DERMATOLOGICA SINICA 36 (2018) 207–210

Contents lists available at ScienceDirect

Dermatologica Sinica

journal homepage: http://www.derm-sinica.com

CASE REPORT

A case of hypopigmented mycosis fungoides successfully treated with 311 nm narrowband ultraviolet B phototherapy

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ARTICLE INFO

Article history:
Received: Nov 30, 2017
Revised: Mar 13, 2018
Accepted: Apr 12, 2018

Keywords:
Lymphoma
T-cell
Cutaneous
Mycosis fungoides
Phototherapy
PUVA therapy
Ultraviolet therapy

ABSTRACT

Hypopigmented mycosis fungoides (HMF) is a rare clinical variant of mycosis fungoides (MF) characterized by hypopigmented lesions involving most commonly trunk and proximal extremities. We report here a case of HMF in 22-year-old Korean woman successfully treated with 311 nm narrow-band ultraviolet B (NB-UVB) phototherapy. She presented with progressive asymptomatic hypopigmented patches on wholebody 1-year ago and diagnosed as HMF based on clinicopathologic findings. She was treated with NB-UVB phototherapy and showed almost complete clearance after 8-month without any side effects.

Introduction

Mycosis fungoides (MF) is the most common primary cutaneous T-cell lymphoma and hypopigmented MF (HMF) is a rare clinical variant of MF. Clinical findings are asymptomatic hypopigmented lesions. Histopathologic findings are similar of classic MF, but immunohistochemistry (IHC) shows a predominance of CD8 T cells, unlike classic MF. Differential diagnosis includes other dermatosis which can show diffuse hypopigmented lesions. It has usually benign clinical course and responds well to therapy. We herein report a case of HMF, successfully treated with narrow-band ultraviolet B (NB-UVB) phototherapy.

Case report

A 22-year-old Korean woman presented with a 1-year history of progressive, asymptomatic hypopigmented patches on trunk and extremities. At first, a few lesions appeared over both knees 1-year ago. Then, the lesions gradually increased in size and progressed to involve almost whole-body sparing face. Skin examination showed generalized, multiple ill-defined irregular hypopigmented macules and patches without overlying erythema and skin atrophy. Some lesions showed fine scales on them (Fig. 1a–c). There was no enhancement of the hypopigmented lesions under Wood's lamp.

She had no systemic symptoms. Past medical and family history were not contributable, with no evidence of recent infections, other dermatosis, or relevant environmental exposure. Physical examination including lymph nodes was unremarkable. Laboratory tests including complete blood count, and liver, renal and thyroid function tests were within normal limits.

Four-mm punch biopsies were taken from a hypopigmented patch on her leg and the adjacent normal skin. Histologic examination revealed decreased basal pigmentation without epidermal change. There was a few atypical lymphocytic infiltration of papillary dermis and single lymphoid cell infiltration in the basal layer linearly. Epidermotropism was seen as well. In some area, they seem to show clustered pattern, like Pautrier's microabscess. But there was no spongiosis nor interface dermatitis. Also there were no melanophages in the dermis (Fig. 1d). High magnification revealed hyperchromatic, atypical lymphoid cells (Fig. 1e). Compared to normal skin, Fontana-Masson stain showed marked reduction of basal pigmentation in the hypopigmented lesion.

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https://doi.org/10.1016/j.dsi.2018.04.004

