Acta Scientific MEDICAL SCIENCES (ISSN: 2582-0931)

Volume 5 Issue 4 April 2021

Research Article

Clinical Profile and Management of Patient with Amyotrophic Lateral Sclerosis in Neurology Unit Antananarivo Madagascar

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Received: February 12, 2021

Published: March 11, 2021

Abstract

Amyotrophic lateral sclerosis (ALS) is a rare and fatal disease. In Madagascar, we don't have more epidemiological data about ALS and no recent publication about its management in our country. The aims of this study were to describe clinical profile and management of patients with ALS in Neurology unit in Antananarivo Madagascar. An observational descriptive study was conduct from January 1st, 2013 to December 31th, 2019 in the department of Neurology at Antananarivo. The study included: incident cases of patients according to the revised El Escorial diagnosis criteria with certain and probable ALS cases or clinically probable ALS and the electroneuromyography findings if patients can afford it abroad Madagascar. Patients were followed by neurologist each one, two or three months after diagnosis. We describe here all health practitioner available in our settings during the management process. Twenty-five patients were retained (0.49%) and one patient was excluded. The majority of ALS begin in the age of 25-70 years-old, it was usual form. Male was more frequent (sex-ratio: 1,27). Disease started with spinal form in 88%. During the diagnosis, spinal and bulbar involvement were frequent in 72%. One familial history was noted. The median ALS FRS-R was 33. Five patients (20%) can buy and take riluzole. Ten patients (40%) were died, 3 patients (12%) were living and twelve patients (48%) were lost for follow-up. Our university hospital includes a respiratory medicine unit for the functional respiratory investigation but cannot assume the ambulatory noninvasive ventilation. Physiotherapist, occupational therapist, nurses and psychologist with neurologists are among the staff for at home management until the illness end course if the patient family car afford it. The clinical profile and outcomes of patients in this study is similar to the literature despite the difficulty faced by patients and neurologists in the country and health practitioner due to the cost and unavailability of many facilities or investigations tools.

Keywords: Amyotrophic Lateral Sclerosis; Clinical Profile; Revised El Escorial Criteria; Madagascar; Management

Introduction

Amyotrophic lateral sclerosis (ALS) is a fatal motor neuron disease characterized by degenerative changes to upper and lower motor neurons [1-3]. Patients experience signs and symptoms of progressive muscle atrophy and weakness, increased fatigue and problems with swallowing, which typically lead to respiratory failure and death [1,2]. It is relatively rare [3]. The meaning survival time is around 20 months after diagnosis [1]. The rate of mortality is variable depending the country [1]. ALS exists all over the world [4], but it is an heterogeneous disease with overlapping phenotypes [5]. To support patient till the end course of the disease, many health practitioner work together. In Madagascar, we have a rare data for ALS. In this study, the aims were to describe clinical profile and management of patients with ALS in the department of neurology at the University hospital in Antananarivo.

Methods

A descriptive observational study was conducted in the department of Neurology in University Hospital Joseph Raseta Befelatanana (HU-JRB) from January, 1st 2013 to December, 31th 2019. The study included incident case of ALS during hospitalization or consultation in department of Neurology. Revised El Escorial (EER) criteria is the standard tools used for diagnosis [6]. The department don't have yet electroneuromyography device (ENMG). The study included then patients with clinically definite ALS or clinically probable ALS with EER criteria, patients with clinically probable ALS and ENMG findings if they can go abroad by their means. All other diagnosis was eliminated. The diagnosis of ALS was done by neurologist for outpatient and by senior neurologist (professor of neurology or assistant professor of neurology) for inpatient. A large ancillary investigation was asked to eliminate other diagnostic: central nervous system lesion was eliminated when cerebral and spinal cord imaging were normal. Peripheral nervous system lesion was eliminated when biological tests were normal (hemogram, CRP, VSH, creatininemia, ionogramme, CPK, LDH, protein electrophoresis, HIV-TPHA/VDRL-hepatitis A, B, C serology, exam of cerebro-spinal fluid). All patients were followed up after diagnosis made, each one, two or three months according to their disease's evolution and their schedules. The study excluded patients with insufficient clinical database. We made a checklist of all medical and allied health practitioner involved in the management of ALS patients available in our settings.

