Mycosis fungoides variants—clinicopathologic features, differential diagnosis, and treatment

Rein Willemze, MD, PhD

Abstract

Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma, which typically presents with erythematous patches and plaques, histopathologically characterized by superficial infiltrates of small to medium-sized atypical epidermotropic T cells. Apart from this classic type of MF, many clinical and/or histopathologic variants have been described. Correct diagnosis of these MF variants is important, but may be difficult, because they may mimic a wide variety of inflammatory skin diseases. In this review, clinical and histopathologic characteristics of distinct variants of MF are presented, and their differential diagnosis and therapeutic options are discussed.

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Mycosis fungoides (MF) is the most common type of cutaneous T-cell lymphoma (CTCL) and accounts for approximately 50% of all primary cutaneous lymphomas.[1] Patients with classical MF present with patches and plaques that are preferentially located on the buttocks and other covered sites of the trunk and limbs (sun-protected areas). Histopathologically, these early stages are characterized by superficial band-like or lichenoid infiltrates of small to medium-sized atypical T cells with cerebriform and sometimes hyperchromatic nuclei, which characteristically infiltrate into the epidermis (epidermotropism). Most patients have a protracted clinical course over years or even decades. However, a proportion of patients may develop nodules or tumors and eventually progress to extracutaneous disease.[2,3] Classic MF, also called Alibert–Bazin type of MF, is discussed in detail in the article by Lorenzo Cerroni in this same issue.

Apart from classical MF, many clinical and/or histopathologic variants of MF mimicking a wide variety of inflammatory skin diseases have been described.[4-6] These include, among others, erythrodermic, hypopigmented, hyperpigmented, bullous/vesicular, poikilodermatous, folliculotropic, syringotropic, granulomatous, and even invisible MF. Most variants have a clinical behavior similar to that of classic MF, and in recent classifications they are therefore not classified separately. In the WHO European Organization of Research and Treatment of Cancer (WHO-EORTC) classification and in the 2017 revision of the WHO classification, only folliculotropic MF (FMF), pagetoid reticulosis, and granulomatous slack skin (GSS) are recognized as distinct variants of MF because of their distinctive clinicopathologic features, clinical behavior, and/or prognosis.[1,7] In this review, the clinical and histopathologic features, differential diagnosis, and treatment of these 3 variants are presented. Hypopigmented MF, which is the most common variant in childhood and adolescence, and other rare variants are shortly discussed.

Department of Dermatology, Leiden University Medical Center, Leiden, The Netherlands.

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Correspondence: Rein Willemze, MD, PhD; rein.willemze@planet.nl; willemze.dermatology@lumc.nl

Folliculotropic MF

FMF is a distinct variant of MF characterized by the presence of folliculotropic infiltrates, often with sparing of the interfollicular epidermis and preferential involvement of the head and neck region.[1] In large series, FMF accounts for approximately 10% of all patients with MF.[2,3] Most cases show mucinous degeneration of the hair follicles (follicular mucinosis) and were originally designated as MF-associated follicular mucinosis. Similar cases, but without follicular mucinosis, have been reported as pilotropic MF.[8]

It should be emphasized that FMF is defined by a combination of clinical and histopathologic criteria. Infiltration of hair follicle epithelium by neoplastic T cells can also be observed in other types of CTCL, such as CD8-positive aggressive epidermotropic cytotoxic CTCL ($CD8^+$ AECTCL), lymphomatoid papulosis (LyP), and cases of classic MF, and is in itself insufficient for a diagnosis of FMF.[9,10]

Clinical features

FMF mostly presents in adults but has also been reported in children and adolescents.[11-16] Men are affected more often than women. Patients may present with (grouped) follicular papules, follicle-based patches, indurated plaques, or tumors, which preferentially involve and are most pronounced in the head and neck area (Figure 1).[11-14,17] Other clinical manifestations are acneiform lesions (comedones, cysts) and keratosis pilaris-like lesions that are mainly localized on trunk and extremities.[18] The skin lesions are often associated with alopecia. Children most commonly present with hypopigmented folicle-based patches with associated alopecia.[15] Infiltrated plaques in the eyebrow region with concurrent alopecia are a common and highly characteristic finding. Pruritus is often severe and may represent a reliable parameter of disease activity. Secondary bacterial infections are frequently observed.[17] In rare cases, FMF may present with a solitary skin lesion (solitary or unilesional FMF) or with erythroderma.[19-21]

Histopathology and immunophenotype

Histopathologically, FMF is characterized by the presence of perifollicular to diffuse infiltrates with variable infiltration of the follicular epithelium by small, medium-sized, or sometimes large T cells with cerebriform and hyperchromatic nuclei (Figure 2).[11-14,17] Many cases show mucinous degeneration of the follicular epithe-

