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Hyperpigmented mycosis fungoides with histological spongiosis in a 61-year-old Syrian male: a case report

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Abstract

Background Mycosis fungoides is a type of cutaneous T-cell malignancy that gives different skin manifestations. Hyperpigmented mycosis fungoides is a very rare type of mycosis fungoides that presents with hyperpigmented patches and macules on the skin, it is reported to affect patients in their 30s, with only few cases reported to date. In this article, we present a unique case of hyperpigmented mycosis fungoides in which histological examination of the skin biopsy showed spongiosis, which is a rare histologic manifestation in mycosis fungoides, which makes the case more exceptional.

Case presentation A 61-year-old Syrian male presented to the dermatology clinic complaining of a persistent pigmented itchy lesion on the right side of the trunk and right thigh. Histological examination of the skin biopsy showed parakeratosic hyperkeratosic epidermis with spongiosis and deposition of melanophages, immunohistochemistry showed $CD3^+$, $CD4^-$, $CD8^+$, and $CD20^-$, and our patient was diagnosed with hyperpigmented mycosis fungoides, and subsequently treated with psoralen and ultraviolet A therapy, a very good improvement was noted, and the prognosis was excellent.

Conclusion Although hyperpigmented mycosis fungoides is an extremely rare condition, clinical practitioners should consider it as a diagnosis that may be encountered when approaching a persistent pigmented skin lesion to provide correct clinical orientation and avoid confusion with differential diagnoses. The diagnosis of hyperpigmented mycosis fungoides should not be excluded based only on the age. Skin biopsy and immunohistochemistry are the irreplaceable investigations to diagnose hyperpigmented mycosis fungoides. Spongiosis, although rare in mycosis fungoides, should not rule out the diagnosis of hyperpigmented mycosis fungoides.

Keywords Hyperpigmented mycosis fungoides, Spongiosis, Mycosis fungoides, Hyperpigmented mycosis fungoides treatment, Skin cancer, Cutaneous T-cell lymphoma, Case report

Background

Mycosis fungoides (MF) is a type of cutaneous T-cell lymphomas (CTCL) and represents a rare blood malignancy characterized by various skin manifestations such as rash, plaques or tumors [1]. Despite its skin manifestations, it is not classified as a skin cancer, since the malignant cells originate in the peripheral epidermotropic memory T cells ($CD45RO^+$), which express the $CD4^+$ immunophenotype and the T-cell receptor (TCR) [1, 2]. MF accounts

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for about 4% of all cases of non-Hodgkin lymphoma and is more likely to occur in men after the age of 50 years [2]. The causes of MF are not clearly known, but there are predisposing factors such as genetic mutations and environmental exposure to certain chemicals and infections [1, 2]. The clinical progression of MF goes through several stages, including the patch stage, the plaque stage, and the tumor stage, and can be diagnosed by skin biopsy or lymph node biopsy [1, 2]. There are various variants of MF, including pagetoid reticulosis and folliculotropic and granulomatous MF [2]. Hyperpigmented mycosis fungoides (HPMF) is an extremely rare type of MF that presents as hyperpigmented patches and macules on the skin. Unlike classic MF, this type affects younger people, especially those with darker skin [3]. Treatment is based on the stage of MF and includes topical steroids, systemic chemotherapy, immunotherapy, and radiation therapy [1, 2]. We believe this case of HPMF in a 61-year-old Syrian male is noteworthy due to the rarity of this variant of MF, as well as the presence of spongiosis, a rare histologic manifestation of MF [4].

Case presentation

A 61-year-old Syrian male with a history of alcoholism and heavy smoking presented to the dermatology department with complaints of itchy pigmented lesions without telangiectasias, scaling, or atrophy on the right side of his trunk and his right thigh. The patient denied prior history of exposure to chemicals or solvents, and there was no family history of skin cancers, skin diseases, or relevant systemic conditions. These lesions were persistent for 3 years, and the patient was previously prescribed a topical 0.1% hydrocortisone cream by a local dermatologist to relieve the itching; the patient used the cream intermittently and only when the itching was severe. Upon clinical examination, hyperpigmented patches on the right side of his trunk and the lateral surface of his right thigh were evident, with no other clinical features (Fig. 1). Blood tests of the patient were all within normal ranges except a slight increase in the white blood cell count. Given the nonspecific features, a skin biopsy was performed for further evaluation, and histopathological examination of the biopsy revealed parakeratosic hyperkeratosic epidermis with slight spongiosis. Papillary dermis was infiltrated moderately by atypical lymphocytes with mild deposition of melanophages. Lymphocytic infiltrate was situated in clusters and in linear basilar distribution along the dermoepidermal junction (Fig. 2). Immunochemistry of the atypical lymphocytes were $CD3^+$, $CD8^+$, $CD4^-$, $CD20^-$. A chest and abdomen computed tomography (CT) scan was conducted, but yielded only normal findings with no lymphadenopathy or organomegaly. The patient was diagnosed with early stage

