

## ADULT T-CELL LEUKEMIA-LYMPHOMA IN A PATIENT WITH HTLV-I/II ASSOCIATED MYELOPATHY

VIRGÍNIA FREITAS\*, IRENIO GOMES\*, ACHILEA BITTENCOURT\*,  
DILSON FERNANDES\*, AILTON MELO\*

---

**ABSTRACT** - Chronic myelopathy associated with T-lymphotropic virus type I (HAM) has been described as an endemic disease in several areas of the world, meanwhile there are few papers describing the association between HAM and adult T cell leukemia-lymphoma. We report the case of a man that, after four years of progressive spastic paraparesis and neurogenic bladder, developed a clinical picture of a lymphoproliferative disorder characterized by dermal and systemic involvement, mimicking mycosis fungoides/Sézary syndrome.

**KEY WORDS:** HTLV-I, HAM, TSP, ATLL, myelopathy, encephalomyeloneuropathy.

### **Leucemia - linfoma de células T do adulto em um paciente com mielopatia associada a HTLV-I/II**

**RESUMO** - Apesar da infecção pelo HTLV-I ser endêmica em várias regiões do mundo, poucos são os relatos da associação entre leucemia-linfoma de células T do adulto (ATLL) e encefalomiceloneuropatia pelo HTLV-I. No presente artigo é descrito um paciente que no curso do comprometimento neurológico pelo HTLV-I desenvolveu quadro de leucemia com infiltração de tecido dérmico semelhante ao encontrado na micose fungóide/síndrome de Sézary.

**PALAVRAS-CHAVE:** HTLV-I, TSP, HAM, ATLL, mielopatia, encefalomiceloneuropatia.

---

Although human T-cell leukemia virus type I (HTLV-I) has been etiologically implicated in a variety of systemic and neurologic diseases<sup>2,5,6</sup>, few reports described lymphoproliferative disorders associated with neurological involvement in HTLV-I patients<sup>3,11</sup>. We report the occurrence of a probable adult T-cell leukemia-lymphoma (ATLL) mimicking mycosis fungoides/Sézary syndrome (MF/SS) in a patient with HTLV-I associated myelopathy (HAM).

### **CASE REPORT**

The patient is a 65 year old black man from Bahia (Northeastern Brazil) who presented with a 10 year history of progressive lower extremity weakness, paresthesia of both legs, urinary urgency and episodes of low back pain. After four years of neurological symptoms, he developed skin abnormalities characterized by itching and generalized descamative lesions beyond cervical, axillary and inguinal adenopathy, hepatosplenomegaly, fever and malaise. At this time he had dry cough and mild dyspnea. Skin and lymph node biopsies were carried out in June 1988. Peripheral blood examination showed HCT 43%; WBC 37.000/mm<sup>3</sup>: 60% lymphocytes. Morphologically many lymphocytes showed marked atypical nuclei (Fig 1). Chemotherapy was started with cyclophosphamide, metoclopramide, procarbazine, prednisone and bleomycin. Partial remission was observed. There was no history of blood transfusion and he denied intravenous drug use and homosexual activity.

On March 1993 physical examination showed besides the generalized exfoliative dermatitis widespread cutaneous infiltration and keratoderma of palms and soles. Hepatomegaly and lymphadenopathy were also present.

---

\*Federal University of Bahia (UFBA). Aceite: 22-fevereiro-1997.

