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Evaluation of clinical, epidemiological and electrophysiological variables for early diagnosis of amyotrophic lateral sclerosis

Avaliação de variáveis clínicas, epidemiológicas e eletrofisiológicas para diagnóstico precoce da esclerose lateral amiotrófica

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ABSTRACT

Motor neuron disease (MND) is a systemic disease with a broad clinical spectrum. It is characterized by primary involvement of the lower or upper motor neuron (UMN), or both, simultaneously, represented by the most common form, amyotrophic lateral sclerosis (ALS). ALS is rapidly progressive and fatal disease that evolve to death due to respiratory failure, on average, in three to five years since the onset of symptoms. This fact attends to the early and correct diagnosis of the disease. **Objective:** To evaluate clinical, epidemiological and electrophysiological variables for the early diagnosis of ALS. **Methods:** This is an observational, descriptive and retrospective study, conducted from the collect of the database, in which the variables were submitted to statistical analysis: Mann-Whitney test and Fisher's exact test. **Results:** When correlating clinical, epidemiological and electrophysiological findings of patients with ALS and other forms of MND, the variables: age of onset of symptoms (P=0,02) hyperreflexia (P=0,001), presence of bulbar symptoms/signs (P<0,001), pathological reflexes (P=0.001), and presence of fasciculation in electromyography (P=0,001) presented statistical significance for the diagnosis of ALS. **Conclusion:** Despite the small sample size, the findings reinforce the importance of well-done neurological examination, to search for signs of involvement of the UMN, in the first evaluation of patients with suspected MND. And that more research is needed to better understand the different phenotypes of the disease in order to obtain an increasingly early diagnosis to offer improvements in the quality of life of these patients.

Key-words: Motor neuron diseases. Amyotrophic lateral sclerosis. Neuromuscular disease.

RESUMO

A doença do neurônio motor (DNM) é uma doença sistêmica com amplo espectro clínico. É caracterizada pelo envolvimento primário do neurônio motor inferior ou superior (NMS), ou ambos, simultaneamente, representados pela forma mais comum de esclerose lateral amiotrófica (ELA). A ELA é uma doença rapidamente progressiva e fatal que evolui para óbito devido à insuficiência respiratória, em média, em três a cinco anos desde o início dos sintomas. Esse fato atenta ao diagnóstico precoce e correto da doença. **Objetivo:** Avaliar variáveis clínicas, epidemiológicas e eletrofisiológicas para o diagnóstico precoce de ELA. **Métodos:** Estudo observacional, descritivo e retrospectivo, realizado a partir da coleta do banco de dados, no qual as variáveis foram submetidas a análises estatísticas: teste de Mann-Whitney e teste exato de Fisher. **Resultados:** Ao correlacionar achados clínicos, epidemiológicos e eletrofisiológicos de pacientes com ELA e outras formas de DNM, as variáveis: idade de início dos sintomas (P=0,02) hiperreflexia (P=0,001), presença de sintomas/sinais bulbares (P<0,001), reflexos patológicos (P=0,001) e presença de fasciculação na eletromiografia (P=0,001) apresentaram significância estatística para o diagnóstico de ELA. **Conclusão:** Apesar do pequeno tamanho da amostra, os achados reforçam a importância do exame neurológico bem feito, na busca de sinais de envolvimento da NMS, na primeira avaliação de pacientes com suspeita de DMN. E que são necessárias mais pesquisas para melhor entendimento dos diferentes fenótipos da doença, a fim de obter um diagnóstico cada vez mais precoce para oferecer melhorias na qualidade de vida desses pacientes.

Palavras-chave: Doença do neurônio motor. Esclerose lateral amiotrófica. Doenças neuromusculares.

