Mycosis fungoides (MF), a low-grade lymphoproliferative disorder, is the most common type of cutaneous T-cell lymphoma. Typically, neoplastic T cells localize to the skin and produce patches, plaques, tumours or erythroderma. Diagnosis of MF can be difficult due to highly variable presentations and the sometimes nonspecific nature of histological findings. Molecular biology has improved the diagnostic accuracy. Nevertheless, clinical experience is of substantial importance as MF can resemble a wide variety of skin diseases. We performed a literature review and found that MF can mimic >50 different clinical entities. We present a structured framework of clinical variations of classical, unusual and distinct forms of MF. Distinct subforms such as ichthyotic MF, adnexotropic (including syringotropic and folliculotropic) MF, MF with follicular mucinosis, granulomatous MF with granulomatous slack skin and papuloerythroderma of Ofuji are delineated in more detail.
regression of lesions can occur; this is sometimes limited to the centre of the lesion. Alopecia may develop in lesional sites or even in clinically unaffected skin. The lesions are asymmetrical and are predominantly located in a ‘swimsuit’ distribution, i.e. preferentially on the abdomen, hips, buttocks and breasts. Lesions are also seen on the medial sides of proximal extremities. The mucosa can be affected at any stage of disease. 8 It is still under discussion whether parapsoriasis with its scattered finger-like striped lesions on the flanks is an entity on its own or is a precursor of MF. The descriptive term ‘mycosis fungoides’, chosen in 1806 by Alibert, already suggests the first differential diagnosis of tinea corporis for a typical MF lesion. The coincidence of dermatophyte infections and MF has been described. 9, 10 Further descriptive terms provide hints for the differential diagnosis: lichenification, lichenoid, eczematous, seborrhoeic, urticarial, erythematous, hypopigmented, pityriasis-like. 11 Thus the differential diagnosis includes nonspecific eczema, nummular eczema, seborrhoeic eczema, contact dermatitis, atopic dermatitis, psoriasis, drug reaction, lichen simplex chronicus and lichen planus (Table 1). 12, 13

Limited involvement of the skin, especially as unilesional typical MF, is not uncommon. 14–17 A well-documented, although not universally accepted, solitary form is the pagetoid reticulosis type Woringer–Kolopp, characterized by a single, scaling and erythematous MF lesion with acral localization. 18 A challenge for the clinician might be the appearance of typical MF in an atypical localization, e.g. MF simulating palmoplantar or periortificial eczema, isolated alopecia or affecting the mucosa (Figs 1 and 2). 19, 20

At the tumour stage IIB (T3N0/1M0) nodules of various sizes are found. They can be flat or dome-shaped. Their colour is yellow-red or red-blue to brown. The lesions are more prominent and deeper than plaques. MF tumours mainly develop in the course of the disease or in conjunction with eczematous lesions. The surface is soft on palpation, which distinguishes the lesions from metastases of solid carcinomas. Ulcerations are frequently seen, which can develop secondary infections. Tumours develop in either pre-existing MF lesions or de novo. The location and configuration of these tumours are comparable with B-cell lymphoma. Another tumorous lymphoma and possible differential diagnosis is lymphomatoid papulosis (LyP). In 1968, Macaulay 21 summarized LyP as a chronically recurring papulonodular dermatosis, sometimes self-limiting. It can be excluded by its brownish-reddish centrally necrotic papules, spontaneous healing within weeks and

---

**Table 1** Differential diagnoses of classical mycosis fungoides (MF) are assembled based on a predominant clinical sign. A representative publication with a clinically imitative MF is given for each differential diagnosis.

