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Case Report

Erythrodermic CD4/CD8 Double-Negative Mycosis Fungoides: A Case Report

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Keywords

Mycosis fungoides · Cutaneous T-cell lymphomas · Erythrodermic mycosis fungoides · CD4/CD8 double-negative mycosis fungoides

Abstract

Cutaneous T-cell lymphoma (CTCL) describes a group of lymphoproliferative disorders characterized by localization of neoplastic T lymphocytes to the skin. Mycosis fungoides (MF) represents the most common type of CTCL and accounts for ~60% of all primary cutaneous lymphomas. Apart from the classic type of MF, many clinical and histopathologic variants have been described. The malignant lymphocytes in MF are usually CD3, CD4 and CD45RO positive and CD8 negative. An unusual immunohistochemical profile of a CD4-negative and CD8-positive mature T-cell phenotype has been reported in a minority of patients; up to 20% of early-stage MF demonstrates a CD8-positive phenotype. There are only a few cases of a double-negative CD4/CD8 MF phenotype reported in the literature. We present the case of a 60-year-old male presenting a double-negative CD4/CD8 MF phenotype.

Introduction

Mycosis fungoides (MF) is the most common variant of cutaneous T-cell lymphomas (CTCLs), comprising up to 62% of cases. It is characterized by a cutaneous invasion of skin-homing malignant monoclonal T lymphocytes [1–3]. It is more commonly seen in men (1.5–2:1), with 55–60 years being the median age at diagnosis. Clinically, MF has an indolent course

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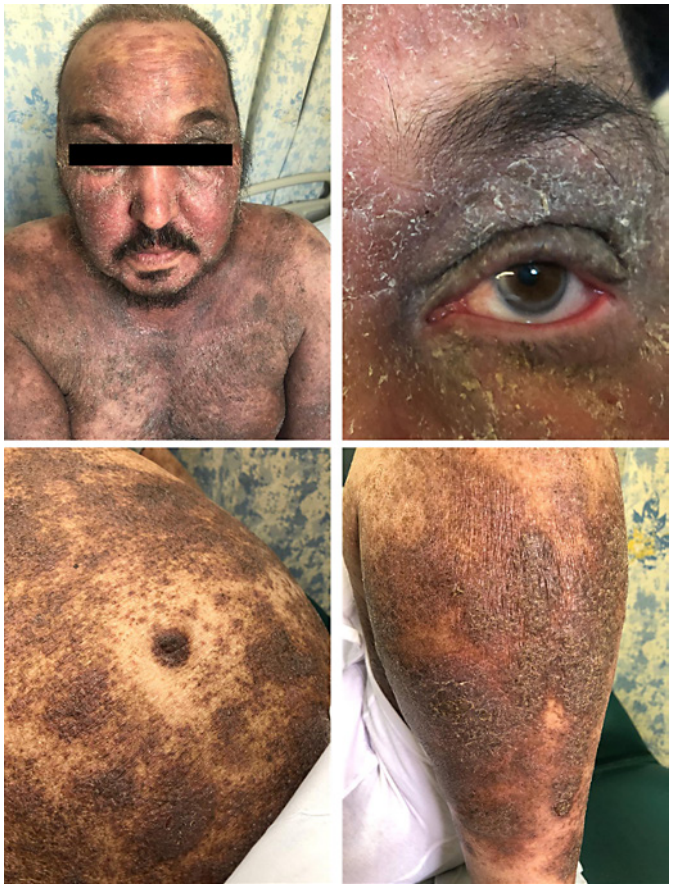

Fig. 1. Erythrodermic mycosis fungoides. Widespread symmetric erythromelanotic scaly patches and plaques involving the upper trunk and face, lower eyelid ectropion, abdomen, and left lower leg.

and can present during early stages as erythematous scaly patches or plaques, or during advanced stages as tumors or erythroderma, with lymph node and/or visceral involvement [4]. MF typically affects unexposed areas such as the trunk, buttocks, and thighs [5]. At early stages, it is commonly misdiagnosed as atopic dermatitis, chronic contact dermatitis, and psoriasis [2].

The malignant lymphocytes in MF are usually CD3, CD4 and CD45RO positive and CD8 negative. However, up to 20% of early-stage MF cases demonstrate a CD8-positive phenotype. CD4-positive T lymphocytes in MF have a variable loss of expression of surface markers such as CD2, CD3, CD5, CD7, and CD26. The loss of CD2, CD5 and/or CD7 expression in a large number of cells within the lesion or in the epidermis alone is highly specific (specificity >90%) for MF [3, 5]. However, there are only a few cases of a double-negative CD4/CD8 MF phenotype reported in the literature [6]. We present the case of a 60-year-old gentleman with a distinctive presentation of a double-negative CD4/CD8 MF phenotype.

