Cranial Nerve IX and X Weakness: An Unusual Initial Presentation of Myasthenia Gravis

EF 1 Nikhita Balabbigari
EF 1 Jaskaran Purewal
EF 1 NFN Sakul
EF 2 Anam Purewal
EF 1 Vijaya Kankanala
E 1 Tiziana Califano

Patient: Female, 51-year-old
Final Diagnosis: Myasthenia gravis
Symptoms: Dysphonia • hoarseness
Medication: —
Clinical Procedure: —
Specialty: Critical Care Medicine • Neurology • Pulmonology

Objective: Challenging differential diagnosis
Background: Myasthenia gravis (MG) is an autoimmune disease characterized by antibodies binding skeletal muscle acetylcholine receptors (AChR). Rarely does the disease manifest with orolaryngeal symptoms before ocular ones. We present a case of MG that on initial presentation had symptoms of cranial nerves (CN) IX and X weakness, including dysphagia and dysphonia.

Case Report: A 51-year-old woman with panic attacks presented to the Emergency Department (ED) with complaints of her throat closing, swallowing difficulty, and hoarse voice. Multiple ED visits revealed no etiology. However, she developed stridor, which prompted further evaluation. Laryngoscopy and imaging studies revealed no gross abnormalities; therefore, her symptoms of dysphonia and difficulty breathing were attributed to anxiety. Her hospital course was complicated by a cardiac arrest requiring intubation. ECHO, CTA chest, and MRI brain were unremarkable. Her cardiac arrest was hypothesized as being secondary to laryngeal spasm. During her ICU course, she failed extubation multiple times due to acute respiratory failure. An autoimmune etiology was suspected, prompting a paraneoplastic screen, which revealed elevated levels of AChR antibodies at 124 mmol/L.

MG was diagnosed and treatment with plasmapheresis and steroids was initiated. However, complications of thrombocytopenia, anemia, and ARDS ensued, so MG treatment was discontinued. The patient was eventually transferred to a LTACH. Thereafter, at outpatient followup, her MG was treated with mycophenolate and prednisone, which led to significant symptom improvement.

Conclusions: MG commonly presents in the third decade with clinical features of ptosis, diplopia, and facial weakness. However, initial and isolated symptoms of dysphagia and dysphonia are rare, leading to missed diagnoses. Our case of a middle-aged woman posed a diagnostic challenge because of her uncommon presentation and co-morbidities of panic attacks and obesity. This case highlights the crucial need for a high index of clinical suspicion for MG in any patient presenting with symptoms of CN IX and X weakness.

MeSH Keywords: Autoimmune Diseases of the Nervous System • Dysphonia • Neuromuscular Junction Diseases • Receptors, Nicotinic

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Background

Myasthenia gravis is an autoimmune disease in which the body produces autoantibodies that bind to acetylcholine receptors on skeletal muscle, thus causing muscle weakness and fatigability [1]. Common presenting symptoms include involvement of the ocular system, resulting in ptosis and diplopia. When the bulbar system is involved, patients present with dysarthria, dysphagia, or dysphonia [1], occurring in approximately 15% of patients [10]. These symptoms commonly occur in the elderly and may be the only manifestations [2]. We discuss an unusual presentation of myasthenia gravis presenting with dysphagia and dysphonia in a middle-aged woman, posing a diagnostic challenge.

Case Report

A 51-year-old woman with a past medical history of severe anxiety and panic attacks presented to the ED multiple times for complaints of feeling her throat closing up, difficulty swallowing and speaking, and hoarseness in her voice. On her initial ED visit, she was sent home on azithromycin for a presumed upper-respiratory infection. She came back to the ED 1 week later with worsening symptoms and a new-onset rash. An allergic reaction to azithromycin was suspected and she was treated with epinephrine, diphenhydramine, and steroids, then was later discharged. Her dysphagia symptoms remained, leading to another ED visit, at which she reported persistent symptoms of difficulty breathing, throat closing, and occasional difficulty swallowing and speaking. She additionally reported progressive dysphagia to solids for 2–3 months, with intermittent hoarseness and stridor. Vitals were overall stable: afebrile (97.4°F [36.3°C]), BP 138/90, HR 88, saturating 100% on room air. A physical exam showed an obese female in no distress, with adequate airway entry bilaterally and equal chest expansion. Chem-7 and complete blood count panel values were all within normal range: WBC 7.85/nL, hemoglobin 14.7 g/dL, platelets 146/nL, sodium 143 mmol/L, potassium 3.2 mmol/L, chloride 105 mmol/L, carbon dioxide 29 mmol/L, BUN 15 mg/dL, creatinine 0.62, alkaline phosphatase 59 U/L, ALT 36 U/L, AST 13 U/L, and glucose 106 mg/dL. Results of a CXR were unremarkable. A CT scan of the soft tissue in her neck showed focal mucosal thickening within the sphenoid sinus, but otherwise no abnormalities. The nasopharynx, oropharynx, hypopharynx, glottis, and subglottic trachea were normal. ENT was called to further evaluate the patient. A bedside flexible fiberoptic laryngoscopy examination revealed fullness at the base of the tongue, with no evidence of asymmetry or obvious mass, posterior laryngeal edema suggestive of reflux disease, and pooling in the piriform sinuses suggesting poor swallowing. Her vocal cords were mobile bilaterally. There was no stridor and her airway appeared widely patent. At this time, given a previous history of Helicobacter pylori infection, abdominal pain, and progressive dysphagia, a gastrointestinal etiology for her symptoms was being considered. She was admitted to the general medical floors for further evaluation.

