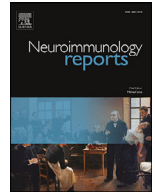




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“A new case of myasthenia gravis following COVID-19 Vaccination”

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ABSTRACT

Background: Myasthenia gravis (MG) is an autoimmune disease of unknown etiology. Infections are known as a major cause of MG exacerbations. A few studies have shown an association between new onset MG and SARS-CoV-2 infection.

Case presentation: We have reported a case of new onset myasthenia gravis in a 68-year-old man presented with bulbar symptoms a few days after receiving COVID-19 vaccine (Sinopharm vaccine). The disease was confirmed by high titer of antibody against acetylcholine receptor and electrophysiological examinations.

Conclusion: Among the adverse effects reported with the COVID-19 vaccine, new onset myasthenia gravis is very rare. The underlying mechanism is unknown but the immune response after vaccination and molecular mimicry theory has been proposed.

Introduction

Myasthenia gravis (MG) is an autoimmune disease involving neuromuscular junction that is characterized by fatigability and intermittent weakness of skeletal muscles due to antibodies against acetylcholine receptors (Chavez and Pougner, 2021, Lee et al., 2022). A few studies have shown an association between new onset MG and SARS-CoV2 infection. This correlation was partly explained by over activation of the immune response that leading to antibodies production by plasma cells against the neuromuscular junction structures (Jōgi et al., 2022). In the reported cases of new onset MG following COVID19 infection, several autoantibodies have been detected (Jōgi et al., 2022).

There have been several case reports regarding the association between vaccine and new onset MG (Sansone and Bonifati, 2022). It is possible that vaccines trigger or aggravate autoimmune diseases including MG (Ruan et al., 2021); however, except for a potential role of the live-attenuated Japanese encephalitis virus vaccine in eliciting of the childhood onset MG, such an association has been assumed to be mostly anecdotal (Sansone and Bonifati, 2022). Nonetheless, there are evidences regarding transient worsening of the symptoms or exacerbation of MG following vaccine administration (Ruan et al., 2021).

So far, there have been few studies on the safety and efficacy of SARS-CoV2 vaccine in MG patients (Sansone and Bonifati, 2022). Here, we have reported a case of new onset MG following COVID19 vaccine.

Case report

A 68-year-old man was admitted to the neurology clinic due to swallowing problems and speech disorder. The symptoms had developed three days following the injection of second dose of inactivated virus COVID-19 vaccine (Sinopharm vaccine) which had progressively worsened within one month. At the time of admission to the clinic, the symptoms were so severe that the patient was very ill and helpless and could not even drink fluids. The patient did not report any recent infection neither before vaccination nor after that. He had a negative drug history and he said that he was completely healthy before the vaccine. The past medical history had been unremarkable so far. The family history had also been negative for autoimmune disorders. The patient did not complain of headache, dizziness or vertigo, blurred vision and diplopia; also, he did not state any focal weakness and numbness of the limbs.

On the neurologic examination, partial ptosis was present in both eyes. The pupils were midsize and reactive to light. Eye movement was normal in all directions. There was neither facial asymmetry nor facial numbness. The patient had nasal speech and drooling (due to inability to swallow saliva). Pharyngeal folds were symmetrical on the both sides. The examination of motor system showed normal proximal and distal muscle power in all limbs. Deep tendon reflexes in upper and lower extremities were normal (2+) and plantar reflexes were flexor on the both sides.

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The patient was admitted to the hospital for further evaluations. Brain MRI was taken and did not show any abnormalities. Laboratory studies including complete blood cell count, blood sugar, urea and creatinine, serum electrolytes (sodium, potassium, Ionized and total calcium, phosphorous, magnesium), erythrocyte sedimentation rate, thyroid function test, were normal. SARS-CoV-2 PCR was negative. With suspected neuromuscular junction disorders, mediastinal CT, electrophysiological examination and acetylcholine receptor and muscle-specific kinase (MuSK) antibodies were requested. Mediastinal CT and MRI did not show thymoma. MuSK antibody was negative, but serum titer of antibody against acetylcholine receptor was elevated (30nmol/L). In slow repetitive nerve stimulation from orbicularis oculi and nasalis muscles, significant decremental pattern was detected, with repair after one minute exercise, typical of postsynaptic neuromuscular junction problems. The patient was treated with oral pyridostigmine (60mg, TID), prednisolon and intravenous immunoglobulins (due to acute course of disease), resulting in significant improvement of symptoms.

