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Case Report

Bilateral Optic Neuritis After Administration of Inactivated COVID-19 Vaccine: A Case Report

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Running Title Bilateral Optic Neuritis After COVID-19 Vaccination

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ABSTRACT

Background: Since the beginning of the COVID-19 pandemic, various efforts have been taken to alleviate the spread of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV2). Studies have shown effective prevention and protection through vaccination. However, there have also been reports of neurologic diseases after vaccination.

Case Presentation: The first case in the Philippines belonged to a 25-year-old female who initially sought a consult for the increased sleeping time associated with retrograde amnesia immediately after receiving her second dose of inactivated SARS-CoV-2 vaccine. She was then managed as a case of viral encephalitis. However, two weeks later, the patient developed a bilateral decline in visual acuity. Diagnostics included visual perimetry, routine EEG, contrast-enhanced cranial MRI, and visual evoked potentials. The patient was then managed as a case of bilateral optic neuritis and was started on pulse methylprednisolone for 3 days with noted gradual but incomplete reversal of the condition.

Conclusion: Autoimmune neurologic events after COVID-19 vaccination are treatable, and the benefits of the vaccination outweigh its risk.

Keywords: COVID-19 vaccines, Demyelinating diseases, Optic neuritis

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Highlights

- This paper presents a case of a 25-year-old female who developed bilateral optic neuritis 2 weeks after receiving the second dose of inactivated COVID-19 vaccine.

- This symptom should be considered in post-vaccination time.

Introduction

The coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and has affected millions worldwide. A study has identified that either direct viral entry or indirect infection of the central nervous system is the mechanism of the virus to cause neurologic symptoms. Another possible explanation is that the virus can enter the bloodstream and spread via retrograde axonal transport or infect the pericytes and astrocytes in the blood-brain barrier [1]. With the information obtained regarding viral pathophysiology, vaccines were developed to alleviate its spread. However, a neuropathological mechanism of COVID-19 is the induction of a hyperinflammatory state, hence the possible correlation between vaccine and inflammatory demyelinating disease [1].

Demyelinating diseases have been reported to be adverse reactions of COVID-19 vaccination, which included acute disseminated encephalomyelitis, transverse myelitis, and optic neuritis [2]. Another study presenting various adverse events after COVID-19 vaccination stated that optic neuritis is a rare phenomenon, and its pathophysiology is not fully understood but may relate to molecular mimicry. The same study hypothesized that demyelination could be attributed to inflammatory mediators activated after vaccination. Such event was mostly associated with mRNA vaccines and viral vectors and a few with inactivated viral vaccines [3]. In cases given Oxford-AstraZeneca (Vaxzevria), the related events of optic neuritis were reported to aggravate the body's reaction to the vaccine in those with undetermined risk factors [4]. In this report, we present a case of a middle-aged female with a progressive blurring of a vision two weeks after receiving the second dose of COVID-19 vaccination.

Case Presentation

A 25-year-old female patient was admitted for blurring of vision. Her symptom started three weeks before hospitalization after receiving her second dose of inactivated SARS-CoV-2 vaccine. The blurring was followed by body malaise, intermittent fever, and generalized pruritic maculopapular rashes. As the rashes were resolving, she developed increased somnolence characterized by sleeping most of the day and unusually waking up in the afternoon. Her mother also reported that she had an episode of retrograde amnesia, not being able to recall previous events. She had no significant past medical history, with no reported adverse events immediately following her first dose of SARS-CoV-2 vaccination. At this time, a viral etiology of encephalitis, including COVID-19 infection, dengue, and viral exanthems, was considered. A nasopharyngeal swab for the real-time polymerase chain reaction for SARS-CoV-2 was requested and came out negative. Complete blood count was within normal ranges, and Dengue antibodies were not detected. Contrast-enhanced cranial CT scan was normal. Electroencephalography (EEG) displayed intermittent generalized slowing (2-3 Hz) of the background activity. A lumbar tap was also offered; however, in a week and the absence of medical intervention, the patient was clinically improving. Hence the lumbar tap was not performed with the impression of resolving viral encephalitis. She was started on valacyclovir 500 mg tablet, BID (2 g/d) for 7 days. Eventually, there was a gradual and continuous improvement of symptoms, with more regular sleep of 8-10 hours per day.

