

## QUIZ SECTION

### Erythematous-to-Brownish Plaques on the Upper Back: A Quiz

Ferdinand Toberer<sup>1</sup>, Wolfgang Hartschuh<sup>1</sup>, Heinz Kutzner<sup>2</sup> and Katharina Flux<sup>3</sup>

<sup>1</sup>Department of Dermatology, Ruprecht-Karls-University of Heidelberg, Im Neuenheimer Feld 440, DE-69120 Heidelberg, <sup>2</sup>Dermatopathologie Friedrichshafen, Friedrichshafen, and <sup>3</sup>Labor für Dermatohistologie und Oralpathologie, München, München, Germany. E-mail: [ferdinand.toberer@med.uni-heidelberg.de](mailto:ferdinand.toberer@med.uni-heidelberg.de)

A 38-year-old woman was referred to our dermatology clinic with a 6-month history of erythematous plaques on her torso. Despite partly severe pruritus, the skin lesions were largely asymptomatic and the patient's general condition was good. The patient reported a vacation in South America prior to the emergence of the skin alterations. The woman suffered from epilepsy, which had been treated continuously for 15 years with the same combined therapy regimen (sodium valproate 500 mg twice daily and phenytoin 100 mg in the morning and 150 mg at night).

Physical examination revealed 6 isolated, non-scaling erythematous-to-brownish plaques on the upper back, around the neckline and the chest (Fig. 1). Basic laboratory tests

(complete blood count, basic metabolic panel) were normal.

Histopathology revealed a dense, subepidermal, band-like lymphocytic infiltrate. Discrete, focal epidermotropism was seen without formation of Pautrier microabscesses (Fig. 2). The infiltrate consisted of small lymphocytes without striking polymorphism admixed with histiocytes. Immunophenotyping revealed an overall mixed-cell infiltrate, predominantly consisting of CD3<sup>+</sup> and CD4<sup>+</sup> T lymphocytes as well as CD20<sup>+</sup> and CD79a<sup>+</sup> B lymphocytes. CD79a<sup>+</sup> cells accounted for 10–20% of the infiltrate. Both biopsies revealed a clonal rearrangement of the T-cell receptor- $\gamma$ -gene.

*What is your diagnosis? See next page for answer.*



Fig. 1. Isolated, erythematous-to-brownish plaque without significant epidermal involvement on the left upper back.

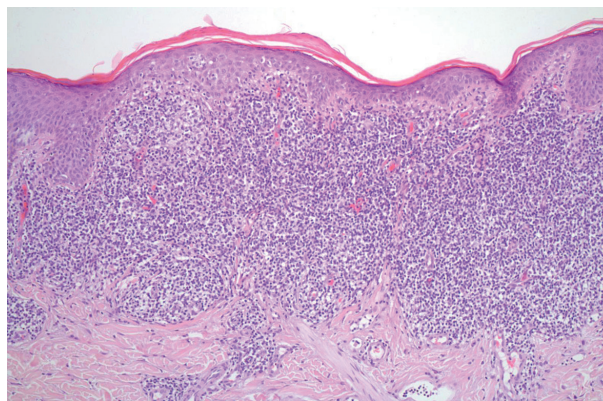


Fig. 2. Histology revealed a subepidermal, band-like lymphocytic infiltrate with discrete epidermotropism (H&E, original magnification  $\times 100$ ).

## ANSWERS TO QUIZ

**Erythematous-to-Brownish Plaques on the Upper Back: A Comment**

Acta Derm Venereol

**Diagnosis: Phenytoin-induced T-cell predominant pseudolymphoma (“pseudomycosis fungoides”) with T-cell clonality**

Phenytoin can act as a trigger of many different allergic skin reactions. In addition to maculopapular exanthemas and the hypersensitivity and Stevens-Johnson syndroms, it can also induce pseudolymphomas. This includes both pseudolymphoma syndrome with pronounced organ involvement and systemic symptoms (fever, lymphadenopathy, hepatitis and alterations in the haemogram) as well as the stimulation of pseudomycosis fungoides (PMF) (1). The PMF syndrome (PMFS) was initially described as a combination of exfoliative erythrodermic dermatitis, epidermal Pautrier’s microabscesses and generalised lymphadenopathy (2). The syndrome mimics the drug reaction with eosinophilia and systemic symptoms syndrome and might even be considered as a variation of the latter (3). However, it is a generally accepted practice to establish a diagnosis of PMFS also in patients without exfoliative erythrodermic dermatitis or generalised lymphadenopathy provided the corresponding histological alterations are present (4). The pathogenesis of phenytoin-induced T-cell infiltrates remains unclear. Phenytoin is capable of inducing late-appearing aberrant immune responses. In the present case, the time elapsed between the start of therapy and the development of pseudolymphoma was about 15 years. To our knowledge, such a long period of time has never been described in the literature before. Once the phenytoin therapy had been discontinued (while sodium valproate was continued), the patient’s skin infiltrations resolved completely within 6 weeks. When phenytoin therapy is discontinued, it should be kept in mind that similar reactions may also be induced by other aromatic anticonvulsive agents (e.g. carbamazepine). This is probably the consequence of a common metabolite created during the metabolism by epoxide hydrolases (1).

However, in cases of T-cell-rich B-cell lymphoma the malignant B-cell population usually shows rearrangement of the immunoglobulin heavy chain (IgH) genes. Clinically, the skin lesions of PMF and T-cell rich B-cell lymphoma might look the same. As in our case, phenytoin-induced pseudolymphomas can also be associated with T-cell clonality. T-cell clonality has been used to differentiate pseudolymphomas from malignant lymphomas in the past. However, rearrangement of the T-cell-receptor  $\gamma$ -genes has also been demonstrated in many infiltrates of clear-cut benign lesions (i.e. lichen planus atrophicus, lichen planus-like keratosis, pityriasis lichenoides, allergic skin reactions, pyoderma gangraenosum). Another important pitfall is the phenomenon of pseudo-clonality (PC). PC is frequently encountered in moderately dense infiltrates of the skin. This also applies to T- and B-cell populations. PC becomes unmasked when the clone appears at a different position during a double (and triple) test.

The present case of phenytoin-induced PMF clearly demonstrates that the feature of T-cell clonality is just one piece in the puzzle but not decisive for the correct diagnosis. Typical distinguishing features are summarized in Table S1<sup>1</sup>.

## REFERENCES

1. Nathan DL, Belsito DV. Carbamazepine-induced pseudolymphoma with CD-30 positive cells. *J Am Acad Dermatol* 1998; 38: 806–809.
2. Rosenthal CH, Noguera CA, Coppola A, Kapelner SN. Pseudolymphoma with mycosis fungoides manifestations, hyperresponsiveness to diphenylhydantoin and lymphocyte dysregulation. *Cancer* 1982; 49: 2305–2314.
3. Cacoub P, Musette P, Descamps V, Meyer O, Speirs C, Finzi L, Roujeau JC. The DRESS syndrome: a literature review. *Am J Med* 2011; 124: 588–597.
4. Wolf R, Kahane E, Sandbank M. Mycosis fungoides-like lesions associated with phenytoin therapy. *Arch Dermatol* 1985; 121: 1181–1182.

<sup>1</sup><https://doi.org/10.2340/00015555-1937>