Review

The Role of Dermoscopy, Ultrasonography and Confocal Microscopy in the Diagnosis of Mycosis Fungoides: Literature Review

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Abstract

Mycosis fungoides (MF), the most prevalent form of cutaneous T-cell lymphoma, is a chronic malignancy often challenging to diagnose in its early stages due to its overlapping clinical features with benign inflammatory dermatoses such as psoriasis, eczema, and atopic dermatitis. This chapter explores the roles of three non-invasive imaging techniques-dermoscopy, high-frequency ultrasound (HF-USG), and reflectance confocal microscopy (RCM)-in improving diagnostic accuracy, disease staging, and monitoring therapeutic responses in MF. Dermoscopy is instrumental in identifying characteristic vascular patterns and pigmentation that differentiate early-stage MF from other inflammatory conditions. HF-USG provides detailed imaging of the skin's internal architecture, with particular emphasis on the subepidermal low echogenic band, which serves as a key diagnostic marker of MF. Additionally, RCM offers near-histological visualization of cellular structures, enabling the detection of epidermotropic lymphocytes and Pautrier microabscesses, which are hallmark features of MF. The integration of these modalities significantly enhances diagnostic precision, reduces the need for invasive procedures, and offers a comprehensive framework for non-invasive evaluation of MF.

Keywords: Mycosis fungoides, dermatoscopy, confocal microscopy, ultrasonography, diagnosis

Introduction

Mycosis fungoides (MF), the most prevalent form of cutaneous T-cell lymphoma (CTCL), is a chronic malignancy with clinical features characterized by early, subtle presentations that may mimic benign inflammatory conditions like psoriasis, eczema, and atopic dermatitis These overlaps, particularly in the early stages, pose challenges for accurate diagnosis.[1]

Traditional methods of diagnosis, such as clinical inspection, histopathology, and immunohistochemistry are invaluable but often invasive and prone to variability, particularly in early-stage MF, where clinical and histopathologic signs can be subtle.[2]

To overcome these challenges, advanced non-invasive diagnostic modalities such as dermoscopy, high-frequency ultrasound (HF-USG), and reflectance confocal microscopy (RCM) have become integral in improving diagnostic precision.

This review focuses on the utility of these imaging tools in detecting, staging, and monitoring MF, emphasizing their non-invasive nature and their ability to complement traditional histopathological methods.

Dermoscopy in Mycosis Fungoides Diagnosis

Dermoscopy is a well-established technique in dermatology for the evaluation of skin lesions, offering a non-invasive

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method to observe vascular patterns, pigmentation, and scaling at a magnified level. In MF, dermoscopy provides valuable insights into the morphology of early lesions, which often present diagnostic challenges when assessed through clinical examination alone.[3]

Key dermoscopic features: Plaque stage: More advanced lesions, such as those seen in the plaque stage of MF, demonstrate dotted vessels and white patches (Figure 1a). These are particularly evident in thicker, more infiltrated lesions, where dermoscopic features become more pronounced.[4,5]

Vascular patterns in early-stage mycosis fungoides: One of the most distinguishing dermoscopic features of early MF is the presence of fine, short linear vessels arranged in a serpentine or spermatozoon-like pattern (Figure 1b). These vessels are usually accompanied by orange-yellowish patchy areas, which represent lymphocytic infiltration and the breakdown of blood by-products, such as hemosiderin. The vascular morphology in MF is often irregular and scattered, reflecting the patchy nature of lymphocytic infiltration in the superficial dermis.[4,5]

Dermoscopic vascular patterns in MF are distinct from other papulosquamous conditions. For instance, the dotted and linear vessels seen in MF are significantly different from the dilated capillaries observed in psoriasis and the irregular capillaries found in chronic eczema. In MF, vessels often run vertically along the dermal papillae and horizontally in the subpapillary dermis.[6,7]

Scaling and surface features: In early MF, fine white scaling is often present, but it tends to be thin and perifollicular, forming around hair follicles rather than covering the entire lesion (Figure 1). This perifollicular pattern contrasts with the thicker and more diffuse scaling seen in psoriasis, where scaling is more widespread and associated with hyperkeratosis. In psoriasis, the scaling tends to be silvery-white and covers a larger portion of the plaque surface.[7,8]

