Original Article

Mycosis Fungoides in Children and Adolescents: A Clinicopathological Study in Jordan, Middle East

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Abstract

Background: Mycosis fungoides usually affects adults but rarely occurs in children and adolescents with a deceptive clinical picture that simulates more common skin diseases at this age; therefore, the diagnosis can be delayed. **Objective:** To determine the clinical and histopathological features in a group of patients who developed mycosis fungoides during childhood and adolescence to share experience and to highlight the early diagnosis of mycosis fungoides in this age group. **Materials and Methods:** A retrospective study was performed, and the clinical and histopathological data for all children and adolescent patients with confirmed mycosis fungoides diagnosis for the last five years were retrieved, reviewed, and analyzed. **Results:** Seven patients were diagnosed with mycosis fungoides with an age ranging from 5 to 17 (mean age, 10) years, comprising five males and two females patients, with a male-to-female ratio of 2.5:1. Three clinical variants of mycosis fungoides were present in our cases: hypopigmented mycosis fungoides in four patients (57%), poikilodermatous mycosis fungoides in two (29%), and classical mycosis fungoides in one (14%). No more than one variant of mycosis fungoides was observed in any patient. **Conclusion:** Although mycosis fungoides rarely occurs in children and adolescents, sufficient clinical and histopathological features are required to make the diagnosis. Therefore, it should always be considered in our clinical differential diagnosis in any appropriate clinical setting. A skin biopsy should not be delayed. **Study Design:** Retrospective study.

Keywords: Adolescents, children, clinicopathological, mycosis fungoides

Introduction

Mycosis fungoides is the most common subtype of primary T-cell cutaneous lymphoma usually affecting older adults with an incidence of 5.6 per million people with male predominance.[1,2] Primary cutaneous T-cell lymphoma and mycosis fungoides rarely occur in children and adolescents, but the latter is the most common clinical presentation of the former in this age group.[3] The incidence of mycosis fungoides in children and adolescents varies in different geographical areas, with a higher incidence in Asia than in Western countries, according to different studies.[4-6] In this study, we will add and share our experiences to add more spotlight to this important subject. The clinical and histopathological features of our cases are presented and analyzed.

Materials and Methods

This was a retrospective study. All patients younger than 18 years with a confirmed diagnosis of mycosis fungoides during our practice at Jordan University Hospital in Amman, Jordan, Al-Karak Governmental Hospital in Al-Karak, Jordan, and our private practice in Amman, Jordan, for the last five years from 2016 to 2021 were included in our study. The clinical and pathological data of all patients diagnosed with mycosis fungoides were retrieved, reviewed, and analyzed. The diagnosis of mycosis fungoides was made according to the International Society for Cutaneous Lymphomas – European Organization of Research and Treatment of Cancer criteria[7] with clinicopathological correlation. Skin biopsies of all patients were interpreted by a dermatopathologist. Due to the presence of sufficient

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diagnostic criteria for the diagnosis of mycosis fungoides based on unequivocal histopathological findings of the skin biopsy and clinical findings (the presence of more than two clinical criteria) in all our cases, T-cell markers CD4, CD8, CD5, and CD7 were evaluated in only a few cases (three cases with hypopigmented mycosis fungoides and one case with classical mycosis fungoides). A clonal T-cell receptor gene rearrangement analysis was not performed.

Results

A total of seven patients aged <18 years were diagnosed with mycosis fungoides from 2016 to 2021, with ages ranging from 5 to 17 (mean age 10) years, comprising five men and two women with a male-to-female ratio of 2.5: 1. Three variants of mycosis fungoides were present in our study: hypopigmented mycosis fungoides (four patients), accounting for 57% of our cases [Figure 1]; poikilodermatous mycosis fungoides (two patients) [Figure 2], and classical mycosis fungoides (one patient) [Figure 3]. No more than one variant of mycosis fungoides was observed in any of our cases. The mean time before diagnosis was 17 months. All our cases were in the early stages of the disease at the time of diagnosis, Stage IA and Stage IB according to physical examination and imaging studies. [Table 1] shows the clinical characteristics of our patients.

