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HTLV-I associated myelopathy in the northern region of Brazil (Belém-Pará): serological and clinical features of three cases

Mielopatia associada ao HTLV-I na região Norte do Brasil (Belém-Pará): aspectos clínicos e sorológicos de três casos

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Abstract *Three patients (males, black, ages 37, 40 and 57) attended a university clinic with a progressive paraparesis of obscure origin. One patient who referred disease duration of more than 16 years, showed diminished deep reflexes, bilateral Babinski's sign, diminished sensation of vibration, abnormal bladder function and back pain. The other two patients (with one and six years of disease duration) complained of weakness in one leg, increased deep reflexes and back pain. Babinski's sign and bladder disturbance were also present in the patient with six years of disease. Blood samples tested by an enzyme immune assay and a discriminatory Western blot were positive for HTLV-I. The familial analysis of one patient showed a possible pattern of sexual and vertical transmission of the virus. To the best of our knowledge, these are the first cases of a proven association between HTLV-I and TSP/HAM in Belem, Para, and emphasize the need to actively look for cases of neurological disease associated to the virus.*

Key-words: *HTLV-I. Myelopathy. TSP/HAM. Neurological disease.*

Resumo *Três pacientes (masculinos, negros, idades 37, 40 e 57) foram atendidos em uma clínica universitária com uma paraparesia progressiva de origem obscura. Um paciente que referiu a duração da doença por mais de 16 anos, mostrou hiporreflexia, sinal de Babinski bilateral, uma sensibilidade vibratória diminuída, disfunção urinária e dor lombar. Os outros dois pacientes (com um e seis anos de duração da doença) queixavam-se de fraqueza em uma das pernas, hiperreflexia e lombalgia. Sinal de Babinski e distúrbio urinário estavam também presentes no paciente com seis anos de doença. Amostras de sangue testadas por ELISA e Western blot foram positivos para HTLV-I. A análise familiar de um dos pacientes, mostrou um possível padrão de transmissão sexual e vertical do vírus. Ao nosso conhecimento, estes são os primeiros casos comprovados de uma provável associação entre o HTLV-I e PET/MAH em Belém, Pará, e enfatiza a necessidade de uma busca ativa de casos de doenças neurológicas associadas ao vírus na região.*

Palavras-chaves: *HTLV-I. Mielopatia. PET/MAH. Doença neurológica.*

Human T-cell lymphotropic virus, type I (HTLV-I) is associated to a neoplastic disorder (Adult T-cell Leukemia and Lymphoma-ATLL), to a characteristic uveitis and a neurological chronic disease, Tropical Spastic Paraparesis or HTLV-I Associated Myelopathy (TSP/HAM). This condition is a chronic myelopathy without spontaneous remission, characterized by a slowly progressive paraparesis, affecting mainly the pyramidal tracts and associated to a variable sphincter disturbance and abnormalities of the sensory system[5,6]. In general, TSP/HAM occurrence follows the same geographical distribution of the virus, presenting high frequencies in Asia, West Indies, America, and Melanesia[10], it affects predominantly individuals from 35 to 49 years of age, with a male/female ratio of 2.5 to 3.0:1, and shows a high frequency among Negroes, mixed race and Asians, although it has also been found among Caucasians[9,12].

In Brazil, the first cases of proven TSP/HAM were reported in 1989[2,4]. Furthermore, clinical and

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seroepidemiological studies have shown cases of TSP linked to HTLV-I antibody detection, in Recife, Salvador, Rio de Janeiro, Sao Paulo and Porto Alegre[1 8].

The present work describes, for the first time, in Belém, Pará (Brazil), a positive association of HTLV-I with three cases of chronic myelopathy.

MATERIAL AND METHODS

Patients examined. Three patients attending a university outpatient clinic (at the Betina Souza e Ferro Hospital, UFPA) with complaints of chronic gait disturbances of obscure origin for more than 6 months, were neurologically examined. In addition, nine other relatives of two of the patients were examined in order to detect clinical signs of neurological abnormalities. Demographic data regarding these patients are presented in Table 1.

Table 1 - Demographic and epidemiological data of three patients with neurological disease associated to HTLV-I in Belém, Pará, Brazil.

Characteristic	Patient 1	Patient 2	Patient 3
Sex	male	male	male
Race	negro	negro	negro
Age	40	37	57
Origin	Buriti Bravo-MA	Santa Cruz do Arari-PA	Cachoeira do Arari-PA
Employment	general services	fisherman	fisherman
History of blood transfusion	no	no	yes
Duration of disease (years)	1	6	16

Serological assays. Serum samples were collected from all three patients and nine of their relatives. Serological diagnostic tests were provided and included an enzyme immunoassay (EIA, Ortho Diagnostic, USA) and a discriminative Western blot (Genelab 2.4, Singapore) that was capable of distinguishing serological reactivity between HTLV-I and HTLV-II, as previously described[7].

RESULTS

Clinical features. The clinical features of the three patients during medical examination and counseling are summarized in Tables 2 and 3, and they presented a neurological disorder clinically diagnosed as Tropical Spastic Paraparesis. None of the examined relatives displayed any sign or symptom compatible with TSP/HAM or any minor neurological abnormalities.

