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CLINICAL REPORT

Oral Involvement in Mycosis Fungoides: Report of Two Cases and a Literature Review

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Oral involvement is uncommon in cutaneous T-cell lymphomas and usually associated with poor prognosis. The clinicopathological and immunohistochemical findings of 2 new cases are described along with a literature review. The first patient had a 10-year history of mycosis fungoides when she developed lesions in the oral tissues. She died 6 months later despite treatment. The immunophenotype was $CD3^+$, $CD4^+$, $CD8^-$, $CD30^-$. The second patient had a mycosis fungoides for 5 years when she developed lesions in the uvula and oropharynx. She was treated with polychemotherapy and she is alive 5 years after oral involvement. The immunophenotype was $CD3^+$, $CD4^-$, $CD8^+$, $CD30^-$. There are conflicting reports about the prognosis in the $CD8^+$ phenotype. The present cases and the literature review seem to indicate that in oral involvement the $CD8^+$ phenotype is not associated with a worse prognosis than the $CD4^+$ subtype. However, it is necessary to study new cases to confirm this statement. ***Key words: cutaneous T-cell lymphoma; oral mucosa; CD8+ phenotype.***

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Mycosis fungoides (MF) is a cutaneous T-cell lymphoma that usually evolves through 3 classical stages: scaly patches, infiltrative plaques, and finally tumours. Lymph nodes and many other organs may be involved in the process but clinical oral involvement is an uncommon manifestation. Thus, Sirois et al. reported a lower than 1% incidence of oral lesions in 824 patients with MF over a 25-year period (1). To the authors' knowledge only 31 cases of oral involvement from cutaneous T-cell lymphoma (MF) have been reported in the English language literature (1–21). The clinicopathological and immunohistochemical features of 2 new patients are described here, along with a literature review.

CASE REPORTS

Case 1

A 45-year-old woman had a 10-year history of classic MF. She had received various treatments: PUVA, PUVA+interferon, methotrexate, topical carmustine, electron-beam therapy and photophoresis, with partial improvement. Nine years after the initial diagnosis she developed lymphadenopathies histologically diagnosed as Hodgkin's lymphoma, and received polychemotherapy and autologous bone marrow transplantation, with a complete response. Eight months later, MF relapsed with numerous disseminated cutaneous plaques and tumoral lesions.

A bone-marrow biopsy specimen at that time was normal. T-cell receptor rearrangement by polymerase chain reaction (PCR) analysis of both peripheral blood and lesional skin biopsies (plaques and tumours) showed clonality. The complete blood cell count showed eosinophilia: 1×10^9/l (normal $< 0.4 \times 10^9$/l). The erythrocyte sedimentation rate was 40 mm/h. Biochemistry, thorax X-ray and thoracic computed tomographic (CT) scan were normal.

Treatment with oral corticosteroids, methotrexate and etoposide was started, but the disease progressed with development of lesions on her tongue, uvula and oropharynx (Fig. 1). The patient died 6 months later. A tongue biopsy specimen showed a dense corial and muscular diffuse infiltrate of large atypical lymphocytes with focal exocytosis. Numerous mitoses and eosinophils were present in significant numbers (Fig. 2). The phenotype of the tongue lesion, cutaneous plaque and tumour was $CD3^+$, $CD4^+$, $CD8^-$, $CD30^-$.

Case 2

In 1990 a 66-year-old woman developed erythematosquamous plaques, papules and nodules on her head, trunk and legs. Biopsy specimens taken from the different lesions were similar and congruent with MF. There was no palpable lymphadenopathy and a systemic workup was negative for extracutaneous involvement. She was treated satisfactorily with systemic interferon, but because of severe lymphopenia the treatment was substituted by topical carmustine with an almost complete response. In 1994 the patient noticed an ulcerated tumour on her leg and a painful enlarged uvula. Microscopically, the uvula surgical excision showed a malignant lymphoid proliferation composed of atypical large lymphocytes with irregular nuclei, prominent nucleoli and numerous mitotic figures.



Fig. 1. Case 1: tongue involvement by ulcerated tumour.

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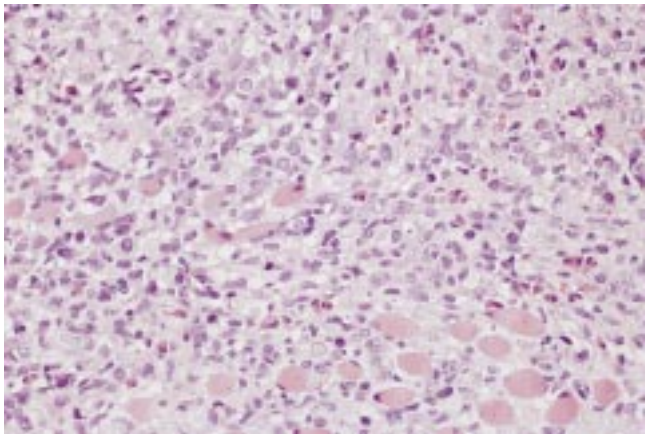


Fig. 2. Case 1: Deeper infiltrate of large atypical lymphocytes around the skeletal muscle fibres.