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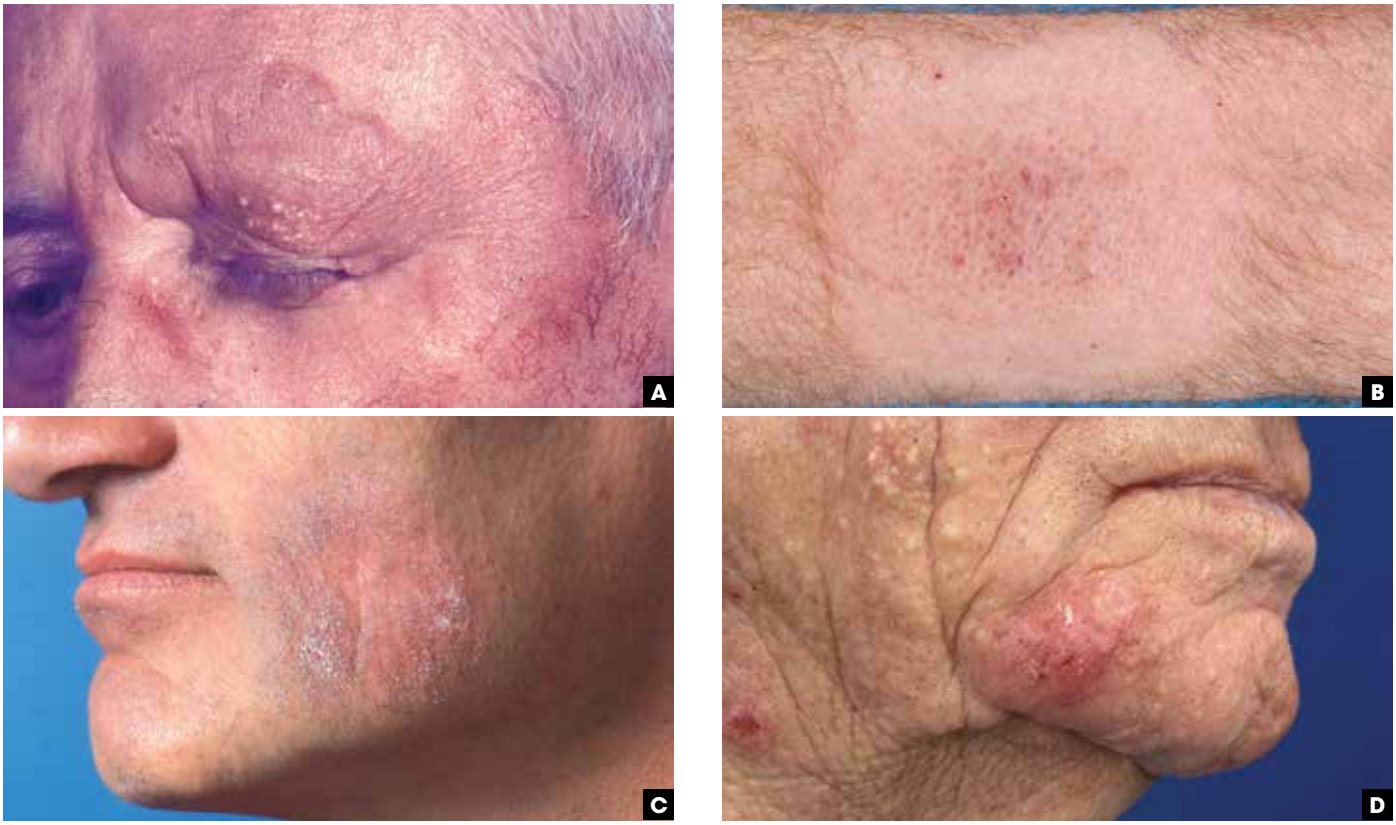


FIGURE 1. Clinical manifestations of FMF. **(A)** Infiltrated plaque with alopecia and cystic lesions above left eye; **(B)** grouped follicular papules on right arm; **(C)** infiltrated plaque with hyperkeratotic papules on left cheek; **(D)** erythematous tumor and many cystic lesions. FMF, folliculotropic mycosis fungoides.

lium (follicular mucinosis), which can be visualized by Alcian blue or colloidal iron staining, but cases without follicular mucinosis have been described as well.[8] Infiltration of the follicular epithelium may be accompanied by infiltration of the eccrine sweat glands (syringotropism), a combination that is often referred to as adnexotropic MF.[21-23] However, concurrent infiltration of the interfollicular epidermis (epidermotropism) characteristic of early-stage classic MF is uncommon. In early-stage lesions, clinically characterized by follicle-based patches or acneiform or keratosis pilaris-like lesions, the perifollicular infiltrates are generally sparse and contain, apart from atypical T cells, variable numbers of small reactive T cells, histiocytes, and occasionally eosinophils. With progression of the skin lesions to more infiltrated plaques or tumors, the dermal infiltrates become more diffuse and may contain increasing numbers of blast cells. There is often a considerable admixture with eosinophils and, in particular, in cases with secondary bacterial infection, plasma cells. In some cases, clusters of small B cells may be present. In cases with destruction of the hair follicle epithelium, a granulomatous reaction can be observed.[22] In cases with diffuse dermal infiltrates with partial or even complete destruction of the epithelial structures, differentiation between FMF and other types of CTCL may be challenging. In such cases, staining with monoclonal antibodies against keratin may be useful to visualize infiltration of residual hair follicles and sweat glands by neoplastic T cells.[21] Large-cell transformation, defined by the presence of more than 25% of blast cells or the presence of clusters of blast cells, has been reported in more than 20% of FMF cases and is more common than in classical MF.[12,14,17]

In virtually all cases, the neoplastic cells in FMF have a $CD3^+/CD4^+/CD8^-$ T-cell phenotype as in classic MF.[22] Admixed blast cells are often CD30 positive. Most cases show clonal T-cell receptor gene rearrangements.[22]