Serological assay. All three patients showed antibodies reactive to HTLV-I/II when tested using the EIA. Western blot serological reactivity was confirmed to be against HTLV-I. The sera of the wife and son of patient nr. 1 showed reactivity to HTLV on the EIA. The Western blot serological reactivity showed an indeterminate pattern (wife) and a characteristic HTLV reaction (son), according to the manufacturer's recommendations for interpretation of the test (Figure 1).

Table 2 - Clinical symptoms observed in three patients with TSP/HAM in Belém, Pará, Brazil.

Clinical characteristic	Patient 1	Patient 2	Patient 3
Difficulty in walking/running during school age	-	-	-
Weakness of the legs within six months of onset of the disease	+	+	+
Leg cramps	+	+	+
Lower limb paresthesis	+	+	+
Back pain with irradiation to the legs	+	+	+
Bladder dysfunction	-	+	+
Male impotence	+	+	+

+ present; - absent

DISCUSSION

The association of HTLV-I to a progressive neuroencephalopathy has been constantly described in Brazil since the initial detection in 1989[1 2 3 4]. The clinical and epidemiological data observed to date, appears to be similar to the cases of TSP/HAM described worldwide[11 12]. In the present paper three cases of clinically diagnosed myelopathy were described with characteristic symptoms of lower limb paresthesis and weakness, incapacity of walking, diminished deep reflexes, bilateral Babinski's sign, back pain, bladder dysfunction and impotence. The three patients fulfilled the clinical criteria as well as presenting serological evidence of HTLV-I infection, sufficient to categorize these as cases of TSP/HAM.

Epidemiological and demographic information also coincide with what is usually observed elsewhere; in that they were black males, with an age range of 37

Table 3 - Neurological abnormalities present in three patients with TSP/HAM in Belém, Pará, Brazil.

Clinical characteristic	Patient 1	Patient 2	Patient 3
Psychic analysis	Normal	Normal	Normal
Motricity of lower limbs			
spastic gait	A	A	P
weakness	P	P	P
hyperreflexia	P	P	P
hyporreflexia	A	A	P
hypertonia	A	A	P
Capacity of walking			
conserved but limited	Y	N	N
use of one or two crutches	N	Y	Y
incapacity	N	N	N
Babinski's sign	Y	Y	Y
Muscle atrophy	N	Y	Y
Superficial sensibility loss in the lower limbs	Normal	Normal	Normal
Deep sensibility loss in the lower limbs	D	D	D
Autonomic disturbances			
bladder dysfunction	A	P	P
constipation	A	A	P
impotence	P	P	P

P= present; A= absent; Y= yes; N= no; D= diminished.

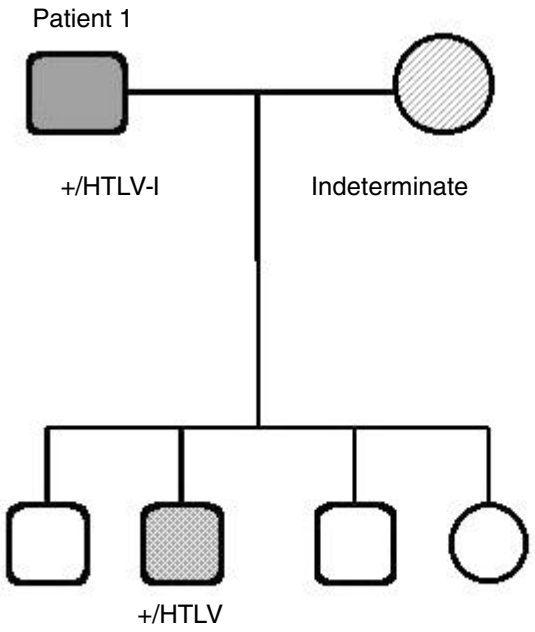

Figure 1 - Presence of antibodies to HTLV-I/II among relatives of patient 1 (results of EIA/Western blot).

to 57 years. The patients resided outside large urban areas, lacking in adequate clinical and laboratory facilities. The association of subtle symptoms at onset of disease, poor diagnostic resources and low income are common and complicating factors that contribute towards the absence of other cases described in the northern region of the Country.

Screening for the presence of antibodies to HTLV among nine relatives of patients 1 and 3 showed that patient 3 was the sole case in the family and transmission of the virus occurred possibly through the parenteral or sexual path. The wife and son (8 years of age) of patient 1 showed evidence of HTLV infection and vertical transmission had probably occurred.

As far as we are aware, these are the first cases of a proven association between HTLV-I and myelopathy (TSP/HAM) described in Belem, but the occurrence of

this or other neurological disorders related to HTLV-I are probably more common. The dissemination of proper information for the clinical and laboratory procedures should be sufficient to improve diagnostic skills, however it is necessary to emphasize the need for a close surveillance and to undertake a further active search for cases of neurological diseases associated to HTLV-I, in this particular geographical region of the Country.

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