
CASE REPORT

A Case of Anti-MuSK Positive Myasthenia Gravis

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SUMMARY

Anti-MuSK Myasthenia Gravis (MG) is a rare autoimmune neuromuscular junction disorder with poor response to conventional management of MG. We're reporting a case with typical presentation and clinical course of this disorder. 28-year-old lady presented with prominent oculobulbar, proximal muscle and respiratory muscle progressively worsened for the past 8 months with demonstrable fatigability with requiring ventilatory support. She responded poorly to intravenous Immunoglobulin (IVIg), conventional immunosuppressive therapy but improved remarkably with plasmapheresis. Her acetylcholine receptor antibody was negative and anti-MuSK antibodies turn out to be positive (1.15nmol/L). The clinical presentation and the clinical course of this patient corresponds to other reported anti-MuSK positive MG cases. Plasmapheresis appears to be an effective treatment for this group of patients in MG crisis.

Keywords: Muscle-Specific Receptor Tyrosine Kinase Antibody, Myasthenia Gravis (MG), Plasmapheresis, Plasma Exchange

INTRIDUCTION

Myasthenia Gravis (MG) is an autoimmune mediated neuromuscular junction disorder. It is usually characterized by the presence of autoantibodies against the skeletal muscle acetylcholine receptor (AChR), muscle-specific receptor tyrosine kinase (MuSK) or low-density lipoprotein receptor-related protein 4 (LRP4)¹. The precise cause of this autoimmune disorder is not known. However, abnormalities of the thymus gland is long known to be playing a role in the anti-AChR antibody mediated MG^{2,3}. MG is a relatively rare disease with rather similar incidence and prevalence rate around the world, except for infantile MG which is more common in the Asian population^{4,5,6}. The prevalence is estimated to be approaching 140 per million and annual incidence of 15 per million in Caucasian^{7,8}. In addition, the annual incidence is noticed to be increasing in the recent years in the elderly age group (>65yrs)⁹. 10-year mortality for MG without treatment is estimated to be about 50%¹⁰. The clinical presentation of the disease is characterized by fluctuating muscular weakness that worsens following repetitive muscular exertion with exclusivity to striated muscle¹¹. It can be either focal (ocular) or generalized. MG can be further classified according to age of onset, thymic disorders and autoantibodies profile¹¹. Despite the availability of advanced diagnostic and therapeutic measures, management

of MG is still a challenging problem in modern medicine. Here, we report a case of anti-MuSK positive MG patient and the difficulties in management.

CASE REPORT

The patient is a 28 year-old Malay lady, no known medical illness, presented to us with proximal muscle weakness of all 4 limbs for the past 8 months. It was progressively worsened over past 3 weeks prior to admission, and was unable to ambulate for 1 day prior to admission. Associated symptoms include drooping of eyelids, diplopia, dysphagia, slurred speech and drooling of saliva for 3 weeks prior to admission. These symptoms were worse in the evening.

On examination, there was bilateral partial ptosis with demonstrable fatigability. Patient had diplopia on bilateral lateral gaze. Gag reflex was weak; and she failed swallowing test. Limbs examination revealed proximal muscle weakness of all 4 limbs, with power 2/5. Tone and deep tendon reflexes otherwise were normal. Plantar reflexes were down-going. No sensory and cerebellar involvements noted. Bedside peak flow was 110 L/min, i.e., 35% predicted.

Initial investigations revealed mild microcytic hypochromic anaemia and type 2 respiratory failure, with PCO₂ of 60 mmHg. Renal profile, electrolytes, liver function test otherwise were normal.

She was admitted to ICU with diagnosis of myasthenia gravis in crisis. She was being put on BiPAP support. IVIg 0.4 g/kg/day for 5 days were completed. Pyridostigmine was started as well. Initially, the patient responded partially to IVIg, with limbs motor power improved to 4/5 and oxygen support was weaned down to ventimask. However,

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she deteriorated again within 1 week of completion of IVIG. She required BiPAP again for type 2 respiratory failure. Azathioprine was commenced.

Subsequently, we traced her acetylcholine receptor antibody results, which turned out to be negative (0.13). No thymoma detected on CT thorax. We were unable to proceed with nerve conduction study and EMG as patient was still on NIV support at ICU.

After 3 weeks of completion of IVIG, trial of 2nd cycle of IVIG 0.4g/kg/day for 5 days was given. Unfortunately, the patient didn't respond to IVIG this time; requiring intubation for worsening CO₂ retention despite on NIV support. Therefore, we decided for plasmapheresis for 7 cycles.

