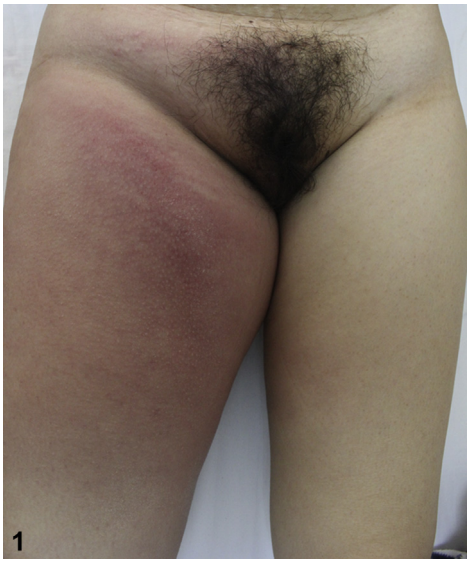
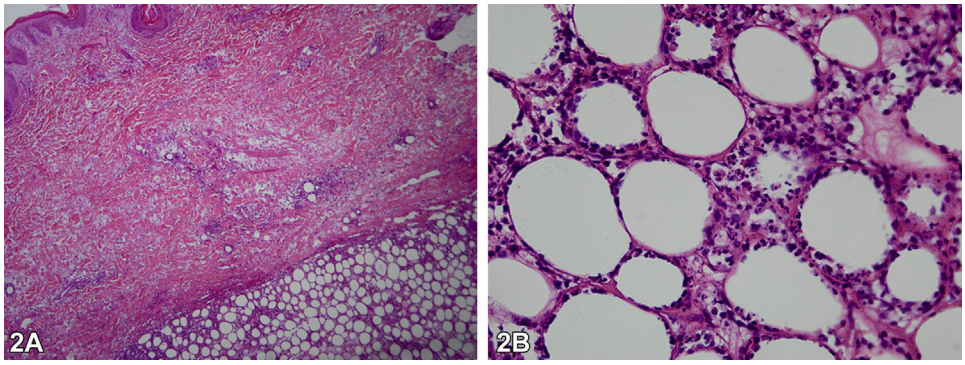
Diffuse painful erythema on right thigh

Manfeng Zhang, MD, Xuhua Tang, MD, PhD, Hui Zhou, MD, PhD, Qiman Liao, MD, Jiande Han, MD, PhD, and Xiaohong Chen, MD, PhD
Guangzhou, China

Key words: cellulitis; erythema; extranodal nasal NK/T-cell lymphoma; lupus erythematosus panniculitis; primary cutaneous gamma-delta T-cell lymphoma; subcutaneous panniculitis-like T-cell lymphoma.





From the Department of Dermatology, The First Affiliated Hospital, Sun Yat-sen University.
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Correspondence to: Xiaohong Chen, MD, PhD, Department of Dermatology, The First Affiliated Hospital, Sun Yat-sen University, Guangzhou, China, 510080. E-mail: chenxh2@mail.sysu.edu.cn.

