International Journal of Research in Medical Sciences
Hirolikar R et al. Int J Res Med Sci. 2024 Oct;12(10):3914-3916
www.msjonline.org
pISSN 2320-6071 | eISSN 2320-6012

DOI: https://dx.doi.org/10.18203/2320-6012.ijrms20242960

Case Report

Breath of hope: unravelling isolated respiratory paralysis through anti musk positive myasthenia gravis

Rushikesh Hirolikar*, Vinod Khandait, Pragati Bhole, Yash Jajoo

Department of Medicine, GMC, Nagpur, Maharashtra, India

Received: 03 August 2024
Revised: 22 August 2024
Accepted: 23 August 2024

***Correspondence:**
Dr. Rushikesh Hirolikar,
E-mail: hirolikar@gmail.com

ABSTRACT

Isolated respiratory paralysis is a rare and perplexing clinical presentation that demands an astute diagnostic investigation. We present a case of 28-year-old woman who presented with sudden onset severe respiratory distress, with no overt signs of generalized muscle weakness, no cranial nerve dysfunction, or any other focal neurological deficit. The initial clinical scenario posed a diagnostic challenge, as the absence of typical myasthenia gravis features led to a myriad of differential considerations. However, through meticulous clinical evaluation, neurophysiological studies, and antibody testing, we unraveled the underlying cause-MuSK positive Myasthenia gravis. Unlike the more common acetylcholine receptor (AchR) positive MG, MuSK positive MG often presents with isolated respiratory involvement posing diagnostic hurdles. Though patient eventually succumbed owing to ventilator associated pneumonia and sepsis, this case exemplifies the necessity of a comprehensive diagnostic approach, even in the face of uncommon presentations, and underscores the importance of tailored therapeutic strategies in improving patient outcomes.

Keywords: Respiratory paralysis, Myasthenia gravis, Muscle specific kinase antibody

INTRODUCTION

Myasthenia gravis is inflammatory neuromuscular disorder that affects AchR receptors at neuromuscular junction.[1] Muscle- specific kinase (MuSK) antibodies are associated with a subtype of myasthenia gravis. This is a rare form of MG characterized by the presence of autoantibodies against MuSK protein, which plays a role in neuromuscular junction.[2] We present to you a case of a 28-year-old female patient which presented to us with isolated paralysis and was diagnosed as MuSK positive Myasthenia gravis.

CASE REPORT

A 28-year-old female came to GMC Nagpur casualty with complaints of throat pain, difficulty deglutition and shortness of breath for 1 month but exaggerated since last 7 days. It was not associated with any diurnal variation or any aggravating or relieving factors. Patient was received in gasping breathing and was intubated and shifted to intensive care unit. Patient did not have any comorbidities and did not have any similar complaints in past. Patient became conscious when received in ICU and was vitally stable. On thorough neurological examination, patient was conscious, cooperative, and following all commands. Patient was moving all 4 limbs, neck holding present, power was 5/5 in all 4 limbs across all joints. No ptosis or any ophthalmoplegia present. Plantar were bilaterally absent, deep tendon reflexes were present and normal. Pupils were normal bilaterally and reacting to light. Occasionally spontaneous fasciculation was present. On admission ABG was suggestive of CO_2 retention with pCO_2 of 49 mm Hg and pO_2 was 512. No

spontaneous efforts of breathing were present as observed on ventilator.

Table 1: Test for respiratory paralysis.

Parameters	ABG on t piece spontaneous breathing	ABG on mechanical ventilation
PAO_2	35.6 mmHg	172 mmHg
$PACO_2$	67.4 mmHg	29.2 mmHg
PH	7.334	7.651
sO_2	63.3%	100.1 %
FO_2Hb	62.3%	99%
FCOHb	0.7%	0.2 %
K^+	2.9 mmol/l	2.3 mmol/l
Na^+	141 mmol/l	139 mmol/l
Ca^{++}	1.25 mmol/l	1.14 mmol/l
Cl^-	96 mmol/l	98 mmol/l
Glucose	7.2 mmol/l	4.6 mmol/l
Lactate	1.1 mmol/l	1.2 mmol/l
HCO_3^-	31.2 mmol/l	34.2 mmol/l

To confirm the diagnosis of respiratory paralysis, ABG on T-piece trial spontaneous ventilation and ABG on mechanical ventilation was done, and shown in the Table 1. Serum cholinesterase was 4772 which was done to rule out OP poisoning. Other laboratory parameters were within normal limits. MRI brain plus cervical spine was done which was normal. Nerve conduction study was done which was normal. Meanwhile patient developed ventilator associated pneumonia and sepsis. Patient developed hypotension and septic shock and patient was put on pressor support and appropriate antibiotics were started.

Samples for anti-AchR antibodies and anti-MuSK antibodies were sent of which anti-MuSK antibodies were positive. Diagnosis of MuSK positive myasthenia gravis was confirmed and patient was started on Injection Intravenous immunoglobulins 2 g/kg over 5 days, tablet pyridostigmine and tab prednisolone. Patient did not show any signs of improvement over course of admission. Owing to septic shock not responding to pressor support, patient succumbed after 7 days of admission.

DISCUSSION

Myasthenia gravis is most common disorder of neuromuscular junction transmission. It is an autoimmune disease characterized by blocking type of type 2 hypersensitivity reaction. It is characterized by fluctuating and variable combination of weakness in ocular, bulbar, and respiratory muscles.[3] In approximately 80% of patients, autoantibodies to the muscle nicotinic AchR are present. These antibodies cause loss of AchR numbers and function, and lead to failure of neuromuscular transmission with muscle weakness.

