Ref: Ro J Neurol. 2021;20(4)
DOI: 10.37897/RJN.2021.4.20

Distal oesophageal spasm as a manifestation of myasthenia gravis

Madhavi Karri, Balakrishnan Ramasamy, Santhosh Perumal

Department of Neurology, PSG Institute of Medical Sciences and Research, Coimbatore, Tamil Nadu, India

ABSTRACT

Myasthenia gravis is an autoimmune neuromuscular junction disorder affecting skeletal muscles. It is characterised by muscle fatigability with fluctuating weakness and diurnal variations. Here, we present an elderly female presented with subacute onset dysphagia predominantly to solids with weight loss for one month. Upper gastrointestinal endoscopy showed a crico-oesophageal spasm. Manometric studies showed distal oesophageal spasm with normal pressures. Clinically, she had proximal muscle weakness of all four limbs with bulbar weakness. Nerve conduction studies done were suggestive of postsynaptic neuromuscular junction disorder. Serum acetylcholinesterase receptor antibodies were elevated. We started her on pyridostigmine and low dose steroids, following which her symptoms improved. Here smooth muscle involvement was considered secondary to myasthenia gravis, which recovered after treatment. Treating physicians should even think of neurological causes in patients presenting with dysphagia predominant to solids.

Keywords: myasthenia gravis, oesophageal spasm, smooth muscle involvement

INTRODUCTION

Myasthenia gravis is a neuromuscular junction disorder mainly affecting the skeletal muscles. In this autoimmune condition, antibodies are directed against the postsynaptic acetylcholine receptors causing neuromuscular transmission blockage. Prevalence was 20 cases per 100,000 population in the US population, with females being more commonly affected than males. Clinically, they can have fluctuating weakness involving the ocular, face, pharyngeal, bulbar, respiratory and limb skeletal muscle groups. Dysphagia can also occur as a sole manifestation [1,2], occurring more commonly in the elderly. Dysphagia for both liquids and solids are noticed, with the former being more predominant in the presentation. Here, we report an elderly female presenting with dysphagia paramount to solids than liquids occurring secondary to myasthenia.

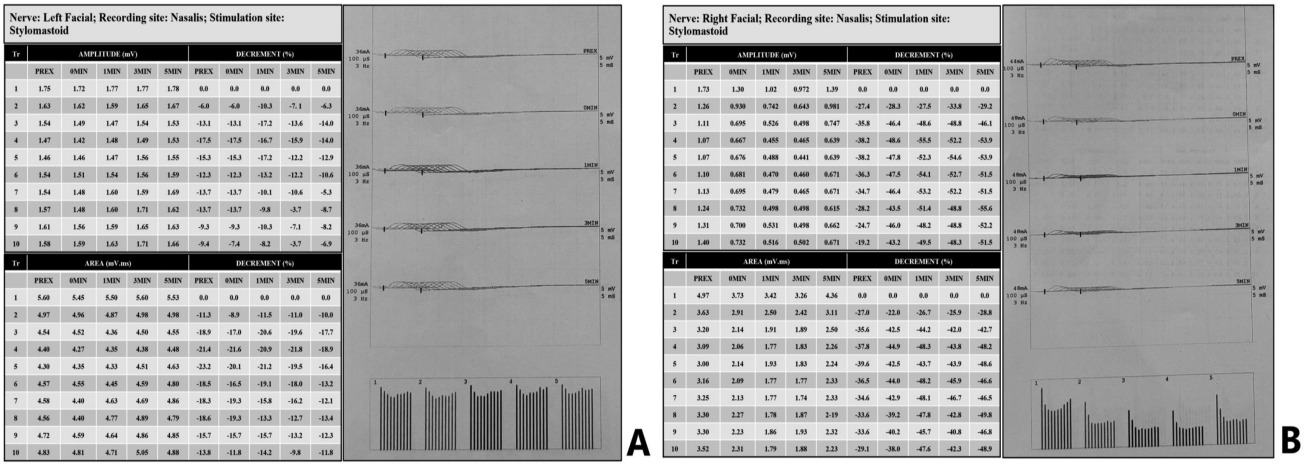
CASE PRESENTATION

Here we describe a 58-years-old female who presented with a history of generalised fatigue and difficulty swallowing both solids and liquids (more for solids) for the past month. She also noticed significant weight loss over one month. She also complained of fatigability and had difficulty doing her daily routine. She did not see any diurnal variation of the symptoms. She had no complaints of numbness, vision disturbances or any recent fever. She had no underlying known co-morbid illness. There was no evidence of any diabetes, malignancy or long term native medication intake in the past.