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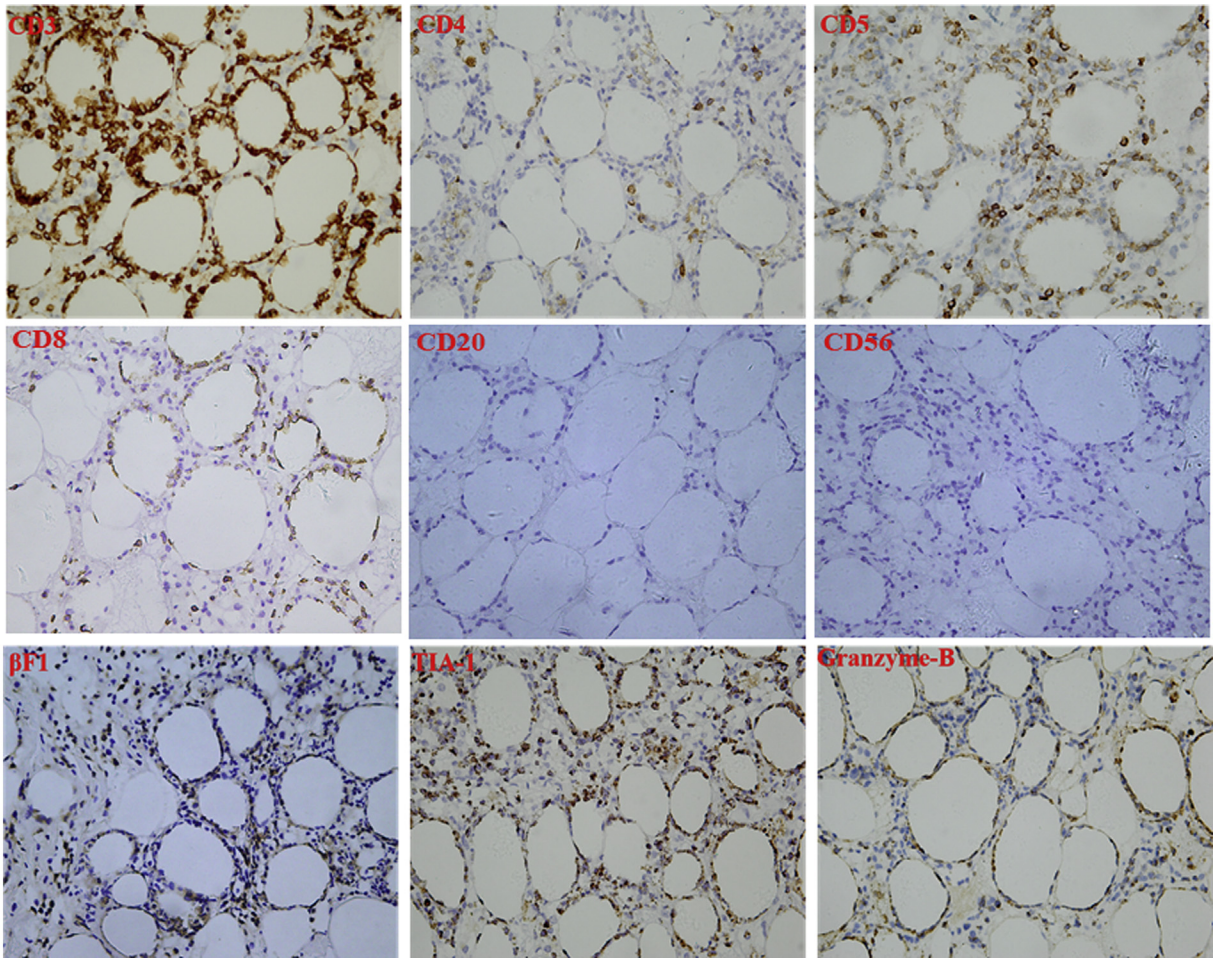

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A 37-year-old otherwise healthy woman presented with a 1-month history of a diffuse, painful, and erythematous swelling on her right thigh (Fig 1), along with high fever (up to 41°C) arthralgia, headache, and night sweats. She was initially treated with multiple antibiotics for infection, but the treatment failed. Routine laboratory tests showed a leukocyte count of 2.40×10^9/L (reference range: 4.00-10.00 $\times 10^9$/L), lactate dehydrogenase 2213 U/L (reference range: 114-240 U/L), alanine aminotransferase 260 U/L (reference range: 1-40 U/L), and aspartate aminotransferase 626 U/L (reference range: 1-37 U/L). Blood culture results were negative. Bone marrow biopsy was unremarkable. Subsequently, biopsies of the right thigh (Fig 2) as well as immunohistochemistry (Fig 3) were performed.

Question 1: Which of the following is the most likely diagnosis?

A. Cellulitis

B. Lupus erythematosus panniculitis (LEP)

C. Subcutaneous panniculitis-like T-cell lymphoma (SPTL)

D. Primary cutaneous gamma-delta T-cell lymphoma (PCGDTL)

E. Extranodal nasal NK/T-cell lymphoma (ENKL)

Answers:

A. Cellulitis — Incorrect. Cellulitis is a common bacterial infection of the skin and underlying tissues. Cellulitis usually occurs in the lower parts of the legs, sometimes in the face, on the arms, and other areas, and appears as swollen, red, painful, and warm lesions. Pathology shows neutrophil infiltration, and antibiotics are usually effective against cellulitis.

B. LEP — Incorrect. LEP is an uncommon variant of lupus erythematosus, which is

histopathologically characterized by lobular panniculitis. LEP often presents with subcutaneous nodules, indurated plaques, or ulcerations involving the face, proximal extremities, and breasts.

C. SPTL — Correct. SPTL is a cytotoxic T-cell lymphoma with a $CD4^-$, $CD8^+$, $CD56^-$, $\beta F1^+$ phenotype and an indolent clinical course.[1] SPTL typically appears as multiple, skin-colored, or erythematous, painless, subcutaneous nodules. It can initially mimic benign panniculitis, psoriasis, dermatitis, eczema, and cellulitis.[2] Histopathologically, numerous atypical lymphoid cells surrounded the adipocytes in a wreath-like manner (Fig 2) and were positive for CD3, CD4, CD5, CD8, βF1, Tia-1, granzyme B, but negative for CD20, CD56 (Fig 3).

