Case Report
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Spiny Hyperkeratosis-Like Follicular Mycosis Fungoides: A Case Report

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Abstract

Folliculotropic mycosis fungoides (FMF) is a rare variant of cutaneous T-cell lymphoma which is categorized as a separate entity. In histopathology, malignant lymphocytes selectively surround and infiltrate hair follicles. FMF has different clinical features in comparison with classic MF which is more refractory to treatment and has a worse prognosis.

In the current study, we describe a 42-year-old patient presenting as follicular papules with keratotic spines and alopecia on the scalp, face, and trunk. Histologic examination of the patient's biopsy revealed follicular and perifollicular T lymphoid cell infiltration without follicular mucinosis. Clonality analysis was interpreted as CD4+ T cell lymphoproliferative disorder. With the final diagnosis of FMF, the patient underwent treatment with oral acitretin and topical corticosteroid and psoralen plus ultraviolet A (PUVA). This case, in addition to the accompanied review of literature, revealed the importance of considering FMF in spiny hyperkeratotic papules in seborrheic areas refractory to antifungal treatments.

Keywords: Mycosis fungoides, Follicular, Lymphoma, Lymphoid cell, Alopecia

Introduction

Mycosis fungoides (MF) represents the most common type of cutaneous T-cell lymphoma and accounts for ~50% of all primary cutaneous lymphomas. Apart from the classic type of MF, many clinical and/or histologic variants have been reported. Clinical variants, such as bullous and hyper- or hypopigmented MF, which have space behavior similar to that of classic MF, folliculotropic MF (FMF), pagetoid reticulosis, and granulomatous slack skin which have distinctive clinicopathologic features, have therefore been included as distinct subtypes of MF.[1] In this report, we describe a case of FMF presenting with an unusual manifestation.

Case Presentation

The ethics committee of Mashhad University of Medical Sciences approved this study (Ethics code: IR.MUMS.REC.1401.023). A 42-

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year-old Iranian man presented with a 10-month duration of patches with keratotic follicular papules, each of which had a keratotic spine. He complained of two patches with the mentioned features on the scalp (occipital part), nasolabial fold, and on his beard. These lesions were associated with moderate pruritus. During the appearance of the lesions, the patient was referred to two dermatologists and the lesions were treated as seborrheic dermatitis with topical azoles, but there were no changes in the lesions except for a slight improvement in pruritus. After six months, due to not receiving adequate response, he was referred to our clinic. He complained of additive involvement of his trunk with alopecia during the prior three months. In our examination, we discovered two alopetic plaques with an erythematous base, follicular papules, and keratotic spines on the occipital part of the scalp. Follicular spicules were found on his face with the preference on nasolabial folds, around the nose, beard, and eyebrows. Furthermore, few alopetic plaques on his chest and abdomen with follicular spicules and spines were found on precise examination (Figure 1). The lesions were asymptomatic except mild pruritus. Some of the lesions had follicular-based pustules and were complicated with superinfection. Therefore, topical clindamycin and oral cephalexin was prescribed empirically. On general physical examination, there was no lymphadenopathy or organomegaly. There was no history of drug ingestion or past medical history. The patient was obese and generally healthy.

The clinical differential diagnosis included follicular mucinosis, FMF, lichen spinulosus, and lichen planopilaris. To differentiate between the mentioned diagnoses, we planned to take two

