

A Case of COVID-19 Vaccine Associated New Diagnosis Myasthenia Gravis

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Abstract

An 82-year-old man presented with intermittent episodes of slurred speech during his evening meals after receiving the BNT162b2 COVID-19 vaccine. Thorough evaluation was conducted including lab work and EMG confirming a new diagnosis of late-onset myasthenia gravis. Despite treatment, the patient progressed rapidly to severe exacerbation requiring intubation and placement of a PEG tube. Infections provoking new diagnosis and exacerbations of myasthenia gravis have been reported. New diagnosis of myasthenia gravis associated with the COVID-19 vaccine is rarely reported. This case highlights the need for clinicians to be aware of the uncommon presenting symptoms in late-onset myasthenia gravis and the possibility of vaccine provoked diagnoses of immune mediated diseases.

Keywords

myasthenia gravis, COVID-19, immunization, immune mediated disease, vaccine

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Case Presentation

An 82-year-old man with a history of laryngeal cancer status post hemi-laryngectomy 40 years previously, Barrett's esophagus, and stage 3a chronic kidney disease presented in late February to the Emergency Department 4 weeks after receiving the first dose, and 2 days after receiving the second dose of BNT162b2 COVID-19 vaccine reporting intermittent episodes of slurred speech. His symptoms had been present for a few weeks, occurring in the evenings, often during his dinner. His symptoms would last approximately 15 min then resolve spontaneously. He described his symptoms as his tongue "being in the way," associated with a sensation of perioral numbness. He reported no associated vision changes or eyelid droop, no difficulty swallowing, no other motor deficits, no cognitive deficits.

In the Emergency Department his physical exam demonstrated a hoarse voice, unchanged from baseline, consistent with history of hemi-laryngectomy, and a normal neurologic exam including no cranial nerve, motor, sensory, or cognitive deficits. CT scan of the head demonstrated age related white matter changes and no evidence of acute intracranial abnormality. He was discharged with follow up in ENT, Neurology and Primary Care.

Outpatient ENT evaluation 1 week after initial presentation to the Emergency Department included direct laryngoscopy

without new mucosal lesion or mass and MRI without laryngeal tumor.

At follow up in primary care in early April he reported ongoing symptoms of slurred speech and difficulty chewing during dinner and a new symptom of trouble spitting when brushing his teeth at night. He continued to deny daytime symptoms and symptoms with earlier meals. Given his persistent, intermittent bulbar symptoms, present in the evenings clinical suspicion for myasthenia gravis was high. Acetylcholine receptor antibodies were ordered demonstrating markedly elevated Ach receptor binding Ab 11.4 (normal < 0.02), Ach receptor modulating Ab 93% (normal 0%-20%) and striational Ab titer 1:245760 (normal < 1:120) and an EMG was performed showing decrement with repeated nerve stimulation confirming the diagnosis of myasthenia gravis. Secondary evaluation for thymoma was negative.

Neurology started treatment with pyridostigmine and speech therapy in early May, and the patient noted initial

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improvement in his speech and swallowing. However, in late May, within 2 weeks of starting treatment, he began to develop eyelid droop. In late June he reported return of difficulty with meals after a dental extraction. In mid July, while on vacation, he developed significant generalized weakness and was hospitalized for a severe myasthenia gravis exacerbation treated with IV pyridostigmine, IVIG and steroids. His hospitalization was complicated by aspiration pneumonia, requirement for ventilator support and inability to swallow requiring PEG tube insertion. He recovered and was discharged to a rehabilitation facility where he continued to improve clinically.

Discussion

Myasthenia gravis is an autoimmune disorder of the neuromuscular junction caused by antibodies to the acetylcholine receptor. It causes fatigable weakness most evident after repeated muscle use or with progression of the day. Although myasthenia gravis is most common in young women, nearly one third of cases present in patients over 50 years old.¹ Late-onset myasthenia gravis is present in a 3:1 male to female ratio and peaks at age 70 in men.¹ Approximately two thirds of patients diagnosed with myasthenia gravis present with ocular symptoms of ptosis and diplopia² while 10% to 15%, most commonly those with late-onset disease, present with bulbar dysfunction, including dysarthria, dysphagia, and dysphonia.^{1,2} Progression to generalized weakness typically occurs within 2 to 3 years and myasthenia crises requiring ventilator support occur in 15% to 20% of patients.² Our patient presented with bulbar symptoms, relatively common for his age and sex. However, he exhibited an unusually rapid progression from mild symptoms to generalized weakness with severe exacerbation requiring hospitalization occurring within 4 months rather than 2 to 3 years.