All cases showed unequivocal diagnostic histopathological features, including lymphocytic atypia, epidermotropism, haloed lymphocytes, disproportional spongiosis, and lymphocytic infiltrate, which were superficial perivascular in most cases with hypopigmented mycosis fungoides [Figure 4]; lichenoid with interface changes in cases with poikilodermatous mycosis fungoides [Figure 5]; and band-like features in the case of classical mycosis fungoides [Figure 6]. In a few cases, T-cell markers were used. The CD-8 phenotype was predominant in all three cases with hypopigmented mycosis fungoides with loss of pan-T-cell markers CD5 and CD7. The CD4 phenotype was predominant in classical mycosis fungoides. [Table 2] shows the histopathological features of all patients.

Discussion

Several reports of mycosis fungoides in children and adolescents have been published in the literature, indicating that mycosis fungoides is not rare in this age as it was previously thought.[8] Mycosis fungoides in children and adolescents account for approximately 4%–5% of cases of mycosis fungoides in the United States.[9] A higher prevalence

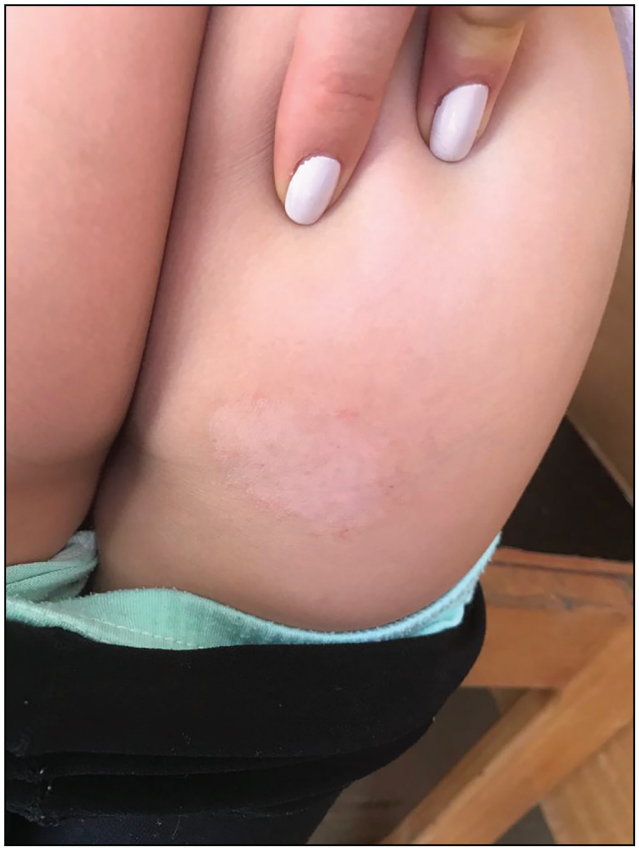

Figure 1: Hypopigmented patch on the buttock of a five-years-old female patient with hypopigmented mycosis fungoides

