Clinical and Histopathological Spectrum of Mycosis Fungoides

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Background: Early diagnosis of mycosis fungoides is essential but difficult and can be easily missed because it mimics many inflammatory skin diseases both clinically and histopathologically.

Objective: To analyze the clinical and pathological features of mycosis fungoides.

Design: A Retrospective Study.

Setting: King Hussein Medical Center, Jordan University Hospital, Al-Karak Governmental Teaching Hospital.

Method: All patients diagnosed with mycosis fungoides from 2000 to 2015 were included in the study. The patients' clinical data were retrieved. The histopathological findings were interpreted by a dermatopathologist. Hematoxylin and Eosin routine stain was used for histopathological interpretation. Immunophenotyping stain was performed for few cases; T-cell rearrangement was not performed.

Result: Sixty-three patients diagnosed with mycosis fungoides were included in this study; 43 were males and 20 females. Male to female ratio was 2.15:1. Age ranged from 11-80 years; the mean age was 45 years. The lesions involved the trunk and proximal extremities in the majority of the cases. Different clinical variants of mycosis fungoides were seen in the patients: 25 (39.6%) classical mycosis fungoides, 7 (11%) hypopigmented mycosis fungoides, 2 (3.1%) hyperpigmented mycosis fungoides, 6 (9.5%) poikilodermatous mycosis fungoides, 1 (1.6%) folliculotropic mycosis fungoides, 1 (1.6%) erythrodermic mycosis fungoides, 1 (1.6%) ichthyosiform mycosis fungoides and 1 (1.6%) purpuric mycosis fungoides.

Conclusion: Mycosis fungoides can mimic different inflammatory skin diseases. However, early proper skin biopsy could be helpful for early diagnosis.

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Mycosis fungoides is the most common subtype of cutaneous T-cell lymphoma. It is characterized by the expansion of skin homing T-lymphocytes. It represents nearly 50% of all cutaneous lymphomas[1]. It is most commonly seen in the elderly, but it can also affect younger age groups[2]. Its clinical course is usually chronic, persistent with the progression of skin lesions from patches to plaques and in some cases tumors[1,3,4].

Mycosis fungoides is associated with a better prognosis compared to other types of cutaneous T-cell lymphoma. However, mycosis fungoides may progress to CD30– or CD30+ large cell lymphoma called transformed mycosis fungoides. The later condition is associated with an aggressive clinical course and poor survival[4,5].

Transformation occurs more frequently in advanced stages and is more common in tumoral lesions[6]. Therefore, early diagnosis is of paramount importance. Early diagnosis of mycosis fungoides is challenging and requires clinical and histopathological correlation.

The aim of this study is to evaluate the clinical and histopathological features of patients diagnosed with mycosis fungoides.

METHOD

Sixty-three patients diagnosed with mycosis fungoides from 2000 to 2015 were included in this retrospective study. Biopsies were taken by a dermatologist using either the punch or wedge biopsy methods. Their clinical data were retrieved and analyzed.

Histopathological features were interpreted by a dermatopathologist. Hemotoxylin and Eosin routine stain was used. Periodic acid–Schiff (PAS) stain was performed to rule out possible fungal infection. Immunophenotyping stains including CD4, CD8, CD3, CD7, and CD5 were performed for few cases. T-cell rearrangement was not available.

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RESULT

Sixty-three patients with mycosis fungoides were included in this study; 43 (68%) males and 20 (32%) females; male to female ratio was 2.15:1. Patient's age ranged from 11 years to 80 years with a mean age of 45 years, see tables 1, 2 and 3.

Table 1: Clinical Characteristics of the Cases in Our Study

Clinical Features	Number	%
Age at Diagnosis		
<40 years	31	49%
40-50 years	9	14%
>50 years	23	36.5%
Sex		
Male	43	68%
Female	20	32%
Site of Lesion		
Unexposed to the sun only	55	87%
Sun-exposed only	-	-
Both exposed and unexposed	63	100%
Symptoms		
Multiple Skin Rash	63	100%
Itching	40	63%
Duration before Diagnosis (range:2mon-10yr)		
<1 year	9	14%
>1 year	54	86%
Palmo Plantar Keratoderma	2	3%