The majority of new myasthenia gravis cases have no identifiable trigger, though infection and stress have been suggested as possible provoking factors in some instances and are commonly associated with myasthenia exacerbations.² Myasthenia gravis exacerbations associated with severe acute respiratory syndrome coronavirus 2 (SARS CoV 2) infection have been described in the literature.^{3,4} New onset myasthenia gravis associated with SARS CoV 2 infection has also been described.⁵⁻⁷

In contrast to associations with infections, onset or flares of autoimmune disorders associated with vaccines are rare.⁸ We found 1 case of myasthenia gravis exacerbation associated with vaccination with the mRNA-1273 COVID-19 vaccine.⁹ New onset myasthenia gravis following COVID-19 vaccination is also rarely reported. A review of vaccine related incidents from health care organizations in 3 countries found only 2 cases of new onset myasthenia gravis

following COVID-19 vaccine.⁸ Both cases involved patients in their 70s and occurred 1 to 7 days after administration of the second dose of the BNT162b2 COVID-19 vaccine.

Although our patient presented to the Emergency Department 2 days after receiving his second BNT162b2 COVID-19 vaccine, his family noted symptoms a few weeks earlier. This correlates with administration of the first BNT162b2 COVID-19 vaccine dose. New diagnosis myasthenia gravis after the first dose of COVID-19 vaccine has not been reported in the literature to our knowledge. Additionally, our patient progressed quickly from symptom onset, diagnosis and initiation of treatment to first severe exacerbation. We found no reported cases of this rapid progression of disease associated with COVID-19 vaccination.

The onset of symptoms in our patient's case correlates with administration of the vaccine, but causality cannot be proven. The plausibility of new diagnosis myasthenia gravis provoked by vaccination is supported by reports of other immune mediated diseases developing as early as 2 days after the first dose of a COVID-19 vaccine.⁸ Proposed mechanisms for vaccine provoked autoimmune disease include molecular mimicry and bystander activation.¹⁰ In a molecular mimicry model involving an mRNA vaccine, antigen produced from the mRNA may be recognized by the immune system as similar to host tissue antigen resulting in T cell activation and antibody formation against host tissue, including the acetylcholine receptor. In our patient's case, the bystander activation model may be more plausible. In this model, previously existing self-antigen is released due to stimulation of the innate immune system as part of the vaccine response resulting in activation of autoreactive T cells.¹⁰ If our patient had pre-existing self-antigen to the acetylcholine receptor that was released due to administration of the BNT162b2 COVID-19 vaccine, this may explain the short time between vaccination and onset of symptoms.

The short time between vaccine administration and new diagnosis may also be explained by exacerbation of dormant or subclinical myasthenia gravis resulting in newly noticeable symptoms.⁵ Subtle symptoms prior to vaccine administration may have been present but missed or ignored. Myasthenia gravis is underdiagnosed in those greater than 80 years old, with symptoms frequently misattributed to subjective fatigue and non-specific age-associated changes.^{1,11} Late onset myasthenia gravis can present with dysphonia which may have been difficult to recognize in our patient due to pre-existing voice changes associated with his history of hemi-laryngectomy. Aside from his history of laryngeal cancer, our patient had very few medical conditions, but co-morbidities in the elderly, especially cardiovascular risk factors, can make diagnosis of myasthenia in this age group difficult.¹²

Conclusion

Myasthenia gravis is a rare disorder. Elderly patients may have co-morbidities and may not present with the most recognizable disease features such as ocular symptoms, making diagnosis challenging. New onset myasthenia gravis associated with COVID-19 vaccination is rare but may become more frequent with increasing vaccination rates and potential recommendation for boosters increasing vaccine numbers. Diagnosis of COVID-19 vaccine associated new onset myasthenia gravis requires awareness and recognition of less common symptoms including dysarthria and dysphagia, and attention to timing of vaccination. Early recognition of myasthenia gravis can lead to timely treatment and prompt management of exacerbations.

Declaration of Conflicting Interests

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