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INTRODUCTION

Motor neuron disease (MND) is a broad clinical spectrum motor neuronopathy that can affect the upper motor neuron (UMN) and/or the lower motor neuron (LMN).[1]

UMN Injuries cause symptoms such as paresis, spasticity, hyperreflexia and/or presence of pathological reflexes.[2] LMN injuries, on the other hand, cause paresis, atrophy, hyporeflexia or areflexia, cramps and fasciculations.[2]

The various forms of MND can develop such symptoms in different segments alone or simultaneously (bulbar, cervical, thoracic, lumbosacral), and has its own peculiarities with distinct evolutions.[1]

Amyotrophic lateral sclerosis (ALS) is the most common sporadic form of MND, presenting with signs of UMN and LMN.[2] It is rapidly progressive, and commonly progresses to quadriplegia and death due to respiratory failure, in three to five years, on average, since the onset of symptoms, which attends to the early and correct diagnosis of the disease.[3-8] The annual incidence of the disease is 1-3 /100,000, and the prevalence is 3-5/100,000, with greater involvement in the sixth decade of life and a slight predominance in males (1.5 to 1).[6,9]

Our study aims to evaluate variables for the diagnosis of ALS in first consultation, and to describe the clinical, epidemiological and neurophysiological characteristics of a reference center for neuromuscular diseases inBrazil.

METHODOLOGY

This is an observational, descriptive and retrospective cross-sectional study of patients with MND cared for at outpatient clinic of neuromuscular disease of the Neurology service of the Antônio Pedro University Hospital, from 2013 to2018.

Screening was performed in the database. The inclusion criterion used was the confirmed diagnosis of MND, and presence of data from the first consultation, regardless of gender or age. Were excluded those who presented another diagnosis, as well as patients with data loss, because they did not present supporting documents or data from the first consultation.

First consultation data were analyzed through medical chart review. Epidemiological, clinical and neurophysiological variables were collected, such as: gender, initial age of symptoms, presence of family history, smoking and alcoholism, time from symptoms to first evaluation, initial segment affected, presence of bulbar symptoms, and physical examination data, such as: change in strength, presence of hyperreflexia, hyporeflexia or areflexia, pathological reflexes, fasciculations, altered sensitivity and muscle tropism. In electroneuromyography (ENMG), data were analyzed as: reduction of compound muscle action potential (CMAP), presence of membrane instability (fibrillations and positive waves), fasciculation potential, neurogenic pattern (motor unit action potential (MUAP) with increased amplitude and duration, and polyphasic potentials with incomplete recruitment) and presence of giant potentials (> 10mV).[9]

After collection, the data were subjected to statistical analysis using the SPSS 20.0 computer programs, and the patients were subdivided into two groups: ALS and non-ALS, and again subjected to statistical analyzes of the Mann-Whitney test and Fisher's exact test.

Clinical, epidemiological and electrophysiological data were then correlated between these groups to verify if there are statistical significance for the diagnosis of ALS in the first consultation. The sensitivity, specificity, positive (PPV) and negative (NPV) predictive values for these findings were also verified.

RESULTS

Description of the general population study

We analyzed database with all (435) patients admitted from the ambulatory of neuromuscular disorders, between 2013 and 2018, 23 patients remained in the study for presented inclusion criteria (Figure 1).

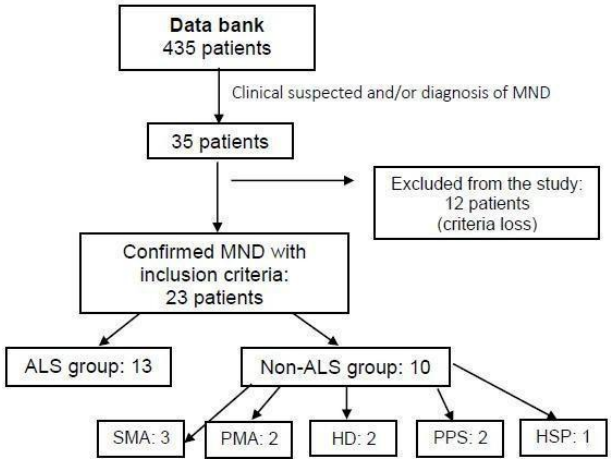

Figure 1: Patient screening flowchart.
Notes: ALS Amyotrophic lateral sclerosis, HD Hirayama disease, HSP Hereditary spastic paraplegia, MND Motor neuron disease, PMA Progressive muscle atrophy, PPS Post-polio syndrome, SMA Spinal muscular atrophy

