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Mycosis fungoides in a Mexican pediatric series: Clinical, immunophenotypic, and therapeutic features

Micosis fungoide en una serie pediátrica mexicana: características clínicas, inmunofenotípicas y terapéuticas

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Abstract

Background: Mycosis fungoides (MF) is a primary cutaneous lymphoma that in pediatric patients is frequently misdiagnosed as a benign dermatosis. Studies in Mexican children are limited.
Objective: To describe the clinical, immunophenotypic, and therapeutic characteristics of MF in a Mexican pediatric series.
Material and methods: It was conducted a cross-sectional study between 2017-2025 at a hospital in Mexico City, which included 17 pediatric patients younger than 18 years of both sexes with a diagnosis of MF.
Results: They were 13 males and 4 females, with a mean age at diagnosis of 11.9 ± 2.8 years and a median disease duration of 3 years; 52.9% of patients were referred with a diagnosis of atopic dermatitis. The most frequent clinical variant was hypopigmented (64.7%). All cases were classified as stage IB. Diagnosis required a median of 2 biopsies, with delays of up to 12 months (range 3-24). All cases showed epidermotropism with CD3 and CD4 positivity (100%), and 88.2% showed CD8 positivity. All patients received topical corticosteroids; 3 received phototherapy, 3 methotrexate, and 3 photopheresis. The classic form of MF was associated with the presence of erythematous patches and erythematous scaly plaques, as well as, in some cases, with the use of methotrexate and phototherapy.
Conclusions: Pediatric MF poses a diagnostic challenge due to its clinical similarity to common dermatoses. Although prognosis is generally favorable, its recurrence requires prolonged follow-up.

Resumen

Introducción: la micosis fungoide (MF) es un linfoma cutáneo primario que en pacientes pediátricos con frecuencia se confunde con dermatosis benignas. Los estudios en niños mexicanos son limitados.
Objetivo: describir las características clínicas, inmunofenotípicas y terapéuticas de la MF en una serie pediátrica mexicana.
Material y métodos: se llevó a cabo un estudio transversal en un hospital de la Ciudad de México entre 2017 y 2025, el cual incluyó 17 casos pediátricos menores de 18 años de ambos sexos con diagnóstico de MF.
Resultados: fueron 13 hombres y 4 mujeres, con edad media al diagnóstico de 11.9 ± 2.8 años y mediana de evolución de 3 años; el 52.9% fue referido con el diagnóstico de dermatitis atópica. La variedad más frecuente fue hipopigmentada (64.7%). Todos los casos se clasificaron en estadio IB. El diagnóstico requirió una mediana de 2 biopsias, con retraso en la toma de hasta 12 meses (rango 3-24). Todos los casos mostraron epidermotropismo con positividad para CD3 y CD4 (100%), y el 88.2% positividad para CD8. Todos los pacientes recibieron esteroides tópicos; 3 casos recibieron fototerapia, 3 metotrexato y 3 fotoféresis. La forma clásica de la MF se asoció con la presencia de manchas eritematosas y placas eritematoescamosas, así como, en algunos casos, con el uso de metotrexato y fototerapia.
Conclusiones: la MF pediátrica constituye un desafío diagnóstico por su similitud con dermatosis comunes; aunque el pronóstico es generalmente favorable, su alta recurrencia requiere un seguimiento prolongado.

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Background

Primary cutaneous lymphomas are malignant lymphoproliferative neoplasms that initially appear in the skin and, in most cases, show no extracutaneous involvement at the time of diagnosis. These neoplasms derive from 2 main cell lineages: T cells and B cells.[1,2] Within this group, cutaneous T-cell lymphomas (CTCL) are rare entities characterized by the proliferation and accumulation of malignant T lymphocytes in the skin, and represent a heterogeneous group of lymphomas ranging from indolent forms, such as mycosis fungoides (MF) and CD30+ lymphoproliferative disorders, to more aggressive subtypes such as Sézary syndrome and primary cutaneous peripheral T-cell lymphomas.[3,4]

