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Case Report

Multiple sclerosis relapse following Moderna SARS-CoV-2 PF vaccination: Case report and review of literature

Ange A. Mele, MD, Henry Ogbuagu, MD, Sahil Parag, DO, Bradley Pierce, MD

Northeast Georgia Medical Center, Internal Medicine Residency Program, USA

Abstract

Multiple sclerosis is a demyelinating disorder of the central nervous system characterized by lesions disseminated in time and space. The diagnostic criteria for laboratory-supported definite multiple sclerosis involves two episodes of symptoms, evidence of at least one white matter lesion on MRI and abnormal oligoclonal bands in cerebrospinal fluid. Patients usually present in their early twenties and on average have up to one flare up per year. While vaccines play an important role in the prevention of many diseases, they have often been purported as a potential trigger of multiple sclerosis and multiple sclerosis relapses. The medical literature provides reliable information concerning the risk of developing multiple sclerosis and multiple sclerosis relapses following administration of most vaccines, but not much is known about the novel Moderna SARS-CoV-2 PF vaccine.

We report the case of 24-year-old male who presented with right sided facial weakness, dizziness, and dysarthria two days after receiving his first dose of Moderna COVID-19 vaccine. Imaging studies noted both acute and chronic central nervous system lesions. He met the diagnostic criteria for laboratory-supported definite multiple sclerosis. His acute flare was treated with intravenous corticosteroids and the patient was subsequently started on Ocrelizumab.

This case serves as an important example of the novel Moderna SARS-CoV-2 PF vaccine as a potential trigger of multiple sclerosis relapse; it reviews the literature for similar occurrences with the other COVID-19 vaccines and provides reliable guidance for COVID-19 vaccination for patients with multiple sclerosis.

Introduction

With the advent of the COVID-19 pandemic, different vaccines have been developed to protect the population and curtail the increasing number of deaths from the virus. The Center for Disease Control and Prevention has reported that patients with neurological disorders were at risk of severe illness from COVID-19. This statement was based on the evidence collected from reviews, cross-sectional studies, and cohort studies [2]. As part of this group, patients with multiple sclerosis were therefore given priority to receive the vaccine first. Several cases of multiple sclerosis relapse have however been reported following the administration of the different COVID-19 vaccines. This occurrence calls for further investigations of the safety of COVID-19 vaccines on the health of multiple sclerosis patients.

Case Presentation

We report the case of a 24-year-old male with a medical history of obesity who presented to the Emergency Department for evaluation of right sided facial weakness, dysarthria, and dizziness two days after receiving his first dose of the Moderna COVID-19 vaccine. He denied a previous similar presentation, headaches, chest pain, shortness of breath and abdominal tenderness. Motor strength was 5/5 bilaterally in both upper and lower extremities, tandem gait was intact, and there were no sensory neurological deficit, dysdiadochokinesia or abnormal Romberg sign.

His chest X-ray was negative for any acute cardiopulmonary disease, EKG consistent with sinus rhythm with a rate of 89 beats per minutes. Transthoracic echocardiogram showed normal left ventricular systolic and diastolic functions with an ejection fraction of 55 to 60%. Bubble study was positive for a trivial intracardiac shunt. CT angiography of the head and neck was negative for acute intracranial processes and did not show any focal narrowing of the cervical or intracranial arteries. Magnetic Resonance Imaging of the brain was notable for an active demyelinating lesion in the left frontal subcortical white matter. Additional regions of white matter signal abnormality, most notably involving the left frontal horn, are expected to be older regions of demyelination. There was no evidence of involvement below the tentorium cerebelli and the optic nerves appeared normal. At this point his acute flare was treated with intravenous corticosteroids.

The patient subsequently underwent lumbar puncture. Meningitis and encephalitis PCR panel was unremarkable. His multiple sclerosis panel was positive for seven oligoclonal bands, consistent with the diagnosis of multiple sclerosis. His immunoglobulin G level in the cerebrospinal fluid was within normal limits. The results of his CSF cell count with differential were all within normal limits. Lupus anticoagulant profile, antinuclear antibodies and aquaporin-4 antibodies were negative, effectively ruling out antiphospholipid syndrome, systemic

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***Corresponding author(s):** Ange A. Mele, MD, Northeast Georgia Medical Center, Internal Medicine Residency Program, USA

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lupus erythematosus and neuromyelitis optica respectively. The patient met the diagnostic criteria for laboratory supported definite multiple sclerosis and was diagnosed with the condition. He was subsequently started on Ocrelizumab.

