Original Research Article

Indian Journal of Pathology: Research and Practice
Volume 7 Number 1, January 2018
DOI: http://dx.doi.org/10.21088/ijprp.2278.148X.7118.7

Principles and Pitfalls in Evaluating Early Mycosis Fungoides: Redefining Criteria and Emphasizing Mimics

Chokka Mahesh Kiran*, Anita Ramdas, Manjiri Phansalkar***, Sheela Kuruvila******

*Associate Professor **,***Professor, Dept. of Pathology, ****Professor, Dept. of Dermatology, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry 605014, India.

Abstract

Background: The diagnosis of early Mycosis Fungoides (MF) is quite challenging because of its overlapping clinicopathologic findings with various reactive dermatoses. A comprehensive assessment of clinical history is absolutely essential as pathologic criteria alone are insufficient. *Aim*: We aimed to diagnose early MF seeking an algorithm proposed by the International Society for Cutaneous Lymphoma (ISCL), define various significant diagnostic criteria and describe the associated clinical and histological mimics. *Materials and Methods* : Formalin fixed, paraffin embedded and H&E stained sections of forty skin biopsies from thirty nine clinically suspected early MF patients (n = 39) were studied initially. Various clinical and histopathological parameters were recorded followed by immunohistochemistry (IHC) with selected markers to arrive at a proper diagnosis. *Results*: Early MF was diagnosed in 9 patients (23.1%), parapsoriasis in 5 patients (12.8%), psoriasiform dermatitis in 7 patients (17.9%) and spongiotic dermatitis in 5 patients (12.8%). Remaining 13 patients (33.3%) were grouped under miscellaneous category comprising of other reactive dermatoses. Atypical lymphocytes were seen in 8 patients with early MF (n = 9) and 2 patients with parapsoriasis (n = 5). No statistical significance was observed between the two groups ($P > 0.05$, Fisher's exact test). *Conclusions*: Some patients with early MF fail to show the typical histological features of the disease. In such instances, multiple biopsies from different lesions are highly useful and the algorithm developed by ISCL is a valid tool in diagnosis. Epidermotropism is considered as histological hallmark. IHC is not needed in all cases, particularly when the clinical and histopathological features are quite obvious.

Keywords: Algorithm; Early MF; Epidermotropism; ISCL; Reactive Dermatoses.

Introduction

Mycosis fungoides was first described in 1806 by Alibert, a french dermatologist who called it "Pian fungoides". However, the current term mycosis fungoides was adopted only in 1832. In 1870, Bazin described the natural history of the disease and its three stages [1].

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL) with an indolent clinical course characterized by evolution of patches and plaques to tumor stage and about less than one-third of the patients developing advanced disease manifested by involvement of lymph nodes, blood and visceral organs [2,3,4]. This represents nearly 50% of all primary cutaneous lymphomas, occuring mostly in elderly adults but also seen in children and young adults with a male-to-female ratio of 2:1 [5,6]. Prominent epidermotropism and small to medium sized pleomorphic lymphocytes with convoluted nuclear contours are useful histologic features [7].

Early MF is mostly evaluated and diagnosed in the absence of classic clinical course, henceforth misdiagnosed as eczema, psoriasis or other reactive dermatoses [6]. The diagnostic histologic features are often not evident and the nuclear atypia of the lymphocytes is also inconspicuous. Features such as psoriasiform epidermal hyperplasia, intraepidermal mucin and spongiosis are sometimes seen mimicking an inflammatory process [7]. At times, biopsies are performed after various treatments thereby altering the histopathological features and rendering diagnosis ineffective [8]. Since accurate diagnosis of early MF is essential for prognostic stratification as well as

Corresponding Author: Chokka Mahesh Kiran, Associate Professor, Dept. of Pathology, Pondicherry Institute of Medical Sciences, Kalapet, Puducherry 605014, India.
E-mail: kirencm@yahoo.com
(Received on 27.10.2017, **Accepted on** 25.11.2017)

determining therapeutic options, the spectrum of reactive dermatoses should be altogether eliminated and this is accomplished by a unique combination of various clinical, histopathological and immunohisto chemical parameters [9].

In the present study we aimed to diagnose patients with a clinical suspicion of early MF through the algorithm proposed by ISCL and redefine all the probable clinical, histopathological and immunohistochemical diagnostic criteria thereby differentiating both clinical and histological mimics.