Mycosis fungoides is the most common primary cutaneous lymphoma in the pediatric population. Its indolent course usually causes symptoms to appear in childhood, although diagnosis may be delayed until adulthood. The disease typically begins between 6 and 8 years of age, but the average age at diagnosis is between 9 and 11 years; it is uncommon in infants and preschool children. During childhood, the male-to-female ratio is similar.[5]

Clinically, MF has a classic clinical presentation that is characterized by slow progression through 3 stages: macules or patches, infiltrated plaques, and tumors, which may present sequentially, coexist, or appear non-sequentially. *Patches* are flat, erythematous or hypopigmented lesions with superficial scaling and variable size, which may be localized or generalized, predominantly affecting sun-protected areas. Unlike adults, children with MF often present with non-classical clinical forms, including hypopigmented, hyperpigmented, folliculotropic, and poikilodermatous variants, and in some cases, multiple clinical presentations coexist at the time of diagnosis. Hypopigmented MF has been described as the most common clinical presentation in the pediatric population. This clinical form can be confused with various non-neoplastic dermatoses, such as post-inflammatory lesions of atopic dermatitis (AD), psoriasis, pityriasis lichenoides chronica, pityriasis alba, eczema, and vitiligo.[6,7]

The diagnosis of MF cannot be established on the basis of clinical findings alone; therefore, skin biopsy is essential for comprehensive histopathological and immunohistochemical evaluation. In the presence of more than 2 lesions, multiple biopsies should be considered, and longitudinal follow-up with repeat biopsies is recommended when a false-negative result is suspected.[8] Histopathologically, it is characterized by an epidermotropic lymphoid infiltrate composed primarily of T-helper lymphocytes (CD3+, CD4+, CD8−); however, in some pediatric cases, more cytotoxic phenotypes (CD8+) may be observed, which are associated with a more indolent clinical course.[9,10] Because the condition may closely resemble other inflammatory disorders in its early stages, repeated skin biopsies may be required in selected treatment-resistant cases to establish a definitive diagnosis.

Although differences in the presentation of MF between children and adults have been recognized in recent years, studies in the pediatric population remain limited, and are even scarcer in Mexico, where most are descriptive and few deliberately explore clinical associations. In this context, the present study aims to characterize the clinical-epidemiological and immunophenotypic features of MF in a Mexican pediatric series, with the goal of facilitating early recognition and describing the local therapeutic approach.

Material and methods

Study type and location

A retrospective observational case series with an analytical component was conducted at the high specialty medical unit (UMAE according to its initials in Spanish) General Hospital “Dr. Gaudencio González Garza”, from the National Medical Center La Raza, in Mexico City, from January 2017 to January 2025. The study was carried out in accordance with the principles of the Declaration of Helsinki, the Belmont Report, and the General Health Law on health research.[11,12] Ethical approval was obtained from the institution’s Research and Ethics Committee (registration number R-2025-3502-096).

Protocol

Electronic medical records of patients with histopathologically confirmed MF were selected for inclusion. Cases included both sexes under 18 years of age, regardless of the presence of comorbidities. Records lacking histopathological confirmation or with incomplete clinical information were excluded. Epidemiological and clinical data were collected, including the following variables: sex, age, nutritional status, underlying diseases or comorbidities, disease duration, family history of cancer, referral diagnosis, type of skin lesion, associated symptoms, lesion topography, disease stage, clinical variant, skin biopsy (number and timing), histopathological features, immunohistochemistry (CD3, CD4, CD8, CD45, CD7, Ki67), baseline lactate dehydrogenase levels, and type of treatment. Data were recorded using a standardized data collection instrument and obtained by a pediatrician and a pediatric dermatologist.

Statistical analysis

Given the low frequency of the disease, all MF cases meeting the inclusion criteria were enrolled, without a prior sample size calculation, using a non-probabilistic, non-random sampling method.