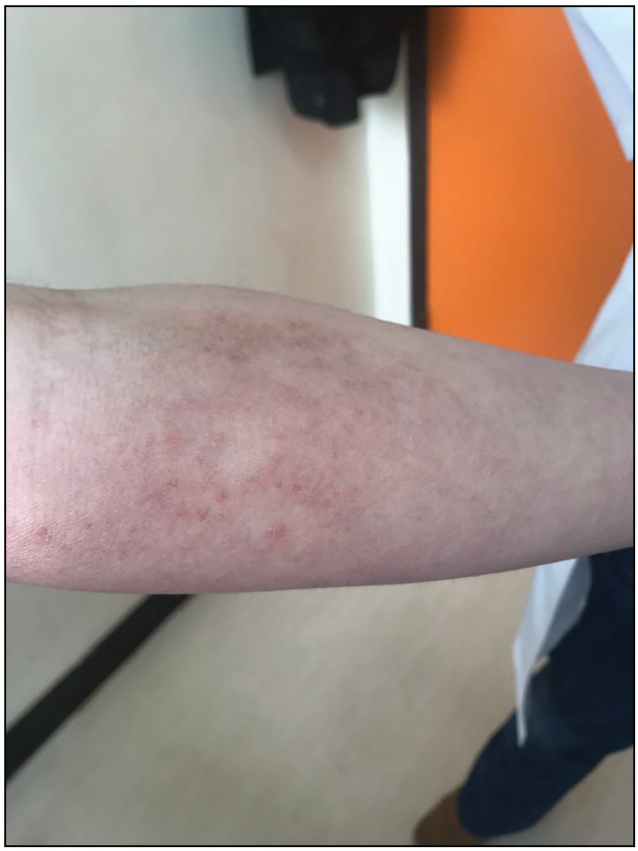

Figure 2: Poikilodermatous patch on the forearm of a 14-years-old female with poikilodermatous mycosis fungoides

of mycosis fungoides in this age group has been reported in Asia, with 16.6% of patients with mycosis fungoidesin children and adolescents in Kuwait,[5] and 11% of patients with mycosis fungoides were children and adolescents in Singapore.[10] In Jordan, we do not have scientific statistics about the prevalence of mycosis fungoides in this age group, and we cannot determine its prevalence based on this study alone, but based on the total number of all cases of mycosis fungoides that we have seen during the period of this study, cases of mycosis fungoides in children and adolescents represent around 14% of them which is similar that in Asia.[5,10] The clinical presentation of mycosis fungoides in this age group can be similar to that of different inflammatory dermatoses, such as eczema, vitiligo, pityriasis alba, and fungal infections. In our study, the initial clinical diagnosis was eczema in three patients, vitiligo in two, and hypopigmented mycosis fungoides in addition to pityriasis alba and tinea versicolor included in the clinical differential diagnosis in the other three. These clinical presentations concur with those of other studies.[4,11] Because physicians sometimes avoid skin biopsies in children, the diagnosis can be delayed. The mean time before diagnosis was 17 months. Due to the increasing awareness of hypopigmented mycosis fungoides, it was recently presented in the clinical differential diagnosis in three of our cases. Hypopigmented mycosis fungoides is the predominant variant of mycosis fungoides in our cases, which concurs with that of other studies.[4-6,8,11,12] The hypopigmented and poikilodermatous variants of mycosis fungoides were often found in children and adolescents,[8] and a similar finding was observed in our cases [Table 3]. In our study, a male predominance was observed, which was also documented in other studies.[6,8,11] All our cases were in the early disease stages at the time of diagnosis (Stage IA and Stage IB, which were also consistent with those in other studies).[4,6,8,13,14]

