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CASE REPORT | ESOPHAGUS

High-Resolution Esophageal Manometry in Myasthenia Gravis

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ABSTRACT

Myasthenia gravis (MG) is an autoimmune disease that affects the postsynaptic membrane at the neuromuscular junction. In MG, antibodies bind to acetylcholine receptors inducing muscle weakness. The weakness typically increases with exercise and repetitive muscle use. Improvement of muscular weakness after rest and/or administration of anticholinesterase drugs (edrophonium) are characteristic of MG. We report a patient with unexplained dysphagia, dysphonia, and dysarthria, whose diagnosis was suggested by high-resolution esophageal motility and edrophonium infusion. We highlight the importance of dysphagia as presenting or dominant symptom in MG and review the esophageal motility findings in this rare, but treatable disorder.

INTRODUCTION

Myasthenia gravis (MG) is an autoimmune disease that affects the postsynaptic membrane at the neuromuscular junction, causing muscle weakness.[1,2] Clinical features vary according to the muscle system involved: ocular (ptosis and diplopia), bulbar (dysarthria, dysphagia, and dysphonia), facial (eyelid closure issues), or limb (proximal muscles and arms greater than legs).[3] We report a patient who presented with unexplained dysphagia and dysphonia referred to our laboratory for high-resolution esophageal motility (HREM). The motility study suggested the diagnosis of MG, which was confirmed by subsequent neurological testing. We highlight the importance of the unusual presentation of MG with dysphagia and draw attention to HREM findings of this case.

CASE REPORT

A 64-year-old man was referred to our motility laboratory for evaluation of unexplained dysphagia to solids and liquids for 3 months. He also noted variable dysphonia and speech difficulties but no additional symptoms. He had no medical history and was not taking any medications. Complete blood count, renal, liver, thyroid testing, and serum electrolytes were normal. An esophagogram and an upper endoscopy revealed a small hiatal hernia, otherwise was normal. Findings during HREM included weak upper esophageal sphincter (UES) and basal pressure 13.7 mm Hg (NL = 26.3–85.1 mm Hg, Figure 1). After the first swallow, a large (>5 cm) peristaltic break in the proximal (skeletal) muscle was noted; otherwise, esophageal parameters were normal (Figure 2). After several swallows, there was progressive muscle fatigue involving the UES, pharynx, and esophagus (Figure 3). Edrophonium infusion restored all peristaltic parameters except for the peristaltic breaks (Figure 4). Given the HREM findings, further neurological testing included positive median nerve stimulation (progressive decline > 10% in the compound muscle action potential amplitude with the first 5 stimuli) that confirmed myoneural junction disease.[4] The tested muscles were reported weak by the examining neurologist. The diagnosis of MG was subsequently established by high-titer acetylcholinesterase receptor antibodies (Ach-Ab) (83 nmol/L, NL = 0–0.5 nmol/L).[3,4] Computed tomography of the chest did not show a thymoma. The patient was treated with azathioprine and pyridostigmine, which resulted in significant clinical improvement. He was offered a repeat HREM but declined.

