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Case Report

Cytotoxic Corpus Callosum Lesions After COVID-19 Vaccination

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ABSTRACT

Background and Aim: Various adverse events have been reported after vaccination against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Cytotoxic lesion of the corpus callosum (CLOCC) is a rare clinical and radiological syndrome linked to various etiologies. This study aimed to report a rare case of CLOCC after receiving the Sinopharm BIBP COVID-19 vaccine.

Case Presentation: A 44-year-old previously healthy man presented with spatial disorientation, memory impairment, and preorbital headache following vaccination against SARS-CoV-2. He had no abnormal findings on initial laboratory tests or cerebrospinal fluid analysis. A brain MRI revealed an ovoid lesion in the splenium of the corpus callosum, which is distinctive for a cytotoxic lesion of the corpus callosum. A biopsy specimen of the lesion was consistent with the diagnosis. The patient showed a transitory response to immunosuppressive therapy. After a dramatic disease course associated with septic shock due to aspiration pneumonia, he developed cardiorespiratory arrest and died two months after the initial presentation.

Results: CLOCC is an autoimmune phenomenon that can occur post-infection and vaccination. CLOCC can be considered as a possible diagnosis in patients with unexplained neuropsychiatric symptoms following SARS-CoV-2 vaccination.

Conclusion: This case underscores the need for increased caution regarding the uncommon complications of SARS-CoV-2 vaccination.

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Introduction

Since the start of the pandemic in December 2019, over 776.8 million confirmed COVID-19 cases and more than 7 million deaths have been reported globally as of November 10, 2024 [1, 2]. Effective vaccines against COVID-19 were urgently needed to control the global pandemic. As a result of the global endeavor of remarkable speed and magnitude, vaccines of different development strategies are currently available to the public [3]. As of January 9, 2022, more than 9 billion vaccine doses against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have been administered [4]. The global immunization of adults with SARS-CoV-2 vaccines has drastically reduced the risk of symptomatic disease, hospitalization, and death rates attributed to COVID-19. However, the initial randomized clinical trials that assessed the vaccines' safety and efficacy were underpowered to detect rare adverse outcomes [5, 6]. Therefore, reports of adverse events are crucial for re-evaluating the potential risks and benefits of vaccine administration and the clinical management of post-vaccination adverse events. A wide range of neurological adverse events has been recorded following SARS-CoV-2 vaccination, most of which are transient and mild. The most common neurological complications associated with SARS-CoV-2 vaccination include headache, Guillain-Barre syndrome (GBS), venous sinus thrombosis (VST), and transverse myelitis. Other neurological adverse effects are much less frequent [7, 8]. Cytotoxic lesion of the corpus callosum (CLOCC), first described by Tada et al. in 2014 [9], is a rare clinical and radiological syndrome that often starts with neuropsychiatric symptoms. It is accompanied by a brain MRI finding of an isolated oval-shaped reversible lesion located in the splenium of the corpus callosum. In most cases, complete recovery without sequelae can be achieved [10]. In August 2021, Youn and Yang [11] reported the first case of CLOCC following SARS-CoV-2 vaccination in a 22-year-old man. We report a case of CLOCC in a 44-year-old man presenting with spatial disorientation, memory impairment, and preorbital headache following SARS-CoV-2 vaccination.