Materials and Methods

We evaluated 40 skin biopsies generated from 39 patients clinically suspected with early MF. All patients with a history of long standing erythematous patches or plaques localized in non-sun exposed areas were included in our study. Patients with a history of drug abuse and diagnosed cases of MF were excluded from the study. This was a prospective study in the Department of Pathology of our institute from Jan 2013 to Dec 2016. The Institutional Ethics Committee of our institute approved the research study and informed consent was obtained from the patients in accordance with the Declaration of Helsinki.

A comprehensive clinical data comprising of age, sex, physical nature of lesion, localization in hidden areas and any prior history of medication was initially obtained. The representative skin biopsies were fixed in neutral buffered formalin immediately after the procedure. Later they were bisected, processed in alcohol, embedded in paraffin, cut into thin sections of four micron thickness and stained by routine hematoxylin and eosin. The slides were assessed thoroughly by two pathologists under x 400 magnification in Olympus CX 41 microscope and 10 criteria were recorded. Each histologic criterion was defined.

a. Epidermotropism: Presence of lymphocytes deposited as solitary units within or near the basal cell layer of the epidermis [9].
b. Atypical lymphocytes : Lymphocytes showing high nuclear-cytoplasmic ratio [9].
c. Patchy lymphoid infiltrate: Lymphocytes distributed in patches [7].
d. Band like lymphoid infiltrate: Lymphocytes distributed in diffuse bands [7].
e. Cerebriform nuclei : Lymphocytes showing folded nuclear margins [9].
f. Dermoepidermal tagging: Four or more lymphocytes closely opposed to basal keratinocytes in a linear arrangement [9].
g. Haloed cells : Lymphocytes surrounded by a clear halo [9].
h. Pautrier microabscess : Collection of four or more lymphoid cells in the epidermis with no significant cytopathic changes in the surrounding keratinocytes [9].
i. Interstitial fibrosis : Bands of fibrosis in upper dermis interrupted by abnormal lymphocytes [7].
j. Spongiosis : Widened and edematous intercellular spaces [9].

Suspicious cases were subjected to IHC for CD3 and CD20 by manual method using rabbit monoclonal antibody. Antigen retrieval was done by heating the tissue sections in a Pascal pressure cooker in 0.01M citrate buffer for 10 to 15 min. After the development of chromogen, the slides were counterstained with hematoxylin and the staining pattern was evaluated under x 400 magnification. Membrane staining was considered positive. Sections from tonsillar tissue were taken as positive control for both CD3 and CD20.

Altogether, a total of 21 criteria (9 clinical, 10 histological and 2 immunohistochemical) were analyzed.

Patients with erythematous patches or plaques localized in hidden areas showing features of epidermotropism and atypical lymphocytes histologically, and CD3 positivity and CD20 negativity on IHC were subjected to the algorithm proposed by ISCL for evaluating early MF and the respective scores were noted. Scoring was in accordance with the algorithm proposed by ISCL. Both clinical and histopathologic parameters included, basic and additional criteria. A score of 2 was given when a basic and 2 additional criteria were present and a score of 1 was given when a basic and 1 additional criteria were present. Clonality was given a score of 1 and CD3 or CD2 positivity was given a score of 1. The minimum score required for a diagnosis of early MF was 4.

Results

A total of 40 skin biopsies were analyzed from 39 patients with a clinical suspicion of early MF. One patient had 2 biopsies from 2 different sites as this patient manifested with erythematous patches localized over sun exposed areas and most of them were ill defined. A diagnosis of early MF was confirmed in 9 patients (23.1%) and rejected in 30

patients (76.9%). Of the 30 patients, parapsoriasis was diagnosed in 5 patients (12.8%), psoriasiform dermatitis in 7 patients (17.9%) and spongiotic dermatitis in 5 patients (12.8 %). Remaining 13 patients (33.3%) showed a wide range of reactive dermatoses like post-inflammatory fibrosis (8 patients), polymorphous light eruption (1 patient), morphea (1 patient) and pityriasis lichenoides chronica (3 patients). The clinicopathological characteristics of all the 39 patients are presented in Table 1.

The mean age of presentation of early MF was 46 years and the M:F ratio was 1.2:1. The clinical presentation ranged from erythematous patches to plaques with 8 out of 9 patients (88.8%) showing lesions in non-sun exposed areas (Figure 1). Classical MF was noted in 8 patients and 1 patient had hypopigmented MF. 5 patients were found to be in patch stage and 4 patients in plaque stage.

