Could Covid-19 Vaccine Induce CNS Demyelination

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Abstract

Background: Despite the fact that immunization against Coronavirus disease-2019 (COVID-19) is still ongoing, numerous adverse reactions to these vaccinations have already been observed, albeit in isolated cases.

Objective: To report different neurological complications developed after COVID-19 virus vaccination.

Method: Six patients had neurological manifestations (vertigo, ataxia, recurrent attacks of loss of consciousness, optic neuritis, myelitis) starting 2-7 days after COVID-19 vaccination. MRI was obtained during the acute period.

Results: Five patients had altered signal intensity, multiple variable-sized, round to oval ill-defined lesions suggestive of multiple sclerosis; and the last one showed findings compatible with cervicodorsal myelitis.

Conclusion: COVID-19 vaccination could result in neurological complications probably secondary to post-vaccination inflammation.

Keywords: COVID-19, Vaccines, Stroke, Facial palsy, Myelitis

Introduction

The current COVID-19 pandemic, which is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), is a global epidemiological concern that will necessitate the introduction of large-scale vaccine production. Given the great diversity of previous coronavirus epidemics, it is necessary to build a vaccine production platform that provides scalability, technological flexibility, and variety. These vaccines must provide high efficacy, safety, and tolerability [1].

For the COVID-19 vaccines, four major vaccine mechanisms have been investigated: DNA-based vaccines, mRNA-based vaccines, protein-based vaccines, and inactivated virus. Using viral vectors, DNA-based vaccines introduce the DNA coding for the SARS-CoV-2 spike protein into cells, inducing cells to produce spike proteins. mRNA vaccines work in a similar way, introducing mRNA into cells via a lipid nanoparticle. Protein vaccines are based on the Spike protein or fragments of it. Finally, several vaccines use inactivated SARS-CoV-2 virus [2].

Numerous shared transient neurological manifestations were reported post-vacination, such as dizzness, headache, myalgia. Moreover, rare cases of tremor, diplopia, tinnitus, dysphonia, seizures, and herpes zoster reactivation have been also observed. The Vaccine Adverse Event Reporting System (VAERS) database also encompasses cases of stroke (17 cases), GBS (32 cases), facial palsy (190 cases), transverse myelitis (9 cases), and acute disseminated encephalomyelitis (6 cases). This, however, does not imply a contributory link with the vaccination [2].

Fears about COVID-19 vaccine-related neurological complications grew in the fall of 2020, when two patients suffered from transverse myelitis post-immunization by Oxford/AstraZeneca vaccine [3]. One case was finally determined to be possibly related to the vaccination (the patient had pre-existing multiple sclerosis), while the other was determined unrelated to vaccine [4]. According to data from the mRNA vaccine clinical trials, seven cases out of 37,000 vaccine receivers had got Bell's palsy, but none of them developed Guillain-Barré syndrome [5].

Methods

We discuss six patients with no history of medical or neurological disorders who developed new neurologic manifestations after receiving the COVID19 vaccination, which led to different neurological diagnoses. Neurologic symptoms started, on average, 4.5 days (range: 2-7 days) after vaccination. All four patients underwent brain MRI within the first week of symptoms. The patients had a minimum of sagittal and axial non-contrast T1 images, axial T2 and T2 FLAIR images, and axial and coronal post-contrast T1 images. We hypothesize that a post-vaccine inflammatory response resulted in the hyperacute presentation of these lesions. These examples highlight the importance of carefully considering and evaluating new neurologic problems after the COVID-19 vaccination.

Results

Case 1

Female patient 23 years old has a positive family history of multiple sclerosis (her uncle is known to have multiple sclerosis) and no history of any medical or neurological disorders, presented 5 days after receiving the first dose of Pfizer COVID 19 vaccine, with acute onset vertigo and unsteadiness which is not related to the position. An MRI brain was performed on sixth-day post-vaccination, which revealed abnormal signal intensity, multiple hyperintense foci are seen at the deep white matter periventricular and perpendicular on the right lateral wall and subcortical lesions were also noted with mild edema, suggestive of demyelinating disease (multiple sclerosis) (**Figure 1**). The patient showed partial improvement after receiving methylprednisolone 1-gram vial daily for 5 days followed by gradual tapering of prednisolone dose.