Revised El Escorial criteria of ALS or Airlie House criteria 1998 include [1,6,7]: clinically definite ALS with upper and lower motor neuron signs in bulbar and at least two spinal (lumbosacral, thoracic, or cervical) regions or upper and lower motor neuron signs in three spinal regions. Clinically probable ALS with upper and lower motor neuron signs in at least two regions (bulbar or spinal) with some upper motor neuron signs rostral to the lower motor neuron signs. Clinically probable ALS-laboratory supported with Clinical evidence of upper and lower motor neuron signs in one body region or of upper motor neuron signs in one region and EMG findings of lower motor neuron involvement in at least two body regions.

Parameters studied were: socio-demographical characteristics with age of onset and sex, clinical characteristics with onset sign, date of onset, type of onset (spinal or bulbar), date of diagnostic, clinical form on diagnosis (bulbar, spinal, or bulbar and spinal), scale of Amyotrophic Lateral Sclerosis Functional Rating Scale – Revised or ALS FRS-R, diagnostic delay, associated sign, familial case, treatment received after diagnosis made and during follow-up, time of follow-up, evolution of patient in the end of study (death, living, unknown).

ALS FRS-R is an instrument to evaluate assessing activities of daily living in patients with ALS. It allows to stratify severity of amyotrophic lateral sclerosis (ALS), including respiratory function [8]. It is based on 12 items: speech, salivation, swallowing, handwriting, cutting food, dressing and hygiene, turning in bed, walking, climbing stairs, dyspnea, orthopnea, respiratory insufficiency. Each question is rated on a 0-4-point scale (0 indicates absence of function or severe impairment and 4 indicates normal function). The maximum score of ALS FRS-R is 48.

The variables were collected in the medical data of patient in the department. The data was writing and analyzing in Excel 2013. Results were representing by absolute number, percent, or mean.

Results

Twenty-five patients (0.49%) were finally included during the study and one patient was excluded from 5032 patients (2932 females and 2197 males). Sixteen patients (64%) were clinically definite ALS and nine patients (36%) were clinically probable ALS. Two patients (8%) were realized an ENMG that found sign of lower motor neuron involvement in at least two body regions.

Age of onset was 47 years between 13 and 76 years. Usual form of ALS (age of onset age is between 25 to 70 years) was frequent (n=20 either 80%). Juvenile form of ALS (age of onset is less than 25 years) was rare (n = 3 either 12%). The study found a predominantly male (n = 14 either 56%) with sex-ratio to 1.27. (Table 1).

The principal sign of onset was represented by spinal sign in 22 patients (88%) like weakness of one or more limbs. During the diagnosis of ALS, spinal and bulbar associated form was predominantly in 18 patients (72%). Delay mean of diagnosis was 25.5 months after onset sign between 2 and 147 months. For associated sign, one patient had a cognitive trouble with memory, language and attention impairment; one patient had attitude tremor of unilateral upper limb; one patient had a cutaneous abnormal with diffuse erythema. ALS-FRS R average during the diagnosis was 33 and

majority of patient (72%) had ALS FRS-R less than 38. The study found one familial case (4%). Five patients (25%) can buy and take treatment by riluzole. Three patients (12%) were need a non-invasive ventilation or NIV (Table 1).

Time of follow-up average was 22 months between 1 to 72 months. After the diagnosis, ten patients (40%) were died, three patients (12%) were living and outcomes of twelve patients (48%) were unknown. The principal cause of death was respiratory failure.

