Case Report

# MuSK Antibody Positive Myasthenia Gravis Mimicking as Myositis

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**Abstract**

Most common neuromuscular junction disorder is Myasthenia gravis (MG) which has variable clinical presentations. Diplopia and drooping of eyelids are the peculiarity of myasthenia gravis. Commonly disease manifests as a fluctuating weakness of skeletal muscles. Although respiratory symptoms may be the initial presenting complaint in a few patients, usually it develops during the later part of the disease course. The initial presentation of isolated prominent respiratory distress is a relatively rare presentation of myasthenia gravis unless accompanied by other clinical features. We report a 40-year-old female patient, who visited our hospital with presenting complaints of breathlessness and generalized myalgia and subsequently developed fatigable weakness during hospitalization.

**Keywords:** *MuSK Ab, myasthenia gravis, myositis*

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## Introduction

Myasthenia gravis (MG) is a well-known immune-mediated neuromuscular junction disorder with a prevalence between 2.19 to 36.71 cases/100.000 population.[1] It has a bimodal age pattern, with early incidence occurring in second to third decades, which has a female preponderance, and the late incidence occurring in sixth to eighth decades, which has a male preponderance.[2]

In myasthenia gravis, autoimmunity is characterized by type 2 hypersensitivity reaction, in which antibodies are directed against acetylcholine receptors (AChRs), muscle-specific kinase (MuSK), and lipoprotein-related protein 4 (LPR4). In 80% of cases of generalized MG, antibodies will be directed against anti-AChR antibodies, while amongst the 20% remaining cases, 70% of patients will have positive serum antibodies against MuSK.[3]

AChR antibodies target the extra-ocular muscles and skeletal muscles, classically resulting in fluctuating muscle weakness, drooping of eyelids and double vision, more marked in the evening or post exercise period. The lifetime risk of myasthenic crisis (acute deterioration leading to respiratory failure) is approximately ten to twenty percent and the annual risk is approximately two to three percent.[4]

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## Case Report

We report a 40-year-old lady who was initially referred for a cardiology consultation by the local physician and subsequently referred to the neurology outpatient department (OPD) as her cardiac evaluations were normal. The patient initially had a fever for a few days and after a few days of recovery from the febrile illness; she developed insidious onset progressive breathlessness, that is, more prominent in during exertion and in lying down position. Within few days her condition deteriorated and she felt difficulty in climbing upstairs and combing her hair. The patient always felt some aching pain in the calves, thighs, and arms, but there is no diurnal variation of symptoms or swelling and redness of joints. This was not associated with dysphagia, dysarthria, nasal regurgitation of liquids, or any ocular symptoms.

On the initial evaluation, the patient was alert and had proximal muscle weakness with intact deep tendon reflexes without cranial nerve, sensory or cerebellar involvement. Her cardio-pulmonary and other examination findings were normal. As the patient had

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a fever proximal muscle weakness, and tenderness, initially inflammatory myopathy was suspected, pending further evaluation.

The initial blood parameters including complete blood count, liver function test, thyroid function test, and renal function tests were normal. X-ray chest and high-resolution computerized tomography (HRCT) thorax did not show any significant abnormality. The serum creatine phosphokinase (CPK) level was 181 U/l (within normal limit).

On day-3 of admission, the patient developed drooping of eyelids, which was more prominent in her left eye. Her dyspnea also started to worsen. An ice pack and neostigmine tests were done to examine neuromuscular junction disorders, but these tests were negative for the same.

We did a repetitive nerve stimulation test (RNST), which showed a decremental response in the facial muscles. A serum sample for acetylcholine receptor antibody was sent for testing. The patient was treated with pyridostigmine for the next four days as we strongly suspected myasthenia gravis by then. But there was no improvement in the patient's condition with pyridostigmine treatment. Instead of any improvement, she developed more severe respiratory distress with a progression of weakness and neck drop. She was shifted to the intensive care unit (ICU) for better airway support and monitoring. Intravenous immunoglobulin (IVIG) was started. We received a negative AchR antibody report, so we planned to test Anti MUSK antibodies. The patient's condition continued to deteriorate requiring invasive ventilation.

After few days, serum anti-MuSK antibodies came out positive. She was immediately scheduled for plasma exchange as her condition continued to worsen despite IVIG and neostigmine treatment. Her symptoms improved drastically just after the first session of plasma exchange. After four sessions of plasma exchange, the patient was discharged with low-dose steroids therapy. She was instructed to avoid certain drugs. The patient has been stable since then, with rituximab prophylaxis without any recurrence of symptoms.

## Discussion

An aforementioned case is a rare presentation of myasthenia gravis. It shows how we should suspect myasthenia gravis, particularly in female patients presenting with unexplainable breathlessness and generalized weakness despite of the absence of classical diurnal variations in symptoms.

MuSK antibodies leading to myasthenia gravis were identified for the first time in 2001.[5] In this variant of myasthenia gravis, the IgG4 subtype of antibodies binds to an Ig-like region, inhibiting the activation of the MuSK-LRP4-Agrin complex and thus leading to the inhibition of transmission across the neuromuscular junction. These antibodies are found in approximately ten percent of myasthenia gravis patients.

The onset of MuSK-MG is classically acute and it progresses rapidly over the next few days. Drooping of eyelids and diplopia are commonly observed clinical signs. Like anti-AChR-associated MG, fatigue and generalized weakness can be seen at the onset. Bulbar onset myasthenia gravis, presenting with slurred speech, nasal intonation, and difficulty in swallowing and chewing is commonly related to rapid worsening, leading to a myasthenic crisis.[5] Our patient who presented with dyspnea on exertion initially lacked majority of the features of bulbar onset myasthenia gravis although she developed them subsequently during the hospitalization due to the progression of the disease.

Despite of negative ice pack and neostigmine test, the repetitive nerve stimulation test in Musk-MG shows a decremental pattern in facial muscles. It may show normal RNS response in limbs.[6]

MuSK-MG shows effective responses with prednisone, rituximab, and plasma exchange over conventional treatment like intravenous immunoglobulins and azathioprine. Thymectomy is also ineffective.[7] Similar to previous studies,[8] our patient who was initially treated with pyridostigmine and intravenous immunoglobulins didn't show any improvement but plasmapheresis was found to be effective.

## Conclusion

MuSK-MG exhibits female preponderance and RNST shows a decremental pattern in facial muscles. Breathlessness and generalized weakness may be initial manifestations despite of the absence of bulbar or ocular symptoms. It may mimic myopathies. This case provides an example of how challenging a diagnosis can be when only proximal muscle weakness is initially involved. While managing such cases, plasmapheresis should be considered as an effective choice of treatment over IV immunoglobulins.

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### Conflicts of interest

There are no conflicts of interest.

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