Amyotrophic lateral sclerosis with sensitive findings: A multisystem disorder?

Esclerose Lateral Amiotrófica com achados sensitivos: Uma doença Multisistêmica?

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ABSTRACT

Introduction. Classical amyotrophic lateral sclerosis (ALS) is not hard to diagnose, but when it comes to atypical forms of motor neuron disease (MND) which account for about 20% in clinical setting, we may face some difficulties in differentiating clearly between atypical forms of ALS/MND and other non-ALS diseases, such as multifocal motor neuropathy, chronic inflammatory demyelinating polyneuropathy and cervical spondylosis. Association between neuropathy and ALS has been reported rarely. **Method.** We report a patient who presented with clinical/electrophysiological features and investigations suggestive of chronic neuropathy but who later progressed with anterior horn and pyramidal signs and received a final diagnosis of ALS according to the original El Escorial criteria. **Conclusion.** Our findings support the hypothesis that ALS is a multisystem neurodegenerative disorder that may occasionally include neuropathy among its non-motor features.

Keywords. Amyotrophic Lateral Sclerosis, Neuropathy, Motor Neuron Diseases.

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RESUMO

Introdução. A esclerose lateral amiotrófica (ELA) clássica não apresenta dificuldades para o correto diagnóstico, entretanto, quando se faz presente em forma atípica de doença do neurônio motor (DNM), fato consumado em 20% dos casos, gera confusão entre formas atípicas de ELA/DNM e outras patologias, tais como neuropatia motora multifocal, neuropatia desmielinizante inflamatória crônica a espondilose cervical. Associações entre neuropatias de causas várias e ELA têm sido relatadas raramente. **Método.** Relatamos o caso de um paciente que inicialmente apresentou achados clínicos/eletrofisiológicos e investigações sugestivas de neuropatia crônica, entretanto, sua condição progrediu rapidamente com sinais piramidais e de ponta anterior da medula espinhal. Recebeu, meses após, o diagnóstico de ELA de acordo com os critérios estabelecidos pelo EL Escorial. **Conclusão.** Nossos achados suportam a hipótese que a ELA é uma desordem neurodegenerativa multisistêmica que ocasionalmente inclui neuropatia entre os achados não-motores.

Unitermos. Esclerose Lateral Amiotrófica, Neuropatia, Doenças do Neurônio Motor.

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INTRODUCTION

There is striking phenotypic variation in sporadic amyotrophic lateral sclerosis (ALS)/motor neuron disease (MND), for example, flail arm syndrome (brachial amyotrophic diplegia), pseudopolyneuritic form, hemiplegic type, ALS/MND with markedly extended involvement beyond the motor system, MND with basophilic inclusion bodies, spinal progressive muscular atrophy, primary lateral sclerosis, progressive bulbar palsy and motor neuron disease with dementia[1]. These variations must be recognized when physicians are to tailor advice on disease progression, prognosis, drug therapy, and care to the needs of the individual.

Clinical trials of new therapeutic agents have been performed, on the assumption that patients with ALS/MND have the same underlying etiology, addressing the heterogeneous population of the patients under a single diagnostic category. This can be detrimental to the well-being of the individual, because clinical heterogeneity may mask drug effects in clinical trials[1,2].

The attempt to categorize subgroups based on the clinical and pathological background within the spectrum of ALS/MND may be a critical step in facilitating clinical research in ALS/MND. Definition of clinicopathologic syndromes in patients with ALS/MND is an important challenging task[1].

Neuropathic involvement is thought not to be a feature of ALS[1,3-6]. However, we have identified a patient with sporadic ALS with neuropathy for which an alternative cause could not be identified.

CASE REPORT

Man, caucasian, 74 years old, taxi driver, relates that there is approximately 1 year began to present difficulties to walk due muscular weakness in the left lower limb (Figure 1). He affirms loss of weight in this period (approximately 10 kg). Remained interned in the University Hospital Antonio Pedro for explanation diagnosis in the first semester of 2008. The neurological exam carried out in 04/11/|2008 revealed compromise of the muscular strength in both lower limbs (distal predominance). Hypopalesthesia and hypoesthesia tactile and painful had been evidenced in distal third of the limbs, predominantly in lower limbs. The reflexes, in its majority, were abolished, with the exception of the patellar (normorreflexia) (Table 1). The electroneuromyographic (ENM) finds were compatible with chronic axonal polyneuropathy. No objective answer to the immunemodulator treatment was observed in that patient that gradually progressed. He returned to the neurology service in 07/09/2008 referring worsening of the chart, mainly in the gait and achievement of instrumental and basic daily life activities. In the re-evaluation was evidenced presence of myofasciculations (lower and upper limbs), exacerbation of the amyotrophy and weakness (Table 2)[7] and presence of the Babinski sign on the right side. After redo the ENM, the finds were compatible with neuronopathy. Received the diagnosis of ALS. He initiated the treatment with Rilutek and Lithium Carbonate.

