

# PRACTICE

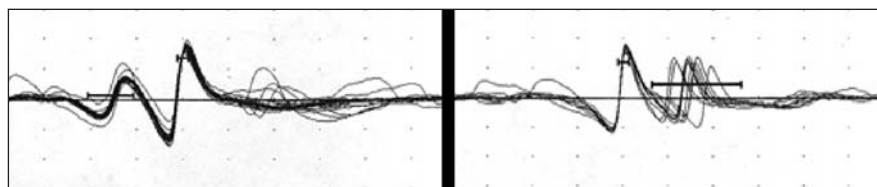
## TEACHING CASE REPORT

### An adult patient with new-onset dysphagia

**The Case:** A 70-year-old man came to the emergency department with a complaint of dysphagia of acute onset. He reported a similar episode a week earlier that had resolved without treatment.

His history included mild cognitive impairment, a remote-left-hip arthroplasty, hip and knee osteoarthritis, and a recent hospital admission for a pelvic fracture that had not required surgical correction. His only medication was acetaminophen. There was no family history of neurologic or autoimmune disorders. The patient denied any diplopia or focal weakness.

Physical examination revealed a healthy-seeming man with a normal heart rate and blood pressure. Cranial nerve examination failed to disclose fatigable diplopia or ptosis. His muscle strength and bulk were normal in both upper and lower extremities. His reflexes were symmetric; plantar response was downgoing. Sensory modalities were intact.



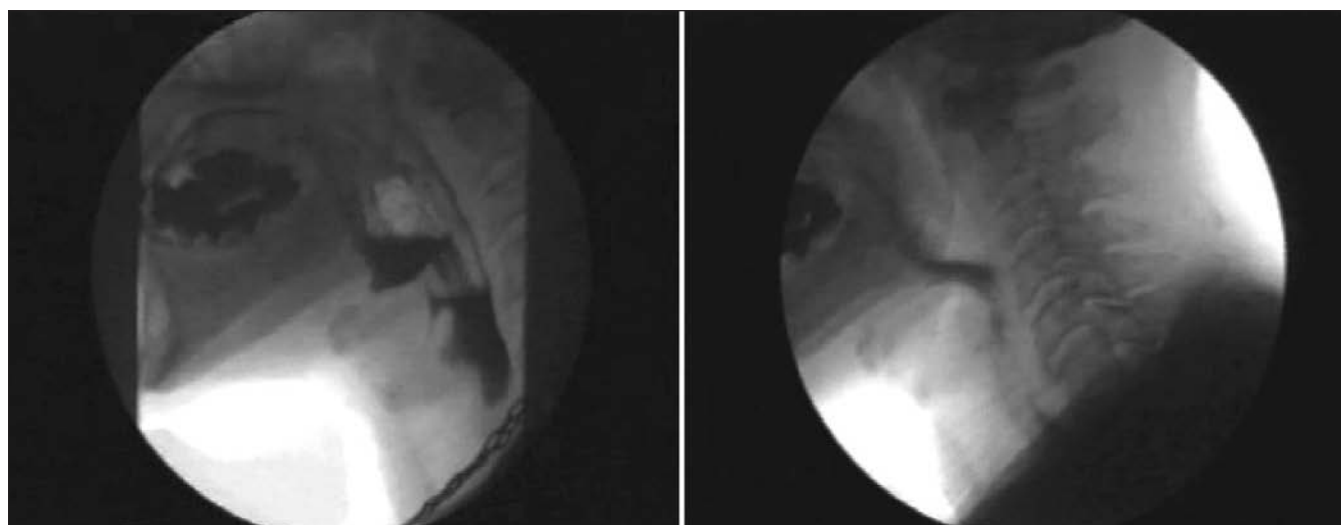
**Fig. 2:** SFEMG (single-fibre electromyography) of a normal control (left) and our patient with myasthenia gravis. Increased variability (known as “jitter”) in our patient (right) was consistent with a neurotransmission abnormality.

Clinical swallowing trials showed signs consistent with a pharyngeal dysphagia, including multiple secondary swallowing efforts, nasal regurgitation, an occasional gurgling voice after swallowing, and frequent throat clearing and coughing during and after swallow trials. Abnormal oral motor findings included fluctuating hypernasality and occasional blocking dysfluencies — sharp interruptions of airflow or phonation that impaired speech. MRIs of the brain and brainstem appeared normal.

