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Anaplastic large cell lymphoma as a cause of rapidly appearing subcutaneous nodules in an HIV-infected patient

Nódulos subcutáneos de rápida aparición como forma de presentación de linfoma Ten paciente con infección por VIH

To the Editor,

AIDS patients have an increased risk of cancer, and one third of them will eventually develop a tumour. The risk of non-Hodgkin lymphomas (NHL) is much higher than in immunocompetent individuals. However, this risk has decreased since highly active antiretroviral treatment (HAART) was introduced, and the frequency has now been reported to be 1–4% in modern series. 2 T-cell derived lymphomas are uncommon and represent less than 3% of NHL, and they usually present worse outcomes than B-cell derived ones. 3 We report a patient with AIDS who developed a rapidly evolving T-cell type NHL.

A 50 year-old patient was admitted to hospital due to fever, weight loss and malaise for the past 3 weeks. He had a history of intravenous drug use and was diagnosed with HIV infection and hepatitis C virus-associated liver disease 11 years earlier. One year before the current admission he suffered P. jiroveci pneumonia, but refused to take HAART or prophylactic drugs against opportunistic infections. The physical examination was remarkable for low body weight (body mass index 17 kg/m2), and enlargement of the liver and spleen. There were no palpable lymph nodes. Blood analyses revealed a normocytic anaemia, a markedly increased ESR, 14 CD4 cells/μl, and 1,480,000 HIV copies/μl. Chest X-ray revealed a slight interstitial pattern. All microbiological tests were negative. A CT scan revealed a 3 cm × 5 cm necrotic mediastinal lymph node, with an inconclusive biopsy. A bone marrow biopsy showed non-specific abnormalities. In the following days subcutaneous painful nodules appeared in the abdomen. They were about 2 cm in diameter, but the size changed, enlarging or decreasing over a few days. An excisional biopsy of one of these nodules revealed a dense infiltrate of lymphoid cells with horse-shoe nuclei in the hypodermis, with abundant expression of Ki67 in most cells (a cell proliferation marker) and positive staining for CD3, CD4, CD30, and EMA, being negative for CD8, CD15, CD20, ALK, LMP1, HVH8, consistent with ALK-negative anaplastic large cell lymphoma of T-cell type. Due to the poor patient status, HAART with atazanavir/ritonavir, lamivudine and abacavir was initiated prior to chemotherapy. However, the patient deteriorated rapidly and died 2 weeks later due to a lung infection. Unlike from lymphomas derived from B-cells, T-cell lymphomas tend to be extranodal, with a higher propensity to affect skin and bone marrow. 4, 5 Among them the peripheral T-cell lymphoma...
is the most frequent, while other subtypes, such as angioimmuno-
blastic and anaplastic large cell lymphoma (ALCL) are less common.
Less than 40 cases of ALCL have been reported in HIV-infected
patients.\textsuperscript{6,7}

ALCL was first characterised by Stein, who described a new type
of lymphoma consisting of large anaplastic lymphoid cells with a
strong expression of CD30, and a tendency to grow cohesively and
invade lymph node sinuses.\textsuperscript{8} As in our case the common type
is characterised by sheets of large lymphoid cells with horseshoe-
shaped nuclei containing multiple nucleoli. Tumour cells have an
abundant cytoplasm with vacuoles and an increased Golgi region.
Most cases of ALCL express T-cell markers. The CD3 complex (TCR)
is one of the most commonly expressed T-cell antigens, whereas
unlike that of our patient CD4 or CD8 expression is less common.\textsuperscript{9}
Some ALCLs are associated with a 2;5 chromosomal translocation
encoding the tyrosine kinase anaplastic lymphoma kinase (ALK).\textsuperscript{10}
It is assumed that both CD30 and ALK are involved in the growth
and replication of the tumour cells.\textsuperscript{7}

ALCL in HIV-infected patients has a distinct course, being much
more aggressive than in immunocompetent patients. Although it
is usually associated with extranodal involvement and systemic
symptoms,\textsuperscript{5} presentation with rapidly appearing painful subcuta-
neous nodes, as in our patient, is very rare. Two clinical forms of
ALCL have been described, systemic and cutaneous.\textsuperscript{7} Although the
skin may be involved in both forms, in systemic cases the hypo-
dermis is affected, but characteristically the dermis is preserved.
This was the pattern in the case reported here. As in this case, ALCL
tends to affect patients with severe immunodeficiency, and con-
trary to cases in non-infected population, rarely expresses ALK,
which is associated with better responses to chemotherapy.\textsuperscript{9,10}
Immune reconstitution by HAART is crucial. Anti-neoplastic regi-
mens are frequently considered, but the prognosis is poor, with a
median survival of 5 months.\textsuperscript{5,10}

Although uncommon, clinicians caring for patients with HIV
infection should be aware of this tumour, especially in patients pre-
senting with swollen lymph nodes, or subcutaneous nodes. Since it
affects patients with severe immunodeficiency, and has an ominous
prognosis, good control of HIV infection and subsequent immuno-
depression is the best preventive strategy.

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Are HIV-infected patients a high-risk population for hepatitis E virus infection in Spain?

¿Son los pacientes VIH positivos un grupo de riesgo para la infección por virus de la hepatitis E en España?

To the Editors,

We read the article by Rodriguez-Frias et al.\textsuperscript{1} with interest. The authors reported a seroprevalence of anti-HEV antibodies (IgG anti-HEV) between 2.2% and 7% in Spain. However, the prevalence of anti-HEV antibodies varies according to the population included in the study, and is even much higher in HIV infected patients. Data on the frequency of anti-HEV antibodies in these patients in Spain are scarce, and it is a controversial issue in other countries, such as England where Feane et al.\textsuperscript{2} reported a similar seroprevalence in controls and patients with HIV infection.

Therefore, we tested 178 plasma samples from 178 HIV-infected patients who attended our Infectious Disease Department for moni-
toring of HAART therapy between December 2011 and January 2012. Among them, 140 (78.65%) were males with a mean age of 46 years (range: 20–78). IgG anti-HEV antibodies were detected in
serum by a commercial enzyme immunoassay (EIA) kit (HEV Ab,
DiaPro Diagnostic Bioprobes, Milan, Italy) following the manufac-
turer's instructions. All positive samples were studied further for
HEV RNA by Western blot analysis (RecomBlot HEV IgG/IgM; Mikrogen, Mar-
tinsried, Germany). In addition, HEV RNA was amplified by reverse
transcriptase (RT)-nested PCR\textsuperscript{3} in all serum samples with IgG or
IgM anti-HEV positive patient. None of them presented clinical symp-
toms related to viral acute hepatitis currently or in recent years.
ALT and AST were normal in all the patients who had IgG, IgM anti-HEV and/or HEV RNA in serum.

The seroprevalence of HEV infection has been studied in other probable risk groups, such as immigrants in Madrid\textsuperscript{4} (Table 1). Our results showed similar frequencies of detection of IgG anti-HEV