Case Report

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Amyotrophic lateral sclerosis with respiratory failure and dysautonomia: a case report

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Introduction and importance: Amyotrophic lateral sclerosis (ALS) is a disease that affects both upper and lower motor neurons, causing a range of symptoms beyond the motor system. Recent research has shown that the autonomic nervous system can also be affected, with symptoms such as orthostatic hypotension, fluctuations in blood pressure, and dizziness being reported.

Case presentation: A 58-year-old male presented with left lower limb limping, difficulty climbing stairs, and left foot weakness, followed by right upper limb weakness and was diagnosed with ALS and received edaravone and riluzole treatment. He presented again with right lower limb weakness, shortness of breath, and wide fluctuations in blood pressure, leading to ICU admission with new diagnosis of ALS with dysautonomia with respiratory failure and was managed with non-invasive ventilation, physiotherapy, and gait training exercises.

Clinical discussion: ALS is a progressive neurodegenerative disease affecting motor neurons but non-motor symptoms can also occur, including dysautonomia, which can result in blood pressure fluctuations. Dysautonomia in ALS is caused by several mechanisms such as severe muscle atrophy, prolonged ventilatory support, and upper and lower motor neuron lesions. Management of ALS involves giving a definitive diagnosis, providing nutritional support, using disease-modifying drugs such as riluzole and non-invasive ventilation to improve survival and quality of life. Early diagnosis is essential for effective management of the disease.

Conclusion: Early diagnosis, use of disease-modifying drugs, non-invasive ventilation, and maintaining the patient's nutritional status are crucial for managing ALS which can have non-motor symptoms as well.

Keywords: amyotrophic lateral sclerosis, case report, dysautonomia, respiratory failure

Introduction

The clinical hallmark of amyotrophic lateral sclerosis (ALS) also known as Lou Gehring disease is the combination of upper and lower motor neuron signs and symptoms because of their degeneration[1]. The symptomatic expressions of ALS are not restricted to the motor system, but rather seem to exhibit a broader range of manifestations[2,3]. Despite the widely held belief that ALS does not exert influence on the autonomic nervous system (ANS), upcoming literature has documented the incidence of ANS-associated symptoms in ALS patients, including but not limited to orthostatic hypotension, fluctuations in nocturnal blood pressure, and episodes of postural dizziness[2,3]. Here, we present the case of a 53-year-old male with ALS with dysautonomia. This case has been reported in line with SCARE criteria[4].

HIGHLIGHTS

- Amyotrophic lateral sclerosis (ALS) is characterized by the degeneration of upper and lower motor neurons with most cases being sporadic.
- ALS is a motor neuron disease that can also exhibit a range of non-motor symptoms such as dysautonomia.
- Dysautonomia can result in blood pressure fluctuations.
- Dysautonomia in ALS might be due to severe muscle atrophy, prolonged ventilatory support, and upper and lower motor neuron lesions.
- Management includes close monitoring of vitals, use of disease-modifying drugs, non-invasive ventilation, nutritional support and physiotherapy.
- Timely identification of the disease is of utmost significance for effective management.

Presentation of case

A 58-year-old male had a history of limping of the left lower limb for 6 months. After 4 months of onset of limping he had difficulty in climbing stairs, getting up from bed, wearing and gripping

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slippers with his left foot. He also had right upper limb weakness for 12 days when he finally went to seek medical attention. He had normal bowel and bladder habits with no history of any sensory symptoms, difficulty in swallowing and speaking, headache, and no trouble in vision. His prior medical and surgical history were not significant. Family history for similar symptoms and other neurological conditions were absent. He was diagnosed to have ALS after thorough neurological examinations and various investigations. He received injection edaravone 60 mg via intravenous route once daily for 14 days for one cycle only and has been receiving tablet riluzole 50 mg twice daily since then. Along with the previous motor symptoms, this time (1 month after being discharged) the patient presented to the emergency department with right lower limb weakness and sudden onset of shortness of breath. He was eventually kept in non-invasive ventilation. His blood pressure showed wide fluctuation ranging from minimum of 70/40 mmHg to maximum of 200/120 mmHg and hence he was admitted to ICU for intermittent inotropic support with continuation of non-invasive ventilation.

On examination, he was conscious and oriented to time, place, and person. Cranial nerve examinations were intact. On motor examination, bulk was decreased proximally in bilateral lower limbs. Power in left upper limbs was 5/5, 2/5 in right upper limb and left lower limb and 3/5 in right lower limb. Deep tendon reflexes were depressed. Sensory examination was normal. Cerebellar signs were absent. There were no signs of meningeal irritation.

The chest X-ray and electrocardiogram was normal and routine blood investigations were within normal limits. Arterial blood gas analysis showed type 2 respiratory failure. Electromyography (EMG) showed fasciculation and fibrillation; features suggestive of motor neuron disease involving lumbar and sacral myotome. MRI of the dorsal spine with the screening of the whole spine showed no definite white matter lesion or demyelinating plaque in the spinal cord; diffuse symmetrical bulges at D3–9 levels, compromising the intervertebral foramina without nerve root impingements. Ultrasonography for diaphragm showed bilateral poor diaphragmatic movement with a reduced diaphragmatic excursion on the right and absent diaphragmatic excursion on left. The patient was diagnosed with ALS with dysautonomia with respiratory failure.

