

Therapy Letters

Low-dose methotrexate combined with superficial X-ray in the treatment of folliculotropic mycosis fungoides: A case report

Sir,

According to the World Health Organization-European Organization for Research and Treatment of Cancer (WHO-EORTC), folliculotropic mycosis fungoides (FMF) is categorized as a variant of mycosis fungoides (MF) because of its distinctive clinicopathologic features.¹ Skin findings include grouped follicular or acneiform papules, such as clustered comedones, nodulocystic lesions, pustules, milia, as well as indurated plaques or tumors. Representative skin lesions typically involve the head and neck, especially the eyebrow, showing plaques and alopecia with severe pruritus.² Histopathologically, the follicular epithelium is infiltrated with atypical lymphocytes, with relative epidermal sparing.³ This variant is associated with a worse prognosis than classical mycosis fungoides because of its resistance to conventional therapies.⁴

A 51-year-old female was admitted to our outpatient department, with a 10-year history of erythematous papules and plaques associated with severe pruritus. Clinical examination revealed alopecia and erythematous, scaly papules, and plaques scattered on the head, neck, trunk, and extremities [Figures 1 and 2]. Alopecia only involved the scalp. Lesions of the head and neck showed infiltration and erosion [Figure 1]. There was no palpable lymphadenopathy or hepatosplenomegaly. Laboratory investigations such as blood count, urinalysis, biochemical profile, serum protein electrophoresis levels, and bone marrow aspiration

were all within normal limits. Imaging studies including chest X-ray, computed tomographic scan, and echocardiography were normal. Skin biopsy revealed intrafollicular or perifollicular infiltration of atypical lymphocytes with minimal epidermal involvement [Figure 3]. In addition, intrafollicular mucin deposits [Figure 4] were observed on Alcian blue stain [Figure 5]. The overlying epidermis showed focal epidermotropism, and few lymphocytes showed mild cytological atypia [Figure 6]. Immunohistochemically, the atypical lymphocytes were positive for CD2, CD3, CD4, CD7, and CD8, with a normal CD4:CD8 ratio, which favored T-cell proliferation. Staining for CD20, CD79a, CD30, and CD68 showed negative results. T-cell receptor



Figure 1: Erythematous papules and plaques, scales, and erosion involving the face and neck



Figure 2: Erythematous papules, plaques, and scales scattered on the trunk

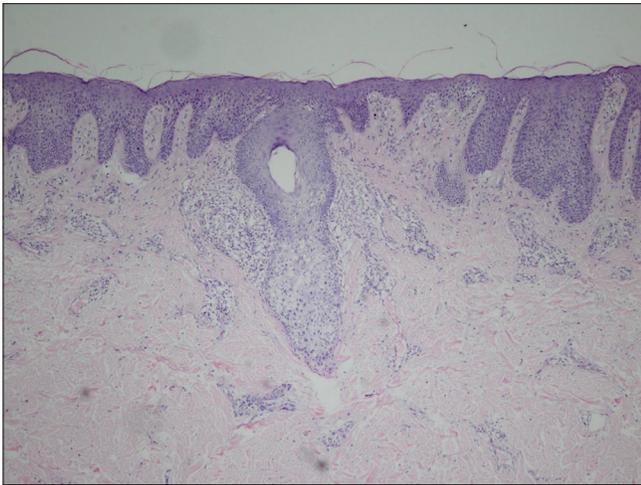


Figure 3: Intrafollicular and perifollicular infiltration with atypical lymphocytes and minimal epidermal involvement (H and E, ×100)

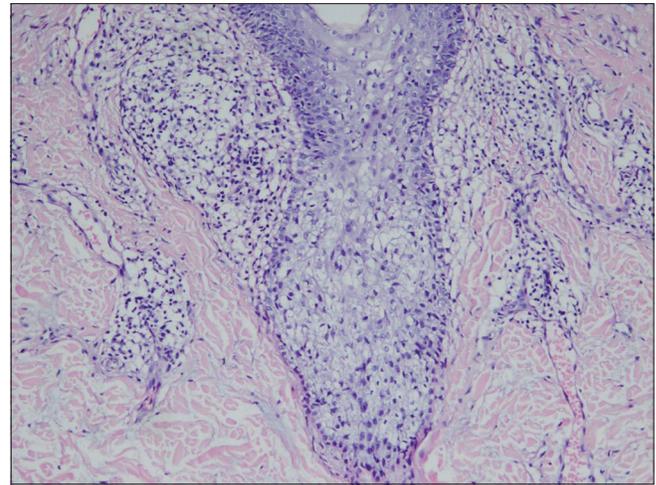


Figure 4: Follicular infiltration with mucin deposition (H and E, ×100)

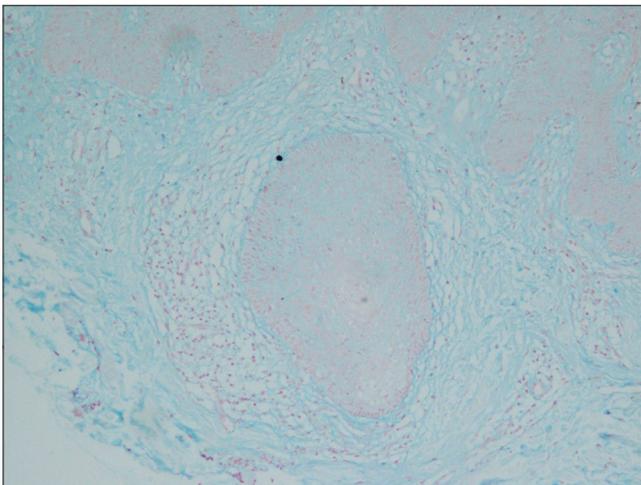


Figure 5: Alcian blue staining showing intrafollicular mucin (×200)