MuSK mediates the agrin-induced clustering of AchR during synapse formation, and is also expressed at the mature neuromuscular junction.[4,5] Anti-MuSK antibodies are of IgG4 type which does not require complement activation. IgG4 undergoes a post-translational modification termed Fab arm exchange that prevents cross-linking of antigens. These findings suggest that MuSK-MG may be different in etiological and pathological mechanisms from AchR-MG.[6]

Myasthenia gravis with antibodies against MuSK is often a severe disease.[7] MuSK positive myasthenia gravis was characterized by a striking prevalence of female patients with age of onset ranging from 6-68 years and around 60% patients presenting under 40 years of age. Muscle weakness is predominantly involving cranial and bulbar muscles with high frequency of respiratory crisis. Limb muscle involvement is comparatively low and if present is less severe and inconsistent.[8] The diagnostic procedure includes MuSK-Ab testing, edrophonium/neostigmine test, and electro neurophysiological studies such as repetitive nerve stimulation (RNS), single-fiber electromyography (SFEMG), and needle EMG. RNS sensitivity appears to be lower in MuSK-MG compared with AchR-MG, especially when performed on distal limb muscles. It has been demonstrated that a similar pattern is usually found also in MuSK- MG, probably due to an underlying presynaptic dysfunction in MuSK-MG patients.[9] The symptomatic treatment with Ach-sterase inhibitors like pyridostigmine and neostigmine is generally unsatisfactory and may be deleterious in MuSK-MG. Moreover, the response to pyridostigmine standard doses, used for AchR-MG, lacks efficacy and has poor tolerance because of side effects.[10]

Prednisone, in combination with plasma exchange or intravenous immunoglobulin, is generally recommended for patients experiencing life-threatening weakness or suffering from severe disease deterioration, though possibility of non-responders is more with IvIg than plasmapheresis.[11] Immunosuppressants like azathioprine, MMF, cyclosporine, tacrolimus, methotrexate can be used as steroid sparing agents though long-term side effects pose a risk.[12] It is important to consider that 10-15% of MuSK-MG patients have a refractory disease or suffer from relapses on tapering immunosuppressive medication. In management of these patients, rituximab, an anti-CD20 monoclonal antibody has shown effectiveness in clinical trials such that immunosuppressants and steroids can later be tapered or stopped.[13]

CONCLUSION

MuSK-MG is a distinctive, frequently more severe, subtype of myasthenia gravis. Onset is usually acute and typically bulbar, with rapid progression of symptoms within a few weeks. Clinical presentation can be atypical: neck weakness, or isolated respiratory paralysis. MuSK-Ab testing confirms the diagnosis when the clinical

picture is highly suggestive. SFEMG plays an important role in diagnosing MuSK-MG in patients with borderline MuSK antibody levels. Response to treatment is often different from that expected in MG patients and achieving a regression of symptoms could be quite challenging.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Mahadeva B. Philips LH 2nd. Juel VC Autoimmune disorders of neuromuscular transmission. Semin Neurol. 2008;28(2):212.
2. Lavrnic D, Losen M, De Baets M, Hajdukovic LJ, Stojanovic V, Trikic R, et al. The features of myasthenia gravis with autoantibodies to MuSK. J Neurol Neurosurg Psychiatry. 2005;76(8):1099-102.
3. Nicolle MW. Myasthenia gravis and Lambert Eaton myasthenic syndrome. Continuum (Minneap Minn). 2016;22(6):1978.
4. Hoch W, McConville J, Helms S, Newsom-Davis J, Melms A, Vincent A. Auto-antibodies to the receptor tyrosine kinase MuSk in patients with myasthenia gravis without acetylcholine receptor antibodies. Nat Med. 2001;7(3):365-8.
5. Guptill JT, Sanders DB. Update on muscle- specific tyrosine kinase antibody positive myasthenia gravis. Curr Opin Neurol. 2010;23(5):530-5.
6. Koneczny I, Stevens JA, De Rosa A, Huda S, Huijbers MG, Saxena A, et al. IgG4 autoantibodies against muscle specific kinase undergo fab arm exchange in myasthenia gravis. J Autoimmune. 2017;77:104-15.
7. Guptill J, Sanders DB, Evoli A. Anti-MuSK antibody myasthenia gravis: clinical findings and response to treatment in two large cohorts. Muscle Nerve. 2011;44(1):36-40.
8. Rodolico C, Parisi D, Portaro S, Biasini F, Sinicropi S, Ciranni A, et al. Myasthenia gravis: unusual presentations and diagnostic pitfalls. J Neuromuscul Dis. 2016;3(3):413-8.
9. Huda S, Waters P, Woodhall M, Leite MI, Jacobson L, De Rosa A, et al. IgG-specific cell-based assay detects potentially pathogenic MuSK-Abs in seronegative MG. Neurol Neuroimmunol Neuroinflamm. 2017;4(4):e357.
10. Morren J, Li Y. Myasthenia gravis with muscle-specific tyrosine kinase antibodies: a narrative review. Muscle Nerve. 2018;58(3):344-58.
11. Reddel SW, Morsch M, Phillips WD. Clinical and scientific aspects of muscle-specific tyrosine kinase-related myasthenia gravis. Curr Opin Neurol. 2014;27(5):558-65.
12. Hehir MK, Hobson-Webb LD, Benatar M, Barnett C, Silvestri NJ, Howard JF Jr, et al. Rituximab as treatment for anti-MuSK myasthenia gravis: multicenter blinded prospective review. Neurology. 2017;89(10):1069-77.
13. Borges LS, Richman DP. Muscle specific kinase myasthenia gravis. Review article. Front Immunol. 2020;11:707.

Cite this article as: Hirolikar R, Khandait V, Bhole P, Jajoo Y. Breath of hope: unravelling isolated respiratory paralysis through anti musk positive myasthenia gravis. Int J Res Med Sci 2024;12:3914-6.