Diagnostic elements in amyotrophic lateral sclerosis: A case report

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Received April 14, 2024; Accepted July 4, 2024

DOI: 10.3892/br.2024.1829

Abstract. Amyotrophic lateral sclerosis (ALS) is a rare neurological disease that involves the degeneration of both upper and lower motor neurons responsible for controlling voluntary muscle activity. Most people with ALS die within 3-5 years due to respiratory failure. The current study presents the case of a 68-year-old woman diagnosed with ALS based on the subjective and objective findings from the patient's initial physiotherapy assessment and on neurophysiological tests. Physiotherapy interventions are aiming to maintain the patient's strength, balance and functional independence for as long as possible. The present case report aimed to highlight that a multidisciplinary team approach is necessary for the management of a progressive degenerative disease such as ALS.

Introduction

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disease that affects nerve cells in the brain and spinal cord. The hallmark of ALS is progressive muscle weakness, accompanied by muscle atrophy, fasciculations, muscle cramps and stiffness and slowness of movements. The main features of ALS include muscle twitches in the arm, leg, shoulder or tongue, muscle cramps, spasticity, muscle weakness affecting the limbs or the neck, slurred and nasal speech, as well as chewing or swallowing difficulties. As the disease evolves, the symptoms may include difficulty breathing, inability to stand or walk independently, weight loss, depression and anxiety (1).

In the evolution of ALS, motor deficits appear at the level of the upper and lower limbs and the respiratory muscles; phonation and swallowing are also affected (1). In conclusion, this degenerative disease is characterized by both central and peripheral motor neuron injuries. The incidence of ALS at the global level is unknown. In Europe, 2.2 per 100.000 individuals are diagnosed with ALS every year; in the United States, the rate of ALS is >1.87 per 100.000 individuals per year (2).

The treatment of ALS is complex and multidisciplinary. The only medication proven to influence the evolution course is rilusole (3). Other treatments, such as respiratory care and nutrition management, can increase the quality of life for patients with ALS (1).

There is no biological marker for ALS. The diagnosis can be established using clinical examination and electrodiagnostic tests. Identifying biological, clinical, neurophysiological and genetic biomarkers of the disease still remains a challenge (4,5). The clinician can use the updated El Escorial diagnostic criteria (EEC) and Awajishima criteria (6,7). According to the EEC, the diagnosis of ALS requires the presence of A-criteria and the absence of B-criteria as follows:

- A1: Degeneration of the lower motor neurons, proved by clinical, electrophysiological or neuropathological exami nation;
- A2: Degeneration of the upper motor neurons, proved by clinical examination;
- A3: Progressive dissemination beyond typical nerve supply areas.
- B1: Electrophysiological or neuropathological findings typical for other diseases that could explain the degeneration of the upper and lower motor neurons;
- B2: Findings of imaging studies that can explain the clinical symptoms. The Awaji criteria are less rigid and are based on the presence of fasciculation potentials in a typical clinical context of ALS.

The current study presented the case of a 68-year-old woman without any medical history, who accessed the ambulatory service of the Medical Rehabilitation Clinic of the Emergency County Hospital of Craiova (Craiova, Romania) for a motor deficit at the level of the upper and lower limbs, installed 1.5 years before the presentation. The diagnosis of ALS was based on clinical features and electrodiagnostic studies. Establishing a correct diagnosis is essential for an appropriate therapeutic approach and consequently for the patient's prognosis.

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Key words: amyotrophic lateral sclerosis, electromyography, diagnosis

Case report

A 68-year-old woman, Caucasian, from a rural environment with a primary education was hospitalized in a Medical Rehabilitation Clinic of the Emergency County Hospital of Craiova (Craiova, Romania) due to dizziness, gait disorders, decreased grip strength and fasciculations. The symptoms began insidiously 1.5 years before the hospitalization. The patient had not previously seen a doctor and had not received any medical treatment, and there was no family history of ALS.

The clinical examination showed that the patient was underweight [body mass index (BMI=18.1 kg/m^2)] and was well-oriented. When examining the cranial nerves, no pathological elements were highlighted, except for the lingual fasciculations. Orthostatism was possible, walking was possible with support but impossible on the toes and tips.

On examination of the hand, the osteoarthritic aspect was noticed, but also the aspect of the 'simian hand', with hypotrophy of the thenar and hypothenar eminences, retraction of the palmar aponeurosis and a grasping deficit. These abnormalities were observed in both hands.

