

Dermatopathology 2018;5:30-33

DOI: 10.1159/000486754 Received: January 3, 2018 Accepted: January 10, 2018 Published online: February 15, 2018 © 2018 The Author(s) Published by S. Karger AG, Basel www.karger.com/dpa



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Research Communication

Lymphocytic Lobular Panniculitis: A Diagnostic Challenge

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Keywords

Panniculitis · Cutaneous lymphoma · Lymphoproliferative disease · Lupus erythematosus

Histological evidence of a lymphocytic lobular panniculitis is always a great diagnostic challenge. The possible diagnosis ranging from benign conditions, such as lupus panniculitis (LP), to indolent or aggressive types of T-cell lymphoproliferative disorders, such as subcutaneous panniculitis-like T-cell lymphoma (SPTL) and primary cutaneous γ/δ T-cell lymphoma (GDTCL). Integration between clinical, histological, and immunophenotypic features is necessary to obtain a definitive diagnosis.

SPTL is a rare cutaneous lymphoma, accounting for <1% of all non-Hodgkin lymphomas. It is related to a favorable prognosis except for cases complicated by hemophagocytic syndrome, associated with a decrease in survival (5-year overall survival 46% compared to 91%) [1]. SPTL had previously been categorized into 2 distinct entities: the α/β subtype, characterized by a good prognosis, and the γ/δ subtype, with a more aggressive behavior. Later, the second subtype was reclassified as distinct entity in the group of rare disease by the name of GDTCL [2]. SPTL occurs frequently in young people and is characterized by subcutaneous nodules and plaques, which can be necrotic but rarely ulcerated (Fig. 1a). The extremities are typically involved. Systemic symptoms, such as fatigue, fever, or weight loss, may be present [3]. The lesions are characterized by a lipotropic infiltrate of predominant small/mediumsized pleomorphic T cells in the subcutaneous tissue, usually sparing the dermis and epidermis. Neoplastic cells, mixed with macrophages, tend to be localized around adipocytes, forming the typical "rimming" and "capping" images (Fig. 1b, c). The phenotype of the neoplastic cells is βF1+, CD3+, CD4-, CD8+, CD45RO+ (Fig. 1d), and they express cytotoxic granules (TIA-1, granzyme, and perforin). Epstein-Barr virus (EBV) is usually not found. Analysis of the T-cell receptor (TCR) rearrangement by polymerase chain reaction (PCR) shows clonal proliferation of the T cells [1].

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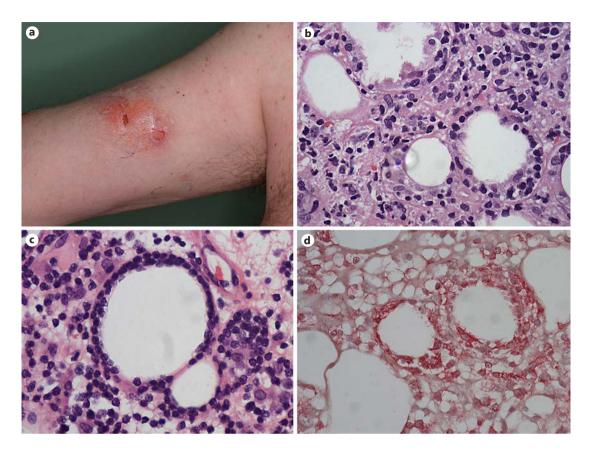


Fig. 1. Subcutaneous panniculitis-like T-cell lymphoma. **a** An erythematous plaque on the right arm. **b** An infiltrate of hyperchromatic small/medium-sized lymphocytes involving the subcutaneous fat. **c** The neoplastic T cells are localized around adipocytes, forming the "rimming" images. **d** CD8 staining reveals positive T cells, especially around adipocytes.

SPTL is frequently associated with autoimmune disorders, especially systemic lupus erythematosus (LE) [4]. GDTCL is similarly characterized by diffuse nodules and plaques, frequently localized on the arms and legs. Ulceration in GDTCL is more common than in SPTL (Fig. 2a). Survival in GDTCL is worse than in SPTL (5-year overall survival 11%) [3]. Unlike in SPTL, in GDTCL the subcutaneous neoplastic infiltrate involves the epidermis and dermis. Tumor cells express markers for TCR- $\gamma\delta$, CD2, CD3, CD45RA, CD56, and cytotoxic proteins. CD4 and CD8 markers are commonly negative (Fig. 2b–d). A clonal rearrangement for the TCR γ gene is frequent [4]. Recently, a mycosis fungoid-like variant has been described, characterized by a better prognosis. It manifests with plaques, papules, and nodules and shows an epidermotropic dermal infiltrate of atypical T lymphocytes without evidence of subcutaneous involvement [5].

