Dermoscopy in the Diagnosis of Mycosis Fungoides: Can it Help?

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ABSTRACT

Introduction: The diagnosis of mycosis fungoides (MF) is challenging since it can mimic a variety of benign skin conditions. Multiple biopsies for histopathologic and immunohistochemical examination are required to diagnose MF. Dermoscopy is an affordable, non-invasive device with expanding indications in dermatology,

Objectives: To investigate the dermoscopic morphology of MF variants and assess the correlation between dermoscopic criteria, histopathologic, and immunohistochemical findings,

Methods: We included 88 patients with several MF variants (classic, hypopigmented, hyperpigmented, poikilodermatous, erythrodermic, and folliculotropic). The diagnosis was histopathologically and immunohistochemically confirmed. Dermoscopic findings were collected, statistically analyzed, and correlated with the results of histopathology and immunohistochemistry,

Results: All patients had MF diagnosis in H&E-stained sections. The majority revealed positive staining with CD3, 4, 8 and negative CD7. Orange-red areas of discoloration, short linear, and spermatozoa like blood vessels are the most frequent dermoscopic findings, while an analysis per MF variant was also performed. The frequently observed dermoscopic structures in classic MF were patchy whitish scales, dotted, short linear vessels, and spermatozoa-like vessels,

Conclusions: Dermoscopy reveals a repetitive dermoscopic pattern in MF (non-homogenous pink to erythematous background, patchy areas of orange discoloration, patchy whitish scales, dotted and short linear blood vessels with some variations according to the clinical variant.

Introduction

Cutaneous T-cell lymphoma is the most frequent extra-nodal non-Hodgkin lymphoma. It comprises a wide variety of types, the most frequent being mycosis fungoides (MF) and Sezary syndrome (SS) [1]. MF is characterized by a significant variability of clinical manifestations. Classically, it evolves in 4 sequential stages (patch, plaque, tumor, and erythrodermic), but several less frequent clinical variants do exist (eg hypopigmented, poikilodermatous) [2]. The diagnosis of MF is very often challenging and necessitates the integration of information acquired by clinical histopathologic and immunohistochemical assessment [1].

In addition to its usefulness in the assessment of pigmented cutaneous lesions [3], dermoscopy gains a role in the diagnosis of non-pigmented skin diseases as well, including inflammatory and infectious diseases [4–6]. Allowing the visualization of vascular structures, scales, color variegations, follicular abnormalities, and other structures, dermoscopy provides a link between clinical evaluation and dermatopathology and is considered an essential device for dermatologists in their daily practice [5]. MF has been reported to display a different dermoscopic pattern compared to chronic eczema, which represents the main differential diagnosis and dermoscopy was suggested to facilitate MF diagnosis by guiding to a more accurate biopsy for histopathologic examination and immunohistochemistry [6].

Objectives

This study aimed to investigate the dermoscopic features of MF, to assess the distribution of these features per clinical variant and to and to correlate these features with histopathologic and immunohistochemical alterations.

Methods

This cross-sectional study included a total of 88 patients with several clinical variants of MF whose diagnosis was based on the clinical presentation of skin lesions and confirmed by histopathological and immunohistochemical examinations. After obtaining the research ethics committee approval from our faculty of medicine, we included all patients diagnosed with MF at the outpatient clinic, cancer institute, and private clinics, in the period between November 2013 and May 2016.

Inclusion criteria were the following:

1. A definitive diagnosis of MF established histopathologically and immunohistochemically. A combination of at least 3 of the following histopathological criteria is the

basis for diagnosis of the studied cases: atypical lymphocytes, epidermotropism with Pautrier microabscesses, some atypical lymphocytes exhibited arrangement along the epidermal side of the dermo-epidermal junction and atypical dermal infiltrate with a variable density as proposed by Smoller et al [7]. Immunohistochemically stained tissues using CD3,4,8, and 7 were performed and assessed according to the percentage of stained cells considering the positive stain if the percentage \geq 30% whereas percent \leq 30% is considered negative [8]. CD3 positive staining with positive CD4 or CD8, and negative staining for CD7 were the immunohistochemical features of most of the included cases.

