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Case Report

Mycosis fungoides: A challenge for the diagnosis

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ABSTRACT

Mycosis fungoides (MF) is the most common primary cutaneous T-cell lymphoma. This cancer characteristically affects the skin, causing different types of skin lesions that progress slowly through several stages, although not all people with the condition progress through all stages. We present a case of MF in a 32-year-old female patient with many years of nonspecific eczematous and psoriasiform skin lesions and non-diagnostic biopsies. The diagnosis of MF can be very difficult and misleading. The wide range of clinical and pathological presentations of MF makes this disease a challenge for diagnosis and, therefore, requires an accurate differential diagnosis integrated by the patient's clinic together with the histological and immunological findings.

1. Introduction

Mycosis fungoides (MF) is a type of blood cancer that is considered the most common cutaneous T-cell lymphoma. The French dermatologist Jean-Louis-Marc Alibert was the first to describe a case of MF in 1806 and interestingly the name MF is somewhat misleading because the term refers to the mushroom-like appearance of the tumors and not to a fungal infection.[1] Although genetic, environmental and immunological aspects have been considered, the etiology of this disease has not been determined.[2] Notably, MF may advance slowly through several stages, although not all affected individuals progress through all stages. In this way, the wide range of clinical and pathological presentations of MF makes this disease a challenge for diagnosis, requiring an accurate differential diagnosis integrated by the patient's clinic together with the pathologic and molecular features. The purpose of this case report is to highlight the main clinical and pathological characteristics of MF with a particular emphasis on differential diagnosis.

2. Case report

A 32-year-old female patient with many years of indolent nonspecific eczematous and psoriasiform skin lesions that caused a lot of itching. Physical examination was notable for a combination of brownish scaly patches, annular and horseshoe-shaped plaques and tumors with ulceration of variable diameters and locations involving more than 35% of the skin surface (Fig. 1A, B, C). Furthermore, oral and zygomatic folliculitis was identified. No lymphadenopathy or organomegaly was observed.

Histological preparations showed thin skin with hyperkeratosis and parakeratosis (Fig. 2A). Exocytosis of small abnormal mononuclear cells with irregular nuclei and surrounded by vacuolated haloes was observed in the thickness of the epidermis, often in a linear configuration, but they do not cause spongiosis (Fig. 2B and C). Meanwhile, a small number of atypical mononuclear cells was also found in the interstitium and around the superficial vascular plexus, where remarkably these cells exhibited an immunological labelling for $CD2^+$, $CD3^+$, $CD4^+$, $CD5^+$, $CD7^+$ and CD8− memory T-cell phenotype (Fig. 3A, B, C). In this way, the morphological and immunophenotypic findings confirmed the diagnosis of MF.

Despite the large area of skin affected by the disease, the combined treatment of interferon-α and PUVA (psoralen and ultraviolet A) has had a relatively good response.

3. Discussion

MF is the most common type of cutaneous T-cell lymphoma (CTCL) characterized by the proliferation of malignant T cells with a particular tropism for the skin. It is a relatively unusual, extranodal, non-Hodgkin's lymphoma with an incidence of approximately 6

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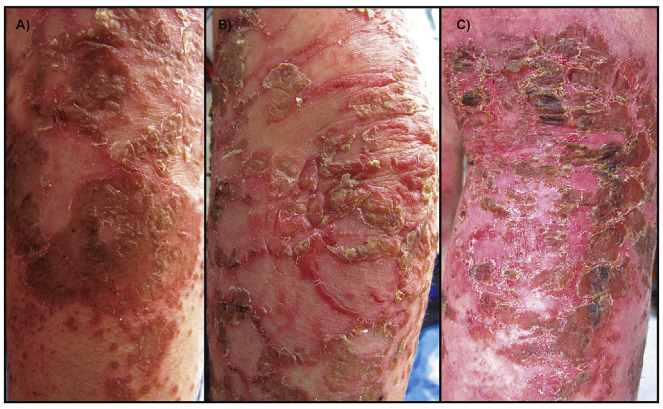

Fig. 1. Clinical manifestations. Combination of A) brownish scaly patches together with B) and C) annular and horseshoe-shaped plaques.