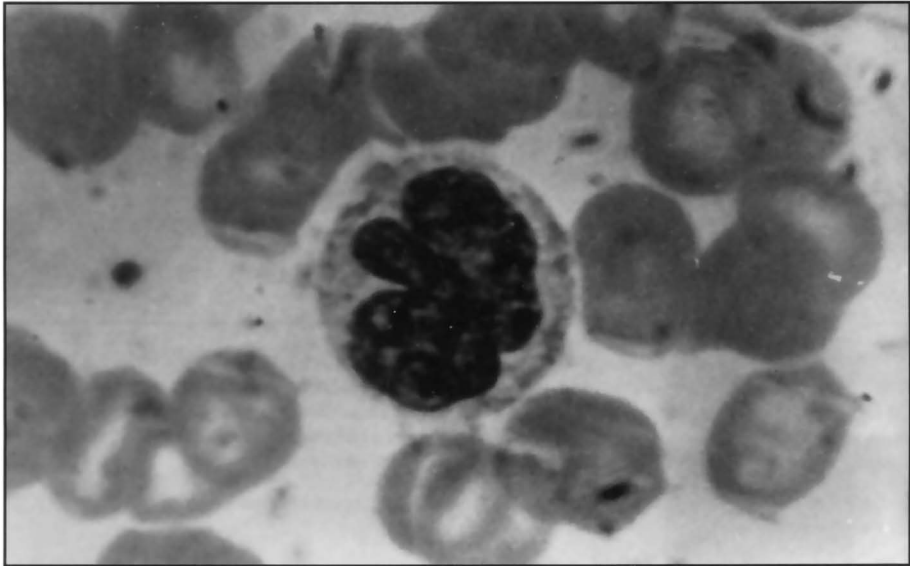


Fig 1. Peripheral blood smear of the patient with HAM/ATLL showing atypical lymphocytes with indented nuclei.

Neurological examination revealed spastic paraparesis, patellar hyperreflexia, hyporeflexia of achilles and bilateral Babinski sign with normal arms reflexes characterizing a neurological picture of myeloneuropathy at thoracic level. There were no objective signs of superficial sensory disturbance. Magnetic resonance imaging showed atrophy of thoracic spinal cord. The cerebrospinal fluid (CSF) was clear with 2.7 cells/mm<sup>3</sup>, proteins 25mg% (normal < 40mg%) and an IgG level of 10.8 (normal: <14 mg/l). An analysis of bronchoalveolar fluid showed that 82% of cells were lymphocytes. Biopsies of skin and lymph node were performed and submitted to pathological examination.

CSF and serum samples tested positive for antibodies to HTLV-I, using commercially available diagnostic EIA kits for screening (Coulter Labs., Hialeah, FL, USA). The EIA-positive serum also tested positive for HTLV-I/II by a new dot blot immunassay using highly purified HTLV-I/II viral and recombinant proteins. Samples were considered positive if antibodies against both gag (p24) and env (p21e) gene products were present.

Pathological studies. Both skin biopsies showed throughout the dermis an infiltration of medium sized neoplastic cells intermingled with plasma cells, mature lymphocytes, eosinophils, and neutrophils, more marked in the second biopsy. The neoplastic cells exhibited round, cerebriform or convoluted nuclei. In the epidermis Pautrier microabscesses were observed (Fig 2). The lymph nodes were obliterated by a infiltration similar to those observed in the skin but with predominance of convoluted cells. The neoplastic cells showed mild to moderate variation in the size of the nuclei. Immunohistochemistry: formalin fixed, paraffin embedded tissue sections were studied by the avidin-biotin complex immunoperoxidase method using the following antibodies: CD 20 (L26) and CD45RO (UCHL1). The neoplastic cells presented with a diffuse cytoplasmatic staining for CD45RO and did not react with CD20 antibodies.

## DISCUSSION

The findings of progressive spastic paraparesis, urinary urgency, thoracic cord atrophy on MRI, lymphocytosis in the bronchoalveolar lavage fluid and antibodies to HTLV-I/II in sera and CSF suggest that the patient had clinically HAM. The presence of large number of atypical T-lymphocytes in the circulation showed that he also had the leukemic variant of a cutaneous lymphoma<sup>2,4,6,7</sup>.

Although there have been many reports of HTLV-1 associated to leukemia/lymphoma or myelopathy, it is uncommon the association of both conditions in HTLV-I infected patients.

