Folliculotropic CD8\(^+\) mycosis fungoides associated with diffuse mucosal involvement

Adèle de Masson, MD, PhD,a,b Laure Frumholtz, MD,a Maxime Battistella, MD, PhD,b,c Marie-Dominique Vignon-Pennamen, MD,\(^c\) Clarence de Belilovsky, MD,\(^d\) Corinne Husson, MD,\(^e\) Caroline Ram-Wolff, MD,\(^a\) Camille Frances, MD, PhD,\(^a,g\) Martine Bagot, MD, PhD,\(^c,b\) and Florence Cordoliani, MD\(^a\)

Paris, France

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INTRODUCTION

Folliculotropic mycosis fungoides (FMF) is a variant of mycosis fungoides (MF) characterized by the presence of atypical T cells in the hair follicles. FMF typically presents with hair loss, comedones, and cystic skin lesions. Syringotropic MF is defined by the eccrine gland infiltration by atypical T cells. Here we report a case of folliculotropic and syringotropic CD8 MF with exceptional diffuse mucosal involvement.

CASE REPORT

A 53-year-old woman presented with a 3-year history of mouth and esophageal burning sensation responsible for a 50-pound weight loss, followed by the appearance of cutaneous lesions.

The oral examination found diffuse, intense erythema. The tongue was reddish, glazed without atrophy. The erythema was predominant on the gingival and cheek mucosa. There was a cheilitis (Fig 1, A). Diffuse vulvar erythema and anal marisca were also present.

The clinical examination found crusted, hyperkeratotic, follicular plaques; open comedones; papulo-pustules of the trunk, pubis, and limbs (Fig 1, B); and rounded erythematous palmoplantar plaques (Fig 1, C).

Linear ulcerations of the esophagus were found by gastroscopy, with lymphoid epitheliotropism on histologic analysis. Antifungal therapy with oral fluconazole and an oral solution of amphotericin B was ineffective. There was no vitamin B12 or iron deficiency. Topical and oral corticosteroids provided no improvement.

The colonoscopy found no abnormality, ruling out inflammatory bowel disease. The serum glucagon levels, pancreas computed tomography scan, and magnetic resonance imaging found no evidence for glucagonoma. The serum zinc levels were in the normal range.

Biopsies of a pustule and a comedone found atypical small CD8 T-cell infiltration with epidermal, follicular, and eccrine epitheliotropism. Further biopsies of the gingival, vulvar, and anal mucous membranes also showed an epitheliotropic CD8 T-cell infiltrate with partial loss of CD7 without any lichenoid pattern (Fig 2). Direct immunofluorescence performed on the skin of the back and gingival mucosa was negative. Indirect immunofluorescence on blood was negative. Antidesmoglein 1 and 3, antienoplakin, and antiperiplakin antibodies were not detected by enzyme-linked immunosorbent assay. The thoraco-abdominal and pelvic computed tomography scan was normal, ruling out a systemic lymphoma with secondary skin involvement. These

From Dermatologie, APHP\(^a\) and Pathologie,\(^c\) Hôpital Saint-Louis; Université Paris Diderot\(^b\); Institut Fournier\(^b\); Hôpital Tarnier\(^b\); Dermatologie, Hôpital Tenon\(^a\); and Université Paris 6.\(^a\) Drs de Masson and Frumholtz are co–first authors.

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Correspondence to: Pr Martine Bagot, Service de Dermatologie, Hôpital Saint-Louis, 1 Avenue Claude Vellefaux, 75015 Paris, France. E-mail: martine.bagot@aphp.fr.

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features were consistent with the diagnosis of folliculotropic and syringotropic CD8 MF with oral, esophageal, and vulvar involvement. Subcutaneous methotrexate led to a partial remission. The patient experienced a relapse, and methotrexate was withdrawn and replaced by liposomal doxorubicin. The patient was still alive 4 years after the onset of the symptoms with no evidence of cutaneous, lymph node, or visceral progression.

**DISCUSSION**

The classical Alibert-Bazin type of MF is characterized by an epidermotropic infiltrate of atypical CD4 cells, and rarely, CD8 T cells. CD8 FMF is rarely reported and was absent from 2 large cohorts of FMF. There was no case of CD8 MF in a recent multicenter series of 29 syringotropic MF cases.

Mucous involvement is estimated to be present in less than 1% of MF cases but might be underreported. Most published cases are advanced-stage MF. The tongue is most frequently affected, followed by the palate, gums, lips, and oropharynx. The gastrointestinal tract was frequently involved at autopsy of MF patients along with the spleen and liver, bone marrow, kidney, and lung. Ocular, perianal, and vulvar lesions have been observed in a few cases.

MF is believed to be mostly a malignancy of resident memory T cells (TRM). CD103+ TRM are enriched in the human epidermis. CD103 (αEβ7 integrin) binds E-cadherin on the keratinocytes. E-cadherin is expressed in the hair follicles. CD103 also mediates adhesion to intestinal microvascular endothelial cell. In fact, CD103 is required for the retention of CD8+ TRM cells in the epithelium. Therefore, the expression of CD103 by the epidermotropic CD8 T cells could explain their preferential localization in the epidermis, hair follicle, and oral and digestive mucosa.

The main differential diagnosis of CD8 MF with mucosal involvement is aggressive epidermotropic cutaneous CD8 lymphoma that presents with rapidly evolving ulcerated or tumoral lesions and can also affect the mucous membranes. The infiltrate is extremely epidermotropic and is mainly composed of intermediate and large cell lymphocytes. Aggressive epidermotropic cutaneous CD8 lymphoma is associated with an extremely poor
prognosis. In our case, the small size of the tumor cells, the clinical presentation (with comedones and erythematousquamous plaques on the skin), and the evolution (the patient being still alive 4 years after the onset of the symptoms with no evidence of progression) make the diagnosis of aggressive epidermotropic cutaneous CD8 lymphoma highly unlikely. Although epidermotropic cutaneous CD8 lymphoma carries a poor prognosis, the prognosis of CD8\(^+\) MF is more controversial. In fact, some investigators have reported a better prognosis of CD8\(^+\) MF compared with classical CD4\(^+\) MF.

Folliculotropic MF has also been shown to be a heterogeneous group. Patients with follicular patches or papules with hair loss, keratosis pilaris–like and acneiform lesions, and a sparse infiltrate on histology have an excellent prognosis. However, folliculotropic MF with infiltrated plaques, nodules or tumors and histologically confluent and diffuse infiltrates, often containing medium-to-large-sized cells, is associated with a more aggressive behavior. There was no evidence of nodules or tumors in our patient.

The paucity of mucosal MF cases reported in the literature makes it difficult to assess the prognosis in this subset of patients. Indeed, most cases of mucosal MF were associated with advanced T stage (tumor stage or erythroderma), which carries a poor prognosis by itself. It is not known whether the mucosal involvement alone negatively affects the prognosis.

In our case, folliculotropic and syringotropic CD8 MF was associated with diffuse mucosal involvement of the vulva, oral mucosa, and digestive tract, leading to functional impairment and profound weight loss.

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