The patient underwent videofluorography before and after receiving edrophonium (Tensilon) intravenously. Edrophonium is a short-acting anticholinesterase that prolongs the presence of the neurotransmitter acetylcholine at the neuromuscular junction.

Videofluoroscopic assessment after its administration revealed a dramatic improvement in swallow function (Fig. 1; a video is available at [www.cmaj.ca/cgi/content/full/175/10/1203/DC1](http://www.cmaj.ca/cgi/content/full/175/10/1203/DC1)). Striking improvements were noted in all parameters, including velopharyngeal closure, base-of-tongue retraction, epiglottic deflection and pharyngeal propulsion. No laryngeal penetration was seen.

These dramatic improvements subsided quickly: swallow trials repeated 4–5 minutes after the edrophonium administration revealed a rapid re-emergence of severe pharyngeal dysphagia. Single-fibre electromyography (SFEMG) confirmed the presence of a neurotransmission dysfunction consistent with myasthenia gravis (Fig. 2). CT



**Fig. 1:** Imaging results during the Tensilon test. Videofluorographs before (left) and immediately after an intravenous administration of 10 mg of edrophonium. The patient's swallowing mechanism showed a rapid and complete recovery in all aspects (right) after receiving the acetylcholinesterase inhibitor. Because edrophonium is a short-acting, the response is transient and useful only as a test.

scans of the patient's chest and mediastinum revealed no abnormalities.

The patient was given a course of oral pyridostigmine, to which he had a partial response. Prednisone was added to the regimen, after which his swallowing returned to normal. Six months after the initial diagnosis, the patient is symptom-free; an attempt to taper the steroid is currently underway.

Myasthenia gravis (MG) is an uncommon autoimmune disease (Box 1) in

which IgG antibodies directed against the acetylcholine receptors at the neuromuscular junction prevent normal muscle contraction and lead to muscle weakness. Originally described (or thought to be described) in a patient with dysarthria, MG is now thought of as the classic autoimmune disease.<sup>1</sup>

The thymus is probably involved in the pathogenesis of MG;<sup>1</sup> thymic tumours should therefore be excluded. Between 30% and 60% of patients with epithelial thymic tumours (thymoma) have MG and, in turn, some 10%–15%

of people with MG have thymoma. Their relationship has yet to be fully elucidated, although the initial steps in the pathogenesis of MG in most cases take place within abnormal thymic microenvironments, whether inflammatory or neoplastic. In about 90% of patients, no cause can be identified.

The classical presentation includes a myasthenic “snarl” and a voice that sounds nasal because of bulbar and facial muscle weakness (Box 2; Table 1). Dysphagia is the only manifestation of MG that has been well documented:<sup>2</sup>