Epidermotropism (100%) and presence of atypical lymphocytes (88%) were the two main histopathological criteria based on which a diagnosis of early MF was made. The salient histopathological and immunohistochemical findings are shown in Figures 2 and 3.

All the 9 patients with histologic features suggesting MF when subjected to the algorithm proposed by ISCL satisfied the required criteria as shown in table 2. 7 patients scored 5 points and rest of the 2 patients scored 4 points, confirming the diagnosis of early MF.

Table 1: Clinicopathological spectrum of study patients

Parameter	Early MF (N=9)		Parapsoriasis (N=5)		Psoriasiform dermatitis (N=7)		Spongiotic dermatitis (N=5)		Miscellaneous (N=13)	
	N	(%)	N	%	N	(%)	N	(%)	N	(%)
Age										
≤ 15	0	0%	0	0%	0	0%	0	0%	2	0%
15-45	6	66.6%	3	60%	5	71%	3	60%	7	53.8%
≥ 45	3	33.3%	2	40%	2	28.5%	2	40%	6	46.1%
Sex										
Male	5	55.5%	1	20%	4	57.1%	5	100%	6	46.1%
Female	4	44.4%	4	80%	3	42.8%	0	0%	7	53.8%
Erythematous plaques	3	33.3%	4	80%`	4	57.1%	3	60%	5	38.4%
Erythematous Patches	5	55.5%	0	0%	1	14.2%	0	0%	1	7.6%
Erythroderma	0	0%	1	20%	0	0%	0	0%	0	0%
Poikiloderma	0	0%	0	0%	0	0%	0	0%	0	0%
Localization in hidden areas	8	88.8%	3	60%	4	57.1%	5	100%	10	76.9%
MF Stage										
Patch stage	5	55.5%	NA	NA	NA	NA	NA	NA	NA	NA
Plaque stage	4	44.4%	NA	NA	NA	NA	NA	NA	NA	NA
MF Histological type										
Classical MF	8	88.8%	NA	NA	NA	NA	NA	NA	NA	NA
Hypopigmented MF	1	11.1%	NA	NA	NA	NA	NA	NA	NA	NA
Epidermotropism	9	100%	0	0%	0	0%	0	0%	0	%
Atypical lymphocytes	8	88.8%	2	40%	0	0%	0	0%	0	%
Patchy LI	8	88.8%	0	0%	3	42.8%	4	80%	5	38.4%
Band like LI	1	11.1%	0	0%	0	0%	0	0%	0	0%
Cerebriform nuclei	6	66.6%	0	0%	0	0%	0	0%	0	0%
Dermoepidermal tagging	3	33.3%	0	0%	0	0%	0	0%	0	0%
Haloed cells	4	44.4%	1	20%	0	0%	0	0%	0	0%
Spongiosis	3	33.3%	1	20%	5	71.4%	5	100%	6	46.10%
Pautrier microabscesses	1	11.1%	0	0%	0	0%	0	0%	0	0%
Interstitial fibrosis	2	22.2%	0	0%	0	0%	0	0%	0	0%
IHC										
CD 3+	9	100%	NA	NA	NA	NA	NA	NA	NA	NA
CD 20-	9	100%	NA	NA	NA	NA	NA	NA	NA	NA

MF - Mycosis fungoides
LI - Lymphoid infiltrate
NA - Not applicable

Table 2: Scoring system (points) for patients with early MF in accordance with ISCL

Sl. No	Criteria			Total score (points)
	Clinical	Histopathological	IHC	
Patient 1	2	2	1	5
Patient 2	2	1	1	4
Patient 3	2	2	1	5
Patient 4	1	2	1	4
Patient 5	2	2	1	5
Patient 6	2	2	1	5
Patient 7	2	2	1	5
Patient 8	2	2	1	5
Patient 9	2	2	1	5

