



# Real-Life Barriers to Diagnosis of Early Mycosis Fungoides: An International Expert Panel Discussion

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## Abstract

Mycosis fungoides (MF) is a rare, primary cutaneous T-cell lymphoma that is challenging to diagnose due to its heterogeneous clinical presentation and complex histology. The subtlety of the initial clinical appearance of MF can result in diagnostic delays and hesitancy to refer suspected cases to specialist clinics. An unmet need remains for greater awareness and education. Therefore, an international expert panel of dermatologists, oncologists, hematologists, and dermatopathologists convened to discuss and identify barriers to early and accurate MF diagnosis that could guide clinicians toward making a correct diagnosis. Confirmation of MF requires accurate assessment of symptoms and clinical signs, and subsequent correlation with dermatopathological findings. This review summarizes the expert panel's guidance, based on the literature and real-life experience, for dermatologists to help include MF in their list of differential diagnoses, along with simple clinical and histopathologic checklists that may help clinicians to suspect and identify potential MF lesions and reduce diagnostic delays.

## 1 Introduction

Mycosis fungoides (MF) is a primary cutaneous T-cell lymphoma (CTCL) characterized by clonal proliferation of skin-resident, epidermotropic T-lymphocytes. MF accounts for  $\geq 50\%$  of all cutaneous lymphomas [1]. Its reported frequency is heterogeneous worldwide [2], with an incidence of  $\sim 0.58$  cases per 100,000 person-years in the United States [3] and 0.2–0.37 cases per 100,000 person-years across Europe [4, 5]; however, its incidence is thought to be greatly underestimated.

Most patients have early-stage MF at diagnosis, presenting typically with erythematous patches and/or plaques without evidence of extracutaneous involvement. Lesions are located mainly in sun-protected (sanctuary) areas of skin [6]. Early MF comprises patches and/or plaques, with or without non-lymphomatous lymphadenopathy, or low-level MF blood involvement [7] (Table 1). Cutaneous tumors and/or erythroderma with possible extracutaneous involvement are seen in advanced stages (stages IIB–IVB) [7, 8]. Although T stage (skin) is the single most important cutaneous prognostic indicator in early MF (T1 is defined as a cutaneous involvement with patches and/or plaques affecting  $< 10\%$

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## Key Points

Diagnosis of early mycosis fungoides (MF) is challenging and often delayed, in part due to the heterogeneity, subtlety, and location of lesions, which may mimic benign inflammatory dermatoses, but also a general lack of physician awareness.

Early diagnosis of MF is critical to avoid distress for the patient, who may be misdiagnosed and receive unnecessary and potentially harmful treatments, and probably to mitigate the risk of disease progression.

There is an urgent need for increased physician education regarding MF to enable expedited specialist referrals, and improved tools facilitating a speedy diagnosis, so that patients may receive guideline-recommended treatments early in their patient journey.

of body surface area [BSA], while T2 is characterized by these clinical features affecting  $\geq 10\%$  of BSA), patients with just patches tend to have a better prognosis than those with plaques [9]. Prognosis is generally good in early-stage MF, and considerably poorer in those with advanced stages presenting with tumors, erythroderma, blood, and/or nodal involvement [1]. Health-related quality of life (HRQoL) is reduced in MF, worsening with disease progression, due to insomnia, anxiety, depression, pruritus, and pain [10, 11].

Early diagnosis is important across all disease stages to allow timely appropriate management and avoidance of potentially harmful treatments, which may worsen cutaneous lesions and fuel disease progression, and to reduce patient distress [12–15]. Early diagnosis may also modify the subsequent disease course [16–18]. Some international guidelines recognize watchful waiting for patients with limited, stage IA MF [19, 20], while National Comprehensive Cancer Network guidelines also recommend interventional treatment [21]. Furthermore, according to a recent international registry report, most patients with early MF, including stage IA, received treatment as a first-line approach [22]. However, clinical diagnosis can be complicated by resemblance of early MF skin lesions to a range of benign inflammatory dermatoses (BIDs) [23], variable histology [23, 24], presence of variants [1, 23], and lack of definitive diagnostic markers [25]. Interobserver variation during histopathologic MF diagnosis has been reported in  $\sim 20\%$  of cases [24]. In one study, significant diagnostic variability was noted among three highly trained observers, which tended to be

greater for evaluation of early MF lesions. Despite using the same criteria during their diagnostic decision making, these observers weighted the criteria differently [26]. Diagnostic delays and/or misdiagnoses are common; one international registry reported delays for 86% of enrolled patients, with a median delay of 3 years (range 1–7.5 years) [25].