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Differential diagnosis</th>
<th>First author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eczematous</td>
<td>Seborrhoeic eczema</td>
<td>Figure 1</td>
</tr>
<tr>
<td></td>
<td>Perioral dermatitis</td>
<td>Wolf 1992*</td>
</tr>
<tr>
<td></td>
<td>Palmoplantar eczema</td>
<td>Spieth 2002*</td>
</tr>
<tr>
<td></td>
<td>Dyshidrotic eczema</td>
<td>Kempf 2005*</td>
</tr>
<tr>
<td></td>
<td>Contact dermatitis</td>
<td>Spieth 2002*</td>
</tr>
<tr>
<td></td>
<td>Atopic eczema</td>
<td>Kazakov 2004*</td>
</tr>
<tr>
<td>Scaling</td>
<td>Psoriasis</td>
<td>Zackheim 2002*</td>
</tr>
<tr>
<td></td>
<td>Psoriasis palmaris</td>
<td>Spieth 2002*</td>
</tr>
<tr>
<td></td>
<td>Psoriasis plantaris</td>
<td>Figure 2</td>
</tr>
<tr>
<td></td>
<td>Parapsoriasis</td>
<td>Ackermann 1996*</td>
</tr>
<tr>
<td></td>
<td>Tinea corporis</td>
<td>Chaves 2002*</td>
</tr>
<tr>
<td></td>
<td>Tinea pedis</td>
<td>Resnik 1995*</td>
</tr>
<tr>
<td>Erythematous</td>
<td>Erythema multifforme</td>
<td>Krebs 1978*</td>
</tr>
<tr>
<td></td>
<td>Annular erythema</td>
<td>Lim 2003*</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cogrel 2005*</td>
</tr>
<tr>
<td>Alopecia</td>
<td>Alopecia areata</td>
<td>Burg 1992*</td>
</tr>
</tbody>
</table>

For a further overview publications of Zackheim and Mccallmont 11—with 23 differential diagnoses—and Kazakov et al. 12 can be recommended.
leukaemic involvement’ describe the difficulty of either delinea-
tion. SS was defined by Sézary and Bouvrain in 193823 as a
triad of erythroderma, lymphadenopathy and atypically large
mononuclear blood cells. It is clinically associated with leon-
ine facies, ectropion, alopecia of the scalp, palmoplantar
hyperkeratosis and fissures and dystrophy of the nails. Similar
but less frequent monosymptomatic forms or new phenomena
such as a vitiligo-like leucoderma with MF and SS hamper the
diagnosis.24–26

A diagnostic discrimination is presented by the Interna-
tional Society for Cutaneous Lymphomas, specifying in add-
tion to erythrodermic MF and SS, ‘other erythrodermic
cutaneous T-cell lymphoma, not otherwise defined’.27 Fur-
ther differential diagnoses include primary and secondary
erthrodermas caused by psoriasis, atopic dermatitis, drug
eruption or age-dependent erythroderma (Table 3). Actinic
reticuloid sometimes exacerbates to erythroderma; however,
it becomes aggravated in sunlight-exposed skin. It is consid-
ered as a form of a cutaneous T-cell pseudolymphoma by
most authors.28

A real clinical challenge is provided by unusual and newly
described variants of MF comprising hyperpigmented, hypo-
pigmented, urticarial, bullous, solely papular, pustular and
hyperkeratotic variants for which diagnosis is easier in con-
junction with typical MF lesions or a positive history of MF
(Table 4).29–31 Hypopigmentation and a vitiligo-like outcome
are predominantly described in individuals with dark skin.
Mainly asymptomatic, irregularly confined, white macules are
seen.12,31 A critical review suggested that only 19 of 106 pub-
lished cases with hypopigmentation were truly MF.34 The bul-
lous form of MF was first described by Kaposi in 1887.
Flaccid or tense, often multiple or even generalized blisters
appear on normal skin or within plaques. A positive Nikolsky
sign is observed. Diagnosis is urgent as bullous lesions of MF
indicate a poor prognosis.35

Some case reports point out single atypical lesions as a clue
for a false diagnosis, e.g. a warty lesion misdiagnosed as a se-
borrhoeic keratosis or Bowen’s disease.36,37 Other clinical
impressions of atypical MF have stimulated diagnoses such as
purpura pigmentosa, vasculitis and pyoderma gangrenosum
(Table 5).38 Especially purpuric eruptions are repeatedly de-
scribed with petechial patches and varying degrees of epider-
mal changes—scaling, vesiculation, lichenification—and
brownish pigmentation from haemosiderin accumulation.33