Recent studies indicate that certain hair shaft abnormalities, including multiple pili torti (observed in 67% of MF cases), 8-shaped hairs, and rapidly tapered hair shafts, are predominantly associated with MF. In contrast, single pili torti appear infrequently in psoriasis (16%) and eczematous dermatitis (8%), suggesting that these findings can aid in distinguishing MF from other inflammatory skin conditions.[9]

Dermoscopic-histopathologic correlation: Dermoscopy findings in MF correlate closely with histopathologic features. Fine, short linear vessels correspond to dermal capillaries within the papillary dermis, infiltrated by atypical T-lymphocytes. Additionally, orange-yellowish patches seen in dermoscopy reflect hemosiderin deposits or dense inflammatory infiltrates, aiding in the differentiation from other dermatoses (Figure 1a).[8]

Dermoscopic findings exhibit notable variation across different clinical types of MF, with each subtype showing specific patterns. In syringotropic MF, for instance, characteristic dermoscopic features include follicular accentuation, plugging, and bluish areas that correlate with eccrine gland involvement. Conversely, folliculotropic MF often presents with follicular obliteration without the bluish hue observed in syringotropic MF. These distinct dermoscopic patterns reflect underlying histopathologic differences between MF subtypes, underscoring dermoscopy's utility in accurately differentiating and diagnosing these variants.[10]

Additionally, purpuric dots are sometimes visible in early-stage MF, corresponding to extravasation of red blood cells due to inflammation-induced vascular damage. These purpuric dots are rarely seen in other inflammatory conditions and can serve as a differentiating feature.[10]

Summary Highlights of the Dermoscopic Findings That Differentiate Other Inflammatory Dermatoses from Mycosis Fungoides

Psoriasis (plaque psoriasis):

- **Vessels:** Regular dotted vessels throughout the lesion, representing dilated capillaries within dermal papillae.
- **Scaling:** Thick silvery-white scaling covering most of the plaque.
- **Pigmentation:** Homogeneous pink to red background, with no orange-yellow areas.
- **Conclusion:** The uniformity of vascular patterns and diffuse scaling in psoriasis differ from the irregular, fine linear vessels and localized perifollicular scaling seen in MF.[2]

Chronic eczema:

- **Vessels:** Dotted vessels similar to psoriasis but more widely spaced and less uniform.

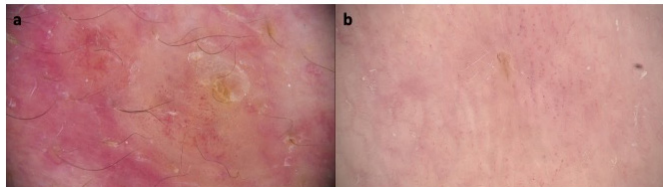

Figure 1. (a) White scale and orange-yellowish pathces. (b) Spermatozoon-like vascular pattern

- **Scaling:** More diffuse scaling, although not as thick as psoriasis.

- **Pigmentation:** Lesions typically exhibit a homogeneous red background with less color variation.

- **Conclusion:** The lack of orange-yellowish areas and less serpentine vascular patterns distinguish chronic eczema from early-stage MF.[2,3]

Atopic dermatitis:

- **Vessels:** Exhibits dotted vessels, but usually within areas of lichenification and xerosis.

- **Scaling:** Tends to show dry scaling associated with lichenification, unlike the fine white perifollicular scaling in MF.

- **Pigmentation:** Often presents with a pale pink background, with little evidence of orange-yellowish pigmentation.

- **Conclusion:** Atopic dermatitis lacks the characteristic vascular features and orange-yellowish patches seen in early-stage MF.[2,3]

In conclusion, the presence of fine, short linear vessels, orange-yellowish patchy areas, and perifollicular white scaling are distinctive markers of early MF. Recognizing these dermoscopic hallmarks is essential for clinicians to improve diagnostic accuracy and initiate appropriate treatment at an earlier stage, potentially altering the disease course and improving patient outcomes.