The Shapiro-Wilk test was used to assess the normality of the data. Variables with a normal distribution were expressed as means and standard deviations, while non-normally distributed variables were reported as medians and interquartile ranges. Nominal variables were summarized using frequencies and percentages. For inferential analysis, the Student's *t* test was applied for comparing means, the Mann-Whitney *U* test for medians, and Pearson's chi-squared test or Fisher's exact test for categorical variables. Statistical analyses were performed using IBM SPSS, version 27, with a 2-sided p value < 0.05 considered statistically significant.

Results

A total of 29 cases were initially diagnosed with clinical suspicion of MF. However, histopathological analysis confirmed MF in 17 patients, while 12 patients did not receive this final diagnosis. Among these, 5 cases were diagnosed with Pityriasis lichenoides chronica, 2 with AD, 1 with vitiligo, and 4 cases showed only histopathological findings without a definitive diagnosis. In these 4 cases, immunohistochemical findings, along with histological descriptions, ruled out malignancy but did not provide a specific diagnosis. In total, 17 pediatric patients with a confirmed diagnosis of MF, who met the inclusion criteria, were included, out of whom 13 were male (76.5%) and 4 female (23.5%). All cases were of mestizo origin. Baseline characteristics of the population are presented in Table I. The mean age at diagnosis was 11.9 ± 2.8 years, and the median disease duration was 3 years (interquartile range 2-4.5 years). More than half of the patients were referred to the unit with a suspected diagnosis of AD. Only 3 patients had a family history of neoplasms, including 1 case of breast cancer, 1 of colon cancer, and 1 of cervical cancer.

Table II summarizes the clinical characteristics of MF in the pediatric population studied. The hypopigmented variant was the most common presentation (Figure 1), and pruritus was documented as an associated symptom in 58.8% of the cases.

Table III presents the histopathological and immunohistochemical findings of the MF cases. The median number of biopsies required to establish a definitive diagnosis was 2, with a delay of up to 1 year in biopsy collection. Only 30% of the biopsies included a detailed report of histopathological findings; in the remaining cases, reports were limited to noting epidermotropism with atypical lymphocytes, followed by the final diagnosis and the immunophenotype. Conse-

Table I Baseline characteristics of the pediatric series with mycosis fungoides

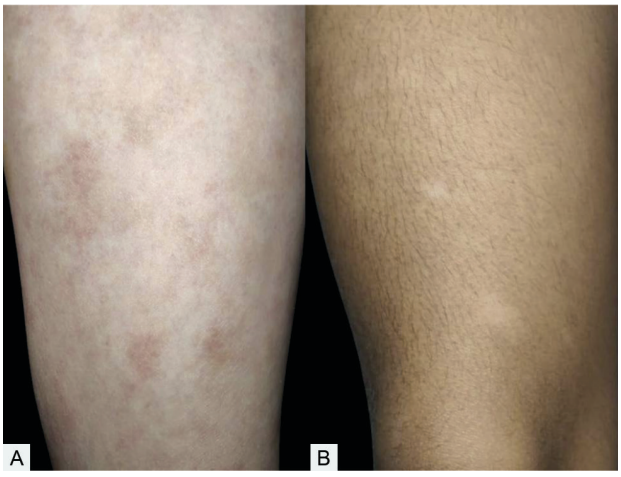
Variable	*n* = 17
Sex, *n* (%)	
Male	13 (76.5)
Female	4 (23.5)
Male-to-female ratio	3.2:1
Age, years, mean (SD)*	
At diagnosis	11.9 ± 2.8
At referral	11.9 ± 2.7
Disease duration, years, median (IQR)†	3.0 (2.0, 4.5)
Nutritional status, *n* (%)	
Undernutrition	5 (29.4)
Normal	9 (52.9)
Overweight	3 (17.6)
Family history of cancer, positive, *n* (%)	3 (17.6)
Referral diagnosis	
Mycosis fungoides	3 (17.6)
Atopic dermatitis	9 (52.9)
Pityriasis lichenoides	2 (11.8)
Psoriasis	2 (11.8)
Tinea corporis	1 (5.9)
Baseline LDH U/L levels, median (IQR)†	258 (193.5, 295.0)