Of the 23 cases of MND, 13 were diagnosed with ALS (56.5%), and ten were non-ALS (43.5%). The diagnosis of the diseases had already been made by a neuromuscular specialist before the study. Of the general sample, 18 were males (78.3%) and five females (21.7%). The age at onset of symptoms in the study population ranged from five to 77 years, with a mean of 40.91 ± 18.94 years (Table1).

Of all cases, ten (43.5%) had isolated involvement of LMN, one (4.3%) of UMN, and 12 (52.2%) simultaneous involvement of both motor neurons, in first consultation.

Table 1: Relevant epidemiological, clinical, and electrophysiological findings in the studied population, in first evaluation

Pt	Diag-nosis	Sex	Age begin spt	Bulbar spt	Hyper-reflexia	Patholo gical reflexes	Fasciculation ENMG
01	ALS	M	77	+	-	-	+
02	ALS	M	42	+	+	+	+
03	ALS	M	44	-	+	+	+
04	ALS	M	42	+	+	+	+
05	ALS	M	64	-	+	+	+
06	ALS	F	50	+	+	+	+
07	ALS	F	37	-	+	+	+
08	ALS	M	47	+	+	-	+
09	ALS	M	38	+	-	+	+
10	ALS	M	69	+	+	+	+
11	ALS	M	54	+	+	+	+
12	ALS	M	42	+	+	+	+
13	ALS	M	43	+	+	+	+
14	SMA	F	5	-	-	-	-
15	SMA	M	5	-	-	-	-
16	SMA	M	6	-	-	-	-
17	PMA	M	49	-	-	-	-
18	PMA	M	36	-	-	-	-
19	HD	M	57	-	-	-	-
20	HD	F	25	-	-	-	-
21	PPS	F	54	-	-	-	+
22	PPS	M	29	-	-	-	-
23	HSP	M	26	-	+	+	-

Notes: ALS Amyotrophic lateral sclerosis, ENMG Electroneuromyography, HD Hirayama disease, HSP Hereditary spastic paraplegia, PMA Progressive muscle atrophy, PPS Post-polio syndrome, SMA Spinal muscular atrophy

Description of ALS group

ALS diagnosis had been previously performed based on Awaji-Shima Criteria. All patients already presented as definitive ALS at the last visit. Of the 13 cases diagnosed as ALS, 11 were male (84.6%) and two female (15.4%). The average age of onset of symptoms was 49.92years.

Of the ALS cases, three (23.1%) had bulbar onset, five (38.5%) in the cervical region and five (38.5%) in the lumbosacral region. Ten (76.9%) patients had bulbar symptoms until the first consultation. Of the ten patients who complained of bulbar symptoms at the first evaluation, four (30.8%) had only dysarthria, three (23.1%), dysphagia associated dysarthria, two (15.4%) dyspnea associated dysarthria, and one (7.7%) patient presented dysphagia with dyspnea.

Eight (61.5%) patients reported other symptoms. Although rare, the most common were urinary symptoms (15.4%), cramps (38.5%) and emotional lability (23.1%).

Six (46.2%) patients reported previous smoking, and nine (69.2%) alcoholism. All denied family history to ALS. On physical examination, all ALS patients (100%) had appendicular paresis, with preferential distribution in the following segments: three (23.1%) in the upper limbs, three (23.1%) in the lower limbs, and seven (53. 8%) in the four segments. Deep reflexes were abolished in one (7.7%) case, hyperreflexia in nine (69.2%), and association of abolished and/or hyporeflexia with hyperreflexia in two cases (15.4%). The patient who had an abolished reflex had pathological reflexes. One (7.7%) patient had normal reflexes. Of the 13 patients, 11 (84.6%) presented pathological reflexes, in which the most evident were: Babinsk (38.5%), Hoffman (30.8%) and pectoral (38.5%). Less frequently, clonus, Mayer signs, Tromner signs, palmomental, orbicularis oris and adductors reflexes were found. Seven (53.8%) patients had two or more pathological reflexes. UMN findings were evidenced in the segments as described (Table 2).

