

Rapid Evolving Unilateral Indurated Oozing Facial Plaques in a Patient with Head-and-Neck Cancer: Peripheral T-Cell Lymphoma Not Otherwise Specified (NOS)

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Abstract

BACKGROUND: The sudden development of facial plaques and nodules may be an alarming clinical sign for underlying malignancies. Nevertheless, a broad range of inflammatory and infectious diseases must be considered as well in the differential diagnosis.

CASE REPORT: We report on a 53-year-old male patient with a left-sided cheek infiltration with oozing but no lymphadenopathy. He had a medical history of head-and-neck cancer. The primary differential diagnosis was herpes zoster with secondary impetiginization or pyoderma facial. About eight weeks later, the patient presented with progressive formation of nodules and plaques on the face and isotretinoin was stopped. Skin biopsy suggested mycosis fungoid and an oral treatment with bexarotene was started. After limited response for another eight weeks, he returned later with massive facial swelling, nodules and impetiginization. Another skin biopsy was performed to exclude diagnostic error or investigate possible disease progression. Microscopic evaluation and multiplex-polymerase chain reaction confirmed the diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTL-NOS), stage Ia (T1 N0 M0). Imaging techniques excluded metastatic spread. By interdisciplinary tumour board, R-CHOP (rituximab, cyclophosphamide, hydroxyl-doxorubicin, vincristine, and prednisolone) was recommended and initiated by hemato-oncologists.

CONCLUSIONS: PTL-NOS confirmed in the present patient has a poor prognosis with a 5-year survival rate of less than 20%.

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Introduction

Sudden development of indurated facial plaques refers to a broader range of benign but also serious life threatening diseases. Various inflammatory disorders are warranting consideration in the differential diagnosis.

Pyoderma facial or rosacea fulminant is characterised by erythematous indurated and painful plaques, sometimes oozing. It can develop unilaterally but is a rare diagnosis in males in contrast to females [1]. Sweet syndrome is a rare neutrophilic disease with rapid onset, fever, neutrophilic leukocytosis and painful cutaneous plaques, which may involve the face [2].

Well's syndrome or eosinophilic cellulitis is a rare disorder characterised by flame figures of

eosinophils in dermal tissue. Pruritic cellulitis-like plaques may masquerade as bacterial facial infection [3]. Granuloma faciale is an uncommon, chronic inflammatory disorder initially described as eosinophilic granuloma, responding to corticosteroids, and shares the apple jelly phenomenon on diascopy with sarcoidosis [4].

Histiocytic diseases may affect the facial skin. Benign cutaneous Rosai-Dorfman disease - a rare, non-Langerhans cell histiocytosis, affects the facial skin in about 11% of cases with erythematous plaques [5]. Disseminated xanthogranuloma typically involves periorbital skin [6].

Among infectious disorders, cutaneous leishmaniasis is emerging in non-epidemic areas. The disease is caused by vector-borne protozoal cutaneous infection by several species of *Leishmania* transmitted by sandflies [7, 8].

In the case of immunosuppression, bacterial papillomatosis and severe facial soft tissue infections may develop [9]. Invasive zygomycosis is another potentially fatal infection [10]. Malignancies need to be taken into consideration in any atypical case of facial nodular plaque-type affection, as the following case report illustrates.

Case presentation

A 53-year-old male patient was admitted to our hospital in July 2016 because of a left sided cheek infiltration with oozing. We observed an oozing indurated nodular plaque of about 6 x 8 cm (Fig. 1A) but no lymphadenopathy. The primary differential diagnosis was herpes zoster with secondary impetiginization or pyoderma facial.

The patient was treated initially with oral acyclovir 5 x 800 mg /d plus 100 mg prednisolone/d (with tapering the dose) for seven days. Oozing diminished but infiltrates were still present.

After that isotretinoin therapy was initiated. Topical treatment consisted of disinfectant washings and fusidinic acid ointment. The marked lymphedema could be explained by a history of head-and-neck cancer (T2 N2 M0 G2 V1 R0) the year before with surgery, neck dissection and radiotherapy.

The patient returned in September 2016 (Fig. 1B). Since there was progress with nodules and lid oedema, isotretinoin was stopped, and a skin biopsy was performed. The working diagnosis was mycosis fungoides. Based on the cutaneous T-cell lymphoma (CTCL) diagnosis the patient was discussed in the interdisciplinary tumour board. Radiotherapy was impossible due to the previous radiotherapy of head-and-neck cancer. Therefore, oral treatment with 525 mg/ d bexarotene was started. There was progress in December leading to a cessation of bexarotene (Fig. 1C).



Figure 1: *Peripheral T-cell lymphoma, not otherwise specified. (A) Initial presentation resembling herpes infection; (B) Worsening with an aspect of mycosis fungoides; (C) Further progression with massive lid oedema and secondary impetiginization*

Another skin biopsy was performed. There was a dense inflammatory infiltrate in dermis and subcutis, but no interface dermatitis and no epidermal infiltration. Hair follicles were partly destroyed. The infiltrate consisted mostly of medium-sized

polymorphous cells with notched nuclei and numerous mitoses. Some small lymphocytic cells and individual plasma cells and mast cells were intermingled (Fig. 2).

