Acute disseminated encephalomyelitis following inactivated COVID-19 vaccine: A case report

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Case Report

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Abstract

Background

Neurological involvement including CNS demyelination syndromes following SARS-CoV-2 infection have been reported as extra-pulmonary involvement in patients with COVID-19. Besides, immune-mediated central nervous system involvement is a rare phenomenon that is considered to be one of the most important and serious complications of vaccines as well. While regarding the recent pandemic and worldwide use of the COVID-19 vaccines investigating serious life-threatening side effects is worth considering.

Case presentation:

This article reported a young male Iranian patient without any past medical history and neurological problems who presented acute disorientation due to acute central nervous system demyelination approximately one month after receiving the first dosage of Sinopharm BIBP COVID-19 vaccine. Based on extended clinical investigations the patient had undergone the treatment with the highly probable diagnosis of acute disseminated encephalomyelitis syndrome.

Conclusion

In this article clinical presentation, diagnosis, and treatment of the patient with the diagnosis of ADEM following COVID-19 vaccine administration have been discussed. It seems for timely diagnosis and access to a safer state in our global immunization, reporting and evaluating the diagnosis approach and challenges in treatment and patient recovery regarding rare and adverse effects is worth considering.

Introduction

Acute disseminated encephalomyelitis (ADEM) is defined as an inflammatory-mediated condition that is characterized by acute onset demyelination of the central nervous system(1). Different kinds of etiology could be considered for the underlying process of encephalomyelitis in patients with ADEM, including post-infectious and post-vaccination situations, and idiopathic causes in some patients(2, 3).

Besides, since the emergence of the COVID-19 pandemic various kinds of extrapulmonary involvements were reported as worth considering aspects of SARS-COV-2 infection(4). Moreover, based on the previous studies, there are clinical case reports of incidence of neurological involvement and CNS demyelination syndromes such as ADEM following SARS-CoV-2 infection which is suggested to consider ADEM as an important differential diagnosis among patients with COVID-19 and neurological involvement(5).In addition, there are a few cases of CNS demyelination including MS and ADEM following different types of approved COVID-19 vaccines are identified as well(6). Here we are reporting a young male patient

without any past medical and neurological history, who presented acute onset of central nervous system demyelination approximately 1 month after receiving the inactivated BIBP-CorV COVID-19 vaccine.

Case Presentation

1–1. Patient Information

A 45-year-old Iranian man was referred to the Imam Khomeini hospital complex (IKHC), a tertiary hospital of Tehran University of Medical Sciences, in December 2021, due to acute onset of mental disorientation to time, place, and person and complete inability to perform personal tasks. The onset of symptoms was accompanied by sudden disorientation, and fever, which started four weeks after taking the first dosage of the Sinopharm BIBP COVID-19 vaccine. It is also worth noting that before the onset of these symptoms, the patient had no history of other medical problems or neurological symptoms.

1–2. Physical Examination

In the physical examination, the patient was awake but not responding and had no eye contact or verbal response to the stimuli. Therefore, an accurate evaluation of the patient's orientation was not possible. On cranial nerve examination, there was no evidence in favor of ophthalmoplegia, ptosis, or facial paresis, and the gag reflex was absent. The pupils were mid-sized, symmetric, and reactive to light, and there was no papillary edema.

On the motor examination, the limbs were spastic especially on the right side, along with reduced motor force in the upper and lower limbs. Deep tendon reflexes slightly increased, and the plantar reflexes were upward. Also Due to the lack of patient cooperation, it was not possible to assess the cerebellar functions and gate examination.

2-Diagnostic Assessment

2-1-Imaging

In multiplanes MRI with pre and post paramagnet injection; There are multiple high T2/FLAIR intensities in periventricular and centrum semiovale, basal ganglia and subcortical regions, corpus callosum, and posterior fossa is seen which was low T1 signal in some lesions. Most of the lesions were enhanced after contrast injection. Generally, numerous variable-size diffuse white matter lesions with enhancement beside extensive peripheral edema were mostly in favor of ADEM. (Fig. 1)

Also based on MR angiography with the time-of-flight (TOF) method and multiple angle views, the Circle of Willis and major intracranial vascular structures was appeared normal. There was no evidence in favor of aneurysm or arteriovenous malformation (AVM).

2–2 Laboratory Findings

Furthermore, extended infections workup has been done and subsequently, TB and brucellosis (which are endemic in our region), syphilis, HIV, HCV, Bacterial meningitis, and endocarditis were ruled out for this patient. Also, according to the importance of evaluating viral markers in reaching a diagnosis, CSF sample analyses regarding HSV, VZV, BK, JC, EBV, CMV, and adenovirus were performed, and the results all were negative. Moreover, the results of the rheumatologic investigation on CSF specimens, including RF, anti-SSB//La, anti-SSA/Ro, anti-DS DNA, anti-cardiolipin, C-ANCA, P-ANCA all were reported negative as well. Also, the Anti-MOG antibody and Anti NMO antibody were assessed for MOG antibody disease (MOGAD) and Neuromyelitis Optica (NMO), and the results were also negative. A summary of the CSF specimen analysis is presented in Table 1.