LP is an uncommon variant of LE and may occur isolated or with a discoid or systemic LE [6]. Typically, LP occurs in females with chronic-relapsing painful subcutaneous nodules and plaques, covered by erythematous patches or discoid LE lesions. They usually heal with evidence of lipoatrophy and depressed scars. Unlike other panniculitides, nodules are usually localized on the upper arms, shoulders, buttocks, and face (Fig. 3a). Histologically, a lobular "cytophagic" panniculitis is frequently associated to epidermal and dermal features of LE, such as epidermal atrophy, vacuolar interface changes, a thickened basement membrane, dermal mucin deposition, and superficial and deep perivascular lymphocytic inflammation





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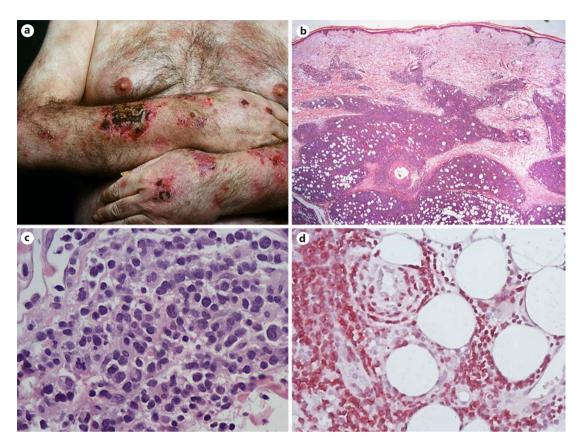


Fig. 2. Primary cutaneous γ/δ T-cell lymphoma. a Multiple erythematous plaques and nodules on the trunk and arms, some of them are ulcerated. b A dense infiltrate involves the whole dermis and subcutaneous fat. c The infiltrate is formed by atypical cells. d Anti-TCR-γδ staining shows the γδ phenotype of the neoplastic cells.

(Fig. 3b, c) [7]. The presence of lymphoid follicles, with a germinal center between the collagen bundles and into the septae, is highly characteristic of LP. The infiltrate is usually mixed, including cytotoxic CD8+ α/β T cells (Fig. 3d), but they are not predominant as in SPTL. Immunofluorescence analysis shows a linear deposition of immunoglobulin M and complement-3 on the dermo-epidermal junction. Serum antinuclear antibodies are commonly positive but few patients show lupus-specific positive serology. The rearrangement of the TCR gene is usually polyclonal, but it can also be monoclonal [3, 8].

In conclusion, it is important to define whether a lymphocytic lobular panniculitis is a benign reactive or a lymphoproliferative process, but this is frequently not easy. The presence of clinical and histological features of a systemic disease, integrated in immunohistochemical and molecular data, is helpful for reaching a diagnosis.

Disclosure Statement

The authors have no conflict of interest to declare.





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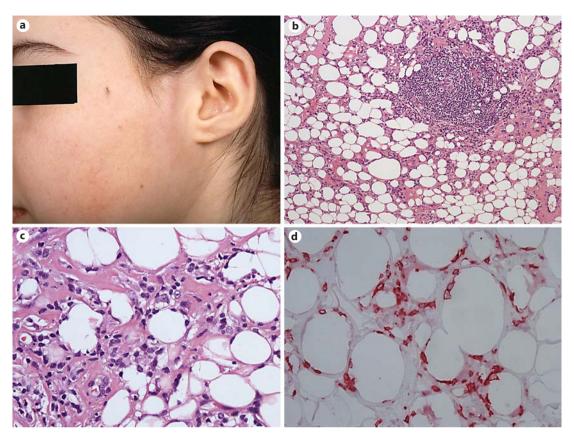


Fig. 3. Lupus panniculitis. **a** A subcutaneous plaque on the left cheek. **b** A lymphoid follicle in the subcutaneous fat. **c** Atypical lymphocytes which tend to be localized around adipocytes forming only a partial "rimming" images. **d** The atypical lymphocytes around adipocytes are CD8 positive.

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