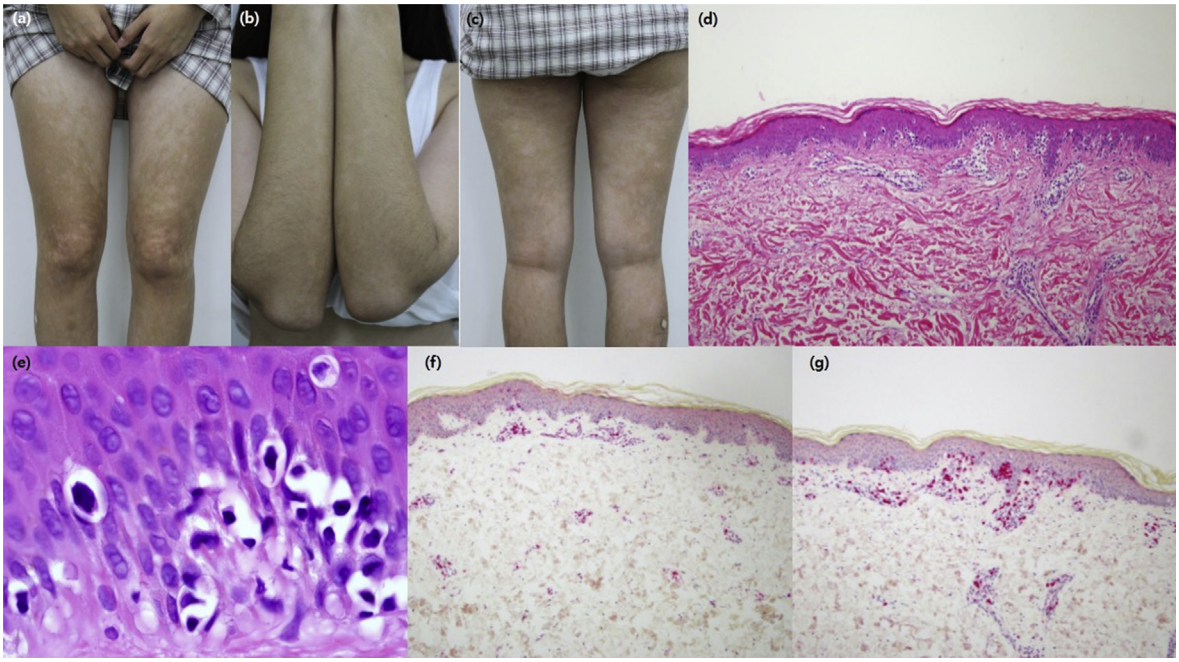

Fig. 1 (a-c) Generalized, multiple ill-defined irregular hypopigmented macules and patches without overlying erythema and skin atrophy. (d) Decreased basal pigmentation without epidermal change. Epidermotropism and Pautrier's microabscess were seen (H&E,×100) (e) High magnification revealed hyperchromatic, atypical lymphoid cells (H&E, ×400) (f-g) CD4, CD8. Immunochemistry revealed positive for CD4 and CD8 but they showed CD8 predominance.

Melan-A stain revealed a few residual melanocytes while the number of melanocytes was within normal in the control.

IHC revealed the atypical lymphocytes were positive for CD3, CD8 and focally positive for CD4 (Fig. 1f–g). They showed CD8 predominance. T-cell receptor (TCR) gamma gene rearrangement analysis showed monoclonal proliferation. Based on above all findings, we diagnosed as stage IB HMF.

She was treated with 311 nm NB-UVB phototherapy twice-weekly with a total number of 66-treatment. The initial treatment dose was 300 mJ/cm^2 and then increased the dose to 1000 mJ/cm^2 over 8-month. No side effects were reported during treatment period. She showed almost complete clearance of hypopigmented lesions by 66-NB-UVB treatments (Fig. 2a–c). Follow up-treatment biopsy specimen showed nearly normal histologic features with a few atypical lymphocytes the number of which was significantly decreased (Fig. 2d).