- 2. The presence of clinical manifestations (even mild) at the time of inclusion. Persistent erythematous patches, plaques, and or nodules with necrosis and ulceration were the criteria of classic MF. While multiple hypopigmented well- defined macules on the trunk with prevalence on the lower back were the characteristic for hypopigmented variant, hyperpigmented variant represented black colored hyperpigmented patches without scaling nor atrophy or telangiectasias. Localized or diffuse patches comprised of atrophy, telangiectasia, hypo or hyperpigmentation were the clinical criteria in the poikilodermatous variant. Regarding erythrodermic variant, there was generalized erythroderma while acneiform lesions, cystic comedones, alopecia, and follicular papules were the most frequent presentations of folliculotropic variant.
- 3. No prior treatment or no treatment within the last 6 months. All patients who accepted to participate in the study signed written consent. Exclusion criteria were the application of any topical treatment, phototherapy, or systemic treatment within the last 6 months, pregnancy or lactation, and the co-existence of other dermatological diseases.

The patients have been classified into the following clinical variants; classic patch stage MF; the commonest variant with gradual progression from patches to more infiltrated plaques and eventually tumors, hypopigmented MF which is rare and characterized by solely hypopigmented patches or in combination with erythematous patches or plaques, poi-kilodermatous MF identified by localized or diffuse large macules and patches of mottled hypopigmentation and hyperpigmentation with atrophy and prominent telangiectasia, folliculotropic MF; a rare variant frequently presented by folliculotropic infiltrates usually involving the head and neck area, erythrodermic MF which is infrequent with intractable progressive erythroderma, and hyperpigmented MF; an extremely rare variant with hyperpigmented plaques without poikiloderma.

All patients were subjected to a thorough dermatological examination to evaluate the morphology and distribution of skin lesions and to exclude any co-existent dermatological disease. The dermoscopic examination was performed using Dermlite II PRO HR (3Gen) using polarized light, magnification x10. Digital images of both clinical and dermoscopic features of the same MF biopsied lesions were taken by digital camera Sony: Cyber-Shoot DSC-W690. The selection of the dermoscopic variables to be included in the analysis was based on pre-existing literature on dermoscopy of MF, adjusted to a consensus paper on the terminology of dermoscopy in general dermatology [5].

Skin biopsies were taken from all patients; formalin-fixed routinely processed paraffin-embedded tissue sections (3-5 μ) and prepared on charged glass slides for confirmation of the diagnosis of MF using light microscopy (Leica DM 500). Immunohistochemical staining of tissue sections was conducted using antibodies against CD3, CD4, CD8, and CD7 and then repeated on a second freshly obtained biopsies after recruiting study participants. All biopsies were obtained from the same sites of dermoscopic examination. Ethical Committee in our institution approved the study.

Statistical Analysis

We calculated the sample size according to Raosoft and all statistical calculations were done using SPSS (statistical package for the social science version 26.00) statistical program. at 0.05, 0.01, and 0.001 level of probability. Qualitative (categorical) data were presented by frequency and percentage was done using chi-square, Pearson linear correlation coefficient (r) was estimated to show the relationship between histopathological features (atypical lymphocytes or epidermotropism with Pautrier micro-abscesses or alignment of atypical lymphocytes or atypical dermal infiltrate) and dermoscopic features [9].

Results

Clinical Results

Out of 88 patients, 48 patients (54.6%) had classic MF, among them 32 (36.4%) presented with the patch stage, and 16 (18.2%) presented with both patch the tumor stages. Twenty patients (22.8%) had hypopigmented MF, 8 patients (9.1%) had poikilodermatous MF, and the study also included 12 patients; 4 patients (4.5%) from each of the following: folliculotropic, erythrodermic, and hyperpigmented MF (Table 1).

