AUCTORES
Globalize your Research

International Journal of Clinical Case Reports and Reviews
Fatemeh Afrashteh *

Open Access

Case Report

# New Onset of Myasthenia Gravis following COVID-19 Vaccination: A Case Report

**Mostafa Almasi-Dooghaee [1], Atefeh Imani [2], Fatemeh Afrashteh [3*]**

[1] Assistant professor, Department of Neurology, Firoozgar Hospital, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

[2] Department of Neurology, Firoozgar Hospital, Iran University of Medical Sciences, Tehran, Iran.

[3] School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

***Corresponding Author:** Fatemeh Afrashteh, School of Medicine, Iran University of Medical Sciences, Tehran, Iran.

**Received Date:** March 13, 2023 | **Accepted Date:** March 24, 2023 | **Published Date:** March 31, 2023

**Citation:** Mostafa A. Dooghaee, Imani A., Afrashteh F., (2023), New Onset of Myasthenia Gravis Following COVID-19 Vaccination: A Case Report, *International Journal of Clinical Case Reports and Reviews*, 13(3); **DOI:** 10.31579/2690-4861/303



**Abstract:**

Myasthenia gravis (MG) is a rare autoimmune disease and the most common neuromuscular junction disorder. The most common symptoms are diplopia, ptosis, and fluctuating weakness of ocular and limb muscles. Here we report a case of MG after COVID-19 vaccination. A 37-year-old Iranian lady presented with generalized weakness, diplopia, and ptosis after three days from taking the second dose of COVID-19 vaccine. Symptoms began three days after taking the second dose of Sinopharm BIBP COVID-19 vaccine (BBIBP-CorV) and worsened within a week. Her past medical history included migraine-type headaches and gastric reflux. She was consuming Rizatriptan and Nortriptyline for her migraine headache and Pantoprazole, Domperidone, and Sertraline for stomach reflux. She had a family history of Essential tremor in her father, uncle, and grandfather. Antibody against the acetylcholine receptor (AChR-Ab) was more than eight times compared to the normal range. The pattern of repetitive nerve stimulation was suggestive for MG. Treatment with corticosteroid, azathioprine, and pyridostigmin led to amelioration of symptoms. Follow-up testing revealed AChR-Ab returned to the normal range.

There are some case reports in that a chronic autoimmune disorder flared up after the COVID1-9 infection or its vaccination. There are several reports of MG exacerbations, acute respiratory distress syndrome, higher ICU admission, and mortality rate and worsening neurological symptoms after COVID-19 infection. There is still debate about the association between neuromuscular disorders and COVID-19 infection and vaccination. This matter is more doubtful for myasthenia gravis.

**Key words:** sars-cov-2; myasthenia gravis; covid-19 vaccination; neuromuscular junction disorder; guillain-barré syndrome

## Introduction

Myasthenia gravis (MG) is a rare autoimmune disease and the most common neuromuscular. MG is mostly caused by binding autoantibodies to the postsynaptic acetylcholine receptor (AChR) at the neuromuscular junction but other types of antibodies including anti-muscle-specific kinase (anti-MuSK) antibodies may be detected in some cases.[1] The binding of an AChR antibody leads to fluctuating skeletal muscle weakness that gets worse by repetitive contraction, commonly involving ocular, bulbar, respiratory, and proximal limb muscles.

At the emergence of COVID-19 pandemics, the literature pointed toward the point that the developing Sars-Cov-2 infection is related to the increased risk of mortality following hospitalization and severe outcomes in patients with MG.[2] After a while, there have been some reports of a new onset of MG after Sars-Cov-2 infection.[3-5]. It is not known whether this is an association or maybe a causal relationship between Sars-Cov-2 infection and MG.

To the best of our knowledge, there is only one report of a case of COVID-19 Vaccine-associated new-diagnosis Myasthenia Gravis [6].

Here, we report a young lady with a typically generalized myasthenia gravis that the symptoms emerged soon after the second dose of COVID-19 vaccination.