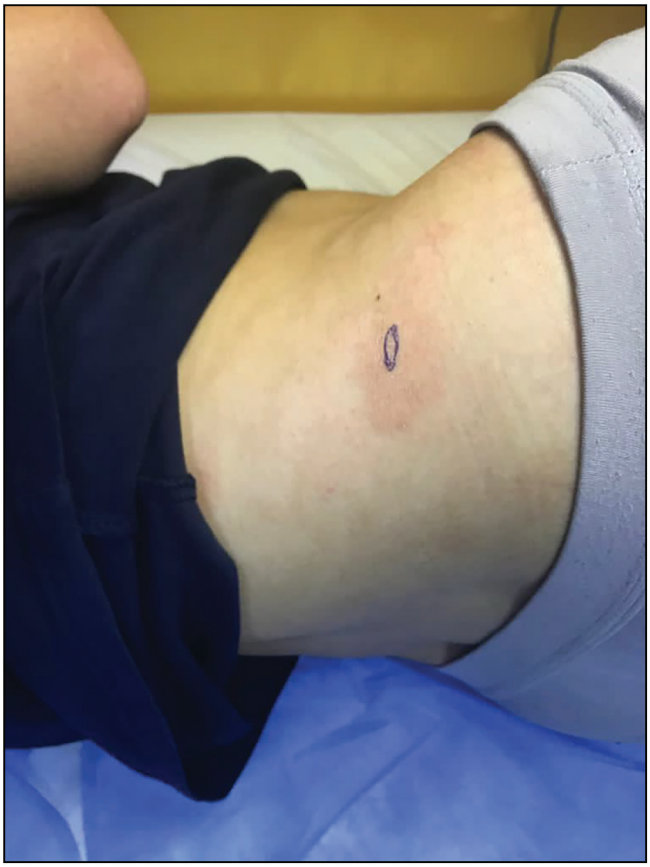

Figure 3: Erythematous scaly patch over the trunk in a 17-years-old male with classical mycosis fungoides

Routine histopathological findings of lymphocytic atypia, epidermotropism, haloed lymphocytes, and disproportional spongiosis were present in all cases

Table 1: Clinical characteristics of patients in the study

Patient no.	Sex	Age	Site	Skin lesions	Time of diagnosis	Symptoms	Clinical diagnosis| differential diagnosis	Stage
1	Male	8 years	Trunk and proximal extremities	Depigmented and hypopigmented patches, ill-defined	6 months	Asymptomatic	1.Vitiligo 2.Hypopigmented mycosis fungoides 3.Pityriasis alba	IB
2	Male	5 years	Trunk and face	Depigmented ill-defined patches	5 months	Asymptomatic	Vitiligo	IA
3	Female	5 years	Trunk and proximal extremities	Depigmented patches ill-defined with peripheral telangiectasia at some lesions	6 months	Asymptomatic	1.Vitiligo 2.Postinflammatory hypopigmentation	IA
4	Female	14 years	Forearm and thigh	Poikilodermatous scaly patches	1 year	Itching	Atopic eczema	IA
5	Male	13 years	Trunk and extremities	Poikilodermatous scaly patches	5 years	Itching	Atopic eczema	IB
6	Male	8 years	Trunk and proximal extremities	Hypopigmented scaly patches ill-defined	6 months	Mild itching	1.Pityriasis alba 2.Tinea versicolor 3.Hypopigmented mycosis fungoides	IB
7	Male	17 years	Trunk and extremities	Erythematous scaly patches and plaques	2 years	Itching	Eczema	IB

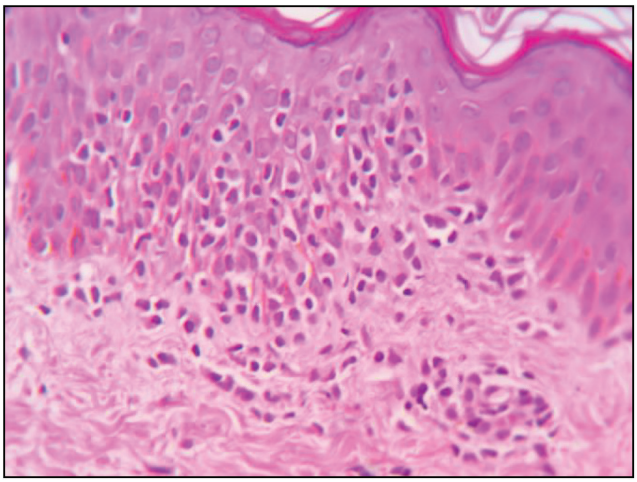

Figure 4: Hypopigmented mycosis fungoides: Mild superficial perivascular lymphoid cell infiltrate with prominent epidermotropism of a typical lymphocyte, haloed lymphocyte, and disproportional spongoisis (HE x400).