## 2 Methodology Used for Expert Panel Discussion

A panel with expertise in both clinical and histopathologic methods was convened (the authors of this work), which included six dermatologists, one hematologist, one oncologist, and two dermatopathologists from seven countries worldwide.

### 2.1 Aim

The objectives were twofold: to identify real-life barriers to early MF diagnosis in the countries represented by the panel; and to provide guidance for clinicians evaluating patients with chronic rash. Guidance was generated by reaching agreement on simple checklists that may be used to make an early diagnosis, including advice on when to include MF during differential diagnosis and how to confirm an uncertain diagnosis.

### 2.2 Methodology

The panel met virtually across different advisory board meetings and were asked to consider two objectives.

1. Identify the optimal patient journey toward a final MF-CTCL diagnosis through open discussion of shared experiences, focusing on the challenges associated with prompt diagnosis of early MF. Commonalities and differences between the geographic regions represented by the participants were noted.
2. Discuss potential tools that could be developed to help improve the diagnostic process for clinicians and patients.

The panelists were divided into two groups, each comprising three dermatologists, a hematologist/oncologist, and a dermatopathologist (with no group overlap), to participate in a virtual workshop. Over an 8-week period (prior to the final virtual meeting in September 2020), each group had access to a virtual room where they shared relevant and diverse experiences; progress was discussed at weekly and/or biweekly calls. The participants' personal experiences were harnessed to define the role and importance of each multidisciplinary team member required to diagnose

**Table 1** TNMB staging in mycosis fungoides and Sézary syndrome [7, 8, 20]

Stage	T	N	M	B
IA	T1: patches and/or plaques over <10% of BSA T1a: patches only T1b: plaques with or without patches	N0: no clinically enlarged nodes	M0: no visceral involvement	B0: < 250 per $\mu\text{L}$ of CD4+CD26- or CD4+CD7- cells by flow cytometry B1: does not meet criteria for B0 or B2
IB	T2: patches and/or plaques over $\geq 10\%$ of BSA T2a: patches only T2b: plaques with or without patches	N0	M0	B0 to 1
IIA	T1 or T2	N1: clinically enlarged nodes but histologically uninvolved (dermatopathic) N1a: clone negative N1b: clone positive N2: early involvement with MF (low level of nodal involvement), aggregates of atypical cells with preservation of nodal architecture N2a: clone negative N2b: clone positive	M0	B0 to 1
IIIB	T3: tumors; lesions $\geq 1$ cm diameter with deep infiltration	N0 to 2	M0	B0 to 1
IIIA	T4: erythroderma > 80% BSA involved	N0 to 2	M0	B0
IIIB	T4: erythroderma	N0 to 2	M0	B1
IVA1	T1–T4	N0 to 2	M0	B2: $\geq 1000$ per $\mu\text{L}$ of CD4+CD26- or CD4+CD7- cells by flow cytometry in the presence of a relevant T-cell clone in blood (identical to skin clone)
IVA2	T1–T4	N3: lymph nodes involved with loss of normal architecture	M0	B0 to 2
IVB	T1–T4	N0 to N3	M1: metastasis	B0 to 2

*B* blood, *BSA* body surface area, *M* metastasis, *MF* mycosis fungoides, *N* node, *T* tumor, *TNMB* tumor/node/metastasis/blood

MF-CTCL. Discussion points were gathered, generating guidance, diagnostic checklists (Boxes 1 and 2) and expert opinions confirmed by all.

### 3 Overview

#### 3.1 Diagnostic Delays

The patient journey from onset of early MF symptoms to diagnosis often involves repeated cycles of incorrect clinical and/or histopathologic diagnoses, and ineffective therapies [25]. Community dermatologists may misdiagnose classical early MF as inflammatory skin disease such as psoriasis, resulting in long-term topical steroid and/or systemic immunomodulatory treatment without a biopsy-driven diagnosis and meticulous follow-up. Partially treated lesions may further mask the disease. In many countries,