She responded well to plasmapheresis. She was extubated and subsequently weaned off oxygen within 1 week after completed plasmapheresis. T. prednisolone 15 mg OD was started after patient was extubated. She was discharged well with no fatigability and focal neurological deficits. The medications upon discharged were pyridostigmine, low dose prednisolone, azathioprine, calcium supplements and proton pump inhibitor. Later, antibody to muscle specific receptor tyrosine kinase (anti MuSK) was traced back and it was positive (1.15 nmol/L).

Unfortunately, patient was readmitted 2 weeks later for MG crisis precipitated by hospital acquired pneumonia (HAP). Three cycles of plasmapheresis were done. Azathioprine was withheld due to sepsis. Again, patient responded well to the therapy, and was discharged 1 week later, planning for outpatient NCS and EMG, as well as considering treatment with rituximab after infection screening.

DISCUSSION

The case we have reported presented with typical clinical presentation of generalized early onset Anti-MuSK MG. The patient is a female and presented with prominent oculobulbar, respiratory weakness with no thymic pathology as expected¹². In term of management, the patient also failed to respond to Acetylcholinesterase inhibitor as per reported in other cases of Anti-MuSK positive MG¹³. The patient was given 2 courses of 5-day Intravenous Immunoglobulin (IVIG), however only partial response before further deteriorated within 1 week. The patient showed mark improvement after plasmapheresis was commenced. The improvement of the patient after plasmapheresis also corresponds to other reported cases of Anti-MuSK MG^{12,13}.

The management of MG usually consist of symptomatic treatment with acetylcholinesterase inhibitors¹¹. Immunosuppressive therapy such as combination of prednisolone and azathioprine to

which the patient failed to respond¹¹. Therefore, rituximab as a second line immunosuppressive therapy has been planned; as there is report showing a good clinical response in this group of patients¹⁴. Furthermore it has been observed that the prednisolone dose was able to be reduced and concomitant immunosuppressant could be withdrawn after the initiation of rituximab¹⁴.

CONCLUSION

Myasthenia gravis is a relative rare autoimmune disorder, however it carries significant morbidity and mortality. (10) Heterogenicity of autoimmune profile and clinical presentation pose a great challenge in the management of MG. Hence, patients with Anti-AchR seronegativity should be promptly investigated for anti-MuSK antibodies or other autoantibodies. In the event of failing to respond to conventional immunosuppressive therapy, plasmapheresis appears to be a promising therapeutic choice. However, larger randomized controlled trials are needed to conclude a better standard of care for this group of patients.

REFERENCES

1. J.P.Sieb. Myasthenia gravis: an update for clinician. British Society for Immunology, Clinical and experimental Immunology, 175: 408-418
2. Berris S, Morel E, Gaud C, Raimond F, LeBrigand H, Bach JF. Anti-AchR antibodies, thymic histology, and T cell subsets in myasthenia gravis. Neurology 1984; 34:66-71
3. Roxanis 1, Micklem K, Willcox N. True epithelial hyperplasia in the thymus of early-onset myasthenia gravis: implications for immunopathogenesis. J Neuroimmunol 2001; 112:163-73.
4. Meyer A, Levy Y – Geoepidemiology of myasthenia gravis. Autoimmun Rev, 2009;9:A383-386.
5. Phillips LH – The epidemiology of myasthenia gravis. Semin Neurol, 2004;24:17-20
6. Chiu HC, Vincent A, Newsom-Davis J et al. – Myasthenia gravis: population differences in disease expression and acetylcholine receptor antibody titers between Chinese and Caucasians. Neurology,1987;37:1854-1857.
7. Heldal AT, Owe JF, Gilhus NE et al. Seropositive myasthenia gravis; a nationwide epidemiology study. Neurology 73, 150-151 (2009)
8. Anderson JB, Engeland A, Owe JF et al. Myasthenia gravis requiring pyridostigmine treatment in a national population cohort. Eur. J. Neurol. 17, 1445-1450 (2010)
9. Pakzad Z, Aziz T, Oger J. Increasing incidence of myasthenia gravis among elderly in British Columbia, Canada. Neurology 2011; 76: 1526-8.
10. Gilhus NE. Autoimmune myasthenia gravis. Expert Rev. Neurother.9,351-358 (2009)
11. Nils Erik Gilhus. Advances in the treatment of myasthenia gravis. Future Neurol. 2012 7(6): 701-708
12. Sanders DB, El Salem K et al. Clinical aspects of MuSK antibody positive seronegative MG. Neurol 200;60 (12): 1978
13. Evoli A, Tonali PA, Padua L et al. Clinical correlates with anti-MuSK antibodies in generalized seronegative MG. Brain 2003; 126 (Pt 10): 2304
14. Diaz- Manera J, Martinez- Hernandez E, Querol L. Long lasting treatment effect of Rituximab in MuSK Myasthenia. Neurology 2012 Jan 17; 78(3): 189-93.

