

Mycosis Fungoides in an Old Patient: A Diagnostic Challenge

Roua Mankai¹, Fatma Daoud¹, Imene Rachdi^{1, *}, Fatma Khanchel², Mehdi Somai¹, Hana Zoubeidi¹, Besma Ben Dhaou¹, Zohra Aydi¹, Aschraf Chadli Debbiche², Anissa Zaouak³, Fatma Boussema¹

¹Internal Medicine Department, Habib Thameur Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia

²Department of Pathology, Habib Thameur Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia

³Department of Dermatology, Habib Thameur Hospital, Faculty of Medicine of Tunis, University of Tunis El Manar, Tunis, Tunisia

Email address:

rachdi.imene14@gmail.com (Imene Rachdi)

*Corresponding author

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Abstract: Mycosis Fungoides is a rare T cell lymphoma. The mean age of onset is about sixty year old, mostly in masculine population. The clinical presentation is dominated by cutaneous signs. We report the case of a 78 year old patient, with a history of erythroderma with pruritus non ameliorated by corticosteroid topics, who was readmitted four years later for osteomyelopathy. At physical examination, he had bilateral axillary lymph nodes. We also noted dry generalized erythroderma with no interval of healthy skin and at the neurologic exam, there was ataxia on walking and a bilateral pyramidal syndrome majorated on the right. The blood count showed hyperleukocytosis with hyperlymphocytosis and chronic hypereosinophilia. The blood smear showed Sezary cells of the order of 2000. The CT scan has confirmed the presence of axillary adenopathies, left breast nodules not found on breast ultrasound, and bilateral adenomegaly of the external iliac and inguinal chains. The first cutaneous biopsy was not conclusive. Axillary node biopsy, 6th skin biopsy and Immunophenotyping of circulating CD4+ T lymphocytes allowed to retain Mycosis fungoides. He was treated with Methotrexate for a year with improvement. Mycosis Fungoides is a rare disease with diagnostic and therapeutic difficulties due to the non contribution of confirmatory examinations which may delay the diagnostic and with a possibility of atypical presentation.

Keywords: Cutaneous Lymphoma, Epidermotropic Lymphoma, Mycosis Fungoides, Sezary's Syndrome

1. Introduction

Sezary syndrome and Mycosis fungoides are rare T-cell lymphomas and account for more than half of all primary cutaneous lymphomas [1] and 5% of cutaneous T-cell lymphomas. The clinical presentation is dominated by cutaneous signs with a mean age of onset of disease is about 60 years [2] and a male predominance, (sex ratio 2/1) [3]. It is important to make the diagnosis of Mycosis Fungoides early. The diagnosis often made with a delay makes the prognosis worse than it is at the beginning. It is a rare disease with diagnostic and therapeutic difficulties due to the non contribution of confirmatory examinations with possibility of atypical presentation.

2. Observation

It is the case of a 78 year old patient, treated in 2003 for high grade infiltrating localized papillary urothelial carcinoma by endoscopy and BCG therapy, currently in remission, hypertensive, treated with a calcium channel blocker and a converting enzyme inhibitor, and having developed supraventricular tachycardia equilibrated by a beta-blocker.

He has presented since 2016 a generalized erythroderma with pruritus. The positive histological diagnosis was inconclusive between atopic dermatitis and mycosis fungoides despite a series of 5 skin biopsies. He was treated by topical corticosteroids, antihistamines and retinoids

without any improvement.

The patient was readmitted to hospital for exploration of gait and balance disorders in 2020. On dermatologic examination, we noted dry generalized erythroderma with no interval of healthy skin covered with non-adherent whitish scales (figures 1, 2), xanthonychia of the fingernails (figure 3), pachyonychia of the toenails, with cracked palmoplantar keratoderma (Figure 4).



Figure 1. Dry generalized erythroderma with no interval of healthy skin covered with non-adherent whitish scales.



Figure 2. Dry generalized erythroderma with no interval of healthy skin covered with non-adherent whitish scales.



Figure 3. Xanthonychia of the fingernails.



Figure 4. Cracked palmoplantar keratoderma.

