

Cutaneous Lymphomas: The Difficulty of Early Diagnosis (The Presentation of Two Cases)

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Abstract: *Mycosis fungoides is the most common type of cutaneous T-cell lymphoma (CTCL). In fact, a variety of inflammatory skin disorders may simulate histopathologically MF, and a precise diagnosis may be impossible. Utilization of the combined clinical and pathologic criteria should be considered for evaluating early MF.*

Keywords: Cutaneous –T-cell lymphoma; Mycosis fungoides; Histopathologic features

1. Introduction

Mycosis fungoides is the most common type of cutaneous T-cell lymphoma (CTCL) and represents nearly 50% of all primary cutaneous lymphomas. It occurs mostly in elderly adults (age > 55 years), but can also be seen in children and young adults. The male-to-female ratio is about 2:1. 1)

There is usually a prolonged clinical course with evolution of patches and plaques to tumor stage in some patients. Less than one-third of patients develop advanced disease involving lymph nodes, blood and visceral organs. 2)

Accurate diagnosis of early MF is essential for staging, prognostic stratification and determining the therapeutic options. In practice, however, the diagnosis of patch and early plaque stage MF can be very difficult, because of its overlapping clinicopathologic findings with various reactive dermatoses as well as conflicting clinical presentations and pathologic features.

In fact, a variety of inflammatory skin disorders may simulate histopathologically MF, and a precise diagnosis may be impossible. Many authors stated that a specific histopathologic diagnosis cannot be made in early lesions of MF because these show features of a non-specific dermatitis. 3)

2. Cases Presentation

First case:

First case was a 44-year-old woman, who had the characteristic clinical presentation of early MF, with a 10-year history of erythematous patches of variable size and shape in the sun-protected areas on the trunk, on the thighs, on the buttocks, and lower abdomen. She had several biopsies (two biopsies), and was initially diagnosed and treated for eczema. The disease continued to progress, despite multiple local and systemic treatments. Looking that clinically this case was concerning for early MF, a rebiopsy was recommended.