Table 2: Histopathological Features

Feature	Number	%
Hyperkeratosis and/or parakeratosis	63	100%
Lymphocytic atypical	63	100%
Epidermotropism of atypical lymphocytes	46	73%
Disproportional spongiosis	63	100%
Haloed lymphocytes	45	71%
Pautrier's micro abscesses	27	43%
Lining up of atypical lymphocytes at the dermoepidermal junction	45	71%
Type of Inflammatory Infiltrate		
Band-like	33	52%
Superficial perivascular	21	33%
Diffuse	3	5%
Lichenoid	6	10%
Epidermal Reaction		
Psoriasiform	52	83%
Lichenoid	5	٪8
Hydropic degeneration	6	10%
Presence of eosinophils	20	32%
Follicular mucinosis	1	2%
Winey papillary dermal fibrosis	42	67%
*Loss of pan-T cell markers CD3 or CD5 or CD7	7	11%

*Note: was done on 7 cases only and this percentage does not represent the all cases.

Table 3: Clinical Variants of Mycosis Fungoides

Variant of Mycosis Fungoides	Number	%
Classical Mycosis Fungoides		
Patch stage	25	40%
Plaque stage	16	25%
Tumor stage	3	5%
Hypopigmented mycosis fungoides	7	11%
Poikilodermatous mycosis fungoides	6	10%
Hyperpigmented mycosis fungoides	2	3%
Erythrodermic mycosis fungoides	1	1.5%
Folliculotropic mycosis fungoides	1	1.5%
Ichthyosiform mycosis fungoides	1	1.5%
Purpuric mycosis fungoides	1	1.5%
Total	**63**	**100%**

Persistent scaly erythematous patches, plaques, and nodules were found in the classical mycosis fungoides, see figure 1; scaly erythematous ichthyosiform patches found in ichthyosiform mycosis fungoides; hyperpigmented patches found in hyperpigmented mycosis fungoides, see figure 2; scaly hypopigmented patches found in hypopigmented mycosis fungoides; scaly purpuric patches in purpuric mycosis fungoides and scaly poikilodermatous patches found in poikilodermatous mycosis fungoides.

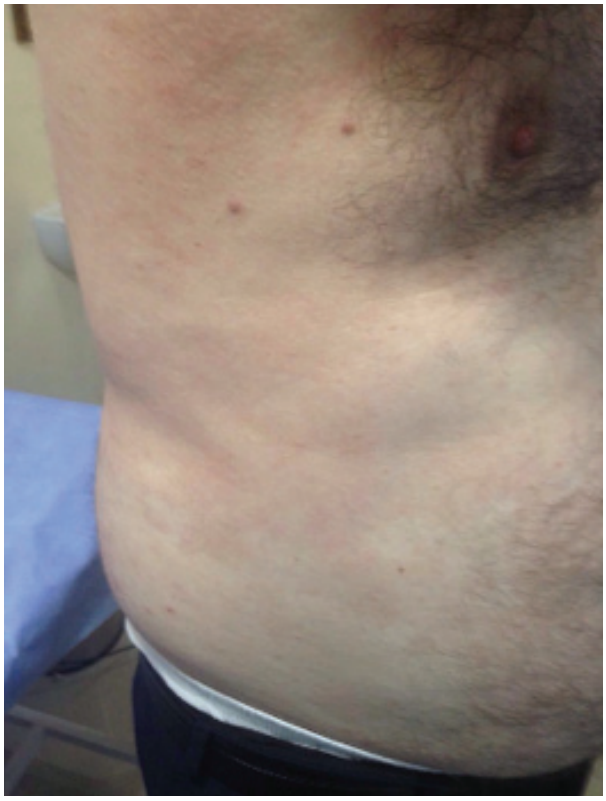

Figure 1: Persistent Irregular Scaly Erythematous Patches on the Trunk in a Patient with Patch Stage Mycosis Fungoides

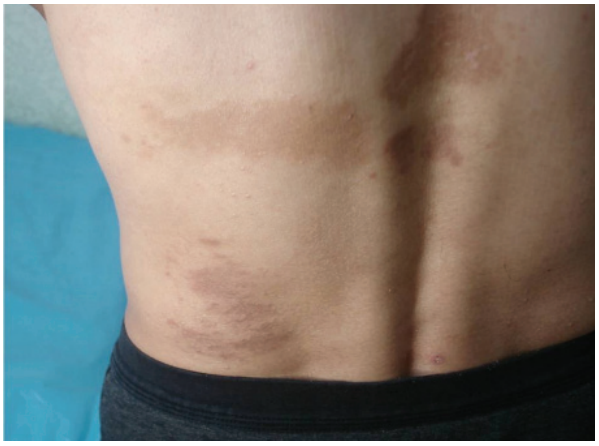

Figure 2: Persistent Hyperpigmented Patches of Variable Sizes on the Back of a Patient with Hyperpigmented Mycosis Fungoides

The patient with folliculotropic mycosis fungoides had nodules on the face, erythematous scaly asymmetrical persistent patches of different sizes and shapes on the trunk and palmoplantar keratoderma. Unexposed areas to the sun were affected in all cases (100%); while sun-exposed areas 9 (14%) cases were affected.