Discussion

MF is the most common type of primary cutaneous T-cell lymphoma characterized by patches, plaques, and tumors stages. There are several distinct clinical forms of MF including granulomatous, pustular, purpuric, hyperkeratotic, verrucous, bullous, invisible, and hypopigmented variants. Among them, HMF is a rare clinical variant of patch stage MF, first described in 1973 by Ryan et al.[1] It differs from the classic MF in clinical, histopathological, and IHC aspects. HMF has younger onset than MF with no gender predilection. And HMF is reported almost in dark-skinned and Asians, because of its predilection for high phototypes. Clinical features are various-sized asymptomatic, hypopigmented lesions occurred mainly on trunk and proximal extremities. Sometimes, it can also involve other part of body like face and distal extremities including palms and soles. Hypopigmented lesions can be the only manifestation of MF, but there are often presences of characteristic erythematous patches or plaques through careful physical examination. There is a case report of showing erythematous plaques and hypopigmented patches and histologically, granulomatous and classic features of MF simultaneously.[2] Overlying skin atrophy and telangiectasia are the other findings which can be shown. Histopathologically, band-like lymphocytic infiltration in papillary dermis and epidermotropism are the characteristic findings, just like classic MF. However, IHC shows a predominance of CD8 T-cells,

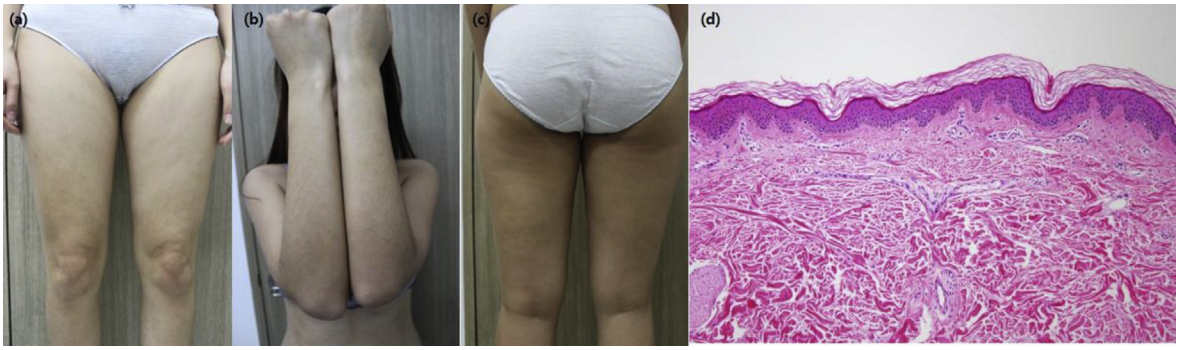

Fig. 2 (a-c) Almost complete clearance of hypopigmented lesions by 66-narrow-band ultraviolet B (NB-UVB) treatments. (d) Follow up-treatment biopsy specimen showed nearly normal histologic features with a few atypical lymphocytes.

unlike classic MF.[3] TCR gene rearrangement may be useful, but it is not entirely specific.

Differential diagnoses should include other dermatosis which can show diffuse hypopigmented lesions like pityriasis alba, vitiligo, postinflammatory hypopigmentation, sarcoidosis, pityriasis lichenoides chronica, pityriasis versicolor, syphilis and other treponematosis, idiopathic guttate hypomelanosis, lichen sclerosus, hypomelanosis of Ito, halo nevus, onchocerciasis and annular lichenoid dermatosis of youth (ALDY).[4,5] Among them, it is important to differentiate HMF, inflammatory vitiligo, and ALDY because they all can show hypopigmented lesions with similar histologic features. Recently, some articles suggested their clinical and histopathologic distinctions.[6,7] The coexisting erythematous patches or plaques, fine scaling, poikiloderma or atrophy favors HMF, and erythematous and papular borders surrounding hypopigmented lesions are features favoring inflammatory vitiligo. In contrast, ALDY shows central hypopigmentation surrounded by slightly raised red-brown colored rim in trunk and groin. Histologically, HMF is more likely to show prominent epidermotropism, band-like lichenoid infiltration, a relatively decreased, but not absent melanocytes, and dermal wiry fibrosis. In contrast, distinguishing features of inflammatory vitiligo include near-complete absence of melanocytes, basement membrane thickening, and focal as opposed to diffuse epidermotropism. Histologies of inflammatory vitiligo are usually consistent with classic vitiligo. But when biopsies taken from the edge of early hypopigmented lesion or raised erythematous border, they can show lichenoid lymphocytic infiltration along the basal layer, exocytosis, spongiosis, and lymphocytic infiltration of dermis.[7] ALDY is an inflammatory condition distinct from MF although there may be some overlapping histopathologic and immunophenotypic features. ALDY shows a lichenoid tissue reaction involving the base of rete ridges and usually shows intact melanocytes. The baseline histology is a lichenoid dermatitis with epithelial injury to involve the tips of rete ridges. Epidermotropism may be seen, but not prominent and lymphoid atypia is not described.

