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HTLV-I ASSOCIATED MYELOPATHY / TROPICAL SPASTIC PARAPARESIS

REPORT OF THE FIRST CASES IN RIO GRANDE DO SUL, BRAZIL

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SUMMARY - The HTLV-I associated myelopathy /tropical spastic paraparesis (HAM/TSP), a myelopathy with predominant involvement of the pyramidal tract with minimal sensory loss and associated with HTLV-I infection, endemic in tropical areas, has been identified in four patients in Porto Alegre (RS, Brazil), a temperate zone.

KEY WORDS: HTLV-I associated myelopathy, tropical spastic paraparesis, HTLV-I, Rio Grande do Sul (Brazil).

Mielopatia associada ao HTLV-I/paraparesia espástica tropical: relato dos primeiros casos no Rio Grande do Sul, Brasil

RESUMO - A mielopatia associada ao HTLV-I/paraparesia espástica tropical (HAM/TSP), uma mielopatia com envolvimento predominante do trato piramidal e com perda sensitiva mínima, que tem o vírus HTLV-I como agente etiológico e é endêmica em várias áreas tropicais, foi identificada em quatro pacientes em Porto Alegre (RS, Brasil), uma zona temperada.

PALAVRAS-CHAVE: mielopatia associada ao HTLV-I, paraparesia espástica tropical, HTLV-I, Rio Grande do Sul (Brasil).

During the 80's, the HTLV-I associated myelopathy/tropical spastic paraparesis (HAM/TSP) was identified in regions such as the Caribe, South Africa, Southern India, Seychelles Islands, Ivory Coast and Southern Japan. Those areas were found to be endemic for the HTLV-I, the etiologic agent for HAM/TSP. Towards the end of that decade and at the beginning of the 90's, several authors have described cases in non-tropical areas or in areas not known to be endemic for the disease as the United States and Europe. Papers published regarding the cases in Brazil have described its presence in the North, Northeastern and Southeastern areas.

In this report we present the first four cases of HAM/TSP with CSF positive tests for HTLV-I in the subtropical State of Rio Grande do Sul, Brazil.

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CASE REPORTS

Case 1. IG, 68 years old, female, white, from Guaíba (RS, Brazil). In 1989, at age 66, she presented pain and weakness in the legs, along with tremor in the hands and constipation. Six months later, she complained of lumbar pain, progressive weakness in the legs and urinary urgency. Computerized axial tomography (CT) of the spine and skull and myelography were negative. Cerebrospinal fluid (CSF) showed pleocytosis with predominant lympho-monocytic cells. In March, 1990, she developed urinary and fecal incontinence. Neurological evaluation showed asymmetric paraparesis, hyperreflexia with spasticity and bilateral Babinski sign. Touch sensation showed slight diminution and pain sensation was increased. Blood samples revealed eosinophylia (23% in 7700 leucocytes). CSF maintained pleocytosis with 23 cells with predominant lymphomonocytes; proteinogram showed slight increase in total protein; the gammaglobulin fraction was 14.4%. After the use of corticosteroids, a slight clinical improvement happened. New CSF exam showed again lymphocytic pleocytosis; immunological tests for syphilis, toxoplasmosis and cysticercosis were negative; electrophoresis of CSF proteins was normal; IgG was not contributory; ELISA for HTLV-I (Serodia - ATLA, Fujirebio) was found positive in the CSF. Magnetic resonance (MR) showed periventricular lesions compatible with demyelinating disease (Fig 1). In May, 1990, the patient presented an urticariform rash, with cough and dyspnea that progressed quickly to ventilatory insufficience, shock and death. Chest X-rays showed diffuse pulmonar infiltrate. Risk factors for HTLV-I virus contamination were not identified.