Combination of psoriasiform epidermal hyperplasia and band-like lymphocytic infiltrate in the same section on low power microscopic examination was present in 30 (47%) cases, see figure 3. At least one or more of the following histopathologic features were present in all cases: epidermotropism of a typical lymphocytes, see figure 4; atypical lymphocytes, haloed lymphocytes in the epidermis, see figure 4; alignment of atypical lymphocytes at the dermo-epidermal junction, see figure 5; combination of psoriasiform epidermal hyperplasia with band-like lymphocytic infiltrate and winey papillary dermal fibrosis or expanded papillary dermis, see figure 3.

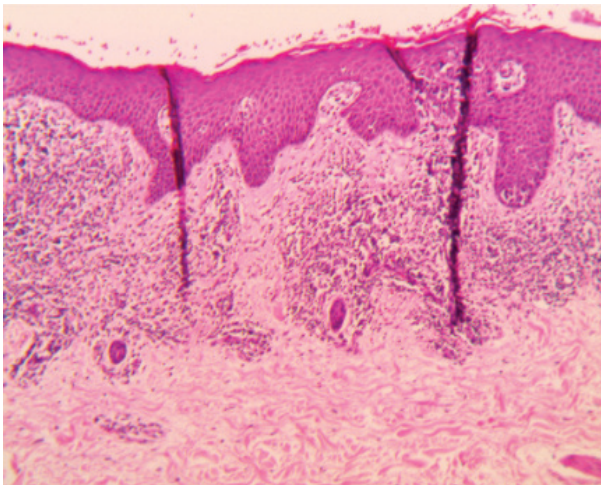

Figure 3: Psoriasiform Epidermal Hyperplasia, Band-Like Lymphoid Cell Inflammatory Cell Infiltrate and Expanded Papillary Dermis in a Patient with Mycosis Fungoides Patients

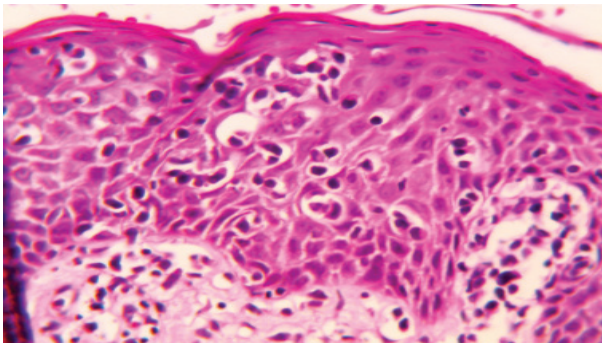

Figure 4: Epidermotropism of Atypical Lymphocytes, Haloed Lymphocytes and Pautrier's Microabscesses in a Patient with Mycosis Fungoides Patients

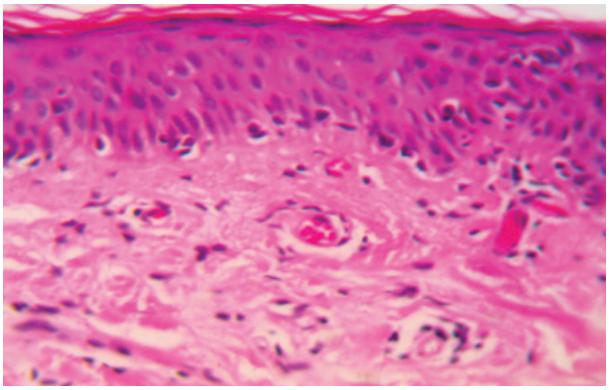

Figure 5: Alignment of Atypical Lymphocytes at the Dermoepidermal Junction in a Patient with Hypopigmented Mycosis Fungoides

T-cell markers CD4, CD5, CD3, and CD7 were performed for 7 (11%) cases where the lymphocytes in the epidermis were predominantly CD4 with loss of CD3 in one case, loss of CD7 in 4 (6%) cases and loss of CD5 in two cases. In one case of hypopigmented mycosis fungoides for which the immune markers were done, the cells in the epidermis were mainly CD8 positive, see figure 6.

