-reactive protein (CRP) ≥10 mg/dL. Our patient was male with a CRP of 3.45 mg/dL, an LDH of 1,871 U/L and an APTT of 38.4 s, thereby having 3 adverse prognostic factors. Histopathological examinations of tattooed skin most frequently reveal dermal fibrosis. In other words, tattooed sites are prone to fibrosis due to chronic foreign-body reactions and persistent inflammation, and they show conspicuous proliferation and the thickening of dermal collagen bundles that non-tattooed skin does not show (12).

As in our case, the presence of tattoos may delay the detection of lesions in SPTCL and may complicate lesion identification due to dermal fibrosis. When tattoos are present, punch biopsies should be performed with careful attention to depth, so as to include the subcutis, or a complete excisional biopsy should be considered. Early PET–CT may be particularly helpful for pinpointing optimal biopsy targets and for detecting extracutaneous lesions. In patients with SPTCL complicated by HLH, knowing the number of established prognostic risk factors can help predict survival expectancy and facilitate accurate, patient-centred informed consent.

ACKNOWLEDGEMENTS

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

The authors have no conflicts of interest to declare.

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