The patients were 44 males (50%) and 44 females (50%). Their ages varied from 10-65 years. The duration of MF lesions ranged from 3 months-20 years. The number of patients who had previous treatment was 32 (36.4%), those patients were either recurrences or who stopped their

treatment due to side effects but still have lesions, while the other 56 (63.6%) received no treatment (Table 2).

Histopathological Examination

Histopathological examination of tissue sections stained with H&E from MF lesions revealed; all patients (100%) had atypical lymphocytes, 84 patients (95%) had epidermotropism escorted with pautrier micro-abscesses, some atypical lymphocytes showed arrangement along the epidermal side of the dermo-epidermal junction in 48 patients (54.5%) and all patients (100%) had atypical dermal infiltrate with variable density (Figure 1). Overall, all patients presented with the typical morphological histopathological criteria recommended by Smoller et al [7].

Immunohistochemical Examination

To begin with CD3, all the patients (100%) revealed positive staining. About CD4, 76 (86.4%) patients showed positivity

Table 1. Classification of the patients according to mycosis fungoides clinical variant.

| Mycosis fungoides variant | No. | % |
|-----------------------------------|-----|------|
| Classic mycosis fungoides | 32 | 36.4 |
| (patch stage) | | |
| Classic mycosis fungoides | 16 | 18.2 |
| (patch/ tumor stages) | | |
| Hypopigmented mycosis fungoides | 20 | 22.8 |
| Poikelodermatic mycosis fungoides | 8 | 9.1 |
| Follicultropic mycosis fungoides | 4 | 4.5 |
| Erythrodermic mycosis fungoides | 4 | 4.5 |
| Hyperpigmented mycosis | 4 | 4.5 |
| fungoides | | |

Table 2. Distribution of the patients according to demographic data.

| 0 1 | | | | | | |
|--------------------|-----|-------|--|--|--|--|
| | No. | % | | | | |
| Sex | | | | | | |
| Male | 44 | 50.0 | | | | |
| Female | 44 | 50.0 | | | | |
| Age/ year | | | | | | |
| ≤30 | 32 | 36.4 | | | | |
| 31 – 40 | 28 | 31.8 | | | | |
| >40 | 28 | 31.8 | | | | |
| Duration/ year | | | | | | |
| ≤ 1 yrs | 32 | 36.4 | | | | |
| > 1 yrs – 6 yrs | 48 | 54.5 | | | | |
| > 6 yrs | 8 | 9.1 | | | | |
| Previous treatment | | | | | | |
| No | 56 | 63.6% | | | | |
| Yes | 32 | 36.4% | | | | |

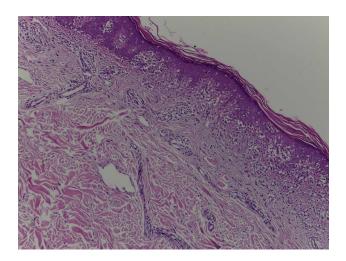


Figure 1. H&E of skin biopsy from classic mycosis fungoides (x10); dermal infiltrate with atypical lymphocytes with alignment at dermo epidermal junction, epidermotropism with Pautrier microabscess.

while 12 (13.6%) were with negative staining. 65 (73.9%) of our patients had positive CD8 stains and 23 (26.1%) were negative. 84 (95%) patients had a loss of CD7 expression. Finally, the CD4/CD8 ratio was more than 4 in 72 (81.9%) of the studied patients.

Dermoscopic Examination

The analytic results of the dermoscopic evaluation are shown in Table 3. The most frequent dermoscopic features in the total study population were (by category):

Background Changes:

a. A pink to the erythematous background was found in 72 patients (81.8%), a non-homogenous background in 68 patients (77.3%), and patchy areas of orange discoloration in 68 patients (77.3%).

