



Case report

Zoster meningitis in an immunocompetent young patient post first dose of BNT162b2 mRNA COVID-19 vaccine, a case report



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ABSTRACT

Recently published observational data suggests an increased risk of herpes zoster infection post-vaccination with the BNT162b2 mRNA vaccine. We describe the case of VZV meningitis post BNT162b2 mRNA vaccination in a young immunocompetent patient. A 39-year-old patient with no medical history presented with a vesicular rash, headache, nausea and fever, days after receiving BNT162b2 mRNA vaccination. CSF analysis revealed a pleocytosis, and VZV DNA was confirmed by PCR testing. The patient received intravenous aciclovir with resolution of symptoms within 48 h. He was discharged after 14 days of treatment. Case reports of herpes zoster reactivation post vaccination and details of subsequent successful vaccination course completion have allowed us to recommend the patient receive his second dose of the BNT162b2 mRNA vaccine. At the time of writing, however, the patient has declined to receive further vaccination due to fears of an adverse event. To the best of our knowledge, this is the first reported case in a young patient of herpes zoster meningitis following COVID-19 mRNA vaccination. The sharing of clinical experiences and reporting of suspected side effects, particularly for vaccines that employ novel technology, increases knowledge of the safety profile of these vaccines and allows clinicians to better aid patients make informed decisions with regard to commencing and completing vaccination.

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Background

We describe the case of VZV meningitis post BNT162b2 mRNA vaccination in a young immunocompetent patient. We would like to highlight this case in order to add to the emerging evidence base which suggests that zoster meningitis may be a possible adverse effect of COVID-19 vaccines. Recently published observational data suggests an increased risk of herpes zoster infection post-vaccination with the BNT162b2 mRNA vaccine (1). While it is not possible to conclude that vaccination has caused VZV meningitis in this instance, the prior case reports have helped to raise clinician

awareness about the possibility of vaccination playing a role in our patient's presentation.

Case presentation

A 39-year-old male presented to his GP with a 3-day history of a vesicular torso rash. The rash and its dermatomal distribution led to a clinical diagnosis of shingles. The patient received oral aciclovir. However, within 24 h, he developed a burning occipital headache associated with nausea, vomiting, and fever. He was referred to hospital for further evaluation.

The patient denied neck stiffness or photophobia. He had chicken pox as a child but otherwise had no medical history. His family history was not contributory. The patient worked in media, was a non-smoker, a rare drinker, exercised regularly and ate a varied diet. He denied any life stressors in the lead up to his presentation. 14 days prior to first noticing symptoms, he had received his first dose of the BNT162b2 Comirnaty® (Pfizer BioNTech) mRNA vaccine.

On examination, the patient was alert, orientated and afebrile. He did not exhibit neck stiffness but did have evidence of a vesicular rash on the right side of his torso in the distribution of the T10

Abbreviations: CSF, cerebrospinal fluid; CT, computed tomography; DNA, deoxyribonucleic acid; GP, general practitioner; HIV, human immunodeficiency virus; mRNA, messenger ribonucleic acid; RNA, ribonucleic acid; RT-PCR, reverse transcriptase polymerase chain reaction; PCR, polymerase chain reaction; WBC, white blood cell count; VZV, varicella zoster virus

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Image 1. Vesicular rash in T10 dermatomal distribution (images taken with patient consent).

dermatome, which was beginning to scab over ([Image 1](#)). The patient had no focal neurological deficits. Cardiovascular, gastrointestinal and respiratory examinations were unremarkable.

Timeline and diagnostic assessment

Routine blood work demonstrated a mild lymphopenia ($1.4 \times 10^9/L$ (reference $1.5 - 4.5 \times 10^9/L$)) and a mildly elevated CRP of 11 mg/L. Renal and liver function tests were within normal limits. A lumbar puncture was performed following normal CT brain imaging. 196 WBC/mm² (reference $0 - 5$ WBC/mm²) were seen in the CSF (90% lymphocytes, 10% polymorphonuclear leukocytes) with an elevated protein level of 102 mg/dL (reference $15 - 45$ mg/dL) and a glucose of 2.99 mmol/L (reference $2.22 - 3.89$ mmol/L). No organisms were seen on gram stain and there was no growth on culture. VZV DNA was detected by PCR on a swab of the patient's vesicular torso rash, and VZV DNA was confirmed by PCR from the patient's CSF, leading to a diagnosis of zoster meningitis. Enterovirus and HSV DNA were not detected.