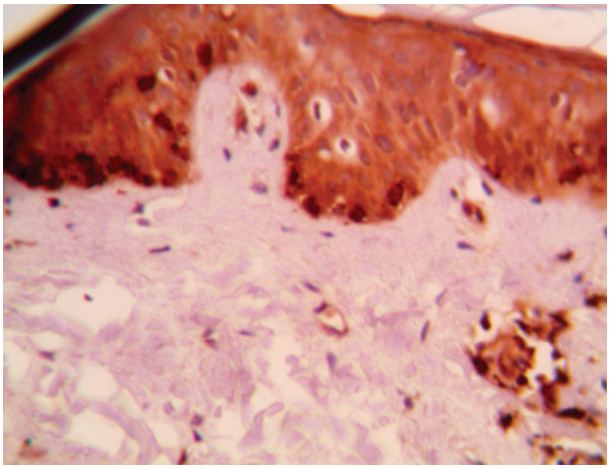

Figure 6: CD8 Positive Lymphocytes at the Dermoepidermal Junction and in the Epidermis in a Patient with Hypopigmented Mycosis Fungoides

DISCUSSION

Mycosis fungoides was first described in France by Alibert in 1806[7]. In the USA, the incidence rate of mycosis fungoides is 0.55 per 100,000 person–years[8]. The incidence of mycosis fungoides in Jordan is not known, and to the best of our knowledge, this is the first clinicopathological study of mycosis fungoides. Mycosis fungoides affects adult males and females; male to female ratio is 2:1. The male to female ratio in our study was 2.15:1 which is similar to other studies[8-11]. The mean age of the patients in our study was 45 years, and the majority of our patients were younger than 40 years[8,11-13].

The diagnosis of mycosis fungoides can be made based on clinical and pathological criteria[14-17]. The clinical criteria of mycosis fungoides include the presence of asymmetric, irregular, persistent erythematous lesions on sun-protected areas that are not improving or recurring after conventional treatment[17]. The immunopathological criteria includes: <50% CD2 positive, CD3 positive and/or CD5 positive T-cells; <10%CD positive T-cells and epidermal/dermal discordance of CD2, CD3, CD5 or CD7.

In our study, itching was present in 63% patients whereas in another study, it was 40.9%[13]. Histopathological features in our study are also consistent with the diagnostic histopathological features of mycosis fungoides[14,17]. Disproportional spongiosis was seen in all patients[14,15]. T-cell markers were done on a few cases in our study, and the findings were consistent with other studies[14,17,19] .

The histopathologic changes of hypopigmented mycosis fungoides and poikilodermatous mycosis fungoides cases in our study showed similar pattern to Khopkar et al[20]. Poikilodermatous mycosis fungoides revealed peculiar histopathological features including epidermal atrophy, vacuolar degeneration, pigmentary incontinence, and telangiectasia, in addition to mycosis fungoides like epidermotropism, lining up of atypical lymphocytes at the dermo-epidermal junction and dysproportional spongiosis. Hyperpigmentation may be the sole presentation, or it may coexist with other skin manifestation of mycosis fungoides[20-24].

In our study, patients with hyperpigmented mycosis fungoides had hyperpigmentation as the sole presentation, and the histopathological image revealed interface changes with melanophages. The histopathological changes in folliculotropic mycosis fungoides show perifollicular and intrafollicular infiltrate of atypical lymphocytes with or without follicular mucinosis and epidermotropism[25,26]. In this study, cases of folliculotropic mycosis fungoides revealed atypical intrafollicular and perifollicular atypical lymphocytes with follicular mucinosis and epidermotropism. In a study, follicular mycinosis in folliculotropic mycosis fungoides was reported in 44% to 96% of patients[25,26]. Patient with folliculotropic mycosis fungoides in this study had aggressive behavior, ichthyosiform mycosis fungoides and purpuric mycosis fungoides[27-29].

Because immunohistopathological testing has not been used for all pathology, the diagnosis of such condition might have been overestimated.

CONCLUSION

Early diagnosis of mycosis fungoides is possible if based on clinical criteria, histopthological, molecular biological and immunohistopathological features. Sixty-three patients were diagnosed with mycosis fungoides in our study.

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Competing Interest: None.

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