general practitioners manage skin diseases and mistakenly treat non-classical MF lesions with antifungal creams, subsequently misdiagnosing eczema or psoriasis if the lesions do not improve. Additionally, MF variants are frequently misdiagnosed [23, 27], and physicians may be unaware of the intra-individual variability of MF lesions. Furthermore, given their subtlety or location in sanctuary sites, lesions can easily be overlooked, resulting in underestimation of the extent of involvement. Delays may also occur during pathologic assessment. Although a shave biopsy can be useful in classical MF, these would be too superficial to allow evaluation of important diagnostic clues for certain variants. Moreover, general dermatopathologists and pathologists may not be sufficiently specialized to recognize the histologic subtleties and lymphoid atypia associated with MF, as cases are encountered rarely. Sampling errors can also cause missed diagnoses, particularly of folliculotropic MF—deeper sectioning of specimens may not be performed

in cases where adnexal structures, principally hair follicles, are absent. Finally, time from biopsy to pathology report can be prolonged, especially when performed by non-specialists; the COVID-19 pandemic has compounded these delays.

Thus, patients may be treated until several lines of therapy have failed before MF diagnosis or referral to a specialized center is considered. Moreover, some may not receive specialist care, such as those with limited or no medical insurance. In some countries, treatment cost is sometimes reimbursed only with a definitive MF diagnosis. While this may be difficult for the patient, it enables optimal treatment and avoids the use of inappropriate or sometimes harmful therapies. In other countries, suspicion of MF is enough to access guideline-recommended therapy.

Historically, ‘parapsoriasis’ has been used to describe conditions that clinically resemble psoriasis but lack some histopathologic MF features and are resistant to therapy. Large-plaque parapsoriasis is now generally considered to be the earliest MF stage [28]; up to 35% of patients advance to unequivocal, well-defined MF [29, 30]. Conversely, the small-plaque subtype (SPP) is considered by many authors as a nosologically separate entity [30, 31] that rarely progresses to MF [29, 32]. SPP shows a distinct clinical presentation characterized by yellow/brown digitate patches located on the flank and proximal extremities. In some regions, the term parapsoriasis continues to be used when a definitive MF diagnosis is difficult, offering the advantage of ongoing monitoring of patients who might develop MF and otherwise be lost to follow-up.

## 3.2 Steps to Arrive at a Correct Diagnosis

### 3.2.1 Physical and Histopathological Examination

Critical diagnostic steps include thorough physical examination, identification of suspected lesions, taking multiple biopsies from representative lesions, and appropriate evaluation of pathologic specimens. Crucially, there must be a correlation between clinical and histopathologic findings [24], sometimes achieved using validated scoring systems.

The International Society for Cutaneous Lymphoma (ISCL) score for early MF diagnosis is based on clinical, histopathologic, and immunohistochemical findings, as well as T-cell receptor (TCR) gene rearrangement [24]. These features can be useful for physicians who see few patients and emphasize the clinical/pathologic correlation in MF. The Guitart et al. criteria allows scoring of pathology based on assessments such as infiltrate density, nature, and extent of epidermotropism, and lymphocytic atypia grade [33]. However, both algorithms are useful for conventional forms of MF, but not variants.

Early MF lesions can be highly variable in size, shape, thickness, scaling, and color. While they are more common in

sanctuary sites [24], lesions can appear in sun-exposed areas (e.g., outer aspects of the upper limbs, head, and neck). Clinical manifestations often resemble common BIDs such as vitiligo, psoriasis, atopic dermatitis, and fungal infection [23, 34]. Suspected clinical presentations warrant thorough scrutiny of the entire skin surface. Experienced physicians may locate a subtle, previously undetected erythematous patch distant from the initial symptomatic site, providing crucial diagnostic information and informing biopsy-site(s) selection [24]. Key lesions can be missed, and suboptimal biopsy sites chosen if patients do not undress completely for the physical examination.

Early histopathologic MF features can be variable or less specific. Classical histology reveals superficial lymphoid infiltrates accompanied by epidermotropism (neoplastic T cells trafficking into the epidermis manifesting as atypical lymphocytes within the epidermis and as lymphocyte tagging at the dermoepidermal junction) [24, 35]. However, histopathologic findings of early-stage lesions often deviate from this classical pattern, with lymphocytes showing minimal/no atypical features and/or little evidence of epidermotropism [36]. Features that overlap with spongiotic, psoriasiform, or lichenoid dermatitis may also be apparent. Further complicating MF diagnosis is the presence of disease variants, three of which are recognized by the World Health Organization: pagetoid reticulosis, granulomatous slack skin, and folliculotropic MF [23, 37, 38].

