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INFLAMMATORY MYOPATHY ON HTLV-I INFECTION

Case report

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ABSTRACT – We describe a 41 years old woman who 17 years ago presented hypotonia and proximal muscular weakness in the upper and lower limbs. On neurological examination, the biceps, triceps and Achilles reflexes were absent; the brachioradialis reflexes were decreased and the patellar reflexes were normal. There was bilateral Babinski sign. The remainder of the neurological examination was unremarkable. In the investigation a myopathic pattern was found in the electromyography. The nerve-conduction study was normal; a ELISA method for HTLV-I antibodies was positive in the blood and in the cerebral spinal fluid. The muscle biopsy showed inflammatory myopathy, compatible with polymyositis. This paper focuses the polymyositis in the beginning of an HTLV-I infection case.

KEY WORDS: HTLV-I, polymyositis, inflammatory myopathy.

Miopatia inflamatória em infecção por HTLV-I: relato de caso

RESUMO – Descrevemos o caso de uma paciente que há 17 anos iniciou sua doença com hipotonia e diminuição da força muscular proximal nos membros superiores e inferiores. No exame neurológico apresentava arreflexia bicipital e tricipital, hiporreflexia estilorradial e reflexo patelar normal; sinal de Babinski bilateral. O restante do exame neurológico era normal. Na eletromiografia de agulha foi encontrado padrão miopático. O exame de condução nervosa estava normal. A pesquisa pelo método ELISA de anticorpos anti-HTLV-I foi positiva no sangue e no líquido cefalorraquidiano. A biópsia muscular mostrou miopatia inflamatória, compatível com polimiosite. O presente artigo enfoca a polimiosite na abertura do quadro clínico de uma infecção pelo HTLV-I.

PALAVRAS-CHAVE: HTLV-I, polimiosite, miopatia inflamatória.

Several syndromes have been associated to the HTLV-I. In neurology, the most frequent picture is the called HTLV-I associated myelopathy / tropical spastic paraparesis. Associated to this, more recently has been described the HTLV-I polymyositis[1], and there are also a few cases of polymyositis alone. This paper reports a case of a patient who started with polymyositis and later developed a myelopathy with HTLV-I antibody positive.

CASE

A 41 years old white woman presented, since 1983, proximal muscle weakness of her left lower limb, and 6 months later also of the right side, with progressive worsening. After 5 years she presented proximal muscle weakness of both upper limbs. There were no sensitive disturbances or urinary incontinence. She also presented moderate myalgia and had several types of treatment without satisfactory result. She was treated with prednisone in the last 3 year and at time of evaluation was taking 5mg/day. She had a past history of hepatitis when was 19 years-old, urinary infection, apendicectomy and had received a blood transfusion.

The neurological examination showed mental and cranial nerves examination with no involvement. There was not muscle atrophy. There was hipotonia in the four limbs. Weakness was presented in the four limbs, and was more prominent in the proximal groups (3/5) than in the distal ones (4/5). The exteroceptive and proprioceptive sensations were normal. The biceps, triceps and Achilles reflexes were absent; the brachioradialis was decreased and the patellar was normal. There was bilateral Babinski sign. The remainder of the neurological examination was unremarkable.

The abnormal investigation were as follows: erythrocyte sedimentation rate (ESR) was 47 mm (normal = 0-20),

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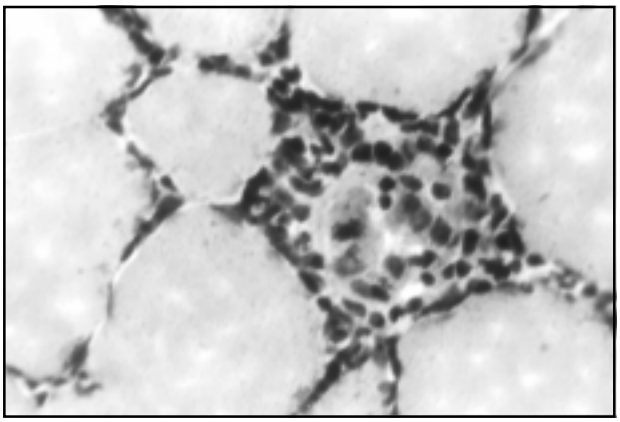

Fig 1. Fibers are focally surrouded and invaded by mononuclear cells (hematoxylin and eosin; 348x).