Clinical examination of the lower limbs indicated a motor deficit in the calf muscles upon muscular testing: The muscular strength (on a scale ranging from 0 to 5) of the anterior tibial muscle was 3/4 right/left, the strength of the common extensor of the toes was 3 bilaterally and the strength of the hallux extensor muscle was 2/3 right/left (6).

The Babinski response was present bilaterally, while osteotendinous reflexes in the upper and lower limbs were abolished (6). Movement coordination was not affected in the patient and no objective sensitivity disorders were noted.

Regarding the imaging investigations, the lumbar spine radiograph showed both degenerative changes and vertebral osteoporosis, a fact confirmed by the osteodensity examination, where a T-score of -3.8 was obtained (dual X-ray absortiometry T-score >-1 means normal; T-score from-1 to -2.5 means osteopenia; T-score <-2.5 means osteoporosis). These comorbidities were not typical for ALS (6).

A specialized neurological examination was requested, following which the diagnosis of neurogenic spinal atrophy was established and the patient was placed under observation for amyotrophic lateral sclerosis.

The electroneuromyography (EMG) for the median and ulnar nerves pointed out the diagnosis of motor chronic demyelinating neuropathy and a needle EMG was needed for confirmation of ALS. Electromyographic examination performed for the brachial biceps muscle, common extensor muscle of the fingers and anterior tibialis muscle revealed an aspect of generalized chronic active neurogenic lesion. This aspect was characteristic ofan injury of motor neurons, confirming the diagnosis of ALS. The recording of the neurogenic pathway was characterized by the spontaneous presence of fasciculations, fibrillation, positive sharp waves, stable and instable neurogenic motor unit potentials with increased duration and amplitude, and a reduced interference pattern by decreased motor neuron recruitment and activation (Figs. 1 and 2, Table I).

ALS is a neurodegenerative disease that occurs in motor nerve cells and leads to gradual amyotrophy and muscle weakness until complete paralysis. The patient of the present study had weakness in the legs, a decreased ability to hold her balance and to go up and down the stairs and required assistance with walking. The patient's arms also showed obvious weakness with arm lifting difficulties and decreased grip strength of both hands, and the patient gradually lost the ability to use the hands and arms. The patient had limb muscle atrophy, muscle bundle tremor and weight loss. The only characteristic sign of cranial nerve damage was lingual fasciculations.

No MRI was performed for this patient, while it is helpful for studying ALS-related changes in the brain or spinal cord. The patient was administered riluzole 50 mg twice daily.

After the diagnosis of ALS, the patient was referred to the neurology outpatient clinic to establish a specialized therapeutic approach. During the 12 days of hospitalization at the Physical Medicine and Rehabilitation Clinic of the Emergency County Hospital of Craiova (Craiova, Romania), the patient underwent a complex kinetic and physical rehabilitation treatment. The individualized physicotherapy program consisted of light aerobic exercises and had the objectives of increasing muscular strength, maintenance of the tone and strength of the unaffected muscles and improvement of the cardiovascular status. This program included walking exercises and a cycle ergometer, also helping the patient fight fatigue and depression. Stretching exercises and mobilization to increase the amplitude of joint movement also aimed to reduce spasticity and combat painful muscle contractions. The patient also responded positively to electrostimulation procedures for lower limb muscles. The patient was monitored through the neurology service and underwent recovery treatment ~6 months later.

Discussion

At present, there is no universally accepted specific diagnostic test for ALS. The diagnosis of the disease is based in particular on the presence of symptoms, signs and laboratory tests that show progressive injury to motor neurons, such as electrodiagnostic tests. Imaging and laboratory tests can be used to rule out other neurological conditions. The classic clinical presentation of ALS is characterized by the asymmetric decrease in muscle strength in the extremities (60-80%) and bulbar muscles (1-9%), axial onset with fall of the cephalic extremity or decrease in the strength of the paravertebral extensor muscles, fasciculations and muscle atrophies (5-7%) (8). Anteflexion of the head due to muscle strenght decrease.

The lack of diagostic tests with sensitivity and specificity for ALS is a major obstacle in the early diagnosis of patients, although in 2000, the diagnostic criteria for this condition were revised (6,8). The diagnosis of patients with ALS with a typical presentation of the disease is relatively easy for the clinician in the presence of signs of upper and lower motoneuron damage and progressive evolution of the disease. However, for patients with a slow evolution of the disease, at the onset of the disease or for those with other concomitant disorders of the central or peripheral nervous system, the probability of misdiagnosis with the 'ALS-mimicking syndromes' is ~7-8% (9). In such cases, peripheral neuropathies, myopathies, spinal muscular atrophy and paraplegia should be ruled out.

