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Interstitial mycosis fungoides

Micose fungoide intersticial

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ABSTRACT

Interstitial mycosis fungoides (IMF) is a rare variant of mycosis fungoides, a cutaneous T-cell non-Hodgkin's lymphoma. It is characterized by an interstitial dermal infiltrate of lymphocytes and histiocytes between collagen bundles. We report the case of a 54-year-old patient with pruritic hypochromic macules on the arms and forearms diagnosed with IMF. Special attention was given to the anatomopathological features that differentiate this entity from its differential diagnoses, such as inflammatory morphea, interstitial annular granuloma, and other variants of the mycosis fungoides itself. We also present a review of the literature on the classification of the IMF.

Key words: lymphoma; lymphoproliferative disorders; mycosis fungoides; granuloma annulare.

RESUMO

A micose fungoide intersticial (MFI) é uma variante rara da micose fungoide, um linfoma cutâneo de células T não Hodgkin. É caracterizada por um infiltrado dérmico intersticial de linfócitos e histiócitos entre feixes de colágeno. Relatamos o caso de um paciente de 54 anos com máculas hipocrômicas pruriginosas nos braços e antebraços com diagnóstico de MFI. Atenção especial foi dada às características anatomopatológicas que diferenciam essa entidade de seus diagnósticos diferenciais, como morfeia inflamatória, granuloma anular intersticial e outras variantes da própria micose fungoide. Apresentamos também uma revisão da literatura sobre a classificação da MFI.

Unitermos: *linfoma; distúrbios linfoproliferativos; micose fungoide; granuloma anular.*

RESUMEN

La micosis fungoide intersticial (MFI) es una variante poco común de la micosis fungoide, un linfoma cutáneo de células T no Hodgkin. Se caracteriza por un infiltrado dérmico intersticial de linfocitos e histiocitos entre haces de colágeno. Presentamos el caso de un paciente de 54 años con máculas hipocrómicas pruriginosas en brazos y antebrazos diagnosticado de MFI. Se prestó especial atención a las características anatomopatológicas que diferencian a esta entidad de sus diagnósticos diferenciales, como morfea inflamatoria, granuloma anular intersticial y otras variantes de la propia micosis fungoide. También presentamos una revisión de la literatura sobre la clasificación de la MFI.

Palabras clave: *linfoma; trastornos linfoproliferativos; micosis fungoide; granuloma anular.*

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INTRODUCTION

Mycosis fungoides (MF) is a cutaneous T-cell non-Hodgkin's lymphoma (CTNHL) characterized by a malignant proliferation mainly of CD4+ cells[1, 2]. MF accounts for about 60% of CTNHL and only 3.9% of non-Hodgkin's lymphomas, with an incidence of 6.4-7.7/1000,000 person/years in the US. There is predominance between 55 and 60 years of age, which is more common in African-Americans and males, and male/female ratio is about 1.6-2:1[1, 2]. The increase in CD4+/CD8+ ratio is not unique to MF, it is also found in inflammatory dermatoses, so it is suggested that MF starts from an inflammatory process that evolves to a malignant form. The MF diagnosis is made by biopsy, accompanied by detailed microscopic evaluation, immunohistochemistry, and clinical history[3]. The most common immunohistochemical pattern of MF is CD2+, CD3+, CD5+, CD4+, CD7-, CD8-, CD45RO+, TCR beta +, and CD30- neoplastic cells, but several T cell markers may be depleted[3-5].

The concept of interstitial MF (IMF), a rare variant of MF, is attributed to Bernard Ackerman in unpublished observations but was first mentioned by Shapiro and Pinto in 1994 in The American Journal of Surgical Pathology. The clinical presentation of IMF is a large, poorly defined, itchy, or scaly erythematous plaques/spots[6] in any part of the body, a fact that shows similarities concerning the features of MF itself. On microscopy, there is a typical interstitial dermal infiltrate predominantly composed of interstitial lymphocytes with some histiocytes between collagen bundles, with no destruction of elastic fibers, at least during the initial phase, as well as the presence or absence of mucin and epitheliotropic effect (**Figure 1**)[7].

Thus, we report a case of interstitial fungal mycosis, one of the rare variants of MF, highlighting their histopathological differential diagnosis and classifications.

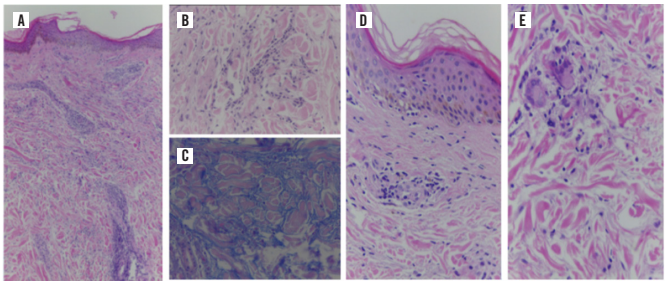

FIGURE 1 – *Perivascular disposition of mononuclear cells in the dermis [(A); HE, original magnification 40×] and interstitium [(B); HE, original magnification 100×] with epidermotropism [(D); HE, original magnification 40×] and sometimes multinucleated histiocytoid cells [(E); HE, original magnification 400×]. Mucin deposition in the reticular dermis [(C); alcian blue pH2.5, original magnification 100×]*

HE: hematoxylin and eosin.