## Case Report

A 37-years-old Iranian lady presented to the neurology clinic with a history of three weeks of diplopia, ptosis, and the weakness of facial and proximal limbs muscles. Symptoms began three days after taking the second dose of Sinopharm BIBP COVID-19 vaccine (BBIBP-CorV) and worsened within a week. She was a Ph.D. student of Health psychology

and noticed that the ocular symptoms gradually worsened after studying or working with her laptop. The muscle weakness worsened after walking for several minutes and climbing the stairs. She denied having similar symptoms before. The patient had no history of trauma, thyroid disease, anemia, bladder or bowel dysfunction, or sensory symptoms. She had no respiratory or swallowing complaint, but she noticed that she got tired sooner after walking. Her past medical history included migraine-type headaches and gastric reflux. She was consuming Rizatriptan and Nortriptyline for her migraine headache and Pantoprazole, Domperidone, and Sertraline for stomach reflux. She had a family history of Essential tremor in her father, uncle, and grandfather. Recently, her mother received a diagnosis of Systemic lupus erythematosus (SLE). She had arthralgia and mild leukopenia for several years. Recently, after the third dose of COVID-19 vaccine (AstraZeneca) injection, some skin lesions appeared. The laboratory tests revealed leukopenia (white blood cells: 3800 *1000/ µL) and increased the titer of anti-nuclear antibody (ANA) and anti-dsDNA.

Neurologic examination revealed asymmetric ptosis, more pronounced on the left side, and was exaggerated after exercise (Figure1). The fore of eye closure was also decreased. Neck flexion and extension and Blowing test were normal. The strength of upper limbs muscles was normal but the Gover's sign was positive, indicating the weakness of proximal muscles of lower limbs.

According to clinical suspicion of myasthenia gravis, some tests were performed to confirm MG. In addition, some laboratory tests were performed to rule out differential diagnoses including Sars-Cov-2 infection and thyroid disorders. The results are shown in Table1. Routine laboratory factors were normal except for hemoglobin and MHC that were lower than the normal range. The titer of the anti-AChR antibody was 3.3 nmol/L which is more than eight times that normal range. Repetitive nerve stimulation (RNS) was performed and a post-exercise exhaustion response (more than 10% decrement) in trapezius and abductor digiti minimi muscles was seen in slow RNS which is suggestive for post-synaptic neuromuscular junction disorders. Besides, other markers in Nerve Conduction Study and Electromyography were normal. Chest CT scan revealed no signs of Thymoma. According to the diagnosis of myasthenia gravis, oral Pyridostigmin, Prednisolone, and Azathioprine were prescribed. The patient's symptoms were significantly resolved.

Six months later after diagnosis of MG, she was on 30mg/day Prednisolone and 100mg/day Azathioprine, and no need for Pyridostigmin. Clinically, she was in clinical remission including no ocular symptoms, no easy fatigability and normal neurologic examination. In addition, the AChR-Ab titer was 0.3 nmol/L indicative of the negative result.

| | Result | Normal Range | | Result | Normal Range |
|---|---|---|---|---|---|
| W.B.C | 4.7 *1000/ µL | 4.5 - 11.0 *1000/ µL | TIBC | 340 µgr/dl | 230-440 µgr/dl |
| R.B.C | 4.45 Mil/ µL | 4.35 - 5.65 Mil/ µL | SI | 51 µgr/dl | 23-134 µgr/dl |
| Hemoglobin | 11.8 gr/dL | 12.0 - 15.5 gr/dL | Ferritin | 10.0 ng/ml | 10-124 ng/ml |
| MCV | 81.3 fL | 80-100 fL | T4 | 7.5 µg/dl | 4.8-11.6 µg/dl |
| MCH | 26.5 pgr | 29 ± 2 pgr | TSH | 3.43 µIU/ml | 0.4-4 µIU/ml |
| Platelets | 189 *1000/ µL | 150- 450 *1000/ µL | CPR | 0.5 mg/L | <6 mg/L |
| Neutrophil | 59.1% | 40-60% | Vitamin D (25OH) | 43.0 ng/ml | 30-100 ng/ml |
| Lymphocyte | 32.4% | 20-40% | Calcium | 8.9 mg/dl | 8.5-10.5 mg/dl |
| Monocyte | 4.5% | 2-8% | phosphorus | 3.6 mg/dl | 2.7-4.5 mg/dl |
| Eosinophil | 3.6% | 1-4% | Vitamin B12 | 422 pg/ml | 193-982 pg/ml |
| Basophil | 0.4% | 0.5-1% | Sodium | 140.2 meq/L | 136-145 meq/L |
| Fasting Blood sugar | 86 mg/dl | 70-110 mg/dl | Potassium | 4.13 meq/L | 3.5-5.1 meq/L |
| Urea | 24.55 mg/dl | <43 mg/dl | Magnesium | 1.9 mg/dl | 1.9-2.5 mg/dl |
| BUN | 11.47 mg/dl | 7-21 mg/dl | Homocysteine | 9.42 micmol/L | 4.4-13.5 micmol/L |
| Creatinine | 1.02 mg/d | 0.6-1.1 mg/dl | LDH | 177 U/I | <480 U/I |
| Total cholesterol | 192 mg/dl | <200 mg/dl | ALP | 124 U/I | 64-306 U/I |
| Triglycerides | 119 mg/dl | <200 mg/dl | AST | 12 U/I | <31 U/I |
| HDL cholesterol | 51 mg/dl | >50 mg/dl | ALT | 10 U/I | <32 U/I |
| LDL cholesterol | 108 mg/dl | <130 mg/dl | CPK | 47 U/I | <167 U/I |
| VLDL cholesterol | 24 mg/dl | 19-52 mg/dl | AChR-Ab | 3.3 nmol/L | <0.05 nmol/L |

