

Psoriasiform mycosis fungoides: a rare form of the disease with review of the literature

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Abstract

Background: Mycosis fungoides (MF) typically presents as erythematous scaly patches or plaques that may progress to cutaneous tumors. Although MF may be presented like other dermatoses, initial presentation as psoriasiform plaques simulating psoriasis is rare. Differentiating MF from psoriasis is important because systemic therapies used for psoriasis can worsen MF. We describe a case of psoriasiform MF and we also review the clinicopathological features of similar cases in the literature. **Case:** A 46-year-old woman was referred to our clinic with a history of psoriasiform plaques for 13 years. She had multiple, generalized, indurated plaques with thick psoriasiform scales that were unresponsive to topical treatments. The histopathology showed marked psoriasiform epidermal hyperplasia with epidermotropic atypical lymphocytes compatible with MF. Immunohistochemical staining showed that atypical lymphocytes were positive for CD3, CD4, CD8, and CD5. Of note, upper dermal and intraepidermal large atypical lymphocytes were CD30 positive. A review of similar psoriasiform MF cases revealed that they had all been treated as psoriasis for many years and finally diagnosed as MF especially after deterioration induced by immunosuppressive therapies. **Conclusions:** In presumed cases of psoriasis that are unresponsive to treatment, progressive, or ulcerative, biopsy should be considered to rule out MF, particularly before starting a potent immunosuppressive agent.

Introduction

Cutaneous T-cell lymphomas are a heterogeneous group of T-cell lymphoproliferative disorders involving the skin, the most common forms of which may be classified as mycosis fungoides (MF). The incidence of MF has been increasing with the highest incidence being reported among middle-aged males [1]. MF typically presents as erythematous scaly patches or plaques that may progress to generalized erythroderma or cutaneous tumors. As the presenting clinical and pathological features of MF are mainly nonspecific, the definitive diagnosis is challenging.

Many patients have symptoms attributed to other dermatoses such as eczema or parapsoriasis for years before obtaining a definitive diagnosis [2]. Differentiating MF from psoriasis is of importance because systemic therapies commonly used for psoriasis, such as tumor necrosis factor (TNF) inhibitors or cyclosporine can worsen MF [3, 4]. In this article we describe an uncommon presentation of psoriasiform MF in a patient who had been treated as psoriasis for a long period and we review similar cases from the literature comparing their clinicopathological features.

Case Synopsis

A 46-year-old woman was referred to the department of dermatology, Razi hospital, Tehran University of Medical Sciences, with a history of psoriasiform plaques for 13 years. Our patient had been diagnosed as having psoriasis for many years and had been treated with topical steroids intermittently. During the last four months her lesions had exacerbated and enlarged significantly without improvement in

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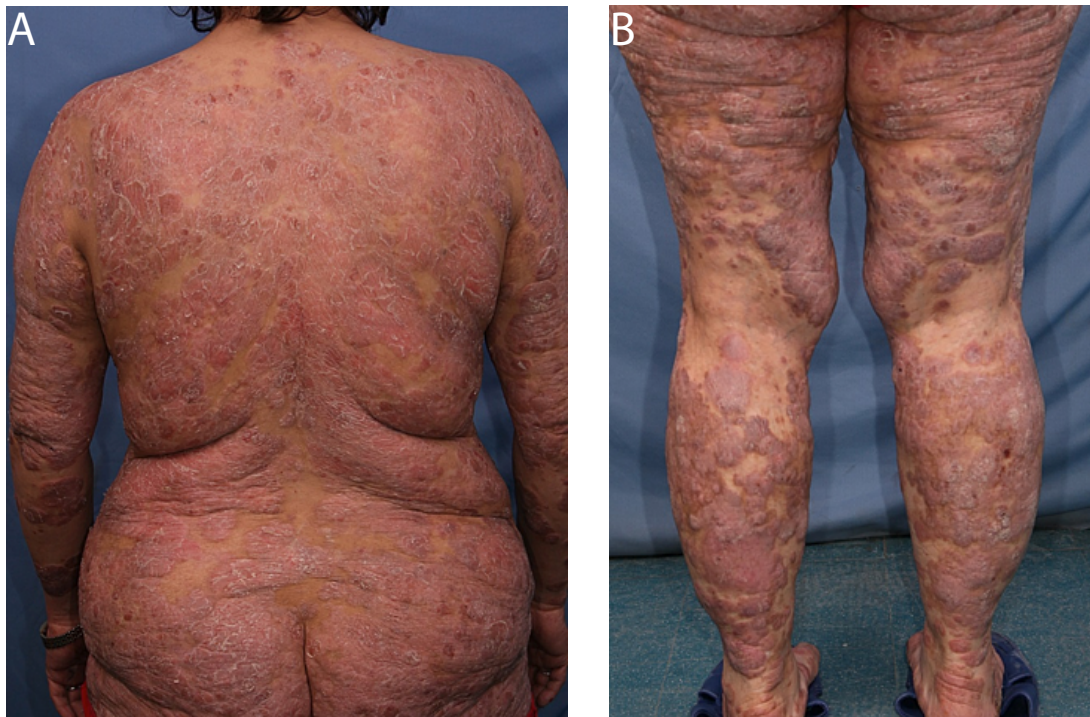