cases per million per year in Europe and the United States.[3] Contrasting with our case, MF mainly affects older adults (between 55 and 60 years),[4] although some cases in children have also been reported,[5] with a male-to-female ratio of 1.6–2.0: 1.[4] Because MF may present one or more of many diverse cutaneous manifestations,[6] before a definite diagnosis our patient had many years of nonspecific eczematous or psoriasiform skin lesions and non-diagnostic biopsies. It has been reported that the time from the onset of symptoms to the diagnosis is usually 3–4 years but can extend up to four decades.[7]

Most affected individuals initially develop some skin lesions called patches, which are flat, scaly, pink or red areas on the skin and mainly affect lower abdomen, upper thighs, buttocks, and breasts. In some patients, patches progress to plaques, which is considered the next stage of the disease and usually are reddish, purplish, or brownish in color. Both the patches and the plaques can cause itching given the mixture of infiltrating cancer cells and the reaction of the skin to these cells. The plaques may remain stable or may progress to tumors.[8] Our patient showed patches, plaques and tumors which together covered approximately 35% of the skin surface, and where the most affected areas were the abdomen, arms and legs. Pruritus was the main malaise that affected our patient and often worsened at the later stages of the disease. Fortunately, she did not show lymphadenopathy or organomegaly, which are common findings that are usually observed in advanced stages of MF together with transformation to large cell lymphoma.[1]

Histology is characterized by superficial lymphoid infiltrate together with a variable number of atypical cells that depend on the stage of disease. Overall, these atypical cells have a small to medium-sized, highly convoluted (cerebriform) and sometimes hyperchromatic nuclei. Despite presenting eczematous lesions, spongiosis was absent in our patient according with other cases of MF.[9] The presence of Pautrier's microabscesses, which are intra-epidermal nests of atypical cells, is a pathognomonic characteristic of MF but is observed in only very few cases. MF tumour cells are characterized by epidermotropic peripheral T lymphocytes whose phenotype is $CD2^+$, $CD3^+$, $CD4^+$ and $CD5^+$. In some cases, T lymphocytes may present a phenotype $CD4^-$and $CD8^+$, $CD4^-$and $CD8^-$, or $CD4^+$ and $CD8^+$. However, atypical MF immunophenotypes do not seem to influence prognosis.[10] Folliculotropic variant and tumour stage diseases have been associated with $CD4^+$ subgroup of MF, while hypopigmented MF has been associated with the $CD8^+$ MF subtype.[11] As the disease progresses, the loss of T cell antigens (CD2, CD3, CD5) is a common finding that results in the presence of

