

Report of varicella-zoster encephalitis caused by human papillomavirus

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Abstract

This article focused on a young woman with normal immune competence and no previous history of varicella or herpes zoster who suffered Varicella-Zoster virus (VZV) encephalitis after Human Papilloma Virus (HPV) vaccination, and VZV was detected by cerebrospinal fluid gene sequencing. The main clinical symptom was headache, which resolved completely after treatment with intravenous ganciclovir.

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Introduction

A 32-year-old young woman was admitted to our department. She had a history of headache in the bilateral temporal and prefrontal regions, which could be relieved by oral analgesics and rest. The patient was vaccinated with the third dose of bivalent HPV vaccine on September 22. Five days after vaccination (September 27), the patient developed headache again. The headache site was basically the same as before, and the pain degree was more serious than before. After oral analgesics again, the headache could only be partially controlled. When the headache was severe, it was accompanied by nausea and vomiting. At the same time, the right hip pain was felt, but no hip skin rash was seen. Physical examination: no herpes on the skin, normal high-level nerve function, normal limb muscle strength and muscle tension, and negative meningeal irritation. Cerebrospinal fluid examination : white blood cell count: $0.698 \times 10^9/L$, total protein: 1719 mg/L, glucose: 2.29 mmol/L. VZV was detected by targeted sequencing of multiple pathogens in the central nervous system (Xi 'an Jinyu Medical

Laboratory). The number of normalized sequences was 382, and no other pathogens were detected. There were no obvious abnormalities in brain MRI and no signs of infection in chest CT. After admission, the patient was treated with intravenous infusion of ganciclovir. The hip pain disappeared after 3 days, and the headache symptoms were completely relieved after 9 days. Lumbar puncture was performed on October 16, and the results of cerebrospinal fluid showed that the white blood cell count was $0.385 \times 10^9/L$, the total protein was 529 mg/L, and the glucose was 2.86 mmol/L. The patient continued to take valaciclovir orally for 2 weeks and was followed up on November 3. No headache occurred.

Discussion

VZV is a neurotropic virus that is a common pathogen causing chickenpox and herpes zoster. It persists in nerve cells in the spinal dorsal root ganglion and trigeminal ganglion after initial infection and can be reactivated by internal or external factors [1,2]. There have been many reports on herpes zoster

or VZV encephalitis caused by COVID-19 vaccination, but there is no case report of VZV infection secondary to HPV vaccination. Headache is one of the common adverse reactions after HPV vaccination [3]. However, there is no research to clarify its mechanism. The patient had no obvious adverse reactions during the first and second HPV vaccination, but had headache and right hip pain after the third vaccination, which was confirmed to be encephalitis caused by VZV infection, and hip pain may be nerve root pain caused by VZV [4]. Whether VZV reactivation is an adverse event or an accidental event of HPV vaccination cannot be determined. VZV reactivation can occur in all stages from infancy to old age [5-7]. It is no longer limited to immune compromised or older people. Due to the prevalence of VZV vaccination, serological antibodies are no longer specific, making the diagnosis of reactivation caused by VZV vaccines relatively difficult [6]. Therefore, it may be difficult to determine the relationship between HPV vaccination and VZV reactivation. However, a meta-analysis of an observational study on COVID-19 vaccination showed that the VZV reactivation rate after COVID-19 vaccination was 14/1000 person-times [1]. Another study found that VZV reactivation after COVID-19 vaccination was higher than that in the cohort without COVID-19 vaccination [8]. The molecular mechanism of VZV reactivation is still unclear. Fathy et al. believed that it may be related to the failure of the immune system caused by the vaccination response [9]. This also provides a possible theoretical basis for the reactivation of VZV after HPV vaccination, because the third dose of vaccine usually produces a stronger immune response, which may cause CD8 + T cells to temporarily lose control of VZV [10]. This article aims to remind patients with headache after HPV vaccination that the possibility of viral encephalitis should be considered to avoid delayed treatment. The overall safety of HPV vaccine is high after entering the large-scale population vaccination from HPV vaccine, but there are still cases of continuous adverse reactions reported [11]. Further research is needed to clarify. For suspected patients, specific detection of anti-IgG and anti-IgM to determine the patient's infection status, but it is relatively difficult to diagnose patients with central nervous system VZV reactivation without rash. The most valuable tests are VZV DNA and anti-VZV IgG in cerebrospinal fluid [12]. In recent years, studies have also taken saliva VZV DNA to diagnose atypical Varicella-zoster [13]. HPV vaccines are considered to be safe and very beneficial interventions for individuals and populations. Although mild adverse reactions may occur after HPV vaccination, the occurrence of serious adverse events is extremely rare. A single case report is not enough to cast doubt on the safety of HPV. At present, there is no substantial evidence to support a clear link between HPV vaccination and VZV reactivation. We believe that continuous monitoring and further research are necessary.

Declarations

Author contributions: Cao Chan provided the case and wrote the whole article. Xiao Ting gives guidance to the idea or design of the work. Zhang YouWen screening and analysis of information Zhang Yimeng retrieves and collects information Shiqiang reviewed and revised the article.

Data availability: All data collected or generated in the course of this study are included in this published article. The original medical records of the study were also archived in the affiliated units.

Ethics approval and consent to participate: The study has

obtained the informed consent of patients.

Consent for publication: Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article.

Competing interests: All authors declare that they have no conflicts of interest. We confirm that we have read the appropriate checklists and affirm that this report is consistent with the guidelines

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