Immunophenotyping of the skin—specifically intraepidermal lymphocytes—plays an important diagnostic role. A panel of markers, including CD3, CD4, CD5, CD7, CD8, and CD20, can aid in diagnosis [8]. Classically, intra-epidermal T cells in early-stage MF exhibit a CD3<sup>+</sup>CD4<sup>+</sup>CD8<sup>-</sup> phenotype; however, CD3<sup>+</sup>CD4<sup>-</sup>CD8<sup>+</sup> and CD3<sup>+</sup>CD4<sup>-</sup>CD8<sup>-</sup> phenotypes have also been observed [39, 40]. Analysis of TCR gene rearrangement, usually identified using polymerase chain reaction (PCR), is an important molecular diagnostic tool, especially in histopathologically suspicious but not diagnostic cases [24, 41]. Although monoclonality is observed in biopsies from some BIDs [42], detection of identical clones at two different sites was 95% specific for MF [43]. However, there may be few malignant cells in early-stage MF with little sign of clonality, rendering PCR testing unreliable in a significant fraction of early cases [41, 44]. High-throughput, next-generation TCR skin biopsy gene sequencing or peripheral blood samples is an emerging technique with potentially higher specificity than PCR-based techniques for differentiating MF from BIDs [44–46].

It should be stressed that while a correlation between clinical and pathologic findings is required for an accurate MF diagnosis, clinical findings should drive the diagnostic process. The central role of clinical features in the diagnosis of early MF was shown in a study assessing the validity of the proposed ISCL algorithm for defining early MF, by applying it in an investigator-blinded fashion to a set of MF cases

and benign clinicopathologic mimics [42]. Interestingly, of all four parameters (clinical, histopathological, immunohistochemical, and genotypical), the only observation that met statistical significance was that clinical criteria were more often achieved in MF cases than in controls [42].

### 3.2.2 Recommendations to Increase Biopsy Yield

1. Topical corticosteroids and other skin-directed therapies should be discontinued  $\geq 2$  weeks before biopsy; sunbathing should be avoided.
2. Perform two or more punch biopsies of the most representative lesions.
  - (a) If lesions are variable, multiple biopsies should be taken from several lesions.
  - (b) Punch size: 6 mm diameter is preferable. Deeper-punch biopsies are preferred in cases of clinical suspicion of adnexotropic/folliculotropic involvement. In case hair follicles are not observed, additional deeper sections should be ordered.

Of note, if the biopsy is inconclusive, lesions should be monitored for changes or progression. Confirmation of an uncertain diagnosis may require multiple biopsies taken over several years [47], which can be distressing for patients. Issues also arise if too few biopsies are taken, the sample is insufficient to allow thorough evaluation, inappropriate sites are biopsied (e.g., to avoid visible scarring), or if biopsies are obtained under suboptimal conditions (e.g., after topical steroid application or sun exposure).

### 3.3 Awareness and Training

Physician education is key to early MF recognition. Efforts are needed to increase awareness, particularly among community dermatologists and oncologists. Dermatologists, especially those practicing remotely from centers of excellence, may refer patients with a recently established MF diagnosis to an oncologist, who may treat them—sometimes inappropriately—with aggressive regimens not necessarily indicated without specialist referral. Patients with clinically suspected MF should be referred directly to centers of excellence for a complete diagnostic workup (clfoundation.org). Where this is impossible, biopsies should be sent to a dermatopathologist or pathologist who specializes in CTCL.

## 4 Diagnostic Checklists

The panel proposed two simple diagnostic checklists to help healthcare professionals recognize signs of MF, allowing identification of patients who should be

referred for further evaluation and appropriate management (Boxes 1 and 2). The clues in these boxes are not listed according to priority; diagnostic prioritization is not possible given the variety of clinical features that can be encountered.