Figure 1. Multiple well demarcated erythematous plaques with psoriasiform scales on her back (A), extremities (B)

spite of topical treatment. Upon examination, the patient had multiple indurated, well-demarcated erythematous plaques with thick psoriasiform scales all over her chest, abdomen, back, upper and lower extremities. Her face was nearly spared. Her hair and nails were normal. There was neither lymphadenopathy nor systemic symptoms (Figure 1).

Histological examination revealed marked psoriasiform epidermal hyperplasia with epidermotropic atypical lymphocytes and scant spongiosis. The epidermis revealed many intraepidermal atypical medium-sized lymphocytes with perinuclear halo and convoluted nuclei linearly arranged along the basal layer. The papillary dermis was filled by a dense infiltration of lymphocytes, which

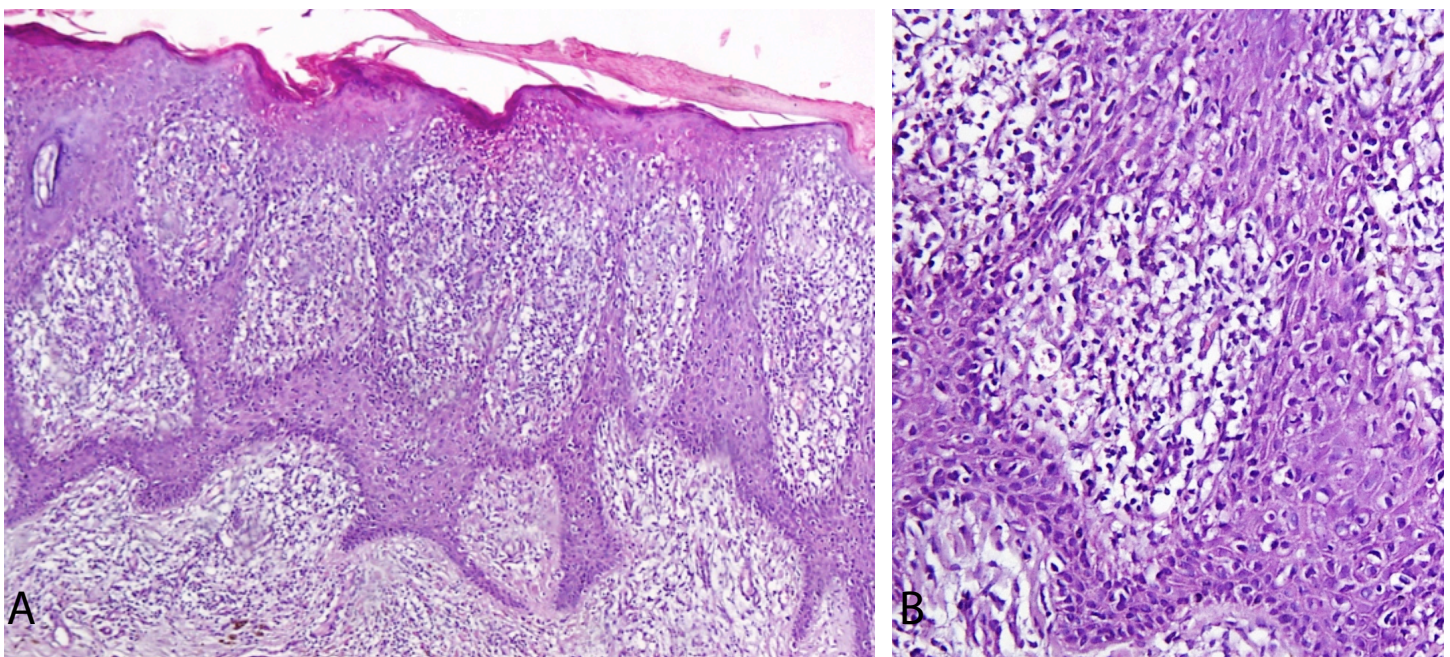


Figure 2. A) Marked psoriasiform hyperplasia with scant spongiosis and superficial dermal fibroplasia, (H&E, 10x). B) Intraepidermal atypical medium-sized lymphocytes with perinuclear halo and filled papillary dermis by dense lymphocytic infiltration, (H&E, 20x).

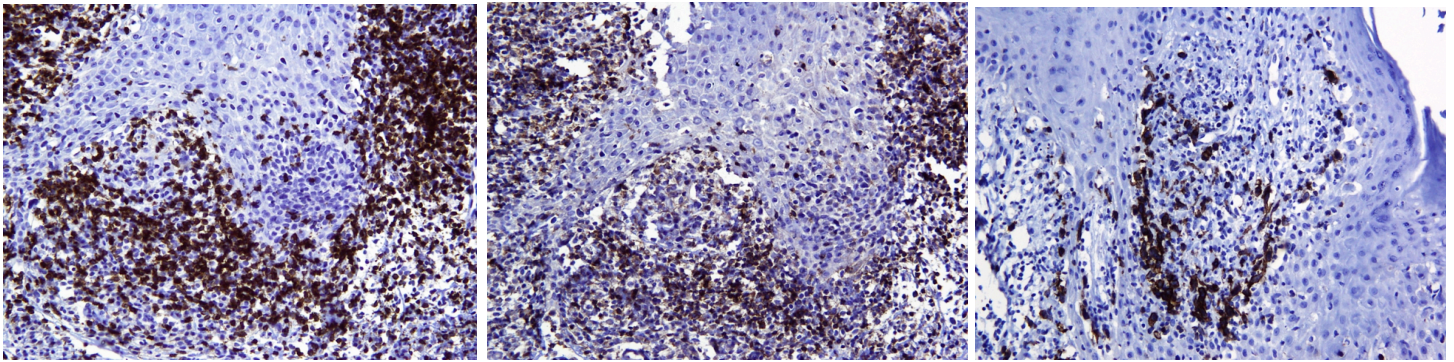


Figure 3. Immunohistochemical staining showed that the atypical lymphocytes were positive for CD30, 20x.

were smaller than the intraepidermal lymphocytes and associated with marked lamellar fibroplasia of the upper dermis (Figure. 2). Immunohistochemical (IHC) staining showed that atypical lymphocytes were positive for CD3, CD4, CD8, and CD5. Of note IHC showed that the upper dermal and intraepidermal large atypical lymphocytes were CD30 positive (Figure. 3). Complete blood count, metabolic panels, liver function tests, ESR, and lactate dehydrogenase were within normal ranges and whole-body computed tomography was normal. The clinicopathological findings were consistent with MF, patch and plaque, affecting more than 10 percent of body surface area (stage IB).

Considering the stage of MF in our patient (stage IB). For treatment, PUVA phototherapy plus systemic acitretin (25mg/d) was chosen, because other skin directed therapies for this stage of the disease like topical nitrogen mustard and total skin electron beam radiation were not available in our country. After three months of therapy the patient experienced significant improvement in her lesions but new lesions were still developing after two months of phototherapy.