A week before admission, two weeks after receiving the said vaccine, she developed gradual and painless blurring of vision bilaterally with a normal initial visual acuity that decreased to counting fingers within a week. She then sought a consult with a neuro-ophthalmologist, where fundus examination and optical coherence tomography findings were unremarkable. Her perimetry showed a generalized visual loss defect. The final diagnosis was atypical bilateral optic neuritis prompting the admission. A cranial MRI with IV contrast showed patchy T2-weighted (T2)/fluid-attenuated inversion recovery (FLAIR) hyperintensities in the bilateral lenticulocapsulothalamic regions with subtle gadolinium enhancement and ill-defined non-enhancing T2/FLAIR hyperintense foci in the bilateral frontal and parietal white matter, ventral pons and cerebellar white matter (Figure 1). Visual evoked potential findings were prolonged latency bilaterally, suggesting a demyelin-

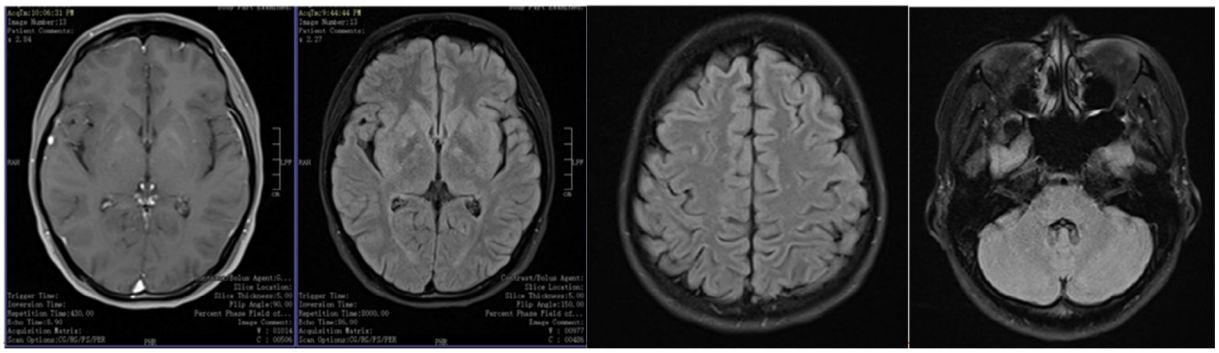

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Figure 1. Cranial magnetic resonance imaging (MRI) with IV contrast displaying patchy T2-weighted (T2)/fluid-attenuated Inversion recovery (FLAIR) hyperintensities in the bilateral lenticulocapsulothalamic regions with subtle gadolinium enhancement and Ill-defined non-enhancing T2/FLAIR hyperintense foci in the bilateral frontal and parietal white matter, ventral pons, and cerebellar white matter

ating etiology. One gram of intravenous methylprednisolone was given for three days. Bilateral visual acuity improved but did not recover completely (Figure 2).

Discussion

Vaccines have been proven to reduce disease spread by increasing herd immunity. Increased administration of these vaccines would result in the prevention of the emergence of vaccine-resistant strains as well as neurological and neuropsychiatric complications associated with COVID-19 itself. Although no medication has been reported without adverse events, recipients of these vaccines may have transient influenza-like symptoms such as headache, myalgia, and fatigue up to 5% of SARS-CoV-2, indicating an appropriate immune response. Severe potential adverse effects in open-label phases of vaccine roll-outs are being collected through national surveillance systems [5].

Previously, cases of autoimmune encephalitis were reported following influenza vaccination. Studies suggest that about 5% of acute disseminated encephalomyelitis (ADEM) events are associated with immunization for varicella, rabies, measles, mumps, rubella, influenza, hepatitis B, Japanese B encephalitis, diphtheria, pertussis, and tetanus [5]. A small increase in Guillain-Barré syndrome cases following H1N1 influenza vaccination was also observed in 1976. Investigators reported adverse effects of the influenza vaccine as follows: optic neuritis (n=38), multifocal disseminated demyelination (n=30), myelitis (n=24), and encephalitis (n=17) [6].

