CASE REPORT

Myasthenia gravis masquerading as dysphagia: unveiled by magnesium infusion

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SUMMARY

Myasthenia gravis (MG) is a neuromuscular disorder that typically affects the ocular, bulbar, neck, proximal limbs and respiratory muscles. Dysphagia can occasionally be the only presenting symptom leading to extensive but ultimately futile gastrointestinal workup. Delay in diagnosis and use of certain pharmacological agents in the interim can lead to a myasthenic crisis, which though diagnostic is life threatening. We document a case of dysphagia as the only symptom of myasthenia, diagnosed after a magnesium infusion precipitated myasthenic crisis. A 70-year-old Caucasian woman who had had progressive dysphagia for 2 years, for which multiple oesophageal dilations were performed. During a hospitalisation for further gastrointestinal workup, she went into myasthenic crisis (respiratory failure) after receiving magnesium replacement. She required ventilatory support and received five plasma exchange (PLEX) treatments after myasthenia was confirmed by the detection of high antiacetylcholine receptor antibody. Though her symptoms improved, she had a prolonged hospital stay (25 days) and required 18 days of mechanical ventilation. This underscores the morbidity associated with a delay in diagnosis of this condition. This case report suggests that neuromuscular causes should be considered early in elderly patients presenting with dysphagia. Timely diagnosis, initiation of management and avoidance of drugs that affect neuromuscular transmission may help reduce the morbidity and mortality associated with myasthenic crisis.

BACKGROUND

Myasthenia gravis (MG) is an autoimmune disease of the neuromuscular junction characterised by the formation of antiacetylcholine receptor antibodies (anti-AchR abs) that block neuromuscular transmission, resulting in skeletal muscle weakness. The disease typically demonstrates features of easy fatigability, and weakness of skeletal muscles in the ocular distribution, causing ptosis and diplopia.^{1 2} Involvement of the facial and pharyngeal muscles affects speech and swallowing, while progression to the proximal limb muscles can cause generalised weakness.^{1 3} Respiratory muscle involvement, including the diaphragm, can result in respiratory failure requiring ventilatory support.^{1 3} Dysphagia has been reported as the sole presenting symptom of myasthenia gravis, more often in the elderly.⁴

Muscular weakness due to myasthenia can be exacerbated by certain drugs acting at the level of the neuromuscular junction to reduce the release of acetylcholine or the sensitivity of the acetylcholine receptor. One such drug, the use of which is almost

spinal in hospital settings, is magnesium. Precipitation of weakness by magnesium, leading to a diagnosis of MG, has been described, most of whom are obstetric patients on a high dose of magnesium for pre-eclampsia.⁵

This case report describes an elderly patient presenting to the university hospital with a 2 year long history of dysphagia, learnt to be due to MG, when she went into myasthenic crisis following magnesium infusion for low serum magnesium levels.

CASE PRESENTATION

A 70-year-old Caucasian woman presented to the emergency department with difficulty in swallowing that initially started out as dysphagia to solids, but gradually worsened to include liquids. She reports unintentional 20 pound weight loss over 2 years and has had multiple esophagoscopy procedures with dilation of stenotic areas that allowed short-term (lasting less than a week) improvement in symptoms. The patient was admitted with increasing inability to eat regular diet and swallow pills over the past week. She denied any weakness, diurnal variation of symptoms, tingling or numbness, or vision changes.

On physical examination, the patient was a pleasant elderly lady, in no acute distress, appeared averagely built but under-nourished and ill. Vitals were stable, and systemic examination did not reveal any significant findings. Routine laboratory tests revealed a low magnesium level of 1.2 mg/dL following which the patient was given 8 mEq intravenously magnesium sulfate intravenously. Immediately after the infusion, the patient began to develop dysphonia and reported that her lips felt heavy. On physical examination, she now had a right-sided ptosis, right facial droop and deviation of the uvula to the left. The MRI performed to evaluate a cerebrovascular accident (CVA) was normal.

In the MRI suite, she developed diplopia on leftward vision, progressive dysphagia and dysphonia. She also was unable to lift her head off the pillow. The possibility of myasthenia was considered, and antiacetylcholine antibody test was ordered. Her respiratory status continued to decline, and she had to be transferred to the intensive care unit for intubation and mechanical ventilation.

Owing to the rapid decline an edrophonium challenge was not performed. The anti-AchR ab levels were high at 45 nmol/L, and the patient was treated with five sessions of plasma exchange and high-dose steroids. Patient's negative inspiratory force and forced vital capacity improved

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from $-18\text{ cm H}_2\text{O}$ and 200 mL to $-60\text{ cm H}_2\text{O}$ and 400 mL, respectively, prior to intubation versus after extubation. The neurological findings resolved gradually, with the neck weakness being the last to improve. The patient on extubation underwent a chest CT scan with contrast to rule out thymoma that revealed no evidence of any mediastinal masses. The patient was discharged to a short stay rehab facility for 10 days and subsequently sent home on medical therapy consisting of azathioprine and pyridostigmine. She was seen in the neurology clinic in a month from discharge and was noted to have significant improvement in her symptoms and muscle strength on examination, and the same course of therapy was continued.

DISCUSSION

MG has an incidence of 2–4/million/annum,⁴ and is twice as common in women.⁶ Disease shows a bimodal age-related distribution with a peak in the second and third decades, affecting more women, and the second peak in the sixth and seventh decades, affecting more men.² Skeletal muscles in the ocular and facial distribution are most commonly involved, and disease typically presents with ptosis and diplopia.⁴ Characteristic features include fluctuating fatigability of muscles and diurnal variation in the severity of symptoms.^{1 2} MG can be limited to the facial and extraocular muscles in 15% of patients,⁷ and eventually progress to involve the proximal limb muscles and the respiratory muscles in about 85%. An initial presentation with only bulbar symptoms is noted in about 6% of patients with MG and is more common with late onset MG.⁶ Dysphagia, due to the involvement of the pharyngeal and striated oesophageal muscles, is seen in 30–60% cases,⁷ and in 15% can be the only symptom.³ Elderly patients can present with atypical features of MG and this treatable condition should be considered in every patient with dysphagia, even in the absence of typical ocular signs and symptoms.