Table 3: Algorithm for diagnosis of early MF

Criteria	Scoring system (Points) by criteria
1. Clinical	2 (basic plus 2 additional)
Basic	1 (basic plus 1 additional)
Persistent and/or progressive patches / thin plaques	
Additional	
1. Non-sunexposed location	
2. Size / shape variation	
3. Poikiloderma	
2. Histopathologic	2 (basic plus 2 additional)
Basic	1 (basic plus 1 additional)
Superficial lymphoid infiltrate	
Additional	
1. Epidermotropism without spongiosis	
2. Lymphoid atypia	
3. Molecular	1 (clonality)
Clonal T-cell receptor gene rearrangement	
4.Immunophenotypic	1 (1 or more criteria)
1. < 50 % CD2+, CD3+, and/or CD5+ T cells	
2. < 10 % CD7+ T cells	
3. T-cell antigen loss confined to epidermis	

Adapted and modified from Pimpinelli et al

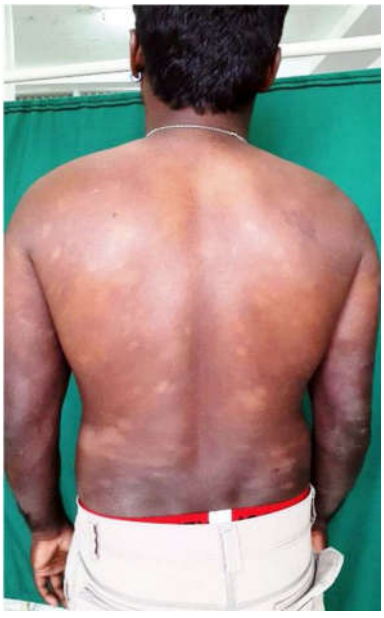

Fig. 1: Patient with erythematous patches of varying size situated over the back.

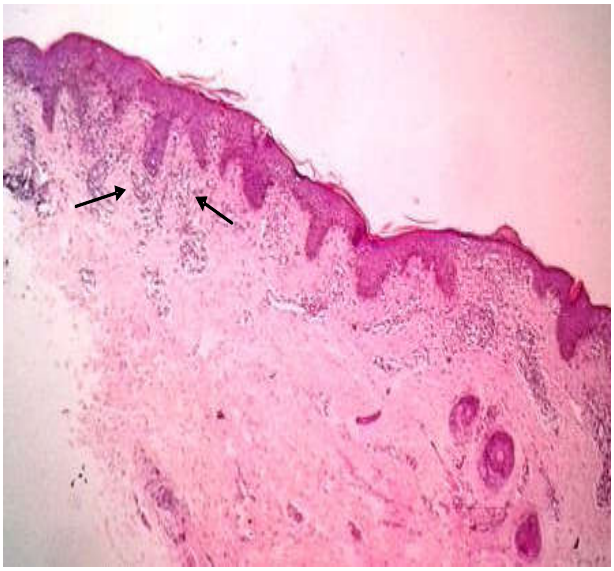

Fig. 2a: Dense lymphoid infiltrtae with epidermotropism (H&E, x100)

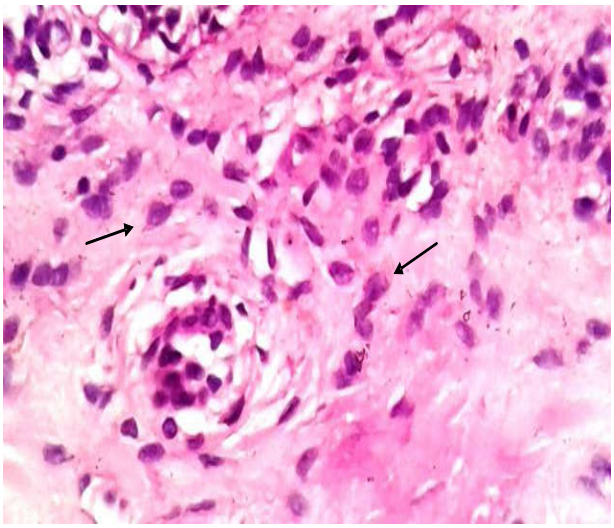

Fig. 2b: Atypical lymphocytes (H&E, x200)