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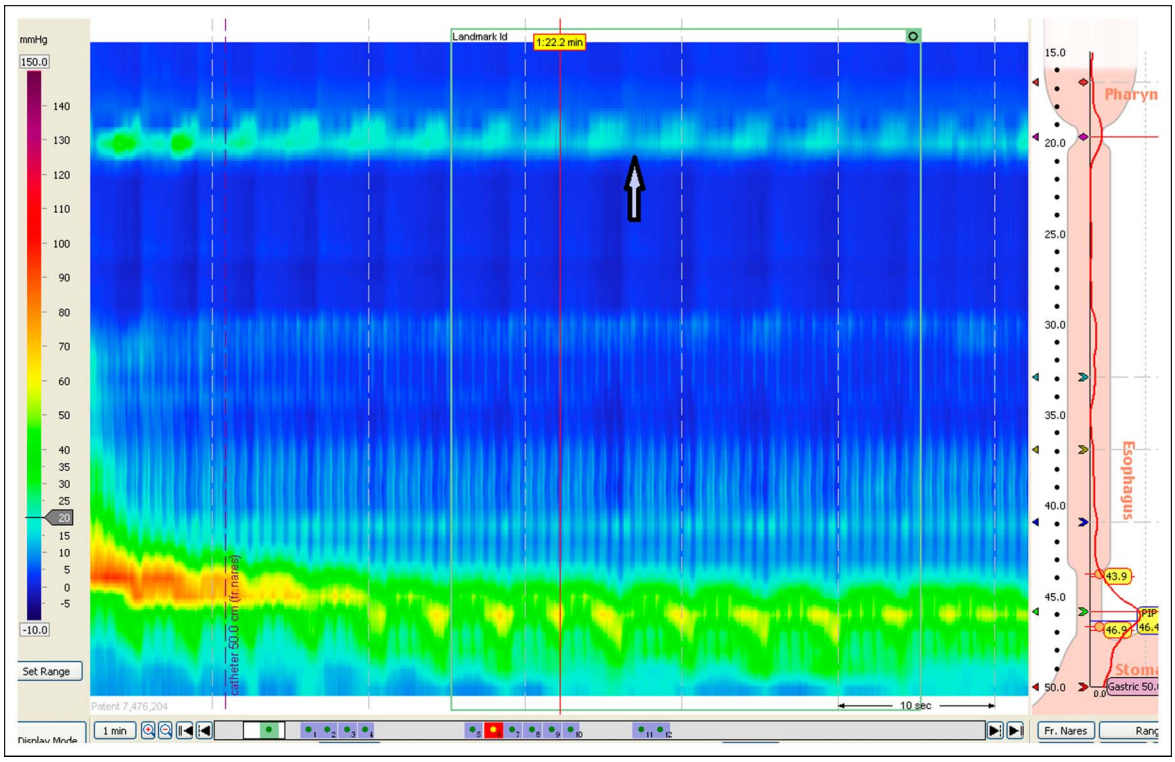

Figure 1. Landmark (baseline) tracing. The arrow shows the weak basal upper esophageal sphincter pressure (light green-blue color on the high-resolution esophageal motility scale) of 13.7 mm Hg (normal 26–3–85.1 mm Hg). The gastroesophageal junction area appears in green/yellow at the bottom of the tracing.