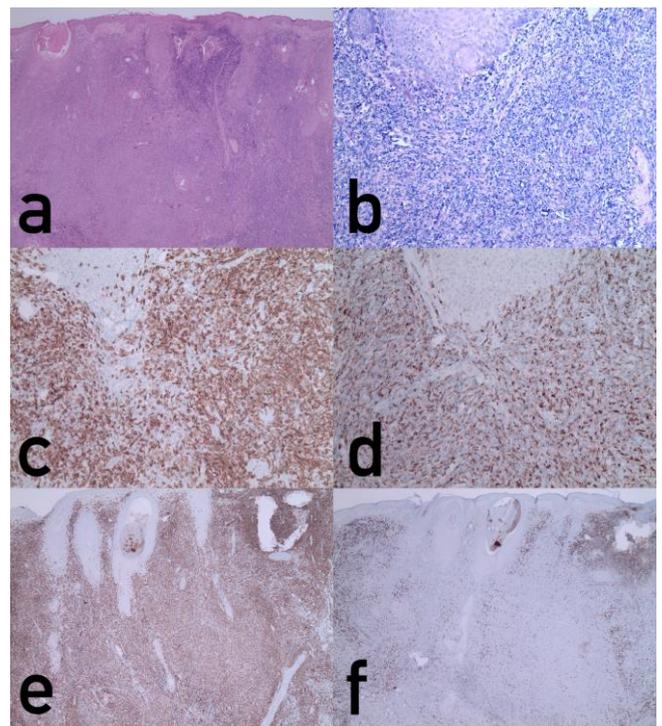


Figure 2: *Histologic investigations. (a) Dense dermal infiltrate (hematoxylin-eosin x 4); (b) Detail – mononuclear cells with cellular atypia and atypical mitoses (hematoxylin-eosin x 10); (c) Strong expression of CD3 (immunoperoxidase x 10); (d) CD8 expression (immunoperoxidase x 10); (e) Beta-F1 expression (immunoperoxidase x 4); (f) Ki67 for proliferating cells (immunoperoxidase x 4)*

Immunohistological findings are summarised in Table 1. After DNA extraction multiplex-polymerase chain reaction (PCR) had been performed to investigate clonality of cells (Institute of Pathology, University of Kiel, Germany) (Table 2). Monoclonality only could be demonstrated for T-cells, not B-cells.

Table 1: **Immunohistological findings**

Marker	Reactivity
CD1a	+ (for single cells only)
CD3	+++
CD4	(+)
CD5	+
CD7	+++
CD8	+++
CD10	-
CD20	+ (focally in the surrounding tissue by small lymphocytes)
CD30	-
CD56	-
CD68	+ (for single histiocytes only)
Bcl-6	-
Beta-F1 (T-cell receptor beta chain)	+++
Cyclin-D1	-
Ki67	++ (up to 60% of medium-sized cells)
PD1	+
Perforin	-

Imaging with diagnostic ultrasound and thoracic X-ray excluded metastatic spread. However, a parotic adenoma was identified. Laboratory investigations revealed an increased ratio of

CD3+CD4+ / CD3+CD8+ of 3.56 (normal range: 1.0-2.3).

The diagnosis of peripheral T-cell lymphoma, not otherwise specified (PTL-NOS), stage Ia (T1 N0 M0), was confirmed.

Table 2: Multiplex-PCR (bp – base pair; negative means polyclonality instead of monoclonality)

Beta-chain T-cell receptor gene		monoclonality
	A-multiplex PCR	247 & 248 bp
	B-multiplex PCR	253 & 261 bp
	C-multiplex PCR	193 & 303 bp
Gamma-chain T-cell receptor gene		
	va-multiplex PCR	negative
	vb-multiplex PCR	negative
Immunoglobulin heavy chain gene		
	F1-multiplex PCR	negative
	F2-multiplex PCR	negative
	F3-multiplex PCR	negative

By interdisciplinary tumour board, R-CHOP (rituximab, cyclophosphamide, hydroxyl-doxorubicin, vincristine, and prednisolone) was recommended and initiated in January by hemato-oncologists. The treatment is continued.

Discussion

Peripheral T-cell lymphoma (PTL) NOS is a rare but aggressive malignancy. The initial stages often resemble non-malignant plaque-type or nodular dermatoses as in the present case. These primary lesions may become infected and imitate an infectious disease [11].

In the differential diagnosis, other lymphomas need to be considered. The most common CTCL – mycosis fungoides - was the first suspicion. The aggressive course and the missing epidermotropism of atypical cells argued against. Because of the dominance of CD8+ lymphocytes in the second biopsy, primary cutaneous CD8-positive aggressive epidermotropic T-cell lymphoma (CD8+ AECTCL) had to be considered. AECTCL is characterised by rapidly evolving erosive or necrotic plaques and nodules. Epidermotropic infiltrates of CD8+ atypical lymphocytes are the hallmark of CD8+ AECTCL, which exhibits a poor prognosis [12]. Again, in the present case, there was no epidermotropism at all, confirming the diagnosis of PTL-NOS.

PTL-NOS may present with single nodules or nodular plaques but tends to disseminate rapidly. Responses to radio- and chemotherapy a short-lived. Our patient has achieved a partial remission during R-CHOP therapy [Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Vincristine (Oncovin®), and Prednisolone].

Negative prognostic factors for PTL-NOS are age > 60, Eastern Cooperative Oncology Group

(ECOG) performance status of ≥ 2 , lactate dehydrogenase levels at normal values or above, and involvement of the bone marrow are independent predictors of decreased survival [13]. Prognosis is poor even with stem cell transplantation and systemic chemotherapy and radiotherapy with a 5-year survival rate of less than 20% [14].

In conclusion, sudden development of facial plaques and nodules can be a red flag of unknown malignancy. Even if routine laboratory tests are unremarkable and lymphadenopathy is absent, an aggressive lymphoma-like PTL-NOS in this case, may be present. Repeated skin biopsies are needed to confirm or exclude diagnosis. PTL-NOS, however, has a poor prognosis not improved substantially by systemic treatment.

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