#### Box 1 Features suggestive of MF or variants

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Main clinical clues for early MF or MF variant that should raise the red flag

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Persistent and/or progressive erythematous patches/plaques, sometimes with skin atrophy, especially in sanctuary areas

Persistent and/or progressive hypopigmented or hyperpigmented patches/plaques, sometimes with skin atrophy, especially in sanctuary areas

Elongated patches/plaques, especially that follow the cleavage lines, or kidney-shaped lesions located along the sides of the trunk and/or inner aspects of the extremities

‘Non-specific dermatitis’ on non-sanctuary areas that may be associated with pruritus, especially if progressive

Any unusual atopic dermatitis:

- Presumed ‘late-onset atopic dermatitis’, especially in the absence of a family/personal history of atopic dermatitis or atopic diathesis during childhood
- Absence of pruritus
- Prominent infiltration/induration of lesions on palpation
- Worsening of an eruption diagnosed as atopic dermatitis during treatment with appropriate therapies: topical agents and systemic treatment

Any unusual psoriasis vulgaris:

- Psoriasiform lesions with erosions/ulceration and/or impetiginization
- Worsening of an eruption diagnosed as psoriasis during treatment with appropriate therapies: topical agents and systemic treatment
- ‘Psoriatic lesions’ with erosions/ulceration and/or impetiginization

Any unusual keratoderma palmaris and/or plantaris after excluding the most common causes:

- Psoriasis, contact dermatitis/atopic dermatitis, and/or tinea

Any unusual follicular-based rash:

- Erythematous, hypopigmented and/or hyperpigmented patches/plaques with follicular accentuation
- Lesions resembling keratosis pilaris but in an unusual distribution and/or in clusters sometimes on faint base
- Acneiform eruptions in the absence of any relevant drug or known relevant associated condition; comedones in locations not characteristic of acne or hidradenitis suppurativa; acneiform and concomitant eczematous or psoriasiform lesions in the same areas
- Localized hair loss on what seems to be ‘dermatitis’ or in areas without lesions but only with scales (also look for focal eyebrow loss)

Any unusual chronic pigmented purpuric dermatosis:

- Patches/plaques in an extensive distribution (beyond the lower legs, occasionally with the buttocks—the usual locations in most cases)
- Coexisting with ‘nonspecific dermatitis’

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MF mycosis fungoides

**Box 2** Histopathologic and immunopathologic checklist

Histopathologic features suggestive of early MF	Pitfalls
<b>Epidermis</b>	
Pautrier micro-abscesses	Spongiotic Langerhans' cell vesicles
Lymphocytic epidermotropism generally without spongiosis	Spongiosis
Epidermal lymphocytes larger than dermal lymphocytes	
Tagging (lining up) of lymphocytes at the dermoepidermal junction	Interface or lichenoid dermatitis
High nuclear variability, hyperchromatic and/or folded nuclei, pericellular halo	Nuclear irregularities seen with interface/lichenoid dermatitis
<b>Dermis</b>	
Superficial dermal band-like lymphoid infiltrate	Lichenoid dermatitis, PPD
Fibrosis of papillary dermis (sign of chronicity)	Chronic/lichenified dermatitis
Variant folliculotropic MF: perifollicular lymphocytic infiltrate with folliculotropism with/without follicular mucinosis	Perifollicular infiltrates may be sparse
<b>Immunopathologic features<sup>a</sup> suggestive of early MF</b>	
Increased CD4:CD8 ratio (CD4 <sup>-</sup> , CD8 <sup>+</sup> or CD4 <sup>-</sup> CD8 <sup>-</sup> )	CD4 <sup>-</sup> CD8 <sup>-</sup> can also be observed after skin-directed (e.g., topical steroid) therapy
Loss of T-cell–marker expression on CD4 <sup>+</sup> lymphocytes	BID (drug- and contact-related) associated with loss of pan T-cell markers, particularly CD7

*BID* benign inflammatory dermatoses, *CD* cluster of differentiation, *MF* mycosis fungoides, *PPD* pigmented purpuric dermatosis

<sup>a</sup>Immunopathologic/molecular examination should be ordered if histologic examination and clinical features suggest MF (no consensus)

## 5 Discussion

Diagnosing MF early may improve patient outcome with mild, nonharmful therapies. Guideline-recommended, skin-directed treatments can have a positive impact on clinical outcomes, improve HRQoL [19, 21], and allow rapid treatment application. Given the indolent nature of MF, with progression occurring over several years, the impact of treatment on overall survival is unknown. However, MF may worsen if patients are misdiagnosed and receive inappropriate treatments [12–15] (e.g., if systemic regimens for eczema and psoriasis are administered). From the patient's perspective, delayed diagnosis prolongs suboptimal therapeutic outcomes, inevitably impacting their confidence in the medical team.