Discussion

The diagnosis of multiple sclerosis can be made based on three diagnostic criteria; namely clinically definite multiple sclerosis; laboratory-supported definite multiple sclerosis and probable multiple sclerosis. Clinically definite multiple sclerosis requires two episodes of symptoms and evidence of two white matter lesions on imaging or clinically. Laboratory-supported definite multiple sclerosis is characterized by two episodes of symptoms as well as evidence of at least one white matter lesion on MRI and abnormal cerebrospinal fluid showing oligoclonal bands. Probable multiple sclerosis requires two episodes of symptoms and either one white matter lesion or oligoclonal bands in the cerebrospinal fluid [1]. As previously discussed, our patient met the diagnostic criteria for laboratory supported definite multiple sclerosis.

The mechanism of action of the Pfizer-BioNTech and Moderna vaccines has been explained by Mascellino et al. According to this journal, the mRNA able to translate and codify for the superficial spike proteins of the virus is isolated and included in a lipid nanoparticle. This nanoparticle is injected intramuscularly as a vaccine, attaches to the host cells, and inserts its mRNA into the cytoplasm to reach the ribosome and synthesize the viral spike proteins. The latter reach the cellular membrane and attract antibodies against the viral spike proteins and the cells of the immune system in particular helper T cells. The interleukins 2, 4 and 5 produced by helper T cells stimulate T cells to proliferate memory T-cells and kill the infected cells [3]. Before receiving the vaccine, our patient did not know he had multiple sclerosis. His MRI noted older regions of demyelination in the left frontal horn as well as new active demyelinating lesion in the left frontal subcortical white matter. He developed a multiple sclerosis relapse after receiving the first dose of the mRNA vaccine. His acute flare was treated with intravenous corticosteroids, and he recovered promptly. The patient received his second dose of Moderna vaccine one month and four days later without further side effects. He was then started on scheduled Ocrelizumab infusions.

Maniscalco et al. also reports a case of multiple sclerosis relapse in a 26-year-old female patient 48 hours after receiving the Pfizer-BioNTech vaccine. The patient presented with paresthesia in her left arm and limbs along with walking difficulties. The patient's MRI showed three new voluminous enhancing lesions. She recovered following five days of methylprednisolone therapy. The authors call for further work to redefine the risk/benefit ratio of COVID-19 vaccination in patients with multiple sclerosis [4]. However, a study that imply a low risk/benefit ratio was conducted by Achiron et al. It was an observational study in one clinical Centre in Israel where 555 multiple sclerosis patients received the Pfizer-BioNTech vaccine. The safety profile was noted to be the same as in premarketing clinical trials where patients mostly experienced fatigue, headache, and injection site reactions. Acute relapses were detected in 2.1% of patients following the first vaccine dose and 1.6% of patients after the second dose [5]. The authors noted increased risks of adverse effects in younger patients aged 18 to 55. This low rate of relapse might be explained by the short follow up period of 20 and 38 days following the first and second vaccine administration, respectively.

To further corroborate the previous findings, Nistri et al. reported a series of 16 cases of multiple sclerosis relapses occurring between 3 days and 3 weeks following administration of the Pfizer vaccine for 10 patients, Moderna vaccine for 2 of them and AstraZeneca for 4 patients between March and June 2021 [6]. Three of these 16 patients were newly diagnosed with multiple sclerosis after COVID-19 vaccination, 13 were known multiple sclerosis patients and 9 of those were being treated with disease modifying drugs. All patients had evidence of newly active lesions on MRI. The authors state that the causative or incidental nature of this relationship remains to be established.