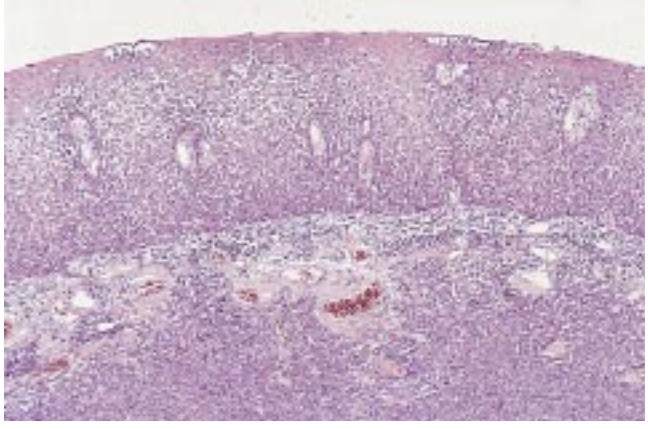


Fig. 3. Case 2: Pleomorphic atypical lymphocytes with epitheliotropism and microabscess formation.

There was intense exocytosis and microabscess formation in the epithelium (Fig. 3). The phenotype was $CD3^+$, $CD4^-$, $CD8^+$, $CD30^-$. These histopathological and immunopathological features were similar to those of the cutaneous ulcerated tumoral lesion.

A CT scan showed asymmetry of the cavum without involvement of deep levels, with enlargement of the soft palate and tonsils. There was no evidence of extracutaneous involvement. A bone-marrow biopsy was unspecific. Treatment with polychemotherapy (CHOP) improved the disease with a complete response. The patient is alive today, without cutaneous or mucosal involvement, 5 years after the occurrence of the oral lesions.

DISCUSSION

Oral involvement in MF is an incidental finding observed in 7.4% to 18% of patients in autopsy studies (22, 23). Despite these findings, *in vivo* mucosal involvement is a rare event, with only 31 cases reported in the English language literature, to the authors' knowledge (Table I). Males and females are equally affected. The age at presentation ranges from 36 to 81 years, with an average of 61 years. The oral sites more frequently involved are the tongue ($n=17$), palate ($n=16$), gingiva ($n=13$), buccal mucosa ($n=6$), lips ($n=3$) and oropharynx ($n=2$). Fifteen cases were affected in more than 1 site. In almost all patients cutaneous lesions preceded mucosal ones, ranging from 7 months to 40 years, with an average of 8 years. There are only 2 case reports with mucosal lesions preceding skin involvement, but it is doubtful that these cases are really MF, and they probably represent peripheral T-cell lymphomas (24, 25).

The histological features consist of a dense infiltrate of atypical pleomorphic lymphocytes. Exocytosis is common and characteristic Pautrier's microabscesses can be found. These features are similar to those seen in cutaneous lesions, although as in these 2 cases a higher number of large lymphocytes and a deeper involvement are frequent. These findings are usually present in tumoral cutaneous lesions of MF, and therefore is logical to find them in oral lesions because they represent an advanced stage of the disease.

A $CD8^+$ phenotype has been reported to have a poor prognosis in cases of MF with oral involvement (18, 26). However, there is not enough information in the literature because the $CD8^+$ immunophenotype has been only reported in 4 patients with MF and oral involvement (1, 14, 18). Moreover, the outcome of the reported cases has been equally poor in both the $CD4^+$ and $CD8^+$ phenotypes. A worse prognosis has not been demonstrated in classical MF with a predominantly CD8 phenotype. However, many papers describe a better prognosis in the $CD8^+$ phenotype (27–29). In the present cases the $CD4^+$ patient had a fatal outcome, while the $CD8^+$ patient remains alive 5 years later.

For these reasons, and despite the conflicting reports, the authors believe that in mucosal involvement the suppressor/cytotoxic (CD8) phenotype does not have a worse prognosis than the helper (CD4) subtype.

Of the reported cases more than 50% died within 1 year of the presentation of oral lesions and almost all died within 3 years. This survival rate is worse than that of patients with lymphadenopathy, erythroderma or tumoral lesions, and similar to that of patients with visceral involvement (21, 22). Therefore, oral involvement in MF must be considered a

Table I. *Summary of characteristics of 33 patients with oral mycosis fungoides (data collected from Refs 1–21 and the present study)*

Site of oral involvement (no. of patients)						Onset to oral involvement[a] (months)	Stage at oral involvement[b]							Survival time[a] (months)
Tongue	Palate	Gingiva	Bucca	Lip	Oropharynx		0	IB	IIA	IIB	III	IV	U	
17	16	13	6	3	2	96 (7–480)	1	6	1	11	3	8	3	16 (2–96)

[a]Mean (range).
[b]U: Unknown; 0: without cutaneous lesions at this moment.

marker for poor prognosis and a manifestation of advanced disease.

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