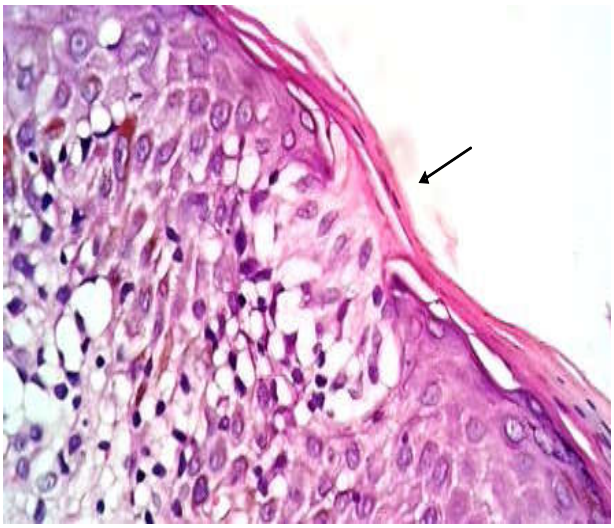

Fig. 3a: Pautrier abscess with spongiosis (H&E, x400)

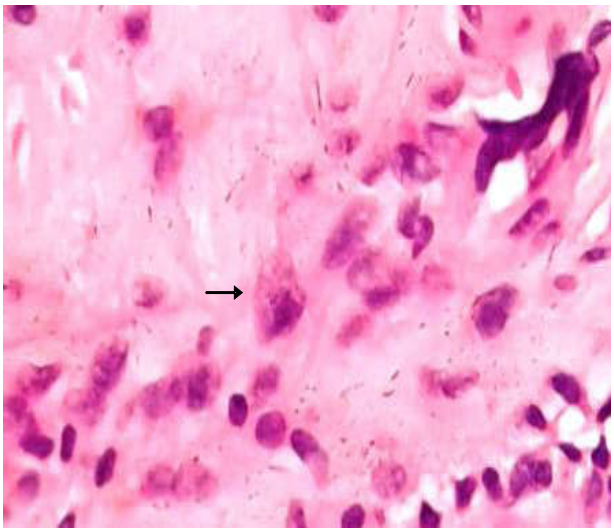

Fig. 2c: Lymphocytes showing cerebriform nuclei (H&E, x400)

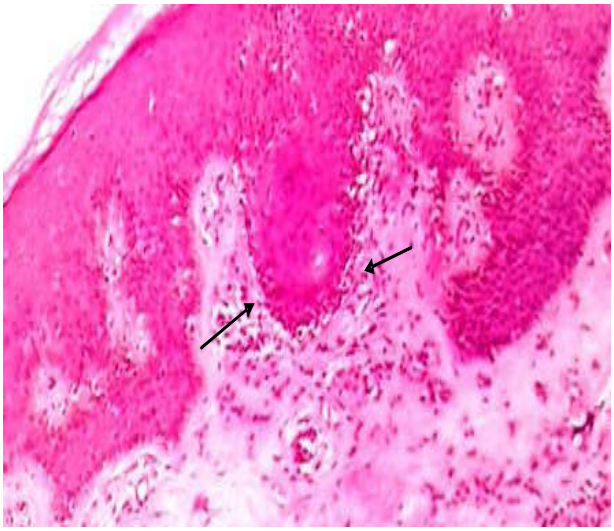

Fig. 3b: Dermoepidermal tagging (H&E, x100)

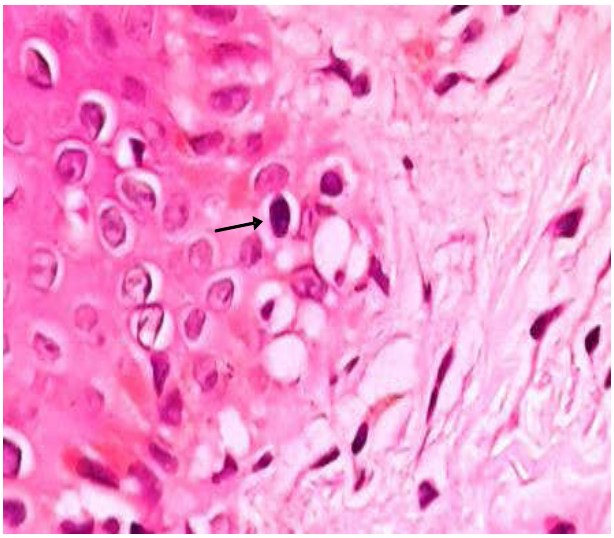

Fig. 2d: Lymphocytes with clear cytoplasm - Haloed cells (H&E, x400)

