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MOTOR UNIT INVOLVEMENT IN HUMAN ACUTE CHAGAS' DISEASE

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SUMMARY — Thirty five patients with acute Chagas' disease who demonstrated parasitaemia at the time of the investigation were submitted to a detailed electromyographical study. With their muscles at rest, 12 patients showed fibrillation potentials and/or positive sharp waves. On volitional contraction, 7 had short duration motor unit potentials (MUPs) and low polyphasic MUPs. On motor and sensory nerve fibers conduction studies, 20 disclosed values below the lower control limit within one or more nerves. Finally, 12 patients produced a muscle decremental response on nerve supramaximal repetitive stimulation. The findings signal that primary muscle involvement, neuropathy and impairement of the neuromuscular transmission, either isolated or combined, may be found in the acute stage of human Chagas' disease.

Compromiso de la unidad motora en la fase aguda de la enfermedad de Chagas humana.

RESUMEN — Treinta y cinco pacientes con el diagnóstico de enfermedad de Chagas en su etapa aguda, todos con parasitemia positiva en el momento de la investigación, fueron sometidos a estudio electromiográfico por técnicas convencionales. En reposo, 12 de ellos mostraron fibrilaciones y/o potenciales positivos. Durante la contracción voluntaria, en 7 pacientes los potenciales de unidad motora eran bifásicos de corta duración y polifásicos de baja amplitud. En 20 se encontró disminución de la velocidad de conducción motora y/o sensitiva en uno o mas de los nervios explorados. Finalmente, 12 pacientes mostraron caida de la amplitud del potencial muscular evocado por estímulo nervioso repetitivo supramáximo. Los hallazgos hechos señalan que durante la fase aguda de la enfermedad de Chagas en el hombre puede producirse alteración primaria del músculo, neuropatía y compromiso de la transmisión neuromuscular, en forma aislada o combinadas entre si.

In the past years, the involvement of the peripheral nervous system has been extensively reported in chronic human Chagas' disease [9-11] and, more recently, the same type of lesion could be demonstrated in chronic experimental models [4,8]. However, only few attempts have been done looking for the eventual damage of the peripheral nervous system in the acute stage of the human disease [2]. Some experimental data obtained from the mouse support the possibility of a very early injury of the peripheral nerve [5], besides the well-known myositis [6], shortly after the inoculation of the animal.

The aim of the present study, has been to make a first approach searching for the involvement of the peripheral nervous system in patients affected by acute Chagas' disease who live in an endemic area. A previous and limited account of these findings has been published elsewhere [1].

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MATERIAL AND METHODS

The whole study was carried out at Santiago del Estero Province, Argentina, where the disease is endemic.

Subjects — Altogether 35 patients were explored. Their ages ranged between 3 and 22 years. Nineteen were females and 16 males. Thirty-three of them lived in rural areas, while just two unhabited within the town. The diagnosis was done at the 'Centro de Chagas y Patología Regional de Santiago del Estero'. All them had positive parasitaemia at the time of the investigation, while only 29 of the studied subjects showed also positive sera tests (immunofluorescence and haemagglutination).

Their clinical initial manifestations were eye-lymph node complex (33 patients), localized swelling at the site of the Triatoma infestans bite (one patient) and widespread subcutaneous oedema (one patient). From this study were rejected all those patients who may have other causes able to induce nervous or muscle damage. The time elapsed between the appearance of the first sign or symptom related to the disease and the observation of the patient varied between 5 and 30 days, with a mean of 13.34 ± 5.6 days. Controls — An age matched group of 25 subjects selected from the same area, without parasitaemia, with negative serum tests, and in good health conditions at the time of the study were employed as controls.

Techniques — Patients and controls were submited to the following procedures: a. *Electromyographical investigation*: Conventional electromyographical (emg) studies, with coaxial needle electrodes, were performed in deltoid, abductor pollicis brevis, quadriceps, tibialis anterior and extensor digitorum brevis muscles. In every case, with the patient resting, a search was made for spontaneous activity, namely fibrillation potentials and positive sharp waves. Thereafter, the subject was instructed to weakly voluntary contract muscles and the characteristics of the motor unit potentials (MUPs) were analized on the screen of a storage oscilloscope. Finally, the subject produced a full contraction and the pattern of MUPs recruitment was observed. b. *Nerve conduction studies*: Conventional maximal motor conduction velocities were studied at the median, ulnar and deep peroneal nerves. Also, conventional sensory conduction velocity was explored, with surface electrodes, at the median nerve by stimulating the IIIrd digit and recording the sensory action potential at the wrist. When performing this investigation, the skin overlying the studied nerve was warmed up and the ambient temperature was mantained at about 28°C. c. *State of the neuromuscular transmission*: Supramaximal ulnar nerve repetitive stimulation at 3, 5 and 10 Hz, through trains of 2 seconds each, was delivered at the wrist. The responses were obtained at the hypothenar muscles with surface electrodes. The amplitudes of the 3rd, 6th and 10th muscle potentials were refered to the first, as percentage.

RESULTS

With the muscles at rest, 12 out of 34 patients explored (35%) disclosed fibrillations and/or positive sharp waves in, at the least, one of the investigated muscles. On full voluntary muscle contraction, all the patients tested (n=34) showed a normal interference pattern. With weaker effort, 7 of them had biphasic short duration MUPs and low amplitude polyphasic MUPs. Two out of these 7 patients had also fibrillation potentials when their muscles were at rest.

