

MOTOR NEURON DISEASES IN THE UNIVERSITY HOSPITAL OF FORTALEZA (NORTHEASTERN BRAZIL)

A CLINICO-DEMOGRAPHIC ANALYSIS OF 87 CASES

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ABSTRACT – In this retrospective (1980-1998) study, we have analyzed clinico-demographically, from the records of the University Hospital of Fortaleza (Brazil), a group of 87 patients showing signs and symptoms of motor neuron diseases (MNDs). Their diagnosis was determined clinically and laboratorially. The WFN criteria were used for amyotrophic lateral sclerosis (ALS) diagnosis. The clinico-demographic analysis of the 87 cases of MNDs showed that 4 were diagnosed as spinal muscular atrophy (SMA), 5 cases as ALS subsets: 2 as progressive bulbar paralysis (PBP), 2 as progressive muscular atrophy (PMA) and 1 as monomelic amyotrophy (MA), and 78 cases of ALS. The latter comprised 51 males and 27 females, with a mean age of 42.02 years. They were subdivided into 4 groups according to age: from 15 to 29 years (n= 17), 30 to 39 years (n= 18), 40 to 69 years (n= 39) and 70 to 78 years (n= 4). From the 78 ALS patients, 76 were of the classic sporadic form whilst only 2 were of the familial form. The analysis of the 87 patients with MNDs from the University Hospital of Fortaleza showed a predominance of ALS patients, with a high number of cases of juvenile and early onset adult sporadic ALS.

KEY WORDS: motor neuron diseases, amyotrophic lateral sclerosis, Fortaleza (Brazil).

Doenças do neurônio motor no Hospital Universitário de Fortaleza (Nordeste do Brasil): análise clínico-demográfica de 87 casos

RESUMO – Neste estudo retrospectivo (1980-1998), analisamos clínico-demograficamente, a partir dos prontuários do Hospital Universitário de Fortaleza (Brasil), um grupo de 87 pacientes que apresentavam sinais e sintomas de doenças do neurônio motor (DNMs). Eles foram diagnosticados clinicamente, e através de exames complementares. Para o diagnóstico da esclerose lateral amiotrófica (ELA), usamos os critérios da Federação Mundial de Neurologia. A análise clínico-demográfica dos 87 casos de DNMs evidenciou a existência de 4 casos de atrofia muscular espinhal (AME), 5 casos de variantes da ELA: 2 de paralisia bulbar progressiva (PBP), 2 de atrofia muscular progressiva (AMP) e 1 de amiotrofia monomélica (AM), e 78 casos de ELA. Esses últimos eram constituídos de 51 homens e 27 mulheres, com uma idade média de 42,02 anos. Eles foram subdivididos em 4 grupos etários: de 15 a 29 anos (n= 17), de 30 a 39 anos (n= 18), de 40 a 69 anos (n= 39) e de 70 a 78 anos (n= 4). Dos 78 casos de ELA, 76 eram da forma esporádica clássica, enquanto que apenas 2 da forma familiar. A análise dos 87 pacientes com DNMs do Hospital Universitário de Fortaleza mostrou predomínio de pacientes com ELA, com um número elevado de casos de ELA juvenil e da forma adulta de início precoce.

PALAVRAS-CHAVE: doenças do neurônio motor, esclerose lateral amiotrófica, Fortaleza (Brasil).

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Motor neuron diseases (MNDs) constitute a group of affective disorders centred on impairment of motor neurons. This group includes diseases such as: (1) motor neuron diseases with parietic motor manifestations (weakness, wasting, fasciculations and loss of reflex) or overactive manifestations (cramps, twitching of muscles, spasms) due to affection of the perikaryon of motor neurons and (2) motor neuron disease that involves syndromes such as amyotrophic lateral sclerosis (with upper and lower motor neuron signs) and its variants: progressive muscular atrophy (PMA) (with lower motor neuron signs only), progressive bulbar palsy (PBP) (with lower, and sometime upper, bulbar motor neuron signs) and primary lateral sclerosis (PLA) (with upper motor neuron signs only)¹.