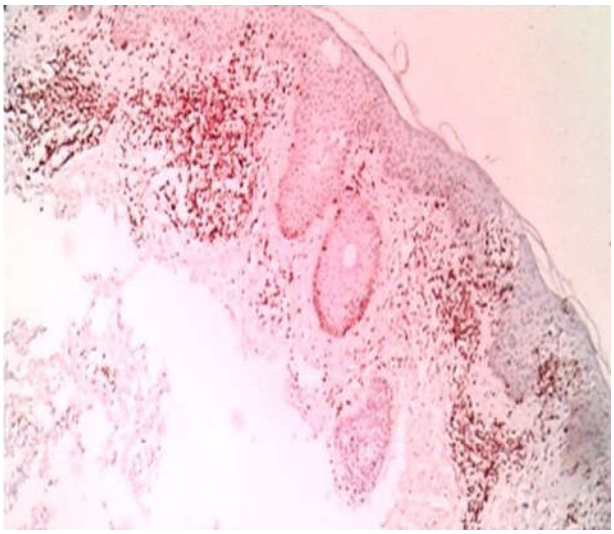

Fig. 3c: IHC showing CD3 positivity in a case of early MF

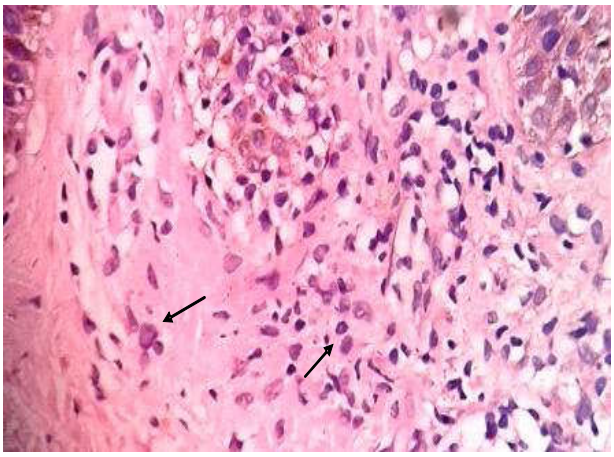

Fig. 3d: A case of parapsoriasis showing mild lymphoid atypia (H&E, x400)

Among the reactive dermatoses, parapsoriasis presenting clinically with erythematous plaques (80%) in non-sun exposed areas (60%) was closely confused with early MF. 2 patients out of 5 (40%) showed atypical lymphocytes histologically (Figure 3d). However, this association was not statistically significant ($P > 0.05$, Fisher's exact test). Spongiotic dermatitis and psoriasiform dermatitis were the other mimickers of early MF manifesting once again with erythematous plaques (60% and 57.1% respectively) in non-sun exposed areas. Other miscellaneous reactive dermatoses like post-inflammatory fibrosis and pityriasis lichenoides chronica mostly presented with erythematous plaques and patches in the non-sun exposed areas. Most of the reactive dermatoses histologically showed mild patchy lymphoid infiltrate without atypia along with spongiosis.

Discussion

MF is the most common primary cutaneous lymphoma and is considered to be rare in Indian population with early MF patients always posing a diagnostic challenge to both the dermatologist and the pathologist [10,11]. The diagnosis of early MF is quite challenging as the clinicopathologic findings overlap with various reactive dermatoses. Moreover, the histopathological findings vary from person to person over time, and even between multiple biopsies from the same person [12,13].

One of our patient had 2 biopsies from 2 different sites. Epidermotropism and atypical lymphocytes were seen in one of the biopsy only and the other biopsy showed perivascular lymphocytic infiltrate. Frequent self-medication in some patients can modify the appearance of the lesions [6,12]. Hence repeat or multiple biopsies from various lesions may be of immense help [12].

In our study early MF was clinically mimicked by conditions such as parapsoriasis, psoriasiform dermatitis, spongiotic dermatitis, pityriasis lichenoides chronica and post-inflammatory fibrosis. All these conditions were biopsy proven. Many research studies confirmed the distinct overlapping histopathologic features between early MF and spongiotic dermatitis, eczema, parapsoriasis, morphea and various other reactive dermatoses [14,15,16,17]. Patients with parapsoriasis showing lymphoid atypia and cerebriform nuclei have been documented [18].