This international analysis of diagnostic challenges in MF revealed many common themes, as well as several geographical/regional differences in clinical practice (Table 2); these include frequency of diagnostic delays, physician lack of awareness/education, limited referral of suspected cases, uncertainty surrounding the value of early diagnosis, and utility of a pre-MF/parapsoriasis diagnosis. Regional differences in diagnosis and management include medical insurance and reimbursement issues, terminology differences (e.g., pre-MF/parapsoriasis), and differences in diagnostic procedures (e.g., use of additional blood testing and imaging depending on MF stage). A recent Italian MF expert consensus reported similar themes [47].

Research is urgently required to improve MF diagnostic tools. While such research is currently underway, an international collaborative effort is needed since validation of precision medicine techniques will require large patient numbers. Efforts are ongoing to develop a gene-expression or transcriptome profile for early MF [48, 49]. Identification of peripheral blood biomarkers (e.g., micro(mi)RNA, exosomes, free-circulant DNA) will be useful for early diagnosis and following treatment response. One potential biomarker, thymocyte selection-associated high mobility group box factor (TOX), is important for the development of CD4<sup>+</sup> cells but is not expressed in mature circulating CD4<sup>+</sup> cells [50, 51]. While TOX expression is not MF-specific, it is expressed in a greater proportion of MF cases versus BIDs and normal skin [41]. Pending confirmatory evidence, cell adhesion molecule 1 expression also has potential as a diagnostic biomarker for early MF, with greater expression being reported in MF than in BIDs [52]. Additionally, later-stage MF can be distinguished from early-stage disease, and CTCL distinguished from dermatitis via differentially expressed miRNAs [53–56].

Evaluation of biopsy specimens has also identified genes related to disease progression, including cell proliferation, immune checkpoints, resistance to apoptosis, and immune response, that are upregulated in late- versus early-stage MF, and thus potentially prognostic [57, 58]. Liquid biopsy sampling also revealed an association between high plasma levels of exosomal miRNA-1246, cell-free miRNA-155, and cell-free miRNA-1246 with advanced MF lesions, which may serve as promising non-invasive biomarkers [59]. However, these techniques are not yet commercially available; flow cytometry and TCR-gene clonality assessment are currently the only routinely available diagnostics for peripheral blood. Other tools include reflectance confocal microscopy, allowing non-invasive visualization of characteristic MF skin morphology [60, 61], and artificial intelligence algorithms based on clinical images and histopathology [62, 63]. However, their place in the diagnostic process for MF remains unclear.

**Table 2** Common themes and geographic/regional differences

Common themes	Details
Diagnostic delays	Delays are common for all regions
Clinical diagnostic uncertainty	Given the diagnostic challenges, some clinicians may try various treatments before referral
Incomplete physical examination	In cases of incomplete dermatologic examination (patients not undressed), physicians may fail to identify key lesions in sun-protected areas
Histopathology importance	Selecting the correct skin site for biopsy is key for MF to be diagnosed Notes: <ul style="list-style-type: none"> <li>• Presence of eosinophils could lead to misdiagnosis as a hypersensitivity reaction</li> <li>• Poikilodermatous MF can mimic the interface of lichenoid dermatitis</li> <li>• Ashy dermatosis/lichen planus pigmentosus and other lichenoid dermatoses can mimic MF; often mild lymphoid atypia are noted, requiring ancillary tests</li> <li>• Hypopigmented MF generally has a normal number of junctional melanocytes or only focal loss, unlike vitiligo, which presents with a significant loss of junctional melanocytes</li> <li>• Folliculotropic MF may show only a sparse perifollicular infiltrate or show features of follicular distortion/destruction, mucin deposition and follicular induction</li> <li>• In patients with suspected folliculotropic MF, in whom adnexal structures are barely seen or not seen at all at initial evaluation, deeper sections should be ordered</li> </ul>
Lack of awareness and education on MF	Education on MF is lacking for clinicians and for students in medical school
<b>Regional differences</b>	<b>Details</b>
Insurance and reimbursement issues	Access to both specialists and treatments varies from country to country
Terminology	Parapsoriasis is historically established and used as a diagnosis before MF is certain in many regions, but rarely in the United States
Staging and testing	Use of point-based staging, blood and lymph node investigation, flow cytometry, and imaging varies across regions

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## 6 Conclusion

This discussion provides a framework for promptly establishing an accurate early diagnosis of MF, which should be driven by clinical findings and subsequent correlation with pathologic findings. The diagnostic aids suggested here could help raise awareness of MF among clinicians and encourage referral of patients with suspected MF to centers of excellence, facilitating early diagnosis and treatment.

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## Declarations

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