Amyotrophic Lateral Sclerosis and the Respiratory System

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KEYWORDS

• Noninvasive ventilation • Diaphragm • Secretion clearance

KEY POINTS

- Amyotrophic lateral sclerosis (ALS) is an incurable disease whereby patients most commonly die of respiratory complications.
- It is important for pulmonary physicians to be aware of this and understand management options, including noninvasive and invasive ventilation and assisted cough techniques.
- Because ALS affects both upper and lower motor neurons, it causes hyperreflexia, spasticity, muscle fasciculations, muscle atrophy, and weakness.

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a progressive neurodegenerative disorder that always affects the respiratory muscles. It is characterized by degeneration of motor neurons in the brain and spinal cord.[1] Respiratory complications, including pneumonia and progressive respiratory failure, are the most common causes of death in ALS and typically occur within 3 to 5 years of diagnosis.[2,3] Because ALS affects both upper and lower motor neurons, it causes hyperreflexia, spasticity, muscle fasciculations, muscle atrophy, and weakness. It ultimately progresses to functional quadriplegia. ALS most commonly begins in the limbs, but in about one-third of cases it begins in the bulbar muscles responsible for speech and swallowing.[4] A small proportion of cases begin with respiratory muscle weakness and can present as unexplained hypercarbic respiratory failure.[5]

Most cases of ALS are idiopathic, but approximately 10% of cases are due to identifiable genetic mutations and are inherited in an autosomal dominant manner.[6] The incidence of ALS in the United States is 1 to 2 cases per 100,000 people, and the average age of onset is in the mid-fifties. There is a male predominance of sporadic cases with a male to female ratio of almost 2:1.[7] There are now 2 medications approved by the US Food and Drug Administration for the treatment of ALS, riluzole and edaravone[8]; but in spite of therapeutic developments, the disease is uniformly fatal and the treatment is largely

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supportive. Much of the therapy for ALS is directed at improving respiratory symptoms and minimizing pulmonary complications.[9] This therapy includes interventions directed at secretion clearance and ventilator support. This article describes the respiratory evaluation and treatment of individuals with ALS.

RESPIRATORY MANIFESTATIONS

ALS causes multiple problems that impact the respiratory system. Fig. 1 provides an overview of the most relevant complications. ALS causes diffuse muscle weakness that ultimately leads to functional quadriplegia and anarthria.

Inspiratory Muscle Weakness

The major muscles of inspiration are the diaphragm, the sternocleidomastoids, the scalenes, and the external intercostals. Weakness of these muscles leads to a decrease in tidal volume, resulting in alveolar hypoventilation and subsequent respiratory insufficiency.

Expiratory Muscle Weakness

The major muscles of expiration are the abdominal muscles, including the rectus abdominis, the internal and external obliques, the transversus abdominis, and the internal intercostal muscles.[10] Decreased strength in expiratory muscles, often coincident with impaired glottic function, can lead to an ineffective cough, retention of upper airway secretions, and subsequent lower respiratory tract infections. Both the inspiratory and expiratory muscle groups become weak in ALS, but this may happen at any time in the disease course; inspiratory muscles can become weak at a different time than the expiratory muscles.

Bulbar-Innervated Muscles Dysfunction

Approximately 30% of patients with ALS present with bulbar dysfunction at the time of diagnosis, which has been linked to poor outcomes.[11] Sialorrhea, dysphagia, and dysarthria are the most important symptoms related to pharyngeal and laryngeal muscle weakness and lead to altered secretion management, decreased calorie intake, and resultant malnutrition. The direct impairment in bulbar-innervated muscles can also lead to an increased risk of aspiration during swallowing, provoking respiratory infections. The recognition of bulbar dysfunction in patients with ALS is crucial for the management of the respiratory complications and will be a key factor in assessing the indication for noninvasive ventilation (NIV) and its subsequent tolerance.

As respiratory muscles become weaker, patients will often develop dyspnea and orthopnea.[12] Additionally, progressive limb weakness can make simple tasks effortful, which can further worsen dyspnea and fatigue. Clinicians need to be aware of the need to elicit more subtle symptoms of respiratory muscle insufficiency, such as disturbed sleep, morning headache, excessive daytime somnolence, orthopnea, and fatigue. As respiratory muscle weakness progresses, patients develop a restrictive ventilatory pattern, which can lead to hypoventilation with hypoxic and hypercarbic respiratory failure. Patients frequently develop atelectasis as the disease progresses, which worsens pulmonary shunt and hypoxia. The combination of inspiratory muscle weakness, expiratory muscle weakness, and poor glottic function makes coughing ineffective; patients have difficulty clearing respiratory secretions and can develop mucous plugging and pneumonia. Bulbar weakness makes swallowing difficult, and patients frequently develop aspiration pneumonia.

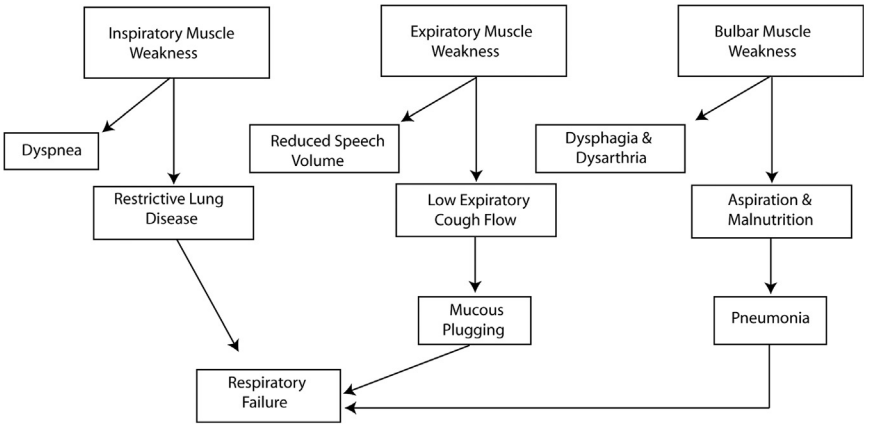

Fig. 1. The major respiratory abnormalities that develop in ALS.