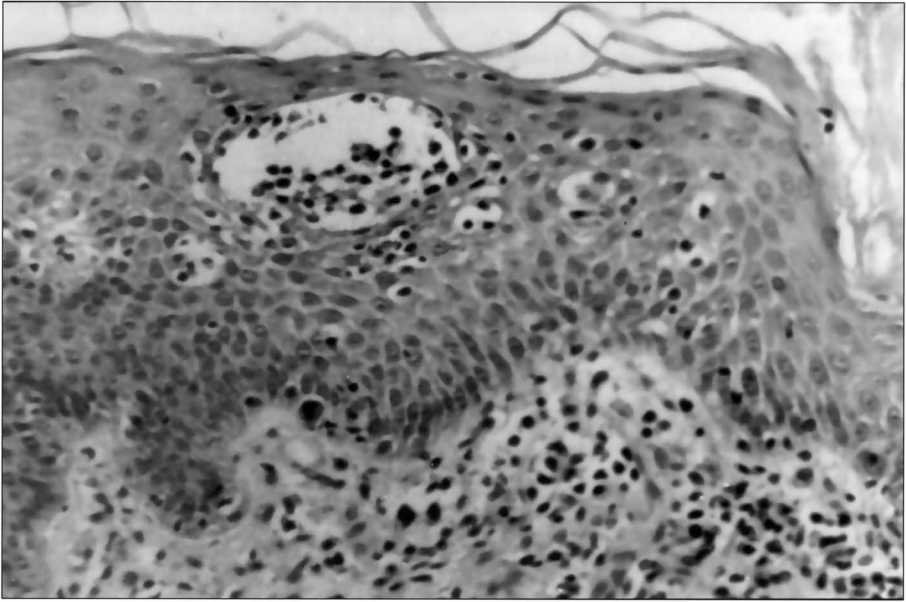


Fig 2. Skin biopsy of the HAM/ATLL patient with acanthosis and mononuclear cell infiltration in dermis. Pautrier abscess are present.

Otherwise, we do not know any previous report of a clinicopathological pattern mimicking MF/SS in HAM patients.

The present case is of special interest because after four years of progressive spastic paraparesis, the patient developed the cutaneous lesions evolving during six years.

HTLV-I positive ATLL has many clinicopathological similarities with MF/SS. This latter condition always involves primarily the skin but HTLV-I positive ATLL may also present with skin lesions in around 50% of cases<sup>4</sup>. Otherwise, in both diseases the neoplastic cells are epidermotropic. However, according to some authors, there are several features of the HTLV-I positive ATLL that may enable a differential diagnosis with MF/SS such as rapid progression of the skin lesions with early spread to lymph nodes and viscera, bone involvement and hypercalcemia<sup>1</sup>. Besides, the nuclei of the malignant cells of the HTLV-I positive ATLL are considered to be extremely pleomorphic<sup>4</sup>.

In the present case the onset of the lymphoma was insidious with a long evolution and hypercalcemia was not observed. By the histopathological pattern alone it would not be possible to differentiate ATLL and MF/SS but, in this case, the neoplastic cells were not as pleomorphic as those usually observed in the HTLV-I-positive ATLL. However the presence in the peripheral blood of a few large atypical lymphoid cells with multilobulated nuclei (flower cells) was very suggestive of ATLL.

The similarities between MF/SS and HTLV-I positive ATLL, that has been found by some authors, has raised speculation about a possible viral origin for MF/SS, at least in some cases, but this is yet matter of controversy<sup>1,7-10</sup>.

## REFERENCES

1. Fine RM. HTLV-I a new human retrovirus associated with cutaneous T-cell lymphoma (mycosis fungoides). *Int J Dermatol* 1988;27:473-474.

2. Gessain A, Gout O. Chronic myelopathy associated with human T-lymphotropic virus type I (HTLV-I). *Ann Intern Med* 1992; 117:933-946.
3. Kawai H, Nishida Y, Takagi M, Nakamura K, Masuda K, Saito S, Shirakami A. HTLV-I associated myelopathy with adult T-cell leukemia. *Neurology* 1989;39:1129-1131.
4. Lennert K, Feller AC. Non Hodgkin's lymphomas. Berlin: Springer Verlag, 1992.
5. Mattos K, Queiroz C, Peçanha-Martins AC, Publio L, Vinhas V, McJo A. Lymphocyte alveolitis in HAM/TSP patients. *Arq Neuropsiquiatr* 1993;51:134-136.
6. Melo A, Gomes I, Mattos K. Mielopatias por HTLV-I na cidade de Salvador, Bahia. *Arq Neuropsiquiatr* 1994;52:320-325.
7. Pancake BA, Zucker-Franklin D. The difficulty of detecting HTLV-I proviral sequences in patients with mycosis fungoides. *J AIDS* 1996;13:314-319.
8. Pancake BA, Zucker-Franklin D, Coutavas EE. The cutaneous T cell lymphoma, mycosis fungoides, is a human T-lymphotropic virus associated disease. *J Clin Invest* 1995;95:547-554.
9. Turbitt ML, Mackie RM. P19 antigen in skin and lymph nodes of patient with advanced mycosis fungoides. *Lancet* 1985;2:945
10. Whittaker SJ, Luzzatto L. HTLV-I provirus and mycosis fungoides. *Science* 1993;259:1470
11. Yasui C, Fukaya T, Koizumi H, Kobayashi H, Ohkawara A. HTLV-I associated myelopathy in a patient with adult T-cell leukemia. *J Acad Derm* 1991;24:633-637.