Differential diagnosis

The distinctive clinical and histopathologic features should facilitate an early and correct diagnosis. However, because of the preferential involvement of the head and neck area, the absence of patches and plaques on the trunk and buttocks, and particularly because of the absence of epidermotropic atypical T cells, the diagnosis of MF or CTCL is often not considered and is misinterpreted as seborrheic dermatitis, atopic dermatitis, or rosacea. Clinicopathologic correlation is also required to differentiate FMF from other types of CTCL. Because the perifollicular infiltrates often contain scattered or clusters of CD30-positive blast cells, histopathologic differentiation between FMF and primary cutaneous CD30-positive lymphoproliferations (cutaneous anaplastic large-cell lymphoma; LyP) may be challenging. In case hair follicles have been destroyed or are completely obscured by diffuse dermal infiltrates, it may be difficult or even impossible to differentiate between FMF and primary cutaneous peripheral T-cell lymphoma, unspecified. In such cases, addi-

tional biopsies and clinical follow-up are needed to make a definite diagnosis.[21] The relationship between FMF and the so-called benign or idiopathic form of follicular mucinosis (alopecia mucinosa) is still a matter of debate, similar to the relationship between classic MF and "parapsoriasis."[24] This idiopathic form of follicular mucinosis usually presents with one or a few localized patches with follicular accentuation and alopecia, particularly in children or adolescents, and has an excellent prognosis.[25] In the case of widespread or persistent lesions, a diagnosis of FMF is more likely.

Treatment and prognosis

Previous studies emphasized that FMF is generally less responsive to several skin-directed therapies (SDTs) and runs a more aggressive clinical course similar to that of tumor-stage classic MF and should therefore be treated accordingly.[11,12] However, more recent studies defined a subgroup of FMF patients with an indolent clinical behavior and an excellent prognosis, with a 5- and 10-year survival similar to that of early-stage classic MF (Table).[17,18,26] Recognition of indolent and aggressive subgroups of FMF is also important from a therapeutic point of view because it implies that early- and advanced-stage FMF require a different therapeutic approach. Recent studies suggest a stepwise, stage-adapted therapeutic approach, similar to in early- and advanced-stage classic MF.[27] Patients with early-stage FMF may benefit very well from nonaggressive SDT, such as topical steroids, psoralen plus ultraviolet A (PUVA), or topical nitrogen mustard. In patients with advanced-stage FMF, these SDTs are less effective. For these patients, PUVA combined with local radiotherapy, PUVA combined with interferon alfa, and/or retinoids or total skin electron beam irradiation have been recommended.[12,14,27] For rare FMF patients presenting with a solitary plaque or tumor, local radiotherapy is highly effective and is the preferred mode of treatment.[19-21] Apart from stage, advanced age, large-cell transformation, and extensive secondary bacterial infection have been reported to be associated with reduced survival.[14,17]

Pagetoid reticulosis

Pagetoid reticulosis is a rare variant of MF, characterized by the presence of localized patches or plaques with an intraepidermal proliferation of neoplastic T cells.[1,28] The term pagetoid reticulosis should only be used for the localized type (Woringer–Kolopp type) and not for the disseminated type (Ketron–Goodman type).[1,28] Nowadays, most patients with generalized disease would be classified as primary cutaneous $CD8^+$ AECTCL, primary cutaneous γ/δ T-cell lymphoma, or tumor-stage MF.[1,29]

Clinical features

Patients characteristically present with a solitary, slowly progressive, psoriasiform or hyperkeratotic patch or plaque, which is usually localized on an extremity, particularly hands or feet (Figure 3).

Histopathology and immunophenotype

The typical histopathologic picture consists of a hyperplastic epidermis with marked infiltration by small to medium-sized atypical pagetoid cells, arranged singly or in nests or clusters (Figure 4). The atypical cells have medium-sized or large cerebriform nuclei and abundant, vacuolated cytoplasm. The superficial dermis may have an infiltrate of mostly small lymphocytes but rarely contains neoplastic T cells. The neoplastic T cells may show either a $CD3^+/CD4^-/CD8^+$ or less commonly a $CD3^+/CD4^+/CD8^-$ or $CD3^+/CD4^-/CD8^-$ phenotype. Cases with a $CD8^+$ or $CD4^-/CD8^-$ phenotype express cytotoxic proteins. CD30 is often expressed.[28]

Differential diagnosis

Pagetoid reticulosis should be differentiated from other types of epidermotropic CTCL, such as MF, LyP, in particular type D, and