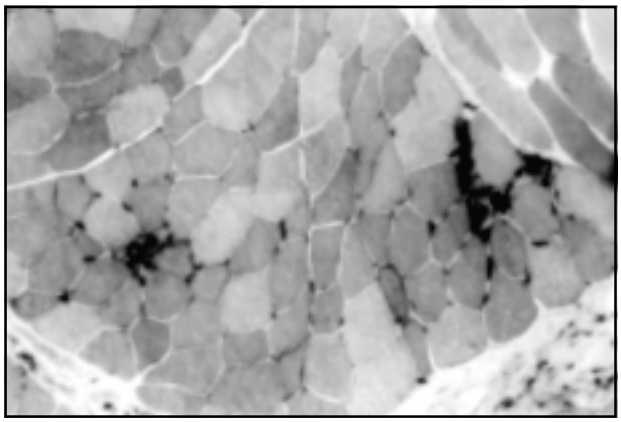

Fig 2. Endomisial mononuclear infiltrade inflammation (hematoxylin and eosin; 174x)

creatine kinase (CK) = 598 IU/l (normal = 10-70), aldolase = 11 IU/l. Serum and cerebrospinal HTLV-I antibody was positive at ELISA; Western blot analysis confirmed the presence of antibodies to HTLV-I polypeptides, including gp 21, p 24, p53, gp 46 and p28 . Rheumatoid factor, antinuclear and DNA antibodies were absent, and there were no LE cells. Needle electromyography of right biceps brachii, deltoid, quadriceps and anterior tibial muscle showed myopathic pattern, with insertion activity, fibrillations and positive waves at the biceps, deltoid and anterior tibial; repetitious discharges complexes at the anterior tibial; voluntary motor activity with short duration and amplitude reduced at the biceps, deltoid and quadriceps. The nerve-conduction study was normal.

The muscle biopsy performed in the biceps brachii showed normal endomisial connective tissue, with no adipose tissue infiltration. The vessels were normal, with little perivascular inflammatory infiltrate. There was a moderate variation of muscular fibers diameter, with some atrofic angulated fibers, with multiple peripherical nuclei. There was simple necrosis and fagocitosis (Fig 1). Inflammatory infiltrate was excessive compared to the necrosis (Fig 2). We also found rare ragged red fiber and basophilics fibers. There was a type 1 fiber predominance. At nonspecific esterase we found increase of interstitial activity and rare atrophic angulated fibers. Rare positive fibers were found at acid phosphatase. There was an increase activity in the interstitial tissue for acid and alkaline phosphatase. Succinate dehydrogenase and cytochrome C-oxidase showed severe subsarcolemal accumulation of mytochondria and rare granular fibers. Oil Red 0, myofosforilasis, PAS and cresil violet were normal.

Along the following years, the patient was treated with layer doses of prednisone, alone or associated with azatioprine, cyclophosphamide and methotrexate with partial improvement of the muscle strength, but there was always some deficit. The best results were obtained with the association of prednisone and methotrexate.

One year ago the patient became worse, with severe muscle weakness of lower limbs and was unable to walk.

DISCUSSION

Epidemiologic surveys have identified regions, such as southern Japan[2,3], the Caribbean[4], South and Central America[5,6] and regions of Africa, where the prevalence of HTLV-I is high, then been considered endemic regions. One survey conduced in Brazil revealed that the prevalence of HTLV-I in this country is high, particularly among homosexual and bisexual men, female prostitutes, patients with AIDS, and men with hemophilia[7].