On examination, the patient was thin built, afebrile with no evidence of lymphadenopathy. Her blood pressure was normal. Neurologically, she had quadriparesis with a power of 4/5 (proximal weakness was more than distal). Deep tendon reflexes were intact, and bilateral plantar was flexor on

Corresponding author:
Madhavi Karri
E-mail: dr.madhavikarri@gmail.com

Article history:
Received: 15 September 2021
Accepted: 20 December 2021



Nerve: Left Facial; Recording site: Nasalis; Stylomastoid

Tr	AMPLITUDE (mV)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	1.75	1.72	1.77	1.77	1.78	0.0	0.0	0.0	0.0	0.0
2	1.63	1.62	1.59	1.65	1.67	-6.0	-6.0	-10.3	-7.1	-6.3
3	1.54	1.49	1.47	1.54	1.53	-13.1	-13.1	-17.2	-13.6	-14.0
4	1.47	1.42	1.48	1.49	1.53	-17.5	-17.5	-16.7	-15.9	-14.0
5	1.46	1.46	1.47	1.56	1.55	-15.3	-15.3	-17.2	-12.2	-12.9
6	1.54	1.51	1.54	1.56	1.59	-12.3	-12.3	-13.2	-12.2	-10.6
7	1.54	1.48	1.60	1.59	1.69	-13.7	-13.7	-10.1	-10.6	-5.3
8	1.57	1.48	1.60	1.71	1.62	-13.7	-13.7	-9.8	-3.7	-8.7
9	1.61	1.56	1.59	1.65	1.63	-9.3	-9.3	-10.3	-7.1	-8.2
10	1.58	1.59	1.63	1.71	1.66	-9.4	-7.4	-8.2	-3.7	-6.9

Tr	AREA (mV.ms)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	5.60	5.45	5.50	5.60	5.53	0.0	0.0	0.0	0.0	0.0
2	4.97	4.96	4.87	4.98	4.98	-11.3	-8.9	-11.5	-11.0	-10.0
3	4.54	4.52	4.36	4.50	4.55	-18.9	-17.0	-20.6	-19.6	-17.7
4	4.40	4.27	4.35	4.38	4.48	-21.4	-21.6	-20.9	-21.8	-18.9
5	4.30	4.35	4.33	4.51	4.63	-23.2	-20.1	-21.2	-19.5	-16.4
6	4.57	4.55	4.45	4.59	4.80	-18.5	-16.5	-19.1	-18.0	-13.2
7	4.58	4.40	4.63	4.69	4.86	-18.3	-19.3	-15.8	-16.2	-12.1
8	4.56	4.40	4.77	4.89	4.79	-18.6	-19.3	-13.3	-12.7	-13.4
9	4.72	4.59	4.64	4.86	4.85	-15.7	-15.7	-15.7	-13.2	-12.3
10	4.83	4.81	4.71	5.05	4.88	-13.8	-11.8	-14.2	-9.8	-11.8