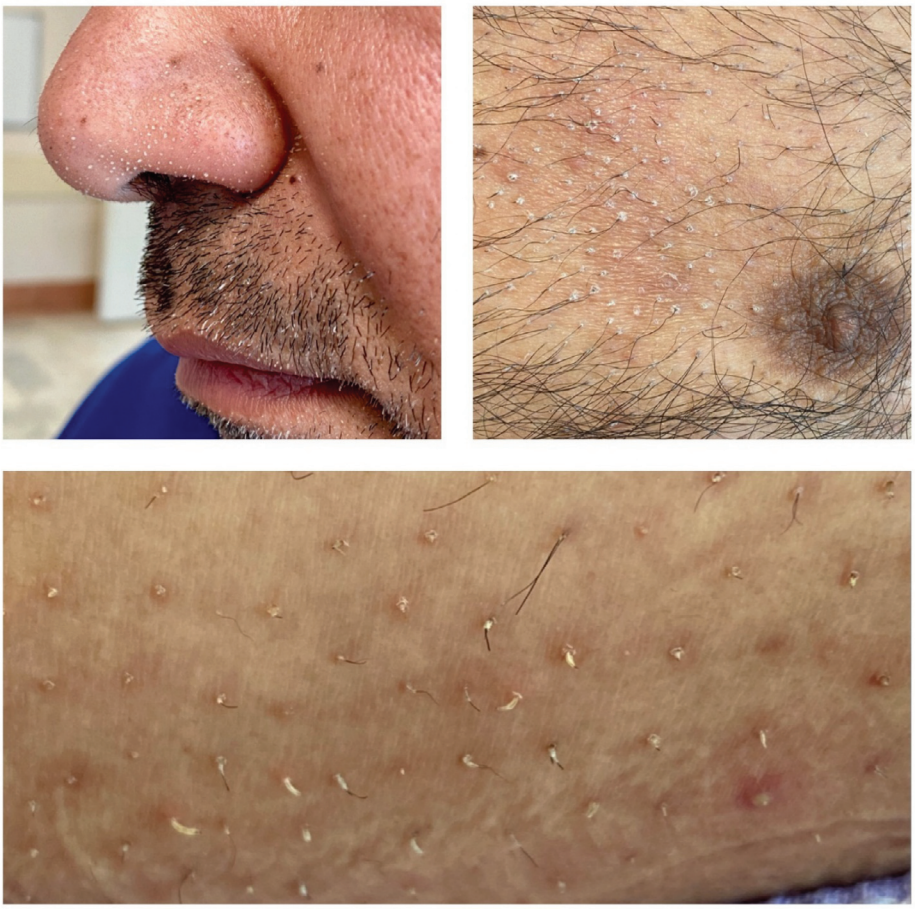

Figure 1. This figure shows the clinical examination and the lesions consisting of follicular papules with keratotic spines on face, scalp, lower abdomen, and chest.

skin biopsies from the patient's scalp and face.

Histopathology

On scalp biopsy, there was a superficial and deep dermal inflammation with follicular and perifollicular T lymphoid cell infiltration (Figure 2). Infiltration of lymphoid cells with mild atypia around vascular network and hair follicles with folliculotropism were seen. In immunohistochemical staining, the majority of lymphoidal cells were T cell CD3+, CD4+, and CD5+ and around the superficial and deep vascular network (Figures 3 and 4). Almost half of the dermal lymphoidal cells were CD7+ and the majority of them were CD7- within the hair follicles. Skin biopsy of the face showed infiltration of lymphoidal cells with mild atypia in the hair infundibulum, infiltration of lymphoidal cells, and fewer eosinophils in pilosebaceous follicles without follicular mucinosis and follicular hyperkeratotic spicules.

The pathologist recommended T-cell receptor (TCR) gene rearrangement analysis. PCR for clonalitity assessment of TCR (β and γ) genes was performed on both scalp and face biopsies. The analysis revealed clonal bands at TCR β and TCR γ chain genes, which was consistent with monoclonal T-cell proliferation. Eventually, morphologic and immunohistochemical studies and clonality analysis were interpreted as CD4+ T cell lymphoproliferative disorder and the final diagnosis of FMF was established.

In laboratory tests containing routine haematologic and biochemical tests, there was only borderline elevated fasting blood sugar and lipid profile. Further investigation, including complete blood count and peripheral blood smear, was normal. Sézary cells were absent. Initial staging and work-up included total-body computed tomographic scanning demonstrated no cervical, axillary, iliac, and inguinal lymphadenopathy. Chest radiography was normal. There was no extracutaneous involvement.

The patient underwent treatment with oral acitretin and topical corticosteroid (Momethasone). After two weeks for better control of the disease, three times weekly psoralen plus ultraviolet A (PUVA) was added to the treatment.

At 12-month follow-up, there was an improvement in the lesions and pruritus was diminished.

Discussion

FMF accounts for less than 4% of all cutaneous T-cell lymphoma cases.[2] FMF has been classified as a separate entity because it has distinctive clinical and histologic features, is more refractory to standard treatment, and has a worse prognosis than classic MF.[2]

FMF presents as a variety of cutaneous lesions, including plaques, erythematous papules, follicular keratotic papules, nodules, eczema-like and