Case Report

A 60-year-old Saudi gentleman presented to King Khalid University Hospital in Riyadh with an 18-month history of erythroderma all over his body and face. It had all started 5 years previously, when he started developing slightly pruritic, slowly progressive erythematous lesions on his trunk and retroauricular area, which was misdiagnosed as severe eczema and was treated with multiple courses of oral prednisolone and oral cyclosporine for 2 months

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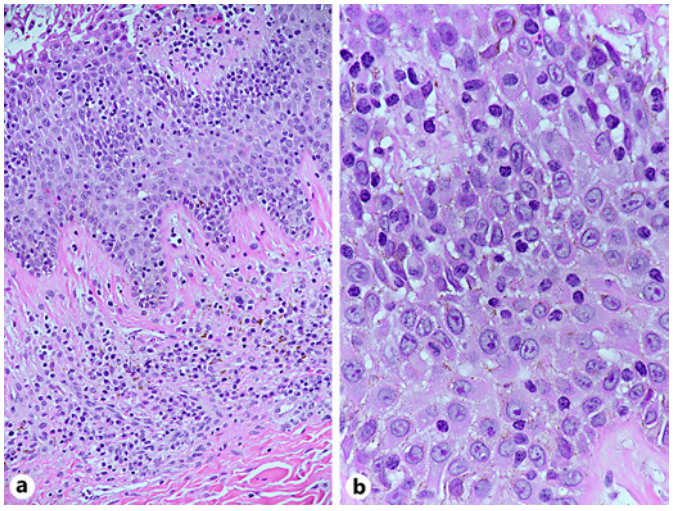

Fig. 2. Band-like infiltrate of lymphocytes in the dermis and fibrosis of the papillary dermis (**a**) (HE, ×200) with intraepidermal medium-sized cerebriform lymphocytes (**b**) (HE, ×600).

with no improvement. On physical examination there were confluent lichenified erythromelanotic plaques and an overlying thick plate of greasy scales involving his face, neck, trunk, genitalia, upper and lower extremities, palms, and soles with sparing of the nails and scalp (Fig. 1). However, there was no lymph node enlargement upon palpation. A bilateral lower lid ectropion was also noticed. Three skin punch biopsies were taken from the lower back, left buttock, and right upper extremity, which revealed epidermotropism of a large number of atypical lymphocytes – single and in clusters. The superficial dermis showed lymphocytic band infiltrate with dermal fibrosis (Fig. 2). However, a skin punch biopsy for immunofluorescence study was negative for fibrinogen, C3, IgA, IgM, and IgG. Immunohistochemically, the tumor cells were positive for CD3 and CD45RO but negative for CD4, CD8, and CD7 (Fig. 3). CD30 showed few scattered positive cells in the dermis, fewer than 25% of the total lymphocytes. The peripheral blood count and smear were normal with no Sézary cells. Flow cytometry of peripheral blood revealed no evidence of monoclonality. A CT scan of the abdomen and pelvis revealed multiple enlarged bilateral external iliac and inguinal lymph nodes, the largest measuring 1.8 cm in diameter. However, there was no evidence of solid organ involvement. A CT scan of the chest revealed no lymphadenopathy by size criterion. An ultrasound-guided incisional lymph node biopsy was performed on the right external iliac lymph nodes, which revealed few scattered large atypical cells, which are suggestive but not diagnostic of MF, but was negative for clonal T-cell receptor gene rearrangement. Based on these findings, the diagnosis of double-negative CD4/CD8 MF of advanced stage was made. The patient was referred to the hematology and oncology unit, where a plan of further staging with an excisional lymph node biopsy was made.

However, unfortunately, the patient developed a septic shock, for which he was admitted to the intensive care unit, and passed away 2 weeks later, about 1.5 months after his diagnosis.

Discussion

CTCLs are the second most common extranodal non-Hodgkin's lymphomas following gastrointestinal lymphomas. The most prevalent CTCL is MF [7]. There were no differences between MF with a classic CD4-positive CD8-negative T-cell phenotype and MF with atypical T-cell phenotypes (CD4-negative CD8-positive, double-negative CD4/CD8, and double-