First case-Figure 1

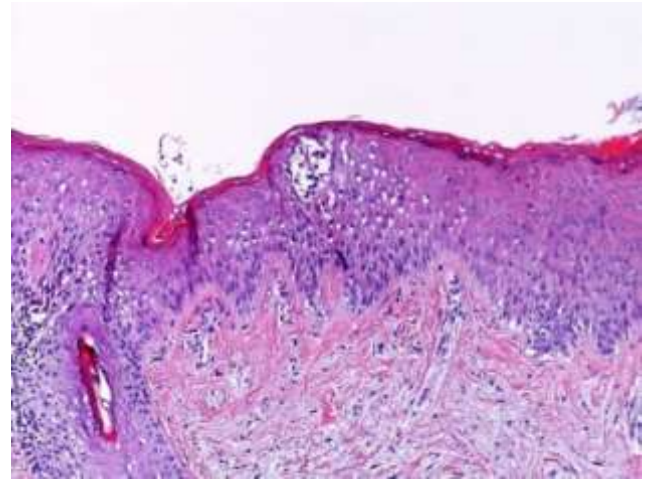


First case – Figure 2

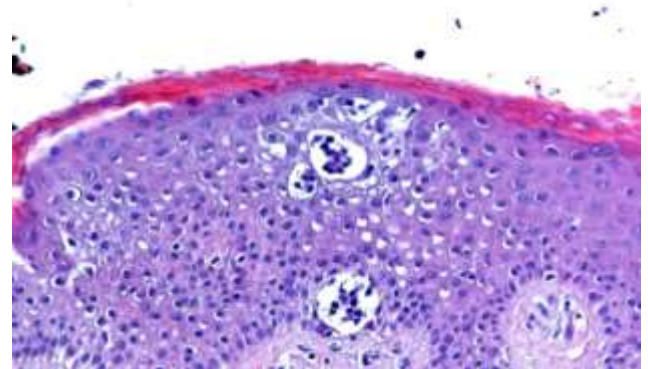


First case- Figure 3

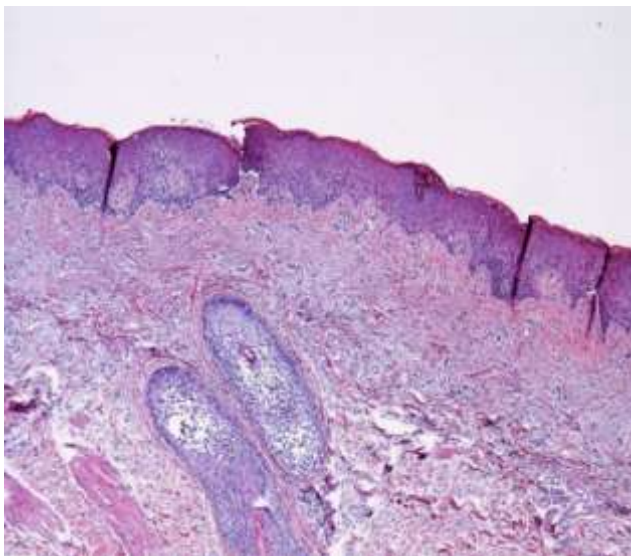
First case :Histopathologic features that favor a diagnosis of MF , include the presence of intraepidermal lymphocytes that are larger than those in the dermis,the presence of follicular mucinosis ,and small Pautrier microabscesses.



First Case- Figure 5: Pautrier microabscesses.



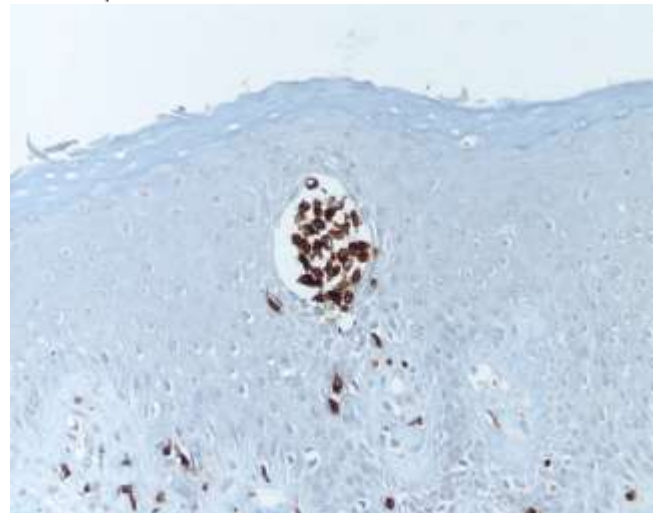
First case – Figure 6: Absence of epidermic spongiosis , Pautrier microabscesses



First case- Figure 4: In the uper dermis,the presence of follicular mucinosis

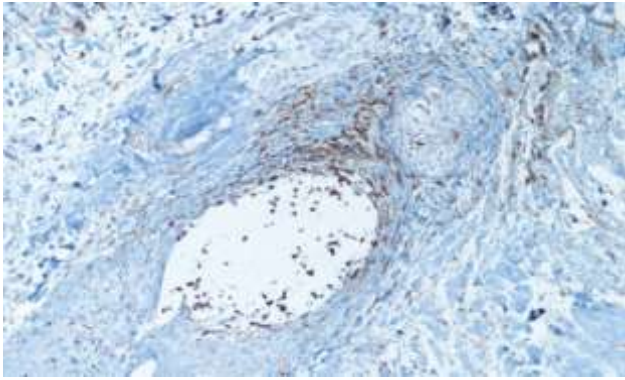
First case Immunohistochemical studies highlight CD3+T cells / expressing CD4+/significant loss of CD7- /CD8-.

CD3epidermic and follicular



First case- Figure 7

First case:Expressing CD4+



First case – Figure 8

Second case

Second case was a women of 57 –year-old,presented with a 1-year history ,of skin patches , dry skin and plaques that were first diagnosed as psoriasis .The patient developed skin tumors and after six months a biopsy was performed.