Numerous tests were carried out to assess the patient's overall immune status. HIV antibody/antigen testing was negative and serum immunoglobulin antibodies (IgA, IgG and IgM) were within normal limits, with no abnormal bands seen on plasma electrophoresis. Lymphocyte subset tests (helper T cells and cytotoxic T cells) were within normal limits as were the patient's HbA1c, thyroid function tests, vitamin B12, folate and ferritin levels. RT-PCR oropharyngeal and nasopharynx testing did not detect the presence of SARS-CoV-2 RNA.

The patient had initially been commenced on empiric meningoencephalitis antimicrobial cover on admission, consisting of intravenous aciclovir, ceftriaxone and vancomycin. Upon receipt of CSF results confirming VZV, this was rationalized to intravenous aciclovir 10 mg/kg q8h. The patient had full resolution of his symptoms within 48 h of treatment commencement.

Follow-up and outcomes

The patient's clinical course remained uneventful and he was discharged after 14 days of intravenous aciclovir. The patient was seen in the outpatient clinic 2 weeks post discharge where he remained well.

Discussion and conclusions

We would like to highlight this case in order to add to the emerging evidence base which suggests that herpes zoster may be a possible adverse effect of COVID-19 vaccines. Recently published observational data suggests an increased risk of herpes zoster

infection post-vaccination with the BNT162b2 mRNA vaccine [1]. While it is not possible to conclude that vaccination has caused VZV meningitis in this instance, the prior case reports have helped to raise clinician awareness about the possibility of vaccination playing a role in our patient's presentation.

Approximately 30% of persons in the United States will experience herpes zoster during their lifetime according to estimates from the Centers for Disease Control and Prevention (CDC) [2]. Meningitis due to VZV reactivation can be seen in a subset of immunocompetent persons with herpes zoster [3,4]. CSF findings typically reveal a pleocytosis and elevated protein. The treatment for neurological complications of zoster, recommended by expert opinion, typically consists of 10–14 days of intravenous aciclovir [5].

After primary infection, VZV remains latent in the dorsal root ganglia. Reactivation as herpes zoster can occur at any time, but is typically influenced by age-related immunosenescence, disease-related immunocompromise, iatrogenic immunosuppression, trauma and/or stress. Reactivation can manifest as a number of different neurological conditions apart from meningitis and encephalitis, such as postherpetic neuralgia, ophthalmic complications, Ramsay Hunt syndrome, and Guillain-Barre syndrome [6]. The most important risk factor in the development of herpes zoster is age [7] and this is thought to be due to a decline in virus specific cell mediated immunity as we age [8]. Cell-mediated immunity plays a crucial role in maintaining latency following infection [9], and reactivation can occur with failure of T cells to maintain infection control.

Case reports and series have described an association between herpes zoster and COVID-19, and though few cases have been reported in the literature, underreporting is likely. It is hypothesized that patients with COVID-19 can experience a functional impairment and decrease of T lymphocytes [10]. Given the importance of cell mediated immunity in maintaining VZV latency [9], such immune changes may make affected hosts more susceptible to zoster reactivation. Elsaie, Youssef, and Nada [11] describe 2 cases of confirmed SARS-CoV-2 infection in older adults who presented with herpes zoster prior to their COVID-19 diagnosis. Tartari et al. report zoster infections in 4 older adults with COVID-19 [12] and Saati et al. describe a case of herpes zoster co-infection in an immunocompetent middle aged male with confirmed COVID-19 [13]. Brambilla et al. [14] describe the emergence of herpes zoster in 3 patients 8–10 weeks after their COVID-19 diagnosis.

The focus of recent literature reports has switched to herpes and COVID-19 vaccination. Bostan and Yalici-Armagan describe a case of zoster reactivation in a 78-year-old male following administration of an inactivated COVID-19 vaccine [15]. Chiu et al. report 3 cases of mild herpes zoster in patients within 7 days of receiving mRNA and adenovirus vector COVID-19 vaccination [16]. Tessler and Kluger report a case of herpes zoster in a 44-year-old male healthcare

provider 1 week after receiving BNT162b2 mRNA COVID-19 vaccine [17]. This patient was treated with oral valaciclovir for 2 weeks before receiving his second dose of the vaccine a month later with no ill effect. A case series from Furer et al. described 6 patients with autoimmune inflammatory rheumatic disease who experienced mostly mild herpes zoster following COVID-19 mRNA vaccination. Five of these patients completed their vaccination course and experienced no further adverse events [18]. One patient, who after COVID-19 vaccination required IV aciclovir for her first episode of herpes zoster ophthalmicus, declined the second dose of the vaccine due to their concern of further complications.