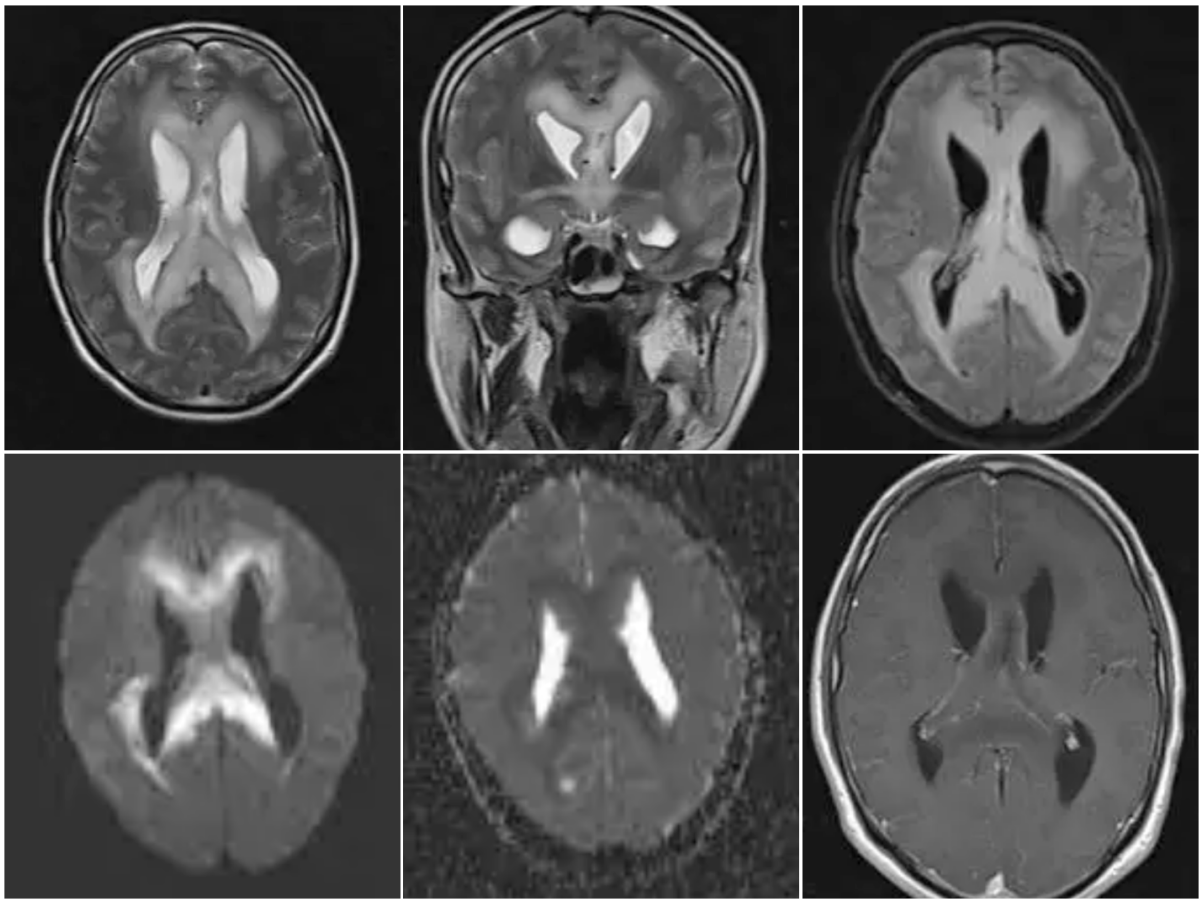
Case Presentation

We describe a 44-year-old previously healthy Caucasian man with no past medical or medication history who developed neurological symptoms shortly after receiving the Sinopharm BIBP COVID-19 vaccine. On day 0, he received the first vaccine dose. Two days later (day 2), he developed acute confusion accompanied by spatial disorientation, difficulty navigating familiar places, progressive recent-memory impairment, and a mild frontal–orbital headache. He reported no fever, dizziness, vertigo, nausea, or respiratory symptoms. Over the following 12 days (day 2–14), the symptoms progressively worsened.

On day 14, he was admitted to the hospital due to worsening confusion and impaired orientation. On neurological examination, the patient was awake and responsive, oriented to time and person, but disoriented to place. Cranial nerve, motor, sensory, and coordination examinations were normal, and no meningeal signs were observed. A non-contrast brain computed tomography (CT) scan revealed diffuse hypodense lesions within the corpus callosum. MRI demonstrated a diffuse cytotoxic lesion involving the splenium and body of the corpus callosum, with restricted diffusion on diffusion weighted imaging/apparent diffusion coefficient DWI/ADC and mild contrast enhancement on T1-weighted images. An additional contrast-enhancing lesion was noted in the left temporal lobe. Magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) were unremarkable.

During hospital days 1–4, extensive diagnostic evaluations were conducted. Laboratory tests, including complete blood count (CBC) and metabolic panel, were normal. Toxicology screening was negative. SARS-CoV-2 polymerase chain reaction (PCR) was adverse. A cerebrospinal fluid (CSF) analysis showed elevated opening pressure (28 cm H_2O) with normal glucose, protein, and cell counts. A CSF bacterial and fungal cultures were negative. A comprehensive viral PCR panel (herpes simplex virus types 1 and 2 [HSV-1/2], varicella-zoster virus [VZV], cytomegalovirus [CMV], Epstein-Barr virus [EBV], JC virus [JCV], SARS-CoV-2) and PCR for *Mycoplasma pneumoniae* were all negative. Autoimmune and paraneoplastic testing revealed positive anti-Yo antibodies (2+). Whole-body CT scans (chest, abdomen, and pelvis) showed no malignancy. A stereotactic brain biopsy demonstrated intracellular edema, mild lymphocytic infiltration, and vascular congestion. Immunohistochemistry revealed LCA-positive lymphocytes and the absence of CD20 expression, consistent with a reactive rather than neoplastic process.

On hospital day 5, the patient experienced his first clinical deterioration, presenting with increased lethargy, slowed responses, hypophonia, and worsening disorientation. High-dose corticosteroid pulse therapy



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Figure 1. There is abnormal signal intensity with mild mass effect and considerable restricted-diffusion in bilateral periventricular white matter with involvement of entire corpus callosum. Patchy enhancement of the lesion is seen between the frontal horns of lateral ventricles and also around the ventricles. Also, abnormal signal intensity with patchy enhancement is present in anterior of left temporal lobe.

was initiated. By hospital day 7, he demonstrated partial clinical improvement, including enhanced alertness and improved ability to follow commands.