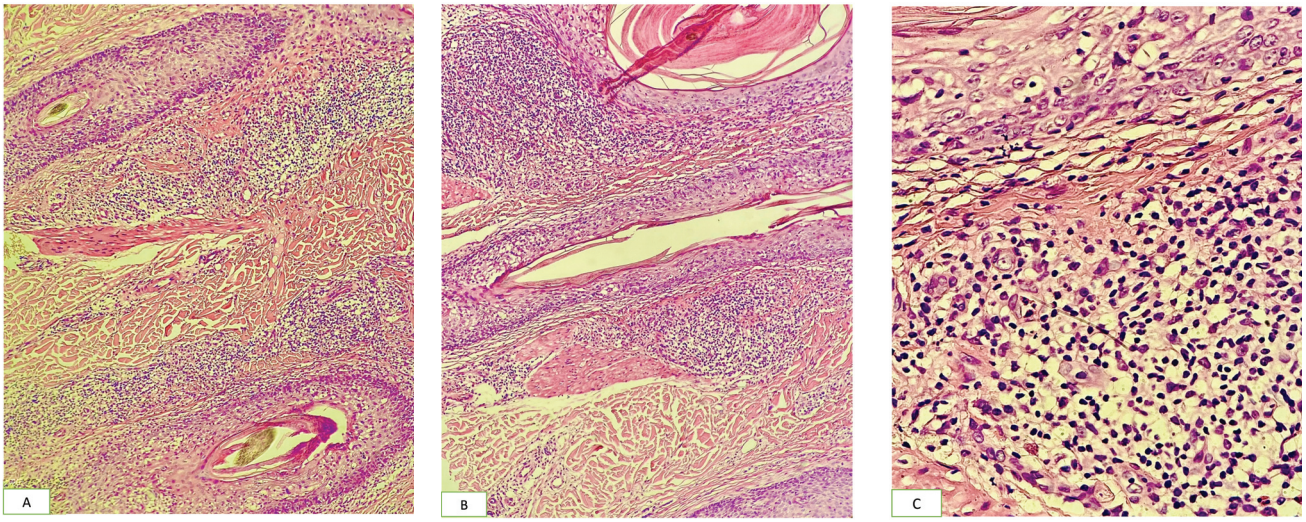

Figure 2. A, B. Histopathologic features with hematoxylin-eosin staining revealed superficial and deep dermal inflammation with follicular and perifollicular T lymphocyte infiltrations (×40, ×100); C. Lymphocytes in the hair infundibulum and pilosebaceous follicles are shown without follicular mucinosis (×400).

comedo-like lesions, cysts, and alopecia.[3] The most common areas of involvement are face, scalp, and upper trunk.[3]

In this case report, we demonstrated an interesting manifestation of spiny hyperkeratosis-like FMF which is not a routine presentation of this disease. The first presentation was with follicular spicules without background erythema on the patient's scalp, nasolabial fold, around the nose, eyebrows, and on the chest and abdomen. At first visits to a dermatologist, it was misdiagnosed as seborrheic dermatitis and did not respond completely to topical antifungals. After several months, the lesions progressed and were complicated with alopecia and superinfection. According to its persistency, associated alopecia, and follicular spicules, we considered further assessment and took biopsies to confirm the diagnosis as FMF.

There are limited FMF cases presenting as thorny spicules. Alopetic plaques with follicular papules and thorny spicules were reported in a single follicular mucinosis case.[4] Additionally, in another report, hyperkeratotic follicular papules similar to spiny lesions were diagnosed as pseudolymphoma of the FMF type secondary to lithium carbonate treatment.[5]

FMF's prognosis is worse than classic patch- or plaque-stage MF and is known to be similar to tumor-stage.[2, 6] However, in recent studies, patients presenting with only patches and/or follicular papules or with the acneiform pattern of lesions have had favorable prognoses.[7, 8] Independent risk factors for disease progression and/or poor survival are clinical stage, age at diagnosis, large cell transformation, and extensive secondary bacterial infection.[7]

In our mentioned case, immunophenotyping and TCR gene rearrangement analysis confirmed our diagnosis. In addition, assessment for hematologic and other organ involvements was performed. Routine hematologic tests, including complete blood count, serum chemistry panel, and computed tomography scans of the chest and abdomen, were normal and revealed no extra-cutaneous involvement.

In our patient's skin biopsies, follicular mucinosis was not detected. In FMF biopsies, mucinous degeneration of the hair follicles (follicular mucinosis) could be recognized, which are defined as MF-associated follicular mucinosis. This feature is detected in 50%-60% of biopsies in case series.[9, 10] In both cases with and without associated follicular mucinosis, the most relevant feature is the deep, follicular, and perifollicular localization of the neoplastic infiltrates, making them less accessible to skin-targeted therapies.[11] The presence of follicular mucinosis is independently associated with higher disease progression rate and MF-related mortality,[11] although another study has found a higher survival rate with extensive follicular mucinosis.[10]

Since FMF is known to be resistant to skin-targeted therapies even in the early-stages,[12] we treated our patient with topical corticosteroid, oral acitretin, and three times weekly PUVA. After a 12-month follow-up, there was a remarkable improvement in the lesions and the associated pruritus.