Because of the diagnostic challenges encountered in early MF, we tried to describe the most reliable diagnostic criteria by which early MF could be distinguished easily from other reactive dermatoses. The criteria we defined were partially the same as those identified by the International Society for Cutaneous Lymphoma in 2005 as well as in 2015 [19]. The most characteristic histopathologic criteria according to us were epidermotropism, atypical lymphocytes distributed in a patchy fashion, cerebriform nuclei, haloed cells and lymphocyte tagging at the dermoepidermal junction. Pautrier microabscesses though considered specific for MF, was not a significant criteria in our study. Epidermotropism, the single most defining criteria is considered as a hallmark of MF and has been reported in up to 96% of patients with early MF [13]. In our study, epidermotropism was reported in 100 % of the patients. The prevalence of Pautrier microabscesses in early MF ranges between 4% to 37% [20,21]. In our study it was 11.1%. Spongiosis is usually seen in 30% of patients with MF [22]. In our study, spongiosis was reported in 33.3% of patients. Interstitial fibrosis has been considered a characteristic feature of advanced disease, rarely seen in early MF [9]. In our study, this was seen in 22.2% of patients. Many studies focused on various histopathological features and confirmed epidermotropism, lymphoid atypia, band like lymphoid infiltrate, haloed cells and dermoepidermal tagging of lymphocytes as the characteristic histopathologic criteria in early MF [10,23-25]. To facilitate accurate diagnosis in patients with early MF, the International Society for Cutaneous Lymphoma has developed an algorithm (Table 3) based on clinical, pathological, molecular and immunohisto-chemical criteria from diverse methodologies. According to the algorithm, a total of 4 points is required for the diagnosis of early MF [6,10]. This algorithm has been subsequently validated in many studies and has been found beneficial with few studies recommending further refinement to improve its accuracy [19].

In our study, we found this algorithm highly valuable. All the 9 patients with histopathological and immunohistochemical features suggesting MF fulfilled the requirements of the algorithm further strengthening the diagnostic accuracy of early MF.

However, our study had certain limitations. Other T cell markers like CD3 and CD5 were not employed. We did not include T-cell receptor gene rearrangement studies. And finally for validating the algorithm proposed by ISCL for diagnosing patients with early MF, we had only 9 patients.

Conclusion

The distinction between early MF and reactive dermatoses still remains one of the most challenging tasks to the dermatologist with spongiotic dermatitis and parapsoriasis being the closest clinical mimics. Apart from these disorders psoriasiform dermatitis, ocassional patients with pityriasis lichenoides chronica, polymorphous light eruption and morphea were the other significant clinical mimics encountered in our study.

The characteristic features which influenced the dermatologists to diagnose early MF in our study were long standing disease and erythematous patches / plaques localized in hidden areas. The role of a pathologist is pivotal in such circumstances and epidermotropism still remains the gold standard histopathologic criterion followed by lymphoid atypia. Finally, the combined dual approach comprising of a combination of clinical and histopathological parameters is of paramount importance. Despite certain limitations, our study throws light on some of the gray zones in dermatopathology providing essential information in distinguishing early MF from various inflammatory mimics.

Acknowledgements

The authors sincerely thank Dr. Renu G'Boy Varghese, M.D, DNB., Professor and Head of the Department of Pathology, Pondicherry Institute of Medical Sciences, Puducherry for her valuable inputs throughout the study.