A

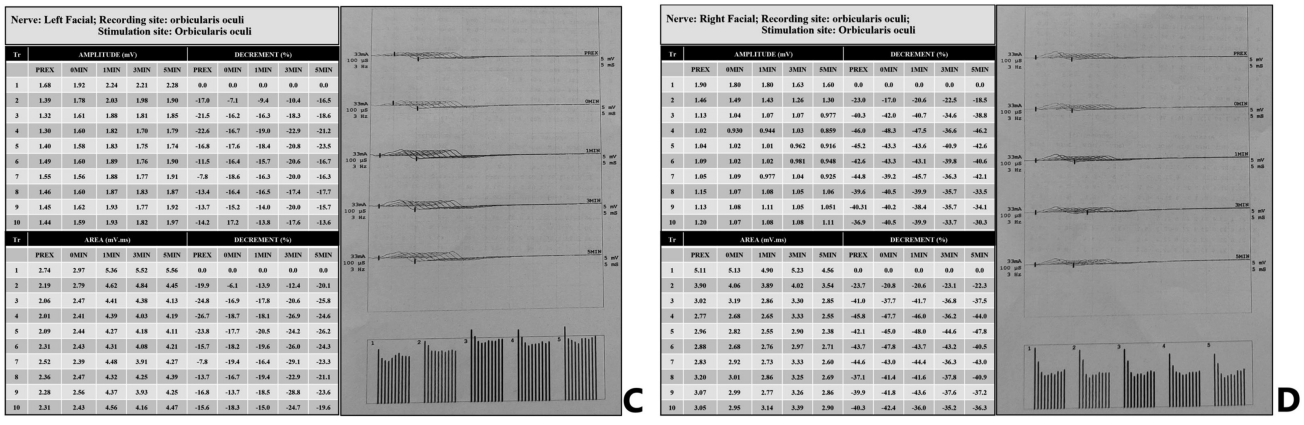
Nerve: Right Facial; Recording site: Nasalis; Stylomastoid

Tr	AMPLITUDE (mV)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	1.73	1.30	1.02	0.972	1.39	0.0	0.0	0.0	0.0	0.0
2	1.26	0.930	0.742	0.643	0.981	-27.4	-28.3	-27.5	-33.8	-29.2
3	1.11	0.695	0.526	0.498	0.747	-35.8	-46.4	-48.6	-48.8	-46.1
4	1.07	0.667	0.455	0.465	0.639	-38.2	-48.6	-55.5	-52.2	-53.9
5	1.07	0.676	0.488	0.441	0.639	-38.2	-47.8	-52.3	-54.6	-53.9
6	1.10	0.681	0.470	0.460	0.671	-36.3	-47.5	-54.1	-52.7	-51.5
7	1.13	0.695	0.479	0.465	0.671	-34.7	-46.4	-53.2	-52.2	-51.5
8	1.24	0.732	0.498	0.498	0.615	-28.2	-43.5	-51.4	-48.8	-55.6
9	1.31	0.700	0.531	0.498	0.662	-24.7	-46.0	-48.2	-48.8	-52.2
10	1.40	0.732	0.516	0.502	0.671	-19.2	-43.2	-49.5	-48.3	-51.5

Tr	AREA (mV.ms)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	4.97	3.73	3.42	3.26	4.36	0.0	0.0	0.0	0.0	0.0
2	3.63	2.91	2.50	2.42	3.11	-27.0	-22.0	-26.7	-25.9	-28.8
3	3.20	2.14	1.91	1.89	2.50	-35.6	-42.5	-44.2	-42.0	-42.7
4	3.09	2.06	1.77	1.83	2.26	-37.8	-44.9	-48.3	-43.8	-48.2
5	3.00	2.14	1.93	1.83	2.24	-39.6	-42.5	-43.7	-43.9	-48.6
6	3.16	2.09	1.77	1.77	2.33	-36.5	-44.0	-48.2	-45.9	-46.6
7	3.25	2.13	1.77	1.74	2.33	-34.6	-42.9	-48.1	-46.7	-46.5
8	3.30	2.27	1.78	1.87	2-19	-33.6	-39.2	-47.8	-42.8	-49.8
9	3.30	2.23	1.86	1.93	2.32	-33.6	-40.2	-45.7	-40.8	-46.8
10	3.52	2.31	1.79	1.88	2.23	-29.1	-38.0	-47.6	-42.3	-48.9

B

FIGURE 1. Repetitive Nerve stimulation at a frequency of 3Hz of nasalis muscle – A: Left B: Right - showing a decremental pattern in the amplitude of compound muscle action potential by the fourth response, after which it stabilises



Nerve: Left Facial; Recording site: orbicularis oculi
Stimulation site: Orbicularis oculi