As medical and allied health practitioner in our University hospital in Antananarivo, working together with neurologists for the management of ALS patients, we identified: pneumologists assessing the respiratory function at the diagnosis time but noninvasive ventilation at the end stage is not available; psychiatrists and psychologists support psychological effects during the evolution of the disease: occupational therapists work only at the hospital but cannot go on bedside at patients home; physiotherapist and nurses are general practioners but assume all activities for bedridden patients at their home with neurologists recommendations for respiratory management and nursing; nutritionist are scarce; gastroenterologist surgeon have skills to perform gastrostomy but no device available and no patients yet undergo gastrostomy at time.

Discussion

This study was among rare study of ALS realized in Madagascar. The department of Neurology HU-JRB in Antananarivo was the only structure that can diagnose and take care ALS patients. This department don't have yet ENMG, and use EER criteria for diagnosis of ALS even if the new criteria using ENMG was recommended: Awaji criteria [9]. This is a monocentric study and it can be a selection bias. In fact, the number of patients can be underestimated (25 patients for 5032). Two reasons can explain this fact. Firstly, the access difficulty for patients to reach specialized facilities in the country due to financial weakness or culture barrier or distance limitation. Secondly, the difficulty to diagnose ALS at the beginning of the disease. The diagnosis was just based on clinical sign which must be complete to confirm the diagnosis of ALS. The diagnosis of bulbar form in the beginning is more difficult without ENMG because ENMG plays an important role in the early diagnosis of bulbar-onset ALS based on Awaji's diagnostic criteria [10].

Variables			n	%
Form about age	Juvenile < 25 years		3	12
	Usual 25-70 years		20	80
	Late > 70 years		2	8
Form about sign	Onset	Spinal	22	88
		Bulbar	3	12
	During diagnosis	Spinal	7	28
		Bulbar	0	0
		Bulbo-spinal	18	72
Associated signs	Cognitive trouble		1	4
	Attitude tremor		1	4
	Cutaneous abnormal		1	4
	Absent		23	88
Diagnostic delay	< 1 year		12	48
	1 year – 2 years		6	24
	> 2 years		7	28
ALSFRS-R	≥ 38		7	28
	< 38		18	72
Treatment	Riluzole	Yes	5	25
		No	20	75
	NIV	Yes	3	12
		No	22	88
	Intubation	Yes	0	0
		No	25	100

Table 1: Clinical characteristics of patients with ALS.

According to the age of onset of ALS, this study found an average age of 47 years. TROPALS study in North, South and west Africa between 2005-2017 confirmed the young age of African patients with ALS around 53 years old [11]. In Pacific Asian and United States, age of onset was higher between 58 to 61 years, but this age was a part of usual form of ALS [6,12]. In the other hand, in Europe, the age of diagnosis was late around 71 years old and this was a part of tardive form of ALS [13]. In fact, the age of installation of disease varies according to the demographic characteristics, geographical origins and ethnicity of population. In Madagascar, the population is mostly young people, less than 20 years old for 53,8% of the population in 2018 [14]. This fact is one of reason of the young

age of onset in our study but juvenile ALS is a rare form. ALS can be underdiagnosed for old people with comorbidity, because the course of the disease can be faster and patients died before definite diagnostic of ALS.

Male patients were more frequent in this study with 1,27 of sex-ratio. A meta-analysis, about incidence of ALS in the world (45 geographical areas and 11 sub-country) between 1952-2011, found 1,41 of sex-ratio [15]. The hypothesis was that: women were less exposed by intensive physical activities, chemical products to the profession, and other environmental risk factors [13,16]. It also appears that estrogen is a neuroprotective factor in women [17].

