# Case Essay

**Problem-based Learning**

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## CASE ESSAY 1: Necrotic Skin Lesions in a 79-year-old Woman

A 79-year-old woman was referred because of multiple necrotic skin lesions. She was healthy until approximately 4 months ago, when she noticed a few small ulcerations on her leg and arm. Initially, she thought it was an insect bite but she developed multiple skin lesions over the following months.

**I found this patient to have a generalized eruption consisting of oval, well-circumscribed lesions covered by a necrotic eschar (Fig. 1). The skin surrounding some lesions was slightly inflamed. Otherwise, the patient appeared healthy. After a first appraisal I would like to exclude infection, especially ECTHYMA GANGRENOSUM.**

Cultures showed growth of Pseudomonas aeruginosa. Routine blood tests revealed lymphocytosis (16×109/l, normal value 0.5-5×109/l). CRP, erythrocyte sedimentation rate and neutrophils were within the normal range.

**Massive lymphocytosis in an elderly patient made me consider CHRONIC LYMPHATIC LEUKAEMIA (CLL). The picture seems to make sense; the clinical impression is ecthyma caused by Pseudomonas, which has previously been observed in immunosuppressed patients with leukaemias. Lack of biochemical signs of infection does not bother me, since CRP and sedimentation rate are often normal in patients with Pseudomonas ecthyma.**

The patient was treated with the antibiotics Meropenem (Meronem®) and Ciprofloxacin. The diagnosis of CLL (B-cell) was confirmed by flow cytometry and bone marrow biopsy. Cytostatic treatment with Fludarabin was given.

**During cytostatic treatment the lymphocyte count fell to normal values. However, neither Fludarabin nor the antibiotics has had any effect on patient's skin lesions. This leads me to think of other possible diagnoses, such as PYODERMA GANGRENOSUM or VASCULITIS, both of which can be associated with lymphoproliferative diseases. LEUKAEMIC SKIN INFILTRATE is also a possibility, though less likely in view of the lack of effect of cytostatics on skin lesions. A biopsy will be necessary.**

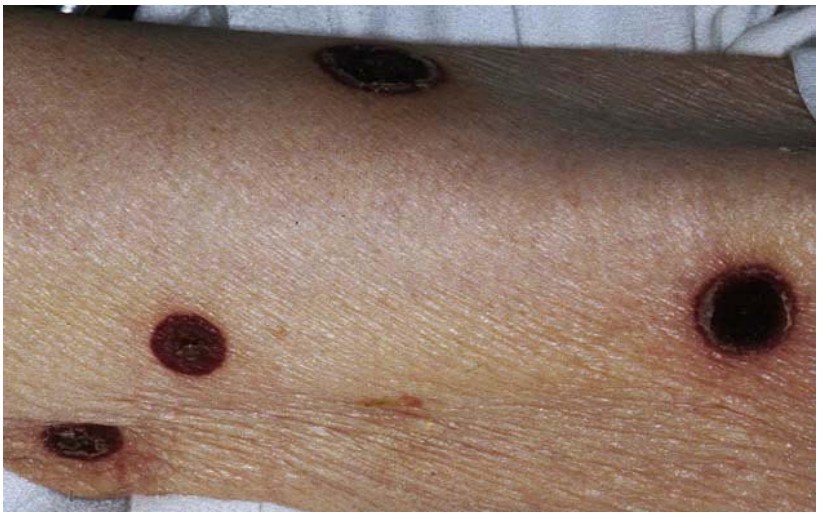

*Fig. 1.* Necrotic skin lesions

Biopsy showed fairly non-specific changes with epidermal necrosis and neutrophilic infiltrate consistent, but not diagnostic for pyoderma gangrenosum. There were no malignant B-cells present in the biopsy.

**SUPERFICIAL GRANULOMATOUS PYODERMA is a possibility, although no association with CLL has been reported. Pseudomonas infection is probably just a secondary phenomenon.**

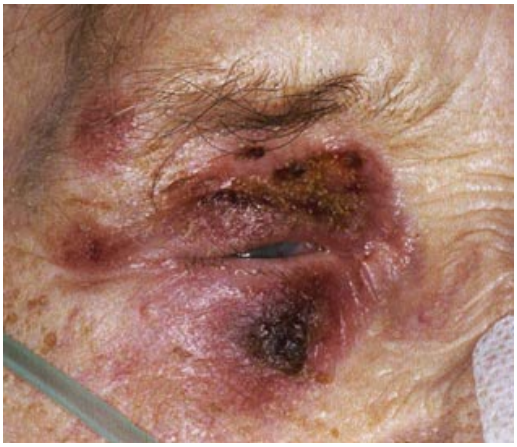

*Fig. 2.* Necrotic skin lesion.

Treatment with prednisolone 50 mg daily was tried. The patient developed more lesions, some of them with ulceration and infiltration.

**I am especially worried about the lesion on the eyelids (Fig. 2) which are quite infiltrated and ulcerated. The diagnosis of pyoderma, which I have never been comfortable with, seems to be less likely, especially in view of the poor response to prednisone. This patient's lesions look malignant to me; I would certainly like to have more biopsies from this patient.**

Three more biopsies were obtained, two of which showed non-specific changes as in the first one. However, the third biopsy showed a malignant epidermotropic lymphoma (Fig. 3). The atypical cells were positive for CD8 and CD3 but negative for CD4. Molecular biology studies showed the presence of a monoclonal T-cell clone, but no monoclonal immunoglobulin gene rearrangement.