D. PCGDTL — Incorrect. PCGDTL is an aggressive non-Hodgkin's lymphoma that does not express CD4, CD8, and βF1. PCGDTL often involves the dermis and epidermis, causing epidermal ulcers. The 5-year survival rate of patients with PCGDTL is nearly 11% owing to a higher incidence of hemophagocytic syndrome (HPS).[1]

E. ENKL — Incorrect. ENKL is an Epstein-Barr virus-associated angiodestructive non-Hodgkin's lymphoma. ENKL is characterized by localized lesions involving the nose, nasopharynx, or oropharynx. ENKL often express NK-cell markers ($CD2^+$, cytoplasmic $CD3^+$, and $CD56^+$).

Question 2: Which of the following is not recommended in the work-up and management of this patient?

A. Epstein-Barr virus-encoded RNA (EBER) detection

B. T-cell receptor (TCR) gene rearrangement analysis

C. Positron emission tomography-computed tomography

D. Antibiotic treatment

E. Combination chemotherapy based on the cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) regimen

Answers:

A. EBER detection — Incorrect. EBER is a diagnostic feature of ENKL and helps to differentiate it from SPTL. Significant Epstein-Barr virus infection is predictive of poor survival in younger patients with peripheral T-cell lymphoma.[3]

B. TCR gene rearrangement analysis — Incorrect. TCR clonal rearrangement was detected in 50% to 88% of patients with SPTL. Although the frequency of TCRδ clonal rearrangement is the lowest in SPTL, it is a specific marker of γ/δ T-cell lineage. The frequency of TCRβ or TCRγ gene clonal rearrangement is higher in SPTL but is not a specific marker for the α/β or γ/δ T-cell lineage. Detection of TCRβ, TCRγ, and TCRδ gene rearrangement enhanced clonality detection to 100% in SPTL.[1]

C. Positron emission tomography-computed tomography — Incorrect. Positron emission tomography-computed tomography is a valuable tool for diagnostic work-up, staging, and response monitoring in patients with SPTL.

D. Antibiotic treatment — Correct. At onset, SPTL can mimic cellulitis and other skin and soft tissue infections; however, it is essentially a rare cytotoxic $CD3^+CD8^+$ T-cell cutaneous lymphoma. Antibiotic treatments are often ineffective.

E. Combination chemotherapy based on the cyclophosphamide, doxorubicin, vincristine, and prednisolone (CHOP) regimen — Incorrect. Anthracycline-based combination chemotherapy (CHOP or CHOP-like) is usually reserved for patients with SPTL who have been treated with corticosteroids, immunosuppressive agents, and radiotherapy without achieving complete remission. Our patient initially showed a good response to CHOP chemotherapy.

Question 3: Which is not a poor prognostic factor in SPTL?

A. HPS

B. Clonal expression of γ/δ TCR gene rearrangement

C. Decreased white blood cell count

D. Elevated lactate dehydrogenase

E. Female gender

Answers:

A. HPS — Incorrect. HPS is characterized by fever, splenomegaly, cytopenia, abnormal liver function, and phagocytosis in bone marrow biopsy. Cytokines and chemokines produced by malignant cells and their cytolytic effects may be involved in the pathophysiology of HPS. HPS is associated with a poor prognosis in patients with SPTL. The mortality rate of SPTL with HPS is as high as 81%.

B. Clonal expression of γ/δ TCR gene rearrangement − Incorrect. SPTL with the clonal expression of α/β TCR is an indolent lymphoma and accounts for approximately 70% of the cases, whereas the γ/δ phenotype is associated with a poor prognosis.[4] The 5-year survival rates of SPTL-α/β and SPTL-γ/δ are 82% and 11%, respectively, owing to the higher incidence of HPS in the latter.[1]

C. Decreased white blood cell count − Incorrect. Leucopenia may be associated with HPS. A retrospective study indicated that a lower white blood cell count is associated with a poor prognosis in patients with SPTL.[5]

D. Elevated lactate dehydrogenase − Incorrect. Higher lactate dehydrogenase is helpful to predicate an aggressive course in patients with SPTL.[5]

E. Female gender − Correct. SPTL affects patients in the 30-40 years age group (median age, 36 years) with a female predominance (male/female ratio, 0.5), and 19% of patients are <20 years of age. However, to date, there is no direct evidence that female patients with SPTL have a worse prognosis than male patients.

Abbreviations used:

CHOP: cyclophosphamide, doxorubicin, vincristine, and prednisolone
EBER: EBV-encoded RNA
ENKL: extranodal nasal NK/T-cell lymphoma
HPS: hemophagocytic syndrome
LEP: lupus erythematosus panniculitis
PCGDTL: primary cutaneous gamma-delta T-cell lymphoma
SPTL: subcutaneous panniculitis-like T-cell lymphoma
TCR: T-cell receptor

Conflicts of interest

None disclosed.

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