Vascular Pattern:

b. In 64 patients (72.7%) dermoscopy revealed dotted and short linear vessels, while spermatozoa-like vessels were detected in 44 patients (50%) and arborizing vessels in 16 patients (18.2%).

Scales:

c. Fifty-six patients (63.6%) had patchy whitish scales, while perifollicular and interfollicular scaling was found in 4 patients (4.5%).

Other Structures:

d. Blue-gray and dark globules were seen in 32 patients (36.4%), 20 patients (22.7%) showed focal white structureless areas in 20 patients (22.7%), while white globules were found in 16 patients (18.2%), and red globules in 12 patients (13.6%).

The analytic results of the dermoscopic evaluation according to the MF variant are shown in (Table 4). In all of the 48 patients with classic MF, dermoscopy revealed a pink to erythematous background with non-homogeneous distribution. The most frequently observed dermoscopic structures were patchy whitish scales (44/48, 91.7%), dotted and short linear vessels (44/48, 91.7%), spermatozoa-like vessels (32/48, 66.7%), and patchy areas of orange discoloration, (24/48, 50%) (Figure 2).

Concerning the most frequent findings in other rare MF variants, the erythrodermic variant exhibited

Table 3. Dermoscopic findings of the studied mycosis fungoides patients.

| | | No. | % |
|--------------------|--|-----|------|
| Background changes | Non-homogenous background | 68 | 77.3 |
| | Pink to erythematous background | 72 | 81.8 |
| | Patchy areas of orange discoloration | 68 | 77.3 |
| Vascular pattern | Dotted blood vessels | 64 | 72.7 |
| | Short linear blood vessels | 64 | 72.7 |
| | Spermatozoa like blood vessels | 44 | 50.0 |
| | Arborizing blood vessels | 16 | 18.2 |
| Scales | Patchy whitish scales | 56 | 63.6 |
| | Perifollicular and interfollicular scaling | 4 | 4.5 |
| Globules | Blue-gray globules | 32 | 36.4 |
| | Dark globules | 32 | 36.4 |
| | Patchy red globules | 12 | 13.6 |
| Pigmentation | Multifocal pigmentation | 4 | 4.5 |
| | Foggy whitish areas | 20 | 22.7 |
| | Hypopigmented areas | 20 | 22.7 |
| | Pearly white globules | 16 | 18.2 |
| Structures | Comedo like openings | 4 | 4.5 |

Table 4. Relation between clinical variants of mycosis fungoides and dermoscopic features.

