

Case Report

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Neurologic complications of COVID-19 vaccine**Kunal M Ajmera^{1*}; Heather Wilkinson²**¹Department of Hospital Medicine, Calvert Health Medical Center, Prince Frederick, MD, USA.²Department of Critical Care Medicine, Doctor's Community Hospital, MD, USA.***Corresponding Author: Kunal M Ajmera**Department of Hospital Medicine, Calvert Health
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Abstract

The neurological complications of coronavirus disease 2019 (COVID-19) are well known and well documented. With advancements in vaccination programs for COVID-19, the pandemic appears to be under control for the most part. With mutating strains of COVID-19 and given that the efficacy of vaccines is still being evaluated, the adverse event profiles of approved vaccines are also becoming clearer. Here, we present a case of severe vertigo in a patient who received a booster dose of the Moderna vaccine. Further neurological complications of the COVID-19 vaccines have also been reviewed and summarized. While the benefits of the vaccines certainly outweigh the risk of adverse events, prospective clinical trials are needed to understand whether specific groups such as those with a personal or family history of autoimmune disease are at a higher risk of developing certain adverse events.

Keywords: COVID-19; COVID-19 vaccine; vertigo; neurological complications.

Introduction

The first case of coronavirus disease 2019 (COVID-19), caused by the novel SARS-CoV-2 virus, was diagnosed and reported in December 2019 in Wuhan, China. Since then, more than 53 million people worldwide have been diagnosed, and more than 800,000 people have died as of January 1, 2022 [1]. As the virus is continuously mutating and with the detection of the delta strain and most recently the omicron strain, the number of affected cases is increasing at an unprecedented rate worldwide. As people start to travel and gather again for various purposes, different preventative strategies including vaccination remain the primary mode of protection.

In the United States, a COVID-19 primary series vaccination is recommended for everyone aged ≥ 5 years to prevent COVID-19. A booster dose of the COVID-19 vaccine is recommended for all persons aged ≥ 18 years, with a minimum of 6 months after completion of an mRNA vaccine (Pfizer-BioNTech or Moderna) primary series, or a minimum of 2 months after completion of a Janssen vaccine primary dose [1]. The most commonly administered vaccines in the US are two mRNA vaccines [2] with $>94\%$ efficacy against the original COVID-19 virus strain,

made by Pfizer–BioNTech (BNT162b2) and Moderna (mRNA-1273), and one modified adenoviral vector vaccine with $<65\%$ efficacy made by Johnson & Johnson (Janssen) [3]. Some of the other vaccines available outside the US are Covishield (modified adenoviral vector vaccine), Covaxin (inactivated virus vaccine), ChAdOx1-nCoV (non-replicating vector vaccine), Gam-COVID-Vac (non-replicating vector vaccine, CoronaVac (inactivated vaccine manufactured), and BBIBP-CorV and WBIP (inactivated virus vaccine). The messenger RNA in the mRNA vaccines contains the genetic information transcribed to produce surface spike proteins. Host immunity then recognizes these spike proteins and produces antibodies. CD4+ helper/inducer cells and CD8+ T cytotoxic/suppressor cells induce the production of cytokines and subsequent removal of the virus from the intracellular compartment [4,5]. The Janssen vaccine carries a modified adenoviral vector with the genetic code for the SARS-COV-2 spike protein antigen, which triggers an immune response [6].

Vaccines against COVID-19 are safe in general. Standard adverse events after the first, second, or booster doses are pain, redness and swelling at the injection site, headaches, myalgias, fever, and nausea. People with a history of anaphylaxis should

be more careful to avoid any complications to vaccination. Here, we present a case of severe vertigo in a patient who received a booster dose of the Moderna vaccine.

Methods

A systematic review of medical literature with the keywords “COVID-19,” “vertigo,” “neurological complications,” “COVID-19 vaccine” was performed on PubMed, Google Scholar, and ScienceDirect databases. Articles that included definition, pathophysiology, mechanism of action, and etiology were identified. All articles, including reviews (narrative and systematic), meta-analysis, literature review, randomized controlled trials (RCTs), case-control cohorts, case series, and case reports, were screened for relevant content. Out of the many articles, full texts of the relevant retrieved articles were accessed and used in this paper, in addition to data obtained from the CDC website. Pertinent information was summarized and organized for ease of understanding.