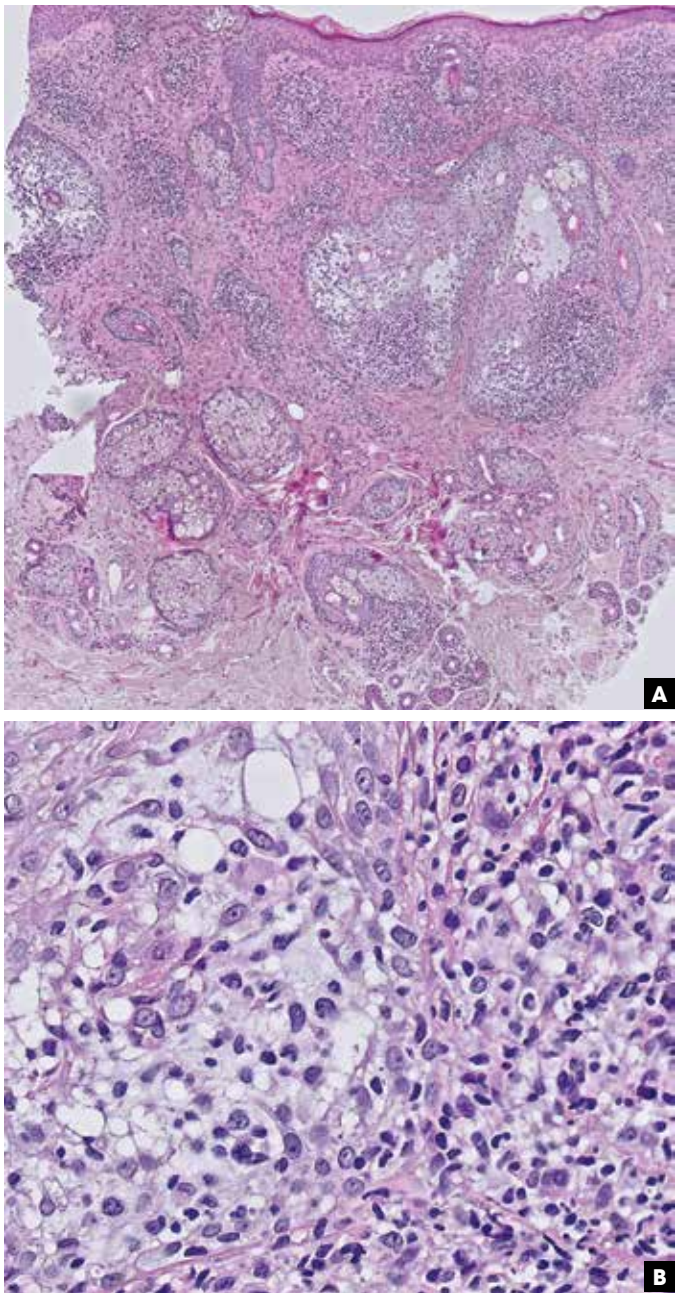


FIGURE 2. FMF. **(A)** Perifollicular infiltrates with extensive follicular mucinosis; **(B)** detail shows infiltration of follicular epithelium by atypical lymphocytes. FMF, folliculotropic mycosis fungoides.

TABLE Differences between early- and advanced-stage FMF[17,18]

	Early-Stage FMF	Advanced-Stage FMF
Clinical presentation	Follicular papules Follicle-based patches Early-stage plaques Acneiform lesions Keratosis pilaris-like lesions	Infiltrated plaques Tumors Nodules Erythroderma
Secondary bacterial infection	Rare	Common
Histopathology	Sparse intra- and perifollicular infiltrates with relatively few mainly small to medium-sized neoplastic T cells	Confluent perifollicular to diffuse dermal infiltrates containing many medium-sized to large neoplastic T cells and often many blast cells
Large-cell transformation	Rare	Common (20%-30%)
Treatment	Topical steroids PUVA Local radiotherapy[a]	PUVA PUVA plus interferon alfa or retinoids PUVA plus local radiotherapy Total skin electron beam irradiation Local radiotherapy[a]
Disease-specific survival		
5-year	96%	65%
10-year	93%	40%
Overall survival		
5-year	92%	55%
10-year	72%	28%

[a]Local radiotherapy as monotherapy for solitary FMF.[19-21]

Abbreviations: FMF, folliculotropic mycosis fungoides; PUVA, psoralen plus ultraviolet A.

CD8+ AECTCL.[10,30] Useful criteria for pagetoid reticulosis include the characteristic clinical presentation and the often strictly epidermal localization of the neoplastic T cells. CD8-positive AECTCL is characterized by a proliferation of epidermotropic CD8+ cytotoxic T cells and an aggressive clinical behavior.[10] Histopathologically, early patch-like lesions may show superficial infiltrates with pronounced pagetoid epidermotropism simulating pagetoid reticulosis.[31] However, unlike pagetoid reticulosis, these patients generally have or soon develop more widespread ulcerating papules, plaques, and tumors, showing diffuse dermal infiltrates of CD8+ neoplastic T cells. Epidermal necrosis and ulceration, as well as invasion and destruction of adnexal structures, are commonly found. LyP type D is characterized by marked epidermotropism of CD8+ cytotoxic T cells simulating CD8+ AECTCL as well as pagetoid reticulosis histopathologically.[30] In contrast with CD8+ AECTCL, CD30 is expressed by the intraepidermal T cells in virtually all cases. Unlike pagetoid reticulosis, which may also express CD30, LyP shows the characteristic clinical course of recurrent, spontaneously regressing skin lesions and is not restricted to one acral site.