| | Classic | Classic MF (patch stage) (n=48) |) (n=4 | (e) | | | Other MF variants (n=40) | its (n=40) | | | | |
|--|-----------------------|---------------------------------|--------|-------|---------------|-------------------------|--------------------------|---------------------------|-----------------|-------|------|--------|
| | Classic- | Classic- patch | | | Erythrodermic | | | | Hyperpig- | | | |
| Dermoscopic features | patch stage (n=32) | stage & tumor (n=16) | Total | % | (n=4) | Hypopigmented (n=20) | Poikelodermatic (n=8) | Folliculotr-opic (n=4) | mented (n=4) | Total | % | ۵ |
| Non-homogenous Background | 100% | 100% | 48 | 100.0 | 100% | %00.0 | 100% | 100% | 100% | 20 | 50.0 | <0.001 |
| Patchy whitish scales | 87.50% | 100% | 44 | 91.7 | 100% | %00.0 | 0.00% | 100% | 100% | 12 | 30.0 | <0.001 |
| Perifollicular and interfollicular scaling | %00.0 | 0.00% | 0 | 0.0 | 0.00% | %00.0 | 0.00% | 100% | %00.0 | 4 | 10.0 | 0.025 |
| Pink to erythematous background | 100% | 100% | 48 | 100.0 | 100% | 20.00% | 100% | 100% | 100% | 24 | 60.0 | <0.001 |
| Patchy areas of orange discoloration | 87.50% | 100% | 44 | 91.7 | 100% | 20.00% | 100% | 100% | 100% | 24 | 60.0 | <0.001 |
| Blue gray globules | 37.50% | 75.00% | 24 | 50.0 | 0.00% | 0.00% | 0.00% | 100% | 100% | 8 | 20.0 | 0.004 |
| Dark globules | 37.50% | 75.00% | 24 | 50.0 | 0.00% | %00.0 | 0.00% | 100% | 100% | 8 | 20.0 | 0.004 |
| Patchy red globules | 12.50% | 25.00% | 8 | 16.7 | 100% | %00.0 | 0.00% | 0.00% | 0.00% | 4 | 10.0 | 0.364 |
| Multifocal pigmentation | 0.00% | 0.00% | 0 | 0.0 | 0.00% | 0.00% | 0.00% | 0.00% | 100% | 4 | 10.0 | 0.025 |
| Foggy whitish areas | %00.0 | %00.0 | 0 | 0.0 | 0.00% | 100% | 0.00% | %00.0 | %0 | 20 | 50.0 | <0.001 |
| Comedo like openings | %00.0 | 0.00% | 0 | 0.0 | 0.00% | %00.0 | 0.00% | 100% | %00.0 | 4 | 10.0 | 0.025 |
| Hypopigmented areas | 0.00% | 0.00% | 0 | 0.0 | 0.00% | 100% | 0.00% | 0.00% | 0.00% | 20 | 50.0 | <0.001 |
| Pearly white globules | 12.50% | 0.00% | 4 | 8.3 | 0.00% | %00.09 | 0.00% | 0.00% | 0.00% | 12 | 30.0 | 0.009 |
| Dotted blood vessels | 87.50% | 100% | 44 | 91.7 | 100% | 0.00% | 100% | 100% | 100% | 20 | 50.0 | <0.001 |
| Short linear blood vessels | 87.50% | 100% | 44 | 91.7 | 100% | %00.0 | 50.00% | 100% | 100% | 20 | 50.0 | <0.001 |
| Spermatozoa like blood vessels | 20.00% | 100% | 32 | 66.7 | 100% | %00.0 | 50.00% | 100% | 0.00% | 12 | 30.0 | 0.001 |
| Arborizing blood vessels | %00.0 | %00.0 | 0 | 0.0 | 100% | %00.0 | 100% | 100% | 0.00% | 16 | 40.0 | <0.001 |
| | | | | | | | | | | | | |

^aP p-value for Chi-square test for comparing between the different categories, significant at p-value < 0.05, highly significant at p-value < 0.001.

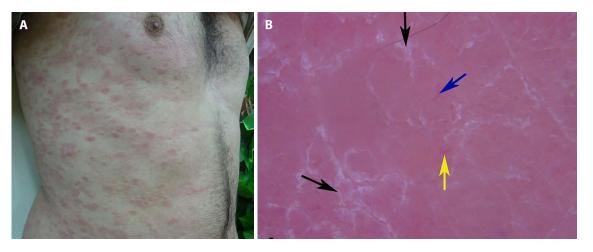


Figure 2. (A) Male patient presented with classic mycosis fungoides, showing multiple erythematous scaly plaques on trunk. (B) Dermoscopic features of lesions on the trunk; patchy whitish scales (black arrows), spermatozoa like blood vessels (yellow arrow), and short linear blood vessels (blue arrow) on pink to erythematous background, polarized light x10.

