

Epidemiology and Clinical Description of Amyotrophic Lateral Sclerosis in Low Income Setting: A Syndrome with Short Survival

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Abstract: Background: Amyotrophic lateral sclerosis (ALS) is a degenerative motor neuron disease. It evolves to loss of autonomy and death. Objective: To describe the cases of ALS clinically definite observed in hospital field. Patients and methods: The retrospective study has covered a period of 10 years (2003-2012) and a total of 10,128 patient's files were analyzed. The neurology department of our level 3 hospital has located the current study. Six patients with no particular medical history have been reported. The inclusion patients are cases where the diagnosis of ALS was clinically definite according to the modified El Escorial classification. About 978 of likely, possible and probable cases of ALS were not included. Results: The mean age was 49 years (24 and 67), all males, with a frequency of 0.59 ‰ and an incidence rate of 0.6 cases per year. The clinical signs were marked by the pyramidal syndrome and peripheral neuropathic motor syndrome. MRI or CT scan signs were marked by the bulbar light atrophy. EMG had shown spontaneous activities with reinnervation signs. The histology exam has found neurogenic fascicular atrophy. The average duration of progression of the disease from the diagnostic to death was 17.6 months (6 to 36). The median of survival all cases combined was 42 weeks. Symptomatic treatment was associated to rehabilitation. Riluzole has been established despite its high cost, but without success. Conclusion: This observation highlighted the major difficulties encountered in the management of ALS and its increasing frequency in south Saharan Africa.

Keywords: Amyotrophic Lateral Sclerosis, Degenerative Diseases, Motor Neuron

1. Introduction

Amyotrophic lateral sclerosis (ALS) or Lou Gehrig's disease is a neurodegenerative disease of both motor neuron pathways, leading to loss of independence and death in mean term. It is revealed by progressive motor deficits that affecting members and oropharyngeal muscles.^[1-3] There is no curative cure up today and the one available, *riluzole*, only slow the disease progression in case of early diagnostic. The treatment is then symptomatic with a multidisciplinary team.^[1,4] The incidence is 1 in 100,000 peoples per year with a peak age between 55 and 70 years old and the prevalence is 0.45 to 0.89 /100,000 with a male predominance.^[5,6]

2. Subjects and Methods

It was a retrospective and descriptive study covered a period of 10 years (2003- 2012). A total of 10,128 patient's files were analyzed. The neurology department of our tertiary hospital had located the present study. The included patients were those who met the criteria of clinically definite ALS according to the consensus of revised El Escorial classification.^[7] All blood and CSF routine analysis were normal. Brain imaging was performed for exclusion diagnostic. Electromyography (EMG) recording and neuromuscular biopsy with histology analysis were the associated tools to retain the definite diagnostic of ALS.

Genetics studies were not available. Many unfulfilled files and the likely, probable and possible cases of ALS were rejected. The patients or relatives have given their informed consent. The study was approved by the ethic committee of the university hospital.

3. Results

Six patients were retained according to the above criteria. All patients were those with ALS clinically definite. The frequency of ALS was 0.59 ‰ and the incidence was 0.6 case /year. The average age was 49 years with extremes of 24 and 67. All patients were males. The median age of diagnosis

was 51 years and mean time to death after the disease onset was 30 months. The clinical signs were marked by the pyramidal syndrome and peripheral neuropathic motor syndrome. MRI or CT scan signs were normal in 3 cases and marked by the bulbar and upper cervical medulla atrophy in other cases. EMG had shown spontaneous activities with reinnervation signs. The histological exam had found neurogenic fascicular atrophy. The average duration of progression of the disease from the diagnostic to death was 17.6 months (6 to 36). The median of survival all cases combined was 42 weeks. The summary of clinical and sociodemographic data of the six patients is reported in table I.

Table I. Summary of clinical and demographic features of the six patients.

Patients	Age (y [†]) /Sex, M*	Time before diagnostic	Clinical signs	EMG (in clinically unaffected muscles)	Biopsy	Imaging (MRI [¶] /CT ^{**})	Survival after diagnostic
1	M/57	14 months	Speech and swallowing troubles, diffuse fasciculations, CMN [‡] and bulbospinal tract signs, tongue atrophy, distal limbs amyotrophy, « monkey’s hands » aspect, drooling, pulmonary infection	Spontaneous activities, signs of reinnervation, no conduction block, normal nerves conduction	Neurogenic fascicular atrophy	Normal	28 months
2	M/47	8 months	Massive fasciculations, diffuse muscular pain, dysarthria, amyotrophy of the tongue and hands , partial PMN [§] signs, rigid pyramidal syndrome of lower limbs	Spontaneous activities, signs of reinnervation, neurogenic pattern, normal nerves conduction	Neurogenic fascicular atrophy	Bulbar and upper cervical medulla atrophy	22 months
3	M/53	36 months	Walking disturbance, fasciculations of tongue and lower limbs muscles, CMN [‡] and PMN [§] signs, bilateral Hoffman sign	Spontaneous activities, signs of reinnervation, normal nerves conduction	Neurogenic fascicular atrophy	Slight bulbomedullar atrophy	18 months
4	M/24	5 months	Lingual amyotrophy, diffuse fasciculations of limbs, swallowing disorder with drooling, CMN [‡] and corticobulbar tract signs with cranial nerves palsy	Spontaneous activities, signs of reinnervation	Neurogenic fascicular atrophy	Bulbar atrophy	3months
5	M/67	24 months	Fasciculations, walking disorders, partial motor deficit of 4 limbs, neurogenic amyotrophy of shoulders and hands, weakness of tendon reflex, CMN [‡] signs	Spontaneous activities, signs of reinnervation	Neurogenic , fascicular atrophy	Normal	26 months
6	M/45	6 months	Phonation and liquids swallowing disorders, amyotrophy and fasciculations of tongue and limbs, CMN [‡] and bulbospinal tract signs, Peripheral motor neuron signs	Spontaneous activities, signs of reinnervation, normal nerves conduction	Neurogenic fascicular atrophy	Normal	18 months