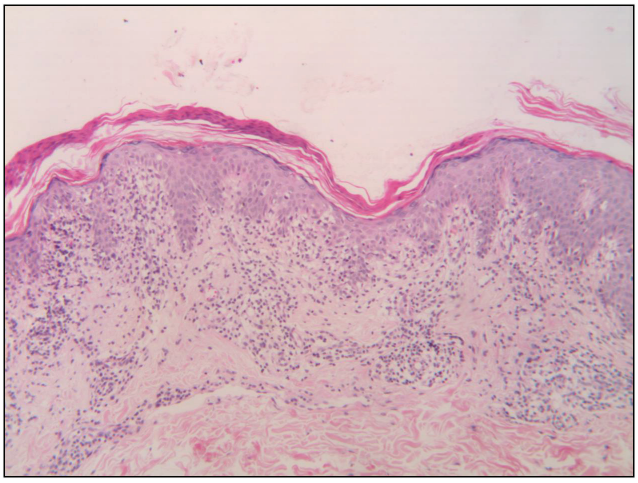

Figure 6: Classical mycosis fungoidis: Parakeratosis, hyperkeratosis, epidermal hyperplasia, epidermotropism of atypical lymphocytes, disproportional spongoisis, band like lymphoid cell infiltrate, and papillary dermal fibrosis (HE x100).

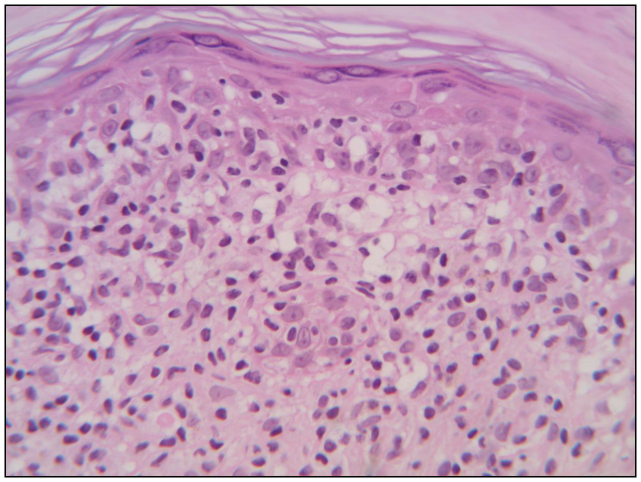

Figure 5: Piokilodermatus mycosis fungoides: Hperkeratosis, epidermal atrophy, lichenoid lymphocytic inflammatory infiltrate, vacuolar changes epidermotropism of atypical lymphocytes, haloed lymphocyte, disproportional spongiosis, and lining up of atypical lymphocytes at the dermo epidermal junction (HE x400).

[Table 2], similar histopathological findings have been reported.[6,12,15] Recent studies have shown that the predominant T-cell phenotype in hypopigmented mycosis fungoides is commonly CD8.[16] Our cases with hypopigmented mycosis fungoides also showed a predominant CD8 T-cell phenotype. Loss of T-cell markers CD3, CD5, and CD7 is considered a helpful diagnostic immunopathologic feature to diagnose mycosis fungoides.[17] In all four cases in which these T-cell markers were performed, at least one of these markers was lost.

Table 2: Histopathological features of patients in the study

Feature	Number of patients	Percent (%)
Disproportional spongiosis	7	100
Lymphocytic atypia	7	100
Epidermotropism without spongiosis	7	100
Haloed lymphocytes	7	100
Pautrier's microabscesses	2	29
Atypical lymphocytes lining up at the dermo-epidermal junction	4	57
Papillary dermal fibrosis	3	43
Dermal infiltrate:		
-Lichenoid	2	29
-Superficial perivascular	2	29
-Band like	3	43
Vacuolar interface	2	29
Predominant T-cell phenotype*		
-CD 4	1	25
-CD8	3	75
Loss of pan: T-cell marker CD5 or CD7**	4	100

* Was done on four cases only

**Was done on four cases only

Table 3: Mycosis fungoides variants in the study *n* = 7 (100%)

Mycosis fungoides variant	Number\ Percentage
Hypopigmented mycosis fungoides	4\57%
Poikilodermatous mycosis fungoides	2\29%
Classical mycosis fungoides	1\14%

Conclusion

Mycosis fungoides is not as rare as it was thought to be. Therefore, it must be considered as a differential diagnosis in children and adolescents. We should not hesitate to perform a skin biopsy if clinical suspicion exists. Clinical, histopathological, and immunopathological features

should be determined for the early diagnosis of mycosis fungoides.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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