non-homogenous pink to erythematous background (4/4, 100%), dotted, short linear, spermatozoa like and arborizing blood vessels (4/4, 100%). (Figure 3) The hypopigmented variant was characterized by foggy whitish areas (20/20, 100%), hypopigmented areas (20/20, 100%), and pearly white globules (12/20, 60%). The poikilodermatous variant revealed patchy areas of orange discoloration (8/8, 100%), dotted (8/8, 100%), and arborizing blood vessels (8/8, 100%), folliculotropic variant (Figure 4) presented perifollicular and interfollicular scaling (4/4, 100%), comedo-like openings (4/4, 100%), dotted, short linear, spermatozoa like (Figure 5) and arborizing blood vessels (4/4, 100%), hyperpigmented variant showed blue-gray globules (4/4, 100%), dark globules (4/4, 100%), dotted and short linear blood vessels (4/4, 100%). Regarding the correlation between the frequently encountered dermoscopic features of MF with histopathological findings (Table 5); non-homogeneous background, showed a statistically significant moderately positive correlation with the presence of atypical dermal infiltrates (ADI) (P < 0.001), while showed a weak positive correlation with atypical lymphocytes (AL), epidermotropism and Pautrier microabscesses (E and PMA) and alignment of atypical lymphocytes (AAL) with high statistical significance (P 0.003, 0.33 and 0.006, respectively). Patchy whitish scales showed a statistically significant strong positive correlation with AL, E, PMA, AAL, and ADI (P < 0.001). Pink to erythematous background showed a strong positive correlation with AL and E, PMA (P < 0.001), on the other hand, showed a weak positive correlation to AAL and ADI (P = 0.03). Patchy areas of orange discoloration and short linear blood vessels showed a strong positive correlation with all findings which was highly statistically significant (P < 0.001). Spermatozoa-like blood vessels showed a strong positive correlation with AL, E, and PMA (P < 0.001) and a moderately strong positive correlation to both AAL and ADI (P < 0.001).

Conclusions

Our study provides novel insights into the dermoscopic morphology of MF according to the clinical variant. Overall, our results are consistent with pre-existing evidence [10].

Classic patch stage MF was dermoscopically typified by a pink to erythematous background, patchy orange-yellowish color, patchy whitish scales, dotted and fine short linear vessels. These results are in perfect agreement with the previous study by Lallas et al [10]. However, a pink to erythematous background, which results from dilatation of dermal blood vessels, was found to be not specific for MF, since it is also frequent in psoriasis, chronic dermatitis, and lichen planus [11].

Patchy areas of orange discoloration which represent serum oozing from erosions [12], were observed in the patch stage of classic MF. This feature was previously suggested as a significant criterion for the differential diagnosis between MF and chronic dermatitis [10]. In our study, we did observe this feature in all clinical variants of MF without significant differences among them.

Dotted and short linear blood vessels, that correlate with vertical vessels [12] and tumor angiogenesis [11] respectively, were observed mostly in patients with patch stage of classic MF. Also, the peculiar vascular structure consisting of a dotted and a linear vessel (spermatozoa like blood vessels) were observed in 66.7% of classic MF patients, and 30% of other rare MF variants including erythrodermic, folliculotropic, and poikilodermatous variants. This feature was previously described as a dermoscopic characteristic of classic MF, but it has not been reported in other MF variants.

We detected patchy whitish scales, that correspond to areas of parakeratosis [11], in classic, erythrodermic, folliculotropic, and hyperpigmented variants of MF. This is in line with the study by Saleh MA and Abdel Halim DM who



Figure 3. (A) Female patient presented with erythrodermic mycosis fungoides, with erythema and scales on the face. (B) Dermoscopic features of lesions of the face; dotted blood vessels (red arrows), patchy whitish scales (yellow arrow), and spermatozoa like blood vessels (blue arrows), all on non-homogenous pink background, polarized light x10. (C) The same patient with erythema on the back of the legs. (D) Dermoscopic features of lesions of the legs; dotted blood vessels (yellow arrow), and spermatozoa like blood vessels (white arrow) on non-homogenous pink background, polarized light x10.

observed these scales in classic and hyperpigmented variants. As scales were observed in MF as well as some inflammatory skin diseases, they were not specific for MF diagnosis [10,11].