Table 2 Differential diagnoses of tumorous mycosis fungoides lesions

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumorous</td>
<td>Lupus erythematosus</td>
</tr>
<tr>
<td></td>
<td>B-cell lymphoma</td>
</tr>
<tr>
<td></td>
<td>Lymphomatoid papulosis</td>
</tr>
<tr>
<td></td>
<td>CD30+ lymphoma</td>
</tr>
<tr>
<td></td>
<td>Hodgkin disease</td>
</tr>
<tr>
<td></td>
<td>Sarcoma</td>
</tr>
</tbody>
</table>

Table 3 Differential diagnoses of erythrodermic mycosis fungoides

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Differential diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythrodermic</td>
<td>Sézary syndrome</td>
</tr>
<tr>
<td></td>
<td>Adult T-cell leukaemia</td>
</tr>
<tr>
<td></td>
<td>Actinic reticuloid</td>
</tr>
<tr>
<td></td>
<td>Atopic dermatitis</td>
</tr>
<tr>
<td></td>
<td>Drug reaction</td>
</tr>
<tr>
<td></td>
<td>Psoriasis</td>
</tr>
<tr>
<td></td>
<td>Age-dependent erythroderma</td>
</tr>
</tbody>
</table>

Fig 2. Mycosis fungoides imitating palmoplantar psoriasis.
More definite clinicopathological findings distinguishing cutaneous lymphoma from pigmented purpuric dermatosis are outlined by Martínez et al. 39

Distinct entities of mycosis fungoides

More clear-cut features lead to the diagnosis of ichthyotic MF, different adnexotropic forms of MF, granulomatous forms of MF, MF with follicular mucinosis and latterly also papuloerythroderma of Ofuji (Table 6).

Ichthyotic mycosis fungoides

MF may be mistaken for an ichthyosis. Clinical aspects of an ichthyotic MF more often reveal extensive skin involvement (Fig. 3). 40 Typical dry scaling affects the trunk and extremities. Sometimes a mild erythroderma-like condition may develop. 41,42 Clinically obvious follicular keratosis, comedo-like lesions and epidermal cysts are mentioned as additional manifestations. 40,42 A coexpression of ichthyotic and follicular MF has been published. 43 In MF, in contrast to other lymphomas, the ichthyosis is not paraneoplastic but is self-defining and has a fairly good prognosis. 43

Adnexotropic mycosis fungoides

This is mainly misdiagnosed as acnetiform lesions and alopecia. Adnexotropic MF can be itemized into subtypes for which different diagnoses are given (Table 7).
Syringolymphoid hyperplasia (SLHA) was first described by Sarkany in 1969.44 Published as lymphomatoid granulomatosi,
its characteristics were alopecia, anhidrosis, hypertrophy of eccrine glands and vasculitis. In 1992 Burg and Schmoeckel45 revealed an association with cutaneous T-cell lymphoma. The clinical presentation is variable, and includes solitary or multiple patches and plaques or skin-coloured to reddish papules, with more extensive skin involvement resembling follicular hyperkeratosis, poikiloderma atrophicans, erythroderma and even palmoplantar hyperkeratosis. Hair loss, hyperaesthesia of the affected skin area and anhidrosis are possible adjuncts. Eight of 15 published cases of SLHA were classified as syringotropic cutaneous lymphoma, for which 13 further cases are now known.46 Besides clinical similarities to SLHA, erythema punctata, sometimes with follicular accentuation and milia, is described for the syringotropic form. The facial localization is reminiscent of discoid lupus erythematosus. The typical histology shows a dense syringotropic lymphocytic infiltrate sometimes surrounding hyperplastic eccrine glands and eccrine ducts. Generally considered a variant of MF, both have a similarly good prognosis.47

Folliculotropic mycosis fungoides

Folliculotropic MF, or follicular MF, is predominantly localized on the head and neck (Fig. 4). Clinically it presents follicular papules (often grouped), alopecia and acneiform lesions.48,49 Patients often complain about severe pruritus.48 Even pseudotumorous forms with nodules have been described, with a marked follicular hyperplasia rather than a lymphocytic proliferation.50 Otherwise perifollicular pleomorphic infiltrates show various degrees of folliculotropism without epidermotropism. Follicular MF is sometimes associated with follicular mucinosis. In 2002, 51 cases of follicular MF were recorded in the Netherlands.48 Diagnostic accuracy and adapted therapeutic regimens seem necessary as follicular MF might be less responsive to standard treatment modalities: this is a possible explanation for disease progression in the Dutch collection.6,48,51