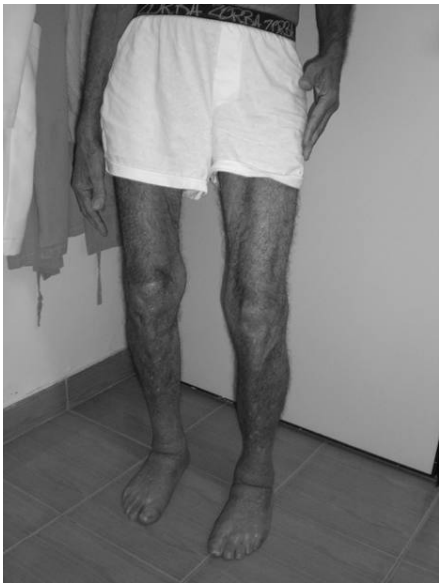

Figure 1. Amyotrophy and walk difficulties.

Table 1. Muscle strength in lower and upper limbs.

Spinal Level	Key muscle	Strenght Grade	
		L	R
C5	Biceps Brachii	(4)	(4)
C6	Extensor Carpi Radialis	(4)	(4)
C7	Triceps	(5)	(5)
C8	Fingers Flexors	(5)	(5)
T1	Dorsal And Palmar Interosseous	(4)	(4)
L2	Iliopsoas	(2)	(3)
L3	Quadriceps Femoris	(3)	(4)
L4	Tibialis Anterior	(0)	(1)
L5	Extensor Hallucis Longus	(0)	(2)
S1	Ankle Plantar Flexors	(0)	(2)

Table 2. Deep reflexes in upper and lower limbs.

Reflexes	Right	Left
Biciptal	(++)	(++)
Estiloradial	(0)	(0)
Triciptal	(++)	(++)
Finger flexor	(0)	(+)
Patellar	(++)	(++)
Achilles	(0)	(0)

* Presence of Babinsk Signal (Lower Limb – Left Side)

DISCUSSION

The association between neuropathy and ALS has been reported rarely and the line distinguishing from motor neuropathies is sometimes blurred. Among MND, the Patrikio´s pseudopolyneuritic form of ALS strictly mimics a kind of neuropathy[8]. We describe the clinical and electrophysiological features in the early stages of the pseudopolyneuritic ALS, and assess the disease progression in an isolated case. The initial symptoms were unilateral foot-drop and gait difficulties, due paresis in lower limb muscles. At the clinical evaluation, weakness of distal leg muscles was detected in our patient. The craniobulbar and hand muscle were spared.

The involvement of the upper and lower motor neurons hardly is established in initial stages of the form pseudopolyneuritic of Patrikio's, fact also identified in our study. The electromyography (EMG) showed active and chronic denervation in upper and lower limbs in the patient. Haematologic and cerebrospinal fluid examinations were normal. Brain and spinal cord showed no abnormalities. The reflexes, in its majority, were diminished. We found the presence of Babinski sign[8].

Our patient also presented sensorial involvement, mainly in distal third of the lower limbs (hypoesthesia tactile/painful and hypopalesthesia). According to Isaacs & cols 4, the sensorial compromise in ALS can generate doubts in the establishment of the diagnosis, however such possibility cannot be discarded in the combined presence of the upper and lower motor neurons signs. Innumerable authors already attempt to ALS as a multisystemic illness, with predilection of involvement of the motor system[9-11].

With the proposal to analyze the nature and the frequency of the sensory involvement in ALS, the data of 103 patients with diagnosis ALS and without co-existing illnesses were revised, between 1997-2004 in the Emory University, Atlanta. The causes of the sensory abnormalities were determinate by handbooks analysis, neurological exam and complementary exams. Sensorial symptoms were presents in 32% of the sample. It is important standing out that the amplitude of the sensorial potential action in the sural nerve was abnormal in 27% of the cases and present pathological abnormalities in 91% of the sample. The myelin fibers of higher caliber were the more compromised (73%) when compared to the small caliber (27%). Teased fiber analysis showed and increased frequency of axonal degeneration and regeneration as well as excessive myelin irregularity. Morphometry confirmed loss of large-calibre fibers[6].