Ten (76.9%) patients had fasciculations on physical examination. The superior segments were preferentially affected, presenting this pattern in all these patients. Two (11.1%) patients presented alteration in the physical examination to the thermoalgesic sensitivity test. Muscle atrophy was seen in eight patients (61.5%), with a preferential pattern by the upper limbs, in which three (23.1%) presented distal predominance, four (30.8%) proximal and one (7.7%) was affected throughout the segment.

In the ENMG, ten (76.9%) patients had altered CMAP with amplitude reduction in at least one nerve. Ten (76.9%) had fibrillation and/or positive waves in one or more segments. Fasciculation potential was seen in at least one segment evaluated of all cases (100%). All patients (100%) presented neurogenic MUAP in two or more segments (Table 2). Six (46.2%) patients had giant potentials.

After analysis of the clinical and electrophysiological findings, the patients were submitted to Awaji-Shima

criteria for ALS classification, based on the data from the first consultation (Table 2).

Description of non-ALS group

Ten (43.5%) patients formed the non-ALS group for presenting the following diagnoses: spinal muscular atrophy (SMA), progressive muscle atrophy (PMA), Hirayama disease (HD), post-polio syndrome (PPS) and hereditary spastic paraplegia (HSP) (Figure 1). Of the ten non-ALS patients, three (30.0%) were female and seven (70%) male.

The average age of onset of symptoms in this group was 29.20 years.

Eight (80.0%) patients had onset of symptoms in the lumbosacral region and two (20.0%) in the cervical region. None presented with bulbar complaints. Only two (20.0%) patients complained of other symptoms such as fatigue (PPS) or deafness (HSP).

One (10.0%) patient reported smoking, and one (10.0%) family history of MND (PMA). All denied alcoholism.

Five (50.0%) patients presented weakness in the four segments, two (20.0%) presented preferentially in the upper limbs and three (30.0%) in the lower limbs. It was evidenced that one (10.0%) presented deep reflex abolished, four (40.0%) hyporeflexia, one (10.0%) hyperreflexia (HSP), and three (30.0%) presented abolished reflex associated with hyporeflexia in another segment. One (10.0%) patient had pathological reflex (Babinsk) (HSP) (Table 1).

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Three (30.0%) presented fasciculations at physical examination (PMA, HD and PPS). Fasciculations were more evident in the upper limbs and/or trunk. Four (40.0%) patients had upper and/or lower limb muscle atrophy.

In the ENMG, six (60.0%) patients had CMAP with amplitude reduction in at least one nerve and six (60.0%), had fibrillation and/or positive waves in at least one segment. One (10.0%) patient had fasciculation potential in ENMG (PPS). Of all patients in this group, eight (80.0%) had neurogenic MUAP, with giant potentials in seven (70.0%) patients.

Correlation between ALS and non- ALS group

By correlating clinical, epidemiological and electrophysiological data between the ALS and non-ALS subgroups, it was found that the variables: age at onset of symptoms, bulbar symptoms, presence of hyperreflexia, pathological reflexes and presence of fasciculation potential, were statistically significant in our study ($P < 0.05$) (Tables 3 and 4).