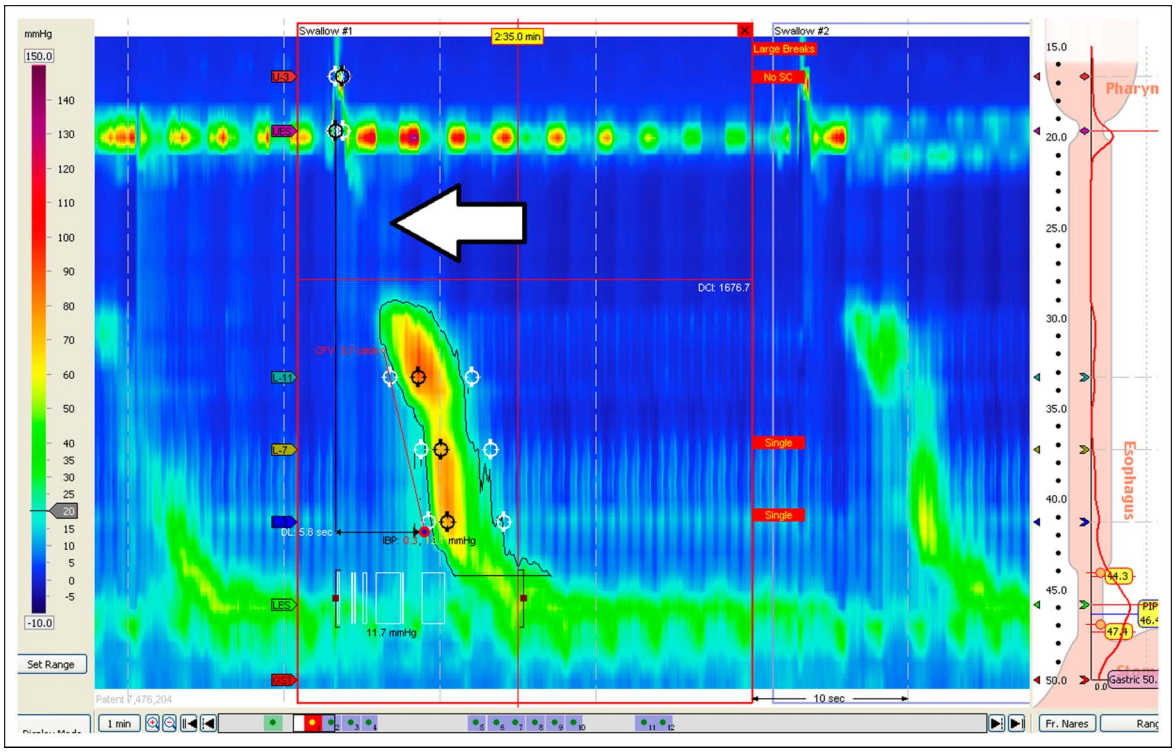

Figure 2. Swallow #1 representing normal esophageal motility findings except for a large peristaltic break > 5 cm in proximal (skeletal) muscle (arrow). Integrated relaxation pressure 11.7 (NL = ≤15 mm Hg), distal contraction integral 1,676.7 mm Hg-cm-s (NL = 450-7,999 mm-Hg-cm-s), and distal latency 5.8 sc (NL = ≥4.5 sc).

