Quick Recertification Series

DANIELLE KRUGER, PA-C, MS

AMYOTROPHIC LATERAL SCLEROSIS

GENERAL FEATURES

- Amyotrophic lateral sclerosis, also known as *Lou Gehrig disease*, is the most common degenerative disease of the motor neuron system. The condition is characterized by loss of upper and lower motor neurons (UMNs/LMNs) while sparing other neurons; it progresses rapidly and is fatal.
- Males have predilection for the disease until after age 65 to 70 years, when incidence in males and females becomes equal. Whites are affected more than nonwhites. The peak age of onset is between 55 and 75 years.
- *Familial ALS* is genetically transmitted, and 5% to 10% of patients have autosomal dominant inheritance.
- *Sporadic ALS* is an idiopathic degeneration of UMN and LMNs; elevated levels of excitatory glutamate have been found in serum and CSF. It is theorized that high levels are toxic. Approximately 90% of affected patients have sporadic ALS.

CLINICAL ASSESSMENT

- Lou Gehrig disease is characterized by a gradual loss of function or slowly progressive weakness in the arms, legs, diaphragm, and cranial nerves.
- The classic finding in an involved limb is a combination of UMN and LMN dysfunction.
  - UMN symptoms: increased tone/spasticity and hyperreflexia, abnormal reflexes (Babinski sign, jaw jerk)
  - LMN symptoms: progressive muscle weakness, atrophy and fasciculation, depressed reflexes
- Limb weakness is the most common manifestation and may begin in either the arms or legs as focal or asymmetric symptoms. Later, all limbs are affected. Other common findings include
  - Reduced finger dexterity/clumsiness, weakness and atrophy of hand muscles
  - Muscle fasciculation (particularly of the tongue) or cramping, myalgias, joint pain, and contractures
  - Wrist or foot drop, difficulty walking, stumbling, slapping gait
- Bulbar symptoms manifest in 20% of cases and include dysphagia, drooling, dysarthria, and hoarseness.
- Pseudobulbar affect, a neurologic disorder that involves emotional lability, involuntary laughing, crying, and depression, is possible.
- The neurons are remarkably sensitive to cell death. The extraocular muscles, sphincters, autonomic functions, bowel and bladder, cardiac and smooth muscle, cognition, hearing, vision, and sensation are spared. No sensory deficit occurs.
- Respiratory muscles and vocal cords are affected late in the disease process and necessitate ventilatory support.
  - Median survival is 3 to 5 years following the onset of weakness.
  - Hypoxia and cardiac arrhythmias are the most common causes of death in patients with ALS.

DIAGNOSIS

- No specific laboratory test can identify ALS.
- El Escorial criteria for diagnosis of ALS require the following:
  - Evidence of LMN degeneration during clinical, electrophysiologic, or neuropathologic examination
  - Evidence of UMN degeneration during clinical examination
  - Progressive spread of symptoms or signs within a region or to other regions, as determined by history or examination
- CT or MRI of the brain and spinal cord should be obtained to rule out the differential diagnosis of UMN and/or LMN disease.
- Nerve conduction studies indicate the potential for widespread denervation and fibrillation.
- Muscle biopsy will show grouped atrophy.
- Forced vital capacity is a sensitive indicator of respiratory muscle weakness.

TREATMENT

- In patients with Lou Gehrig disease, treatment focuses on patient education in combination with the following adaptive and supportive treatments:
  - Riluzole (Rilutek), a glutamate pathway antagonist that prolongs tracheostomy-free survival by 2 to 3 months
  - Noninvasive or invasive ventilatory support, percutaneous

>>QUESTIONS<<

1. A 56-year-old male with no significant past history presents with complaints of bilateral weakness in the arms and legs that had progressively worsened over the past 3 months. Which of the following clinical manifestations does not support a diagnosis of ALS?

a. Muscle fasciculation
b. Ataxia
c. Extraocular muscle weakness
d. Hyperactive deep tendon reflexes
e. Muscle atrophy

2. Which of the following is a bulbar symptom of ALS?

a. Dysphagia
b. Tongue fasciculation
c. Spasticity
d. Jaw jerk reflex

For answers, please see the online version of this article at www.jaapa.com

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endoscopic gastrostomy (PEG)
- The primary cause of death among patients who elect to use ventilatory support is pulmonary infection.

MULTIPLE SCLEROSIS

GENERAL FEATURES

- Multiple sclerosis (MS) is a recurrent autoimmune, inflammatory, demyelinating, CNS disease involving selective destruction of the myelin sheath of the optic nerve and white matter of the cerebellum, brain stem, basal ganglia, and spinal cord.
  - The disease spares gray matter and the peripheral nervous system.
  - Nerve conduction delay or block is worsened with increased body temperature caused by fever, hot shower or bath, or food.
  - MS is an immunologic disorder with antibodies to myelin basic protein (MBP) in the blood and CSF; it involves T-cell dysfunction.
- Pathologic hallmark is inflammation and demyelination-remyelination, in which lesions evolve into chronic, burned-out plaques.
  - Underlying axonal transections may occur during acute exacerbations, resulting in permanent clinical disability.
- MS affects genetically susceptible individuals with the HLA-DR2 serotype who were exposed to an environmental trigger (ie, viral or geographic).
  - The disease is more common in patients who are geographically far from the equator.
  - Risk is entirely associated with time spent in a temperate climate (ie, Northern Europe) during childhood (< age 15 years).