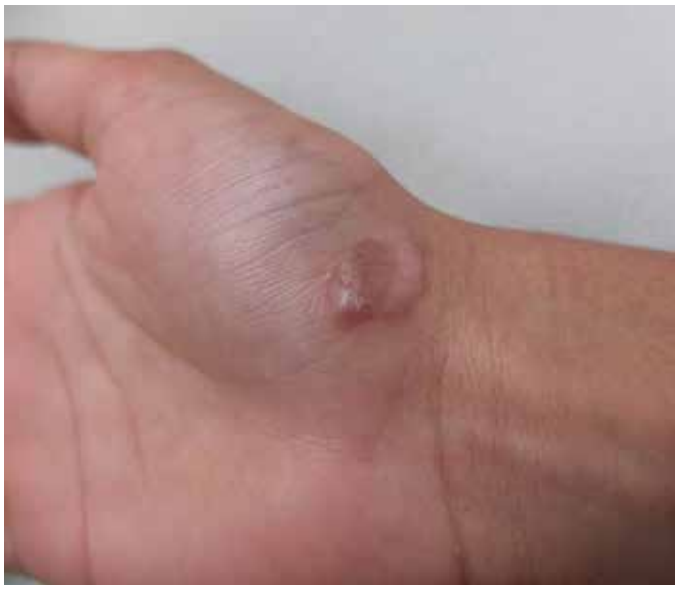
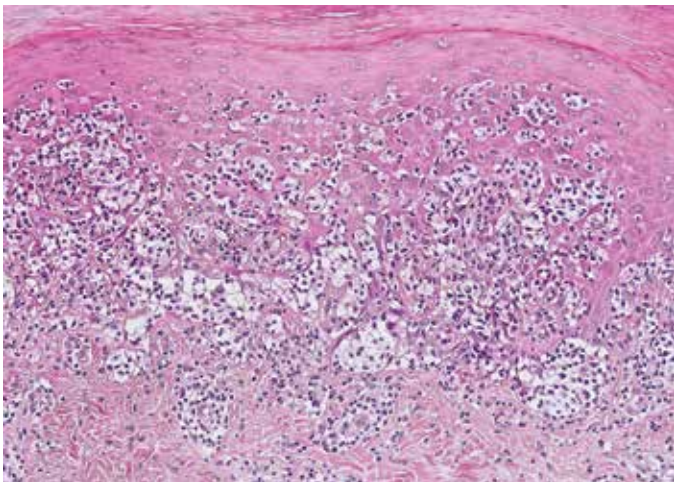


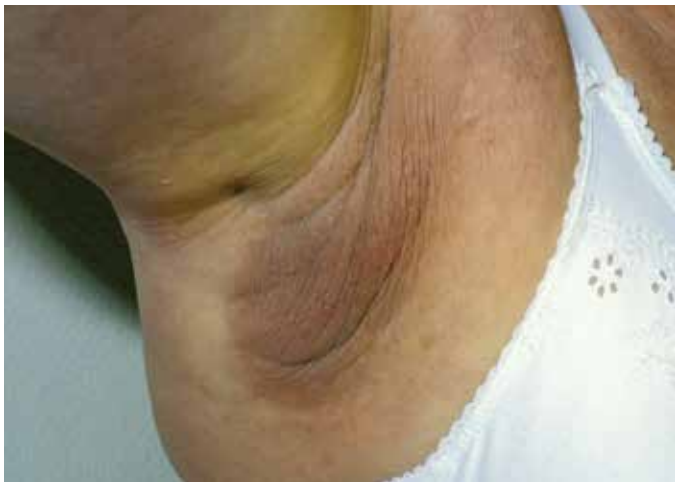
FIGURE 3. Pagetoid reticulosis presenting with a solitary hyperkeratotic plaque on the right wrist.

Treatment

The preferred mode of treatment is radiotherapy or surgical exci-



■ **FIGURE 4.** Pagetoid reticulosis. Epidermal hyperplasia and extensive epidermotropism of small to medium-sized atypical lymphocytes in a pagetoid pattern.



■ **FIGURE 5.** GSS showing bulky skin folds in the right axilla. GSS, granulomatous slack skin.

sion. The prognosis of pagetoid reticulosis is excellent. In contrast with classic MF, extracutaneous dissemination or disease-related deaths have never been reported.[29]

Granulomatous slack skin

GSS is an extremely rare variant of MF, characterized by the slow development of folds of lax skin and a granulomatous infiltrate with clonal T cells.[1,32]

Clinical features

Initial skin lesions in GSS are patches and plaques as in classical MF, which evolve to bulky, pendulous folds of atrophic skin in the flexural areas (axilla and groins), resembling cutis laxa (Figure 5).[33,34] In approximately one-third of the reported patients, an association with other malignant lymphomas, including MF and Hodgkin lymphoma, has been reported.[34] Extracutaneous dissemination is exceedingly rare, and most patients have an indolent clinical course.[2,33]

Histopathology

Histopathologically, GSS is characterized by dense infiltrates throughout the entire dermis of small to medium-sized clonal T cells admixed with numerous macrophages and many scattered multinucleated giant cells (Figure 6). The presence of multinucleated giant cells containing more than 10 nuclei per cell is considered a characteristic feature, but has also been observed in cases of granulomatous MF.[33] Loss of elastic tissue, elastophagocytosis, and emperipolesis (engulfment of lymphocytes) by multinucleated cells are commonly observed. The epidermis may be infiltrated by small atypical T cells with cerebriform nuclei, as in classic MF. Most cases have a $CD3^+/CD4^+/CD8^-$ T-cell phenotype and show clonal T-cell receptor gene rearrangement.[33] In one case, a t(3;9)(q12;p24) has been reported.[35]

Differential diagnosis

Granulomatous MF is an unusual histopathologic variant that may be found in microscopic sections of patients with otherwise classical MF, as well as in other variants, such as FMF.[36] Granulomatous changes that develop in patients with well-established MF do not usually form a diagnostic problem. However, the diagnosis may be difficult if granulomatous MF is the first manifestation of the disease, in particular in case the neoplastic T-cell infiltrate is obscured by an extensive granulomatous reaction.[37] In a recent EORTC study, it was found that granulomatous MF shares many histopathologic features with GSS, including the presence of a granulomatous infiltrate with variable numbers of multinucleated giant cells, loss of elastic fibers, and a population of small to medium-sized mainly $CD4^+$ neoplastic T cells.[33] Because of these overlapping histopathologic features, histopathologic differentiation between GSS and granulomatous MF is often not possible, and the final diagnosis is ultimately based on the typical clinical presentation of GSS. Patients with granulomatous MF are reported to have a poorer response to SDTs, a worse prognosis than patients with classic MF, and a higher risk of developing a second malignant lymphoma.[33,36]