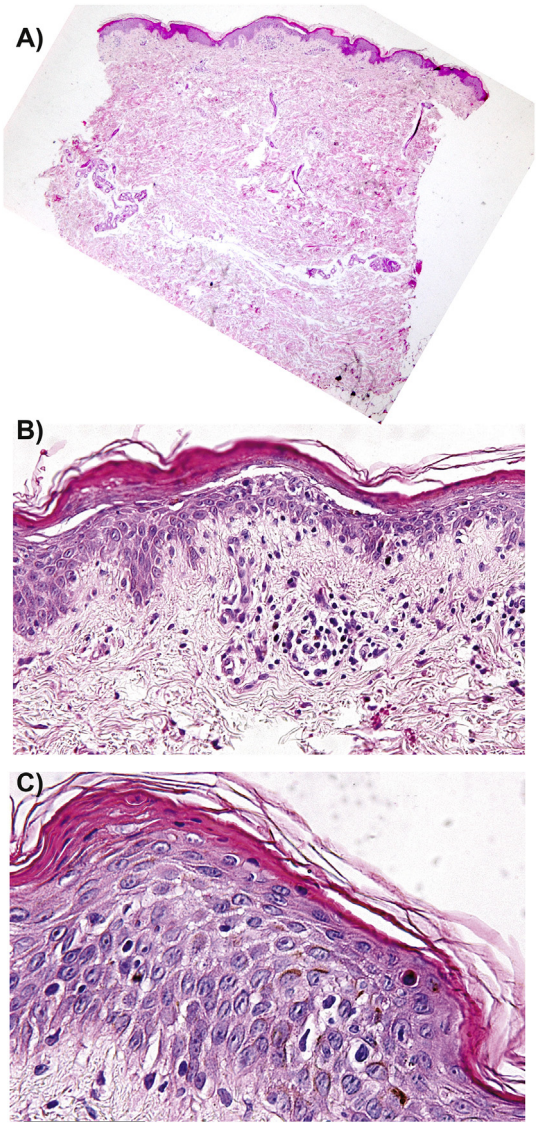

Fig. 2. Histological preparations. A) Hyperkeratosis and parakeratosis are observed together with B) few interstitial and perivascular mononuclear cells (H&E 25× and H&E 200×). C) Exocytosis with haloes without spongiosis are detailed (H&E 400×).

aberrant phenotypes. The case described here presented a $CD2^+$, $CD3^+$, $CD4^+$, $CD5^+$, $CD7^+$ and CD8− memory T-cell phenotype.

Regarding the differential diagnosis three categories should be considered. The first category includes benign dermatoses such as several types of eczema, psoriasis, superficial fungal infections and drug reactions. A second category involves several benign conditions such as lymphomatoid contact dermatitis, lymphomatoid drug reactions, and actinic reticuloid. Finally, the third category includes other types of CTCLs, where immunological labeling is required to define the malignant clone. In this way, combining information about clinical, pathologic, and molecular features is essential to making an accurate diagnosis.

There is currently no cure for MF and the only goal of treatment is disease control. In general, skin-directed therapies (SDTs) are used to treat the disease in the early stages, whereas the most

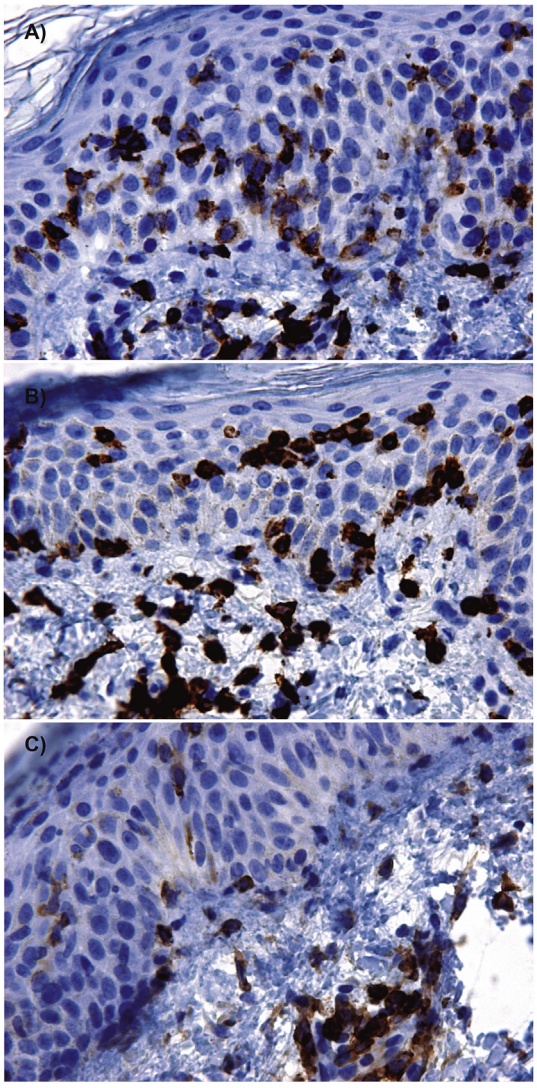

Fig. 3. Memory T-cell immunophenotype. The immunological labeling of the atypical cells found in the skin showed a positive result for A) $CD2^{+}$ (400×), B) $CD3^{+}$ (400×), C) $CD4^{+}$ (400×), which agree with memory T cells.

advanced stages require the combination of systemic therapy and SDTs. SDTs include topical or intralesional corticosteroids, topical cytotoxic agents, phototherapy and radiotherapy.[12]

4. Conclusions

Since MF shows a wide range of clinical and pathological presentations, this disease is actually a challenge, where many cases require several years for an accurate diagnosis that would be integrated into the patient's clinic along with the pathological and molecular characteristics.

Conflict of interest

The authors declare no conflict of interest.

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