Case 2

A previously healthy 29 years old man with no history of COVID 19 infection, presented 7 days after receiving the first dose of Pfizer COVID 19 vaccine, with one episode of loss of consciousness without convulsion that lasted about 10 minutes approximately, and the patient gradually regained his normal consciousness. After two weeks, a similar condition occurred. An MRI brain was performed, which revealed there are multiple abnormal high signal foci at the periventricular white matter with subcortical lesion noted, with no perifocal edema or mass effect **(Figure 2).** The EEG revealed a focal sharp slow epileptiform discharge in the bitemporal area. Lumbar puncture and CSF analysis were negative for the oligoclonal band (negative for multiple sclerosis), as well as negative laboratory markers for autoimmune disease.

Case 3

Male patient 31 years with no history of medical or neurological disorders, presented to the emergency department 2 days after receiving the first dose of Pfizer COVID 19 vaccine, with acute onset pain during movement of the left eye, which is associated by acute diminution of vision up to

Figure 1. a) Coronal FLAIR, b) Sagittal T2, and c) and d) axial T2 of the brain at the ventricular level supratentorial region show multiple hyperintense foci seen at the deep white matter periventricular and perpendicular on the right lateral wall (red and black arrows) and subcortical lesions also noted (blue arrow) with mild edema.

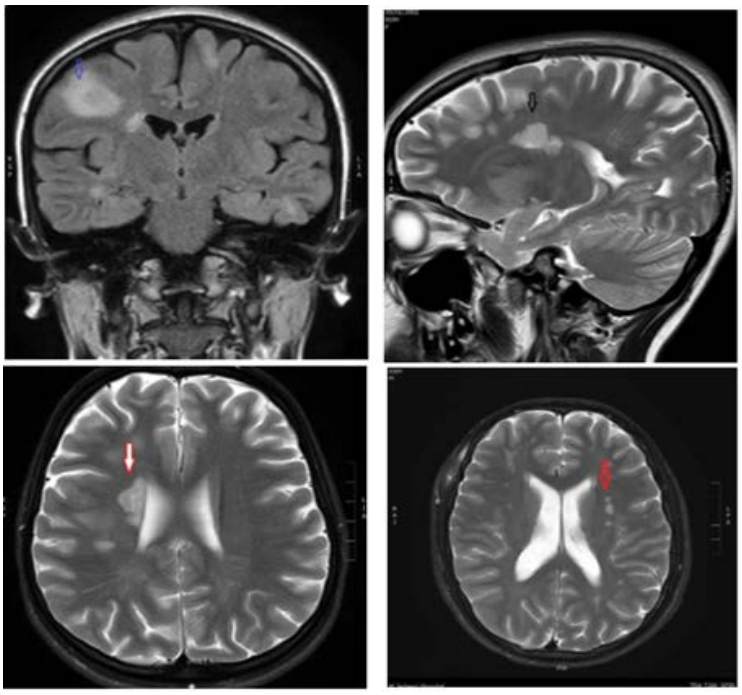
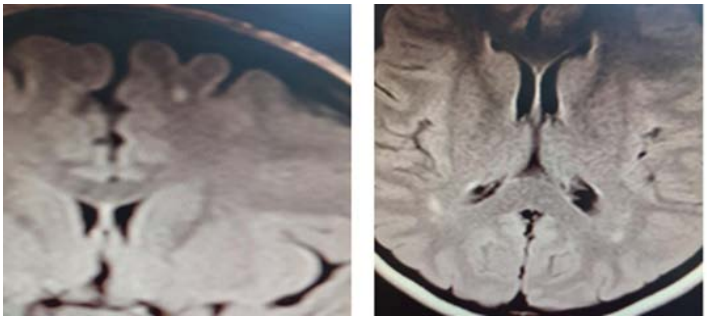


Figure 2. a) Coronal FLAIR and b) Axial FLAIR of the brain at the ventricular level there are multiple abnormal high signal foci at the periventricular white matter with subcortical lesion noted (red arrows). No perifocal edema or mass effect.



complete loss of vision within 5 days, and color vision impaired more to red and green. After seeking medical help, the patient was diagnosed with left optic neuritis. Multiple variable-sized, round to oval ill-defined lesions involving bilateral fronto-parietal and occipital lobes at juxtacortical, at gray-white matter junctional areas, deep white matter, and juxta-ventricular areas that suggestive demyelinating disease (multiple sclerosis) were seen on MRI brain and complete spinal cord **(Figure 3).** There was an aberrant pattern of the left optic nerve (expressed by prolonged P 100 delay) on VEP. The patient was given a 1-gram vial of methylprednisolone daily for 5 days, followed by a progressive tapering of prednisolone, which resulted in a partial improvement in vision up to 6/18, but the patient's color vision remained compromised. Lumbar puncture and CSF investigation for the oligoclonal band revealed no oligoclonal band in CSF (negative for multiple sclerosis), as well as negative NMO aquiporine 4 antibodies.