Discussion

Myasthenia gravis is an autoimmune disorder of neuromuscular junction that causes intermittent fatigability and weakness of skeletal muscles (Chavez and Pougner, 2021, Lee et al., 2022). Most patients present with ocular symptoms (ptosis and diplopia) but, 10-15% present with bulbar symptoms including dysarthria, dysphagia and dysphonia (Chavez and Pougner, 2021). Although infection and stress are known as the causes of MG exacerbation, but in most cases of new onset myasthenia gravis there is not any identifiable factor (Chavez and Pougner, 2021, Tagliaferri, Narvani and Grist, 2021).

MG following SARS-CoV2 infection has been reported in the literatures; the causal relationship between the two conditions is difficult to understand. In all reported cases, the symptoms of MG have developed with latency from the SARS-CoV2 infection but not in the acute phase of the infection (Jögi et al., 2022). This indicates the autoimmune mechanism in the pathogenesis of the disease. Another hypothesis is that infection in the context of the genetic predisposition makes a person susceptible to the disease. Particular HLA haplotypes such as HLA DQA1, DQB1 have been implicated in some cases of late onset MG (Jögi et al., 2022). An alternative theory has suggested that infection or some medications used to treat SARS-COVID19 infection (including Azithromycin and other macrolides) uncover the preexisting mild MG disease (Jögi et al., 2022). However, MG exacerbation with various infections especially respiratory tract infections is more common in practice.

Our patient presented with bulbar dysfunction a few days after receiving the second dose of COVID-19 vaccine (Sinopharm). Among the adverse effects reported with the SARS-CoV2 vaccine, new onset myasthenia gravis was very rare. The underlying mechanism was unknown but the immune response after vaccination and molecular mimicry theory were proposed (Chavez and Pougner, 2021, Lee et al., 2022).

So far, a few cases of MG related to COVID-19 vaccine have been reported. Maher and colleagues reported the first case of ocular MG that triggered by the viral vector Oxford-AstraZeneca COVID-19 vaccine. Their patient was treated with pyridostigmine and oral corticosteroids (Maher, Hogarty and Artsi). Huang described another case of new onset ocular MG with high anti-AchR antibody titer after chAdOx1 nCoV-19 vaccine (Huang et al., 2022).

Our case is the first case of new onset myasthenia gravis following Sinopharm vaccine that is associated with high antibody titer against the acetylcholine receptor and a dramatic response to the acetylcholine esterase inhibitor drugs and oral corticosteroid.

Also, Chavez and Pougner reported a new case of myasthenia gravis at the old age (late onset MG) with bulbar manifestations and high antibody titer against the acetylcholine receptor after receiving the BNT 162b2 COVID-9 vaccine (Chavez and Pougner, 2021).

Myung Ah Lee, et.al described myasthenia gravis at the young age (early onset MG) after receiving COVID-19 mRNA vaccine (Pfizer-BioNTech) which showed thymus hyperplasia on the chest CT scan and was associated with a negative antibody titer and a favorable response to the acetylcholine esterase inhibitor drugs (Lee et al., 2022).

There have also been several cases of MG exacerbation with SARS-CoV2 vaccine (Sansone and Bonifati) which it seems unrelated to pre-vaccine disease severity (Sansone and Bonifati, 2022). Because of the benefits of vaccination for the MG patients outweigh the potential risks, it is recommended to these patients (Sansone and Bonifati, 2022); however, the patients should be aware of the possible exacerbation or transient worsening of symptoms after vaccination.

The cases of myasthenia gravis following hepatitis B vaccine have also been reported with a favorable prognosis (Stübgen, 2010). Recently, myasthenia gravis following immunotherapy drugs such as checkpoint inhibitors and Bacillus Calmette-Guerin (BCG) therapy in the treatment of bladder cancer has been reported (Suzuki et al., 2017, Takizawa et al., 2017).

Therefore, there is a possibility of MG after receiving SARS-CoV2 vaccine. If muscle weakness, ocular and bulbar symptoms occur, MG should be considered, even if this seems a rare event. Although, there are not enough data about the appropriate treatment for MG caused by the vaccine and its prognosis, but in the reported cases, an optimal response to the acetylcholine esterase inhibitor drugs and corticosteroids has been seen.

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Authorship

All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this article, take responsibility for the integrity of the work as a whole, and have given their approval for this version to be published.

Ethics approval

No ethical approval was required as this manuscript is a case report. However, the necessary written informed consent was obtained from the patient himself.

Conflict of interests

The authors declare that no conflict of or competing interests existed or occurred in this manuscript.

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