Our patient showed most of the features favoring HMF. She did not have annularity, and the lesions tend to be generalized, with microscopic evaluation showing prominent epidermotropism with lymphoid atypia. Also TCR gamma gene rearrangement showed monoclonality.

In diagnosing HMF, clinicohistologic correlation is very important. If there is an absence of certain characteristic clinical and histologic findings of MF, immunohistological analysis of neoplastic T-cells and monoclonal TCR gene rearrangement can be helpful to diagnosis.[5] However only 50%–80% of patch stage MF shows monoclonality and monoclonality may also be seen in benign disorders, including inflammatory vitiligo.

In classic MF, neoplastic cells are typically CD4 T cells with variable loss of other T-cell markers and infiltration of CD8 T cells is uncommon. While classic MF shows typically atypical CD4 T cells, the characteristic immunochemical analysis of HMF is predominantly CD8 infiltration with marked epidermotropism contrary to mild-to-moderate dermal infiltration. Clusters of lymphocytes within the epidermis (Pautrier'smicroabscess) are seldom reported and these also can be observed in inflammatory dermatoses. Other findings include slight psoriasiform epidermal hyperplasia, sparse superficial perivascular, periadnexal or patchy lichenoid dermal lymphocytic infiltration and dermal wiry fibrosis. Other characteristic immunochemical profile is that decreased CD7 expression.[8] Greater presence of CD1a Langerhans cells in the epidermis may be useful in distiughishing early MF from imflammatory dermatoses.[9]

The exact mechanism of the pigment disturbance of HMF is unclear. Ultrastructural studies by Breathnach et al.[10] showed the degenerative changes of melanocytes and abnormal melanogenesis but there were no evidence of blockade in melanosome transfer from melanocytes to keratinocytes. The authors suggested that these changes would be non-specific response to cell injury associated with inflammation. It can be hypothesized that the neoplastic CD8 lymphocytes release factors that may inhibit the process of melanogenesis and these result in hypopigmented lesion of HMF.

HMF usually follows a benign clinical course and has a good response to therapy, but its potential lethality should not be underestimated.

Treatments include topical nitrogen mustard and carmustine, topical corticosteroids, phototherapy, and psoralen plus ultraviolet A photochemotherapy (PUVA).[11]

NB-UVB has become a standard treatment for typical patch-stage MF, but there are few publications reporting use of NB-UVB for HMF.[12] Recent studies reported twice-weekly regimen of NB-UVB phototherapy was an effective and well-tolerated treatment for HMF.[13,14] Wongpraparut and Setabutra[15] found that both PUVA and NB-UVB were effective modalities for HMF and PUVA was superior to NB-UVB. However, NB-UVB has advantages over PUVA that its availability and better safety profile.

In conclusion, we reported a rare case of HMF, successfully treated with NB-UVB phototherapy. HMF is a challenging diagnosis because it can resemble benign skin disorders. This case suggests that skin lesions suspicious for HMF should be biopsied to avoid diagnostic delay, especially in young population.

Conflict of interest

The authors declare that they have no financial or non-financial conflicts of interest related to the subject matter or materials discussed in this article.

Acknowledgement

This work was supported by the Soonchunhyang University Research Fund.

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