



## Case Report

# First Paediatric Case of mRNA COVID-19 Vaccine Associated New Onset Systemic Myasthenic Crisis

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### Abstract

Myasthenia gravis (MG) is an autoimmune disorder characterized by abnormal neuromuscular conduction. The thymus is believed to play a key role in the pathogenesis of MG; therefore, thymectomy is an important treatment option for the disease. As MG exacerbations and new-onset MG cases following Coronavirus Disease 2019 (COVID-19) vaccinations have been previously reported in the literature, various complications highly related to autoimmunity, such as Guillain-Barré syndrome, have also been described after vaccination. A previously healthy girl developed her first life-threatening systemic MG attack following administration of the messenger RNA (mRNA) BNT162b2 COVID-19 vaccine. Despite receiving treatment targeting MG, her clinical status did not show significant improvement, which led to the decision to perform thymectomy via the video-assisted thoracoscopic surgery (VATS) approach. After the procedure, a significant improvement was observed in her clinical condition. We aimed to contribute to the literature on this rarely encountered condition by reporting the first paediatric case in our country presenting with BNT162b2 vaccination-associated generalized weakness and severe respiratory distress, who was diagnosed with MG and thymoma during follow-up, in the light of contemporary literature. This case also serves as a warning for other mRNA vaccines.

**Keywords:** BNT162b2, COVID-19, Myasthenia gravis, paediatric, thymoma.

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The vaccine against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), introduced after the declaration of the COVID-19 pandemic by the World Health Organization (WHO) in March 2020, markedly limited the spread of the virus and reduced mortality. Although it has been proven that the vaccines have a satisfactory safety profile in randomized clinical studies, severe and unexpected neurological complications were reported in 2022: Guillain-Barré syndrome, cerebrovascular events, and autoimmune disorders including myasthenia gravis (MG).<sup>[1,2]</sup>

Myasthenia gravis (MG) is an autoimmune neurological disorder characterized by abnormal neuromuscular conduction. Antibodies against acetylcholine receptors (AChRs), muscle-specific kinase (MuSK), and protein 4 bound to the low-density lipoprotein receptor (LRP4) are the dominant autoantibodies in MG. The disease is more common in women (3:1) and in young people between 20 and 30 years of age, whereas it affects both sexes equally later in life. The thymus is believed to play an important role in the pathogenesis of MG; it shows morphological

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changes such as lymphofollicular hyperplasia, thymoma, and thymic atrophy. The general guidelines of the Centers for Disease Control and Prevention (CDC) recommend that most MG patients should be vaccinated with any COVID-19 vaccine.<sup>[1-3]</sup>

In this study, we aimed to report a previously healthy paediatric MG patient who experienced her first disease attack after being vaccinated with the BNT162b2 mRNA COVID-19 (Pfizer–BioNTech) vaccine, had persistent attacks despite immunotherapy, and showed regression in attack frequency a short time after undergoing video-assisted thoracoscopic (VATS) thymectomy.

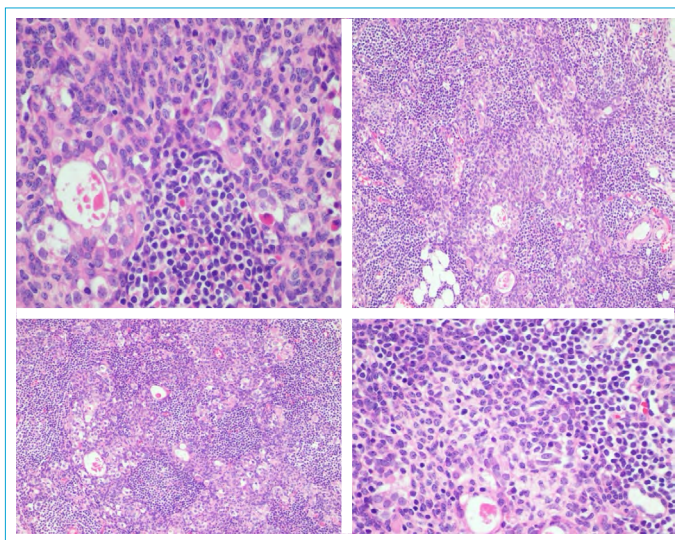
### Case Report

A 15-year-old female patient presented to our paediatric emergency department with difficulty swallowing, followed by generalized weakness and respiratory distress, 36 hours after receiving the first dose of the BNT162b2 mRNA COVID-19 (Pfizer–BioNTech) vaccine. Her physical examination was remarkable for dysphagia, respiratory distress, and tachypnoea. She had normal deep tendon reflexes; her gag reflex was positive, but she had difficulty speaking. Her body temperature was 36.8°C, blood pressure 116/72 mmHg, and pulse rate 103/minute. She had difficulty with swallowing and mastication. Her eye movements were normal, and there was no ptosis.

Twenty-four hours after admission to the paediatric ward, her symptoms, most notably respiratory distress, worsened; thus, she was transferred to the paediatric intensive care unit. She was intubated shortly thereafter. A repeat neurological examination revealed positive DTRs and no ophthalmological abnormalities, including ptosis. Her blood tests (serum biochemistry, creatine kinase, CRP, sedimentation rate, free T4, and TSH) were normal. None of her smear or blood PCR tests, including the COVID-19 PCR, was positive.

An electromyogram (EMG) performed using the polyneuropathy protocol revealed no abnormalities. A repetitive stimulation test produced a decremental response. After sending the anti-AChR and anti-MuSK antibody tests, she was started on intravenous immunoglobulin (0.4 mg/kg/day×5 days), pyridostigmine, and methylprednisolone at a dose of 30 mg/kg/day for 3 days. The patient's complaints rapidly regressed after the initiation of treatment; she was extubated at the 18th hour and transferred to the regular ward 60 hours later. All of her symptoms resolved by the 72nd hour of therapy.