Tr	AMPLITUDE (mV)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	1.68	1.92	2.24	2.21	2.28	0.0	0.0	0.0	0.0	0.0
2	1.39	1.78	2.03	1.98	1.90	-17.0	-7.1	-9.4	-10.4	-16.5
3	1.32	1.61	1.88	1.81	1.85	-21.5	-16.2	-16.3	-18.3	-18.6
4	1.30	1.60	1.82	1.70	1.79	-22.6	-16.7	-19.0	-22.9	-21.2
5	1.40	1.58	1.83	1.75	1.74	-16.8	-17.6	-18.4	-20.8	-23.5
6	1.49	1.60	1.89	1.76	1.90	-11.5	-16.4	-15.7	-20.6	-16.7
7	1.55	1.56	1.88	1.77	1.91	-7.8	-18.6	-16.3	-20.0	-16.3
8	1.46	1.60	1.87	1.83	1.87	-13.4	-16.4	-16.5	-17.4	-17.7
9	1.45	1.62	1.93	1.77	1.92	-13.7	-15.2	-14.0	-20.0	-15.7
10	1.44	1.59	1.93	1.82	1.97	-14.2	17.2	-13.8	-17.6	-13.6

Tr	AREA (mV.ms)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	2.74	2.97	5.36	5.52	5.56	0.0	0.0	0.0	0.0	0.0
2	2.19	2.79	4.62	4.84	4.45	-19.9	-6.1	-13.9	-12.4	-20.1
3	2.06	2.47	4.41	4.38	4.13	-24.8	-16.9	-17.8	-20.6	-25.8
4	2.01	2.41	4.39	4.03	4.19	-26.7	-18.7	-18.1	-26.9	-24.6
5	2.09	2.44	4.27	4.18	4.11	-23.8	-17.7	-20.5	-24.2	-26.2
6	2.31	2.43	4.31	4.08	4.21	-15.7	-18.2	-19.6	-26.0	-24.3
7	2.52	2.39	4.48	3.91	4.27	-7.8	-19.4	-16.4	-29.1	-23.3
8	2.36	2.47	4.32	4.25	4.39	-13.7	-16.7	-19.4	-22.9	-21.1
9	2.28	2.56	4.37	3.93	4.25	-16.8	-13.7	-18.5	-28.8	-23.6
10	2.31	2.43	4.56	4.16	4.47	-15.6	-18.3	-15.0	-24.7	-19.6

C

Nerve: Right Facial; Recording site: orbicularis oculi;
Stimulation site: Orbicularis oculi

Tr	AMPLITUDE (mV)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	1.90	1.80	1.80	1.63	1.60	0.0	0.0	0.0	0.0	0.0
2	1.46	1.49	1.43	1.26	1.30	-23.0	-17.0	-20.6	-22.5	-18.5
3	1.13	1.04	1.07	1.07	0.977	-40.3	-42.0	-40.7	-34.6	-38.8
4	1.02	0.930	0.944	1.03	0.859	-46.0	-48.3	-47.5	-36.6	-46.2
5	1.04	1.02	1.01	0.962	0.916	-45.2	-43.3	-43.6	-40.9	-42.6
6	1.09	1.02	1.02	0.981	0.948	-42.6	-43.3	-43.1	-39.8	-40.6
7	1.05	1.09	0.977	1.04	0.925	-44.8	-39.2	-45.7	-36.3	-42.1
8	1.15	1.07	1.08	1.05	1.06	-39.6	-40.5	-39.9	-35.7	-33.5
9	1.13	1.08	1.11	1.05	1.051	-40.31	-40.2	-38.4	-35.7	-34.1
10	1.20	1.07	1.08	1.08	1.11	-36.9	-40.5	-39.9	-33.7	-30.3