Legend: M*= male; y[†]= years; CMN[‡]=Central motor neuron signs; PMN[§]=Peripheral motor neuron signs; EMG^{||} :electromyography; MRI[¶] : Magnetic Resonance Imaging ; CT^{**}= computer tomography

4. Discussion

4.1. Methodology

We have reported 6 cases of ALS clinically definite in a period of 10 years. This retrospective clinical cases study has some weaknesses. It concerns solely the patients who were followed up in neurology. The diagnosis is based on clinical signs and symptoms of ALS. The patients with likely and possible diagnostic of ALS were rejected. In other hand, some ALS clinically definite may not expect the hospitals, and used to attend basic clinics. All these recruitment bias

reduced the sample size and show that the study is not exhaustive. However, the consistency and relevance of our results with the literature give validity to the reported data.

4.2. Epidemiological Aspects

The age of 1st , 3rd , 5th and 6th patients is similar to that reported in the literature, but the 2nd and 4th are younger than the peak age of onset reported in several previous studies.^[1,5,6] The juvenile forms may have a familial origin in 30%.^[8-10] The presence of juvenile forms should lead to perform genetic testing in search of SOD1 mutation in a young patient.

In our case, a family survey was conducted in patient age of 24 years, in the lack of the genetic studies.

The reported prevalence in this study of ALS may be biased by undiagnosed. Indeed, cases of probable or possible ALS which should be confirmed by appropriated diagnostic tools were not included. The suspected patients must pay themselves for the clinical investigations. EMG and histology are not locally available and the patient must travel to abroad country to perform these tests. Data from different hospitals scattered studies in Africa show that ALS is a reality in the continent, but still rare.^[1,3,5]

4.3. Clinical Features of ALS

Concerning our patients, the presence of loss of 2 spinal territories of the peripheral and one territory of central motor neurons at least is compatible with the El Escorial criteria for clinically definite ALS. To these signs, are added the gradual evolution and especially the absence of sensory, visual, sphincters, autonomic and basal ganglia disturbances.^[7] The diagnosis of ALS is based on clinical criteria of El Escorial revised in 1998, but some additional tests (EMG and neuromuscular histology) can confirm the diagnosis or eliminate certain diseases that may mimic it. There are diseases that mimic ALS where the affected nerve territory is either only at the central or peripheral motor neurons.^[11-14] These diseases have been eliminated through careful neurological examination and biological and radiological investigations. ALS is a progressive and irreversible disease.

Brain imaging (MRI and CT) is not the tool to confirm or to reject the ALS diagnosis, as it can be normal in many cases in where it was done. These observations raised the capital interest of a thorough neurological examination as the solely diagnostic weapon we have in African regions to diagnosis ALS.

Regarding the course of the disease, we believe that there must been a delay in diagnosis of patients 3 and 5, because they have generalized their symptoms, with all the different clinical phases of ALS. The onset time of symptoms was 2 years for the 3rd and 3 years for the 5th. For other patients, it may be a case for rapid evolution or the onset of the disease has been poorly evaluated. Diagnostic delays affect about 25% of patients who died before they meet the criteria of the disease.^[15,16] These diagnostics are mostly encountered delays in cases where the clinic is rough, often misleading and mimic many other neurological disorders.

The existence of cognitive impairment should not exclude the diagnosis of ALS. Indeed signs of fronto temporal lobe dementia (FTD) may occur before or after the ALS symptoms in 40 % of cases especially in the bulbar form.^[17]

4.4. ALS Management

Concerning the medical care, only symptomatic treatment was offered to our patient. Treatment with *Riluzole* has been established for those who were able to buy it on abroad because it is non- availability in the country. In these cases where *Riluzole* was used, any significant improvement was

not observed. In the literature and according to different consensus, typical ALS support is based on three lines:

1-Neuroprotective treatment made by glutamate-release antagonists (*Riluzole*, *Verapamil*, *Topiramate*) which has been shown to slow the course of ALS, but this does not proved its effective effects in several studies.^[2,3,18,19]

2-Symptomatic treatment should be done by multidisciplinary team to improve the quality of life,^[1] and finally followed by palliative and end-of-life cares.^[2]

Noninvasive positive pressure ventilation (NIPPV) is a therapeutic option used for many patients with less than 50% of vital capacity. The NIPPV may be replaced by a tracheostomy with permanent ventilation if necessary. The use of mechanical ventilation varies between countries with cross-cultural and ethical differences. Many studies suggest that the use of NIPPV improves survival and quality of life in patients admitted to multidisciplinary team centers.^[20,21]

The introduction of percutaneous endoscopic gastrostomy (PEG) has given a real comfort to patients suffering from severe swallowing disorders.^[22] The drooling, bronchial secretions, insomnia and pseudobulbar signs were supported by anti emetics, amitriptyline, atropine, and physiotherapy.^[3,4,23]

The management of neuralgic pain was provided by good nursing and a delicate engagement with regular change of position of the patient. The adjuvant treatment includes analgesics, anti-inflammatory and antispasmodics.^[1,2,4,23,24]

The patient quality of life depends strongly on medical, psychosocial and existential accompany in life. Fatigue, depression, anxiety and hopelessness are common among these patients. The treatment of these symptoms improves significantly the quality of life of patient with ALS.^[23-25]

5. Conclusion

Carefully clinical examination is essential in case of suspected ALS. The management of ALS remains difficult in all continents. The ALS is still under diagnosis in Africa. The data on this disease are highly variable, rare and sparse in Africa.

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