In addition, we found associated mammary nodule at the union of the left upper and lower quadrant with bilateral axillary adenopathies. At the neurologic exam, there was ataxia on walking and a bilateral pyramidal syndrome majorated on the right. The blood count showed hyperleukocytosis at 11600 elements/mm³ with hyperlymphocytosis at 4960 elements/mm³ and chronic hypereosinophilia at 1163 elements/mm³. LDH was normal at 198 IU/L. The blood smear showed Sezary cells of the order of 2000.

Immunophenotyping of circulating CD4+ T lymphocytes did not show an aspect in favour of Sezary syndrome.

Thoraco-abdomino-pelvic CT scan confirmed the presence of axillary lymph nodes, left breast nodules not found on breast ultrasound, and bilateral adenomegaly of the external iliac and inguinal chains.

The breast ultrasound has concluded to the absence of mammary nodes, it has shown only bilateral axillary adenomegaly.

The angio-cerebro-medullary magnetic resonance imaging showed an ischemic cerebellar vascular accident with degenerative cervical myelopathy C3-C4 that explain his neurologic symptoms.

The sixth skin biopsy showed basal infiltration of the epidermis by lymphocytes. Immunohistochemical studies show intense CD3+ labelling of dermal and epidermal cells. CD8+ labelled much less intensely than CD3 (almost 50% of the cells are CD3+ labelled). CD7 labelled about 75% of the cells with no obvious CD7 phenotypic hole. This is a morphological aspect compatible with mycosis fungoides (figure 5).

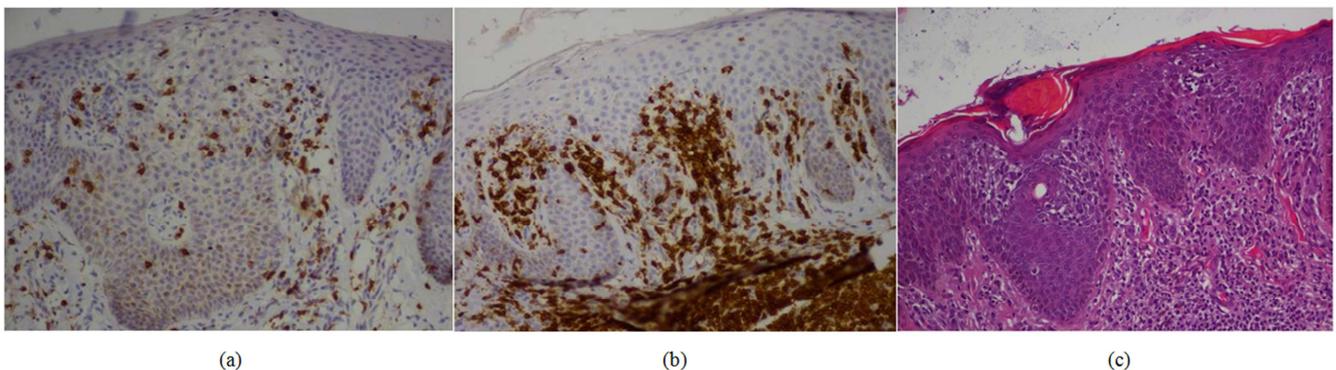


Figure 5. Skin biopsy showing. (a) marked epidermotropism (HE x200); the infiltrate is composed predominantly of atypical small to intermediate sized lymphocytes; (b) most lymphocytes, in the infiltrate, both at the dermis and epidermis, highlighted by the T-helper cell marker CD4 (immunohistochemistry for CD4x200); (c) scattered lymphocytes in the dermis and epidermis highlighted by T-cytotoxic cell marker CD8 (immunohistochemistry for CD8 x200).

Axillary biopsy revealed that the partial nodal architecture of the cortical area has been erased and replaced by a cell population sometimes histiocytic or interdigitated and sometimes lymphocytic, grouped into lymphocyte clusters or lobules. The immunohistochemical study showed positive labelling of lymphocytes with respect to CD3, CD4 with a histiocytic reaction population, CD68+ and CD1a+. CD20 made it possible to label lymphoid follicles with a clear centre with a decrease in their number in the periphery. This resulted in partial lymph node infiltration of T-cell lymphoma (mycosis fungoides). (figure 6).