**Table 1:** Similar-seeming conditions to consider during the differential diagnosis of suspected myasthenia gravis

Condition	Distinguishing features
<b>Ocular/bulbar myasthenia</b>	
Brainstem stroke or lesion	<ul style="list-style-type: none"> <li>• Acute onset; persistent symptoms</li> <li>• Upper-motor-neuron signs, other signs of pseudo-bulbar palsy</li> </ul>
Multiple sclerosis	<ul style="list-style-type: none"> <li>• Relapsing-remitting symptoms at different times and anatomic locations</li> <li>• Onset is rare in people &gt; 60 years of age</li> <li>• Sensory symptoms are common</li> <li>• Classic findings include internuclear ophthalmoplegia, optic neuritis</li> <li>• Typical MRI findings include T2 hyperintensities in the periventricular and subcortical white matter, corpus callosum, brainstem or cerebellum</li> </ul>
Thyroid ophthalmopathy	<ul style="list-style-type: none"> <li>• Proptosis</li> <li>• Absence of ptosis</li> <li>• No fluctuations in diplopia</li> <li>• Enlargement of extraocular muscles (visible via MRI or CT scan)</li> </ul>
Leptomeningeal process causing cranial nerve palsies*	<ul style="list-style-type: none"> <li>• Presenting symptoms often include fever, headache, change in mental status, weight loss</li> </ul>
Oculopharyngeal muscular dystrophy	<ul style="list-style-type: none"> <li>• Extraocular muscles not usually involved</li> <li>• Autosomal dominant disorder: strong family history</li> </ul>
Mitochondrial disease: chronic progressive external ophthalmoplegia	<ul style="list-style-type: none"> <li>• Typical lack of diplopia despite profoundly limited extraocular movement</li> <li>• Slowed saccades</li> <li>• Positive family history</li> <li>• Systemic involvement (diabetes, short stature, etc.)</li> </ul>
<b>Generalized myasthenia</b>	
Amyotrophic lateral sclerosis (ALS)	<ul style="list-style-type: none"> <li>• Progressive disease with upper- and lower-motor-neuron features: muscle weakness, wasting and fasciculations, hyperreflexia, spasticity</li> <li>• No ocular involvement</li> </ul>
Lambert-Eaton syndrome	<ul style="list-style-type: none"> <li>• Areflexia or hyporeflexia that can transiently improve after brief activation of muscles (e.g., knee extension)</li> <li>• No involvement of ocular or bulbar muscles</li> <li>• Autonomic dysfunction may be present</li> <li>• Commonly associated with small-cell lung cancer</li> <li>• Repetitive 20-Hz nerve stimulation or 10-s maximal exercise incrementally and markedly increases compound muscle action potential (CMAP) amplitude</li> </ul>
Botulinism	<ul style="list-style-type: none"> <li>• Symptoms begin 12–36 hours after ingestion of foods improperly canned/preserved/stored</li> <li>• Descending paralysis (i.e., progressive muscle weakness that first affects muscles innervated by the cranial nerves, then descends to include the muscles of respiration, etc.) with a rapid onset</li> </ul>
Congenital myasthenic syndrome	<ul style="list-style-type: none"> <li>• Onset in infancy/early childhood (usually &lt; 2 years old)</li> <li>• Strong family history of muscle weakness</li> <li>• No response to acetylcholinesterase inhibitors</li> </ul>

\*E.g., leptomeningeal carcinomatosis, tuberculous or fungal meningitis.

about 20% of cases involve the bulbar muscles. MG can be diagnosed by means of serology, nerve conduction studies with SFEMG, or the classic Tensilon test. Since about 85% of patients with generalized disease will have antibodies to the acetylcholine re-

ceptor, a positive result is diagnostic for MG; unfortunately, this test is not routinely available.

A long-acting oral anticholinesterase such as pyridostigmine is the first line of treatment. Immunosuppression with prednisone is used when symptom improvement is inadequate; azathioprine or mycophenolate mofetil can also be added. Thymectomy is considered for all patients younger than 55 years who have generalized myasthenia or a resectable thymoma. Plasmapheresis and intravenous immune globulin therapy are reserved for acute exacerbations, when the need is for a rapid benefit.

This case demonstrates the importance of considering neurotransmitter

diseases in the approach to new-onset focal weakness that involves the bulbar musculature. MG was diagnosed in our patient, who presented purely with swallowing abnormalities, via videofluorography during a Tensilon test.<sup>3</sup> This novel diagnostic approach should be considered for patients with suspected bulbar MG.

#### Kieran McIntyre

Department of Medicine

University of Toronto

#### Simon McVaugh-Smock

Department of Speech Language

Pathology

St. Michael's Hospital

#### Ophyr Mourad

Department of Medicine

University of Toronto

Division of General Internal Medicine

St. Michael's Hospital

Toronto, Ont.

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#### Box 1: Incidence patterns of myasthenia gravis for age, sex

- Estimated annual incidence, per 100 000 population: 0.25-2.0
- Incidence rises with old age
  - Increase is especially evident among men in their 60s
  - Women have 2 incidence peaks, at ages 20-40 and 70+ years

#### Box 2: Symptoms and signs of myasthenia gravis

- Acute or subacute symptom onset
- Fluctuating ptosis and diplopia are the most common presenting symptoms
- Muscle fatigability and weakness, usually of the eye, the proximal limb, or both
  - When the eye is involved, the orbicular muscles tend to be the ones affected
  - Distal limb weakness, when present, most frequently affects the finger extensors
  - Muscle weakness is often asymmetric
- Difficulty chewing or swallowing; nasal regurgitation of liquids
- Slurred or nasal speech
- No sensory involvement
- Improvement in symptoms after waking or rest, and worsening late in the day or after prolonged use
- Occasional spontaneous remission

#### REFERENCES

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