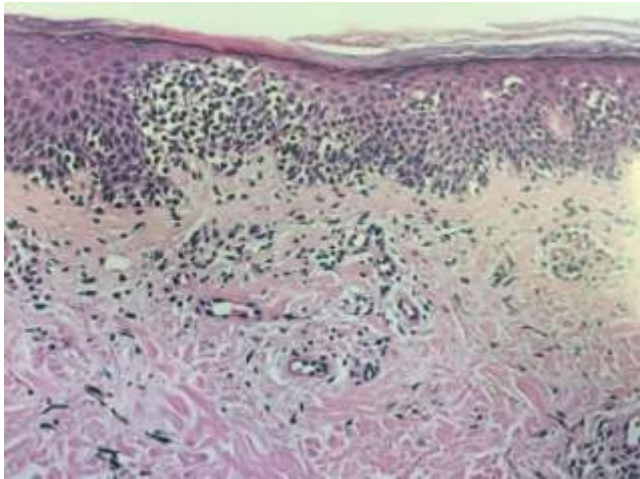


Second case- Figure 9 & 10



Second case: Figure 11 & 12

Second case: Biopsy specimen of a tumor reveals extensive and dense lymphoid infiltrate with interstitial edema.No Pautrier microabscesses were detected. Immunophenotypic analysis demonstrates T cells expressing CD3(+++) , CD8(+++),negative ,CD5(+++), with loss of CD4(---),CD 20(---), CD10(---),CD15(---),CD30(---),CD21(---),CD23(---).



Second case – Figure 13

3. Discussion

Early MF, as the name implies, is evaluated and diagnosed without the benefit of having a classic clinical course of evolution from patches to plaques and, in some cases, to tumor lesions. It may lack the characteristic features of epidermotropism, including formation of Pautrier microabscess, which occurs in about 20% of the cases. Therefore, it may be indistinguishable from reactive dermatoses and is often misdiagnosed initially as eczema or psoriasis as seen in this case.4;5;6)

MF is usually a chronic indolent disease, and most patients have a long history of patch or plaque lesions on non-sun-exposed skin. The diagnosis should not be made without knowledge of the clinical findings.

At present there is no "golden standard" for the histopathologic diagnosis of early MF that is universally accepted.

Sanchez and Ackerman suggested that the most important feature for histopathologic diagnosis of early MF is the presence of an increased number of lymphocytes distributed as solitary units or in small collections within an epidermis devoid of spongiotic microvesiculation (so-called "disproportionate epidermotropism").7)

Atypia of lymphocytes is neither a prominent nor a reliable criterion for the diagnosis of early MF.

King-Ismael and Ackermann further expanded the criteria to include lymphocyte size (epidermal lymphocyte larger than those in the dermis) and dermal changes (presence of wiry collagen bundles in the papillary dermis).8)

Smoller et al suggested that "haloed" lymphocytes (lymphocytes with hyperchromatic nuclei surrounded by a clear cytoplasm resembling a halo) are the most important discriminator of MF from non-MF cases.

Santucci et al. found that the presence of cerebriform lymphocytes in the epidermis and clustered in the dermis was the only highly reliable feature for the differentiation of early MF from inflammatory skin disorders.9)

Finally, Naraghi et al. recently stated that the clinicopathologic correlation is the golden standard in the diagnosis of early lesions of MF. They demonstrated by multivariate analysis that several histopathologic criteria do not have any additional discriminating power, including presence of Pautrier's microabscesses, "haloid" lymphocytes, disproportionate epidermotropism, epidermal lymphocytes larger than those in the dermis, hyperconvoluted lymphocytes in the epidermis and dermis, absence of dyskeratosis, and papillary dermal fibrosis.

No single criterion can be considered as a "golden standard". Histopathologic diagnosis relies on careful analysis of specimens and correlation of histopathologic features with the clinical picture.10)

4. Conclusion

To diagnose early MF with confidence, a comprehensive assessment of clinical history is absolutely essential and pathologic criteria alone may be insufficient.

Because morphologic findings of early MF or treated lesions often show only minimal to mild epidermotropism without Pautrier microabscess, obtaining repeat or multiple biopsy specimens from various lesions may be helpful.

In doubtful cases with early lesions, it is preferable to defer a definite diagnosis of malignancy to follow-up biopsies. Differential diagnosis includes both benign and neoplastic conditions, such as adult T-cell leukemia/lymphoma, which can mimic MF when they involve the skin.

Although patients with MF may have erythroderma and circulating neoplastic cells, they should not be confused with cases of SS, which requires erythroderma, lymphadenopathy, and a significant population of neoplastic circulating Sezary cells for the diagnosis.

Although the histopathologic features are not always diagnostic, they should be considered consistent with MF and do not rule out the diagnosis.

Utilization of the combined clinical and pathologic criteria should be considered for evaluating early MF.

For cases that are clinically concerning for early MF but do not display clear-cut diagnostic features, rebiopsy is recommended.11)

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