Given the complexity of the disease, >40 clinical randomized controlled trials performed over the last decades failed to show any influence on disease progression or life expectancy

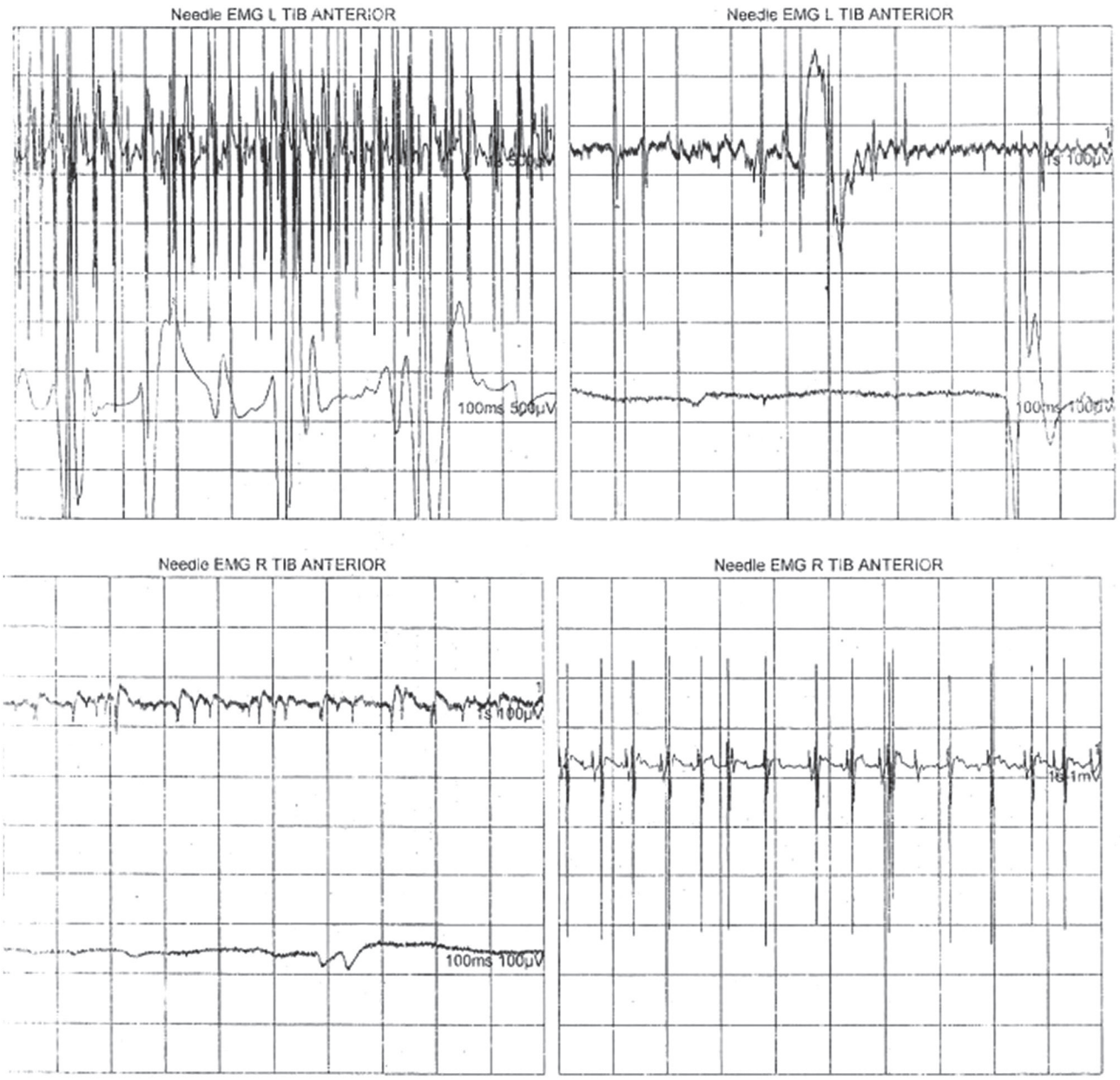

Figure 1. Needle EMG for anterior tibialis muscle: Spontaneous positive short-wave activity, fasciculations, fibrillation with increased amplitude motor unit potentials and decreased recruitment and activation, suggestive of a neurogenic pathway. EMG, electroneuromyography; L, left; R, right; TIB, tibial.

in patients with ALS (10). In most European countries, riluzole 50 mg twice daily is the only medication used for the treatment of patients with ALS due to its antiglutamatergic effects and it is a disease-modifying drug proven to prolong life by 3-6 months (11,12).

