CORPUS PUBLISHERS

Current Research in Emergency Medicine (CREM)

ISSN: 2832-5699

Volume 3, Issue 1, 2023

Article Information

Received date : 17 May, 2023

Published date: 12 June, 2023

*Corresponding author

Balasubrahmanyam CH, Citizen's Specialty Hospital, Nallagandla, Hyderabad, India

DOI: 10.54026/CREM/1052

Key Words

Autoimmune Disorder; Neuromuscular Weakness; Myasthenia Gravis; Dysphagia; Laryngoscopy; Emergency Department

Case Report

Myasthenia Gravis: Rare Disease with Rarer Presentation

C Manisha, Sushrut S Palepu, Balasubrahmanyam CH*, Santosh Kumar P, Sasidhar P, Bharath kumar Pamulapati, Seerapani Gopaluni, Aparna VijayKumar

Citizen's Specialty Hospital, Nallagandla, Hyderabad, India

Introduction

Myasthenia Gravis (MG) is an autoimmune disorder affecting the neuromuscular junction, in which antibodies are directed against post-synaptic nicotinic acetylcholine(nAch) receptors. Autoimmunity in this disease is mediated by a type-II antibody reaction in which antibodies directed against post-synaptic nAch receptors attack the myoneural junction and damage the post-synaptic membrane via complement fixation. This results in the failure of action potential propagation across the neurons, eventually leading to a neuromuscular weakness without stiffness [1]. The annual incidence of Myasthenia gravis is relatively less with 0.21-2 patients per 100,000 population [2]. Incidence rates have a bimodal distribution in women, with peaks around age 30 and 50. In men, the incidence increases steadily with age and with the highest rates between age 60 and 89 [3]. Women are more commonly affected before age 40, with a female: male ratio of 3:1 for early-onset MG. In the fifth decade of life, women and men are equally affected, while men have a higher proportion after age 50, with a male: female ratio of 3:2 [4]. The clinical hallmark of MG is the presence of fluctuating fatigable muscle weakness that worsens with activity and improves on rest. Up to 50% to 85% of patients with MG present with ocular symptoms with or without generalized weakness, and 50% to 60% of patients with MG who initially present with isolated ocular involvement go on to develop generalized weakness, often within 3 years after onset of symptoms. The disease remains exclusively ocular in only 15% to 25% of patients throughout their course [5,6]. Approximately 20% of patients with MG may present with prominent bulbar symptoms [4] along with weakness of head extension and flexion. Limb weakness may be more severe proximally than distally, isolated limb muscle weakness is the presenting symptom in about 5% of patients [7]. Myasthenic crisis is a complication of myasthenia gravis characterized by worsening of muscle weakness, resulting in respiratory failure that requires intubation and mechanical ventilation.

Case report

A 68-year-old lady presented to our Outpatient Department (OPD) with complaints of dysphagia since past one year that had aggravated in last three days, difficulty in breathing for three days, cold and cough for three days. Her past medical history included multinodular goitre (euthyroid) and she had also undergone multiple upper GI endoscopies for evaluation of dysphagia and was diagnosed to have Gastro-Oesophageal Reflux Disease (GERD). Her family history was unremarkable. On examination she was found to be tachypnoeic and was referred to the emergency room from OPD. On arrival she was found to be gasping and had a respiratory arrest which was managed with endotracheal intubation and mechanical ventilation. The initial blood gas analysis showed features of type 2 respiratory failure. After stabilising the vitals, she was shifted to medical intensive care unit (MICU), where mechanical ventilation was continued for a day, after which her blood gases improved to p/f ratio of 300. By then she was completely awake and was obeying commands. She tolerated a spontaneous breathing trial well enough to be weaned off mechanical ventilation and getting extubated.

However, within the next 15-20 minutes she had hoarseness of voice and had difficulty in breathing for which she had to be re-intubated and ventilated. Direct laryngoscopy at the time of intubation revealed that she has oropharyngeal oedema, and her vocal cords were not moving adequately. With the background of dysphagia, type 2 respiratory failure, difficulty in breathing, vocal cord palsy and oropharyngeal oedema we had the following as our differential diagnosis: diffuse oesophageal spasm, GERD, Parkinson's disease, supra-bulbar palsy, Guillain-Barre syndrome, Myasthenia gravis, neoplasms in neck causing vocal cord palsy and tracheal compression and pneumonia. To narrow down our diagnosis we got C1 esterase inhibitor function and C4 levels done which were normal, there was no h/o NSAID or ACEI use or similar family history, CNS examination, brisk reflexes, sensory & motor examination -normal. Examination by ENT specialist showed no features of pseudo-membranes / tonsillitis EBV antigen & throat swab for diphtheria were negative. Thyroid function test normal. USG Thyroid and FNAC were negative for malignancy. A CT head and neck done which revealed diffuse extensive oedematous soft tissue thickening involving the tonsils, nasopharynx, oropharynx, and laryngopharynx. There were no signs of neoplasm or any other cerebral pathology. CT chest showed no s/o infection. We also ordered for a nerve conduction study and sent samples for anti-cholinesterase antibody levels.

