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## Case Report

## Varicella zoster meningitis following COVID-19 vaccination: a report of two cases

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## ABSTRACT

Most of the adverse effects reported in patients who have received COVID-19 vaccines have been mild. However, possible serious adverse effects are being monitored cautiously. There have also been a number of case reports of reactivation of varicella zoster infection within 28 days after immunization with mRNA COVID-19 vaccines. A few cases have also been reported after viral vector and inactivated COVID-19 vaccination. The incidence of meningitis following varicella zoster virus infection is rare. In the current study, we report two cases of male patients who received two different types of COVID-19 vaccine (inactivated and viral vector) and developed varicella zoster meningitis within 10 days after vaccination.

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## Introduction

In Thailand, immunization against COVID-19 began in February 2021. The two major types of vaccines used are inactivated (CoronaVac or Sinovac®) and viral vector (AstraZeneca®). Globally, there have been a number of case reports of reactivation of varicella zoster infection within 28 days after immunization with mRNA COVID-19 vaccines (Chiu et al., 2021; Furer et al., 2021; Lee et al., 2021; McMahon et al., 2021; Psychogiou et al., 2021; Rodríguez-Jiménez et al., 2021). A few cases have also been reported after viral vector and inactivated COVID-19 vaccination (Aksu and Öztürk, 2021; Arora et al., 2021; Bostan and Yalici-Armagan, 2021; Chiu et al., 2021). Maruki et al. (2021) reported the one case of varicella zoster meningitis following the first dose of BNT162b2 mRNA COVID-vaccine. In the current study, we report two cases of male patients who received two different types of COVID-19 vaccine (inactivated and viral vector) and developed varicella zoster meningitis within 10 days after vaccination.

## Case 1

## Patient history

The first patient was a 34-year-old man with underlying asthma who had contracted varicella twice at a young age and had never been vaccinated for herpes zoster. Five days after the patient had received his first COVID-19 vaccine, an inactivated COVID-19 vaccine (Sinovac®), he developed a vesicular lesion on the left side of his waist. A local pharmacist diagnosed him as having herpes zoster viral infection and prescribed oral acyclovir 800 mg five times daily. Nine days post-vaccination, the patient presented at the emergency department with severe headache. He indicated a pain score of 10 out of 10. He vomited twice during the ER visit. The patient had no history of fever, weakness, numbness, or alteration of consciousness.

## Physical examination

The patient had a body temperature of 36.6 degree Celsius, blood pressure of 124/76 mmHg, heart rate of 74 bpm, average respiratory rate of 20 bpm, and oxygen saturation of 100% on room air. Heart, lung, and abdominal examinations were unremarkable. However, vesicular lesions were observed on the patient's left

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lower back area at the T11 dermatome. Further neurological examination revealed signs of stiff neck with normal consciousness and no focal neurological deficit.

#### Laboratory results

Cerebrospinal fluid (CSF) opening pressure was normal (17 cm H<sub>2</sub>O). CSF white blood cell count was 185 cell/mm<sup>3</sup> (77% lymphocyte, 19% monocyte, and 2% neutrophil) and glucose level was 50 mg/dL (serum glucose was 114 mg/dL). CSF protein was 92 mg/dL. The CSF culture was negative for any organism.

#### Treatment

The patient was clinically diagnosed with varicella zoster meningitis and was given intravenous acyclovir 500 mg every eight hours for fourteen days. Contact precaution was applied to the patient. Polymerase chain reaction (PCR) analysis later revealed varicella zoster virus. The patient was discharged without any immediate complications. At a two-week follow up, he had fully recovered without any neurological complications. The patient was advised to receive his second dose of COVID-19 vaccine one month from the first dose to avoid confusing the adverse side effects of the vaccine. The care team did not advise against the Sinovac vaccine. However, the patient received the AZD1222 (the AstraZeneca® viral vector vaccine) following the national vaccination program. He did not have any adverse effects following the AZD1222 vaccination.