*Standard deviation; †Interquartile range: (25th, 75th percentiles)

Table II Main clinical findings of mycosis fungoides in the pediatric study series

Variable	*n* = 17
	n (%)
Skin lesions	
Hypochromic patches	11 (64.7)
Erythematous patches, erythematous scaly plaques	6 (37.3)
Signs and symptoms, present	
Xerosis	12 (70.6)
Pruritus	10 (58.8)
Affected topography	
Head and trunk	3 (17.6)
Trunk and extremities	13 (76.5)
All body segments	1 (5.9)
Disease stage	
IB, skin involvement > 10% of body surface area (T2 N0 M0 B0)	17 (100)
Clinical variant	
Classic	6 (35.3)
Hypopigmented	11 (64.7)

Figure 1 Clinical variants of mycosis fungoides



A: Case of mycosis fungoides with a classic clinical presentation, characterized by the presence of erythematous patches and erythematous scaly plaques. B: Case of mycosis fungoides with hypochromic clinical presentation

quently, a global synthesis of histological findings was not possible. Regarding immunohistochemistry, all cases demonstrated epidermotropism with positivity for CD3 and CD4 (100%), confirming the T-cell origin of the infiltrate and the classical phenotype; however, 88.2% (15/17) also exhibited CD8 positivity, indicating a high proportion of cytotoxic lymphocytes. This finding could reflect a mixed infiltrate, in which the neoplastic CD4+ population coexists with a reactive CD8+ component, or a predominant cytotoxic phenotype (CD8+) with possible aberrant co-expression of CD4/CD8, a pattern more frequently observed in pediatric populations and associated with a more indolent clinical course. Finally, in the 11 cases evaluated for Ki-67, the median proliferation index was 5%, corresponding to a low proliferative rate (<10-20%). This result aligns with the early stages of MF (patches/plaques) and further suggests a relatively indolent clinical course in this pediatric series.

Table IV summarizes the main treatments administered to patients with MF throughout the course of the disease. All patients received topical steroids at some point for the management of skin lesions. Additionally, phototherapy was prescribed in 3 cases, methotrexate in 3 cases, and extracorporeal photopheresis in 3 cases.

Table IV Therapeutic management of pediatric cases with mycosis fungoides

Variable	*n* = 17
Number of treatments, median, IQR*	2 (1,3)
Type of treatment, *n* (%)	
Topical steroid	17 (100)
Methotrexate	3 (17.6)
Dose used, mg/kg/week, IQR*	0.23 (0.16,0.41)
Treatment duration, months, IQR	15 (10,19)
Phototherapy, *n* (%)	3 (17.6)
Extracorporeal photopheresis	3 (17.6)

*IQR, interquartile ranges (25th, 75th percentiles)

Table V presents the clinical, epidemiological, histopathological, immunophenotypic, and therapeutic characteristics of MF stratified by clinical presentation. The classical form was significantly associated with the presence of erythematous macules and erythematous scaly plaques (100% vs. 0% in the hypopigmented variant; $p < 0.01$), as well as with the use of methotrexate (50.0% vs. 0%; $p = 0.02$) and phototherapy (50.0% vs. 0%; $p = 0.02$). In contrast, the hypopigmented variant was exclusively associated with the

Table III Main histopathological and immunohistochemical findings in the pediatric series with mycosis fungoides

Variable	*n* = 17		
Histopathological study, *n* (%)	17 (100)		
Number of biopsies, median, IQR*	2 (1, 2)		
Time to biopsy, months, IQR*	12 (3, 24)		
Histopathological features, *n* (%)			
Epidermotropism of atypical lymphocytes	17(100.0)		
Immunohistochemistry, positive, *n* (%)	Positive	Negative	Not Done
CD3	17 (100)	-	-
CD4	17 (100)	-	-
CD8	15 (88.2)	2 (11.8)	-
CD45	1 (5.9)	1 (5.9)	15
CD7	12 (70.6)	-	5
Ki-67	11 (64.7)	-	6
Ki-67 %; median, IQR*	5% (5.0%, 10.0%)	-	6

*IQR: interquartile ranges (25th, 75th percentiles)

presence of hypochromic macules (100% vs. 0% in the classical form; $p < 0.01$).

