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Morphological Characterization of Erythrodermic Mycosis Fungoides

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Abstract

Mycosis fungoides (MF) is the most common variant of primary cutaneous T-cell lymphoma (CTCL). CTCLs constitute 65% of all cutaneous lymphoid malignancies, of which 50% are patients with MF. The erythrodermic variant of MF, a malignancy of mature, skin homing, clonal T lymphocytes, is a very rare clinical sub type that usually presents in mid- to late adulthood. We report a case of a 70-year-old man with intractable progressive erythroderma of a 2 year-duration, accompanied by severe persistent pruritus. Upon histological and immunohistochemical diagnosis, the most provocative challenge was ruling out leukemization confirming Sezary syndrome. A short critical overview of literature sources disputing this rightful verification is herein highlighted.

Key words: mycosis fungoides, erythroderma, Sezary syndrome

Introduction

Mycosis fungoides is the most common type of cutaneous T-cell lymphoma. MF is a primary cutaneous mature T-cell epidermotropic non-Hodgkin lymphoma [4]. It is considered a low-grade malignancy initially presenting in the skin, however, it can be aggressive and spread to lymph nodes, blood, and other organs, such as the liver, spleen, and gastrointestinal tract. Clinical features of MF include presence of progressive skin lesions such as patches, plaques, papules, tumor, erythroderma. The prognosis worsens in late stages.

Case report

A 70-year-old man was afflicted with large confluent erythematous pruritic patches with scaling dated back from 15 years. They gradually increased in size and number, mostly in the last 2 years, involving over 90% of his body surface area. There was no lymphadenopathy or hepatosplenomegaly. The patient had received previous topical corticosteroid treatment for chronic atopic dermatitis with no beneficial effect. His medical history was notable for hypertension and hypothyroidism.

On dermatological examination, diffuse, erythematous and scaly lesions were present on the trunk, arms, legs and face. A clinical diagnosis of MF was made, and multiple skin biopsies were taken from different sites. On histopathological examination the hematoxylin and eosin-stained section of the skin showed variable acanthosis, epidermotropism of atypical lymphocytes (characteristic "haloed cells") without spongiosis (**Figs. 1, 2**). On immunohistochemisty, lymphocytic infiltrate was positive for T-cell marker CD4 and to a much lesser extent for CD8 (**Figs. 3, 4**). Peripheral blood flow cytometry analysis showed a normal CD4/CD8 ratio (<10) and the Sezary cells were less than 5%, with the absolute number being 183 cells/mm3 (<1000 cells/mm3). Bone marrow aspiration cytology, chest X-ray and abdominal ultrasound exam appeared normal.

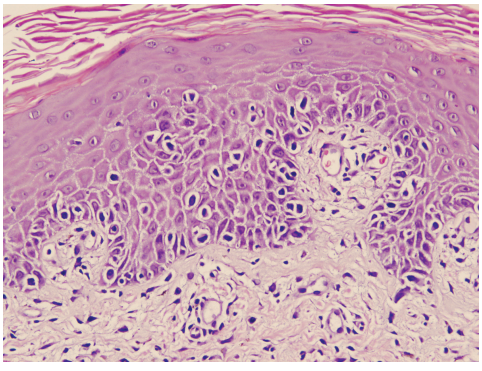

Fig. 1. Hyperkeratosis, acanthosis, epidermotropic atypical lymphoid cells in the low portion of the epidermis. (Hematoxylin-Eosin, × 200)

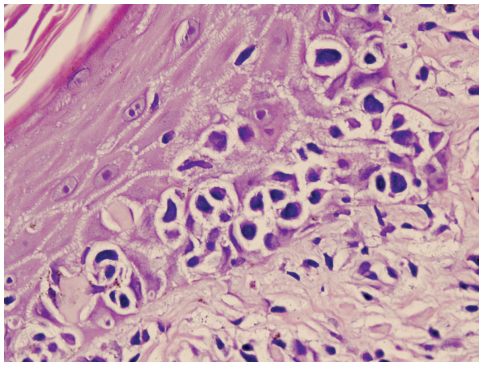

Fig.2. Pautrier's microabscesses. (Hematoxylin-Eosin, × 400)