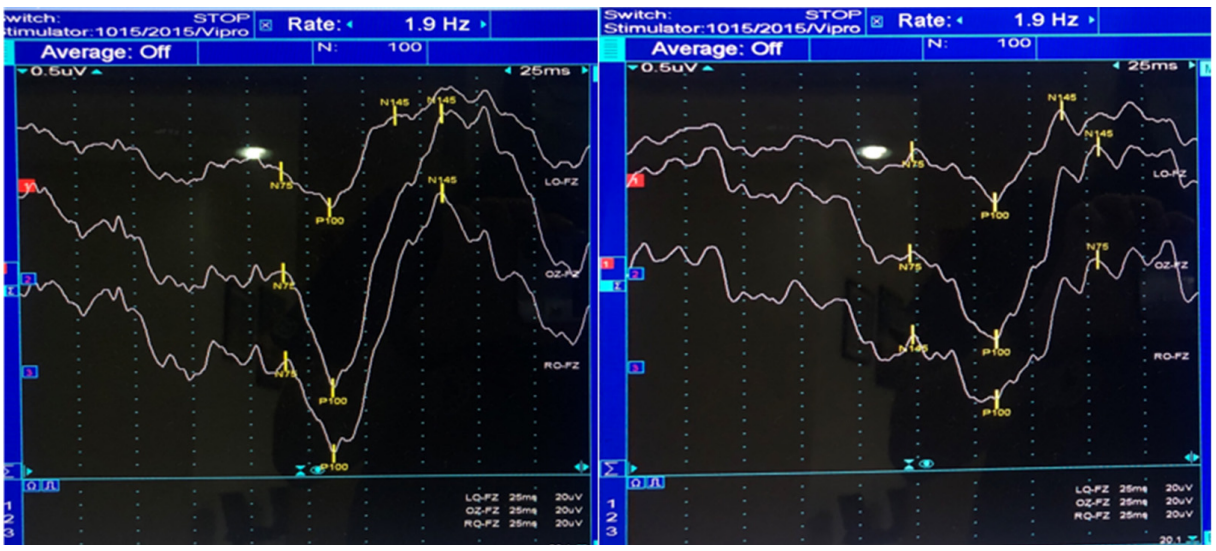

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Figure 2. Visual evoked potentials displaying prolonged P100 Latencies from the right (135 ms) and left eye (157 ms)

Optic neuritis (ON) is often bilateral and is much more common as a presenting symptom of both post-viral and post-vaccine ADEM than in multiple sclerosis. In other studies, there were reports of vaccines causing ocular adverse reactions such as conjunctival and eyelid reactions, ON, and intraocular inflammation. The vaccines were hypothesized to stimulate innate immunity through cytoplasmic nucleic acid receptors, including toll-like receptors resulting in an immune response [7]. As of this writing, there are published reports of ADEM with bilateral ON 14 days after receiving the first dose of the AstraZeneca vaccine [2]. A study conducted a PubMed search and revealed 48 cases of vaccination-related ON, from which 32 had isolated ON, 9 occurred as the first symptom of neuromyelitis optica spectrum diseases, and 6 were associated with the clinical course of ADEM. The occurrence of post-vaccination ON likely exists but is rare. Optic neuritis is presumably immune-mediated, and reported cases had a good prognosis for visual recovery. Administration of intravenous corticosteroids may facilitate the recovery of visual function of patients with post-vaccination ON [8]. In another study, 69 patients were involved, in which 67% received the viral vector vaccine, 26% received mRNA, and 7% received the inactivated vaccine. Post-vaccination optic neuritis is an extremely rare adverse event occurring in 0.0017 per 100000 persons vaccinated vs 3.74 per 100000 persons in the UK for those having ON alone. These patients also had a good outcome of visual acuity. The same study concluded that a causal relationship is plausible, but the overall risk-benefit balance favors SARS-CoV-2 vaccination [9].

In this writing, we report a patient presenting with encephalopathy and bilateral ON following the second dose of inactivated SARS-COV-2 vaccine. The mechanism of developing demyelinating neurologic events after vaccination includes the fulminant activation of lymphocytes by microbial superantigens, leading to direct injury to the central nervous system, which then results in exposure of myelin antigens causing autoimmune damage to the myelin. Another cause would be an immune response directed to the virus, which damages the myelin sheath due to molecular mimicry between these two substances [10].

As in the case of our patient, cranial MRI with IV contrast revealed patchy T2/FLAIR hyperintensities in the bilateral lenticulocapsulothalamic regions with subtle gadolinium enhancement and ill-defined non-enhancing T2/FLAIR hyperintense foci in the bilateral frontal and parietal white matter, ventral pons, and cerebellar white matter, which are consistent with demyelinating disease. Furthermore, the patient also underwent visual evoked potentials elicited with alternating checkerboard patterns, revealing prolonged P100 latencies bilaterally, suggesting a demyelinating lesion in the visual pathways.

In a study done in Germany, similar clinical and laboratory findings of patients having neurologic sequelae of COVID-19 were found in those with neurologic autoimmune reactions postvaccination. The proposed mechanism involved polyclonal or bystander activation, epitope spreading, or molecular mimicry. Hence, patients with existing autoimmune diseases may have enhanced responses to vaccination by unmasking asymptomatic autoimmunity. These reactions were shown to be responsive to immunosuppressive therapy. The study then concluded that autoimmune neurologic events are rare after COVID-19 vaccination, and the benefits of the vaccination outweigh its risk [11].

Conclusion

The cases reported for adverse effects of COVID-19 vaccination are only very few compared to the million vaccination doses administered worldwide, hence the difficulty of establishing direct causality. Given the possible immune mechanisms behind developing demyelinating conditions, the cross-reactivity or heightened immune response from vaccine introduction to the system may have been associated with demyelinating conditions. This study presented the possibility of having optic neuritis post-vaccination.

Ethical Considerations

Compliance with ethical guidelines

All study procedures were in compliance with the ethical guidelines of the Declaration of Helsinki 2013.

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Authors contributions

Conceptualization, writing, review, editing and investigation: Evaliza Villoria, Prima Quintay, and Artemio Roxas Jr; Writing the original draft: Evaliza Villoria; Resources: Evaliza Villoria and Prima Quintay; Supervision: Artemio Roxas Jr.

Conflict of interest

The authors declared no competing interests.

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