The anti-AChR antibody level was 2.6 nmol/L (<0.25 nmol/L), while anti-MuSK antibodies were negative. Azathioprine treatment was added to the regimen, and steroid



**Figure 1.** Appearance compatible with thymoma containing lymphoid stroma.

therapy was planned to continue for 6 months. However, her complaints recurred after tapering the steroid dose. As her symptoms did not abate despite azathioprine and pyridostigmine treatments, she underwent thymectomy via the video-assisted thoracoscopic surgery (VATS) technique. Examination of the pathology specimen revealed micronodular stage 1 thymoma (Fig. 1). She did not experience recurrent attacks during a 1-year follow-up after thymectomy.

### Discussion

Myasthenia gravis is an autoimmune disorder of the neuromuscular junction caused by antibodies against the acetylcholine receptor. Juvenile MG constitutes approximately 10% of all MG cases. Weakness leading to exhaustion after repetitive use of muscles or as the day progresses is the most prominent feature of the disease and is most commonly seen in young women.<sup>[1,3]</sup>

The thymus gland has an incompletely understood yet very important role in the pathogenesis of MG. While the thymus gland is expected to lose its function and involute with puberty, it is well known that this fails to occur in a significant portion of generalized MG patients with AChR antibodies and that these patients have a thymic abnormality. This abnormality is in the form of thymic hyperplasia in more than 80% of patients with early-onset, generalized MG with positive AChR antibodies and as thymic epithelial tumor (thymoma) in 10–15% irrespective of age. In the pathogenesis of MG, AChR-specific CD4+ T helper (Th) cells are essential for AChR antibody production. Because the thymic gland contains muscular cells with acetylcholine receptors on their surface and there is

an abnormal number of cells with an increased T4/T8 ratio in the thymus of MG patients, it is thought that the thymus gland is the site where the autoantibodies responsible for MG are largely produced.<sup>[4-7]</sup> Furthermore, TGF- $\beta$  causes Treg cell development by inducing Focp3 (“fork-head box P3”), a Treg cell-associated transcription factor.<sup>[5]</sup> Inducible Treg cells and Th17 cells are reciprocally regulated during differentiation; TGF- $\beta$  plays a role as an inducer in this pathway and establishes the relationship between thymoma and MG, with increased cytokine levels contributing to this process by directly affecting TGF- $\beta$ .<sup>[6]</sup> The authors attributed the detection of thymoma in our patient, whose first findings appeared after vaccination, to increased cytokine levels and the autoimmunity triggered by them, as stated in the literature.

Farina et al.<sup>[7]</sup> reported that few side effects occurred after COVID-19 vaccination; clinical worsening was rare, but the BNT162b2 vaccine was more frequently encountered in cases of clinical worsening. Ishizuchi et al.<sup>[8]</sup> reported that clinical worsening occurred in three patients, two of whom received the BNT162b2 vaccine. The timing of post-vaccination worsening ranged from the first 2 days after the first vaccine to 14 days after the second dose. Watad et al.<sup>[9]</sup> reported two newly diagnosed cases of MG after the second dose of BNT162b2, with one of those patients having been intubated. The first pediatric case of systemic MG following BNT162b2 vaccination was reported by Ramdas et al.<sup>[10]</sup> in a 13-year-old child, and our patient represents the first case reported from our country. In our patient, the symptoms appeared after the first dose, and the patient suffered severe clinical progression leading to intubation. The appearance of the findings after the first dose and the detection of thymoma are both very important findings because they are rare situations.

The relationship between vaccines and autoimmunity is a highly debated topic. The proposed mechanisms for vaccine-induced autoimmune diseases include molecular mimicry between SARS-CoV-2's spike protein and the host's own antigens and “bystander” activation. However, there is strong suspicion that a mechanism similar to a cytokine storm may underlie the condition.<sup>[8-12]</sup> The strong response of our patient's clinical signs to immunotherapy in the first attack supports this view.

Two adult patients were reported from Türkiye by Yılmaz et al.,<sup>[13]</sup> one diagnosed with systemic MG and the other with ocular MG after an mRNA COVID-19 vaccine. In the systemic MG case, thymectomy was reported to be planned by the authors. In this regard, the significance of our case lies in the fact that it involves a pediatric patient who underwent thymectomy via the VATS approach.

## Conclusion

In conclusion, although MG is a rare condition, the high morbidity and mortality rates associated with COVID-19 infection require raising awareness of vaccines. The fact that COVID-19 vaccines have adverse effects as rare as other vaccines should not discourage patients and, more importantly, should not prevent neurologists from recommending vaccination to MG patients. However, if there is severe involvement, such as severe bulbar symptoms and myasthenic crisis, it will be safer to postpone the COVID-19 vaccine. In Türkiye, the first newly discovered pediatric MG case after the BNT162b2 vaccine, which we presented in our study, indicates that, just like in adults and similar to other autoimmune conditions, MG can affect children after vaccination. This condition should be remembered after mRNA vaccines, which have become increasingly important, particularly in children giving a vaccination history. It corroborates the notion that MG should be considered if the tests for coronavirus are negative in cases of clinical worsening.

## Disclosures

**Ethics Committee Approval:** This is a single case report, and therefore ethics committee approval was not required in accordance with institutional policies.

**Informed Consent:** Written informed consent taken from patient family.

**Conflict of Interest:** The authors declare that there is no conflict of interest.

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