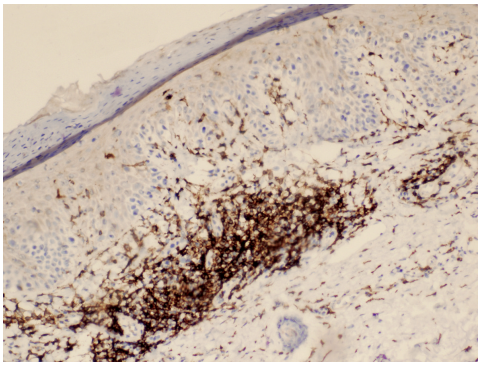

Fig. 3. CD4+ lymphoid cells. (× 400)

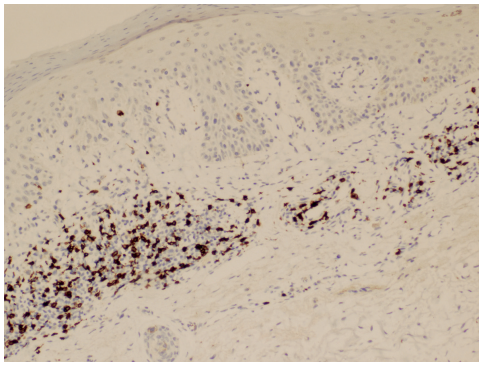

Fig. 4. CD8+ lymphoid cells. (× 400)

The patient's findings were consistent with an erythrodermic variant of MF, stage IIIA (T4N0M0B0) according to the ISCL/EORTC revised classification system.

Psoralen plus UVA therapy and IFN-alpha 2a (3 MIU SC 3 times weekly) resulted in partial clearance of lesions.

Discussion

Mycosis fungoides and Syndroma Sezary are the most common types of cutaneous T-cell lymphomas. MF is a malignancy of mature, skin homing, clonal T lymphocytes [9]. Sezary syndrome (SS) is an erythrodermic and leukemic variant of CTCL. It is defined by the triad of erythroderma, generalized lymphadenopathy and the presence of neoplastic T cells (Sezary cells) in the skin, lymph nodes and peripheral blood [7]. According to EORTC/WHO classification, a case of SS must demonstrate one or more of the following criteria: an absolute Sezary count of > 1000 cells/mm^3, a CD4/CD8 ratio of >10, T-cell clonality in the peripheral blood by flow cytometry, or a chromosomal abnormal T-cell clone [5]. The lack of monoclonal atypical lymphoid invasion in the peripheral blood ruled out SS and categorized our patient as an erythrodermic MF.

The erythrodermic MF variant was originally described in 1892 [8]. MF usually affects mid-aged adults with a slight male preference (2:1) [6]. The etiology and the pathogenic mechanisms involved in the development and step-wise progression of MF are largely unknown. Genetic, environmental and immunologic factors have been considered [3]. The diagnosis is based on standard histopathological findings, showing small cerebriform lymphoid cells that solitary or in groups (Pautrier's microabscesses) invade the lower portion of the epidermis. Usually those cells express CD4+/CD7- immunohistochemical profile. Interestingly, the invasive lymphoid population may transform into lower differentiated, more aggressive in biological behavior subtypes (CD30+ anaplastic T cells). Therefore, regular clinical and histological monitoring is essential in all MF cases.

Skin-directed therapies are preferred in early MF stages [2]. Topical corticosteroids, retinoids (bexarotene) or chemotherapeutic agents (nitrogen mustard), psoralen plus UVA phototherapy, and total skin electron beam irradiation (TSEB) are among the most effective treatment options. Systemic therapy is strictly preserved for advanced disease. Conventional chemotherapy (methotrexate, doxorubicin, vincristine), oral retinoids, IFN-alpha, alemtuzumab (monoclonal antibody), and histone deacetylase inhibitors such as Vorinostat and Romidepsin are the most common treatment of choice [1]. Ruling out SS utilizes better prognosis and a less aggressive treatment approach. The combined interferon – systemic photochemotherapy regimen initiated in our case proved beneficial, leading to partial clearing of the skin lesions.

Conclusion

Physicians should have a high index of suspicion for primary cutaneous lymphoid proliferation in any patient with therapy-resistant persistent pruritus. MF should be ruled out in patients with long-standing erythematous papules and plaques, progressing from confluent patches to generalized exfoliative dermatitis (erythroderma). Chronic erythroderma with atypical epidermotropic lymphoid cells, arranged in Pautrier's microabscesses and obscuring the dermal-epidermal junction is compatible with mycosis fungoides. The lack of peripheral blood monoclonal lymphoid cell inva-

sion ruled out SS, verifying erythrodermic MF. Regular follow-up visits and repeated skin biopsies are required to monitor the progression of MF to SS for better patient survival and outcome.

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