New-Onset Myasthenia Gravis Following COVID-19 Vaccination

Case Presentation

A 28-year-old woman with no family history of neuromuscular or autoimmune disease and no significant medical history suddenly suffered generalized weakness, myalgia, and diplopia three weeks after her first BioNTech coronavirus disease 2019 (COVID-19) vaccination. She presented to our department with slurred speech, diplopia, and blurred vision after the second dose of the Pfizer-BioNTech COVID-19 vaccine. After three days of these symptoms, she had difficulty raising her arms and neck flexion. Neurological examination revealed decreased muscle strength with a Medical Research Council grade 4/5 in the upper and lower extremities.

Symptoms had been present for several weeks and showed diurnal fluctuations, often during dinner. She was barely able to swallow food.

Her physical examination revealed a nasal voice and normal mental functions, bladder symptoms, and sensory deficits. The routine hematological and biochemical parameters were normal. Cranial computed tomography (CT) scan of the head was normal. She had a negative real-time reverse transcription polymerase chain reaction (RT-PCR) for COVID-19 infection by nasopharyngeal swab test, and a normal thorax CT. In the past, as far as she knew, she had not had COVID-19.

Given her persistent, intermittent bulbar symptoms, which also occurred in the evening, clinical suspicion of MG was high. The patient's serum AchR antibody titer was <0.01 nmol/L and her muscle-specific kinase antibody titer was <0.01 nmol/L; both were within normal ranges, and LRP-4 antibodies was negative. Motor and sensory nerve conduction studies were normal. Repetitive nerve stimulation test showed a significant decrement response of the nasalis muscle and it was compatible with a post-synaptic neuromuscular transmission disorder. A single-fiber electromyography (EMG) from the frontal muscle proved abnormal.

Based on the combination of the variability of symptoms, response to neostigmine, and typical electromyographic findings, we diagnosed the patient as seronegative MG. After investigations (clinical features, normal computed tomography of the brain, and nerve conduction studies), we ruled out other diagnoses, such as other neuromuscular diseases, acute inflammatory demyelinating polyneuropathy, myopathy, brain stem ischemia, and motor neuron disease. There were no additional features that can be seen in congenital MG, such as cognitive impairment, dysmorphism, neuropathy, epilepsy, and muscle weakness that increases with exertion. The severity of MG was class IIa according to the Myasthenia Gravis Foundation of America. The patient was administered IVIG with a diagnosis of seronegative bulbar MG. Oral pyridostigmine 240 mg/day was started to the patient who had not received any immunosuppressant treatment before. The patient made a full recovery, and she was uneventfully discharged. In the control examination three months later, the patient did not have any complaints, and her treatment was continued.

Discussion

MG is the most common autoimmune disease that affects the neuromuscular junction and can lead to weakness in various patterns of muscle groups. The most commonly affected muscles in MG are the levator palpebra superioris, extraocular muscles (medial and superior rectus), neck flexors, and facial muscles. MG needs to be promptly recognized and treated because the potential for improvement and remission is very high. The primary abnormality in MG is autoantibodies to AChRs or adjacent proteins (MuSK, LRP-4, or Agrin) that allow receptor accumulation. Disruption of the neuromuscular signaling pathway results in decreased stimulation of muscles, which manifests as fatigable muscle weakness. This may be generalized or focal, affecting, particularly the ocular and bulbar regions, and in severe cases may lead to respiratory impairment.[1] Diagnosis can be made by clinical, laboratory, or neuromuscular testing.

Bacterial-viral infections, vaccines, and stress are triggers for myasthenic crisis in patients with MG. Exacerbations of MG associated with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been reported in the literature.[2] However, there are insufficient data on the infection and vaccine causing myasthenia gravis in healthy patients. New diagnoses of MG associated with the vaccine COVID-19 are rarely reported.

In a review of vaccine-related incidents at health organizations in three countries, only two cases of new-onset MG were noted after COVID-19 vaccination.[3] All two cases involved elderly patients with additional chronic conditions, and the complaints occurred one to seven days after administration of the second dose of BioNtech COVID-19 vaccine. The difference in this case is that our patient was young and had no concomitant diseases. She exhibited an unusually rapid progression from mild symptoms to generalized weakness with severe exacerbation within several weeks. The onset of symptoms was associated with the administration of the first dose of vaccine. The temporal relationship between the COVID-19 vaccination and the onset of symptoms suggests that this new-onset MG is related to the vaccination. The pathophysiologic mechanism of disease after vaccination is not clear and requires further investigation. Although the underlying pathophysiologic mechanism is not known, it is suspected that the immune response in the post-vaccination period may trigger an autoimmune process leading to the production of autoantibodies. The possibility of new diagnosis MG provoked by vaccination is supported by the reports of other immune-mediated diseases developing as early as two

days after the first dose of a COVID-19 vaccine.[3] The role of molecular mimicry and latent MG activation is thought to be the cause of the onset of the disease.[4] In the mRNA vaccine-induced molecular mimicry model, the antigen produced from the mRNA can be recognized by the immune system similar to the host tissue antigen, resulting in T cell activation and antibody formation against the host tissue, including the acetylcholine receptor. In the latent MG activation model, pre-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. Considering the short time between vaccination and the onset of symptoms, the latent MG activation model is more appropriate for our patient.

Treatment is aimed at symptomatic improvement with pyridostigmine and immunosuppressive treatments to control antibody production and reduce disease severity.

We present a case of MG diagnosed after administration of two doses of Pfizer BioNtech's COVID-19 vaccine based on electrodiagnostic findings and clinic. Given the pandemic and vaccination studies, it is important to recognize the development of neurologic complications that may be associated with the vaccine. Early recognition of vaccine-related MG can lead to timely treatment and rapid management of exacerbations. It should be remembered that because of the small number of cases, results are limited and only associations can be drawn. Observation of more cases is needed to consolidate our findings.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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