

# Familial Lateral Sclerosis with Juvenile Onset: About 3 Cases and Review of the Literature

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**How to cite this paper:** Mamady, C., Djigué, B.S., Male, D., Lamine, T.M., Tafsir, D.M., Laïla, T., Seny, Y., Ibrahimsory, K., Fatoumata, B.L., Salif, C.M., Idrissa, C., Idrissa, D., Bachir, D.H., Lamine, C.M. and Abass, C.F. (2023) Familial Lateral Sclerosis with Juvenile Onset: About 3 Cases and Review of the Literature. *Journal of Biosciences and Medicines*, 11, 55-62. <https://doi.org/10.4236/jbm.2023.1110006>

**Received:** August 14, 2023

**Accepted:** October 8, 2023

**Published:** October 11, 2023

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## Abstract

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease deadly. In Africa, little data exists on this condition and the form familial is the most common with a younger age of onset. Our observations relate to three brothers, born from a consanguineous marriage. The diagnosis of amyotrophic lateral sclerosis was certain placed in all patients according to the criteria of Awaji. The average age of patients was 16.66 years, and the average age of onset of symptoms was 10.33 years old. The female gender was the most represented with a sex ratio of 0.5. Our patients benefited from rilusole, vitamin D and physiotherapy. A only patient presented with dysphagia. However, no cases have been observed at this day.

## Keywords

ALS, Familial, Juvenile

## 1. Introduction

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disease deadly [1] [2]. Juvenile-onset ALS (JALS) is defined by an appearance before the age of 25 [3]. In Africa, little data exists on this affection and the familial form is the most common. Patients from Africa of West have a younger age of onset compared to those of South Africa North and Southern Africa ( $p = 0.0001$ ) [4]. The incidence of JALS is 0.7 at 5 cases per 100,000 people [5] [6] [7]. About 10% of cases of ALS are familial, they are caused by a genetic mutation that is usually transmitted in an autosomal fashion dominant [8] [9]. The age of onset of ALS is usually 62 years old [10]. However, the familial form is associated with earlier onset and

longer survival [11]. There is no diagnostic test or biomarker for the diagnosis of ALS. The diagnosis is based on clinical and paraclinical arguments. The Awaji criteria allow early diagnosis and identification of different forms [12]. Currently, there is no curative treatment for ALS and management burden rests on symptomatic and palliative care [13].

## 2. Case Presentation

We report three (3) cases of ALS observed in three brothers from a marriage by consanguinity, of which a maternal uncle had presented towards the fifty years, weakness in all four limbs and deformation of the extremities before dying four years later.

### 2.1. 1<sup>st</sup> Observation

This is the eldest Mrs. M, she is 20 years old. She consulted for a gait disorder, deformity and weakness of all four limbs. The beginning of the symptoms dates back to the age of 9, marked by progressive onset of limb weakness and deformity lower than upper limbs. Vital parameters on admission were normal. On neurological examination, hyper-reflexia is noted. osteotendinous of the lower and upper limbs. In the upper limbs, we observe amyotrophy of the eminences thenars and hypothenars, and interosseous bones of the upper limbs (**Figure 1** and **Figure 2**). At lower limbs the patient has muscular strength of 3/5, an amyotrophy



**Figure 1.** Amyotrophy of thenar and hypothenar muscles.



**Figure 2.** Amyotrophy of the interosseous muscles of the hand.

of the soleus and interosseous muscles of the lower limbs with *bau varus* appearance of the feet. No sensory disturbance, no problems oculomotor or sphincter disorders. Brain and cervical MRI were normal. Brain fluid analysis spinal cord was unremarkable. Infectious serologies (HIV, VDRL, TPHA, HbsAg) were negative. The electroneuromyogram concluded that potentials fibrillation and denervation. The diagnosis of definite ALS was made according to the Awaji criteria. The patient benefited from riluzole at a dosage of 100 mg per day divided into two doses, vitamin D at 50,000 IU every two (2) weeks and one physiotherapy for muscle strengthening.

### 2.2. 2<sup>nd</sup> Observation

This is Mr. M, 17 years old, a student and with no personal history. He has been received for weakness in all four limbs and deformity of the extremities, progressive and ascending installation over a period of 11 years. Vital parameters were normal on admission. On neurological examination, muscle testing was 3/5 in all four limbs. Upon examination by members superiors we have amyotrophy of the deltoid, biceps, triceps, the forearm, thenar, hypothenar and interosseous eminences with a monkey-handed appearance. In the lower limbs we note amyotrophy of the soleus and interosseous muscles of the lower limbs and feet in beam. We notes a hyper-osteo-tendinous reflex of the four limbs. No trouble sensory, no oculomotor disorders, nor sphincter disorders. Brain and cervical MRI were normal. Brain fluid analysis spinal cord was unremarkable. Infectious serologies (HIV, VDRL, TPHA, HbsAg) were negative. On the electroneuromyogram, we note the detection fibrillation and slow denervation. The diagnosis of certain ALS was made according to the criteriaof Awaji The patient was given riluzole at a dosage of 100 mg per day divided into two doses, vitamin D at 50,000 IU every two (2) weeks, and it has also benefit from physiotherapy. The patient presented one month later a swallowing disorder and dyspnea on exertion, he benefited from a respiratory physiotherapy.