In the following days, several rapid responses were called. The evening following admission, she experienced chest tightness and difficulty breathing. An EKG was done and was not significant for any new changes. Her symptoms were believed at the time to be due to her severe anxiety, and lorazepam was ordered, with subsequent improvement in her symptoms. The same night, rapid response was called again, as she appeared lethargic, with an extremely faint voice, whispering “I can’t talk.” She received diphenhydramine for possible allergic reaction, and was placed on supplemental oxygen, saturating 100% on a 2-L nasal cannula. Psychiatric consultation was requested for further evaluation of acute anxiety. Her family members at bedside revealed a history of anxiety and panic attacks occurring in the past 2–3 years since the death of the patient’s mother. Family members described her attacks as sudden inability to speak and episodes of her throat closing up. At this time, the diagnosis of conversion disorder was considered.

On the third day of hospitalization, another rapid response was called. She was observed sitting at the edge of the bed after ambulating from the bathroom, but looked uncomfortable. She was pale and tachypneic with RR 40 and extremely faint voice. She suddenly lost consciousness without any palpable pulses. CPR was immediately started, she was intubated, and ROSC was quickly achieved with compressions only. An EKG after arrest showed ventricular bigeminy, 15 beats of ventricular tachycardia, and then 3 minutes of accelerated idioventricular rhythm. She was transferred to the ICU for further care. A cardiac etiology of her arrest was judged to be less likely. An echocardiogram showed normal LV and RV systolic function with no significant valvular abnormalities, and a cardiac catheterization done 3 months prior to presentation showed nonobstructive coronary arteries. Due to the sudden onset of shortness of breath, pulmonary embolism was also considered, but a CTA chest was unrevealing. An intracranial process was also considered due to her loss of consciousness, but a CT head was also unremarkable. Given the sequence of events and symptoms she experienced since admission, it was thought that she had laryngeal spasms causing significant hypoxia, thus resulting in cardiac arrhythmia.

The following morning, she was extubated and within minutes developed acute respiratory failure, requiring immediate reintubation. During the intubation, visualization of her vocal cords showed normal anatomy with some arytenoid edema, so a steroid taper was initiated starting with intravenous dexamethasone 4 mg 4 times daily. Gastroenterology was consulted to evaluate esophageal abnormalities; however, given that
she was intubated, an adequate work-up could not be done at the time. Extubation was attempted again; however, she was reintubated within days due to tachypnea, hypoxia, and hypercapnia. Arterial blood gas showed pH 7.0, pCO$_2$ 116, O$_2$ 103, bicarbonate 29, and O2% 93% on a non-rebreather mask.

At this time, a paraneoplastic and autoimmune work-up for the etiology of her acute respiratory failure was performed. Surprisingly, acetylcholine receptor binding antibodies were elevated at 124 mmol/L (reference range <0.02 mmol/L); thus, the diagnosis of myasthenia gravis was considered. Neurology was consulted and plasma exchange with 3.6 L albumin was initiated for a total plan of 5 sessions every other day. She was continued on intravenous steroids tapered down to hydrocortisone every 6 hours and subsequently to prednisone 60 mg daily. Given that she was sedated and mechanically ventilated, the response to treatment was unable to be appreciated in the acute setting. Her hospital course was further complicated by sepsis and acute respiratory distress syndrome due to hospital-acquired multilobar pneumonia. Due to her sepsis, steroids were discontinued while she remained on antibiotics. She also experienced severe anemia and thrombocytopenia requiring transfusions, and thus only completed 2 sessions of plasmapheresis before discontinuation. Her prolonged and complicated ICU stay eventually ended with placement of a tracheostomy and PEG tube and transfer to a long-term care facility. After completing her antibiotics, she resumed treatment with prednisone, with an up-titration of 10 mg every 5 days starting at 10 mg and reaching a maintenance dose of 60 mg for 2 months with a subsequent taper. She was soon maintained on treatment with prednisone 20 mg every other day, pyridostigmine 60 mg 3 times daily, and mycophenolate 500 mg twice daily, with considerable improvement in her initial bulbar symptoms.