Diagnosis of MG is suspected based on the history and clinical examination and is confirmed by pharmacological, serological and electrodiagnostic tests. Pharmacological test demonstrates improvement in muscle weakness with use of edrophonium and can be performed at the bedside, but was not used in our patient due to rapid respiratory failure.⁸ Serological tests involve detection of AChR antibodies, present in up to 85% of the patients.⁹ In patients with respiratory and bulbar symptoms, but absence of anti-AChR antibodies, antimuscle-specific tyrosine kinase (anti-MuSK) antibodies may be detected.¹⁰ Electrodiagnostic tests include repetitive nerve stimulation studies that demonstrate progressive decline in the amplitude of compound muscle action potentials.⁸ Treatment involves the use of plasmapheresis, immunosuppressive therapy and anticholinesterases. The response of pharyngeal swallow dysfunction to an acetylcholinesterase inhibitor and immunosuppressive therapy is variable and may be less satisfactory than do other muscle groups.¹¹ table 1 describes the difference between the characteristic features of early and late onset MG.¹²

In our patient, infusing magnesium in response to low serum magnesium levels led to worsening of muscle weakness. Magnesium precipitated muscle weakness, leading to a diagnosis of MG, has been reported.¹³

Mechanism: Acetylcholine release at the neuromuscular junction is driven by calcium entry into the presynaptic nerve terminal. Magnesium is known to have both presynaptic and postsynaptic effects detrimental to neuromuscular transmission. It can competitively inhibit calcium entry at the presynaptic nerve terminal and impede acetylcholine release,¹⁴ and

Table 1 Difference between early onset and late-onset MG¹²

Characteristics	Early-onset MG	Late onset MG
Age peak (years)	30	65
Female: male ratio	4:1	1:3
Proportion of total MG cases	65–70%	Up to 30%
Presenting symptoms	Weakness and fatigue are more common Ocular and extremity weakness frequently present	Peripheral weakness and fatigue can be absent Ocular signs less common Bulbar signs are more common
Presence of thymoma	Rare	More common
Acetylcholine receptor antibody test (AChR-abs)	Present in up to 90%	Absent in up to 40% (seronegative MG)
HLA associations	HLA-DR3	None

Ocular signs include ptosis, gaze paresis and diplopia. Bulbar signs include dysphagia, dysphonia, tongue weakness, slurred speech and chewing problems. AChR-abs, Acetylcholine receptor antibody test; HLA, human leucocyte antigen; MG, myasthenia gravis.

simultaneously decrease motor end plate sensitivity to acetylcholine.¹⁵ In MG, the reduction in acetylcholine release and receptor sensitivity, in the presence of receptor blockade by antibodies, can have an additive effect and precipitate severe muscular weakness with minor elevations in the serum magnesium concentration.¹⁶ This effect of magnesium can be reversed by the use of intravenous calcium gluconate.^{11 17 18}

Literature review indicates various pharmacological agents that can have detrimental effects on neuromuscular transmission and must be used with caution/avoided in MG as shown in table 2.^{19 20}

This case aims to emphasise the importance of having a high suspicion for neuromuscular disorders in elderly patients with dysphagia and create awareness about the pharmacological precipitants of neuromuscular weakness, which must be used with great caution in such patients. Early diagnosis and avoidance of drugs that potentiate muscular weakness can reduce episodes of myasthenic crisis as well as morbidity caused by severe malnutrition, aspiration pneumonia and other complications associated with MG.⁴

Table 2 Guide to drug use in MG^{19 20}

Absolute contraindication	Contraindicated	Caution (may exacerbate weakness in some)
<ul style="list-style-type: none"> ▶ Curare ▶ D-penicillamine ▶ Botulinum toxin ▶ Interferon α ▶ Sedatives (benzodiazepines, barbiturates) 	<ul style="list-style-type: none"> ▶ Antibiotics—aminoglycosides (gentamycin, kanamycin, neomycin, streptomycin, tobramycin); macrolides (erythromycin, azithromycin, telithromycin, biacin); fluoroquinolones (ciprofloxacin, norfloxacin, levofloxacin) ▶ Quinine, quinidine, procainamide ▶ Magnesium salts, intravenous magnesium replacement 	<ul style="list-style-type: none"> ▶ Calcium channel blockers ▶ β-blockers ▶ Lithium ▶ Statins ▶ Iodinated contrast agents

MG, myasthenia gravis.

Learning points

- ▶ Myasthenia gravis can present with dysphagia as the sole symptom.
- ▶ It is essential to keep neuromuscular causes of dysphagia in mind when evaluating an elderly patient with dysphagia, as bulbar symptoms on diagnosis are seen more commonly in the elderly population.
- ▶ Early recognition and treatment are important to prevent myasthenic crisis, which has high morbidity and mortality rates. Once the diagnosis is suspected, periodic negative inspiratory force and vital capacity monitoring are performed to monitor respiratory status and the need for intubation, while hospitalised.
- ▶ Avoidance of drugs associated with worsening of myasthenic weakness is important to prevent iatrogenic worsening that can precipitate myasthenic crisis. Commonly used drugs like β -blockers, calcium channel blockers, magnesium, aminoglycoside and fluroquinolone antibiotics must be used with caution in patients with suspected myasthenic weakness.

Competing interests None.

Patient consent Obtained.

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