Most cases of folliculotropic MF show mucinous degeneration of the hair follicles and are traditionally designated as MF-associated follicular mucinosis. However, this is not a prerequisite and, with or without associated follicular mucinosis, these forms are named ‘follicular MF’ or ‘folliculotropic MF’. The difficulty of a diagnostic assignmet of follicular mucinosis towards MF or of delineation as a primary and exclusive clinical manifestation is reflected in ongoing discussions.52–57 The differentiation cannot be assisted by PCR of the T-cell receptor, as the primary or idiopathic follicular mucinosis might also exhibit monoclonal T-cell populations. Furthermore, follicular mucinosis has been observed in association with other MF subforms, such as the adnexotropic form, already

### Table 7 Differential diagnoses of adnexotropic forms of mycosis fungoides

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Differential diagnosis</th>
<th>First author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adnexotropic</td>
<td>Rosacea</td>
<td>Sherertz 1986113</td>
</tr>
<tr>
<td></td>
<td>Eczema</td>
<td>Bonta 2000114</td>
</tr>
<tr>
<td></td>
<td>Seborrhoeic dermatitis</td>
<td>van Doorn 200228</td>
</tr>
<tr>
<td></td>
<td>Comedones, cysts</td>
<td>Oliwiecki 1992115</td>
</tr>
<tr>
<td></td>
<td>Epidermal cysts</td>
<td>Lacour 1993116</td>
</tr>
<tr>
<td></td>
<td>Comedones, cysts, alopecia</td>
<td>Peris 1999117</td>
</tr>
<tr>
<td></td>
<td>Follicular hyperkeratosis</td>
<td>Klemptke 199951</td>
</tr>
<tr>
<td></td>
<td>Poikilodema vasculare atrophicans</td>
<td>Brecher 2002118</td>
</tr>
<tr>
<td></td>
<td>Idiopathic syringolymphoid hyperplasia</td>
<td>Kazakov 2004112</td>
</tr>
<tr>
<td></td>
<td>Discoid lupus erythematosus</td>
<td>Thein 200446</td>
</tr>
</tbody>
</table>

© 2006 British Association of Dermatologists • British Journal of Dermatology 2007 156, pp1–10
characterized, and papuloerythroderma of Ofuji for which clinical description and differential diagnoses will follow.58

The coexistence of syringotropic and folliculotropic cutaneous lymphomas also results in acneiform manifestations with follicular papules, comedones, milia, cysts, dry skin and alopecia.47 Some authors suggest inclusion of these clinical variants, as well as other pilotropic forms of MF, under the term ‘adnexotropic cutaneous lymphomas’.59,60

Granulomatous mycosis fungoides and granulomatous slack skin

Ackerman and Flaxman61 proposed the term ‘granulomatous MF’ in 1970. In 1978 Ackerman62 added the term ‘granulomatous slack skin disease’. In 1968 Bazex et al.63 described a clinical form similar to cutis laxa as ‘Besnier–Boeck–Schau mann disease’. In 1997 and 2005 ‘granulomatous slack skin’ was included in the EORTC64 and then the WHO–EORTC classification6 as a provisional entity. So far up to 42 cases have been reported. Granulomatous T-cell infiltrates and loss of elastic fibres lead to asymptomatic skin wrinkles, mainly in the flexures (Fig. 5).65 Sometimes pruritus and erythema are described. Granulomatous MF may be preceded by erythematous scaling patches or macules, and may coexist with classical MF lesions. Benign as well as progressive courses were described. In 50% of cases coexistence with Hodgkin disease or nodal non-Hodgkin disease is observed.

From a histological point of view it is discussed whether granulomatous MF and granulomatous slack skin belong together.59,67 The pathogenesis of granuloma formation in lymphoma is unknown and its occurrence is not specific for MF. Similar histological formations have been described in pleomorphic T-cell lymphoma, panniculitis-like T-cell lymphoma and in B-cell lymphomas.68 A case report of a CD30+

Fig 4. Adnexotropic form of mycosis fungoides.