Case 4

Female patient 44 years old, with no history of medical or neurological disorders, presented 7 days after receiving the first dose of Pfizer COVID 19 vaccine, with acute onset weakness of both UL and LL up to patient wheelchair-bound, more severe in right side associated with numbness and paresthesia of both upper and lower limbs with a sensory level at the root of neck. An MRI brain was performed, and the results were normal., while MRI of the cervicodorsal spine revealed the spine shows a long segment of intramedullary hyperintense signal with mild increase cord caliber expansion with a corresponding hypointense signal on T1, a picture suggestive of transverse myelitis **(Figure 4).** VEP showed a normal pattern (normal P 100 latency without significant interside difference) of both optic nerves. The patient was treated with a 1-gram vial of methylprednisolone daily for 5 days, followed by a gradual tapering of prednisolone with partial improvement in the muscle power. The patient can now walk with minimal assistance. Lumbar puncture and CSF analysis for the oligoclonal band were performed, and there was no detection of the oligoclonal band in CSF (negative for multiple sclerosis), as well as NMO aquiporine 4 antibodies.

Case 5

Female patient 39 years old, with no history of medical or neurological disorders, presented 5 days after receiving the second dose of Pfizer COVID 19 vaccine by an acute diminution of vision of right eye up to counting fingers over one-meter distance with impairment of color vision and pain with movement of the right eye, fundus examination was normal, visual evoked potential p100 124 on the right eye. MRI brain showed multiple abnormal high signal foci at the periventricular white matter with subcortical lesion noticed, with no edema or mass effect, a picture suggestive of MS **(Figure 5)** Positive CSF for the oligoclonal band. The patient was improved on 1 gm methylprednisolone for 5 days.

Case 6

Female patient 35 years old, with no history of medical or neurological disorders, presented 7 days after receiving the first dose of Pfizer COVID 19 vaccine by myoclonic jerks, which progressed within two days to generalized tonic-clonic convulsions. Neurological examination was normal. MRI brain showed multiple abnormal high signal foci at the periventricular white matter noticed, with no edema or mass effect **(Figure 6).**

Figure 3. a) Coronal FLAIR and b) Axial T2 of the brain at the ventricular level there are multiple abnormal high signal foci at the periventricular white matter prominent at the left side (red arrows) with no edema or mass effect.

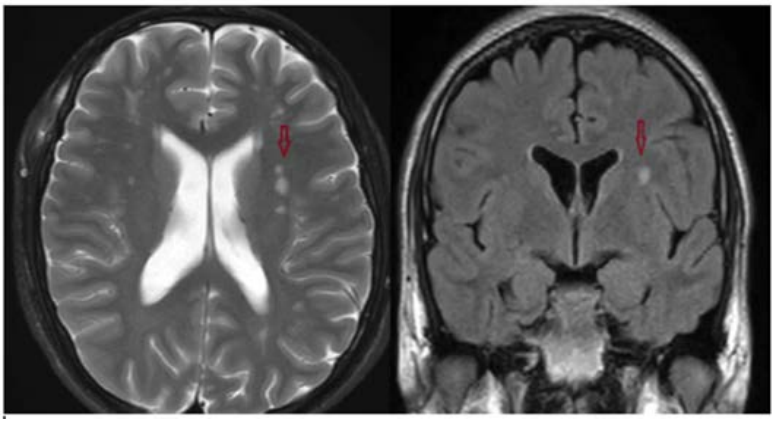


Figure 4. a): Sagittal T2, b) Sagittal T1, and c) axial T2 of the spine show a long segment of intramedullary hyperintense signal with mild increase cord caliber expansion with the corresponding hypointense signal on T1 Sugg. Of transverse myelitis.