Table 2: Clinical and electrophysiological findings of ALS patients in first consultation

Patient	UMN 3 segments	UMN 2 segments (one rostral)	UMN 2 segments	Bulbar symptom	Fibrilation and/or Positive wave in ENMG	Fasciculation potential in ENMG	Chronic denervation in ENMG	Awaji-Shima Criteria
01	-	-	-	dysarthria dysphagia	-	3 segments	3 segments	Does not fill
02	+	-	-	dysarthria dysphagia	3 segments	2 segments	3 segments	Definite
03	+	-	-	-	3 segments	3 segments	3 segments	Definite
04	-	-	+	dysarthria flaccid / dyspnea	2 spine segments	2 spine segments	2 spine segments	Possible
05	+	-	-	-	3 segments	1 segment	3 segments	Definite
06	-	-	+	dysphagia dyspnea	1 segment	1 segments	3 segments	Possible
07	+	-	-	-	-	1 spine segment	2 spine segments	Definite *
08	-	-	+	dysarthria flaccid	2 spine segments	2 spine segments	2 spine segments	Possible
09	-	+	-	dysarthria dyspnea	2 spine segments	2 spine segments	2 spine segments	Probable
10	+	-	-	dysarthria spastic / Dysphagia	3 segments	2 segments	3 segments	Definite
11	+	-	-	dysarthria	2 segments	3 segments	3 segments	Definite
12	+	-	-	dysarthria spastic / Dysphagia	-	3 segments	3 segments	Definite
13	-	-	+	dysarthria flaccid	3 segments	2 segments	3 segments	Possible

Table 3: p-value of age of beginning of symptoms of ALS diagnosis in the sample studied

MANN-WHITNEY Test					
Variable	Non-ALS		ALS		
	Average	Median	Average	Median	value
Age of beginning of symptoms	**29,2**	27,5	**49,9**	44,0	**0,02**

this data was not statistically significant, since the non-ALS group also showed a higher prevalence in males (70%), a fact that occurs in several MND, such as PMA, progressive bulbar palsy, spinal and bulbar muscular atrophy, HD, brachial amyotrophic diplegia and leg amyotrophic diplegia.[11,15]

Table 4: p-value, sensitivity, specificity, positive and negative predictive value of variables statistically significant for diagnosis of ALS in the sample studied.

Variables / Categories		Non-ALS		ALS		p-value	Sensitivity	Specivity	PPV	NPV
		N	N%	N	N%					
Bulbar symptom	No	10	100,0%	3	30,0%	**<0,001**	**76,9%**	**100,0%**	**100,0%**	**76,9%**
	Yes	0	0,0%	10	100,0%					
Hyperreflexia	No	9	90,0%	2	15,4%	**0,001**	**84,6%**	**90,0%**	**91,6%**	**81,8%**
	Yes	1	10,0%	11	84,6%					
Pathological reflexes	No	9	90,0%	2	15,4%	**0,001**	**84,6%**	**90,0%**	**91,6%**	**81,8%**
	Yes	1	10,0%	11	84,6%					
Fasciculation potential in ENMG	No	6	90,0%	0	0,0%	**<0,001**	**100%**	**85,7%**	**92,8%**	**100,0%**
	Yes	1	10,0%	13	100,0%					

DISCUSSION

The heterogeneity of MND associated with unfavorable prognosis of some types it even harder to task of an early diagnosis, what bothered us the need for more accurate physical examination and evaluation to distinguish the forms of MND.[9]

In order to have a clinical suspicion of MND, there must be an objective complaint of weakness, in the absence of complaint or sensory symptoms, as was the case in all patients evaluated in our study.[4,10,11] Two (8.7%) cases, diagnosed as ALS, had alteration in thermoalgesic sensitivity during the physical examination, but this isolated fact did not exclude the initial diagnostic suspicion. Harms *et al*. (2013) reported in their study that sensory changes such as these have already been described due to changes in the dorsal root ganglion.[2]

The prevalence of ALS in our study (2.98% of cases in the database) was high because it was a study conducted at a neuromuscular disease center. Higher prevalence was found in males (84.6%), as in the reviewed studies, including studies in a Brazilian cohort as reported by Linden Junior *et al.* (2013) and Prado *et al.* (2016).[1,9,10,12,13] Palermo *et al*. (2009) reported in their literature review that male prevalence is seen in studies worldwide.[14] However,