The primary routes of HTLV-I are four: transmission from mother to child through breast milk[8], sexual transmission (male to male, male to female, and rarely female to male)[9,10], transfusion of infected blood[11-13] and use of drugs sharing needles/syringe[14].

The majority (98%) of HTLV-I seropositives are asymptomatic[1,15]. Why the disease is manifested in some people is not completely known, and the same is true about why one syndrome choose one group of patients. Several processes have been suggested as the pathogenesis of HTLV-I myelopathy; two of them are considered the most important: the first hypothesis suggests the infection of the glial cells as the initial process, then a cytotoxic immune response against the infected cells results in demyelination[16], other suggestion is that the HTLV-I infection leads to the activation of a autoimunne process T cell mediated[1]. The involvement of the HTLV-I in the genesis of polymyositis is almost confirmed, particularly after the identification of the HTLV-I in some muscle biopsy of seropositives patients with polymyositis[17-20]. However, some investigators did not get success in that attempt[21]. The pathogenesis of the HTLV-I polymyositis is not clearly known, and seems to be related to an immunological process and/or direct infection of the muscle fibers by virus[22-23]. Recent data argues

against the direct viral infection; HTLV-I and HTLV-I positive lymphocytes probably do not infect the muscle *in vivo* and *in vitro*[17,21]. The polymyositis is likely to be caused by a T-cell-mediated and major-histocompatibility-complex Class I (MHC-I)-restricted myocytotoxicity[24-25] , but muscle fibers in polymyositis without HTLV-I also express MHC-I antigen[22,26]. Muscle fibers in patients HTLV-I-positive also expressed MHC class II antigens in one study[26], specially when associated with myelopathy, and it was not observed in HTLV-negative patients, suggesting a different immune environment .

Some investigators have reported cases of polymyositis following HTLV-I myelopathy[18,28,29], and also just polymyositis in HTLV-I infected patients. In Brazil, there are only two studies that describe muscle involvement in the HTLV-I infection[30,31]. In the bigger one[30], 4 of the 11 patients reported had muscle biopsy suggesting polymyositis. However, these are reports of patients that have myelopathy and associated muscle involvement, and is no reference about typical clinical history of polymyositis in the beginning of clinical presentation. From 1993 to 1999, 13 patients were diagnosed with neurological disorders associated to HTLV-I in the Hospital de Clínicas-PR-Brazil; this is the first case of polymyositis.

A study confronting idiopathic forms of polymyositis and HTLV-I seropositive polymyositis tried to distinguish these two diseases, considering clinical aspects[32]. They found dysphagia only in the seronegatives patients. Babinski sign was found only in the seropositives, and other reflexes were abnormal (decreased or brisk) in almost all the seropositives, while only one of the seronegatives patients showed decreased reflexes. Some of the seropositives patients had bladder disturbances, but not the seronegatives. Moreover, the evolution of the patients was different: progressive worsening in the seropositives despite the treatment, in contrast to the full recovery of the great part of the seronegatives. As already reported, our patient did not have dysfagia, the reflexes were diffusely decreased and there was bilateral Babinski sign. Moreover, even presenting some improvement, she did not never recovered fully, and there were periods of worsening when the drug doses were reduced.

Besides the clinical history, the diagnosis of polymyositis is based on the muscle biopsy, the electromyography and serum level of some enzymes (CK, aldolasis). As already reported, the detection of the HTLV-I in the muscle biopsy is possible, but not always.

The main treatment is the corticotherapy[28,29,32], but also can be included immuno-suppressive drugs[32]. It has been proposed the use of high-dose intravenous immune globulin infusion for refractory cases, with good results[33].

We report this case for its atypical presentation, with the myopathy always predominant, and the upper motor neuron disease beginning just at the end of the clinical presentation (in opposite of the usual).

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