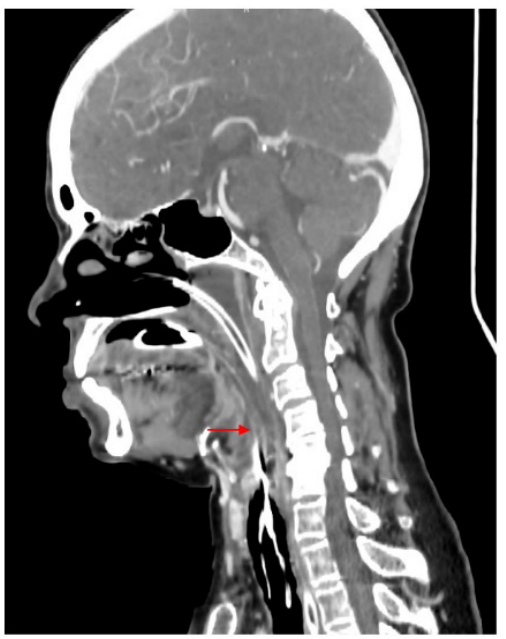
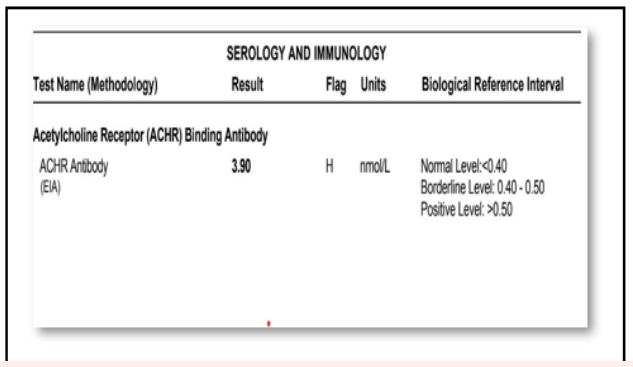


Figure 1: CT HEAD AND NECK-Showing oedematous soft tissue thickening of oropharynx and laryngopharynx

While waiting for the results, the patient had recovered from the effects of muscle relaxant and was able to move all the four limbs without much effort, but we noticed that she had a fibrillating tongue. Further detailed questioning of the family revealed that she is generally weak and gets tired easily for the past forty years and had a change in voice for the past one year which they thought was a consequence of recurrent respiratory tract infection. It was also conveyed that she had ptosis after a cataract surgery, which was ascribed to the local anaesthesia administered during surgery. In the light of the newly discovered symptoms our diagnosis was more in favour of myasthenia gravis. This was confirmed by anti cholinesterase antibody levels of 3.9nmol/L (Figure 2). The repetitive nerve stimulation study (RNS) was ordered which revealed decremental response on repetitive stimulation, (Figure 3) which is also a feature of MG.



SEROLOGY AND IMMUNOLOGY

Test Name (Methodology)	Result	Flag	Units	Biological Reference Interval
Acetylcholine Receptor (ACHR) Binding Antibody				
ACHR Antibody (EIA)	3.90	H	nmol/L	Normal Level:<0.40 Borderline Level: 0.40 - 0.50 Positive Level: >0.50

Figure 2: Acetylcholine receptor antibody report

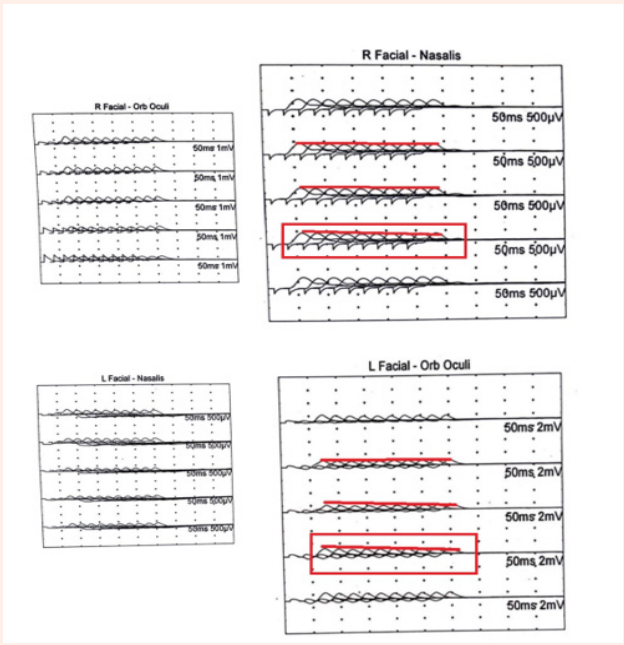


Figure 3: Repetitive nerve stimulation test-showing decremental response in Rt.Facial and Lt.Orbicularis oculi.