The criteria for diagnosis of Amyotrophic Lateral Sclerosis (ALS) have been defined by the World Federation of Neurology² and have guided the clinical definition of this condition in the different studies from then on. However, a revision and new criteria (Airlie House revision) are being recently proposed³. ALS is an universal disease, which shows regional differences due to population and ecological characteristics, which have been outlined in certain epidemiological studies⁴.

The aim of the present study was to analyze clinico-demographically a small retrospective series of 87 cases of motor neuron diseases, obtained from the records of the University Hospital of Fortaleza (Northeastern Brazil).

METHOD

We analyzed, retrospectively from 1980-1998, the records of the Service of Neurology of the University Hospital of Fortaleza (Northeastern Brazil), from which 87 patients presenting symptoms and signs of motor neuron diseases were ascertained. According to these records, the following exams were performed in many of them: electromyography, nerve conduction velocity, muscle biopsy and myelography. In some patients, blood studies for cells and muscle enzymes were carried out. Due to economic restrictions, MRI (magnetic resonance imaging) of the crano-cervical region was not performed. In addition, analysis of the cerebrospinal fluid (CSF) was occasionally performed. Since most of these cases did not return to the Hospital and consequently were not followed-up, we were not able to determine prospective evolution and time of death.

Regarding ALS diagnosis, we have adhered to the criteria proposed by the WFN².

RESULTS

The retrospective analysis of the records of the University Hospital of Fortaleza (Northeastern Brazil) identified 87 cases of motor neuron disease. Of these, 4 cases were diagnosed as spinal muscular atrophy, 5 of ALS subsets: 1 as monomelic amyotrophy, 2 as progressive bulbar paralysis and 2 as progressive muscular atrophy, and 78 were diagnosed as ALS (Table 1).

From the 4 patients with spinal muscular atrophy, 3 belonged to the same family (AFL, AFL, MFL) and from the 4th patient we could not have information on familial antecedents. They were 3 males and 1 female, with a mean age of 19.2 years. Their disease had a mean evolution of 10.7 years (Table 1).

Among those with motor neuron disease, 78 had ALS and 5 were variants of it. Of these 5 ALS variants, 2 patients had progressive bulbar palsy. The latter were both females, with a mean age of 38.5 years, and a clinical evolution of 1 year at the time of the evaluation. The other 2 patients with progressive muscular atrophy, were a male and a female, with a mean age of 38.5 years and a clinical evolution of 5.5 years. The only patient with monomelic amyotrophy was a 52 years-old man, with a clinical evolution of 1 year (Table 1).

The clinical aspects of the 78 ALS cases have already been reported in a previous number of this journal⁵. The demographic analysis of the 78 ALS patients showed that 51 were male and 27 female (ratio of 1.8:1). The patients had a mean age of 42.02 years (SD: 15.51; SEM: 3-9, Range: 15-78) (Table 1), and were divided accordingly into 4 subgroups: a juvenile ALS group between 15 and 29 years (n= 17); an early onset adult ALS group between 30 and 39 years (n= 18); an age-specific ALS group between 40 and 69 years (n= 39); and a late-onset ALS group between 70 and 78 years (n= 4). From the 78 ALS patients, 76 were of the classic sporadic form with only 2 having familial members possibly affected.

The possible risk factors to which these ALS patients have been exposed included familial incidence (2/78, 2.56%) and farming activity (1/78, 1.28%).

Table 1. Motor neuron diseases in the University Hospital of Fortaleza (Northeastern Brazil) between 1980 and 1998 (n= 87).