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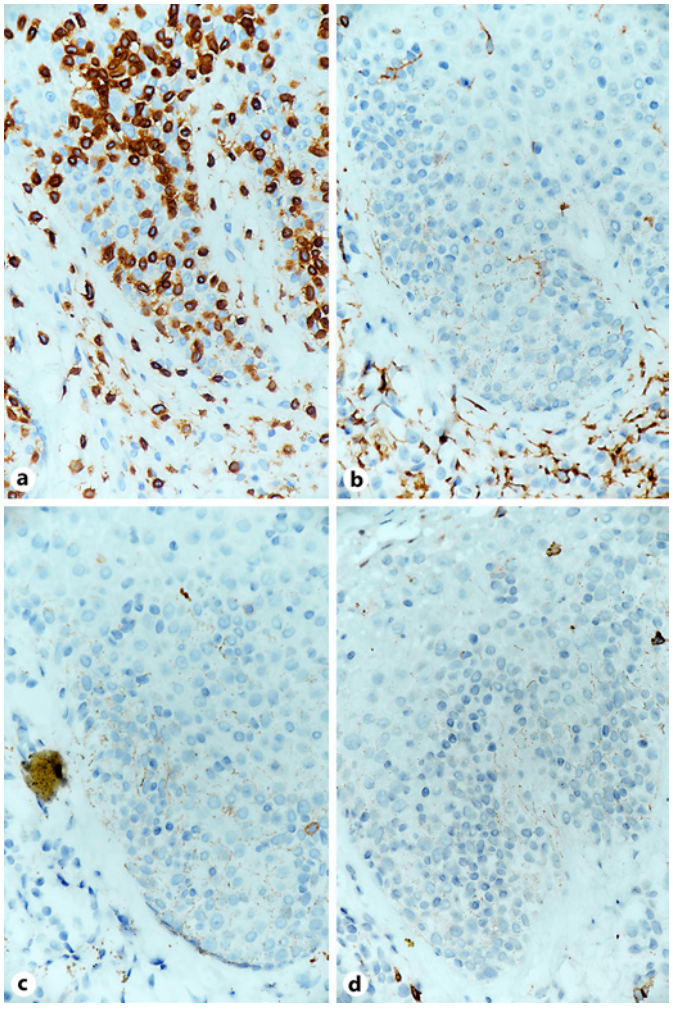

Fig. 3. The intraepidermal lymphocytes were positive for CD3 (**a**) (×400) and negative for CD4 (**b**) (×400), CD8 (**c**) (×400), and CD7 (**d**) (×400).

positive CD4/CD8) when comparing stage at presentation and risk of progression of the disease [8]. Most of the double-negative CD4/CD8 MF cases had unusual presentations, but their course was similar clinically to classic MF [6]. Other CTCLs with a double-negative CD4/CD8 phenotype in the differential of double-negative CD4/CD8 MF are cutaneous γ/δ T-cell lymphoma, extranodal NK/T-cell lymphoma, nasal-type lymphoma, and primary cutaneous peripheral T-cell lymphoma, unspecified [7, 9].

There are 35 reported cases in the literature with double-negative CD4/CD8 MF. They include 14 males and 13 females. Twelve cases were 55 years old or older, 5 cases were 14 years old or younger, and 10 cases were between 15 and 54 years old. These cases showed multiple presentations, including 8 with the classic MF presentation, 7 with hypopigmented MF, 3 with localized MF, 1 with erythema gyratum repens-like MF, 1 with purpuric MF, and 1 with ichthyosiform MF [6].

Twenty-eight of the reported cases were early-stage MF (IA–IIA). Eighteen cases of those with early-stage MF were treated with skin-directed therapy and had an indolent course. Seven were treated with phototherapy or IFNα with an indolent course. Two had a partial response to phototherapy. One had a complete response to psoralen plus UVA, etretinate, and chemotherapy. Five of the reported cases were of advanced-stage MF. Three out of these 5 cases exhibited a more aggressive behavior, either due to large cell transformation or metas-

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tasis to lymph nodes and bone marrow or to the liver, and they died after 3, 6.8 and 3.9 years, respectively. One of the remaining 2 cases of advanced-stage MF responded partially to treatment with psoralen plus UVA, and the other one had an indolent course with narrowband UVB. Our patient died 5 years after the start of his symptoms and 45 days following diagnosis.

Conclusion

The presence of a double-negative CD4/CD8 MF immunophenotype is rare and commonly has unusual clinical presentations. This is the first reported case in the literature with clinical presentation of erythrodermic MF and immunohistochemical findings of a double-negative CD4/CD8 T-cell phenotype. Most of the reported patients had nonclassic presentations and early stages of indolent MF. Five reported cases in addition to our case had advanced stages of MF.

Statement of Ethics

The authors certify that they have obtained the appropriate patient consent form. In this form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that his name and initials will not be published, and due efforts have been made to conceal his identity, but anonymity cannot be guaranteed. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

There are no conflicts of interest.

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Author Contributions

M.A.A. and F.A. conceived and designed the study. A.M.S. and N.G.A. drafted the manuscript. M.A.A., F.A., and N.K. participated in history-taking and making pictures. All authors read and approved the final manuscript.

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