Case Discussion

Herein we report a patient with MF that had exhibited psoriasiform plaques for 13 years before being seen in our department. She was misdiagnosed and treated as psoriasis for many years. During the last months she had experienced exacerbation in her lesions that were unresponsive to previous topical therapies. The clinicopathological findings and IHC were consistent with MF, and the CD30 positive atypical cells and new lesions still developing during treatment suggest a more aggressive behavior.

MF is a cutaneous lymphoma with a wide spectrum of clinicopathological presentations that are mainly nonspecific at onset. Because of the initial nonspecific cutaneous signs, distinguishing MF from various inflammatory dermatoses such as chronic eczema or atopic dermatitis may prove difficult [5]. Although MF presenting with psoriasiform plaques which mimic psoriasis is less common, differentiating MF from psoriasis is very important, especially when systemic immunosuppressive therapies for psoriasis are indicated. There are reports of deterioration and aggressive behavior of MF after starting immunosuppressive therapies such as cyclosporine and TNF inhibitors for cases misdiagnosed as psoriasis.

Herein, a brief review of these reports is given [3, 4, 6-8], (Table1). In 2002, Zackheim et al. reported a 52-year-old woman who was misdiagnosed to have severe psoriasis for 8 years and was treated with cyclosporine, which was followed by rapid development of an aggressive cutaneous T-cell lymphoma. The patient died of large cell lymphoma almost 1 year after cyclosporine therapy was started. The article concluded that distinguishing some cases of MF from psoriasis, both clinically and pathologically, can be difficult and conversion of MF to a highly aggressive lymphoma with fatal outcome after treatment with cyclosporine is possible [4]. In 2009, Lafaille et al. presented a 47-year-old man with recent progression of erythematous scaly plaques. The patient had been diagnosed 5 years previously as having psoriasis that had been treated by methotrexate (MTX) for a few years. The patient began treatment with etanercept, 50mg twice weekly for better control of the disease. Over the next few months he had a marked deterioration in his

Table 1. Clinical and immunohistochemical features of psoriasiform MF cases in this study, and previous studies.

| Study(year) | Case | Age (sexF/M) | Clinical presentation at the time of last visit | Ulceration (YES/NO) | Duration of skin disease treated as psoriasis(year or month) | Previous treatments | IHC | Outcome |
|-----------------------------------|------|--------------|--|---------------------|--|--|-------------|--|
| Zackheim et al. (2002) [4] | 1 | 52(F) | Palmoplantar desquamation Widespread erythematous patches and plaques | No | 9(y) | Topical steroids, calcipotriene, MTX, cyclosporine | N/A | Death due to highly aggressive large cell lymphoma |
| Lafaille et al. (2009) [3] | 2 | 47(M) | Generalized erythematous scaly plaques, alopecia, large ulcerating plaque on scalp | Yes | 5(y) | MTX, NBUV-B, PUVA, Etanercept | CD4+ Tcells | Final Dx: MF, Improved with a combination of NBUVB, IFN alfa-2b & bexarotene 2-year F/u: stable |
| Weenig et al. (2009) [6] | 3 | 52(M) | widespread ulceration with red, indurated borders | Yes | 20(y) | Topical steroids, acitretin, alefacept | CD2,3,5,7+ | finalDx:CTCL Thx:syst.CS+IFN alpha2a. Death due to multisystem organ failure |
| | 4 | 75(M) | generalized, indurated, and erythematous plaques. Many were ulcerated | Yes | 2(y) | Topical steroids, acitretin | CD3,5,7,8+ | Final DX:CTCL PUVA+Gemcitabine Death:sepsis |
| | 5 | 67(M) | Widespread ulceration | Yes | 20(y) | Topical CS, cyclosporine, MTX | CD2,3,5,7+ | Final Dx:CTCL Thx:Gemcitabine Death:MI |