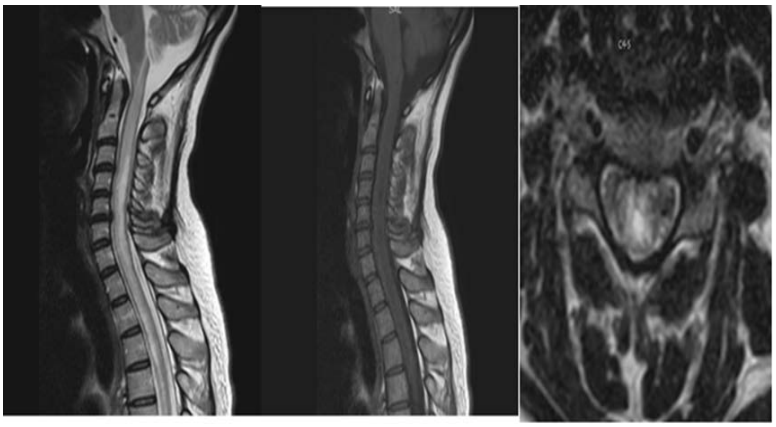


Figure 5. a) Axial FLAIR and b) Sagittal FLAIR of the brain at the supraventricular level there are multiple abnormal high signal foci at the periventricular white matter with subcortical lesion noted (blue arrows). No perifocal edema or mass effect.

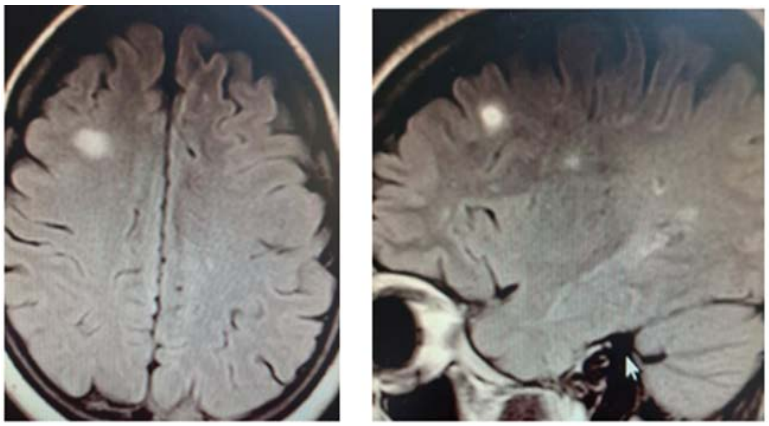
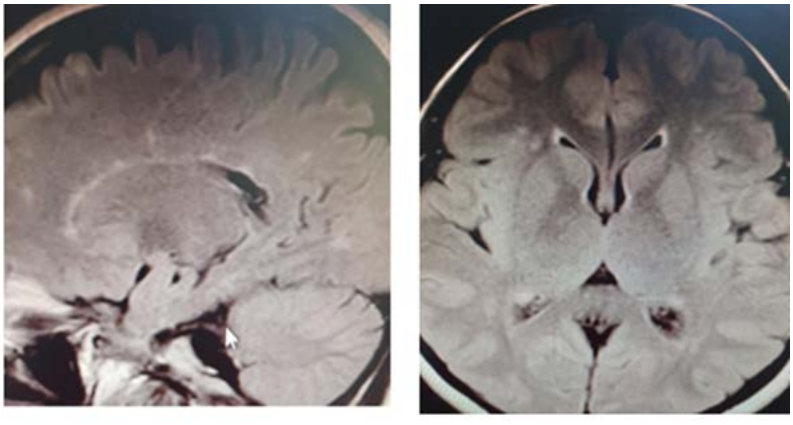


Figure 6. a) Sagittal FLAIR and b) Axial FLAIR of the brain at the ventricular level there are multiple abnormal high signal foci at the periventricular white matter (black arrows). No perifocal edema or mass effect.



Discussion

Covid-19 vaccination is a chief preventive tool for reducing disease incidence, morbidity and mortality. COVID-19 sequelae and complications are still being studied, but it is clear that multiple organ systems, including the nervous system, can be affected. The most common neurological complaints associated with COVID-19 infection are anosmia, ageusia, and headache, as well as more serious complications such as stroke, seizures, and encephalopathy [6]. But, neurologic symptoms induced by vaccination are tremendously rare [7,8].