The mean age at onset of symptoms in the ALS group was 49.94, compared to 29.20 in the non-ALS group, and was statistically significant for the ALS diagnosis (P=0.02). In the literature, the mean age at onset of symptoms in this population ranged from 50 to 70 years, and it has been reported that other forms of MND commonly have a younger age at onset.[1,9,15-17] However, the Brazilian literature reports that the average age of onset of symptoms in ALS is lower than studies in Europe and Asia.[14] Palermo *et al*. (2009) reported that the age at onset of symptoms was 52 years, while in the Prado *et al.* (2016) cohort was 54.9 and Silva *et al.* (2018) 51 years, on average.[13,14,18]

All patients diagnosed with non-ALS had signs/symptoms of LMN or UMN alone.

When there is clinical suspicion of MND, to have hypothesis of ALS, physical examination often requires asymmetric paresis associated with signs of LMN and UMN involvement.[1,5,9,19] Recognition of UMN involvement, as well as LMN, as pathogenesis of ALS, was initially described by Charcot in 1869.[19]

Of the 13 patients diagnosed with ALS, 12 had signs of UMN since the first evaluation, evidenced by hyperreflexia and/or pathological signs in two or more segments. The presence of hyperreflexia and/or pathological reflexes presented in our study a significant predictive value for ALS (P=0.001), with specificity of 90% and PPV of 91.6%, which corroborates to more accurate diagnosis of definitive ALS based on El Escorial, Airlie House and Awaji-Shima criteria, all of which include the findings of UMN associated with LMN.[1,19,20] The presence of signs/symptoms of UMN in all these criteria for definitive, probable and possible, diagnosis

associated with the findings of our study proved the importance of these clinical signs.[1,9,20,21]

Alvarez *et al.* (2018) reported in their study that all ALS patients show signs of UMN at some point in the disease, but in their initial assessment, 26.1% of patients did not show any signs.[22] Signs of hyperreflexia (69.2%) and Babinski (49.2%) were the most frequent in their population, and were present in 11 (84.6%) and 5 (38.5%) patients, respectively, in our study.[19] Werneck *et al*. (2017) in a study in southern Brazil, showed that hyperactive deep tendon reflexes happened in 65.7% of cases, while Babinski's sign was present in 32.6%, data similar to ours.[23]

Due to the presence of subclinical signs of UMN at the first visit, studies emphasize the importance of imaging studies of the pyramidal pathway, but so far, physical examination is still irreplaceable for this evaluation.[22,24,25]

We had in our sample a patient (patient 1 – table 1) who at the first consultation had no clinical signs of UMN, but during the course of the condition, and after two months of reevaluation, signs of UMN appeared. This corroborates the diagnostic difficulty of physicians and generalist neurologists at the first visit, because in early stages there may be no clinical UMN presentation to confirm the diagnosis.[26]

Statland *et al.* (2015) reported that data such as weakness characteristics (symmetry, asymmetry, axial, proximal, distal), presence of sensory symptoms, and signs of UMN involvement, for example, helped to distinguish ALS and other forms of MND, from disease that potentially simulated these.[1] By showing the involvement of the UMN without sensory signs, they showed that ALS, primary lateral sclerosis (PLS) and HSP were the main suspects.[1] The clinical findings of these entities commonly distinguish them.[1]

The PLS for presenting preferentially asymmetrical involvement of the upper

limbs and bulbar region, with predominance in advanced age, represents the main differential diagnosis of ALS among these entities.[1] Yedavalli *et al.* (2018) demonstrated in their study that it is possible to differentiate clinically and with imaging studies such as positron emission tomography and ENMG, PLS from ALS.[24]