She was tracheostomised and a decision to initiate plasmapheresis was made in consultation with nephrology team and pulse dose steroids were started. After two cycles of plasmapheresis she started to tolerate pressure support ventilation. Plasmapheresis was continued for another three cycles under the supervision of nephrologist, and we also started her on pyridostigmine and azathioprine were initiated. Over a period of next 10 days her clinical condition improved, she was decannulated and was able to speak well. Check laryngoscopy revealed decreased oropharyngeal oedema and she was discharged from hospital with maintenance therapy of pyridostigmine, steroids and immunosuppressants.

Discussion

The Myasthenia Gravis Foundation of America Clinical Classification divides MG into 5 main classes and several subclasses [7]:

- Class I: Any ocular muscle weakness; may have weakness of eye closure; all other muscle strength is normal.
- Class II: Mild weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity.
- Class IIa: Predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles.
- Class IIb: Predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both.
- Class III: Moderate weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity.
- Class IIIa: Predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles.

- Class IIIb: Predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both.
- Class IV: Severe weakness affecting other than ocular muscles; may also have ocular muscle weakness of any severity.
- Class IVa: Predominantly affecting limb, axial muscles, or both; may also have lesser involvement of oropharyngeal muscles.
- Class IVb: Predominantly affecting oropharyngeal, respiratory muscles, or both; may also have lesser or equal involvement of limb, axial muscles, or both.
- Class V: Defined by the need for intubation, with or without mechanical ventilation, except when used during routine postoperative management. The use of a feeding tube without intubation places the patient in class IVb.

Myasthenic crisis is commonly triggered by infection, surgery, pregnancy or tapering dose of immunosuppressive agents [8]. Medications are another large source of triggers for myasthenic crisis. The most important dictum for managing myasthenic crisis in emergency department is establishing a secure airway. A simple bedside test to recognise an impending respiratory failure is single breath count test, difficulty in counting till twenty in a single breath signifies expiratory muscle weakness [9]. In selected patients who can co-operate spirometry can be done to measure forced vital capacity (FVC) and maximal inspiratory pressure (MIP). Elective intubation should be considered in patients with FVC <15 or MIP between 0 to -30 [10]. Up to 20% of patients with myasthenic crisis could potentially be managed with non-invasive ventilation, and its early use has shown to reduce ventilator days, length of ICU stays and rate of reintubation [11]. But one should not delay establishing an advance airway in a patient with respiratory collapse. The anti–acetylcholine receptor (AChR) antibody test for diagnosing MG has a high specificity up to 100%. It is Positive in as many as 85% of patients who have generalized MG but in only 50% of patients who have purely ocular MG [12]. False-positive anti-AChR antibody test results have been reported in patients with thymoma without MG, Lambert-Eaton myasthenic syndrome, Small cell lung cancer, Rheumatoid arthritis treated with penicillamine, 1-3% of the population older than 70 years.

RNS is abnormal in more than 50% to 70% of patients with generalized MG but are often normal in patients with purely ocular form of MG. A decrement in RNS can be seen in other conditions like neuropathies, motor neuron disease, inflammatory myopathies and myotonic disorders. Patients with MG rarely have a decreased response in a clinically normal muscle. Thus, testing a proximal weak muscle gives a better yield than testing an unaffected distal muscle. The two primary pharmacologic therapies available for myasthenic crisis are intravenous immunoglobulin (IVIg) and plasma exchange (PE) [2]. The usual dose of IVIg is 400 mg/kg daily for 5 days. Patients should be screened for IgA deficiency to avoid anaphylaxis from IVIg [2]. For PE, 5 exchanges (1 plasma volume or 3-4 L per exchange) are usually performed every other day over 10 days [14, 15]. A comparison between the two primary modalities is given below (Table 1). High dose corticosteroids (1-1.5mg/kg/day of prednisone) can be used in conjunction with IVIg and PE. There is no role of steroids in a setting of myasthenic crisis, rather, high dose corticosteroids precipitate early exacerbation of myasthenia gravis and increase the need for mechanical ventilation.