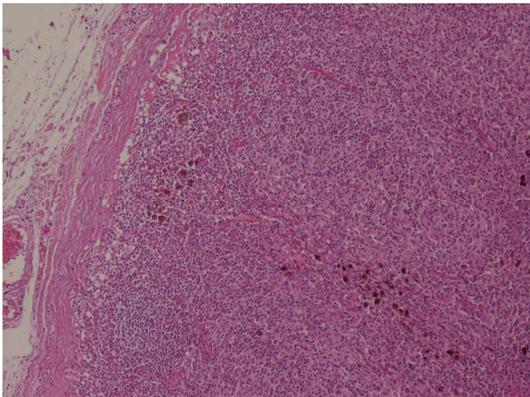


Figure 6. Lymph node biopsy showing features of dermatopathic lymphadenitis (HEx100) with presence of mycosis cells (in set; HEx1000).

In total, the positive diagnosis of Mycosis fungoides was retained with a T4N2M0B2 class. The patient was treated with Methotrexate at a dose of 25 mg/week for a year with regression of lymph nodes and skin lesions.

3. Discussion

This case shows the diagnostic and therapeutic difficulties in this 78-year-old patient with Mycosis Fungoides.

Indeed, the etiological diagnosis of his skin disease was not easy, made with a delay of 4 years because of the results of the series of skin biopsies which did not allow to retain the diagnosis despite a typical but isolated initial skin presentation.

In fact, the histological diagnosis is not easy because the cells are often very small and can be confused with benign chronic inflammatory dermatoses. At a retrospective study over a 16-year period, 32 histological sections were analysed from 24 patients with mycosis fungoid at the non-tumour stage, 13 histological sections showed chronic inflammatory dermatoses simulating mycosis fungoides [4].

Therefore, in the case of our patient we were looking for solutions especially because there was not an improvement in his symptoms. So we looked for other localizations that may confirm the tumor stage and make the positive diagnosis easier. The neurological and the mammary localization were eliminated only the lymph node involvement was confirmed. Generally, it is the most common, followed by pulmonary, splenic and bone marrow involvement. We also multiplied

cutaneous biopsies to finally retain the positive diagnosis in the sixth time after four years. It is well recognized that patients may experience symptoms for months or even years before a biopsy-proven diagnosis is made. Forty-eight patients reported having lesions or symptoms for a minimum of 2 months before diagnosis of MF/SS; among these patients, the median time from first symptoms/lesions to biopsy proven diagnosis was 3 years (range, 0.2-40 years). [5].

For the therapeutic issue, not all the patients respond the same way. Our patient has taken topical corticosteroids and acitretin for two years without any improvement. Effectively, all retinoic acid have been used for the treatment of cutaneous T cell lymphomas alone or in combination. With retinoids as monotherapy, moderate response rates can be achieved [6-11].

It is still controversial, the view that a more aggressive therapeutic approach may be indicated is gaining support. How aggressive this approach should be and whether it should include nodal irradiation and/or systemic chemotherapy are therapeutic problems yet to be solved [10-12] Current comparative therapeutic trials are under way in the United States in the hope that the therapeutic advances achieved in Hodgkin's disease and other lymphomas may be repeated in mycosis fungoides. [13] Our patient is now receiving metotrexate and Chop regimen.

The prognosis is generally bad because current treatments cannot guarantee long-term remission [14, 15]. In addition, advanced age over 60 years, the appearance of extracutaneous localizations, high LDH, significant blood hypereosinophilia, partial or complete loss of CD26 or CD7 by circulating CD4 T cells are factors with a poor prognosis as well as the extent of skin involvement, the largest prognostic study includes 106 erythrodermal ECLTs, the median survival observed was 3.6 years. [14] That's why, in our case, the patient is classified with bad prognosis since he is 78 years old, he has hypereosinophilia, multiple infiltrated nodes and a general erythroderma.

4. Conclusion

Mycosis Fungoides is a rare disease with diagnostic and therapeutic difficulties posed by the frequency of non contribution of confirmatory examinations with the possibility of atypical presentation. The diagnosis often made with a delay makes the prognosis worse than it is at the beginning.

Conflict of Interest

The authors declare that they have no competing interests.

Author Contributions

FD, IR, RM: initiated the preparation of this manuscript.

All authors were involved in the clinical management of this patient and contributed to the preparation of this

manuscript.

FK, ACD: analysed pathology images.

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