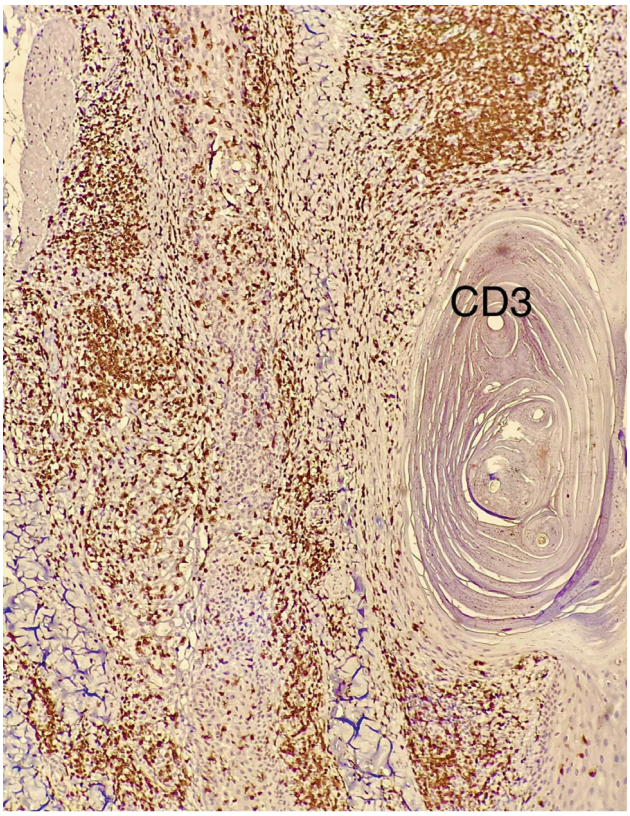

Figure 3. This figure shows the immunohistochemical staining illustrating CD3+ T lymphocytes within the perifollicular inflammatory infiltrate (×100).

Conclusion

In summary, the recognition of FMF may pose diagnostic challenges due to the variety of clinical and histopathological findings. Since the description of FMF, the presentation of keratotic spines as the only feature of FMF is somehow uncommon and misdiagnosed as follicular mucinosis or seborrheic dermatitis. An increased awareness and consideration of FMF will result in early diagnosis and treatment. Eventually, the presence of follicular papules with hyperkeratotic spines together with alopecia on seborrheic areas, which does not respond to antifungal agents, should increase the possibility of FMF.

Informed Consent

The patient signed the informed consent prior to the treatment.

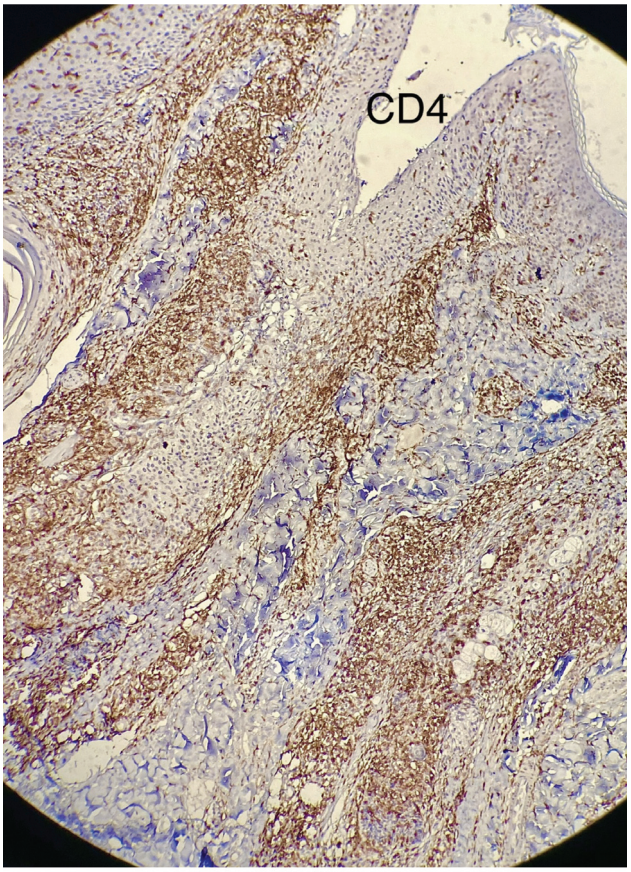

Figure 4. This figure shows the immunohistochemical staining demonstrating CD4+ T lymphocytes within the perifollicular inflammatory infiltrate (×100).

Conflict of Interest

None declared.

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