However, on hospital day 10, he experienced a sudden clinical decline, developing fever, tachypnea, and hypoxia (oxygen saturation 92% on room air). Neurologically, he became lethargic and non-verbal. Pulmonary CT angiography demonstrated thromboembolism. Anticoagulation was initiated, and a repeat SARS-CoV-2 PCR test was positive. EEG showed diffuse background slowing consistent with encephalopathy without epileptiform activity. He was transferred to the intensive care unit (ICU) and underwent therapeutic plasma exchange in combination with corticosteroid therapy. Based on partial clinical response and the biopsy findings, rituximab therapy was initiated; however, the patient developed ventricular tachycardia, prompting discontinuation of rituximab and transition to cyclophosphamide.

After 20 days of hospitalization, the patient was discharged with a stable cardiac status and mild improvement in mental function. Two weeks after discharge, he returned for scheduled cyclophosphamide administration. Follow-up brain magnetic resonance imaging (MRI) showed mild enlargement of the callosal lesion, though the patient demonstrated slight clinical improvement and was discharged again (Figure 1).

Two weeks later (approximately two months after symptom onset), the patient presented to the emergency department with decreased level of consciousness and a recent episode of generalized tonic–clonic seizures. He was febrile and hemodynamically unstable. Given his respiratory status and neurological decline, aspiration pneumonia with septic shock was suspected, and management was initiated accordingly. Twelve hours after admission, he developed cardiopulmonary arrest and died after one hour of resuscitative efforts. An autopsy was recommended, but declined by the family.

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Discussion

CLOCCs are secondary lesions related to a variety of disease entities, including malignancy, infection, subarachnoid hemorrhage, metabolic disturbances, drugs, trauma, and vaccination [12]. Corpus callosal lesions with diffusion restriction on diffusion weighted imaging (DWI) and low ADC values on brain MRI are consistent with cytotoxic edema [13]. Cytotoxic edema is caused by water entrapment within cells. Glutamate plays an essential role in excitotoxicity and is responsible for the inward shift of water through acting on sodium-potassium pumps. Increased levels of inflammatory cytokines interleukin-1 (IL-1) and interleukin-6 (IL-6) initiate a cascade that leads to increased glutamate release from astrocytes, resulting in cytotoxic edema [12, 14]. Infection with SARS-CoV-2 initiates innate and adaptive immune responses, resulting in alterations in immune cell populations and their respective T-cell, B-cell, and NK-cell subsets. This systemic inflammatory response can cause excessive expression of pro-inflammatory cytokines, such as IL-1 and IL-6, leading to cytokine storms [15, 16]. Vaccines can induce an excessive inflammatory response and increase peripheral pro-inflammatory cytokines [17]. Cytokines that pass through the blood-brain barrier trigger glial cells - such as astrocytes, microglia, and oligodendrocytes – and might lead to cytotoxic edema through excitotoxic mechanisms, depending on the individual's immunogenetic background and innate immune memory [11]. It is not yet established whether vaccination against SARS-CoV-2 can induce an overactive immune response resulting in cytokine storms in a subset of recipients. Adverse events with autoimmune mechanisms have been reported after SARS-CoV-2 vaccination in the literature. GBS, VST, and transverse myelitis are the most frequently reported complications [8]. Other less frequent immune-mediated neurological adverse effects include vaccine-induced acute disseminated encephalomyelitis [18], Bell's palsy [19], neuromyelitis optica spectrum disorder [20], and multiple sclerosis [21, 22]. However, they do not suggest a causal link with the vaccination. There is no clear consensus that SARS-CoV-2 vaccination increases the risk of these complications beyond the expected rate in the general population [19, 21]. Our case nearly resembles a recently reported case of CLOCC in a patient who received the SARS-CoV-2 mRNA vaccine (BNT162b) [11]. Accordingly, we assume that the development of CLOCC in our patient was secondary to an autoimmune response triggered by cytokine release following SARS-CoV-2 vaccination. The temporal relationship supports this hypothesis, raised pro-inflammatory markers, and the absence of other etiological factors for encephalopathy other than SARS-CoV-2 vaccination.

Conclusion

We presented a case of CLOCC in a patient who received the first dose of the Sinopharm BIBP COVID-19 vaccine, with a transient response to immunosuppressive therapy. We hypothesized that an excessive immune response and the subsequent increase in the concentrations of pro-inflammatory cytokines have led to this phenomenon. However, the underlying mechanism needs further research in larger populations of vaccinated patients. Vaccination is highly recommended to achieve herd immunity against SARS-CoV-2. However, the possible adverse reactions must not be ignored. Clinicians must be aware of both common and uncommon adverse events associated with SARS-CoV-2 vaccination to better care for patients seeking medical support post-vaccination.

Ethical Considerations

Compliance with ethical guidelines

Written informed consent was obtained from the patient for the publication of the article and any associated images.

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Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interception of the results, and manuscript drafting. Each author approved the submission of the final version of the manuscript

Conflict of interest

The authors declared no conflict of interest.

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