Case report

Our patient was a 74-year-old woman with a long-standing medical history significant for essential hypertension, brain stroke, lupus, paroxysmal atrial fibrillation (AF), Marfan’s syndrome, mitral valve prolapse, and hyperlipidemia who presented to the emergency room (ER) secondary to severe vertigo. The patient had never been diagnosed with COVID-19. She had received the first and second doses of Moderna vaccine 6 months prior to receiving the booster dose, which she tolerated well without any significant adverse events. After receiving the booster dose in the morning, she slept for most of the day. While watching television the same evening, she suddenly started to feel the room spinning and experienced severe nausea and numbness/tingling around her face. Eventually, she had to keep her eyes closed for a prolonged duration to prevent this sensation. She did not have any difficulty with her speech or vision, weakness or heaviness of her arm or leg, facial droop, or difficulty with speech or swallowing. She consulted her primary care provider who advised her to come to the emergency room (ER) for further evaluation. While the patient was being evaluated, she started having left-sided non-radiating, 8 out of 10, heavy pressure-like sensations, and shortness of breath, which lasted for roughly 30 min. The chest pain eventually resolved without further intervention but vertigo continued. She denied having any associated lightheadedness, dizziness, or tinnitus. The patient’s family history was significant for stroke (father) and Parkinson’s disease (mother). The patient did not have any surgical history. The patient was a non-smoker and did not consume alcohol and had no history of substance abuse. The patient was on regular, long-term metoprolol. The patient was not on any anticoagulants for AF or immunosuppressants for lupus at home. In the ER, physical examination revealed a temperature of 98.1 F, pulse rate of 68 bpm, respiratory rate of 15/min, blood pressure of 176/113 mmHg, and oxygen saturation of 98% in room air. Orthostatic vital signs remained negative. Chest auscultation revealed a 2/6 ejection systolic murmur heard at the base. There was no evidence of carotid bruit, jugular vein distention, or pedal edema. Neurological examination showed no motor or sensory deficits and no facial droop or dysarthria; her reflexes and vision were normal. Blood work including complete blood count and comprehensive metabolic panel

remained within the standard limit and are described in detail in Table 1. Electrocardiogram showed normal sinus rhythm with a heart rate of 74, PR interval of 164, QRS duration of 76 ms, QTc interval of 444 ms; no ST/T elevation or depression was noted. Chest radiography showed no acute cardiopulmonary abnormality. Computed tomography (CT) of the head without contrast showed no acute intracranial abnormalities, and CT angiography of the head and neck showed no large vessel occlusion or hemorrhage. No carotid/vertebral artery stenosis, dissection, or occlusion was observed. Magnetic resonance imaging (MRI) of the brain showed only chronic infarction. The patient’s troponin remained negative thrice and was cleared from a cardiac standpoint by the cardiologist. Chest pain was thought to be secondary to elevated blood pressure, possibly related to the vaccine booster dose. The patient had a normal echocardiogram from 4 months before this hospitalization episode and was not repeated. The patient was diagnosed with vertigo, likely a postvaccination adverse event, by the neurology department, and she was started on meclizine and ondansetron which improved her symptoms. Given the prior stroke history, the patient was started on aspirin and statin. Aggressive blood pressure control was recommended. The patient was eventually discharged in a stable condition on day 3 of hospitalization with a referral for vestibular rehabilitation.

Discussion

Vaccines against COVID-19 have been available for almost over a year now. With time, we also have a better understanding of the short- and long-term vaccine-related adverse events. Vaccine Adverse Events Reporting System (VAERS) is a passive vaccine adverse events reporting system in the US. It is crucial to remember that VAERS is a passive data reporting system, and the data presented might be inaccurate. It is also possible that the incidence rate of real-world adverse events is actually higher than that reported by VAERS. There is always a chance that some of these adverse events might be coincidental and unrelated to the vaccine. Data certainly does not establish causal association but only indicates the temporal association between adverse events and vaccine administration. According to VAERS, there have been 8,136 documented cases of vertigo post-COVID-19 vaccination, of which almost 6,000 cases were reported in female vaccine recipients (Table 2) [7]. Out of these, 10 vaccine recipients had died (seven female and three male), and at least 444 recipients (294 female and 147 male) required hospitalization. It is also worth noting that >200 million people have been fully vaccinated with both doses, and almost 70 million have already received a booster dose. Thus, the incidence of vertigo can be considered a non-serious and rare adverse event, per the World Health Organization’s definition [8].