High-Frequency Ultrasound in Mycosis Fungoides Diagnosis

HF-USG is a pivotal imaging modality for evaluating the structural and morphological changes in MF lesions. Unlike dermoscopy, which primarily assesses surface characteristics, HF-USG provides a detailed view of the skin's internal architecture, including the epidermis, dermis, and subcutaneous layers.[11]

HF-USG uses sound waves to produce detailed images of the skin's structural layers. It is a non-invasive imaging modality that has proven valuable in dermatological practice, particularly for measuring skin thickness and assessing the depth of infiltration in various cutaneous conditions.[12]

HF-USG operates at frequencies typically between 20 MHz and 50 MHz, which allows for high-resolution imaging of superficial structures like the epidermis, dermis, and upper subcutaneous tissue.[11] The depth of penetration of HF-USG is inversely proportional to its frequency, meaning higher frequencies provide more detailed images but can only assess superficial layers up to 15-25 mm.[11,12]

The ultrasound image is generated based on the reflection of sound waves from tissues of different densities. As the ultrasound waves encounter boundaries between different tissues (e.g., the epidermis and dermis), they are reflected back to the transducer. The intensity and timing of these reflections are translated into an image based on the echogenicity (brightness) of the tissues.[11]

Subepidermal low echogenic band: The presence of the subepidermal low echogenic band (SLEB) is one of the hallmark ultrasound findings in MF (Figure 2). This band represents the infiltration of atypical T-cells in the superficial dermis and is a key differentiator between MF and other inflammatory dermatoses.[13]

The SLEB is typically seen as a hypoechoic (dark) band located just below the epidermis. In MF, this band is significantly thicker compared to inflammatory conditions like psoriasis and eczema. The thickness of the SLEB correlates with the degree of infiltration of malignant cells in the dermis and can serve as a reliable diagnostic marker.[14]

In comparison to other dermatoses, the SLEB in MF is more prominent and persists even in patch-stage lesions, where other inflammatory conditions may show a thinner or absent SLEB.[15]

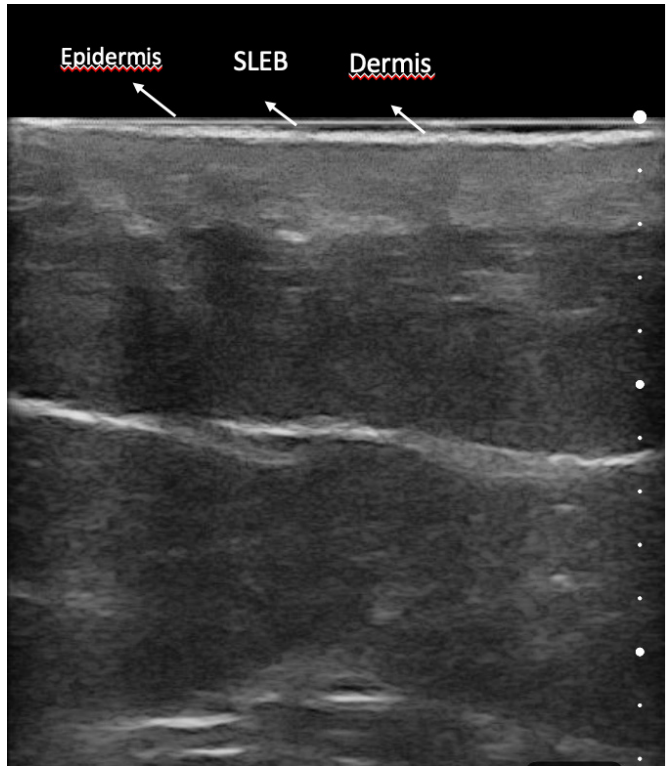

Figure 2. SLEB in MF lesion
SLEB: Subepidermal low echogenic band, MF: Mycosis fungoides