**Discussion**

Myasthenia gravis is an autoimmune disease in which the body produces autoantibodies against acetylcholine receptors on skeletal muscle, impairing transmission at the neuromuscular junctions either by direct inhibition of acetylcholine binding to the muscle or accelerating the degradation of acetylcholine receptors, thus decreasing the number of receptors. As a consequence, patients experience skeletal muscle weakness and fatigability. Clinical presentation of the disease varies widely among patients. Extraocular muscle weakness, diplopia, and ptosis are present in 90% of patients diagnosed with myasthenia gravis, being the initial complaint in about 50% [2]. Surprisingly, our patient and her family members did not report any history of ocular symptoms, thus posing a diagnostic challenge.

Myasthenia gravis can occur at any age, but typically occurs in a bimodal distribution. The peak incidence is at 30 years in females and 65 years in males [3]. Furthermore, myasthenia can be divided into late-onset and early-onset. Approximately 65–70% of all MG cases are early-onset (<50 years), whereas up to 30% are late-onset [3]. Late-onset myasthenia, peaking at 70–80 years in both sexes, frequently presents with bulbar symptoms such as dysphagia, dysphonia, and dysarthria [4], and ocular symptoms are less common. Dysphagia occurs in 15–40% of patients in generalized myasthenia, but it is uncommon for it to be the only manifestation of the disease [5]. The diagnosis of myasthenia in a patient with these isolated symptoms should be considered. Unfortunately, our patient’s history of severe anxiety and panic attacks, atypical age range, and atypical presentation with only bulbar symptoms deterred us from considering an autoimmune etiology, thus delaying diagnosis.

About 20–30% of patients diagnosed with myasthenia gravis are affected by myasthenic crisis, and in some cases, this is the initial presentation [6]. In a study of 51 myasthenic patients, Quereshi et al. described 7 patients (approximately 14%) with no previous diagnosis of MG presenting with acute respiratory failure. Of these 7 patients, most demonstrated predominantly bulbar symptoms along with ocular involvement [7]. However, only 1 patient was found to have isolated bulbar involvement, similar to our patient, again posing a diagnostic challenge.

Identification of myasthenia gravis includes multiple approaches. Apart from clinical symptoms and physical examination findings, diagnostic testing includes presence of autoantibodies, slow repetitive nerve stimulation, and single-fiber electromyography. The most specific diagnostic test, and the test used in our case, is elevated acetylcholine receptor antibodies in the serum, which is positive in 85% of patients with generalized myasthenia and in only 50% of patients with only ocular myasthenia gravis [8]. However, seronegative disease is not uncommon, and the diagnosis of myasthenia gravis should not be overlooked. In fact, Renard et al. presented a case of laryngeal myasthenia gravis in which the patient showed a lack of antibodies, normal repetitive nerve stimulation, and absence of extra-laryngeal involvement, whose symptoms improved upon initiation of therapy despite a negative myasthenia work-up [9].

It is rare to see acute respiratory failure as the presenting symptom of myasthenia gravis, as witnessed in our patient. It is reasonable to believe that her symptoms of myasthenia may have presented when she was diagnosed with anxiety, as she experienced symptoms of dysphagia and dysarthria during her assumed panic attacks. Unfortunately, it may have been left undiagnosed due to anchoring bias. In patients experiencing such a crisis, timely initiation of plasma exchange and intravenous immunoglobulins reduces the duration of mechanical
ventilation [7]. Unfortunately, given our patient’s complications during her hospital course resulting in long-term tracheostomy and ventilation, we were unable to assess her response to plasma exchange.

Conclusions

Late-onset myasthenia gravis can mimic psychiatric panic diseases and anaphylactic reactions because of the bulbar presentation. Misdiagnosis due to lack of recognition of appropriate symptoms is common. Myasthenia gravis should be ascertained with a low threshold as a differential diagnosis of acute-onset dysphagia, dysphonia, and/or dysarthria in middle-aged to elderly people. Recognition of these symptoms should prompt early work-up of autoimmune etiology and initiation of therapy to prevent severe complications of myasthenic crises and acute respiratory failure.

References:


Conflicts of interest

None.

Abbreviations

MG – myasthenia gravis; AChR – acetylcholine receptors; CN – cranial nerve; ED – Emergency Department; URI – upper-respiratory infection; ECHO – echocardiogram; CTA – computed tomography angiography; MRI – magnetic resonance imaging; LTACH – long-term acute care hospital; PEG – percutaneous endoscopic gastrostomy; ARDS – acute respiratory distress syndrome; CXR – chest x-ray; CPR – cardiopulmonary resuscitation; EKG – electrocardiogram; LV – left ventricle; RV – right ventricle