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Myasthenia Gravis Presenting after Administration of the mRNA-1273 Vaccine

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ABSTRACT

The mRNA-1273 SARS-CoV-2 vaccine received emergency use authorization in December 2021. We present a case of myasthenia gravis (MG) which became clinically apparent following vaccination against SARS-CoV-2. A 30-year-old man developed acute onset diplopia, 2 days after receiving his first mRNA-1273 vaccination against SARS-CoV-2. He reported blurred vision with horizontally displaced images, which worsened with increased eye strain. Diplopia resolved when one eye was covered. He also had fatigable arm weakness, but denied dysphagia, dysarthria, dysphonia or dyspnoea. On examination, he had left-sided ptosis and esotropia at rest which worsened with sustained upward gaze and prolonged focus. He also had fatigable weakness of neck flexion and extension (4+/5), and generalized, fatigable weakness (4/5). His single-breath count was 38. Cranial nerves, sensory examination and deep tendon reflexes were normal. A 2-min ice-pack test and neostigmine test temporarily improved his diplopia and ptosis. The acetylcholine receptor (AChR) antibody was borderline high and muscle-specific tyrosine kinase (MuSK) antibody was negative. Chest CT and brain MRI with contrast were unremarkable. The patient was diagnosed with MG and oral pyridostigmine and prednisone therapy were initiated.

We present a case of newly diagnosed MG after administration of mRNA-1273 vaccination against SARS-CoV-2. Although there has been long-standing discussion regarding the potential for vaccines to exacerbate autoimmune conditions, data remain sparse and consensus has not been reached. Consequently, this case is important to make providers aware of potential side effects of a novel vaccine, and may also help guide the selection of vaccination candidates and monitoring parameters.

LEARNING POINTS

- We present a case of newly diagnosed myasthenia gravis after administration of the mRNA-1273 SARS-CoV-2 vaccine.
- mRNA-1273 vaccination against SARS-CoV-2 may exacerbate subclinical cases of myasthenia gravis.
- Recognition of new vaccine side effects may guide the selection of vulnerable patients.

KEYWORDS

Myasthenia gravis, SARS-CoV-2, mRNA-1273

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INTRODUCTION

Myasthenia gravis (MG) is an antibody-mediated autoimmune disorder in which antibodies bind to acetylcholine receptors or to functionally related molecules in the postsynaptic neuromuscular junction [1]. It is characterized by fatigable weakness involving ocular, bulbar, limb and respiratory muscles [1]. A positive ice-pack test is a helpful bedside test that can support the diagnosis, with a sensitivity of 82%, specificity of 96% for generalized myasthenia, and sensitivity of 94%, specificity of 97% for ocular myasthenia [2]. Additionally, the neostigmine test, another bedside test, has been reported to be a useful test to support the diagnosis [3].

Subclinical MG may become apparent after some medications, vaccinations and underlying illness [4–6]. A case of MG crisis induced by the mRNA-1273 (Moderna) SARS-CoV-2 vaccine has been reported [7]. We describe a case of newly diagnosed MG after administration of the mRNA-1273 SARS-CoV-2 vaccine.

CASE DESCRIPTION

A 30-year-old man developed acute onset diplopia, 2 days after receiving his first mRNA-1273 vaccination against SARS-CoV-2. He reported blurred vision with horizontally displaced images, which worsened with increased eye strain. Diplopia resolved when one eye was covered. With directed history taking, the patient recounted a 6-month history of early fatigue while performing overhead manual labour. He denied dysphagia, dysarthria, dysphonia or dyspnoea. He had no family history of autoimmune diseases. On examination, he had left-sided ptosis and esotropia at rest which worsened with sustained upward gaze and prolonged focus. He also had fatigable weakness of neck flexion and extension (4+/5), and generalized, fatigable weakness predominantly in his left hemibody (4/5). His single-breath count was 38. Cranial nerves, sensory examination and deep tendon reflexes were normal. A 2-min ice-pack test and neostigmine test temporarily improved his diplopia and ptosis. The acetylcholine receptor (AChR) antibody was borderline high at 0.3 nmol/l (normal <0.24 nmol/l), and muscle-specific tyrosine kinase (MuSK) antibody was negative. Chest CT and MRI with contrast of the brain were unremarkable. Given the limited access to electrodiagnostic studies at this location, electromyography results were not available. The patient was diagnosed with MG and oral pyridostigmine 30 mg three times a day and prednisone 10 mg a day were initiated. The prednisone was increased weekly by 10 mg per day. During treatment, the patient felt his symptoms improved but continued to fluctuate. Ultimately, his dose of prednisone was lowered to 10 mg daily due to side effects. At the time of this submission, immunosuppressants had not yet been started.