Vaccines with other mechanism of action have also been implicated in multiple sclerosis relapse. This is the case of the Sputnik vaccine in Russia. Its mechanism of action involves two adenovirus viral vector (recombinant-adenovirus 5 and 26). According to Etemadifar et al., a 34-year-old rituximab-treated multiple sclerosis patient who was diagnosed with relapsing-remitting multiple sclerosis 13 years ago developed hemiplegia and ataxia following administration of the Sputnik vaccine [7]. The journal states that this occurred three months after his last Rituximab infusion and three days following his first dose of Sputnik vaccine. Moreover, it further raises concerns about the safety and efficacy of the vaccine in multiple sclerosis patients treated with anti-CD20 monoclonal antibodies. Her anti-SARS-COV-2 antibodies were below the lower detectable limit. The patient however received the second dose of the Sputnik vaccine without additional side effects. The authors postulate that the efficacy of COVID-19 vaccination is limited in patients who are being treated with anti-CD20 monoclonal antibodies and recommend planning a delay in such treatments to enable patients to receive the vaccine and develop anti-SARS-CoV-2 immunity.

According to Bagnato et al., multiple sclerosis patients and those on immunosuppressive medications were excluded from clinical trials lead by Pfizer-BioNTech; the Moderna study did not mention multiple sclerosis as a comorbidity and did not make it part of an exclusion criteria either; and the Johnson and Johnson phase 3 clinical trial were not fully public yet [8]. As such, the use of these vaccines in MS patients on disease modifying therapies is mainly based on previous studies of other vaccines. Based on these studies, it claims that immunization in general is considered safe in people with multiple sclerosis and recommends receiving the vaccine if MS patients do not have any other known contraindications to doing so. The Multiple Sclerosis centers of Excellence further postulates that COVID-19 vaccines were important and safe for veterans with multiple sclerosis [9].

Concerning MS patients who are on immunosuppressive medications, a discussion with their primary neurologist is

recommended to understand the importance of vaccination, the minimal risks associated with it and to decide if any treatment modification is necessary. Furthermore, Righi et al. states mRNA based or inactivated vaccines are also considered safe in multiple sclerosis patients undergoing immunomodulatory or immunosuppressive treatments [10]. Finally, according to guidance from the National Multiple Sclerosis Society, discontinuing disease modifying agents is associated with significant risks of relapse and worsening of clinical course. As such, the NMSS recommends continuing these medications unless otherwise advised by their primary neurologist [11].

The American Academy of Neurology (AAN) also released guidance on the vaccination of multiple sclerosis patients on different types of disease modifying therapies [12]. The first recommendation is for patients on beta interferons, glatiramer acetate, teriflunomide, dimethyl or monomethyl fumarate or natalizumab. The AAN advised against discontinuing these disease modifying agents and does not recommend a delay or adjustments in dosing or timing of administration of these medications. The second recommendation is for MS patients on anti-CD20 monoclonal infusions. Patients on these medications are prone to an attenuation of humoral response. It is therefore advised to be vaccinated ≥ 12 weeks after the last infusion and to resume infusion 4 weeks after the last dose of the vaccine to maximize the efficacy of the vaccine. The third recommendation concerns patients on Alemtuzumab. Given its effects on CD52+ cells, it is advised to be vaccinated ≥ 24 weeks after the last infusion and to resume infusion 4 weeks after the last dose of the vaccine. MS patients starting Alemtuzumab are advised to be fully vaccinated first and starting the medication 4 weeks or more after completing the vaccine. The fourth recommendation concerns MS patients on sphingosine 1 phosphate receptor modulators, oral cladribine and ofatumumab. MS patients starting these medications are also advised to be fully vaccinated and then starting these disease modifying agents 2 to 4 weeks after completing the vaccine. Patients are not advised to change the schedule of administration. When possible, however, patients should restart taking their doses of cladribine or ofatumumab 2 to 4 weeks after the last dose of the vaccine. These recommendations should be followed only when there is enough disease stability to allow delays in treatment. Complete blood count with differential should be collected to obtain an estimate of white blood cell count and lymphocyte in patients with markedly suppressed immune system.

Conclusion

Overall, it can be concluded that many cases of multiple sclerosis relapses have been reported following the administration of COVID-19 vaccines with different mechanism of action. The National Multiple Sclerosis Society and the Multiple Sclerosis Centers of Excellence advocate for the safety of the vaccine in MS patients. Moreover, the American Academy of Neurology has released guidelines for the vaccination of MS patients on different disease modifying therapies. Further research needs to be done to better comprehend the mechanism of these relapses following the administration of the different COVID-19 vaccines. In the meantime, following these guidelines, as well as continued patient education and clinical monitoring will contribute to mitigating these incidental side effects.

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