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Case Report

# Varicella-Zoster Virus (VZV) Meningitis in an Immunocompetent Adult after BNT162b2 mRNA COVID-19 Vaccination: A Case Report

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ABSTRACT

We present, to our knowledge, the second case report of a 46-year old female who developed varicella-zoster virus (VZV) meningitis after BNT162b2 mRNA COVID-19 vaccination. The patient is immunocompetent and has no known predisposing risk factors for developing VZV meningitis. The patient received acyclovir therapy and subsequently had a complete recovery. We describe possible mechanisms of VZV meningitis after mRNA COVID-19 vaccination.



## Introduction

The introduction of vaccines against SARS-CoV-2 brought hope to end the pandemic, save lives, begin economic recovery, and restore social life. An unprecedented number of mass vaccination campaigns globally were initiated to curb transmission, prevent hospitalizations and deaths, and reestablish normalcy (Our World in Data, 2021). The mRNA-based BNT162b2 COVID-19 vaccine has demonstrated a high efficacy rate with an acceptable safety profile and was rapidly rolled out through several nationwide vaccination campaigns (Frenck et al., 2021; Polack et al., 2020; Our World in Data, 2021). In the United Arab Emirates (UAE), 100% and 91.3% of the population have received either 1 or 2 doses of the vaccine against SARS-CoV-2, respectively, including the BNT162b2 mRNA vaccine, as of December 19, 2021 (NCEMA, 2021). Although the safety profile of the BNT162b2 mRNA vaccine established in clinical trials was favorable (Polack et al., 2020), recent real-world data reported some adverse events that were not apparent during phase 3 of the clinical trial (Barda et al., 2021). Some of those side effects, although they can be potentially serious, occurred at a much lower frequency in the vaccinated population when compared with those who contracted the natural infection (Barda et al., 2021; Shasha et al., 2022).

One of those concerning vaccination-related adverse events is Herpes Zoster (HZ) infection. It has been reported mainly as cutaneous shingles (Barda et al., 2021; Maruki et al., 2021; van Dam et al., 2021), and was theorized to be responsible for the increased incidence of Bell's palsy in the vaccinated population (Barda et al., 2021).

Herein, we report a rare case of varicella-zoster virus (VZV) meningitis in an immunocompetent adult after BNT162b2 mRNA COVID-19 vaccination and discuss the potential mechanisms.

## Case report

A 46-year-old female with a previous medical history of dyslipidemia and surgical history of left-sided cervical tuberculosis (TB) lymphadenitis, status postsurgical excision, and anti-TB treatment, more than 20 years ago.

She presented to the emergency department with a 3-day long severe headache. The headache involved the occipital region with referral to the frontal region of exploding type; it was diffuse, continuous, and not responding to medications. It ranged in severity

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from 7 to 10 of 10, associated with light-headedness, photophobia without phonophobia, nausea, or vomiting.

There were no associated symptoms such as transient loss of vision, doubling of vision, or associated cranial nerve symptoms. She denied any associated focal motor weakness of the upper or lower limbs, nor in the coordination of the upper or lower limbs, even though the patient was too weak to walk because of her severe headaches. There was no history of loss of consciousness, involuntary movements, or seizures in the past. She denied the presence of any headaches in the past. She also denied any history of trauma. There was no history of fever, cough, breathing difficulty, or other associated systemic symptoms. The patient denied exposure to any sick contacts, recent travel, or exposure to livestock. The patient has received the 2-dose COVID-19 vaccination series with the inactivated SARS-CoV-2 vaccine (Sinopharm), and the last dose of this 2-dose series was administered on March 1, 2021. She received the first dose of the BNT162b2 mRNA COVID-19 vaccine (Pfizer-BioNTech) as a booster dose on August 24, 2021, 3 weeks before the emergency department (ED) visit. The patient did not receive any VZV vaccinations in the past.

When she arrived at the ED, she was hypotensive with a blood pressure of 80/64 mmHg and a low-grade fever of 37.7°C, which was not reported by the patient during history taking. The review of systems was unremarkable aside from terminal neck stiffness. In addition, there was no evidence of any skin rash or skin manifestation on physician examination.