Reactivation of herpesvirus infections have been reported previously following hepatitis A, influenza, rabies, and Japanese encephalitis vaccinations [19], with a hypothesis that reactivations could be the result of vaccine-related immunomodulation. Japanese researchers have published what they believe to be the first report of aseptic meningitis in a young immunocompetent patient [20] and more recently PCR confirmed VZV meningitis in an older (71 year old) immunocompetent patient, both one week post their first BNT162b2 mRNA COVID-19 vaccination [21]. Abu-Rumeileh et al. performed a retrospective study of patients presenting to their centre with VZV-induced neurological disease and identified 3 such patients (aged 63, 70 and 82 years) who presented between 12 and 41 days after receiving COVID-19 vaccination [22]. These patients showed no difference in clinical features, results of diagnostic investigations, or outcome when compared to other patients presenting to their centre with VZV-induced neurological disease prior to COVID-19 vaccination.

Research by Sahin et al. [23] demonstrates the strong humoral and adaptive immune responses induced in the host following BNT162b2 vaccination. In their publication exploring the reactivation of VZV following BNT162b2 vaccination in 7 patients (aged 51–94 years), Psychogiou et al. [24] theorize that, following BNT162b2 vaccination, the host's VZV-specific adaptive immune cells may be rendered temporarily incapable of controlling latent VZV infection due a massive shift in the host's T cell response following vaccination. They liken this phenomenon to immune reconstitution inflammatory syndrome (IRIS) in certain profoundly immunosuppressed HIV patients, where the host, in the presence of a pre-existing infection, can experience a paradoxical clinical deterioration following antiretroviral therapy initiation due to their regained capacity to mount an inflammatory response.

Current Irish national guidelines state the contraindications to COVID-19 mRNA vaccination as (1) anaphylaxis following a previous dose of the vaccine or any of its constituents, (2) anaphylaxis following another mRNA vaccine or (3) a previous history of myocarditis after a dose of an mRNA vaccine [25]. The literature shows that COVID-19 vaccination courses have been successfully completed without adverse events in several patients who developed herpes zoster following their first dose, including in a patient who presented, similar to our patient, with zoster and headache (though this patient did not undergo lumbar puncture) [18].

To the best of our knowledge, this is the first reported case of zoster meningitis in a young immunocompetent patient following COVID-19 mRNA vaccination. The patient was seen in the outpatient clinic 2 weeks post discharge where he remained well. In light of his presentation to hospital following vaccination, the patient had some concerns about completing the vaccine course. However, following a review of the literature and local multidisciplinary team discussion, the patient was reassured and advised to complete the vaccine course, similar to the older immunocompetent patient in Makuri et al.'s case report [21]. The patient had not received the second dose of vaccine at the time of writing.

The case reports and series have provided valuable information regarding the successful completion of vaccination courses following first dose adverse events and have allowed us to advise the

patient accordingly. Thankfully, COVID-19 vaccine hesitancy has not been an issue in Ireland, where vaccine uptake is “the envy of Europe” [26]. However, as the old Irish proverb goes; “Ní neart go cur le chéile” (“There is no strength without unity”), and high vaccination uptake is required not just nationally but globally to stymie the development of new variants and reduce COVID-19 related morbidity and mortality. Post-vaccination adverse events, whose causality cannot be fully attributed, risk deterring patients from completing vaccination and receiving maximum protection from COVID-19.

Robust pharmacovigilance is vital in detecting new safety issues that may emerge during vaccination campaigns. The sharing of clinical experiences and reporting of suspected side effects, particularly for vaccines that employ novel technology, increases knowledge of the safety profile of these vaccines and allows clinicians to better aid patients to make informed decisions with regard to commencing and completing vaccination.

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CRediT authorship contribution statement

Colm Kerr: Conceptualization, Visualization, Writing – original draft, Writing – review & editing. **Susan O'Neill:** Writing – original draft. **Anna Szucs:** Writing – original draft. **Oliver Darmody:** Writing – original draft. **Claire Williamson:** Writing – original draft. **Ciaran Bannan:** Supervision, Writing – review & editing. **Concepta Merry:** Supervision, Writing – review & editing.

Competing interests

None of the authors have any competing interests to declare.

Data availability

Not applicable.

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Informed consent

The patient provided informed written consent for this case report.

Ethics approval and consent to participate

The patient has provided written consent for this case report.

Consent for publication

The patient has provided written consent for this case report.

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