Statland *et al.* (2015) reported that symmetrical axial weakness with bulbar symptoms and signs of UMN were very suggestive of ALS.[1] Yunusona *et al.* (2010) stated that bulbar involvement is an important feature of ALS, and has been reported for years.[27] Although, on average, only 30% of ALS patients start with bulbar symptoms such as dysphagia, dysarthria and dyspnea, the vast majority will progress especially towards dysarthria.[27] This data was similarly visualized in our study, in which three (23.1%) patients had onset of symptoms in the bulbar region, and ten (76.1%) reported bulbar symptoms at some point. Our findings were similar to the study of Prado *et al.* (2016) that reported that 70.5% of the cases started in the spinal segments, and 9.8% in the bulbarregion.[13]

These findings showed that bulbar symptoms, regardless of being the first findings of the disease, has statistical significance (P<0.001) for ALS diagnosis, and presented 100% specificity and PPV in oursample.

As reported in the literature, the difficulty of the criteria includes patients with subclinical involvement of UMN and/or LMN.[20,26] Subclinical involvement of LMN was resolved by including neurophysiological findings as equivalent to clinical findings of this neuron in the Awaji-Shima criteria.[25,26] Finding denervation and reinnervation in at least three segments is necessary for definitive diagnosis of ALS in the absence of clinical signs.[25,28] Fasciculation potential was added to the Awaji-Shima criteria as a sign of active denervation, even in the absence of fibrillation potentials or positive wave.[9,28] Tao *et al.* (2017) reported that this criteria significantly improved diagnostic sensitivity, although it is not specific and may be absent in some ALS patients.[21]

In our study, fasciculation potential was evident in all patients in the ALS group, and only 1 (10%) in the non-ALS group, showing statistical relevance for diagnosing ALS (P=<0.001) with sensitivity and NPV of 100%. These data show the importance of fasciculation potential for the diagnosis of ALS.[9]

Almost half (46.2%) of patients in the ALS group reported smoking. Although more frequent in this group than in non-ALS, this data had no statistical relevance (P=0.99). However, smoking has been described as a risk factor in other previous studies, as by Csobonyeiova *et al.* (2017).[29] Although alcoholism was frequent in our patients (69.2%), we did not find this data as a risk factor in our literature review, and did not show relevance in our study (P=0.133). All patients denied family history for ALS, which states the highest frequency of sporadic ALS in the general population, described in the literature in 90-95%, and in our group presented 100% of cases.[30-33]

Our study had limitations because it was a retrospective study, obtaining bias for collecting information in the database, such as data loss, which resulted in a reduction in the sample size. This fact also justifies the absence of other variants of the MND, and limits a better evaluation of the sample, since these diseases may progress and the diagnosis may change over time.

However, we observed that there were statistically significant findings for the diagnosis of ALS.

CONCLUSIONS

The findings of our study suggested that in the first evaluation of patients with suspected MND (motor symptoms without sensory complaints), the variables: age at onset of symptoms (P=0.02), presence of bulbar symptoms (P<0.001), hyperreflexia (P=0.001), pathological reflexes (P=0.001) and fasciculation potential (P<0.001) are statistically significant for the early diagnosis of ALS.

In the clinical history, the presence of bulbar symptoms presented specificity and PPV of 100%, and sensitivity and NPV of 76.9%.

On physical examination, the presence of signs of UMN involvement, such as hyperreflexia and pathological reflexes, also presented specificity values of 90%, sensitivity of 84.6%, PPV of 91.6% and NPV of 81.8%, and were fundamental for the diagnosis ofALS.

In ENMG, the fasciculation potential presented sensitivity of 100%, specificity of 85.7%, PPV of 92.8% and NPV of 100%.

Although certain variables presented high sensitivity and specificity, the small sample of our study limited the accuracy of the data.

We conclude that, despite the small sample size, the findings reveal the importance of a well-done neurological examination directed to the tireless search for signs of involvement of the first motor neuron in this group of patients.

More research is needed to better understand the different phenotypes of the disease in order to obtain an increasingly early diagnosis to offer improvements in the quality of life of these patients.

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