Evaluation and Management of Amyotrophic Lateral Sclerosis

Nojan Valadi, MD

KEYWORDS

• Amyotrophic lateral sclerosis (ALS) • Motor neuron disease (MND)
• Neurodegeneration • Diagnostic criteria • Neuromuscular disease

KEY POINTS

- Consider amyotrophic lateral sclerosis (ALS) and motor neuron disease in patients who have upper and/or lower motor weakness without sensory problems (eg, extensor plantar responses plus atrophy and fasciculations).
- Consider ALS in patients with combined upper and lower motor neuron signs plus weakness in facial muscles.
- Obtain MRI of the brain and cervical spine, as well as electrodiagnostic and laboratory studies to exclude other diseases.
- Consider treatment options with supportive measures (multidisciplinary support to help cope with disability; drug treatment for symptoms such as spasticity, cramps, and pseudobulbar affect).

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a neurodegenerative motor neuron disease (MND) that results in progressive neuromuscular weakness. ALS, also known as "Lou Gehrig's disease," after the famous baseball player with the disorder, is the most common MND. Although most MNDs affect only the lower motor neurons, ALS can affect both upper motor neurons in the motor cortex in the brain and lower motor neurons in motor nuclei in the anterior horn of the spinal cord and the cranial nerve nuclei in the brainstem. Other MNDs are listed in **Table 1**, of which ALS is most common. The clinical presentation is typically one of atrophy, weakness, and fasciculations of muscles involved, all signs of lower motor neuron involvement

Disclosures: The author has no relationship with any commercial company that has a direct financial interest in the subject matter or materials discussed in the article.
St. Francis Neurology, 2300-A Manchester Expressway, Suite 201, Columbus, GA 31904, USA
E-mail address: nvaladi@gmail.com

Prim Care Clin Office Pract 42 (2015) 177–187
http://dx.doi.org/10.1016/j.pop.2015.01.009 **primarycare.theclinics.com**
0095-4543/15/$ – see front matter

Table 1
Motor neuron diseases

Motor Neuron Diseases	Upper Motor Neuron Involved	Lower Motor Neuron Involved
Amyotrophic lateral sclerosis	Yes	Yes
Primary lateral sclerosis	Yes	No
Progressive muscular atrophy	No	Yes
Progressive bulbar palsy	No	Yes
Spinal muscular atrophy	No	Yes
Spinobulbar muscular atrophy (Kennedy disease)	No	Yes
Poliomyelitis	No	Yes
Postpolio syndrome	No	Yes
Multifocal motor neuropathy	No	Yes

together with involvement of cranial nerves that can cause speech and swallowing difficulties. The diagnosis is made based on clinical suspicion and confirmed with supportive testing. Imaging and genetic or infectious disease laboratory tests can either confirm or rule out specific differential diagnoses or mimics. Much can be done in supportive care for patients with ALS, but ALS is a progressive and fatal disease in which patients typically suffer respiratory failure. Treatment options at this time are very limited.

EPIDEMIOLOGY

Incidence and Prevalence

The incidence of ALS in Europe and North America is between 1.5 and 2.7 per 100,000 per year, with a prevalence of 2.7 to 7.4 per 100,000 and an overall lifetime risk of developing the disease of 1:400.[1,2] Men have a higher incidence (3.0 per 100,000 person-years; 95% confidence interval (CI) 2.8–3.3) than women (2.4 per 100,000 person-years; 95% CI 2.2–2.6), although the incidence between men and women is about the same in familial disease.[1] Roughly 20,000 Americans currently have ALS and another 5000 people are diagnosed with the disease annually. The disease onset peaks between ages 58 and 63 for sporadic ALS with a mean age of onset at 56, and that of familial ALS being approximately 10 years earlier.[1] Average disease duration from onset of symptoms is approximately 3 years, but it can vary significantly. ALS is familial in 5% to 10% and sporadic in 90% to 95% of cases.[3]

Risk Factors and Genetics

Age and family history, as well as smoking, seem to be risk factors for the disease.[4,5] There are weak or conflicting data for other risk factors, including exposure to welding or soldering, exposure to heavy metal, military service, agricultural work, heavy manual labor, repetitive muscle use, work in the plastics industry, playing professional soccer, trauma, and electrical shock.[6–10]

Several genes have been identified in families with ALS and in some patients with sporadic ALS. These include mutations the *SOD1*, *FUS*, *OPTN*, *SETX*, *ANG*, *TARDBP*, *C9ORF72*, *SQSTM1*, and *ANG* genes.[11–19] *SOD1* accounts for 20% of familial ALS, causing a toxic gain of function with an autosomal dominant penetrance. Expansions