Table 1
CSF specimen analysis

CSF Specimen Analysis	Unit	Result	Normal Value
Opening pressure	mm H20	140	70–180
Glucose	mg/dl	74	50–70
Protein	mg/dl	22	15–60
LDH	U/L	30	< 40
IgG	mg/dl	4.3	< 8
IgG index	-	0.39	< 0.7
Alb	mg/dl	23	< 35
Oligoclonal band	-	1 band (intermediate)	-

CSF = Cerebrospinal fluid

According to the previous Studies, CSF findings in ADEM syndrome could vary in different patients although in most cases there are no notable findings in CSF analysis(7). Also, Oligoclonal bands may be transiently reported in the CSF of patients with ADEM(8).

3-Therapeutic Intervention

Based on clinical and para-clinical findings and the high probability of a diagnosis of ADEM, the patients underwent four sessions of plasmapheresis with the replacement of 2500 cc plasma alongside five sessions of pulse corticosteroid therapy. Then considering the absence of significant improvement in symptoms, cyclophosphamide and rituximab (1000 mg) were added to the patient regimen. A summary of the timeline of symptoms and interventions is presented in Fig. 2.

4- Outcomes

At the time of discharge, the patient's condition was stable. Also, despite the treatments, the patient still had no verbal response. Besides, on the motor examination, the muscle force was slightly improved. Also,

based on the imaging findings, no obvious changes in lesions progression in comparison with the results of the previous ones were reported.

Discussion

Vaccination is one of the most significant achievements of modern medicine; it effectively diminishes mortality and morbidity due to infections. However, in rare cases, vaccines may lead to inflammatory conditions and even initiate autoimmune diseases by inducing the production of autoantibodies. (9, 10) Demyelination is the damage to the protective layer surrounding the nerve cells, which is called myelin, and it can lead to neurological problems such as acute transverse myelitis (ATM), ADEM, and MS. (11, 12)

This article reported a case of a 45-year-old man without any history of medical and neurological problems, who developed severe disorientation, motor weakness, and severe disability four weeks after taking the first dosage of inactivated COVID vaccine. As a result of clinical and laboratory studies, he underwent treatment with the diagnosis of ADEM.

The idea that vaccines could trigger autoimmune demyelination has been discussed in studies for many years. (9, 13, 14) In their literature review, a study by Karussis et al. referenced 71 case reports with various post-vaccination CNS demyelinating syndromes. The most-reported ones were influenza, HPV, and hepatitis A or B. The symptoms usually appeared in about two weeks, but some reported cases had delayed presentation of symptoms after Vaccination (4 weeks and up to 5 months post-vaccination). Acute optic neuritis was the most common post-vaccination isolated CNS syndrome reported in the literature, and after that, ATM, multifocal disseminated demyelination, encephalitis, and also chronic disease such as MS or NMO have been reported frequently. (15)

Furthermore, in a study by Baxter et al., an association was found between the incidence of acute demyelination and inactivated vaccines such as influenza, measles, mumps, rubella vaccine, and varicella vaccines. (16)

Since the beginning of the COVID-19 pandemic, several cases of CNS inflammatory diseases have been reported after SARS-CoV-2 infection, including ADEM and ATM. (17, 18). Besides, concerns about the possible association of autoimmune demyelinating syndromes and the COVID-19 Vaccination have been raised since few cases have been reported after injection.

According to the four randomized clinical trials for ChAdOx1 nCoV-19 across the UK, Brazil, and South Africa, studied by Voysey and colleagues, three cases of ATM occurred among participants, and one of them was considered possibly vaccine-related. (19)

Although the exact pathophysiology leading to ADEM is unknown, several mechanisms such as a virus or viral products or vaccine-associated products have been accused of causing damage to myelin and leading to ADEM.(20, 21)

CNS demyelination was reported following all types of approved COVID-19 vaccines. Although the mRNA-based COVID-19 vaccines resulted in most post-vaccine demyelinating syndromes, inactivated vaccines such as Sinovac/Sinopharm also had an important role, including 5 cases from the 32 total cases (15.6%). Also, Cao et al. reported a patient diagnosed with ADEM after 2weeks of receiving one dose of an inactivated SARS-CoV-2 vaccine. (22).

Conclusion

Severe central nervous system involvement is one of the very rare side effects of vaccines. In the case of COVID-19 vaccination, these side effects are also very rare compared to its global achievements. However, the recognition of serious life-threatening side effects in some cases and related risk factors, in order to prevent, diagnose and treat these complications more effectively seems necessary.

Declarations

Consent for publication

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

consent to participate

The informed consent has been obtained.