Muscle spasticity in patients with ALS can be influenced using baclofen and stretching exercises (13). For the treatment of muscle cramps, carbamazepine or gabapentin and also magnesium supplements can be used. Antidepressant medication may also be used for emotional lability. Nutrition changes and speech therapy can also be useful for patients with ALS (14).

The success of the treatment of patients with ALS is ensured by a multidisciplinary collaboration (15). Future therapy may include edaravone (16,17), a drug that has been approved for the treatment of ALS in several countries, or masitinib, a tyrosine kinase inhibitor, drugs used in clinical trials (18). Genetic studies for ALS treatment are also in progress (19), as well as stem cell treatments (20,21).

The patient presented in this case study had an asymmetric decrease in muscle strength at the extremities level, at the clinical examination, which could suggest the diagnosis of ALS. When first seen, the patient of the present study had asymmetric weakness of the extremities that was consistent with ALS, but this lack of muscle strength in the extremities can also indicate a demyelinating neurological disease (22). Fasciculations may also be characteristic of this condition, but may be associated with other neurological diseases. These symptoms may be significant to clarify the diagnosis of ALS when they are accompanied by changes in the motor unit highlighted by the needle EMG examination (7). Electrodiagnostic analysis is essential in

Table I. Needle electroneuromyography parameters for tibial anterior, biceps and extensor digitorum communis muscles highlight an aspect of chronic active generalized neurogenic injury characteristic of motor neuron disease.

	Spontaneous					MUAP			
Muscle	IA	Fib	PSW	Fasc	H.F.	Amp	Dur	PPP	Engagement pattern
L. Tibial anterior	N	2+	1+	2+ (slow)	None	Giant	3+	3+	Reduced
R. Tibial anterior	N	1+	3+	None	None	Giant	3+	3+	Discrete
L. Biceps	N	2+	1+	2+ (slow)	None	2+	3+	3+	Reduced
R. Extensor digitorum communis	N	1+	1+	2+ (fast)	None	Giant	3+	3+	Reduced

L, left; R, right; MUAP, motor unit action potential; IA, insertional activity; Fib, fibrillation potentials; PSW, positive sharp wave; Fasc, fasciculation; H.F, harmonic focus activation; Amp, amplitude; Dur, duration; PPP, phase.