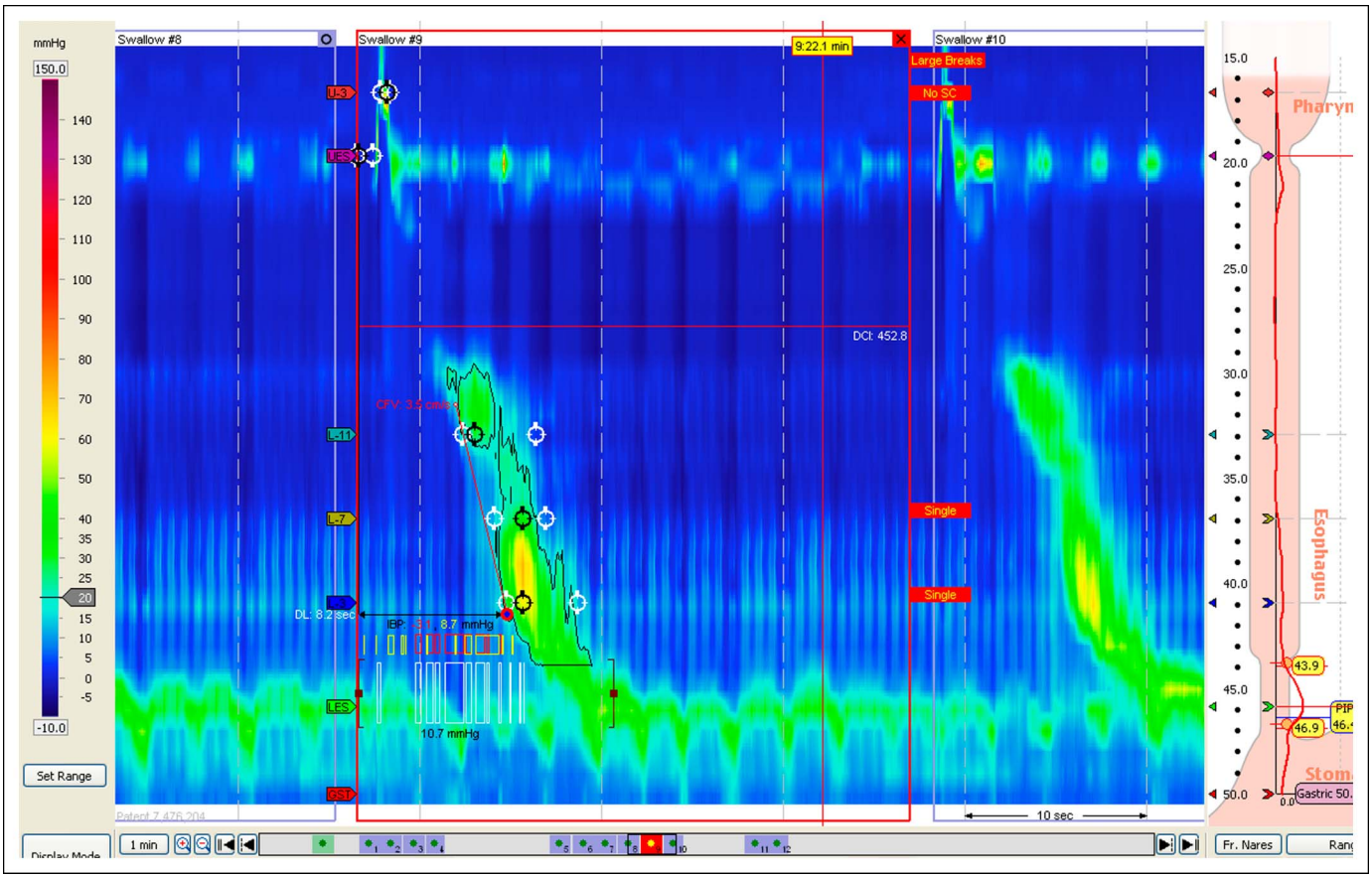

Figure 3. Swallow #9 in which substantial fatigue can be observed (demonstrated by the cooler green-blue color contour in the high-resolution esophageal motility) in the upper esophageal sphincter and pharyngeal and esophageal contractions. When compared with swallow #1, upper esophageal sphincter basal pressure decreases from 26 mm Hg to 0.4 mm Hg, pharyngeal contraction is reduced from 121.1 to 71 mm Hg, and DCI decreased from 1,676.7 mm Hg-cm-s to 452.8 mm Hg-cm-s. Note persistent peristaltic break > 5 cm in skeletal muscle.

DISCUSSION

There is limited available information about esophageal involvement in MG, and to our knowledge, there are no previous reports of HREM in MG. We describe a patient referred for HREM for unexplained dysphagia whose findings suggested the diagnosis of MG confirmed by additional neurological testing. We review the pertinent literature about MG presenting with dysphagia and the outcome of previous studies on esophageal motility testing in this condition. We underscore the need for gastroenterologists to consider this uncommon, but treatable disorder in patients with undiagnosed dysphagia.

MG is a rare disease but the most common disorder of the neuromuscular junction.[3] The estimated annual incidence is 8 to 10 cases per 1 million persons, with a prevalence of 150 to 250 cases per 1 million.[5] MG can involve any striated muscle group, especially those innervated by oropharyngeal or laryngeal musculature causing dysarthria, dysphonia, or dysphagia.[1–3,6] The diagnosis of MG is based on the combination of relevant symptoms and signs, abnormal neurophysiological tests (electromyographic), and a positive test for specific autoantibodies (Ach-Ab).[4,7]