Tr	AREA (mV.ms)					DECREMENT (%)				
	PREX	0MIN	1MIN	3MIN	5MIN	PREX	0MIN	1MIN	3MIN	5MIN
1	5.11	5.13	4.90	5.23	4.56	0.0	0.0	0.0	0.0	0.0
2	3.90	4.06	3.89	4.02	3.54	-23.7	-20.8	-20.6	-23.1	-22.3
3	3.02	3.19	2.86	3.30	2.85	-41.0	-37.7	-41.7	-36.8	-37.5
4	2.77	2.68	2.65	3.33	2.55	-45.8	-47.7	-46.0	-36.2	-44.0
5	2.96	2.82	2.55	2.90	2.38	-42.1	-45.0	-48.0	-44.6	-47.8
6	2.88	2.68	2.76	2.97	2.71	-43.7	-47.8	-43.7	-43.2	-40.5
7	2.83	2.92	2.73	3.33	2.60	-44.6	-43.0	-44.4	-36.3	-43.0
8	3.20	3.01	2.86	3.25	2.69	-37.1	-41.4	-41.6	-37.8	-40.9
9	3.07	2.99	2.77	3.26	2.86	-39.9	-41.8	-43.6	-37.6	-37.2
10	3.05	2.95	3.14	3.39	2.90	-40.3	-42.4	-36.0	-35.2	-36.3

D

FIGURE 2. Repetitive Nerve stimulation at a frequency of 3Hz of Orbicularis oculi muscle – C: Left D: Right - showing a decremental pattern in the amplitude of compound muscle action potential by the fourth response, after which it stabilises

both sides. She had a bulbar weakness with a weak gag reflex**.** The rest of the examination was normal.

Dysphagia to solids being predominant symptom – she evaluated for the same. Her complete blood picture was normal, and the erythrocyte sedimentation rate was 20. Renal functions, liver functions and electrolytes were normal. Her TSH levels (2.86) and cortisol levels (18.85 microg/dl) were normal. As dysphagia was predominant in solids - she had undergone upper gastrointestinal endoscopy to rule out the structural lesion. Results showed mild cricopharyngeal spasm. Oesophageal manometry studies showed evidence of distal oesophageal spasm with normal sphincter pressures. Because of proximal weakness, creatine phosphokinase (CPK) levels were normal (63U/l). Nerve conduction studies of all four limbs reported being normal. Repetitive nerve stimulation(RNS) of bilateral orbicularis oculi, abductor pollicis brevis and nasalis muscles were done. RNS showed decremental response – suggestive of the postsynaptic neuromuscular junctional disorder. Anti-acetylcholine receptor antibodies were positive (> 80 nmol/l), and anti-muscle-specific kinase antibodies were negative. CT chest showed no evidence of thymoma. After evaluation, she was diagnosed with Myasthenia gravis and started on pyridostigmine, following which her symptoms improved. After six months of follow-up, she can do her regular activities without any support and swallow normally.

DISCUSSION

Isolated dysphagia and dysarthria are often rare in myasthenia [3]. Dysphagia occurs in about 15-40% of generalised myasthenia gravis. It is due to dysfunction of the oropharyngeal phases of swallowing [4]. The weakness of the oesophageal striated muscle portion causes oesophageal dysmotility leading to dysphagia. Another probable pathogenesis was the weakness of buccopharyngeal muscles with the relaxation of constrictors, which was considered to cause dysphagia in myasthenia [5].

Distal oesophageal involvement in myasthenia gravis is said to be a rare entity with limited information. The involvement of smooth muscle in myasthenia is a rarity, where there is a profound alteration in the motility of oesophageal segments composed of smooth muscles solely [6]. But the mechanism behind the smooth muscle involvement was unknown. One of the probably considered explanations was voluntary muscle involvement, and there was reduced afferent feedback from the distal oesophagus. Another possibility considered was transmission block between neurons of dorsal vagal nerve and neurons of myenteric plexus, mediated by nicotinic (ganglionic type) ach receptors. It was characterised that these receptors crossover reactivity with myogenic receptors. Distal oesophageal spasm, generally defined as the replacement of normal peristaltic contraction by nonperistaltic contractions. For a normal oesophageal transit, these nonperistaltic contractions are not effective. Due to the loss of the deglutitive inhibition with impaired inhibitory nerve function, localised to the oesophageal body, the regular transit is impaired.