### 2.3. 3<sup>rd</sup> Observation

This is the youngest of the family, aged 13 and without a medical history staff. She consulted for weakness of the lower limbs and gait disorder, the onset of symptoms dates back to the age of 11. On admission vital parameters were normal. The particularities of the neurological examination were as follows: hyper osteotendinous reflexia of four limbs, amyotrophy of the eminences thenars, hypothenars and interosseous bones in the upper limbs. We notice also a decrease in muscle strength rated at 3/5, amyotrophy soleus and interosseous muscles of the lower limbs (**Figure 3** and **Figure 4**). No trouble sensory, no oculomotor disorders, nor sphincter disorders. Brain and cervical MRI were normal. Brain fluid analysis spinal cord was unremarkable. Infectious serologies (HIV, VDRL, TPHA, HbsAg) were negative. The electroneuromyogram revealed at the detection of fibrillation potentials and slow denervation at rest. The diagnosis of



**Figure 3.** Amyotrophy of thenar and hypothenar muscles.



**Figure 4.** Amyotrophy of the interosseous muscles of the hand.

definite ALS was made according to the Awaji criteria. The patient benefited from rizudole at a dosage of 100 mg per day divided in two doses, vitamin D at 50,000 IU every two (2) weeks and one physiotherapy for muscle strengthening.

### 3. Discussion

The familial form of ALS represents 5.1% of cases [14]. The cause of ALS is unknown although some genetic risk factors have been identified [15] [16]. Causal mutations in superoxide dismutase-1 (SOD1) are identified in 10 to 20% of FALS [17]. The rates of C9ORF72 variants and TARDBP are elevated in genetically isolated populations such as Finland or Sardinia [9] [18]. The risk of developing ALS varies between continents and regions ethnic groups [15]. Prevalence is 50 to 100 times higher in the Western Pacific than elsewhere in the world [19] [20]. It is increased in Guam, Japan and the New Guinea [21]. The incidence of ALS gradually increases from of 40 years with a peak between 60 and 70, followed by a sharp decrease [22]. Advanced age and bulbar appearance are markers of poor important prognoses [23]. The phenotype and course of ALS vary according to the ancestral origin of the population [24]. A study in the

State of Washington had shown that the African origin was associated with a time of survival longer than the others, with a risk of death of 2.2% after adjustment for age, sex and ethnicity [25]. ALS is more common in men than women [21]. Lateral sclerosis refers to the hardening of the corticospinal tracts anterior and lateral when the motor neurons in these areas degenerate and are replaced by gliosis, and “Amyotrophy” refers to the atrophy of fibers denervated muscles [26]. The exact molecular pathway causing the motor neuron degeneration in ALS is unknown [27] Tobacco is considered the main factor associated with development of ALS [28]. However, recent studies on the role of environmental risk factors in the causation of ALS concluded that it is no consistent association between a single environmental factor and the risk of developing ALS [29]. There is no diagnostic test for ALS, several diagnostic criteria have been established including the revised Lambert and E1 Escorial criteria, however these criteria cannot diagnose early ALS [30] [31]. The Awaji classification seems today diagnostic criterion most appropriate than precedents for ALS diagnosis [32] [33]. The spinal form is the most common, it affects nearly 70% of patients. There bulbar form is observed in approximately 25% of cases [5]. The bulbar appearance is more common in women and older patients [11]. The disorders of swallowing can lead to bronchial aspiration and poor food. The weight loss for which these are responsible is correlated with a shorter survival [20]. Cognitive or behavioral impairment is observed in up to 50% of patients [7]. Although ALS is thought to be painless, most patients experience non-neuropathic pain [34]. Cerebrospinal fluid analysis, and skeletal muscle biopsy or other tissues are not necessary for diagnosis except to exclude a mimicry syndrome [35] [1]. Electroneuromyography (ENMG) confirms the existence of signs of denervation in an anatomical region [12].

According to a recent meta-analysis, riluzole 100 mg extends survival by 2 to 3 months when taken for a period of 18 months [36]. About half of patients die within 30 months of onset. symptoms, while approximately 20% of patients survive between 5 and 10 years [37]. Low levels of vitamin D are seen in ALS, but studies recent studies suggest that vitamin D is not a prognostic marker independent [38].

#### **4. Conclusion**

Juvenile-onset familial lateral sclerosis is a rare form of ALS, it presents no clinical particularity, despite the early onset of the symptomatology life expectancy seems to be better. A more study extent could provide information on this clinical entity.

#### **Conflicts of Interest**

The authors declare no conflicts of interest regarding the publication of this paper.

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