Vertigo results from an imbalance within the vestibular system. There can be a peripheral or central cause of vertigo such as benign paroxysmal positional vertigo, migraine, vestibular neuritis, Meniere’s syndrome, and vertebrobasilar insufficiency. Treatment should be directed to the specific underlying cause; however, meclizine and antiemetics help with symptomatic management when the underlying cause remains unidentified. Neurologic complications of COVID-19 disease such as those related to the central nervous system (vertigo, cerebrovascular accident, headache, altered mentation, seizures) and peripheral nervous system (anosmia, vision impairment, neuropathic pain)

Table 1: Blood work on day 0.

		Reference range
WBC	7.8	4.0-11.0 10 ³ /ul
Hb	12.9	13.0-18.0 g/dL
MCV	98.5	80-95 fl
Platelet	221	150-450 10 ³ /uL
Na	142	136-145 mmol/L
K	3.9	3.5-5.1 mmol/L
Glucose	132	75-100 mg/dL
AG	07	8-16 mEQ/L
S. Creat	1.0	0.6-1.3 mg/dL
GFR	>60	(>60 mL/min)
Ca	9.2	8.5-10.1 mg/dL
Mg	2.2	1.8-2.4 mg/dL
T. Bili	0.4	0.2-1.0 mg/dL
AST	23	15-37 U/L
ALT	17	12-78 U/L
Alk Phos	89	45-117 U/L
Albumin	3.7	3.4-5.0 g/dL

WBC: White Blood Cell, Hb: Hemoglobin, MCV: Mean Corpuscular Volume, Na: Sodium, K: Potassium, AG: Anion Gap, S. creat: Serum Creatinine, GFR: Glomerular Filtration Rate, Ca: calcium, Mg: magnesium, T. Bili: Total Bilirubin, AST: Aspartate Aminotransferase, ALT: Alanine Aminotransferase, Alk Phos: Alkaline Phosphatase.

are well documented. Patients with more severe COVID-19 infection tend to show more severe neurological complications. The proposed mechanisms include direct viral damage to neurons and indirect damage due to hypoxia [9] or hyper/autoimmune response [10]. However, it remains unclear why some vaccine recipients develop neurological complications, reported by VAERS, such as stroke (in 6,924 recipients), Guillain-Barre Syndrome (in 575 recipients), transverse myelitis (in 250 recipients), facial palsy (in 1,112 recipients), encephalomyelitis (in 47 recipients), and multiple sclerosis (in 824 recipients). Post-vaccination headaches probably have the highest incidence rate, with almost 130,000 vaccine recipients reporting this adverse event. Even though headache is mostly a benign adverse event related to vaccination, it can be a warning sign of a more severe underlying problem. Intractable headaches can sometimes be a sign of underlying vaccine-induced immune thrombocytopenic purpura causing life-threatening cerebral venous thrombosis (in 137 recipients, including 11 deaths) or cerebral arterial thrombosis (in two recipients, including one death). Cerebral thrombosis can cause further complications such as stroke or intracranial hemorrhage. The proposed mechanism includes autoantibody formation against platelet factor 4 secondary to viral spike protein or one of the vaccine components such as vaccine adjuvants (i.e., polyethylene glycol) causing thrombosis [11]. Thrombosis can also occur at other typical sites causing pulmonary emboli or deep venous thrombosis. This is a well-known complication with the Janssen vaccine. The role of autoimmunity has already been proposed in developing rhabdomyolysis [12] post-COVID-19 vaccination. Our patient had a personal history of lupus, an autoimmune disorder. It is possible that a dysregulated immune system as in an autoimmune disorder can start producing autoantibodies

Table 2: Incidence of Vertigo post-COVID-19 vaccination.

Vaccine type	Sex	Events reports
JANSSEN	Female	386
	Male	200
	Unknown	22
	Total	608
Moderna	Female	2,464
	Male	869
	Unknown	56
	Total	3,389
Pfizer-BioNTech	Female	3,067
	Male	1,019
	Unknown	43
	Total	4,129
Unknown	Female	7
	Male	3
	Total	10
Total		8,136

against its own neurons once stimulated by the vaccine and cause damage to the vestibulocochlear nerve causing vertigo. A similar hypothesis can be proposed for other adverse events such as transverse myelitis, Guillain-Barre Syndrome, Bells palsy, or encephalomyelitis. There are no guidelines available for vaccination in patients with autoimmune disorders.

Conclusion

It is imperative to have better guidelines on vaccination for patients with autoimmune disease. COVID-19 vaccines are safe in general, and the benefits certainly outweigh adverse events. No neurologic condition is an absolute or relative contraindication to receiving the COVID-19 vaccine. However, a better understanding of neurological and other adverse events related to the vaccine is undoubtedly needed. Prospective clinical trials can certainly help improve our understanding.

Declarations

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