

Cutaneous T-cell Lymphoma and Human Immunodeficiency Virus Infection: 2 Cases and a Review of the Literature

M. A. MUÑOZ-PÉREZ¹, J. J. RÍOS-MARTÍN², A. RODRIGUEZ-PICHARDO¹ and F. CAMACHO¹

Departments of ¹Dermatology and ²Pathology, Virgen Macarena Hospital, School of Medicine of Sevilla, Spain

Cutaneous non-Hodgkin's lymphomas are rare in patients with HIV-1 infection and almost all of the cases reported are of T-cell lineage with histopathological features of mycosis fungoides or Sezary syndrome. We studied 2 cases of mycosis fungoides in HIV-1-positive patients who were intravenous drug abusers and were in stage II and IV C2 (CDC'86), respectively. The first patient (stage II) had multiple, erythematous and infiltrated large plaques on the abdomen, back, arms and legs, whereas the second patient (stage IV) had smaller erythematous, slightly scaly and infiltrated pruritic plaques on the trunk and limbs. Their CD4 lymphocyte counts were 634 and 250 cells/mm³, respectively. Biopsies showed features consistent with mycosis fungoides, with an epidermotropic pattern. The immunohistochemical study revealed a T-cell lineage of this atypical infiltrate. Both patients partially responded to topical steroid ointment, showing moderate improvement. Further biopsies performed 6 months later confirmed the prior diagnosis of mycosis fungoides. No tumour stage was observed during a 2-year follow-up. We conclude that mycosis fungoides is rare in HIV-positive patients, but must be included in the differential diagnosis of erythematous plaques in these patients. In suspected, but non-diagnostic cases of mycosis fungoides in HIV-positive patients, only a close clinical and histopathological follow-up can confirm the diagnosis. **Key words:** *mycosis fungoides; HIV infection; EBV.*

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F. Camacho Martinez, Departamento de Dermatología, Hospital Virgen Macarena, Avda Dr Fedriani s/n, ES-41009 Sevilla, Spain. Camacho@meditex.es.

Non-Hodgkin's lymphomas (NHL) may be as much as 100 times more common in patients with AIDS than in the general population and they occur in about 10% of HIV-infected patients (1). Most of them are of B-cell phenotype (2–3) and extranodal, mainly located in the central nervous system and gastrointestinal tract (4). On the other hand, cutaneous NHLs are rare in patients with HIV-1 infection and almost all of the cases reported are of T-cell lineage with histopathological features of mycosis fungoides (MF) or Sezary syndrome (5–10). A few cases of T-cell neoplasms are large cell NHLs without epidermotropism (11–12) and Kerschmann et al. (5) in a review of 25 cases described two forms of HIV-associated cutaneous lymphoma, the first an indolent disease resembling mycosis fungoides or Sezary's syndrome, and the second representing large cell lymphomas with a poor prognosis, whose cells often had a CD30+ T-cell phenotype and harboured the Epstein-Barr virus. HTLV-I has also been associated with T-cell leukaemia/lymphoma.

CASE REPORTS

Case 1

A 28-year-old white man was referred to our Department of Dermatology in March 1995 because of multiple erythematous, infiltrated, pruritic and lichenified plaques (2–20 cm in diameter) on the face, trunk and limbs (Fig. 1A). He was an intravenous drug user and had been HIV-1-positive since 1985. He was in stage II (CDC'86) and had a CD4 lymphocyte count of 634 cells/mm³. A series of biopsy specimens showed features consistent with MF, with a dense band-like infiltrate of atypical hyperchromatic lymphoid cells in the upper dermis and around follicles and vessels (80% of atypical lymphocytes for high-power field). Foci of epidermotropism were also seen with formation of Pautrier's microabscesses (Fig. 1B). The immunohistochemical study was realized with a pan-T-cell marker on paraffin sections (CD3, prediluted, Concepta Laboratory), revealing the T lineage of this atypical infiltrate. The majority of atypical cells were positive to anti-CD4 antigen antibody (CD4, 1:50, Novocastra Laboratory), and only scattered cells showed positivity to anti-CD8 antigen antibody (CD8, 1:50, Novocastra Laboratory), revealing the predominant CD4 nature of the atypical infiltrate. Immunohistochemical detection of latent membrane protein of Epstein-Barr virus (EBV) was negative (LMP-1, 1:50,