Her workup in the ED included computed tomography of the head and a computed tomography angiogram with unremarkable findings. Lab tests revealed a white blood cell count of $8.8^{*}10^{9}$/L, hemoglobin 110 g/L, and hematocrit 0.34 L/L. She had a normal metabolic profile, C-reactive protein (3.3 mg/L), and a negative SARS-CoV-2 nasopharyngeal swab.

A lumbar puncture was performed, and the cerebrospinal fluid (CSF) showed lymphocytic pleocytosis with an elevated white blood cell count ($794 \times 10^{6}$/L), lymphocyte (89%), normal CSF glucose (2.96 mmol/L), and elevated CSF protein (0.81 g/L). The acid-fast stain smear and *Mycobacterium tuberculosis* polymerase chain reaction (PCR) from the CSF were negative. Herpes simplex virus 1 and 2 qualitative CSF PCR was negative. The VZV PCR from the CSF was positive. The CSF fluid gram stain and culture did not reveal any growth.

Magnetic resonance imaging of the brain with intravenous (IV) contrast revealed no acute/subacute ischemic infarction, intracranial hemorrhage, or mass lesion, and no abnormal enhancement was seen. There were a few high signal foci in the deep white matter of the frontal region.

The patient received empirical treatment for bacterial meningitis in the ED, including acyclovir 750 mg IV once, ceftriaxone 2 g IV once, vancomycin 1 g IV once (15 mg/kg/dose), and dexamethasone 10 mg IV once. Due to the abnormal CSF findings and her previous history of TB lymphadenitis, she was prescribed the RIPE regimen (rifampin, isoniazid, pyrazinamide, and ethambutol); however, therapy was not administered. The VZV PCR result came back positive, and a diagnosis of varicella-zoster meningitis was confirmed. Her antibiotics were discontinued, and acyclovir was continued at a dose of 750 mg IV every 8 hours with subsequent significant improvement in her headaches. The patient received a 3-week regimen of IV acyclovir and had a complete recovery.

## Discussion

To the best of our knowledge, this is the second case report of VZV meningitis in an immunocompetent adult. The first case of VZV meningitis after COVID-19 vaccination was reported in a patient with Immunoglobulin A nephritis who was not on any immunosuppressive therapy (Maruki et al., 2021).

It's been documented that mRNA-based COVID-19 vaccination induces a strong T cell response and that booster doses of the SARS-CoV-2 mRNA vaccines induce cellular response with increased CD8+ T cell and T helper type 1 CD4+ T cells (Collier et al., 2021; Ciabattini et al., 2021; Schrezenmeier et al., 2021). An interesting hypothesis to explain HZ reactivation is that VZV-specific CD8+ cells are incapable of controlling VZV disease because of a resultant shift of VZV-specific CD8+ cells in the setting of COVID-19 vaccination (Psichogiou M et al., 2021). Another possible mechanism that has been proposed is the involvement of toll-like receptor signaling, which plays a role in the reactivation of HZ (West et al., 2012; Zhang et al., 2019; Furer et al., 2021).

We share our case with the medical community to consider VZV meningoencephalitis in the context of COVID-19 infection and vaccination, especially in clinical practices where meningoencephalitis PCR diagnostics are not readily available.

More studies are required to establish the incidence of HZ reactivation after COVID-19, and whether it is more likely to occur in vaccinated versus unvaccinated individuals. COVID-19 vaccines are only expected to be more widely used because of increased availability and acceptance, administration of booster doses, and potentially becoming a periodic vaccine similar to the influenza vaccine. Until the picture is clearer, it is perhaps best to vaccinate for varicella in patients eligible by virtue of age or co-morbidities.

## Conflict of Interest Statement

The authors of this case report have no conflicts of interest to disclose

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## Ethical Approval statement

This publication was exempted from Institution Review Board (IRB) approval, and consent was obtained from the patient for publication of this case report.

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