Absence of HTLV-1 Proviral Sequences in Patients with Lymphomatoid Papulosis

To the Editor:

Lymphomatoid papulosis (LyP) is a chronic self-healing cutaneous lymphoproliferative disease that is clinically benign but histologically mimics a malignant lymphoma (Macalay, 1968; Cabanillas et al., 1995). Thomasen and Lange Wantzin (1987) found specific antibodies to human T-cell lymphotrophic virus (HTLV) type 1 in three of 18 patients, “indicating a relationship to the pathogenesis” of this disease. Others have reported specific antibodies to HTLV-1 in isolated patients of LyP (Oshima et al., 1992); however, in a previous study we were unable to find HTLV-specific antibodies in any of our 18 cases (Ortiz Romero et al., 1992). As far as we know, polymerase chain reaction (PCR) technology has not previously been used to identify HTLV-1 proviral sequences in LyP patients.1

To indicate a possible link between LyP and HTLV-1 we performed the following study. Seven patients from the center of Spain were included and diagnosis of LyP was carried out according to clinicopathologic features (Willemze et al., 1982). None of the patients presented specific antibodies against HTLV-1 (enzyme-linked immunosorbent assay). One of the patients developed typical mycosis fungoides more than 3 y after taking the cutaneous sample studied.

We analyzed genomic DNA taken from lesional skin biopsies of six patients. DNA from peripheral blood lymphocytes was also studied in four of the above, including the patient that developed mycosis fungoides. Furthermore, one DNA sample from peripheral blood lymphocytes taken from another LyP patient was also studied.

PCR was used to amplify the pol (primers SK110 and SK111) and tax/rex (primers SK43 and SK44) genes. These sets of primers are common in both HTLV-1 and HTLV-2. LTR, and env gene were also amplified in a nested-PCR procedure. This method consists of a first round of amplification which amplifies both viruses, and a second round that uses specific primers for each virus. DNA of prototypic HTLV-1 and HTLV-2 cell lines, MT-2 and MoT, respectively, were used as positive controls. DNA of donor peripheral blood lymphocytes was used as negative control. PCR and Southern blot were performed as previously described (Vallejo and Garcia Sáiz, 1995).

We did not find HTLV-related sequences in the samples studied, even under low stringency conditions of PCR and Southern blot hybridization, whereas the β globin gene could be amplified in all of them.

In five of the patients, the DNA extracted from cutaneous lesions was used to study T cell receptor gene rearrangement by the Southern blot technique as previously described (Ortiz Romero et al., 1992); two of them showed a clonal pattern. The other three, including the patient that developed mycosis fungoides, presented a polyclonal pattern.

The absence of antibodies to HTLV-1 surface proteins in our series (Ortiz Romero et al., 1992) was not enough to disprove a relationship between LyP and HTLV-1. It is well known that proviral DNA can be found without specific antibodies to HTLV-1 in peripheral blood (Zucker-Franklin et al., 1991; Pancake et al., 1995). Defective forms of HTLV-1 may play a role in the development of T cell lymphomas.

Studying the possible relationship between HTLV-1 and LyP was particularly interesting. Several findings made LyP a good candidate to find viral DNA: first, HTLV-1 antibodies were found in 16% of the patients of the Thomson and Lange Wantzin series (Thomson and Lange Wantzin, 1987). Secondly, most of the patients with LyP have a benign clinical course. In about 10–20%, however, LyP is preceded by, associated with, or followed by malignant lymphoma, mostly mycosis fungoides, Hodgkin’s disease, and CD30 positive large-cell lymphoma (Beljaards and Willemze, 1992). HTLV-1 DNA was found in a number of cases of mycosis fungoides and CD30+ large-cell lymphoma (Agastopoulos et al., 1990; Zucker-Franklin et al., 1991). Thirdly, large atypical cells in LyP lesions express CD30. In vitro experiments showed that HTLV-1 is a powerful inducer of CD30 expression in T cells (Stein et al., 1985).

Our findings do not support the possible link between LyP and HTLV-1; however, the geographic origin of the patients may be important, as previously suggested. Spain is an area of low prevalence for HTLV-1. Broader studies on patients from different regions will be needed to confirm or discard this relationship.

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REFERENCES


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Abbreviation: LyP, lymphomatoid papulosis.

1After submission of this letter, we have found the paper of Wood et al. (1997) in which 14 lymphomatoid papulosis cases were also negative for human T-cell lymphotropic virus type 1 by polymerase chain reaction/Southern blot and dot blot.