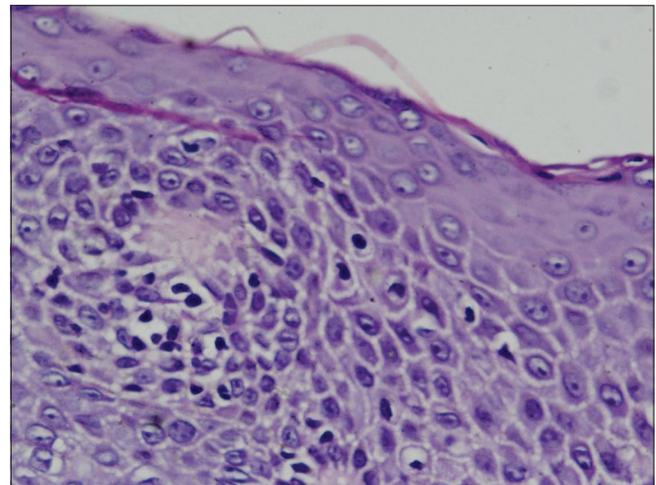


Figure 6: Epidermis showing focal epidermotropism and few lymphocytes showing mild cytological atypia (H and E, ×200)

gamma (TCR gamma) rearrangement confirmed a monoclonal proliferation of the atypical T lymphocytes. Considering the clinical and histopathological examination, diagnosis of stage IIA folliculotropic mycosis fungoides was made.

Initially, the patient was treated with interferon α -2b, isotretinoin, nitrogen mustard, and psoralen-UVA for 1 month, resulting in minimal improvement. Subsequently, methotrexate was added for 1 month, which resulted in an excellent response [Table 1]. The initial dose of methotrexate was 10 mg per week and the maximal dose was 15 mg per week. Most lesions on the trunk and extremities disappeared after these treatments. However, some persistent plaques remained on the head and neck. The patient was then treated with a combination of methotrexate 10 mg weekly plus superficial X-ray (100 kV, 400 cGy~500 cGy, a total dose of 40 Gy for 9 cycles) per week for 3 months [Table 2], which resulted in dramatic remission [Figure 7]. The patient continues to be in clinical remission after 10 months.

Folliculotropic mycosis fungoides, a distinct variant of mycosis fungoides, is characterized by the presence of folliculotropic

Therapy	Dose	Duration	Side effects
Interferon a-2b	300 IU 3 times/qw	2 weeks	Fever
Isotretinoin	10 mg BID-TID	5 months	Dry mouth
Methotrexate	10-15 mg qw	4 months	None
Nitrogen mustard	Local application 2 times/qd	All the time	None
Psoralen and ultraviolet A	3 times/qw	3 months	None

infiltrates, that often spare the epidermis and preferentially involve the head and neck area.¹ It is associated with a worse prognosis than classical mycosis fungoides, due to resistance to conventional therapies such as isotretinoin, methotrexate, PUVA, and interferon.⁴In our patient, most lesions responded well to conventional therapies, except for persistent lesions on the head and neck area. Agar *et al.*⁵ reported that a patient with



Figure 7: Lesions on the face and neck almost disappeared

Table 2: Treatment plan used from September 2015 November 2016

Month	1	2	3	4	5	6-15
Interferon a-2b	a					
Isotretinoin mg/day	30	20	*	*	*	b
Methotrexate mg/qw		10→15	10	*	*	c
Nitrogen mustard	d	*	*	*	*	*
Psoralen and ultraviolet A	e	*				
Superficial X-ray			f	*	*	g

*Treatment is the same as the previous month, ^aThree-million units three times a week. Because of fever, interferon a-2b was stopped after 2 weeks, ^bDuring the 10-month (6th-15th month) follow-up, isotretinoin was used intermittently, ^cDuring the 10 months (6th-15th month) follow-up, there was mild recurrence. MTX was used discontinuously, ^dNitrogen mustard (concentration: 0.02%): External application, ^ePsoralen-UVA: Three times a week, ^fSuperficial X-ray (100 kV,400-500 cGy) per week, ^gDuring the 10 months (6th-15thmonth) follow-up, superficial X-ray was used intermittently

localized thick plaques on the head, was treated successfully with superficial radiotherapy. Demirkesen *et al.*⁴ reported that patients with folliculotropic mycosis fungoides, who received more aggressive and combined treatments such as PUVA, methotrexate, interferon, and radiotherapy, achieved a higher survival rate. Kelly *et al.*⁶ reported that patients in stages I–III, who were treated with topical carmustine as monotherapy, with or without an added systemic agent demonstrated a high degree of response. In addition, a 16-year-old patient who presented with a single, firm, well-circumscribed erythematous infiltrated plaque over the forehead was successfully treated with local electron beam therapy.⁷ Since the persistent lesions were localized in our patient, we chose X-ray as an additional treatment. She showed dramatic remission—a fact which may help direct future treatment guidelines

of this condition. We were unable to find previous reports of the combination treatment of methotrexate with superficial X-ray in our literature search.

This regimen – methotrexate with superficial X-ray therapy – may be a new viable therapeutic option for recalcitrant mycosis fungoides, especially the folliculotropic variant.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that name and initial will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest

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