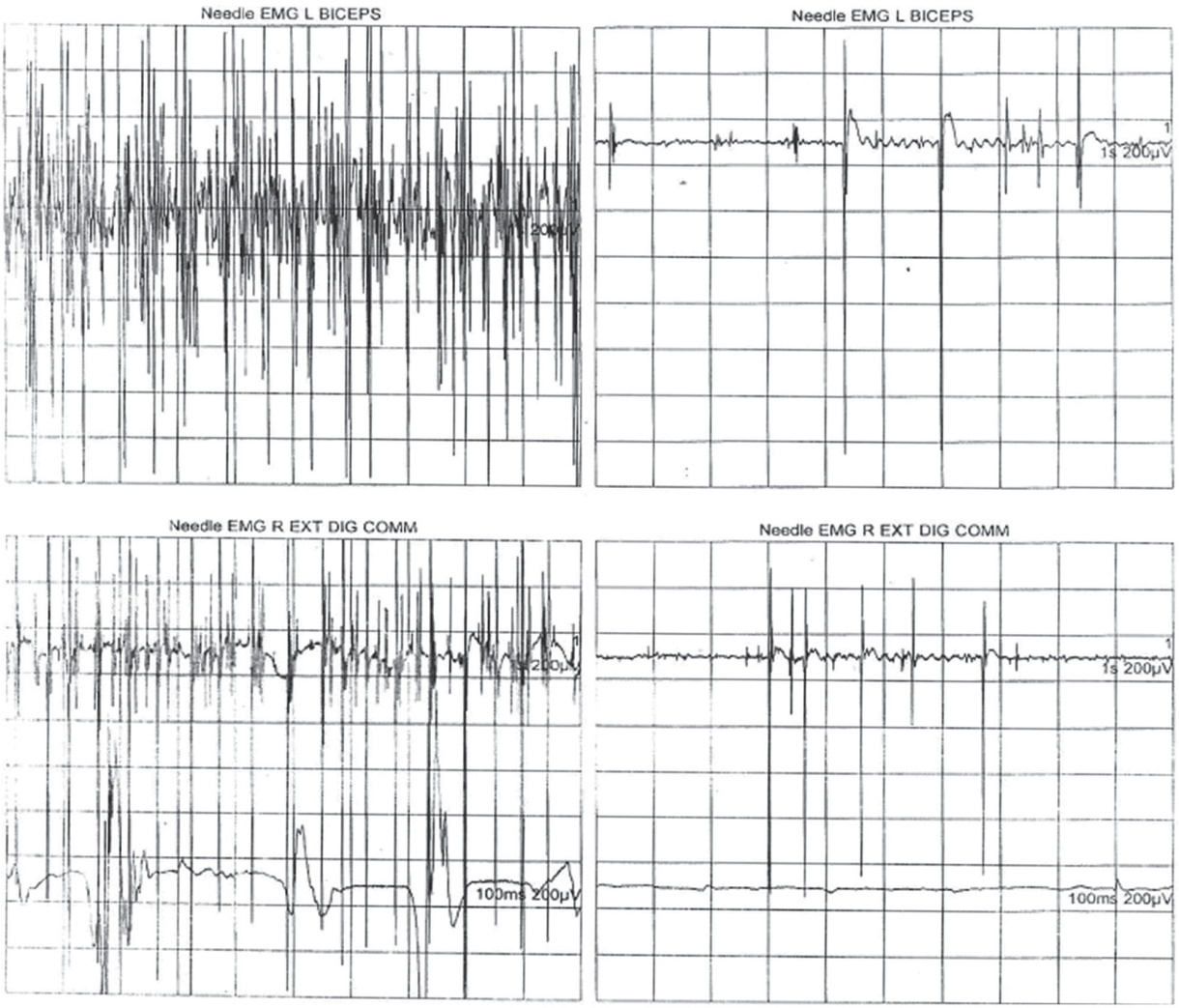

Figure 2. Needle EMG for common extensor muscle of the fingers and biceps muscle: The presence of motor unit potentials with increased amplitude and duration and decreased recruitment is observed, also suggestive of a neurogenic pathway. EMG, electroneuromyography; L, left; R, right; EXT DIG COMM, extensor digitorum communis.

patients with this condition, both to confirm the diagnosis of ALS and to identify other potentially treatable neurological disorders.

Patients with ALS frequently exhibit weight loss that occurs late in the course of the disease. There are multiple causes of weight loss, which may include decreased muscle strength in

the upper limbs and seizure disorders, dysphagia, dyspnea during swallowing, chewing problems and a hypermetabolic status (23). The patient presented in the current study was underweight, with a BMI of 18.1 kg/m^2. According to clinical studies, a BMI <18.51 kg/m^2 caused by weight loss in patients with ALS is a negative prognostic factor and is associated with a decreased survival time (23).

This situation in which the patient with ALS first presented at the Medical Rehabilitation service is rare, which was an additional reason why establishing the diagnosis was challenging, requiring a multidisciplinary evaluation (medical rehabilitation doctor, neurologist specializing in electromiography, physioterapists).

In conclusion, as there are no disease-specific diagnostic tests, diagnosing ALS is a challenge for the clinician. The neurological clinical examination must be associated with a series of paraclinical investigations necessary for the differential diagnosis of other neurological diseases. In this sense, the importance of electrodiagnostic tests is highlighted, particularly electromyography, as well as imaging, the most useful being nuclear magnetic resonance. At times, muscle or nerve biopsy is required, determination of serum levels of thyroid and parathyroid hormones, as well as detection of heavymetals in urine. The average survival time in patients with ALS is between 2 and 5 years after diagnosis, but in numerous cases, it can be exceeded.

Acknowledgements

Not applicable.

Funding

No funding was received.

Availability of data and materials

The data generated in the present study may be requested from the corresponding author.

Authors' contributions

IRM contributed to the data acquisition. OCR contributed to manuscript writing and critical revision for important intellectual content. RP contributed to the systematization of the data. VP and DD contributed to analysis and supervision. All authors have read and approved the final version of the manuscript. IRM and DD checked and confirmed the authenticity of the raw data.

Ethics approval and consent to participate

Not applicable.

Patient consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Competing interests

The authors declare that they have no competing interests.

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