References

1. Yamashita T, Abbade LPF, Marques MEA, Marques SA. Mycosis fungoides and Sézary syndrome: clinical, histopathological and immunohistochemical review and update. An Bras Dermatol. 2012;87(6):817-30.
2. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. Blood. 2005;105:3768-85.
3. Ralfkiaer E, Cerroni L, Sander CA, et al. Mycosis fungoides. In: Swerdlow SH, Campo E, Harris NL, et al, eds. WHO classification of tumors of haematopoietic and lymphoid tissues. 4th ed. Lyon, France: IARC Press; 2008:296-98.
4. Kim YH, Liu HL, Mraz-Gernhard S, et al. Long-term outcome of 525 patients with mycosis fungoides and Sézary syndrome: clinical prognostic factors and risk for disease progression. Arch Dermatol. 2003;139:857-66.
5. Hwang ST, Janik JE, Jaffe ES, et al. Mycosis fungoides and Sézary syndrome. Lancet. 2008;371:945-57.
6. Song SX, Willemze R, Swerdlow SH, Kinney MC, Said JW. Mycosis fungoides: Report of the 2011 Society for Hematopathology / European Association for Haematopathology workshop. Am J Clin Pathol 2013;139:466-90.
7. Rajan Dewar, Aleodor Alexandru Andea, Joan Guitart, Daniel A. Arber, Lawrence M. Weiss. Workup of cutaneous lymphoid lesions in the diagnosis of primary cutaneous lymphoma. Arch Pathol Lab Med. 2015;139:338-50.
8. Maha Arafah, Shaesta Naseem Zaidi, Hala Kassouf Kfoury, Ammar Al Rikabi, Khalid Al Ghamdi. The Histological Spectrum of Early Mycosis Fungoides: A Study of 58 Saudi Arab patients. Oman Medical Journal. 2012;27(2):134-39.
9. Inchara Y K, Rajalakshmi T. Early mycosis fungoides vs. inflammatory mimics: How reliable is histology?. Indian J Dermatol Venereol Leprol 2008;74:462-66.
10. Pimpinelli N, Olsen EA, Santucci M, , Vonderheid E, Haeffner AC, Stevens S, *et al* . Defining early Mycosis fungoides. J Am Acad Dermatol 2005;53:1053-63.
11. Zacheim HS, Mc Calmont TH. Mycosis fungoides: The great imitator. J Am Acad Dermatol 2002;47:914-8.
12. A. Kelati, S. Gallouj, L. Tahiri, T.Harmouche, F.Z. Mernissi. Defining the mimics and clinico-histological diagnosis criteria for mycosis fungoides to minimize misdiagnosis. International Journal of Women's Dermatology 2017;3:100-106.
13. Massone C, Kodama K, Kerl H, Cerroni L. Histopathologic features of early (patch) lesions of mycosis fungoides: A morphologic study on 745 biopsy specimens from 427 patients. Am J Surg Pathol 2005;29:550-60.
14. Ackerman AB, Breza TS, Capland L. Spongiotic simulants of mycosis fungoides. Arch Dermatol 1974;109:218-20.
15. Solomon A, Cosgarea R, Ruzicka T, Braun-Falco M. Palmoplantar eczema as initial sign of mycosis fungoides. J Eur Acad Dermatol Venereol 2016;30:e124-5.

16. Goldberg I. Parapsoriasis-to be or not be (mycosis fungoides). Harefuah 2012;151:581-4.
17. Fujimoto M, Basko-Plluska JL, Petronic-Rosic V, Shea CR. Early morphea simulating patch-stage mycosis fungoides. Am J Dermatopathol 2015;37:409-12.
18. Sarveswari K N, Yesudia n P. The conundrum of parapsoriasis versus patch stage of mycosis fungoides. Indian J Dermatol Venereol Leprol 2009;75:229-35
19. Vandergriff T, Nezafati KA, Susa J, Karai L, Sanguinetti A, Hynan LS, et al. Defining early mycosis fungoides: Validation of a diagnostic algorithm proposed by the International Society for Cutaneous Lymphomas. J Cutan Pathol 2015;42:318-28.
20. Burg G, Kempf W, Cozzio A, Feit J, Willemze R, Jaffe ES, et al. WHO/EORTC classification of cutaneous lymphomas 2005: Histological and molecular aspects. J Cutan Pathol 2005;32:647-74.
21. Naraghi ZS, Seirafi H, Valikhani M, Farnaghi F, Kavusi S, Dowlati Y. Assessment of histologic criteria in the diagnosis of mycosis fungoides. Int J Dermatol 2003;42:45-52.
22. Shapiro PE, Pinto FJ. The histologic spectrum of mycosis fungoides / Sézary syndrome (cutaneous T-cell lymphoma). A review of 222 biopsies, including newly described patterns and the earliest pathologic changes. Am J Surg Pathol 1994;18:645-67.
23. Guitart J, Kennedy J, Ronan S, Chmiel JS, Hsiegh YC, Variakojis D. Histologic criteria for the diagnosis of mycosis fungoides: Proposal for a grading system to standardize pathology reporting. J Cutan Pathol 2001;28:174-83.
24. Nickoloff BJ. Light-microscopic assessment of 100 patients with patch / plaque-stage mycosis fungoides. Am J Dermatopathol 1988;10:469-77.
25. SantucciM, Biggeri A, Feller AC, Massi D, Burg G. Efficacy of histologic criteria for diagnosing early mycosis fungoides: An EORTC cutaneous lymphoma study group investigation. European Organization for Research and Treatment of Cancer. Am J Surg Pathol 2000;24:40-50.