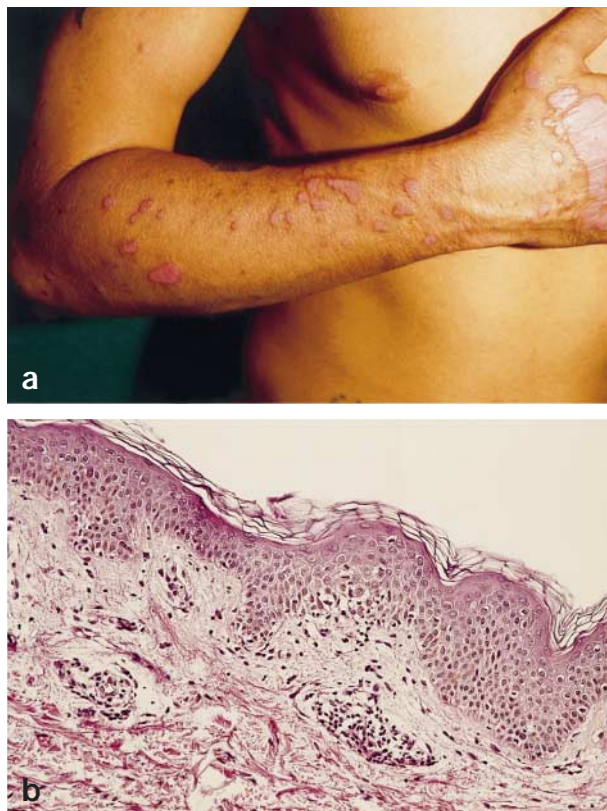


Fig. 1. (A) Multiple erythematous, infiltrated, pruritic and lichenified plaques on the upper limb of patient 1. (B) The first skin biopsy specimen shows foci of atypical lymphocytes in the upper dermis and formation of a Pautrier's microabscess (H & E, ×120).

Novocastra Laboratory). *In situ* hybridization for LMP-1 was not done. PCR analysis for HTLV-1 was not available, neither for TCR rearrangement to prove the clonality of the lesions. HTLV-1 serology was negative. The patient denied any treatment except clobetasol propionate 0.05% cream, and the plaques slowly improved, with recurrence 3 months later. A new biopsy specimen confirmed the diagnosis of MF 6 months later. In July 1997, and after therapy with D4T (Estadivine), 3TC (Lamivudine) and Saquinavir, the cutaneous plaques improved significantly and the viral load decreased to 2,000 copies/ml, but with a CD4 count of only 83 cells/mm³. In May 1998 the patient returned to drug abuse, stopped all treatment, the viral load increased to 81,700 copies/ml and the CD4 to 130 cells/mm³, but no changes in cutaneous lesions were observed at that moment. The patient refused new biopsies.

Case 2

A 41-year-old white man was seen at our Department of Dermatology in April 1994 with multiple erythematous, slightly scaly and infiltrated pruritic plaques (1–5 cm in diameter) on the trunk and limbs. He was an intravenous drug abuser and had been HIV-1-positive from 1986. He was in stage IV C2 (CDC'86) and had a CD4 lymphocyte count of 250 cells/mm³. A biopsy specimen showed features consistent with incipient MF, with a slightly band like infiltrate of atypical lymphoid cells in the upper dermis and around vessels and also numerous atypical lymphocytes disposed as a row in contact with the basal layer of the epidermis and only a few Pautrier's microabscesses. The immunohistochemical study on paraffin sections also revealed a T lineage of this infiltrate. Immunohistochemical results using the antibodies cited before were similar to case 1, revealing that 70–75% of atypical cells corresponded to CD4 lymphocytes. HTLV-1 serology was negative. Treatment with clobetasol propionate 0.05% cream was started with moderate improvement. A new biopsy was performed 6 months later that confirmed the diagnosis of MF. Six months later the patient's cutaneous lesions were unchanged. The patient did not come to our clinic again.