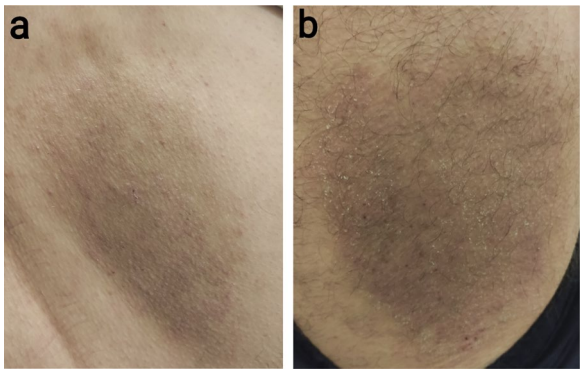

Fig. 1 Persistent hyperpigmented patches on the right side of the patient's trunk (**a**) and right thigh (**b**)

HPMF and was subsequently referred to a specialized hospital to receive the treatment. Our patient underwent psoralen and ultraviolet A light (PUVA) therapy, with oral 8-methoxypsoralen two times a week, and was prescribed a topical 0.1% betamethasone dipropionate. After 12 weeks of treatment, the itching was relieved, and the hyperpigmentation regressed, but did not disappear. The patient's long-term prognosis is excellent, and he was instructed to apply moisturizer and avoid sun exposure and is being evaluated every 6 months to detect any further relapse or new lesions on other areas of the body.

Discussion

MF is the most prevalent among CTCLs, arising from the peripheral epidermotropic memory T cells ($CD45RO^+$). It affects black individuals more than Asian or white individuals [2]. While the exact causes of MF remain unclear, various etiologies had been proposed. The genetic etiology of deletions and translocations involving several different chromosomes or chromosomal segments had been suspected by several studies, and since particular TP53 polymorphisms were linked to various malignancies, Laura Y McGirt *et al.* concluded that the Pro72Arg polymorphism could be linked to MF [2, 5]. The environmental exposure etiology was recognized since several studies suggested that the exposure to aromatic hydrocarbons, hydrazine, and formaldehyde might be associated with MF. Furthermore, an infectious etiology related to human T-lymphotropic virus Type 1 (HTLV-1) had been linked to the disease as well [2]. Our patient was a Syrian male who had no history of exposure to chemicals or relevant infections. The presentation of MF varies significantly depending on the disease stage. The initial stage, known as the patch stage, is characterized by an erythematous, scaly patch that may exhibit moderate atrophy. As the disease advances, it progresses to the plaque stage, and the lesions become elevated with well-defined edges,