The patient was kept on NIV for type 2 respiratory failure and tablet riluzole was continued. He was also managed with physiotherapy and gait training exercises.

Discussion

The term amyotrophic refers to the atrophy that occurs as a result of muscle inactivity and means no muscle feeding[5]. Upon examination of the spinal cord after autopsy, a sclerosis is felt that is caused by the growth of astrocytes and scarring of the lateral columns of the spinal cord[5]. A paper by Salvany *et al*.[6] highlighted the pathological characteristics of ALS because of early buildup of misfolded superoxide dismutase 1, motor neuron degeneration, and microgliosis. The majority of ALS cases are sporadic, while 5–10% of them are familial[7]. Viruses, neurotoxins, heavy metals, flaws in the immune system, and deviant enzymes are a few potential causes[7]. Among the familial cases, the common mutations are C9orf72 repeat expansions, SOD1, TARDBP, and FUS[7].

The appropriate investigations depend on the clinical presentation and may include nerve conduction studies and needle EMG, various imaging including MRI, blood and cerebrospinal fluid studies, or other tests[8]. Only 10% of patients have familial ALS with a hereditary cause; thus, genetic diagnosis is not always required[8]. The El Escorial criteria, revised in 2015, proposed that a diagnosis of ALS requires at least one of the following: (a) progressive upper motor neuron and lower motor neuron deficits in at least one limb or region of the body for possible ALS; and (b) lower motor neuron deficits as defined by clinical examination (one region) and/or by EMG in two body regions (defined as bulbar, cervical, thoracic, lumbosacral); with the EMG findings consisting of neurogenic potentials and fibrillation potentials and/or sharp waves[5]. Our patient satisfied the above criteria and in addition, we evaluated for a variety of possible causes by performing various investigations before making the final diagnosis of ALS.

The development of extra neurological symptoms or other organ involvements suggests a different diagnosis because ALS has generally been thought of as a pure motor disease in which sensory function and coordination remain intact[1]. Nevertheless, it is becoming more well acknowledged that non-motor symptoms can happen and although dysautonomia symptoms are not common in ALS, they have lately been documented[9–11]. Disorder in ANS most commonly results in functional collapse such as hypotension, but hypertension due to overactivity has also been described[2,10]. Our patient experienced high blood pressure episodes that stabilised after weaning off inotropes as well as bouts of low blood pressure that were treated with inotropes. Mechanisms responsible for sympathetic overactivity thus leading to hypertension might include severe muscle atrophy and long-term bedridden state, psychological stress, prolonged ventilatory support, upper and lower motor neuron lesions[12]. With the progression of disease, hyposensitivity or downregulation of the a-adrenoreceptors of peripheral blood vessels may result in intemperate blood pressure falls particularly during sleep where there is low sympathetic activity[13]. Oscillation in autonomic regulation could also be due to involvement of the central and basolateral nuclei of the amygdala and the hypothalamus, which can also lead to emotional fluctuation[14,15]. Furthermore, the progressive decrease in ventilatory capacity, as observed in the progression of ALS, can cause intermittent hypoxia initially which can lead to both sympathetic and parasympathetic activity, as a normal response to hypoxia, resulting in dysautonomia[16]. Because of effective compensatory mechanisms in ANS and decreased daily activity in ALS patients, subtle autonomic dysfunction might not manifest clinically initially leading to infrequent dysautonomia signs and symptoms being visible in early ALS[17].

ALS symptoms continue to deteriorate, and some drugs have been reported to delay progression; therefore, only early definitive ALS diagnosis can lead to a better quality of life in patients with ALS[18]. Management of patients with ALS starts with the giving of diagnosis and continues to the terminal phase of the disease[18,19]. Riluzole is an approved disease-modifying drug in ALS which is described to lengthen median survival by 2–3 months[19]. Non-invasive ventilation improves the survival of ALS patients without severe bulbar dysfunction more than that of riluzole and improves the quality of life in all ALS patients[19]. Nutritional status also impacts survival in ALS, hence is crucial to maintain[19].

Conclusion

Although classically thought of as a pure motor disease, non-motor symptoms such as dysautonomia have been documented in ALS. Effective management of ALS involves early diagnosis, use of disease-modifying drugs like riluzole, non-invasive ventilation, and maintaining the nutritional status of the patient. Further research is needed to fully understand the pathophysiology of dysautonomia in ALS and its impact on disease progression and quality of life.

Ethical approval

Not required.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Author contribution

S.C., N.K., R.L. and R.K.: led data collection, concept of study, contributed in writing the case information. R.A.: literature review, writing case information, revising, editing the manuscript and preparation of final version. B.P. and A.K.: Literature review, revising and editing the manuscript.

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