

## Cutaneous Gamma-delta T-cell Lymphoma with an Initially Indolent Course Mimicking Lupus Panniculitis

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Primary cutaneous  $\gamma$ - $\delta$  T-cell lymphoma (CGD-TCL) is a rare disease characterized by a monoclonal proliferation of mature activated  $\gamma$ - $\delta$  T cells and an unfavourable prognosis. CGD-TCL represents approximately 1% of CTCLs as well as an entity of its own in the WHO classification (1). Thus far, there is sparse literature on this entity. We report here an atypical case of CGD-TCL, which showed an indolent course for almost 2 years, thus mimicking lupus panniculitis, prior to a rapid progression to the typical clinical presentation.

### CASE REPORT

A 68-year-old woman presented to our clinic with multiple indurated erythematous plaques and nodes on the right upper leg as well as one painful, immobile subcutaneous node on the left lower leg (Fig. 1A). These nodular lesions had developed over 9 months and had been pretreated with topical steroids with no success.

Haematoxylin and eosin (H&E) histology of a biopsy taken from the lesions revealed a dermal and subcutaneous infiltrate of atypical lymphocytes with mitoses, plasma cells and neutrophils as well as a vacuolar degeneration of basal cells. The pattern of panniculitis was predominantly lobular without rimming of adipocytes by atypical lymphocytes (Fig. 2A). Furthermore, histopathology showed a distinct dermal accumulation of mucin (Fig. 2B). Immunohistochemistry revealed CD3 expression of the pleomorphic lymphocytes, whereas CD79a and CD8 were negative (Fig. 2C). T-cell receptor (TCR)- $\gamma$ , as well as TIA-1, granzyme-B and perforin expression, was significant in the pleomorphic cells (Fig. 2D). A monoclonal TCR- $\gamma$  gene rearrangement was identified.

Anti-nuclear antibodies showed a titre of 1:320, lactate dehydrogenase was slightly elevated with 318 U/l.

Based on these results it was initially difficult to distinguish between CGD-TCL and lupus panniculitis, whereas  $\gamma$ - $\delta$ -derived mycosis fungoides or lymphomatoid papulosis could be excluded.

Staging via computed tomography (CT) and magnetic resonance imaging (MRI) showed no suspect lesions within the organs and lymph nodes.

Given the discrepancy between the rather aggressive histological and largely indolent clinical course we favoured the diagnosis of lupus panniculitis and started treatment with topical corticosteroids and hydroxychloroquine. With this therapy, the lesions showed a stable clinical course with no improvement, and with no aggravation for more than one year. When the patient developed further lesions of the abdomen and the legs with rapid growth and central ulceration (Fig. 1B) more than one year later, however, the clinical picture matched the threatening histological findings. Thus we could clearly confirm the diagnosis of CGD-TCL. We subsequently started polychemotherapy following the CHOP regimen (cyclophosphamide, doxorubicin, vincristine, and prednisone). Before obtaining an allogeneic stem cell transplantation complete remission was achieved after 5 months of polychemotherapy.

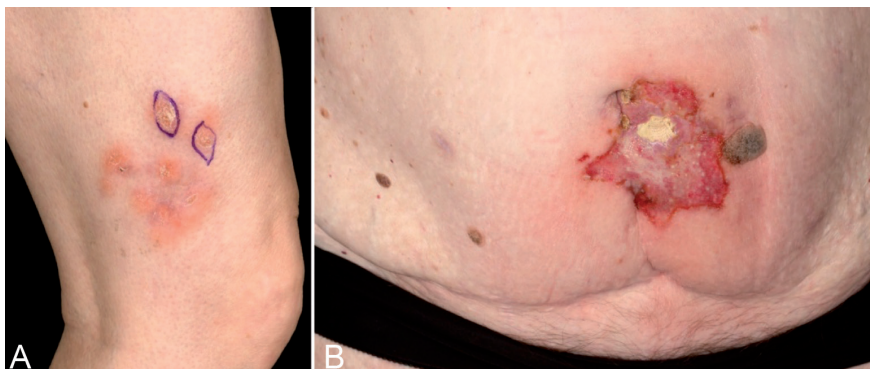
The patient developed opportunistic infections and a graft-versus-host disease of the gastrointestinal tract during the following months and died due to cardiac and renal failure following a haemolytic-uraemic syndrome.