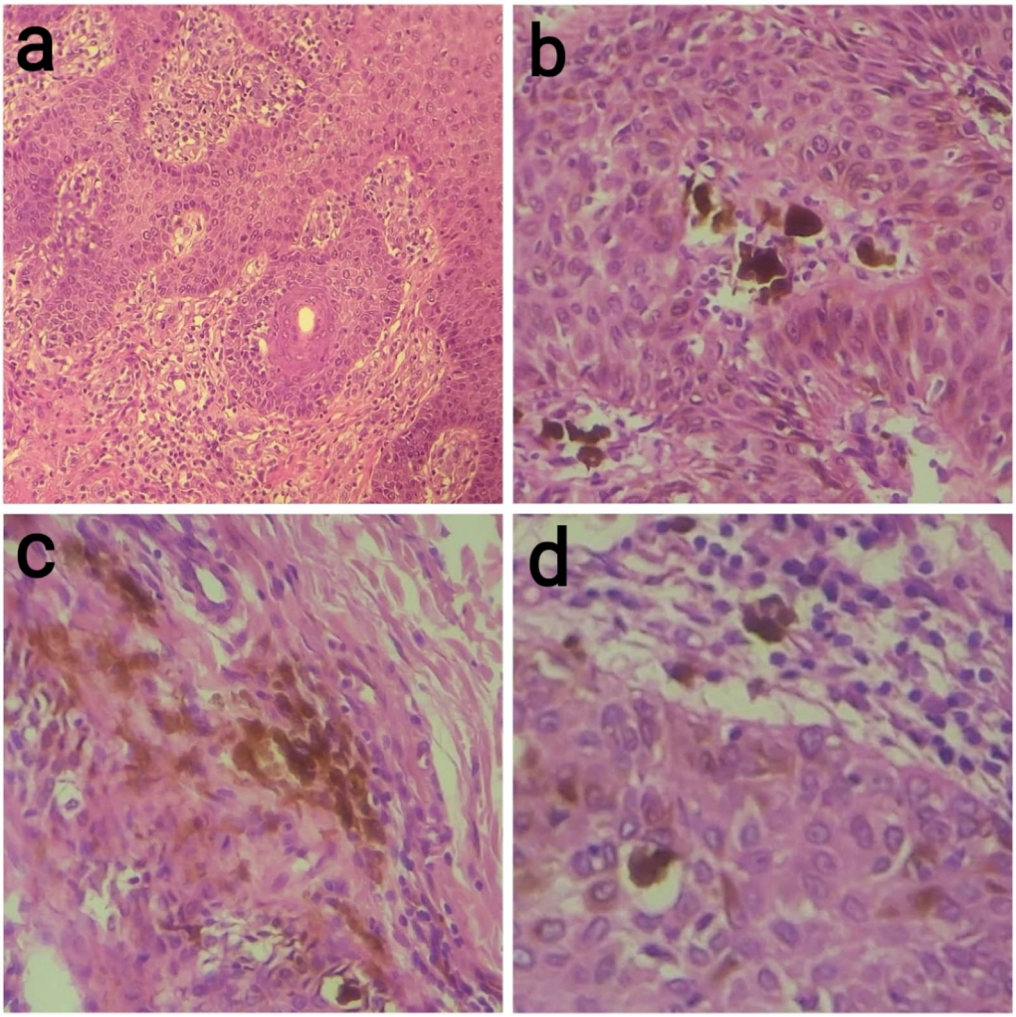

Fig. 2 Microscopic study of the skin biopsies with hematoxylin–eosin staining shows the presence of spongiosis (**a**), as well as depositions of melanophages and atypical lymphocytes infiltration (**b**, **c** and **d**)

and new lesions emerge with an asymmetrical distribution. In the tumor stage, erythematous nodules or papules develop, typically larger in diameter than those seen in the previous stages. The clinical presentation could also be accompanied by organomegaly or lymphadenopathy, but only in advanced cases [2, 6]. There are several clinical variants of MF, including hypopigmented, granulomatous, and hyperpigmented MF. HPMF represents the rarest variant, with only a few cases reported in literature [3]. HPMF is more common in Black people. It usually occurs at the age of 35 years and younger, while classic MF affects patients 50 years of age[2, 3, 6]. In our case, the patient was 61 years old at presentation. Clinical examination of HPMF patients typically reveals hyperpigmented patches or plaques, but no poikilodermatous changes are noted. Defined hyperpigmented patches can be a characteristic of various conditions including contact dermatitis, postinflammatory hyperpigmentation, parakeratosis variegate, erythema dyschromicum perstans, and poikiloderma vasculare atrophicans. The diagnosis of early-stage MF through histopathology can be challenging. It may require the evaluation of multiple biopsies conducted over several months and a thorough correlation between the pathological and clinical findings to validate the clinical suspicions and distinguish MF from other differential diagnoses such as poikilodermatous variegata or contact dermatitis [3]. Our patient only had hyperpigmented patches at presentation, and a skin biopsy was performed for further evaluation. Histopathology of HPMF is marked by a dermal lymphocytes infiltration and epidermotropism, and hematoxylin–eosin staining revealed melanophages with