**It seems that this patient has a second malignancy: a PRIMARY CYTOTOXIC EPIDERMOTROPIC CD8+ T-CELL LYMPHOMA. Malignant histology and the presence of monoclonal T-lymphocyte clone provide solid basis for this diagnosis. There are two epidermotropic CD8+ lymphomas that can give these kinds of symptoms: the disseminated PAGETOID RETICULOSIS and the recently described PRIMARY CD8+ LYMPHOMA OF THE SKIN. The clinicopathological features are consistent with the latter diagnosis.**

The patient was further treated with Cyclophosphamide and Rituximab with no apparent effect. She died of disseminated cutaneous lymphoma 4 months later.

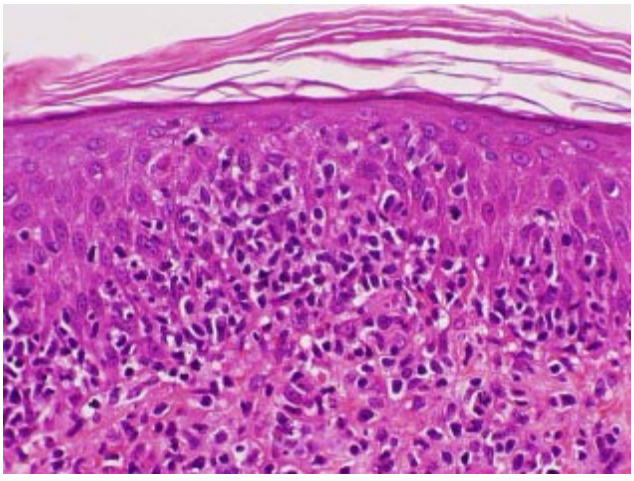

*Fig. 3a.*

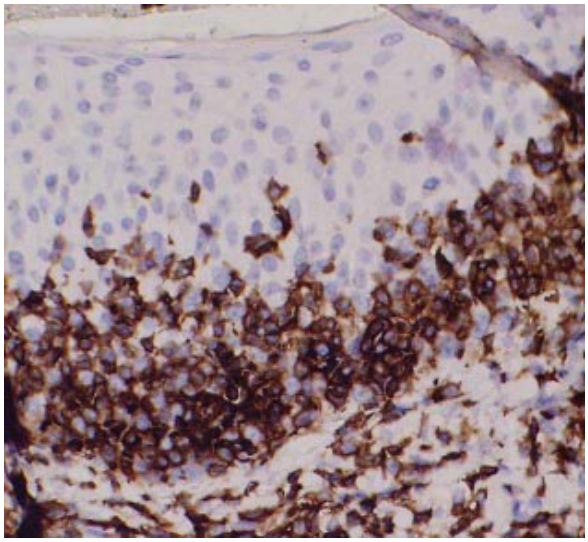

*Fig. 3b.*

Table I. *CD8+ Lymphomas of the skin*

| Entity | Clinical appearance | Pathology | Prognosis |
|---|---|---|---|
| PRIMARY CD8+ LYMPHOMA OF THE SKIN | SUPERFICIAL, OVAL NECROTIC LESIONS | EPIDERMOTROPIC CD8+ LYMPOMA | SEVERE, MEAN SURVIVAL 32 MONTHS |
| Pagetoid reticulosis | Scaly patches, usually on the extremities | Pagetoid epidermotropic CD8+ infiltrate | Excellent |
| CD8+ mycosis fungoides | Patches, plaques, tumour. Changes identical to classic mycosis fungoides | Like classic mycosis fungoides | Good in early stage |
| Subcutaneous panniculitis-like lymphoma | Panniculitis, subcutaneous tumours, ulcerations | Infiltration of subcutaneous fat by pleomorphic lymphocytes | Severe, mean survival approximately 20 months |

## Comment

The molecules CD4 and CD8 are essential components of the normal T-cell antigen receptor complex and are expressed on the helper and cytotoxic T-lymphocytes, respectively. For some reason most cutaneous T-cell lymphomas (e.g. classic mycosis fungoides, lymphomatoid papulosis, anaplastic lymphomas, etc) tend to differentiate into the CD4+ phenotype. Only approximately 4 different clinical entities, all quite rare, are CD8+ (cytotoxic) lymphomas (Table I). The so-called PRIMARY EPIDERMOTROPIC CYTOTOXIC LYMPHOMA OF THE SKIN has been described only recently by the Willemze group (1). It is an extremely aggressive neoplasm with an invariably fatal prognosis, which makes it differ from CD8+ mycosis fungoides and pagetoid reticulosis. The clinical features are characteristic: presence of round, often ulcerated and infiltrated necrotic skin lesions. Tumours may develop in latter stages. Mean survival is 32 months despite chemotherapy.

This case illustrates the difficulties encountered with the early diagnosis of cutaneous lymphomas. It is important to be aware of the clinical picture of these diseases since the histology at the early stages is often unspecific. Erroneous diagnosis of an inflammatory disease instead of skin lymphoma has previously led to tragic therapeutic mistakes: some patients were treated with cyclosporine that resulted in disease dissemination and death. Patience and multiple biopsies are required when in doubt. The last lesson is that some skin lymphomas may be associated with other malignancies, in this case with CLL. The presence of one malignant disease does not exclude the development of another malignancy.

## Reference

1. Berti E, Tomasini D, Vermeer MH, Meijer CJ, Alessi E, Willemze R. Primary cutaneous CD8-positive epidermotropic cytotoxic T cell lymphomas. A distinct clinicopathological entity with an aggressive clinical behavior. Am J Pathol 1999; 155: 483–492.