## Case 2

#### Patient history

The second patient was a 32-year-old man with underlying asthma and chronic hepatitis B with seroconversion. He was not on inhaled or systemic corticosteroids or undergoing any immunosuppressant therapy. Five days after receiving his first COVID-19 vaccine, AZD1222, he developed bilateral temporal headache with fever. He indicated a pain score of 4 out of 10 before visiting the hospital. He visited the emergency department on day 6 after being vaccinated due to persistent headache.

#### Physical examination

The patient had a body temperature of 36.5 degree Celsius, blood pressure of 93/64 mmHg, heart rate of 97 bpm, average respiratory rate of 18 bpm, and oxygen saturation of 98% on room air. Neurological examination showed neither a signs of stiff neck nor a focal neurological deficit. Heart and lung parameters were within the normal limits. We failed to find any skin lesion.

#### Laboratory results

Due to the persistent severe headache, a CT scan of the brain was performed, the results of which were normal. We decided to perform a lumbar puncture. Opening CSF pressure was normal (18 cmH<sub>2</sub>O). CSF profiles revealed a white blood cell count of 288 cell/mm<sup>3</sup> (93% lymphocytes, and 6% monocytes, no neutrophils). CSF glucose level was 55 mg/dL (serum glucose was 92 mg/dL) and protein was 102 mg/dL. The CSF culture was negative. A PCR for herpes virus was performed.

#### Treatment

Based on the CSF results, the doctor decided to treat the patient for herpes viral meningitis with intravenous acyclovir 500mg every

eight hours). Contact precaution was implemented. Two days after admission, the patient developed a vesiculopapular lesion on his back. After 6 days of treatment, a PCR for varicella zoster virus in the CSF came back positive. PCRs for other organisms, such as mycobacteria, human herpes virus type 6 and 7, and enterovirus RNA, were negative. Intravenous acyclovir 500 mg every eight hours was continued for a total of fourteen days. At a two-week follow up, the patient had completely recovered without any complications or neurological deficit. The patient had the second dose of AZD1222 one month later. He only complained of having a low-grade fever. Serious adverse effect was not observed.

## Discussion

The mechanism behind varicella zoster reactivation post COVID-19 vaccination is not fully understood. There may be a relationship, or it could simply be a coincidence. Meningitis following varicella zoster virus infection is rare, occurring in less than one percent of cases (Yasuda et al., 2019). Psychogiou et al. (2021) proposed that the mechanism underlying varicella zoster reactivation following COVID-19 vaccination may resemble that of immune reconstitution inflammatory syndrome (IRIS) after administration of antiretroviral therapy in HIV patients, as antiretroviral drugs can worsen occult infection.

Previous studies have shown that vaccination can alter the proportion of T cells and their functions in the body. For instance, one week after the tetanus vaccination, healthy participants had a decreased of the proportion of naïve T cells and an increase the proportion of memory T cells (Li Causi et al., 2015). Patients with herpes zoster infection also had a lower number of CD3+ T cells and CD8+ T cells (Wei et al., 2017). We hypothesize that COVID-19 vaccination could have altered human immunity and allowed reactivation of occult varicella zoster virus. Another possible explanation is that vaccination might induce physical and emotional stress (Chen et al., 2022), resulting in alteration of the immune system and reactivation of herpes zoster (Segerstrom and Miller, 2004).

Our study cannot provide the association between Covid -19 vaccines and varicella zoster reactivation. Due to a small number of cases, we cannot conclude that the vaccine increased the risk of reactivation. Safety monitoring of patients undergoing COVID-19 vaccination and a larger study of the association between varicella zoster reactivation and COVID-19 vaccination are required.

## Conclusion

It is possible that herpes zoster meningitis is reactivated following COVID-19 vaccination. However, we do not have evidence that the COVID-19 vaccine causes immune dysregulation or reactivates herpes zoster infection. COVID-19 vaccination should not be discouraged as its benefits outweigh its known risk.

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## Ethical approval

This research was reviewed and approved by the Khon Kaen University Committee for Ethics in Human Research (HE 641448).

## Conflict of interest

The authors declare no conflicts of interest.

## Declaration of 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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