Treatment

Treatment of GSS is unsatisfactory. Patients have been treated with PUVA, radiotherapy, surgical excision, interferon, and other systemic therapies, but complete responses have never been reported. GSS is characterized by an indolent and slowly progressive clinical course. Because of the increased risk of a second malignant lymphoma, long-term follow-up is needed.[33,38]

Hypopigmented MF

Hypopigmented MF is found often in dark-skinned individuals and is the most common variant in children and adolescents.[15,16,39] In white patients, hypopigmented lesions usually coexist with erythematous lesions typical of classic MF. Patients present with asymptomatic hypopigmented patches that are mainly located on trunk and extremities. Histopathology shows the typical features of early patch-stage MF. However, in contrast with classic MF, hypopigmented MF usually has a $CD8^+$ T-cell phenotype.[15,39] Patients respond very well to SDTs, preferably narrow-band UVB, and usually have an excellent prognosis.[16]

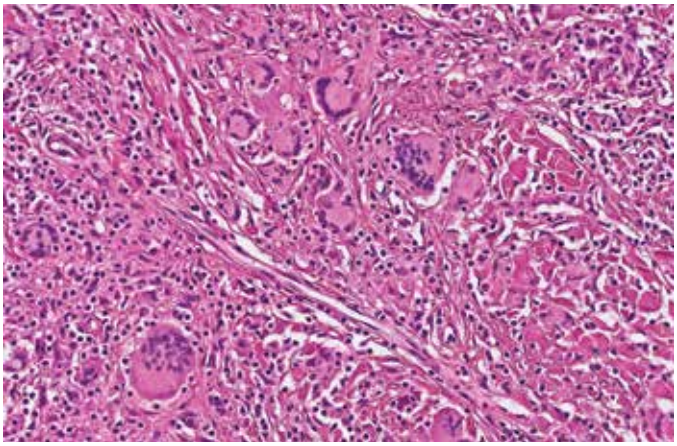


FIGURE 6. GSS showing a diffuse lymphoid infiltrate with many multinucleated giant cells. GSS, granulomatous slack skin.

Other variants of MF

Apart from the variants discussed in more detail above, several other clinical and/or histopathological variants of MF have been described. Variants like hyperpigmented, bullous/vesicular, poikilodermatous, pigmented purpura-like, pustular, ichthyosiform, palmoplantar MF, and still others are named after their specific clinical manifestations. However, they generally have the same typical histopathologic features, and in most instances the same clinical course, as classic MF and have therefore not been included as separate entities in recent classifications for cutaneous lymphomas.

Immunophenotypical variants of MF

In addition to clinical and/or histopathological variants, phenotypical variants of MF can be distinguished also. Early-stage classic MF characteristically shows a $CD3^+$, $CD4^+$, $CD8^-$, $CD45RO^+$ T-helper memory cell phenotype, but a minority of cases may show a $CD4^-$, $CD8^+$ cytotoxic T-cell phenotype or, even more uncommon, a $CD4^-$, $CD8^-$ or $CD4^+$, $CD8^+$ T-cell phenotype.[40-42] A $CD8^+$ phenotype is more common in pediatric MF and in some variants of MF, including pagetoid reticulosis, hypopigmented, hyperpigmented, and poikilodermatous MF.[39,43,44] Moreover, in rare cases of otherwise classic early-stage MF, the neoplastic T cells may express CD30 or CD56 or may have a γ/δ T-cell phenotype rather than the normal α/β T-cell phenotype.[40-42] However, these aberrant phenotypes in early-stage MF do not have independent prognostic significance.

Conclusion

MF and its variants demonstrate a broad spectrum of clinical and histopathologic manifestations. By mimicking a wide variety of inflammatory dermatoses, the diagnosis of MF and in particular its variants may be challenging. Clinicopathologic correlation and integration of immunophenotypical and genetic data is essential for correct diagnosis and adequate treatment.