DISCUSSION

Whilst B-cell phenotype NHLs are extremely common in AIDS patients (13), T-cell lineage NHLs are rare (5–10). We have found only these 2 cases of cutaneous T-cell lymphoma in 1,161 patients of our prospective study about cutaneous findings in HIV-1-positive patients (14). In a review of 25 cases collected during 8 years in San Francisco General Hospital, Kerschmann et al. (5) described two forms of HIV-associated cutaneous lymphoma. The first ($n=8$) was an indolent disease resembling mycosis fungoides or Sezary's syndrome with relatively high counts of CD4 lymphocytes (600 cells/mm³), epidermotropism, Epstein-Barr virus (EBV) DNA negativity and a mean survival of 38.9 months. The second form ($n=17$) was characterized by a single or a few violaceous nodules, histologically classified as large cell lymphoma, without epidermotropism and whose cells often had a CD30+ T-cell phenotype and harboured the EBV. The prognosis was worse (mean survival of 6.7 months) and was associated with severe immunosuppression (50 CD4 lymphocytes/mm³). Our two cases belong to the first group. The initial prognosis is good and no evolution to tumour stage was observed in a 2-year follow-up.

Estève et al. (15) found 8 cases of cutaneous lymphomas occurring in HIV-positive patients: 7 non-epidermotropic lymphoma and only 1 case of MF. The median survival was 8 months and the immunophenotype was T-cell in 4 cases, B-cell in 3 and non-determined in 1. In this report the non-epidermotropic type of cutaneous lymphoma is also the most frequent.

Our first case reminded us clinically of lichen planus but histopathology showed MF. In the second case the lesions reminded us initially of MF but the biopsy was not so demonstrative as the first case. Repeated biopsies and a clinical follow-up were necessary to confirm the diagnosis in both patients. Usually, the diagnosis of MF in HIV-positive patients is based mainly on the histopathology of the skin lesions and the analysis of 1 or 2 pan-T-cell markers on paraffin sections. Biopsies must be evaluated carefully because other dermatoses characterized by lymphocyte-rich infiltrates, including drug eruptions, seborrheic dermatitis, contact dermatitis, atopic dermatitis, interface dermatitis or psoriatic erythroderma, can be misdiagnosed as MF in HIV-positive patients. Zhang et al. (10) compared cases of probable MF in HIV-positive patients with cases of MF unassociated with HIV infection, finding less concordance among dermatopathologist in making a diagnosis, a greater proportion of CD8+ than CD4+ T-cells in the cutaneous infiltrate in the HIV-positive group, and concluded that CD8 T-cell predominant dermatosis may simulate MF in HIV-positive patients. We also corroborate that, in suspected but non-diagnostic cases of MF in HIV-positive patients, only a close clinical and histopathological follow-up can confirm the diagnosis of MF.

Regarding the mechanism of development of CTCL in HIV-positive patients, several proposals may be considered. A few reports have indicated either the presence or the absence of EBV in Hodgkin's disease in HIV-positive patients. Hamilton-Dutoit et al. (16) demonstrated EBV-DNA in 12 of 24 cases of AIDS-related lymphomas, but all of them were of B or non-B, non-T phenotype. Dreno et al. (12) detected EBV-DNA in lesions of an AIDS-related anaplastic T-cell lymphomas, suggesting a causal relationship between viral infection and tumour cells. Kerschman et al. (5) found that EBV was absent in the epidermotropic lymphomas, but it was present in 73% of the non-epidermotropic cases. EBV was not detected in our 2 cases.

HTLV-I has a mode of transmission similar to that of HIV and has been associated with T-cell leukaemia/lymphoma (17–19). It has been suggested that HIV-1 itself may be a casual agent in the development of T-cell neoplasias (3). This suggestion is based on similarities between the transactivator genes in HIV-1, HTLV-I, and HTLV-II. The transactivator gene in HTLV-I and -II is believed to turn on growth-promoting genes which in turn may lead to the ultimate malignant transformation of the infected cells. HTLV-1 serology was negative in our two cases. A different proposal is that the development of T-cell-lymphoma in patients with AIDS may be a result of chronic antigenic stimulation of T-cells. Furthermore, EBV may act as a chronic antigenic stimulant (6).

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