CASE REPORT

A 54 years-old female patient, brown-skinned, from Brazil, whose main complaints were "white spots on the body". The itching started in the arms then spread to the body, culminating in the appearance of lesions. The patient presented a condition characterized by hypochromic macules, some slightly infiltrated with a rounded erythematous halo in the arms and forearms. Besides, the sensitivity test was normal and no palpable lymph nodes were present. The suspicions raised were borderline tuberculosis leprosy, MF, and eczema. The immunohistochemical pattern presented by the specimens was CD2+, CD3+, CD5+, CD7-, CD20-, CD1A+, CD68+ (**Figures 2** and **3**). After biopsies and immunohistochemistry of the right arm and left forearm fragments, the IMF diagnosis was established (Figures 1, 2, and 3).

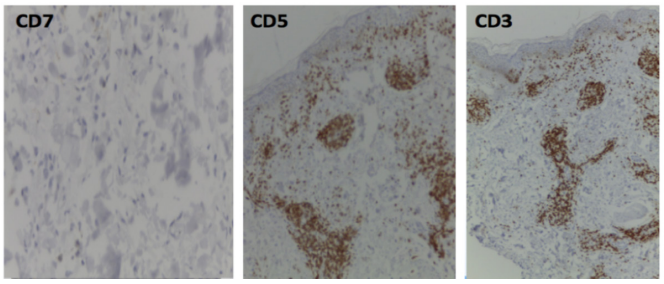

FIGURE 2 – *Immunoreactivity for CD5 and CD3 (original magnification 40×), also immunonegativity for CD7 (original magnification 100×)*

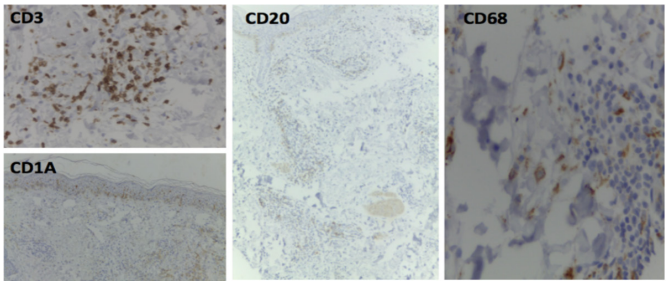

FIGURE 3 – *Immunonegativity for CD20 (original magnification 40×) and immunoreactivity for CD68, CD3 (original magnification 100×), and CD1A in the epidermis (original magnification 40×)*

DISCUSSION

The IMF has histopathological features similar to interstitial granuloma annulare (GAi), interstitial granulomatous dermatitis, inflammatory morphea, autoimmune conditions, drug reactions, and Borrelia bacterial infection[8]. In addition to other rare MF subtypes and other T-cell malignancies: acquired

cutis laxa, granulomatous MF, cutis laxa-like MF, and other types of cutaneous T-cell lymphomas that may have granulomatous histological features, such as Sézary syndrome, cutaneous anaplastic large-cell lymphoma, and subcutaneous panniculitis-like T-cell lymphoma[3].

The morphea or localized scleroderma is an idiopathic skin disease characterized by local inflammation followed by fibrotic changes in the skin and subcutaneous tissue. Both morphea and IMF have lymphoid interstitial infiltrates, whereas plasma cells are common in the morphea and rare in the IMF. However, several histological aspects can distinguish them. Finally, aggregates can be found in the dermis-subcutaneous junction, lymphocyte infiltrates, plasma cells, and histiocytes, only in inflammatory morphea. Moreover, there is a moderate presence of B lymphocytes and few T lymphocytes, while in IMF T cells are predominant[5].

We emphasize the importance of differentiating IMF from GAi. Both diseases share a dermal interstitial mononuclear infiltrate, occasionally associated with an increase in mucin. Clinical findings may be similar when GAi appears as macules or a well-developed raised or papular borderless set. Fibroplasia in the papillary dermis is found in IMF rather than GAi[5].

It is also noteworthy that IMF can be confused with an interstitial granulomatous drug reaction, given the significant histiocytic infiltrate, fragmentation of elastic and collagen fibers, as well as a relationship with dermatitis not seen in IMF. However, a population of T clones is not observed in drug reaction, and clinical association with drug use must be present[8].

Granulomatous MF, IMF, and cutis-laxa MF are all variants of MF that may resemble the early stages of the so-called granulomatous slack skin syndrome (GSSS)[9]. Thus, another fundamental issue arises: how to classify IMF given their clinical and morphological characteristics?

The GSSS is an uncommon form of CTNHL, with few cases published, and also a variant of MF, by World Health Organization (WHO) classification. It is characterized by flexural folds of redundant skin with low elasticity and granulomatous infiltrate with elastolysis and multinucleated giant cells[9]. Virmani *et al*. (2016)[6] in a review of the European Organization for Research and Treatment of Cancer (WHO-EORTC) classification incorporates IMF within another variant of similar morphology, granulomatous MF, but considers it to be a different entity from GSSS, both clinically. As for histology, however, some argue that these two histopathological variants should be kept separate[2, 6].

Finally, there is the theory that all these variants of MF, including GSSS itself, would be part of the same disease spectrum, with a variable clinical-pathological presentation, based on the stage of evolution. After all, all these variants represent a granulomatous immune response against neoplastic T cells[4]. Therefore, the MFI may represent an early stage of GSSS[3, 7].

CONCLUSION

It is evident that the diagnosis of IMF is difficult, either due to its infrequent presentation or a large number of differential diagnoses. Besides, there are cases such as our patient, which escape the most frequent epidemiologic characteristics. Because of these facts, a tripod-based diagnosis is required: clinical, histopathology, and immunohistochemistry. We also highlight the need for more studies related to IMF, to better understand their classification.

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