Dermoscopic examination of hyperpigmented MF revealed multifocal pigmentation and dark and blue-gray globules that represent epidermal or horny layer melanin or blood and melanophages in the papillary dermis respectively [11]. This was observed previously by Saleh and Abdel Halim. Thus, it can be concluded that these globules are of value in the diagnosis of the hyperpigmented variant.

Blue-gray globules were also detected in folliculotropic variant, which is a novel finding in the literature. In addition, the folliculotropic variant was characterized by perifollicular, interfollicular scaling, and comedo-like openings that represent keratin filled invagination of the epidermis [13] and could be found in many scalp and hair disorders [14]. Still, they are not specific for MF diagnosis, they may differentiate folliculotropic variant from other variants.

The hypopigmented variant of MF showed whitish areas that represent areas of hypomelanosis [12], and pearly white

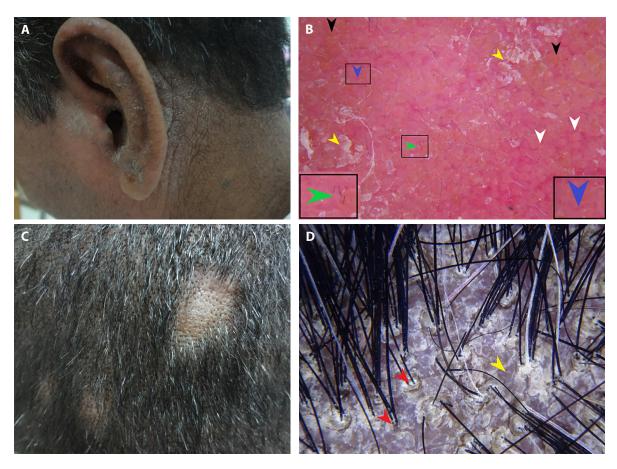


Figure 4. (A) Male patient presented with folliculotropic mycosis fungoides, showing erythematous scaly plaques behind the left ear. (B) Dermoscopic features of the postauricular area; pink to erythematous background with areas of orange discoloration (black arrows), patchy white scales (yellow arrows), arborizing blood vessels (white arrows), spermatozoa like blood vessels (green arrow) and short linear blood vessels (blue arrow), polarized light x10. (C) The same patient with hairless plaque on the scalp. (D) Dermoscopic features of the scalp lesions; inter and perifollicular scaling (red arrows) and large blue-gray globules (yellow arrow). Polarized light x10.

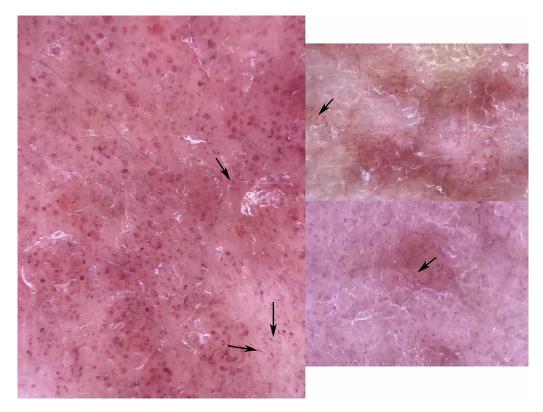


Figure 5. Dermoscopic features of poikilodermatous mycosis fungoides showing spermatozoa like blood vessels (black arrows).