interface changes. The hyperpigmentation observed in the clinical examination could be a result of the melanophages interface changes in addition to the influence of stem cells and mast cells promoting the melanocytes to produce melanin [3]. Spongiosis is a rare histologic manifestation in MF. It is characterized by wide spaces between the surrounding keratinocytes, as well as condensation of cells, and extended intercellular bridges, indicating the presence of intercellular epidermal edema [4]. Histopathological examination of skin biopsies of our patient revealed spongiosis alongside depositions of melanophages and atypical lymphocytic infiltration. Classic MF exhibits a clonal proliferation of $CD4^+$, and less commonly $CD8^+$, but the immunohistochemistry of HPMF is often characterized by a $CD8^+$ phenotype, and less frequently by a CD4–CD8 phenotype [3, 6]. Our patient immunohistochemistry revealed a $CD8^+$ phenotype. MF diagnosis is challenging even in advanced countries, as it mimics various conditions such as chronic eczema, psoriasis, or atopic dermatitis. However, the diagnosis of HPMF is further complicated due to its rarity and the possible differential diagnoses, especially in resource-limited countries, which may result in the misdiagnosis of HPMF [2, 4, 7]. The rare presence of spongiosis in MF adds more difficulty to the diagnostic process since spongiosis may occur in benign inflammatory conditions [4]. Although HPMF can occur solely, it may also intermix with other pigmentary variants of MF, such as pigmented purpura-like and hypopigmented MF, complicating the diagnosis process. Therefore, the evaluation of numerous biopsies and a prolonged follow-up are necessary to affirm the diagnosis [3, 4]. Radiological imaging, such as chest and abdomen CT may be performed to assess for potential lymphadenopathy or visceral involvement, depending on the stage of the disease [2]. CT imaging of the chest and abdomen of our patient revealed only normal findings. HPMF is an indolent disease, mimicking the early stage of classic MF, although the classic MF with a $CD8^+$ phenotype tends to be more aggressive in some cases. Incilay Kalay Yildzhan *et al.* concluded that the $CD8^+$ phenotype in MF is typically associated with an indolent and slower-progressing type of MF, and that skin-directed treatments are effective for its management [3, 8]. Prognosis of MF varies depending on several factors. The poor prognosis is associated with older age, the extracutaneous involvement, elevated lactate dehydrogenase (LDH) levels, and specific variants such as folliculotropic MF [2]. Similar to classic MF, the treatment of HPMF is based on the clinical stage. Systemic chemotherapy is indicated for patients exhibiting advanced symptoms such as lymphadenopathy or organomegaly. However, for early stages, the standard therapy is photochemotherapy. However, PUVA and topical chemotherapy, oral retinoids, and topical corticosteroids can be used [2, 3]. Our patient reported a very good improvement in the symptoms after PUVA therapy with 0.1% betamethasone dipropionate. Since there is no complete cure for mycosis fungoides, the main goal of the follow-up is to improve the patient's quality of life and long-term prognosis, and to detect relapse occurrence. In addition to the mentioned therapeutic measures, the patient should be advised to use adequate moisturizers to prevent skin dryness and to wear long-sleeved clothing when outside to minimize the sun exposure [2]. Upon returning to the literature, we reviewed four similar cases of HPMF, including a case of 55-year-old Japanese male with reticular pigmentation with an erythematous, itchy periphery on the face [9], and other two other cases, a 67-year-old Kosovar male and a 45-year-old female presenting with pigmented lesions spread over several areas of the body [10, 11], as well as a case with $CD4^+$ predominance presenting with lichen planus pigmentosus-like lesions in a 72-year-old elderly male with a dark complexion [12]. In contrast to these cases, our patient was Syrian and had only two hyperpigmented patches on his trunk and right thigh, and the skin biopsy exhibited spongiosis.

Conclusion

Clinicals should consider the diagnosis of HPMF, although rare, as a differential diagnosis in patients presenting with persistent hyperpigmented patches, and a skin biopsy and immunohistochemistry are necessary to confirm the diagnosis. The diagnosis of HPMF should not be excluded based only on the age. Further research is needed to elucidate the epidemiological data of HPMF. Hyperpigmentation might be the only manifestation of HPMF, and regular follow-up is needed for better evaluation. Histological features such as spongiosis, although rare in MF, should not rule out the possibility of HPMF. Photochemotherapy remains an effective treatment of HPMF.

Methods

This work has been reported in line with the CARE criteria [13].

Abbreviations

MF	Mycosis fungoides
CTCL	Cutaneous T-cell lymphomas
TCR	T-cell receptor
HMPF	Hyperpigmented mycosis fungoides
CT	Computed tomography
PUVA	Psoralen and ultraviolet A light
HTLV-1	Human T-lymphotropic virus Type 1

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Author contributions
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Competing interests
None.

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