Finally, all cases remained at stage IB during pediatric follow-up; 4 patients lost eligibility for care at the institute and discontinued follow-up, while 2 continued their care in Adult Dermatology after reaching adulthood.

Discussion

The clinical and epidemiological characteristics of MF observed in this study are consistent with those previously reported in the literature. These include: a) age at diagnosis (11.9 ± 2.8 years), comparable to that described in pediatric studies involving Latino and U.S. children; b) sex distribution, with a male predominance, in agreement with several prior reports; c) duration of follow-up, with a median of 3 years, consistent with earlier studies; d) laboratory findings, with lactate dehydrogenase (LDH) levels remaining within normal ranges, as reported in pediatric patients with MF;[13,14,15] e) clinical presentation, in which the hypopigmented variant was the most frequent, similar to other pediatric series that associate this subtype with younger age at onset; and f) disease stage, with stage IB being the most prevalent.[16,17] In addition, the histopathological and immunohistochemical findings were similar to those previously described in the literature.[18]

Mycosis fungoides represents a diagnostic challenge due to its clinical similarity to more common dermatoses, particularly AD, as both conditions may present with erythematous scaly plaques. However, in AD, lesions typically predominate in flexural areas and are associated with intense pruritus, whereas in MF they more commonly involve non-sun-exposed areas.[9] In early stages, MF presents with nonspecific lesions, such as minimally infiltrated erythematous or hypochromic macules, and follows an indolent course characterized by fluctuating lesions, partial response to topical corticosteroids, and absence of systemic symptoms. These features favor alternative diagnoses and delay clinical suspicion, compounded by subtle and often inconclusive early histopathologic findings. Because primary care physicians are more familiar with AD, MF is rarely considered at the initial evaluation, and diagnosis is often established only after failure of conventional therapies. In our cohort, AD was the leading reason for referral in 52.9% of cases, underscoring the diagnostic overlap and the consequent delay in performing a skin biopsy. Although previous studies have reported a mean disease duration of approximately 3 years and 6 months prior to diagnostic confirmation,[13] the time to biopsy and definitive diagnosis in our series was up to 12 months, likely reflecting a structured referral pathway to our tertiary care center and the implementation of a multidisciplinary approach involving dermatology, oncology, and pediatrics.

Histopathological findings in pediatric MF are not always conclusive, requiring clinical surveillance and, in many cases, multiple biopsies to confirm the diagnosis. Castano *et al.* reported an average of 3 biopsies to establish the disease, whereas in our cohort the median was 2.[19] In the immunohistochemical analysis of our series, all cases were CD3+ and CD4+, but the concomitant expression of CD8+ in most cases

Table V Clinical-epidemiological, histopathological, immunophenotype, and therapeutic characteristics of mycosis fungoides according to clinical presentation

	Classical *n* = 6	Hypopigmented *n* = 11	*p*-value
Age, years, mean (SD)*			
At diagnosis	12.6 ± 2.0	11.5 ± 3.1	0.43†
At referral	11.3 ± 2.2	10.6 ± 3.2	0.65†
Duration of disease, median (IQR)	48 (24.0, 75.0)	24 (24, 48.0)	0.35‡
Clinical presentation, present, *n* (%)			
Hypochromic patches, *n* = 11	0	11 (100.0)	< 0.01*
Erythematous patches + erythematous-scaly plaques, *n* = 6	6 (100.0)	0	< 0.01*
Symptoms, positive, *n* (%)			
Xerosis, *n* = 12	6 (100.0)	6 (54.5)	0.10*
Pruritus, *n* = 10	5 (83.3)	5 (45.5)	0.30*
Histopathology			
Number of biopsies, *n* (%)	2 (1,3)	1 (1,2)	0.21‡
Time to biopsy, months, IQR§	21 (4.2, 30.0)	6 (3.0, 24.0)	0.35‡
Type of treatment, *n* (%)			
Methotrexate, *n* = 3	3 (50.0)	0	0.02*
Phototherapy, *n* = 3	3 (50.0)	0	0.02*
Extracorporeal photopheresis, *n* = 3	0	3 (27.3)	0.51*