DISCUSSION

We present a case of a newly diagnosed MG which became clinically apparent following administration of mRNA-1273 vaccination against SARS-CoV-2.

The mRNA-1273 vaccine was approved in the USA with an emergency use authorization on 18 December 2021 [8]. Although there has been long-standing discussion regarding the potential for vaccines to exacerbate autoimmune conditions, data remain sparse and consensus has not been reached. The influenza vaccine has been the most widely investigated vaccine, but myasthenia exacerbation has not been supported [9].

Data regarding the safety and efficacy of mRNA vaccines in patients with autoimmune conditions is currently limited [10]. Although we cannot definitively attribute our patient's presentation to the mRNA-1273 vaccine, his MG symptoms became apparent after administration of the vaccine, without other environmental changes. We hypothesize that this pathophysiology may be related to generalized upregulation of the immune system. Furthermore, a more specific interaction has been noted between the SARS-CoV-2 spike glycoprotein and nicotinic acetylcholine receptors, which may lead to new or exacerbation of neuromuscular junction conditions, such as myasthenia gravis [11]. Although AChR was borderline high and MuSK antibodies were negative in this case, the patient had documented a characteristic fatigable diplopia and weakness, with clinical improvement after ice-pack bedside testing, neostigmine and pyridostigmine. We were not able to test for low-density lipoprotein receptor-related protein 4 antibodies and a repetitive nerve stimulation test and single fibre electromyography were inaccessible due to hospital limitations. The patient was diagnosed with MG and responded appropriately to treatment.

Lee et al. recently described a similar case of early-onset MG in which symptoms developed on the same day after the patient received their second dose of a SARS-CoV-2 vaccine [12]. Most et al. also described a case of MG 2 days after administration of the first dose of a SARS-CoV-2 vaccine [13]. Although similar, these patients received the BNT162b2 (Pfizer-BioNTech) SARS-CoV-2 vaccine, while our patient received the mRNA-1273 (Moderna) SARS-CoV-2 vaccine. Interestingly, all cases tested negative for AChR antibodies and MuSK antibodies, and presentations occurred within 2 days of vaccination [12, 13]. This is a short timeline to produce antibodies, raising the question of alternative pathophysiology or exacerbation of an underlying condition in the setting of upregulation of the immune system. The patient in our case reported a 6-month history of early fatigue, and his presentation may represent illness exacerbation after injection of the vaccine. In the case of MG exacerbation described by Tagliaferri et al., the patient presented to the emergency room with dysphagia beginning within 2 days after receiving his second dose of the mRNA-1273 SARS-CoV-2 vaccine [7]. Alternatively, the seronegative status may imply that

there is a novel antibody that cannot be detected with the current assay methods. The patient described by Lee et al. developed symptoms after their second dose of a SARS-CoV-2 vaccine, with the possibility that pre-existing antibodies allowed for early clinical symptoms [12]. Further research and case presentations may help to clarify the potential underlying mechanisms for the development of MG in the setting of vaccination against SARS-CoV-2.

Our case illustrates the potential for unrecognized side effects in a patient population that may already be vulnerable and suffer from respiratory compromise. Consequently, this report is not only important to make providers aware of the potential side effects of a novel vaccine, but also may help guide the selection of vaccination candidates and monitoring parameters. The need for monitoring and potential escalation of care for patients with severe myasthenia who may experience an exacerbation secondary to vaccine administration undoubtedly has implications for resource-scarce healthcare environments and readiness.

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