Figure 1 shows the results obtained in 35 patients who underwent nerve conduction studies. Twenty two of them showed some nerve involvement. The commonest was the slowness of the sensory fibers of the median nerve (14 out of 33 patients studied, 42.4%) followed by the involvement of the motor median nerve (8 out of 21, 38%) and of the ulnar nerve (6 out of 31, 19.3%) and, finally, of the deep peroneal nerve (5 out of 31, 16.1%). The most frequent type of peripheral nerve damage was the slowness of an isolated nerve (63.6% of the patients). Two nerves were affected in 18% of the patients, 3 in 13.6% and 4 only in 4.5% of them.

Seven patients who showed neuropathy disclosed also spontaneous activity (31.8%) and 4 associated neuropathy with an emg of the primary muscle involvement type (18.1%). Twelve out of 33 patients explored (36.3%) disclosed a decremental muscle response, larger than 15% (s) of the amplitude of the first potential, on repetitive nerve stimulation. Six of the 12 patients with this abnormal response showed also neuropathy. Three had neuropathy plus signs of primary muscle involvement, while the remaining three patients had no other associated abnormality.

It was observed that there was a positive relationship between the timing of the infection and the appearance of abnormal electrophysiological signs. So, the neuropathy was

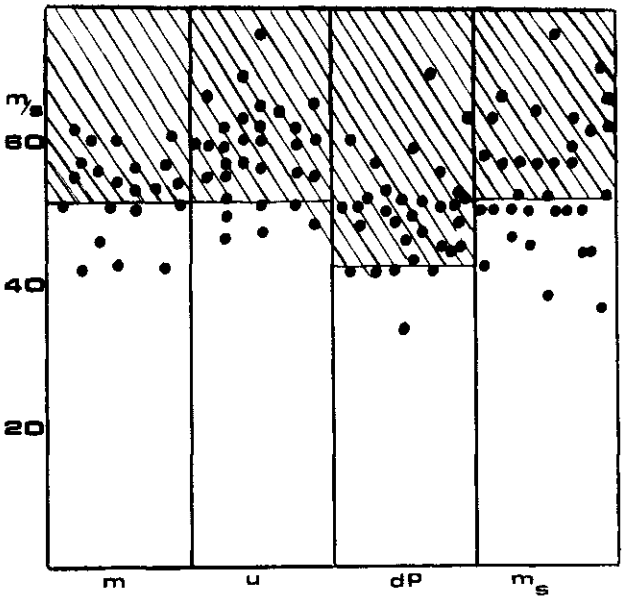

Fig. 1 — Values of maximal motor and sensory conduction velocities. Hatched areas signal control range: m, median nerve (motor); u, ulnar nerve; dp, deep peroneal nerve; m_s, median nerve (sensory).

detected in 37% of the patients within the first 10 days post-infection (pi); in 71.4% of them in the second 10 days pi; in 66% in the last 10 days ($r=0.61$). Signs of primary muscle involvement were found in 12.5%, 19% and 33% of the patients within equal periods ($r=0.96$) and, finally, decremental responses to repetitive nerve stimulation were observed in 12.5%, 33.3% and 66% of them also in similar time periods ($r=0.98$).

When electrophysiological findings were compared with laboratory tests results, it was observed that out of the 6 patients who showed negative serological tests (17%), 4 had neuropathy. One of them had also signs of primary muscle involvement, other spontaneous muscle activity, and a third subject involvement of the neuromuscular transmission.

COMMENTS

As a whole, the findings in this study point out to the motor unit as one of the target structures which are damaged during the acute stage of the infection in humans. The different components of the motor unit seem to be involved almost simultaneously leading to an electrophysiological complex picture where signs of denervation coexist with signs of primary muscle involvement. The combination of both pathologies could be found in some patients, while in others the predominance of one of them was observed. This situation resembles quite closely the findings of Losavio et al.[7] and Jones et al.[5] in their mouse experimental model where, either electrophysiologically or anatomically, a similar behaviour was detected at early post-infection stages. Those authors suggested that this was due to vasculitis, and consequent ischaemic processes, which could be found at the nerve trunk and muscle levels. Despite the lack of anatomical evidence, one is tempted to attribute the human findings to a similar mechanism.

A second point to be discussed is the cause of the damage. At present it is hard to give an adequate answer. Nevertheless, it seems likely that the parasitaemia, which was present in every patient, may play a significant role.

The other feature which deserves some comment is the impairement of the neuromuscular transmission found in 12 subjects, either combined with denervation or with primary muscle involvement. Even though we cannot rule out a direct effect of the infection onto the end-plate. A more likely explanation is that a damage of the end-plate appears following the muscle harm. This would imply that, most probably, a reduced number of acetylcholine post-synaptic receptors might be the cause of this finding, at the least, in the primary muscle involvement.

The abnormalities found seem to be time-dependent, because they involved an increasing number of subjects when the time of infection was more prolonged, a feature which could mean progressive damage of the structures involved.

Despite of the electrophysiological evidences, none of the patients had clinical signs or symptoms of peripheral nerve or muscle involvement. This may be related to the amount of damage imposed by the infection which has to be mild enough as not to produce clinical manifestations.

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