Table 1: Comparison between IVIg and Plasma Excahnge [2]

	IVIg	Plasma exchange
Dose	400mg/kg/day	One plasma exchanges every other day over 10days
response	Improvement in 4-5 days; effect for 4-8 weeks	Improvement in 2 days
		effect for 3-4 weeks
Advantages	More readily available	Faster treatment response
Disadvantages	Slower treatment response	Need for special venous access, equipment, and personnel
Contraindications	IgA deficiency	Hemodynamic instability, unstable coronary artery disease, current internal bleeding.
Serious complications	Aseptic meningitis, cardiac arrhythmia, thrombocytopenia, thrombotic events	Hemodynamic instability, cardiac arrhythmia, myocardial infarction, haemolysis

Conclusion

The mainstay of treatment for myasthenia gravis is pyridostigmine, with adjunctive corticosteroids for all patients with myasthenia gravis who have not reached treatment goals following a trial of pyridostigmine. If steroids are not tolerated by the patient, a non-steroidal immunosuppressant can be used, such as cyclosporine, azathioprine or methotrexate. If refractory to these measures, chronic IVIG should be initiated in a speciality centre for myasthenia gravis [16]. Timely diagnosis and appropriate treatment will have a good survival benefit even in the elderly. Presence of symptoms like dysphagia in elderly group draws a false attention towards a non-existent GI disease which may result in more severe life-threatening presentation in the form of myasthenic crisis as it happened in our case. Hence, it is important to have high index of suspicion for MG even in the absence of classical features.

Conflicts of interest: None

Funding: None

References

1. Breen E, Bleich L, Loeser C (2014) Myasthenia gravis presenting with dysphagia in an elderly male: a case report. Am J Med 127(9): e7-e8.
2. Wendell L, Levine J (2011) Myasthenic crisis. Neurohospitalist 1(1): 16-22.
3. Carr AS, Cardwell CR, McCarron PO, McConville J (2010) A Systematic Review of Population Based Epidemiological Studies in Myasthenia Gravis. Bmc Neurol 10: 46.
4. Ciafaloni E (2019) Myasthenia Gravis and Congenital Myasthenic Syndromes. Continuum Minneap Minn 25(6): 1767-1784.
5. Strauss AJL, Seigal BC, Hsu KC, Burkholder PM, Nastuk WL (1960) Immunofluorescence demonstration of a muscle binding complement fixing serum globulin fraction in Myasthenia Gravis. Proc Soc Exp Biol 105(1): 184.
6. Patric J, Lindstrom JM (1973) Autoimmune response to acetylcholine receptor. Science 180(4088): 871-872.
7. Jaretzki A 3rd, Barohn RJ, Ernstoff RM, Kaminski HJ, Keesey JC, et al. (2000) Myasthenia gravis: recommendations for clinical research standards. Task Force of the Medical Scientific Advisory Board of the Myasthenia Gravis Foundation of America. Neurology 55(1): 16-23.
8. Berrouschot J, Baumann I, Kalischewski P, Sterker M, Schneider D (1997) Therapy of myasthenic crisis. Crit Care Med 25(7): 1228-1235.
9. Juel VC (2004) Myasthenia gravis: management of myasthenic crisis and perioperative care. Semin Neurol 24(1): 75-81.
10. Godoy DA, Mello LJ, Masotti L, Di Napoli M (2013) The myasthenic patient in crisis: an update of the management in neurointensive care unit. Arq Neuropsiquiatr 71(9A): 627-639.
11. Seneviratne J, Mandrekar J, Wijdicks EF, Rabinstein AA (2008) Noninvasive ventilation in myasthenic crisis. Arch Neurol 65(1): 54-58.
12. Padua L, Stalberg E, LoMonaco M, Evoli A, Batocchi A, et al. (2000) SFEMG in ocular myasthenia gravis diagnosis. Clin Neurophysiol 111(7): 1203-1207.
13. Younger DS, Raksadawan N(2001) Therapy in neuromuscular disease. Neurol Clin 19(1): 205-215, vii.
14. Ahmed S, Kirmani JF, Janjua N, Alkawi A, Khatri I, et al. (2005) An update on myasthenic crisis. Curr Treat Options Neurol 7(2): 129-141.
15. Shemin D, Briggs D, Greenan M (2007) Complications of therapeutic plasma exchange: a prospective study of 1,727 procedures. J Clin Apher 22(5): 270-276.
16. Sanders D, Wolfe G, Narayanaswami P (2017) Author response: International consensus guidance for management of myasthenia gravis: executive summary. Neurology 88(5): 505-506.