Epidermal and dermal changes: HF-USG can assess the thickness and echogenicity of the epidermis and dermis. In MF, there is a reduction in dermal echogenicity, which reflects the presence of atypical lymphocytes infiltrating the skin. This reduction is due to the displacement of normal collagen and dermal structures by the infiltrating cells, resulting in decreased reflection of the ultrasound waves.[16]

In addition to the decreased echogenicity, MF lesions often show increased epidermal thickness**,** particularly in plaque-stage MF. This thickening is a result of epidermal hyperplasia and infiltration by malignant cells, which can be clearly visualized in HF-USG.[16]

Vascular involvement: HF-USG is also capable of detecting changes in the vascular structures of the skin. In MF, increased blood flow to the affected area, as well as dilated blood vessels, can be identified using color Doppler ultrasound, which is an adjunct to HF-USG. These vascular changes often correlate with the inflammatory nature of the lesions and the presence of malignant infiltrates within the skin.[17]

Unlike psoriasis, which often shows prominent vascular changes related to dilated capillaries in dermal papillae, the vascular alterations in MF tend to be less uniform and may reflect localized areas of lymphocytic infiltration.[14,18]

Clinical utility of HF-USG: HF-USG is an helpfull tool for distinguishing between patch and plaque stages of MF. In patch-stage MF, HF-USG shows superficial dermal involvement with minimal deep tissue changes. In contrast, plaque-stage lesions exhibit deeper infiltration into the dermis, which can be quantitatively measured using HF-USG. The SLEB observed in HF-US is not exclusive to MF or Sézary syndrome (SS), thus limiting the diagnostic specificity of HF-US for these conditions. Consequently, while HF-US provides valuable structural and staging insights, its diagnostic value remains relatively restricted in distinguishing MF/SS from other dermatoses.[17]

HF-USG has demonstrated effectiveness in monitoring treatment response in MF patients undergoing PUVA and UVA1 phototherapy. The SLEB was present in all patients prior to treatment. After phototherapy, significant thinning or complete disappearance of the SLEB was observed, correlating with clinical improvement. In cases of complete response, the SLEB vanished entirely, while in cases of partial response, there was a reduction in SLEB thickness. These findings indicate that HF-USG can serve as an objective, non-invasive tool to evaluate the efficacy of MF treatments by quantifying changes in SLEB thickness and dermal echogenicity, which correspond to treatment outcomes.[19]

Reflectance Confocal Microscopy in MF Diagnosis

RCM offers a high-resolution, cellular-level view of the epidermis and superficial dermis, providing a near-histological assessment without the need for biopsy. RCM allows real-time imaging, which is particularly useful in early-stage MF where histopathologic features may be subtle.[20]

In early-stage MF, RCM typically reveals epidermotropic lymphocytes, which appear as round, refractile cells scattered within the epidermis.[21] This corresponds to the histological finding of atypical T-cells invading the epidermis.[22]

In some cases, RCM can detect spongiosis, characterized by intercellular edema, which correlates with early MF histology.[22,23]

More advanced lesions in plaque-stage MF may show Pautrier microabscesses, which appear as vesicle-like structures filled with refractile material. These are considered diagnostic of MF and can be visualized using RCM.[24]

Limitations of RCM: Despite its advantages, RCM has some limitations, including limited imaging depth (typically up to 200-300 microns), which makes it less effective for evaluating deeper dermal involvement. Moreover, RCM may struggle to distinguish between certain cell types, particularly in the context of complex inflammatory infiltrates.[25]

RCM is a valuable adjunct to traditional histopathology. It is particularly useful for selecting optimal biopsy sites, reducing false-negative biopsy results, and providing additional information in ambiguous cases.[22]

Conclusion

The integration of dermoscopy, HF-USG and RCM offers a robust, non-invasive diagnostic framework for MF. Each modality provides unique insights that, when combined, significantly enhance diagnostic accuracy.

- Dermoscopy provides detailed surface-level information on vascular patterns, scaling and pigmentation.

- HF-USG adds depth by evaluating lesion infiltration, SLEB thickness, and dermal changes.

- RCM offers near-histologic resolution of epidermal and dermal structures, identifying atypical lymphocytes, microabscesses, and other key features.

Footnotes

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