Availability of data and materials

Not applicable.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Authors' contributions

SS: Conceptualization, Project administration, Original draft preparation, Writing- Reviewing and Editing **BH**: Conceptualization, Original draft preparation, Writing- Reviewing and Editing curation.**MM:** Conceptualization, Resources **VK:** Resources, **HA:** Supervision, Writing- Reviewing and Editing:

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Figures

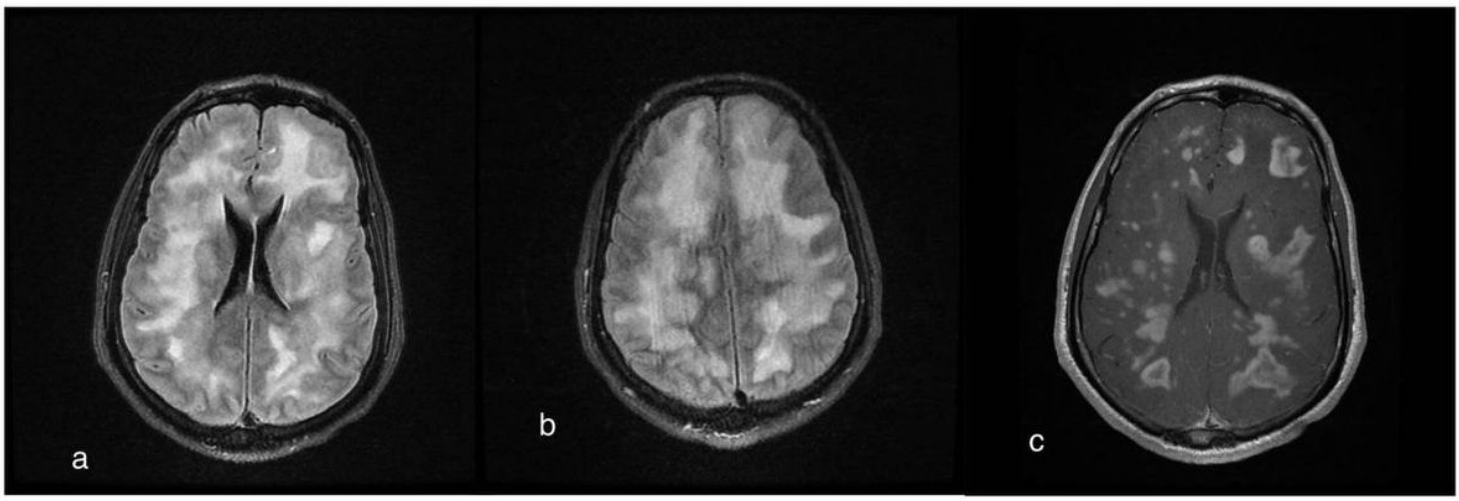

Figure 1

a: Axial FLAIR MRI, b: T2 weighted MRI, c: T1 weighted MRI with GAD

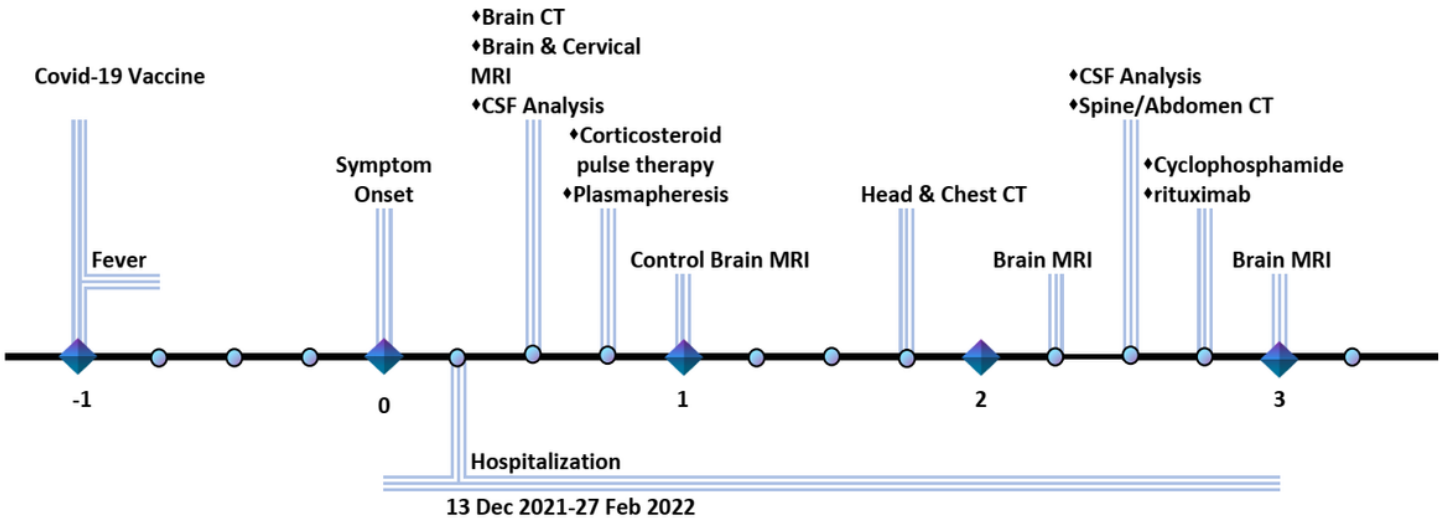

Figure 2

Timeline of symptoms onset and interventions the time scale is month