Our patient was referred for esophageal motility testing primarily for the evaluation of unexplained dysphagia. Dysphagia can be the dominant or presenting symptom in MG.[8] In one study of 1,036 patients with MG, 6% presented exclusively with dysphagia.[9] In another investigation, nearly 17% of patients with MG had their initial symptoms referable to oropharyngeal muscles (dysphagia, dysphonia).[10.] Late-onset MG (occurring in the mid-60s, such as in our patient) often presents with bulbar symptoms, including dysphagia, dysphonia, and slurred speech.[11,12] A recent review of 30 MG cases involving the oropharynx/larynx found that the most frequent primary symptoms were dysarthria (14/30), followed by dysphagia (11/30), slurred speech (4/30), and dysphonia (1/30). Only 23% of patients were diagnosed with MG at the first clinic visit.[13] These findings underscore the need for gastroenterologists to be aware of MG as a cause of dysphagia.

There are few reports about esophageal motility testing in MG and, to our knowledge, none include HREM. Previous motility studies have described a spectrum of findings including decreased UES pressures and esophageal aperistalsis.[14] Other less detailed studies in a small number of patients (n = 3) noted

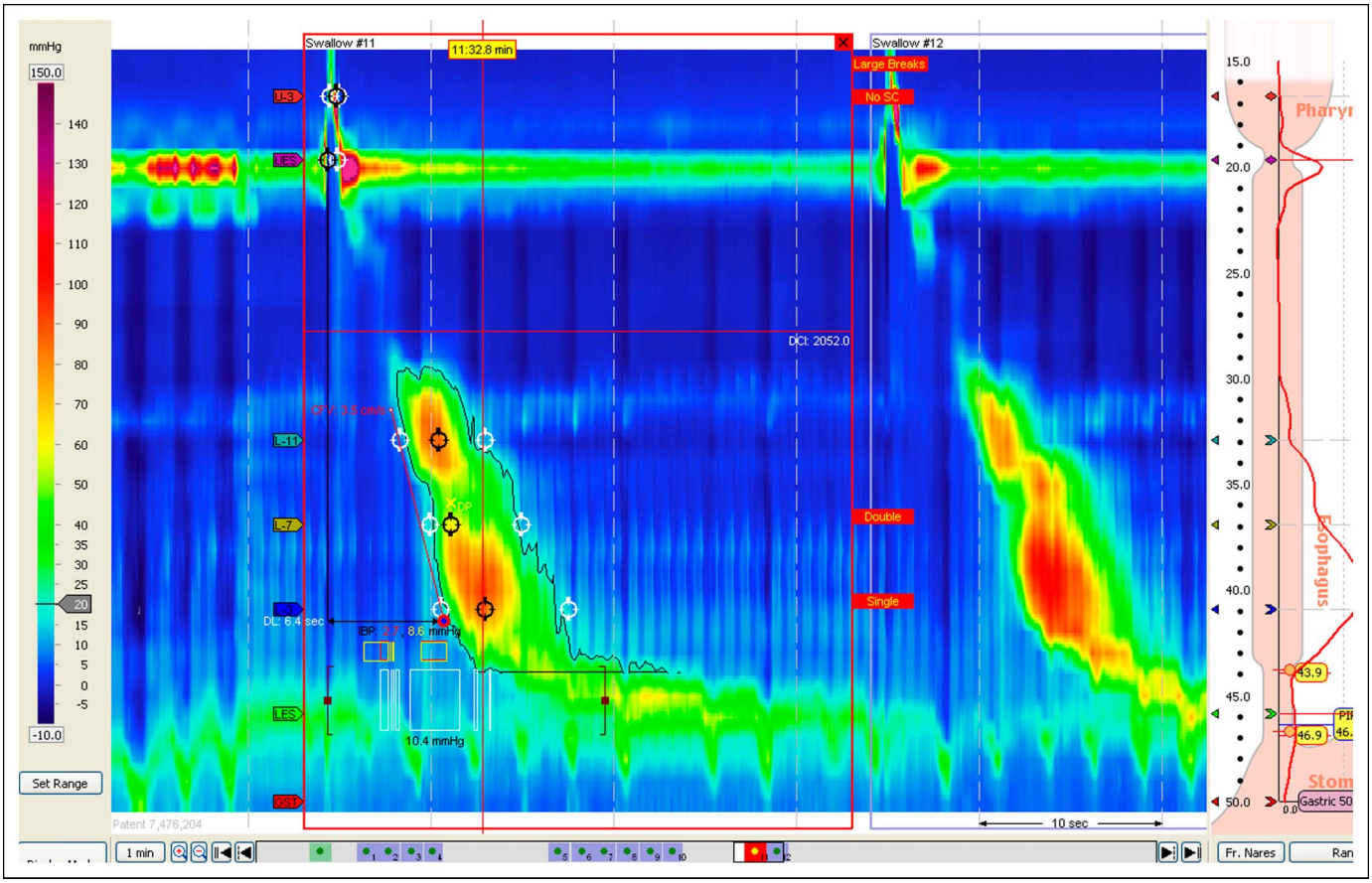

Figure 4. After administration of edrophonium (85 μ/kg IV) (swallow #11), the upper esophageal sphincter and pharyngeal and esophageal contractions are seen more clearly (notice yellow and red colors in the high-resolution esophageal motility scale). There is a marked increase in basal upper esophageal sphincter pressure to 51.6 mm Hg, pharyngeal contraction to 301 mm Hg, and distal contraction integral to 2,052 mm Hg-cm-s. There is persistent peristaltic break (>5 cm) in the proximal skeletal muscle, likely because of complete anticholinergic antibody blockade in this area of the esophagus.

"minimal decreased motility," "decreased motility," and "normal motility."[15] Llabrés et al in 2 patients found decreased UES pressures and esophageal amplitude, with a further reduction of esophageal amplitude after successive swallows.[8] In the largest study to date, 25 randomly selected Chinese patients with documented MG were compared with 20 controls. UES pressures and amplitude of esophageal peristalsis were significantly lower in MG. Up to 96% of the patients with MG had abnormal motility.