Nuclear Protrusions and Marker Chromosomes in Lymphocytes of Two Patients with Cutaneous T-Cell Lymphoma

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In 1980, Liang et al. [1] reported the first observation of nuclear protrusions in lymphocytes of a patient affected with Sézary syndrome (SS). These authors correlate this anomaly with the presence of long marker chromosomes, a constant finding in this disease [2, 3]. SS, with mycosis fungoides (MF) and some cases of lymphomatoid papulosis, represents a group of chronic T-cell malignancies called cutaneous T-cell lymphoma (CTCL).

The absence of anti-HTLV-1 (human T-cell leukemia-lymphoma virus, type 1) serum antibodies in the large majority of these patients suggested the lack of relations between CTCL and HTLV-1 associated malignancies, called ATLL (mature adult T-cell leukemia-lymphoma) and known to be clustered in Japan, Africa, North America and the Caribbean [4]. Nevertheless, recently HTLV-1 proviral sequences were detected in lymphomatous cells of a French patient with SS, in spite of the absence of anti-HTLV-1 serum antibodies [5].

We recently observed 1 case of SS (N.N., female, 77 years old) and 1 case of MF (C.P., male, 49 years old), the latter with a small number of Sézary cells. Both patients showed clear nuclear protrusions in nondividing white blood cells and absence of anti-HTLV-1 serum antibodies, while large marker chromosomes were observed in mitogen-stimulated peripheral lymphocytes of the SS patient. The diagnosis was made on the basis of peripheral blood, bone marrow, skin and lymph node examination. TEM analysis of peripheral mononuclear cells of both patients revealed the typical morphology of Sézary cells, with cerebriform nuclei in different percentages. The 90% of peripheral lymphocytes in SS and the 40% in MF were CD4 positive (T-helper). The sera of the patients examined for detection of HTLV antibodies by an ELISA assay [6] were found negative. Evident nuclear protrusions were detected in 20% of nondividing cells in the SS patient and in 9% of the MF case (fig. 1a). The cytogenetic investigations, performed on peripheral lymphocytes, stimulated with PHA and PWM, and on bone marrow cells without mitogen, revealed a normal diploid karyo-type in bone marrow cells of both patients. The analysis was carried out on patients off of therapy for at least 4 months. The karyotype of

peripheral lymphocytes of the MF patient was normal diploid. In the SS patient, only 9 out of 58 examined cells had a normal karyotype. 34 cells were pseudodiploid with at least one large-sized marker chromosome and 10 cells were hyperdiploid, 1 with 47 chromosomes and 9 with 49 chromosomes, with markers. Most of these markers were long submetacentric chromosomes (designated as M1) and, in little percentage, median-small submetacentric chromosomes (designated as M2) (fig. 1b).

The survival time of the SS patient was higher than 3 years, while that of the MF patient was 15 months. Our cytogenetic findings are in agreement with those of the 32 cases of SS described so far by other authors, especially as far as long submetacentric marker chromosomes are concerned [2]. The normal diploid karyotype of our MF patient differs from the karyotype of the 9 cases reported which show constant an-euploidy, sometimes with markers [7]. With regard to the nuclear protrusions, a correlation between this anomaly and the presence of long marker chromosomes is suggested by Liang et al. [1]. The same relation was suggested by others in neoplastic and nonneoplastic diseases, associated with abnormally long

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m m
cáat
B

M2

Fig. 1. a Some nuclear protrusions in the lymphocytes of patients with MF (left $\times 2,000$) and SS (right $\times 3,200$). b M1 and M2 marker chromosomes from 7 SS cells (G-banded). The first M1 is probably derived from one No. 12.

chromosomes [8]. This hypothesis is suggestive, but it does not explain the evidence of such a finding in our MF patient whose lymphocytes never revealed the presence of marker chromosomes of large size. Nuclear protrusions could also be related with a cytopathic effect of HTLV-1 virus, but sera of our patients were HTLV-1 antibody negative. Nevertheless, the recent report of detection of HTLV-1 proviral sequences in a SS patient, whose serum had been found negative for viral antibodies [5], maintains open this last hypothesis.

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