In this study, the form of disease was a classical form of progression of ALS. ALS begins by spinal form (88%) with weakness of one or more limbs and extension progressively to bulbar form. At the time of diagnosis, patients presented bulbar and spinal signs. Some studies found a predominance of spinal form at the onset of disease: 77, 3% in Africa by TROPALS; 65,5% in Europa in the French registry of ALS in Limousin [11, 13]). Spinal form can manifest by weakness of upper or lower limb as in our study. but also, by hemiplegia or pseudo polyneuropathy [18]. ALS can be associated with another diseases: fronto-temporal dementia (FDT), Gougerot-Sjögren syndrom, or parkinson disease [19-21]. Association to ALS/FDT was more frequent. More than 100 genes are known to contribute to ALS/FTD [22]. In the recent research, the presence of pathological tau processing was been demonstrated [23]. In our study, one case of cognitive impairment was found but the diagnosis of fronto-temporal dementia was not established.

The median scale of ALS FRS-R in this study was 33. It was the same in the study by Marin B and al in the French register in Limousin [13]. In the TROPALS study in Africa, the median scale was 38,5 [11]. The same result was found in New-York [24]. The ALS FRS-R was used in a lot of study especially clinical trials, it permits to predict survival time of ALS patient [1,8,24]. But Kimura F and al in Japan, did not find significant difference to compare two groups with ALS FRS-R ≥ 38 and < 38 about survival time in ALS [25].

One case familial was found (4%) in this study. The review and meta-analysis for the rate of familial form of ALS by Susan Byrne and al, confirm this rate (5%) [26]. Some genes were identified: SOD1, FUS, TARDP43, OPT, VCP and C9ORF72 explain 70% of familial form [6]. In our study, genetic identification was not done for the patient. Because, the biological laboratory was lack of materials and the patient did not have money to send genetic identification in outside.

In this study, rare patients can afford riluzole because it is very expensive and rare drugstore can sell it. In our unit, riluzole was the only molecule that we used for etiological treatment. We are not using edavarone yet although there are studies on it. Japan, United States and South Corian are using edavarone since 2015 [27]. However, until now, no treatment can cure this disease [28,29] but only slowed the disease course.

About the outcome of patients, half of patient was lost (12 patients) of follow-up and only half was known (13 patients). The follow-up of patient in the lower country like Madagascar is yet difficult because the majority of patient have not money to follow treatment correctly. Their family prefer to take care them at home, sometimes they can dead at home. In this study, ten of patients was dead (40%), the principal cause was respiratory failure, they were dead between one to five years after diagnosis. The results were compatible with the others studies [30,31]. ALS is a fatal disease, a mean survival time was around 20 months after diagnosis [1,32]. According to the study realized by Pupillo E and al in Italy, conditions associated with prolonged survival were younger age, the diagnosis of possible/suspected ALS, spinal onset, and disease duration >12 months at diagnosis [21,33].

Our neurology unit works with other department to manage ALS at the time of diagnosis till the end stage of the disease. We don't have yet a specific unit for ALS but all neurologists performed training abroad Madagascar especially in France. We don't have ENMG. Our nurse and physiotherapist take care of bedridden patient at their home according to the neurologist recommendations. Respiratory medicine actually has functional respiratory investigation that we ask at the time of diagnosis. Noninvasive ventilation is not available for the advanced stage of the disease. Gastrostomy was never done for all our patients. Device of gastrostomy is not available even our surgeon was trained for such activities. We give ourselves nutrition adjustment due to the lack of nutritionist. Psychiatrist and psychologist help us for the mental support during the disease for the patient and the family. Occupational therapists are now trained in our settings but still rare so all their intervention is at their department only.

Conclusion

Patients with ALS in Madagascar is young aged, predominantly male. Spinal form is the most frequent form at the beginning but bulbar form existed also. It revealed the difficulties encountered by patients and neurologists in low income country as Madagascar. Few patients can afford riluzole and ENMG not available in our settings. Medical and allied health professional work together in the management of these patients even the weak of investigations and care facilities. A multicentric study would be better in the future to have a better idea of the distribution and the risk factor of this disease in the Malagasy people.

Conflict of Interest

No conflict of interest.

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