[16] Our patient showed UES and pharyngeal and esophageal body pressures, which diminished after repeated swallows (muscle fatigue) and improved following edrophonium infusion. In addition, we noted persistent peristaltic breaks in the cholinergic innervated skeletal muscle, likely caused by complete acetylcholine receptor blockade in this segment of the esophagus. Muscular weakness in myasthenic patients typically worsens with the duration of mastication and swallowing.[15–17] Alleviation of muscular weakness and fatigability after rest and/or administration of anticholinesterase drugs (edrophonium) are consistent with MG.[16,17] Joshita et al reported that after edrophonium test, all 7 patients with MG developed increased swallowing pressures.[17] Our findings agree and confirm the observations of previous studies performed with traditional line systems.[8,14–17] Although typical involvement of MG includes the skeletal muscle, we and others found smooth muscle esophageal involvement.[8,14–16,18,19] The exact explanation for the involvement of the esophageal smooth muscle in MG is not entirely clear. Studies in human and animal models have identified atropine sensitive swallow-induced peristalsis, indicating that the final contraction of the esophageal smooth muscle is also related to intramural cholinergic stimulation.[20]

In summary, we present a patient with primarily unexplained dysphagia and dysphonia. HREM identified UES, pharyngeal, and esophageal contraction fatigue reversed partially by edrophonium. These findings raised the possibility of MG which was confirmed by electromyographic and high titers of Ach-Ab. We review the relevant studies of esophageal involvement in MG and previous reports describing the spectrum of esophageal motility findings in this condition. Gastroenterologists should be aware of dysphagia as a dominant or presenting feature of MG.

DISCLOSURES

Author contributions: G. Herrera-Quiñones and G. Torres-Barrera wrote the manuscript. SI Scharrer, DE Benavides-Salgado, and HJ Maldonado-Garza edited and revised the manuscript for intellectual content. SR Achem wrote the manuscsript and reviewed the literature. G. Torres-Barrera is the article guarantor.

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