*Fisher's exact test, †Student's *t* test, ‡Mann-Whitney *U* test, §interquartile ranges (25th, 75th percentiles)

suggests either a mixed infiltrate with reactive cytotoxic T lymphocytes or a cytotoxic neoplastic phenotype, described more frequently in pediatric MF. This profile, together with the low proliferative index (Ki-67), supports a more indolent clinical course of the disease.[5,20]

According to the 2023 consensus of the European Organisation of Research and Treatment of Cancer (EORTC), first-line treatment for MF in early stages (IA, IB, and IIA) includes a watch-and-wait policy in selected cases (primarily T1a), as well as skin-directed therapies (SDT). Options include topical corticosteroids, topical chlormethine, narrowband ultraviolet B (nbUVB) phototherapy, psoralen plus UVA (PUVA) photochemotherapy, and localized radiotherapy. In cases of therapeutic failure or disease progression, second-line systemic treatments are recommended, such as retinoids, interferon-alpha (IFN-alpha), total skin electron beam therapy (TSEB), and biological agents such as brentuximab vedotin and mogamulizumab; in addition, low-dose methotrexate is another alternative.[21]

In our series, therapeutic management followed international guidelines, with some association observed between clinical presentation and treatment administered. The classic form was related to the use of methotrexate and phototherapy; however, the latter may be limited in some hospitals due to equipment availability, lack of pediatric expertise, and the need for greater patient cooperation. The classic presentation also showed a higher frequency of extracorporeal photopheresis use, although without statistical significance. While this modality is usually reserved for advanced MF, Sézary syndrome, or refractory cases, reports have documented complete and sustained remissions in early stages.[22,23,24] At our institution, extracorporeal photopheresis was available and used in refractory patients; nevertheless, although prolonged or sustained remissions are expected, this could not be assessed due to the cross-sectional nature of our study.

Pediatric MF generally has a favorable prognosis; however, it is associated with a high recurrence rate, necessitating long-term follow-up. Given the limited number of large-scale studies guiding long-term therapeutic management in this population, some authors advocate for a watchful waiting strategy and an individualized treatment approach. This recommendation is based on the typically indolent course of early-stage disease and the need to consider potential safety concerns and quality-of-life impacts associated with treatment.[25,26]

The main limitations of this study were its cross-sectional and retrospective design, which precluded longitudinal follow-up of the patients; the small sample size, limiting representativeness to the beneficiary population served at our unit; the exclusive inclusion of Mexican patients, restricting extrapolation to other populations; the absence of molecular studies; potential interobserver variability in histopathological and immunohistochemical interpretation; and the lack of a standardized assessment of therapeutic response due to the cross-sectional nature of the study.

Conclusions

Mycosis fungoides in the pediatric population is an uncommon entity that poses a diagnostic challenge because of its clinical similarity to common dermatoses, often leading to delays in patient referral and biopsy. In our series, male sex, the hypopigmented variant, and a CD8+ phenotype predominated, all of which were associated with a more indolent clinical course. This study contributes by providing a clinical, immunophenotypic, and therapeutic characterization of MF in Mexican children, while also documenting diagnostic delays reflected by the frequent need for multiple biopsies to confirm the diagnosis and the limited availability of therapies, such as phototherapy. Although the overall prognosis is favorable, the high recurrence rate requires prolonged follow-up, highlighting the need to increase clinical suspicion and to conduct multicenter studies to standardize management and better define prognosis in this population.

Conflict of interest disclosure: The authors have completed and sent the Spanish-translated form of the Declaration for Potential Conflicts of Interest of the International Committee of Medical Journal Editors, and no conflicts of interest were reported related to this article.

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