Case 2. ADS, 39 years old, white, male, from Porto Alegre (RS, Brazil) was normal untill 1980, when started to present progressive weakness in lower extremities, which affected predominantly the right leg. At that time, myelography was normal and CSF was suggestive of neurosyphilis which was properly treated. In the same year, despite the use of corticosteroids, he became worse. After 2 years, paraparesis progressed with appearence of hyperreflexia, knee and ankle clonus and bilateral Babinski sign. Cranial nerves, upper extremities, and cortical functions were normal. He complained of feet and legs pain and was constipated. Corticosteroids were used again but paraparesis slowly worsened. In 1986, new CSF sample showed increase in gammaglobulin levels (17.3 %) and oligoclonal bands; IgG was high and suggested immunoliberation at the central nervous system (CNS). In the same year, MR of brain and spinal cord failed to show abnormalities. In 1987, ELISA (Behring) for HIV was negative. Nine years after the first symptoms, he had severe paraparesis and bladder control disturbances. New CSF made in 1991, showed again high gammaglobulin levels (23.5%) and ELISA (Genetic System and Fujirebio) to HTLV-I was reactive. The patient was homosexual. Treatment with danazol was of no benefit.

Case 3. PRHB, 26 years-old, white, male, from Porto Alegre (RS, Brazil) was a drug user, alcoholist who had received a blood transfusion in 1985. In September, 1989, he started with paresthesias in lower extremities, paresis in the left leg, that progressed into paraparesis in 2 months. In February, 1990, he used corticosteroids with subjective improvement. In March, he showed constipation, urinary hesitance. Neurological evaluation

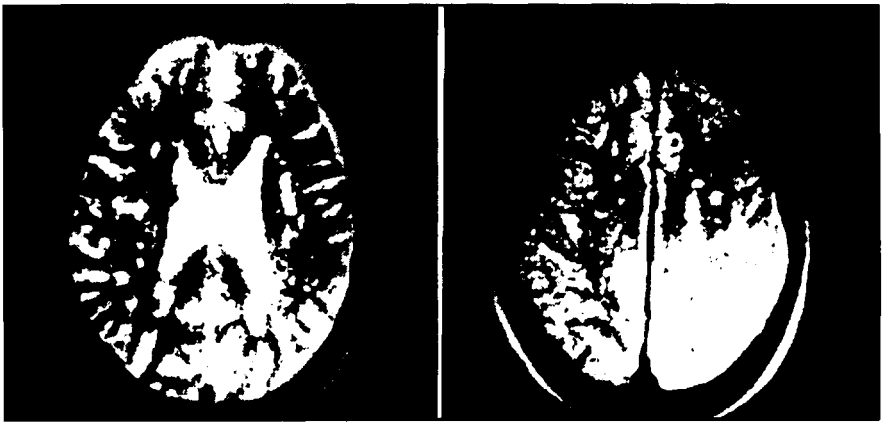

Fig 1. Case 1. MRI showing periventricular lesions compatible with demyelinating disease.

disclosed diffuse hyperreflexia particularly in the lower extremities and severe paraparesis. At this time, his brother, who had AIDS and also showed paraparesis, died. Myelography and vertebral CT were normal. Tests for syphilis were negative as well as ELISA for HIV. CSF sample was normal, except for elevated gammaglobulins levels (30.4%) with oligoclonal bands; ELISA (Fujirebio) for HTLV-I in CSF was positive. From March to May, 1990, he received corticosteroids again, but had no improvement.The patient failed to return for new evaluations after 1990.

Case 4. MMP, 43 years-old, white, female, married, from Pelotas (RS, Brazil). In 1974, when she was 29 years-old, started with difficulty to move the right foot. At this time, only the CSF showed pleocytosis with 10 cells, with predominance of lympho-monocytes. She progressed to paraparesis and in 1976 it was already difficult for her to walk. At the same time, urinary incontinence occurred. New CSF study in 1979 was similar to that examined in 1974. Urodynamic evaluation disclosed a neurogenic bladder. She used corticosteroids and baclofen with slight improvement. Sensibility was normal until 1981, when she refered alterations in legs's sensations. New evaluation in 1982 showed worsening of the paraparesis, which was still asymmetric, lumbar pain, constipation and urinary urge-incontinence. In 1984, mobilization of the legs was difficult, she had diurnal urinary urgency and frequent nocturnal incontinence. The constipation persisted. Three years later, she had severe paraparesis and important walking difficulties. In 1988, MR of spinal cord was normal. In 1992, new evaluation disclosed CSF with slight pleocytosis with 7 leucocytes and 25 mg/dl of protein; ELISA (Behring) test for HIV-1/HIV-2 was negative but positive for HTLV-I (EMBRABIO). The mode of transmition was not identified.