**Table 1:** The laboratory findings of the patient at the time of clinical presentation including the results of Hematology, biochemistry, serology and hormones markers.

W.B.C: White Blood Cells, R.B.C: Red Blood Cells, MCV: Mean Corpuscular Volume, MCH: Mean Corpuscular Hemoglobin, BUN: Blood Urea Nitrogen, HDL: High-Density Lipoprotein, Low-Density Lipoprotein, VLDL: Very-Low-Density Lipoprotein, TIBC: Total Iron-Binding Capacity, SI:Serum Iron, TSH: Thyroid Stimulating Hormone, CRP:C-Reactive Protein, LDH: Lactate Dehydrogenase, ALP:Alkaline Phosphatase, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, CPK: Creatinine Phosphokinase, AChR-Ab: acetylcholine receptor Antibody.

**Figure 1:** Bilateral ptosis, more prominent at the left side, which could be enhanced after exercise (not shown here) in the patient.

## Discussion

There are several reports of MG exacerbations, acute respiratory distress syndrome, higher ICU admission, and mortality rate and worsening neurological symptoms after COVID-19 infection [7, 8]. Not only the prognosis of COVID-19 infection is more severe in MG patients, but the medications used in COVID-19, such as azithromycin and hydroxychloroquine, also worsen the course of MG disease and taking immunosuppressive drugs due to weakened immune systems in MG patients after COVID-19 infection is still challenging [2].

There are various reports of neurological complications in 78% of COVID-19 infected patients. Encephalopathy, myalgia, seizure, myopathy, optic neuritis, headache, cerebrovascular disease, immune-mediated neuropathy was reported in the course of COVID-19 infection as neurological complications [9].

To the best of our knowledge, this is the second case of new onset MG after the COVID-19 vaccination. In this study, our patient was a 37-year-old lady with a negative history of MG who developed limb and eye muscle weakness, three days after the second dose of BBIBP-CorV vaccine. BBIBP-CorV vaccine is a type of inactivated virus COVID-19 vaccine which was provided by Sinopharm's Beijing Institute of Biological Products. Ancillary tests including AChR antibody and RNS study confirmed the diagnosis of MG. treatment with immunosuppressive and Acetylcholine esterase inhibitors led to amelioration of the symptoms. After six months, clinical remission was achieved and the level of AChR-Ab returned to normal value. In addition, recently her mother was diagnosed to have SLE that its dermatologic manifestations also evolved after injection of third dose of COVID-vaccine.

Recently, an 82-year-old man was reported with intermittent bulbar symptoms after 2 days of injecting the second dose of nucleoside-modified RNA COVID-19 vaccine. The presenting symptoms were intermittent episodes of slurred speech which was more pronounced in the evening. This patient had no ocular symptoms. Clinical suspicion was confirmed with the results of RNS and antibodies titer. The RNS revealed decrementing pattern and the AChR binding Ab, AChR modulating Ab and striational Ab titer were elevated [10].

Besides, a case of MG exacerbations after receiving the Moderna COVID-19 vaccine approximately five and one weeks prior to worsening symptoms has been reported. He was a 77-year-old male with a history of MG and new onset of dysphagia within one week after the COVID-19 vaccination [11]. This could be due to a weak defensive power of T and B lymphocytes because of taking immunosuppressive drugs in these patients, and therefore the COVID-19 vaccination may not be effective in these patients. To treat the patient's symptoms, a low dose of corticosteroids was prescribed to reduce the number of inflammatory cytokines in his body.