### DISCUSSION

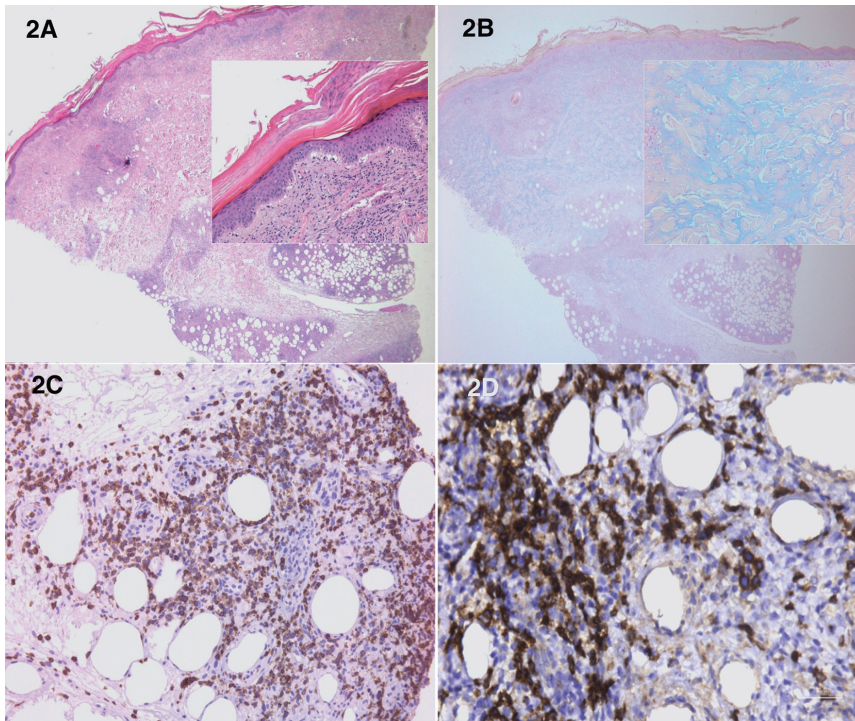
In most cases CGD-TCL has a poor prognosis with a median survival time of 15 months (1). In contrast, benign lupus erythematosus panniculitis (LEP) has a prolonged clinical course with a favourable prognosis. In addition it is important to distinguish CGD-TCL from subcutaneous panniculitis-like T-cell lymphoma (SPTCL), which bears an alpha-beta phenotype and displays a favourable prognosis (2).

Most patients with primary CGD-TCL present deeply infiltrated plaques and early ulcerations, especially on the legs (3). Lupus panniculitis, however, commonly shows erythematous nodes and plaques on the trunk, face, shoulders and proximal extremities.

Histopathology in CGD-TCL usually presents with epidermotropism as well as dermal and subcutaneous infiltrates of atypical lymphocytes. Rimming of adipocytes



**Fig. 1. Initial and late clinical characteristics.** (A) Initial clinical presentation of the patient's right leg at first visit to our hospital. Two of the nodular lesions are marked with violet paint for excision. (B) Clinical presentation of the growing ulceration at the patient's abdomen upon disease progression.



**Fig. 2. Histology and immunohistochemistry.** (A) Predominantly lobular panniculitis with dermal infiltration by lymphocytes (haematoxylin and eosin (H&E) staining, original magnification  $\times 20$ ) and vacuolar degeneration of the epidermis with parakeratosis (inset  $\times 200$ ). (B) Diffuse interstitial mucin deposition (Alcian blue  $\times 20$ , inset  $\times 200$ ). Immunohistochemistry shows numerous pleomorphic lymphocytes expressing CD3 (C) and T-cell receptor (TCR)- $\gamma$  (D) (original magnifications  $\times 200$  (C),  $\times 400$  (D)).

can occur, but is not specific (4). Immunohistochemistry usually shows a  $\beta F1^{-}$ ,  $CD3^{+}$ ,  $CD4^{-}$ ,  $CD2^{+}$ ,  $CD5^{-}$ ,  $CD7^{+/-}$  and  $CD56^{+}$  phenotype with strong expression of TIA-1, granzyme-B and perforin. Histopathology of lupus panniculitis, however, is rather characterized by interface dermatitis, dermal and subcutaneous infiltrate of lymphocytes, plasma cells and granulocytes as well as a strong accumulation of mucin.

Furthermore the monoclonal gene rearrangement and positivity for TCR- $\gamma$  in our case support a diagnosis of CGD-TCL. However, besides marked interface dermatitis we found a significant amount of plasma cells and mucin accumulation, favouring lupus panniculitis. Combined with the indolent clinical course, our patient showed many clinical and histological criteria for either of the diagnoses. The histopathological distinction is further complicated by the fact that cases of LEP with atypical lymphocytes are described (4). Magro et al. (5) described these lesions as a form of cutaneous lymphoid dyscrasia with characteristics of lobular lymphocytic panniculitis. The same authors discuss the presence of mucin accumulation in LP. As several cases of T-cell lymphoma with mucin accumulation have been published, this criterion alone is also unsuitable for the clear distinction between these entities (6).

There are several publications emphasizing that CGD-TCL can have an indolent course for years, before it shows the typical rapid disease progression (5–10). Still, it is crucial to exclude other CTCLs, such as mycosis fungoides or lymphomatoid papulosis with a  $\gamma$ - $\delta$  phenotype that, in general, show a far more indolent course (1).

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