Type	Number	%	Demographic aspects			Time of evolution (years)
			Mean of age (years)	Gender		
				Male	Female	
Amyotrophic lateral sclerosis*	78	89,6	42,02	51	27	-
Definite	36	46,1	-	-	-	-
Probable	20	25,6	-	-	-	-
Possible	15	19,2	-	-	-	-
Suspect	7	8,9	-	-	-	-
Progressive bulbar paralysis	2	2,2	38,50	-	2	1,0
Progressive muscular atrophy	2	2,2	38,50	1	1	5,5
Monomelic amyotrophy	1	1,1	52,00	1	-	1,0
Spinal muscular atrophy (type III)	4	4,5	19,20	3	1	10,7

*According to *El Escorial* WFN Diagnostic Criteria (1994)².

DISCUSSION

In this series of 87 cases of MNDs, a small group of 4 patients had spinal muscular atrophy, which represents 4.5% of the series. All cases were of the Wohlfart-Kugelberg-Welander type III form, with a protracted evolution ranging from 4 to 22 years up to the time of clinical analysis. From these 4 cases 3 were of the same family of ten children, whose parents were cousins, pointing to a possible recessive inheritance.

Regarding the other forms of motor neuron disease (MND), in our series only rare cases of progressive bulbar palsy (2.2%) and progressive muscular atrophy (2.2%) were observed, whose frequency is similar to that previously described⁶.

Among the different forms of MND, ALS is predominant⁷, and in our series, it represents 89.6% of the MND cases (Table 1). For this reason, a detailed analysis will be done only for the ALS form.

The ALS (Charcot's disease, Lou Gehrig's disease) accounts for about 0.1% of adult-deaths⁸. It has an overall incidence of 0.2-2.4/100,000 and the prevalence of the disease has been estimated at 0.8-7.3/100,000^{9,10}. The incidence and prevalence of ALS in Brazil is, however, not yet fully known.

ALS is subclassified into sporadic (95%), familial (5-10%) and Guamanian ALS-Parkinsonism-Dementia complex¹¹. Our series showed predominantly the classic sporadic ALS (89.7%) and rare cases are possibly familial (3.7%).

In terms of gender and onset-age, our sporadic ALS series revealed a predominance of males and a mean age of 42.02 years, with a range from 15 to 78 years. These results agree with those of the literature showing the predominance of male over female cases, with a respective ratio of 2.5 to 1.4^{8,10}.

The main peculiarity of this study of sporadic ALS patients resides on the age curve. In our study we have found 4 important age peaks: the classical one with patients between 40 and 70 years old^{10,12-16}; a late onset ALS group between 70 and 78 years, related to a higher mortality rate^{12,13,14,10}; and 2 young groups. These young groups are subdivided into a juvenile one with age below 29 years, and an early onset adult group, between 30 and 39 years. The sporadic juvenile ALS is extremely rare¹⁷⁻²⁰, while the familial juvenile form is more frequent^{21,22}. If a higher prevalence of it in Brazil is confirmed, this may represent an important area of study regarding its etiology. There are few cases of familial juvenile ALS in our series, exempting further comment. Furthermore, it is known that the familial juvenile form is recessive, with a linkage to chromosome 2q33-q35, and usually occurs in the

second decade of life²³. The familial ALS etiologies and mechanisms are still unknown. However, a subset ($\pm 15\%$) of familial adult autosomal ALS is associated with mutations in the cytosolic antioxidant enzyme Cu/Zn superoxide dismutase (SOD1) located in chromosome 21^{24,25}. Since some of the classical sporadic ALS may also be possibly related to SOD1 mutation²⁶, a search for this etiology should also be carried out in juvenile sporadic cases from Brazil. Moreover, other differing etiologies (slow viruses, intoxication, auto-immunity with low titers of anti-GM1 antibodies) should be looked for^{27,28}.

In conclusion, this analysis of the 87 cases of MNDs in the University Hospital of Fortaleza (Northeastern Brazil) reveals a predominance of ALS and a high percentage of young cases of sporadic juvenile and early-onset adult ALS.

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