References

1. Willemze R, Jaffe ES, Burg G, et al. WHO-EORTC classification for cutaneous lymphomas. *Blood*. 2005;105(10):3768-3785. doi: 10.1182/blood-2004-09-3502.
2. van Doorn R, Van Haselen CW, van Voorst Vader PC, et al. Mycosis fungoides: disease evolution and prognosis of 309 Dutch patients. *Arch Dermatol*. 2000;136(4):504-510.
3. Agar NS, Wedgeworth E, Crichton S, et al. Survival outcomes and prognostic factors in mycosis fungoides/Sezary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. *J Clin Oncol.* 2010;28(31):4730-4739. doi: 10.1200/JCO.2009.27.7665.
4. Nashan D, Faulhaber D, Ständer S, Luger TA, Stadler R. Mycosis fungoides: a dermatological masquerader. *Br J Dermatol*. 2007;156(1):1-10. doi: 10.1111/j.1365-2133.2006.07526.x
5. Kazakov DV, Burg G, Kempf W. Clinicopathological spectrum of mycosis fungoides. *J Eur Acad Dermatol Venereol*. 2004;18(4):397-415. doi: 10.1111/j.1468-3083.2004.00937.x
6. Martínez-Escala ME, González BR, Guitart J. Mycosis Fungoides Variants. *Surg Pathol Clin*. 2014;7(2):169-189. doi: 10.1016/j.path.2014.02.003.
7. Swerdlow SH, Campo E, Harris NL, et al, eds. *World Health Organization Classification of Tumours of Hematopoietic and Lymphoid Tissue*. Revised 4th edition. Lyon: IARC Press, 2017.
8. Vergier B, Beylot-Barry M, Beylot C, et al. Pilotropic cutaneous T-cell lymphoma without mucinosis. A variant of mycosis fungoides? French Study Group of Cutaneous Lymphomas. *Arch Dermatol.* 1996;132(6):683-687.
9. Kempf W, Kazakov DV, Baumgartner HP, Kutzner H. Follicular lymphomatoid papulosis revisited: a study of 11 cases, with new histopathological findings. *J Am Acad Dermatol.* 2013;68(5):809-816. doi: 10.1016/j.jaad.2012.12.952.
10. Robson A, Assaf C, Bagot M, et al. Aggressive epidermotropic cutaneous CD8+ lymphoma: a cutaneous lymphoma with distinct clinical and pathological features. Report of an EORTC Cutaneous Lymphoma Task Force Workshop. *Histopathology*. 2015;67(4):425-441. doi: 10.1111/his.12371.
11. van Doorn R, Scheffer E, Willemze R. Follicular mycosis fungoides, a distinct disease entity with or without associated follicular mucinosis: a clinicopathologic and follow-up study of 51 patients. *Arch Dermatol*. 2002;138(2):191-198.
12. Gerami P, Rosen S, Kuzel T, Boone SL, Guitart J. Folliculotropic mycosis fungoides: an aggressive variant of cutaneous T-cell lymphoma. *Arch Dermatol*. 2008;144(6):738-746. doi: 10.1001/archderm.144.6.738.
13. Lehman JS, Cook-Norris RH, Weed BR, et al. Folliculotropic mycosis fungoides: single-center study and systematic review. *Arch Dermatol*. 2010;146(6):607-613. doi: 10.1001/archdermatol.2010.101.
14. Wieser I, Wang C, Alberti-Violetti S, et al. Clinical characteristics, risk factors and long-term outcome of 114 patients with folliculotropic mycosis fungoides. *Arch Dermatol Res.* 2017;309(6):453-459. doi: 10.1007/s00403-017-1744-1.
15. Hodak E, Amitay-Laish I, Feinmesser M, et al. Juvenile mycosis fungoides: cutaneous T-cell lymphoma with frequent follicular involvement. *J Am Acad Dermatol.* 2014;70(6):993-1001. doi: 10.1016/j.jaad.2013.12.029.
16. Boulos S, Vaid R, Aladily TN, Ivan DS, Talpur R, Duvic M. Clinical presentation, immunopathology, and treatment of juvenile-onset mycosis fungoides: a case series of 34 patients. *J Am Acad Dermatol*. 2014;71(6):1117-1126. doi: 10.1016/j.jaad.2014.07.049.
17. van Santen S, Roach RE, van Doorn R, et al. Clinical Staging and Prognostic Factors in Folliculotropic Mycosis Fungoides. *JAMA Dermatol*. 2016;152(9):992-1000. doi: 10.1001/jamadermatol.2016.1597.
18. Hodak E, Amitay-Laish I, Atzmony L, et al. New insights into folliculotropic mycosis fungoides (FMF): A single-center experience. *J Am Acad Dermatol.* 2016;75(2):347-355. doi: 10.1016/j.jaad.2016.03.009.
19. Kempf W, Kazakov DV, Schermesser M, et al. Unilesional follicular mycosis fungoides: report of two cases with progression to tumor stage and review of the literature. *J Cutan Pathol.* 2012;39(9):853-860. doi: 10.1111/j.1600-0560.2012.01965.x.
20. Amitay-Laish I, Feinmesser M, Ben-Amitai D, Fenig E, Sorin D, Hodak E. Unilesional folliculotropic mycosis fungoides: a unique variant of cutaneous lymphoma. *J Eur Acad Dermatol Venereol*. 2016;30(1):25-29. doi: 10.1111/jdv.12851.
21. van Santen S, Jansen PM, Vermeer MH, Willemze R. Folliculotropic mycosis fungoides presenting with a solitary lesion: clinicopathological features and long-term follow-up data in a series of 9 cases. *J Cutan Pathol.* 2018;45(2):122-128. doi: 10.1111/cup.13077.
22. Gerami P, Guitart J. The spectrum of histopathologic and immunohistochemical findings in folliculotropic mycosis fungoides. *Am J Surg Pathol*. 2007;31(9):1430-1438. doi: 10.1097/PAS.0b013e3180439bdc.
23. de Masson A, Battistella M, Vignon-Pennamen MD, et al. Syringotropic mycosis fungoides: clinical and histologic features, response to treatment, and outcome in 19 patients. *J Am Acad Dermatol*. 2014;71(5):926-934. doi: 10.1016/j.jaad.2014.06.033.
24. Cerroni L, Fink-Puches R, Bäck B, Kerl H. Follicular mucinosis: a critical reappraisal of clinicopathologic features and association with mycosis fungoides and