| Study(year) | Case | Age (sexF/M) | Clinical presentation at the time of last visit | Ulceration (YES/NO) | Duration of skin disease treated as psoriasis(year or month) | Previous treatments | IHC | Outcome |
|----------------------------------|------|--------------|--|---------------------|--|--------------------------|---------------|---|
| Dakouki et al. (2009) [7] | 6 | 52(M) | Red-brown ulcerated tumors, indurated erythematous plaques with superficial erosion | Yes | 6(y) | Topical CS | CD3, 4+ | N/A |
| Jinno et al. (2015) [8] | 7 | 54(M) | erythema with pityroid scales, indurated, well demarcated erythema with thick scales | No | N/A | Topical CS, Cyclosporine | CD3,CD4+ | Final Dx:MF Thx: improvement with phototherapy+ topical CS |
| Our study | 8 | 46(F) | Well demarcated red-brown plaques with thick scale | No | 13(y) | Topical CS | CD3,4,5,8,30+ | Final Dx:MF Thx:marked improvement with PUVA+ acitretin |

skin lesions, including a progression of the plaques and alopecia. Large, ulcerating, infected plaques appeared on his scalp. Treatment with etanercept was stopped, biopsy and IHC were done, and the histopathological findings were in favor of MF with the presence of CD4-positive atypical T cells by IHC [3]. Also In 2009, Weenig et al. described 3 men with similar clinicopathological features (Table1). All had long duration (2-45 years) of indolent, chronic, generalized scaly dermatitis or psoriasis-like skin lesions who had undergone a rapidly progressive, ulcerative evolution. Histopathology showed a lichenoid tissue reaction pattern and IHCs were compatible with cutaneous T-cell lymphomas with aggressive behavior that led to death in all the patients. Weenig et al. cautioned about aggressive cytotoxic CTCL that should be in the differential diagnosis of patients who present with ulcerated plaques similar to psoriasis but atypical [6]. In 2009 Doukaki et al. reported an unusual case of MF (Table1) in a 52-year-old man who exhibited psoriasiform plaques on the palms and soles for 6 months. He rapidly developed additional ulcerated lesions on the scalp, limbs, and trunk. The biopsy and IHC were compatible with MF. The patient rapidly developed skin tumors and lymphadenopathy over a 2-month interval. They suggested skin biopsy in patients with presumed psoriasis before introducing systemic therapy to prevent the risk of T-cell lymphoma deterioration. In 2015, Jinno et al. reported a 54-year old man (**Table 1**) with erythematous lesions all over his body who had shown a poor response to topical steroids and cyclosporine. He had a biopsy based diagnosis of psoriasis. The patient had two types of lesions. Clinically, some lesions presented with erythematous plaques with fine scales and other lesions were indurated, well demarcated erythematous plaques with thick scales. Biopsy and IHC were both compatible with MF and the psoriasiform lesions gradually changed into MF [8]. In summary the psoriasiform MF cases reported have been mostly male, with a mean age of 54 years and a history of misdiagnosed psoriasis for a duration of 6 months to 45 years (average 13 years). Typically, the correct diagnosis was made when exacerbation and ulceration occurred. A summary of clinicopathological features of these cases are shown in **Table 1**.

Our patient with MF had an unusual presentation of thick, scaly, erythematous psoriasiform plaques that had been treated as psoriasis for many years, but her biopsy and IHC findings were compatible with MF. Her IHC was in favor of a more aggressive behavior type (CD30 positive). Also we reviewed previous cases of psoriasiform MF and they had common features such as long term cutaneous lesions mimicking psoriasis, recent exacerbation in their lesions, and deterioration induced by systemic immunosuppressive therapies. Many exacerbations showed ulcerated plaques, lichenoid infiltration histologically, and atypical CD4- and CD3-positive lymphocytes [3-8].

Conclusion

In conclusion special attention should be paid to psoriasiform MF. In probable cases of psoriasis that are unresponsive to conventional treatment, progressive, or ulcerative, biopsy should be considered. In atypical cases, in particular before starting a potent immunosuppressive agent, a biopsy for definitive diagnosis of psoriasis and ruling out MF is highly suggested.

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