Danielle Kruger is an industrial professor at the Saint John's University PA program, Queens, New York. She also works in the emergency department at Coney Island Hospital, Brooklyn, New York. The author has indicated no relationships to disclose relating to the content of this article.

- Females are affected more than males (3:2), and whites are affected twice as often as nonwhites. The peak age of onset is between 18 and 45 years.
  - Males present for evaluation of the condition 1 to 2 years later than females and have greater tendency for the primary progressive subtype at onset.

CLINICAL ASSESSMENT

- Symptoms are variable and can include sensory, motor, autonomic, cerebellar, and cognitive/psychiatric dysfunction.
  - Transient sensory loss is the most common initial finding.
- Other symptoms include numbness, paresthesias, fatigue (70%), muscle weakness and cramping, upper motor neuron symptoms (ie, spasticity, hyperreflexia, Babinski sign), scanning speech, dysphagia, dysarthria, ataxia, intention tremor, bowel, bladder issues (ie, urinary retention, constipation), and sexual dysfunction.
  - Psychocognitive symptoms can also occur, including depression and altered attention span, concentration, memory, and judgment.
- Optic neuritis that involves unilateral visual blurring, decreased acuity and color perception, flashes of light, and scotomas is the initial manifestation in 15% to 20% of cases. Approximately 90% of patients experience complete recovery within 8 to 12 weeks, with 20% to 35% experiencing recurrence.
- *Internuclear ophthalmoplegia*, a disorder of conjugate lateral gaze in which eye movement reveals impaired adduction and abduction with nystagmus, can be present. This disorder can lead to diplopia.
- *Lhermitte sign*, neck flexion that results in an electric shock-like feeling in the torso or extremities, is also possible.

>>QUESTIONS<<

1. The classic finding of internuclear ophthalmoplegia (INO) is caused by a lesion in which part of the brain?

a. Basal ganglia
b. Primary motor cortex
c. Cerebellum
d. Medial longitudinal fasciculus
e. Hippocampus

2. Which of the following is not a typical manifestation of MS?

a. Weakness in the lower extremities
b. Ascending paralysis
c. Spasticity
d. Ataxia
e. Nystagmus

For answers, please see the online version of this article at www.jaapa.com

CATEGORIES OF MS

- **Relapsing-remitting**
  - Seventy percent of affected patients experience these acute exacerbations, which last weeks to months with gradual, full, or partial remissions.
  - 20% to 35% of patients experience complete or nearly complete recovery of acute exacerbation within 8 weeks, particularly when it occurs early in the disease course.
- **Primary progressive**
  - These patients experience a gradual decline and accumulated disability without remission; they also have less visual, more axonal involvement.
- **Secondary progressive**
  - Relapsing-remitting patients eventually enter this stage of continuous deterioration.

DIAGNOSIS

- No specific laboratory test can identify MS.
- MRI with gadolinium will show multiple asymmetric plaques with characteristic periventricular distribution.
- CSF analysis reveals mononuclear

pleocytosis, elevated protein, normal glucose, elevated immunoglobulin G antibodies with oligoclonal bands, and increased myelin basic protein levels.
- Visual, auditory, and somatosensory evoked potentials are helpful for assessing nerve transmission.
- Revised McDonald criteria for MS include the following: ≥2 episodes of ≥2 signs (imaging/clinical) that reflect pathology in anatomically noncontiguous white matter tracts of the CNS.

TREATMENT

- IV steroids are given for acute exacerbations.
- Supportive treatment focuses on controlling the precipitants of exacerbation; aggressive treatment of infections and/or fever; medications for spasticity (baclofen [Lioresal Intrathecal]), urinary symptoms (self-catheterization), constipation, and mood disorders; and skin care.
- In relapsing form, interferon beta-1a (Avonex, Rebif) or interferon beta-1b (Betaseron) can slow the accumulation of disability and decrease the frequency of clinical exacerbations.
- Glatiramer acetate (Copaxone), a synthetic myelin basic protein that mimics myelin to alter T-cell destruction of CNS protein, can reduce relapse frequency in relapsing form.

PROGNOSIS

- Untreated, more than 30% of patients will develop significant physical disability within 20 to 25 years of onset.
- Disease-modifying agents may slow the progression of disability.
- Male patients with primary progressive MS have the worst prognosis, with a less favorable response to treatment and rapidly accumulating disability. Life expectancy is shortened slightly, and mortality is linked to disability and secondary complications such as pulmonary embolus or pneumonia. JAAPA

Dawn Colomb-Lippa, MHS, PA-C; Amy M. Klingler, MS, PA-C, department editors