COMMENTS

The four cases described here are in white patients. This has been previously described[2,3,9]and may represent the ethnic composition in the area. Considering the small number of cases it is not possible to analyse the differences of incidence according to sex of patients. The age of first symptoms in our patients is similar to the described in the literature[1,2,7,8,11,13] except in Case 1, who presented the disease after the age of 60[2,11,16].

We did not test these patients for the HLA haplotype, but family history was negative, except for Case 3, whose brother had died of AIDS[2,10]. We failed to identify the mode of transmission of the HTLV-I in Cases 1 and 4. Patient 2 is homosexual. In Case 3 there was a history of drug addiction and blood transfusion. The literature reports that horizontal transmission occurs in 0.4 to 60.8%[2,6-8,11-14,16].

Several studies showed that patients infected by means of transfusions of whole blood or its sub-fractions would develop the first neurologic symptoms in a shorter period of time[16], would be younger and would have a faster progression of the disease[12]. Patients infected by other ways would have a slower progression[11,14,15]. A rapid and premature course occurred on Case 3, and also in the Case 1, whose mode of infection was not identified, but certainly was not related to transfusion of blood or its components.

All four patients fulfilled the clinical and laboratory criteria for the diagnosis proposed by Vernant and col. in 1987. The four cases had positive tests for HTLV-I in the CSF by ELISA[2,3,6,8,16,19]. Serial eosinophylia was found in the peripheral blood in Case 1 as previously reported[20]. All of our four patients had negative tests for HIV. In Case 1, MRI showed periventricular lesions similar to what is seen in multiple sclerosis, but was normal in Cases 2 and 4. Both types of finding are seen with this pathology[6,8,11,13].

Cases 2, 3 and 4 progressed according to what was expected, however Case 1, who died, presented pulmonary infiltrates possibly related to the perialveolar lymphocytic reaction secondary to the circulation of immunecomplexes described in the literature[8,12,19].

Treatment with corticosteroids caused partial and transient improvement in Cases 1 and 2 and none in Cases 3 and 4. This may be related to the mode of transmition. This is consistent with what has been described in the literature[1,7,8,14]. Cases 2 and 4 showed no improvement with the use of danazol.

In 1986, Tadakoro and col. reported the prevalence of positive tests for HTLV-I in Japanese immigrants arrived from the region of Okinawa (Japan) and in their descendants living in the cities of Campo Grande and São Paulo (Brazil). They found a 10% positivity for HTLV-I in the serum of persons tested[18].

In 1988, Johnson and col. reported cases of TSP in Peru affecting residents living in a region not known to be endemic and in caucasians who had no previous history suggestive of contamination by the HTLV-I virus[9].

More recently, in 1989, Costa and col. published 10 cases of TSP in Fortaleza (Brazil) but did not perform the tests for HTLV-I[5]. Castro and col. published a preliminary report on the serum positivity in São Paulo (Brazil)[4]. In 1990, Spina-França and col. studied the CSF of 150 patients in order to determine the incidence of serum positivity for HTLV-I in some risk groups in São Paulo (Brazil). The results ranged from 16.5 to 55% of positivity[17]. In 1993 the first cases in Rio de Janeiro were published[3].

The prevalence of HTLV-I in the State of Rio Grande do Sul is not known, since no epidemiologic survey has been made with such purpose so far. However, due to technical difficulties, only now several other cases of spastic paraparesis detected in our service are being tested for HTLV-I.

The legal obligation for the performance of testing in blood donors in our country, and particularly in our state has raised the problem of what to do with the persons with positive tests and, so far, do not present, if ever will present, clinical symptoms. It appears, at the moment, that persons with positive tests must be oriented not to donate blood, not to brest feed, and to use systematically comdom.

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