Fig 5. Mycosis fungoides with granulomatous slack skin.
The diagnosis can only be confirmed during the course of disease. Whole-body inspection often allows identification of typical lesions besides atypical lesions, thus guiding towards the correct diagnosis. Taking all information together and adding histology, differential diagnoses are no longer a problem. Once a lymphoma has been diagnosed a consequent follow-up is also required to detect possible recurrence or manifestation of other associated conditions.

We end with a statement by Zackheim and McCalmon13 who called MF ’the great imitator’. They compared the chameleon-like diversity in clinical presentation of MF with the variability of clinical conditions seen in syphilis.

Acknowledgments

We thank Professor Rein Willemze for revision and constructive advice.

References


Table 8 Differential diagnosis of granulomatous forms of mycosis fungoides

<table>
<thead>
<tr>
<th>Clinical sign</th>
<th>Differential diagnosis</th>
<th>First author</th>
</tr>
</thead>
<tbody>
<tr>
<td>Granulomatous</td>
<td>Granuloma annulare</td>
<td>Jouary 2002</td>
</tr>
<tr>
<td>Sarcoidosis</td>
<td></td>
<td>Bessis 1996</td>
</tr>
<tr>
<td>Necrobiosis</td>
<td></td>
<td>Woollons 1999</td>
</tr>
<tr>
<td>Skin atrophy</td>
<td>Cutis laxa</td>
<td>van Haselen 1998</td>
</tr>
</tbody>
</table>

Lymphoma with granulomatous slack skin exists, so not even granulomatous slack skin is a specific subtype of MF. Therefore clinically and histologically granulomatous MF variants have to be differentiated from other cutaneous T-cell lymphomas and from sarcoidosis, granuloma annulare and infectious granulomas (Table 8). The so-called ‘sarcoidosis–lymphoma syndrome’ includes the association of sarcoidosis and lymphoma, among other entities described in association with MF.

Papuloerythroderma of Ofuji

Is papuloerythroderma of Ofuji no more a differential diagnosis but a precursor of MF? Papuloerythroderma of Ofuji was first described in 1984. It is characterized by red-brownish, partly confluent flat papules; the flexors remain unaffected, and this is described as a ‘deckchair distribution’. Reports describe the association of papuloerythroderma of Ofuji and cutaneous lymphoma as well as the development of a cutaneous lymphoma after primary diagnosis of papuloerythroderma of Ofuji. Case reports demonstrate the similarity to MF with eosinophilia, with elevated serum IgE and similar histological and molecular biological criteria.

Distinguishing diagnoses

Based on clinical evaluation, the progress of MF and transformation into other lymphoma subtypes can be assessed. The coexistence of different primary cutaneous lymphomas and secondary cutaneous lymphomas presents a challenge for differential diagnosis. Coexisting dermatological conditions such as psoriasis or neurofibromatosis and atopic dermatitis also have to be taken into account. The correct diagnosis. Taking all information together and adding histology, differential diagnoses are no longer a problem. Once a lymphoma has been diagnosed a consequent follow-up is also required to detect possible recurrence or manifestation of other associated conditions.

Conclusion

Knowledge of cutaneous lymphoma is advancing. According to Koiz et al., in every chronic disease resistant to treatment lymphoma has to be considered. Therefore, if lymphoma is suspected then the diagnosis must be confirmed by clinical, histological and molecular examinations perhaps repeated in the course of the disease. In about 10% of cases the diagnosis can only be confirmed during the course of disease. Whole-body inspection often allows identification of typical lesions besides atypical lesions, thus guiding towards the correct diagnosis. Taking all information together and adding histology, differential diagnoses are no longer a problem. Once a lymphoma has been diagnosed a consequent follow-up is also required to detect possible recurrence or manifestation of other associated conditions.

We end with a statement by Zackheim and McCalmon who called MF ’the great imitator’. They compared the chameleon-like diversity in clinical presentation of MF with the variability of clinical conditions seen in syphilis.

Acknowledgments

We thank Professor Rein Willemze for revision and constructive advice.

References

Diversity of mycosis fungoides, D. Nashan et al.