Table 5. Correlation between dermoscopic and histopathological features (H&E stain).

| Dermoscopic Features | Histopathological Features | | | | | | | |
|--|----------------------------|-------|--|-------|---|-------|-------------------------------|-------|
| | Atypical Lymphocytes | | Epidermotropism With Pautrier Microabscesses | | Alignment of Atypical Lymphocytes | | Atypical Dermal Infiltrate | |
| | R | P | r | P | r | P | r | P |
| Non-homogenous Background | 0.312 | 0.003 | 0.227 | 0.033 | .289 | 0.006 | 0.627 | 0.000 |
| Patchy whitish scales | .889 | 0.000 | .883 | 0.000 | .930 | 0.000 | .889 | 0.000 |
| Perifollicular and interfollicular scaling | .219 | 0.040 | .227 | 0.033 | .308 | 0.003 | .965 | 0.000 |
| Pink to erythematous background | .965 | 0.000 | .963 | 0.000 | .308 | 0.003 | .308 | 0.003 |
| Patchy areas of orange discoloration | 1.000 | 0.000 | 1.000 | 0.000 | .937 | 0.000 | .937 | 0.000 |
| Blue-gray globules | .646 | 0.000 | .671 | 0.000 | .937 | 0.000 | .937 | 0.000 |
| Dark globules | .646 | 0.000 | .671 | 0.000 | .690 | 0.000 | .690 | 0.000 |
| Patchy red globules | .384 | 0.000 | .399 | 0.000 | .594 | 0.000 | .646 | 0.000 |
| Multifocal pigmentation | .219 | 0.040 | .227 | 0.033 | .482 | 0.000 | .482 | 0.000 |
| Foggy whitish areas | .502 | 0.000 | .521 | 0.000 | .339 | 0.001 | .339 | 0.001 |
| Hypopigmented areas | .219 | 0.040 | .227 | 0.033 | .690 | 0.000 | .690 | 0.000 |
| Pearly white globules | .502 | 0.000 | .521 | 0.000 | .690 | 0.000 | .963 | 0.000 |
| Dotted blood vessels | .446 | 0.000 | .463 | 0.000 | .594 | 0.000 | .646 | 0.000 |
| Short linear blood vessels | .963 | 0.000 | .962 | 0.000 | .855 | 0.000 | .772 | 0.000 |
| Spermatozoa like blood vessels | .963 | 0.000 | .962 | 0.000 | .482 | 0.000 | .446 | 0.000 |
| Arborizing blood vessels | .772 | 0.000 | .802 | 0.000 | .289 | 0.006 | 0.627 | 0.000 |

globules. These features, that were not reported before in any previous study, can differentiate hypopigmented variant from other variants of MF.

Regarding the pearly white globules, an interesting observation in the present study in some patients who previously received phototherapy; was observed before in the active vitiligo lesions [15,16] and it was described by Jha et al as "tapioca sago" appearance [15]. We suggest that it may be a sign of photodamaging. This relates to Friedland R et al who stated that MF patients who were treated with phototherapy may acquire an eruption resembling idiopathic guttate hypomelanosis as a side effect [16].

Another noteworthy finding of our analysis was that all MF variants except hypopigmented MF were characterized by a non-homogenous distribution of structures and colors. Malvehy et al stated that the non-homogenous distribution of structures and colors was not observed previously in the dermoscopic examination of benign skin disorders [12]. Thus, it could be added as a dermoscopic feature indicative of malignancy.

Our analysis revealed a very good correlation between histopathologic alterations and dermoscopic structures. The combination of dermoscopy with histopathology results in a better tumor examination with two distinct but balancing tools. While histopathology reflects the vertical sight of the lesions, dermoscopic images offer a horizontal assessment. Therefore, it is always hard to correlate both tools, however, the horizontal perception which is added by dermoscopy is complementary to histopathology [11]. Dermoscopy is similarly valuable in barely visible vascular components and color deviations so it may associate clinical examination and dermatopathology [17].

Our study has several limitations. First, we included only MF cases and, therefore, our results do not provide information on the usefulness of described criteria for the differential diagnosis between MF and clinical simulators. Besides, some rare clinical variants included in the study were represented by a small sample, which did not allow a more robust statistical analysis to assess differences among clinical variants.

In conclusion, our study confirms previous evidence on dermoscopy of MF and provides novel information on the distribution of the dermoscopic criteria according to the clinical variant, which might be clinically relevant.

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