The sensory nerve dysfunction in 19 patients with ALS were determined using clinical and neurophysiological tests. This assessment was repeated on 12 patients after intervals of 6–18 months. Twelve controls were also studied. The ALS group, only 2 patients had noticed mild sensory symptoms and none had sensory signs. Between successive studies the vibration thresholds increased, but not to a significant degree. ALS patients showed a significant fall in amplitude of the sensory nerve action potentials in the median, radial, and sural nerves ($P < 0.04$); sensory nerve conduction velocity did not alter. The median nerve somatosensory evoked potential N19 latency showed a highly significant increase ($P < 0.008$). Significant subclinical deterioration in sensory nerve function occurs in ALS, and parallels the progressive motor decline. The autors considered that ALS is not restricted to motor neurons[11].

A morphometric study were performed on sural nerve biopsies to evaluated the sensory nerve pathology in ALS patients and seek a correlation between the severity of peripheral nerve pathology and disease duration. Nerve biopsies from ALS individuals showed evidence of early axonal atrophy, increased remylination and a shift in the diameter distributions curve towards smaller fiber diameters. In addition, the severity of sensory nerve pathlogy in ALS patients correlated with disease duration. The peripheral nerve sodium pump concentration of patients was not reduced. The group concluded that an ingravescent dorsal root ganglion neuronopathy is seen in the incipient stages of ALS, preferentially affecting the largest neurons and resulting in turn in progressive axonal atrophy, secondary demyelination-remyelination and finally in nerve fiber degeneration. Etiologically, a parallel involvement of motor and sensory neurons suggests a more widespread metabolic disturbance in ALS than simply "sick" motor neurons[12].

CONCLUSION

ALS is a progressive degenerative disease of up-

per and lower motor neurons. Reports of the nature and frequency of sensory nerve involvement in ALS have varied. Our findings support the hypothesis that ALS is a multisystem neurodegenerative disorder that may occasionally include sensory neuropathy among its non-motor features.

REFERÊNCIAS

1.Sasaki S. Phenotypes in ALS-clinical features and pathology. Brain Nerve; 2007;59:1013-21.

2.Rajabally YA, Jacob S. Chronic inflammatory demyelinating polyneuropathy-like disorder associated with amyotrophic lateral sclerosis. Muscle Nerve; 2008;38:855-60.

3.Cappellari A, Ciammola A, Silani V. The pseudopolyneuritic form of amyotrophic lateral sclerosis (Patrikios' disease). Electromyogr Clin Neurophysiol; 2008;48:75-81.

4.Isaacs JD, Dean AF, Shaw CE, Al-Chalabi A, Mills KR, Leigh PN. Amyotrophic lateral sclerosis with sensory neuropathy: part of a multisystem disorder ? J Neurol Neurosurg Psychiatry; 2007;78:750-3.

5.Pugdahl K, Fuglsang-Frederiksen A, Johnsen B, de Carvalho M, Fawcett PR. A prospective multicentre study on sural nerve action potentials in ALS. Clin Neurophysiol; 2008;119:1106-10.

6.Hammad M, Silva A, Glass J, Sladky JT, Benatar M. Clinical, electrophysiologic, and pathologic evidence for sensory abnormalities in ALS. Neurology; 2007;69:2236-42.

7.Medical Research Council. Aids to the investigation of peripheral nerve injuries. War Memorandum (revised 2nd edition). London: HMSO, 1943, p.11-46.

8.Cappellari A, Ciammola A, Silani V. The pseudopolyneuritic form of amyotrophic lateral sclerosis (Patrikiu´s disease). Electromyogr Clin Neurophysiol; 2008;48:75-81.

9.Higashihara M, Sonoo M. Electrodiagnosis of ALS. Brain Nerve; 2007;59:1031-41.

10.Rule RR, Suhy J, Schuff N, Gelinas DF, Miller RG, Weiner MW. Reduced NAA in motor and non-motor brain regions in amyotrophic lateral sclerosis: a cross-sectional and longitudinal study. Amyotroph Lateral Scler Other Motor Neuron Disord; 2004;5:141-49.

11.Gregory R, Mills K, Donaghy M. J Neurol 1993;240:309-14.

12.Heads T, Pollock M, Robertson A, Sutherland WHF, Allpress S. Acta Neuropathologica; 1991;82:316-20.