Dysphagia to solids is the most under-recognised entity in myasthenia gravis [7]. Similar, Llabres et al. reported three cases of myasthenia presented with dysphagia to solids [6]. In this, all patients had an outstanding response with pyridostigmine, with one among them had plasmapheresis. Another case report was reported by Romo Gonzalez et al. from Argentina [2] and another from Ferreira et al. from Lisbon [3] with a similar presentation and other features of myasthenia and had a dramatic response with pyridostigmine.

Manometric studies of the oesophagus can aid as a valuable tool in the assessment. They help assess lower oesophageal sphincter pressures, location, relaxations and identify any motility disorders or local pathology. Routinely these studies are not done in patients with myasthenia gravis in clinical practice. In these studies, decreased upper oesophageal sphincter pressures and amplitude with successive swallows was frequently observed in myasthenia. Attribution to these observations, due to weak peristaltic contractions of the oesophagus [8]. With the advent of cinefluorography, routine swallowing evaluation and understanding of swallowing dynamics have become more accessible. Specifically, videofluoroscopic swallow studies (VSSs) and video endoscopy are valuable in identifying and tracing manoeuvres that facilitate swallowing and prevent aspiration [9,10]. Early identification and initiation of treatment strategies play a pivotal role in preventing severe consequences and mortality related to the disease [11].

CONCLUSIONS

Dysphagia predominant to solids may mostly be considered secondary to mechanical non-neurological causes. Myasthenia gravis needs to be kept as one of the differentials for isolated dysphagia for solids. Myasthenia gravis is a serious but potentially treatable condition for dysphagia. Timely considerations in evaluating and treating dysphagia in myasthenia gravis are essential to prevent complications and improve quality of life.

REFERENCES

1. Klair JS, Rochlani YM, Meena NK. Myasthenia gravis masquerading as dysphagia: Unveiled by magnesium infusion. BMJ Case Rep. 2014 Apr 17;2014:bcr2014204163.
2. Romo González RJ, Chaves E, Copello H. Dysphagia as the sole manifestation of myasthenia gravis. Acta Gastroenterol Latinoam. 2010 Jun;40(2):156-8.
3. Ferreira S, Lage P, Claro I, Alcântara J, Nunes J, Nobre Leitão C. Dysphagia and dysarthria: unusual presentation of myasthenia gravis. Acta Med Port. 2007 Sep-Oct;20(5):463-6.
4. Ertekin C, Yüceyar N, Aydoğdu I. Clinical and electrophysiological evaluation of dysphagia in myasthenia gravis. J Neurol Neurosurg Psychiatry. 1998 Dec;65(6):848-56.
5. Viets HR. Diagnosis of myasthenia gravis in patients with dysphagia. J Am Med Assoc. 1947 Jul 19;134(12):987-92.
6. Llabrés M, Molina-Martinez FJ, Miralles F. Dysphagia as the sole manifestation of myasthenia gravis. J Neurol Neurosurg Psychiatry. 2005 Sep;76(9):1297-300.
7. Rison RA. Reversible oropharyngeal dysphagia secondary to cricopharyngeal sphincter achalasia in a patient with myasthenia gravis: a case report. Cases J. 2009 Aug 7;2:6565.
8. Torres-Barrera G, Herrera-Quiñones G, Scharrer SI, Benavides-Salgado DE, Maldonado-Garza HJ, Achem SR. High-Resolution Esophageal Manometry in Myasthenia Gravis. ACG Case Reports J. 2020 Mar 16;7(3):e00340.
9. Cook IJ, Kahrilas PJ. AGA technical review on management of oropharyngeal dysphagia. Gastroenterology; 1999 Feb;116(2):455-78.
10. Juan HC, Tou I, Lo SC, Wu IH. Efficacy of postural techniques assessed by videofluoroscopy for myasthenia gravis with dysphagia as the presenting symptom: A case report. J Med Case Rep. 2010 Nov 19;4:370.
11. Khan OA, Campbell WW. Myasthenia Gravis Presenting as Dysphagia: Clinical Considerations. Am J Gastroenterol. 1994 Jul;89(7):1083-5.