We reported six patients with neurological symptoms concomitant with MRI changes. Three patients had altered signal intensity, multiple variable-sized, round to oval ill-defined lesions involving bilateral parietooccipital at juxtacortical, at gray-white matter junctional areas, deep white matter, and juxtaventricular areas; and the last one showed findings compatible with cervicodorsal myelitis, all of which were mostly related to the COVID-19 vaccine.

Optic neuritis is a type of optic nerve inflammation caused by demyelination, infection, post-immunization, or autoimmune diseases. A viral infection is the most common cause of optic neuritis in children. As a result, it appears that vaccines may also cause a similar condition by stimulating the host's immune system [9]. Despite the exact mechanism being still unknown, but type IV hypersensitivity reaction due to T-cell activation, and crossing the blood-brain barrier, resulting in damages to the optic nerve's myelin sheath [10]. Encoded spike proteins may cross the BBB after vaccination and boost inflammatory responses to nascent pathology in the brain.

Many studies have described post-vaccination optic neuritis, such as DiMario et al. [11], who reported a case of a 16-year-old girl presented with nearly complete visual loss in association with chiasmal neuritis following recent HPV immunization. Following the H1N1 vaccine, two cases of central nervous system involvement were reported in 2011. The first case involved a previously healthy child who developed optic neuritis a few weeks after vaccination, and the second involved a health care worker who developed seizures and retrograde amnesia with CSF changes after receiving the H1N1 influenza vaccine [12,13].

Several case reports have suggested a link between CNS demyelinating syndrome and several different vaccines [14,15]. Of that, influenza vaccines were the most commonly reported, probably due to the H1N1 outbreak between 2009 and 2012 [13,14]. Moreover, apart from optic neuritis, they also presented with other clinical syndromes, such as neuromyelitis optica, myelitis, or acute disseminated encephalomyelitis [16-18].

Transverse myelitis (TM) is a spinal cord inflammatory demyelinating disorder caused by an autoimmune process. Longitudinally extensive transverse myelitis occurs when a lesion extends beyond three vertebral segments in length [19].

Transverse myelitis is a rare condition, and vaccine-associated TM cases are even rarer. It has been stated to occur after receiving a wide range of vaccines, including diphtheria and tetanus toxoids and pertussis vaccine, measles, mumps, and rubella virus vaccine, Haemophilus influenzae type B vaccine, oral poliovirus vaccine, Japanese encephalitis virus vaccine, hepatitis B vaccine, cholera vaccine, typhoid vaccine, rabies vaccine, and seasonal influenza virus vaccine [20-23].

Only 37 reported cases of transverse myelitis were associated with various vaccines given to infants, children, and adults, according to Levin A [23]. The majority of these associations lasted between a few weeks and three months. The first clinical manifestation of relapsing MS after vaccination with the Pifzer BioNTech COVID-19 vaccine was reported by Havla et al. [24]. She began to develop MS six days after the initially well-tolerated first immunisation. We diagnosed relapsing MS using the 2017 McDonald criteria after ruling out all other possible diagnoses.

Conclusion

We came to the conclusion that the CNS involvement of covid-19 vaccination-related complications is more varied than previously reported. Steroids were used in all cases, and the imaging and clinical outcomes improved significantly. Furthermore, a temporal association between vaccination and adverse effects does not always imply causation, and much remains to be learned about the effects of COVID-19 vaccination. Population-based studies are needed to assess the adverse effects of these vaccines and whether there is an increase in the number of neurological adverse effects associated with their use. Nonetheless, one thing is certain: the advantages of vaccination far outweigh the risks.

Aknowlegement

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Authors Contribution

Dr. Yasser Hamed: conception and supervision of the work.

Dr. Abd Elaziz Shokry: Data collection, analysis, and interpretation of data

Dr. Tareq Mohamed M. Mansour: Performing and description of MRI

Dr. Salma Mokhtar: Drafting the manuscript

Dr. Khaled Mohamed Ali Shehata: supervision of the work.

Ethical Approval and Consent to Participate

The study is in accordance with the Declaration of Helsinki and approved by the appropriate ethical committee of El-Azhar university. Informed consent to participate in the study was obtained from participants..

Disclosure statement

The authors report no conflicts of interest.

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