Our current knowledge about the consequences of COVID-19 vaccines is limited. One of the neurological consequences of vaccination is Guillain-Barré syndrome (GBS) which has been reported for the first time following two weeks after injection of the Pfizer COVID-19 vaccine in a patient. She was 82-year-old and her symptoms were generalized body pain, paresthesia, and difficulty walking [10]. After that, a GBS onset in a 62-year-old woman after 11 days from Oxford/AstraZeneca COVID-19 vaccine injection with the complaint of paresthesia and progressive weakness of her lower limbs was reported. She received intravenous immunoglobulin (IVIG) at a dose of 2 g/kg for 5 days and but her symptoms worsened and she was admitted to the ICU with mechanical ventilation [12]. Recently, an interesting study compared the incidence of GBS after two types of COVID-19 vaccines including Ad.26.COV2. S (Janssen) and mRNA vaccines. The results showed the risk of GBS for Ad.26.COV2.S (Janssen) vaccines is more than 20 times than mRNA vaccines (adjusted RR= 20.56 (95% CI: 6.94-64.66)) [13].

Because of limited studies, there is still debate about the association between neuromuscular disorders and COVID-19 infection and vaccination (Figure2). This matter is more doubtful for myasthenia gravis. It is not clear if this relationship is just an association or there may be a causal relationship between them. We suppose that the vaccination may induce the immune system, not only for immunization against the virus but also for flare-up the latent autoimmune disorder which had not been unfolded before [14]. One evidence for our claim is that the titer of ACHR-Ab in our patient reached the normal value, six months afterward. Although this may be due to passing time after vaccine-induced autoimmunity, but also the effect of treatment may not be excluded. Another clue is the flare-up of the symptoms in her mother who had the diagnosis of SLE, recently. Her mother was under the supervision of a doctor for arthralgia and leukopenia for several years without any well-known diagnosis. Surprisingly, her lupus was evident after the injection of COVID-19 vaccine and the criteria are fulfilling now. In addition, the positive history for another autoimmune disorder in a family member is a sign of innate susceptibility to an autoimmune disorder.

There are some case reports in that a chronic autoimmune disorder flared up after the COVID1-9 infection or its vaccination. In a study published on 2021 April, 27 subjects had an episode of acute immune-mediated diseases (IMD) after COVID-19 vaccination. Among them, 17 individuals had a flare-up after a well-known IMD and 10 had a new-onset IMD. Interestingly, 21/27 of the patients had a least one previous autoimmune/rheumatic disease diagnosis prior to the vaccination. The authors suggested that the rate of both flares and new-onset IMD after COVID-19 vaccination is rare [14].

One another important issue is the medication choosing, typically immunosuppressive agents for patients with immune-mediated disease including myasthenia gravis. The choice of medication in patients who already have myasthenia gravis and active COVID-19 infection or those who develop MG after infection or vaccination is still controversial.