Sezary syndrome. *Arch Dermatol*. 2002;138(2):182-189.
25. Alikhan A, Griffin J, Nguyen N, Davis DM, Gibson LE. Pediatric follicular mucinosis: presentation, histopathology, molecular genetics, treatment, and outcomes over an 11-year period at the Mayo Clinic. *Pediatr Dermatol.* 2013;30(2):192-198. doi: 10.1111/pde.12019.
26. Tomasini C, Kempf W, Novelli M, et al. Spiky follicular mycosis fungoides: a clinicopathologic study of 8 cases. *J Cutan Pathol*. 2015;42(3):164-172. doi: 10.1111/cup.12399.
27. van Santen S, van Doorn R, Neelis KJ, et al. Recommendations for treatment in folliculotropic mycosis fungoides: report of the Dutch Cutaneous Lymphoma Group. *Br J Dermatol*. 2017;177(1):223-228. doi: 10.1111/bjd.15355.
28. Haghighi B, Smoller BR, LeBoit PE, Warnke RA, Sander CA, Kohler S. Pagetoid reticulosis (Woringer-Kolopp disease): an immunophenotypic, molecular, and clinicopathologic study. *Mod Pathol*. 2000;13(5):502-510. doi: 10.1038/modpathol.3880088.
29. Steffen C. Ketron-Goodman disease, Woringer-Kolopp disease, and pagetoid reticulosis. *Am J Dermatopathol*. 2005;27(1):68-85.
30. Saggini A, Gulia A, Argenyi Z, et al. A variant of lymphomatoid papulosis simulating primary cutaneous aggressive epidermotropic CD8+ cytotoxic T-cell lymphoma. Description of 9 cases. *Am J Surg Pathol*. 2010;34(8):1168-1175. doi: 10.1097/PAS.0b013e3181e75356.
31. Guitart J, Martinez-Escala ME, Subtil A, et al. Primary cutaneous aggressive epidermotropic cytotoxic T-cell lymphomas: reappraisal of a provisional entity in the 2016 WHO classification of cutaneous lymphomas. *Mod Pathol*. 2017;30(5):761-772. doi: 10.1038/modpathol.2016.240.
32. LeBoit PE. Granulomatous slack skin. *Dermatol Clin*. 1994;12(2):375-389.
33. Kempf W, Ostheeren-Michaelis S, Paulli M, et al. Granulomatous mycosis fungoides and granulomatous slack skin: a multicenter study of the Cutaneous Lymphoma Histopathology Task Force Group of the European Organization for Research and Treatment of Cancer (EORTC). *Arch Dermatol.* 2008;144(12):1609-1617. doi: 10.1001/archdermatol.2008.46.
34. van Haselen CW, Toonstra J, van der Putte SJ, van Dongen JJ, van Hees CL, van Vloten WA. Granulomatous slack skin. Report of three patients with an updated review of the literature. *Dermatology.* 1998;196(4):382-391.
35. Ikonomou IM, Aamot HV, Heim S, Fosså A, Delabie J. Granulomatous slack skin with a translocation t(3;9)(q12;p24). *Am J Surg Pathol.* 2007;31(5):803-806. doi: 10.1097/PAS.0b013e31803071a4.
36. Li JY, Pulitzer MP, Myskowski PL, et al. A case-control study of clinicopathologic features, prognosis, and therapeutic responses in patients with granulomatous mycosis fungoides. *J Am Acad Dermatol*. 2013;69(3):366-374. doi: 10.1016/j.jaad.2013.03.036.
37. Scarabello A, Leinweber B, Ardigó M, et al. Cutaneous lymphomas with prominent granulomatous reaction: a potential pitfall in the histopathologic diagnosis of cutaneous T- and B-cell lymphomas. *Am J Surg Pathol*. 2002;26(10):1259-1268.
38. Clarijs M, Poot F, Laka A, Pirard C, Bourlond A. Granulomatous slack skin: treatment with extensive surgery and review of the literature. *Dermatology.* 2003;206(4):393-397. doi: 10.1159/000069967.
39. El-Shabrawi-Caelen L, Cerroni L, Medeiros LJ, McCalmont TH. Hypopigmented mycosis fungoides: frequent expression of a CD8+ T-cell phenotype. *Am J Surg Pathol*. 2002;26(4):450-457.
40. Massone C, Crisman G, Kerl H, Cerroni L. The prognosis of early mycosis fungoides is not influenced by phenotype and T-cell clonality. *Br J Dermatol.* 2008;159(4):881-886. doi: 10.1111/j.1365-2133.2008.08761.x.
41. Rodríguez-Pinilla SM, Ortiz-Romero PL, Monsalvez V, et al. TCR-gamma expression in primary cutaneous T-cell lymphomas. *Am J Surg Pathol.* 2013;37(3):375-384. doi: 10.1097/PAS.0b013e318275d1a2.
42. Hodak E, David M, Maron L, Aviram A, Kaganovsky E, Feinmesser M. CD4/CD8 double-negative epidermotropic cutaneous T-cell lymphoma: an immunohistochemical variant of mycosis fungoides. *J Am Acad Dermatol*. 2006;55(2):276-284. doi: 10.1016/j.jaad.2006.01.020.
43. Pavlovsky L, Mimouni D, Amitay-Laish I, Feinmesser M, David M, Hodak E. Hyperpigmented mycosis fungoides: an unusual variant of cutaneous T-cell lymphoma with a frequent CD8+ phenotype. *J Am Acad Dermatol*. 2012;67(1):69-75. doi: 10.1016/j.jaad.2011.06.023.
44. Abbott RA, Sahni D, Robson A, Agar N, Whittaker S, Scarisbrick JJ. Poikilodermatous mycosis fungoides: a study of its clinicopathological, immunophenotypic, and prognostic features. *J Am Acad Dermatol*. 2011;65(2):313-319. doi: 10.1016/j.jaad.2010.05.041.