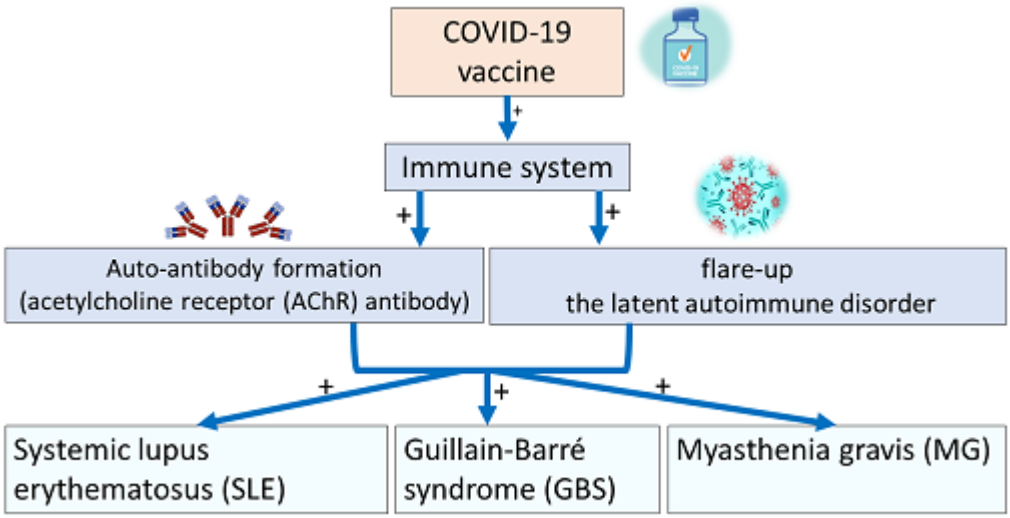


**Figure 2:** The immunologic consequences of COVID-19 vaccine

## Abbreviations

ACHR: acetylcholine receptor

ALP: Alkaline Phosphatase,

ALT: Alanine Aminotransferase

ANA: anti-nuclear antibody

AST: Aspartate Aminotransferase

BBIBP-CorV: Sinopharm BIBP COVID-19 vaccine

BUN: Blood Urea Nitrogen

CPK: Creatinine Phosphokinase

CRP: C-reactive protein

GBS: Guillain-Barré syndrome

HDL: High-Density Lipoprotein

IMD: acute immune-mediated diseases

LDH: Lactate Dehydrogenase

LDL: Low-Density Lipoprotein

MCH: Mean Corpuscular Hemoglobin

MCV: Mean Corpuscular Volume

MG: Myasthenia gravis

MUCK: anti-muscle-specific kinase

R.B.C: Red Blood Cells

RNS: Repetitive nerve stimulation

SI: Serum Iron

SLE: Systemic lupus erythematosus

TIBC: Total Iron-Binding Capacity

TSH: Thyroid Stimulating Hormone

VLDL: Very-Low-Density Lipoprotein

WBC: white blood cells

## Author contribution

MA contributed conception and manage the patient. FA contributed writing and data collection. AI contributed writing. All authors contributed to manuscript revision, read and approved the submitted version.

## Conflicts of interest

The authors declare that they have no conflict of interest.

## Ethical approval

Not applicable

## Consent to participate

Informed consent to participate in this study was given from the patient.

## Consent to publication

Not applicable

## Availability of data and materials

Not applicable

## Funding

Not applicable

## References

1. Gilhus NE, Verschuuren JJ. (2015). Myasthenia gravis: subgroup classification and therapeutic strategies. *Lancet Neurol*. 14:1023-1036.
2. Muppidi S, Guptill JT, Jacob S, Li Y, Farrugia ME, et al. (2020). COVID-19-associated risks and effects in myasthenia gravis (CARE-MG). *Lancet Neurol*. 19:970-971.
3. Huber M, Rogozinski S, Puppe W, Framme C, Höglinger G, et al. (2020). Postinfectious Onset of Myasthenia Gravis in a COVID-19 Patient. *Front Neurol*. 11:576153.
4. Sriwastava S, Tandon M, Kataria S, Daimee M, Sultan S. (2021). New onset of ocular myasthenia gravis in a patient with COVID-19: a novel case report and literature review. *J Neurol*. 268:2690-2696.

5. Karimi N, Okhovat AA, Ziaadini B, Haghi Ashtiani B, Nafissi S, et al. (2021). Myasthenia gravis associated with novel coronavirus 2019 infection: A report of three cases. *Clin Neurol Neurosurg*. 208:106834.
6. Chavez A, Pougnier C. (2021). A Case of COVID-19 Vaccine Associated New Diagnosis Myasthenia Gravis. *J Prim Care Community Health*. 12:21501327211051933.
7. Camelo-Filho AE, Silva AMS, Estephan EP, Zambon AA, Mendonça RH, et al. (2020). Myasthenia Gravis and COVID-19: Clinical Characteristics and Outcomes. *Front Neurol*. 11:1053.
8. Mirfazeli FS, Sarabi-Jamab A, Pereira-Sanchez V, Kordi A, Shariati B, et al. (2022). chronic fatigue syndrome and cognitive deficit are associated with acute-phase neuropsychiatric manifestations of COVID-19: A 9-month follow-up study. *Neurol Sci*; 10:1-9.
9. Mirfazeli FS, Sarabi-Jamab A, Jahanbakhshi A, Kordi A, Javadnia P, et al. (2020). Neuropsychiatric manifestations of COVID-19 can be clustered in three distinct symptom categories. *Sci Rep*. 10:20957.
10. Waheed S, Bayas A, Hindi F, Rizvi Z, Espinosa PS. (2021). Neurological Complications of COVID-19: Guillain-Barre Syndrome Following Pfizer COVID-19 Vaccine. *Cureus*. 13: e13426.
11. Tagliaferri AR, Narvaneni S, Azzam MH, Grist W. (2021). A Case of COVID-19 Vaccine Causing a Myasthenia Gravis Crisis. *Cureus*. 13: e15581.
12. Hasan T, Khan M, Khan F, Hamza G. (2021). Case of Guillain-Barré syndrome following COVID-19 vaccine. *BMJ Case Rep*. 14.
13. Hanson KE, Goddard K, Lewis N, Fireman B, Myers TR, et al. (2021). Guillain-Barré Syndrome after COVID-19 Vaccination in the Vaccine Safety Datalink. *medRxiv*.
14. Watad A, De Marco G, Mahajna H, Druyan A, Eltity M, et al. (2021). Immune-Mediated Disease Flares or New-Onset Disease in 27 Subjects Following mRNA/DNA SARS-CoV-2 Vaccination. *Vaccines (Basel)*. 9.






**DOI:10.31579/2690-4861/303**