

A Case of Herpes Zoster Due to Varicella-Zoster Virus Vaccines in a 14-Month-old Girl

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Abstract: Herpes zoster (HZ) due to Varicella-Zoster virus (VZV) vaccines is rare and the accurate incidence remains unknown. We report a case of HZ due to VZV vaccines presented in an immunocompetent 14-month-old girl 62 days after vaccination which is the youngest case from the first dose of the VZV vaccine in immunocompetent children.

Keywords: Herpes Zoster, immunocompetent children, vaccine-strain Varicella-Zoster virus

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Varicella-zoster virus (VZV) vaccines have been implemented worldwide in regular childhood vaccination programs and are considered safe for immunocompetent children. The widely used Oka strain for VZV vaccines was collected from a boy named Oka at our hospital in 1971, and the VZV vaccine was developed by Takahashi in 1974. Voluntary single-dose vaccination for varicella started in 1987 and was included in the regular childhood vaccination program as a 2-dose vaccination in 2014 in Japan. Since then, the incidence of varicella has decreased dramatically. Although this trend reflects the high efficacy of VZV vaccines, it has been hypothesized that an increase in the incidence of herpes zoster (HZ) can occur due to waning herd immunity against varicella.¹ This waning herd immunity develops due to the reduced chance of re-exposure to varicella, which boosts immunity in people who have been previously infected with varicella. HZ due to VZV vaccines is extremely rare, and its incidence remains unknown. Therefore, it is vital to distinguish HZ caused by wild-type varicella from the vaccine strain to identify the incidence of HZ due to VZV vaccines precisely, especially after the implementation of the vaccine. We report a case of HZ due to VZV vaccines in a 14-month-old girl 62 days after vaccination, which is the youngest case of HZ due to VZV vaccines in immunocompetent children.

ETHICAL APPROVAL

Written informed consent was obtained from the parents of this patient. This research was approved by the ethical board in Osaka Police Hospital.

CASE PRESENTATION

A 14-month-old girl presented with a clustered rash with crusts on her right shoulder and anterior axilla. She was in good health with no known significant medical or family history or history of varicella. However, 5 days before her first consultation,

pictures taken by her mother showed a vesicular rash at the same lesion. The clinical findings were compatible with HZ involving the right T2 dermatomal region. Although oral acyclovir was considered for treatment, it was not prescribed because of the resolution of the lesion. The rash healed, and left hypopigmentation of the skin occurred within a week without any medication (Fig. 1).

She was subcutaneously vaccinated with the Oka vaccine strain at 12-month-old on her right upper arm at the same time as MR (measles and rubella) and mumps vaccine on her left upper arm. HZ was present 62 days after vaccination. A sample for the polymerase chain reaction (PCR) was collected from the crust's surface on her right shoulder. PCR results showed amplified products of the VZV sequence, and the vaccine strain was identified by electrophoresis of the product digested with *Sma*I.¹

Blood tests revealed normal complete and differential blood counts and IgG, IgM, IgA, IgE and serum complement levels. Results of human immunodeficiency virus testing were negative. The enzyme immunoassay of VZV-IgM was negative, and VZV-IgG was 31.4 (OD₄₅₀ values). She had no significant medical events until the age of four after this event.

DISCUSSION

Primary VZV infection causes varicella infection. The virus becomes latent in the dorsal root ganglia and reactivates as HZ in later life.² On the other hand, primary VZV infection may present atypically and HZ can occur without an apparent history of varicella even after the VZV vaccine.^{1,2} This may confuse HZ caused by wild-type or the vaccine strain after VZV vaccines. In addition, the appearance of HZ resembled the rash caused by herpes simplex and bullous impetigo. Considering the difficult aspects of HZ differentiation due to VZV vaccines, the incidence may be underestimated.

VZV vaccines induce immunity against VZV without clinical presentation and prevent clinical varicella and HZ. After implementing VZV vaccines in the regular childhood vaccination schedule in 2014 in Japan, the incidence of varicella decreased by 78.1% in 2018 compared to the mean incidence from 2000 to 2011.³ In contrast, the incidence of HZ has been increasing gradually. Although it might be affected by aging in the population, the case of HZ has steadily increased from 1997 to 2017, especially since the implementation of VZV vaccines in 2014.⁴ This trend may support the hypothesis that re-exposure to varicella boosts the immunity against VZV and prevents HZ.⁵ Rising cases of HZ has also been reported outside of Japan. Leung et al⁶ reported HZ incidence from 1993 to 2006 in the United States. The cases have increased continuously across all age groups regardless of the coverage levels of VZV vaccines. In addition, although the cases of HZ in children decreased significantly from 2010 to 2015 in Germany after the implementation of the same 2-dose schedule of VZV vaccines as in Japan in 2009, the incidence of HZ in adults dramatically increased in the same period.⁷

The incidence of HZ due to VZV vaccines was reported as 0.11 per 100,000 doses in children. Only 15 cases have been reported between 2005 and 2020 in Japan.⁸ In 15 previously reported cases, 3 cases were reported in immunocompromised children. The child that we report is the youngest from the first dose of

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FIGURE 1. The appearance of HZ due to the VZV vaccine. A: Clustered vesicular rash presented at her right back shoulder. B: The first consultation with us. The rash turned to crusts. C: The lesion healed and left hypopigmentation. [full color online](#)

the VZV vaccine until the presentation of HZ in an immunocompetent child. HZ due to VZV vaccines tend to appear at the vaccination site, and the vaccine strain was detected in half of the cases of zoster-like skin rashes after vaccination. Comparing the vaccine strain with wild-type VZV in HZ, HZ due to VZV vaccines occurs in younger children (median age 1 vs. 9.5) and a shorter time from vaccination (median days 167 vs. 2506).⁹

HZ caused severe outcomes in immunocompromised children before the wide use of acyclovir treatment; however, the severity has become similar in children diagnosed with hematologic cancer in hospital settings.¹⁰ Even though distinguishing HZ due to VZV vaccines from the wild-type varicella is still important because about half of the cases of HZ due to VZV vaccines relate to reduced immunity of the vaccinee and could be a prodromal sign of undiagnosed immunodeficiency, leukemia or both.¹¹

It is uncertain whether the vaccine strain becomes latent at the dorsal root ganglia of the vaccinated dermatomal area and reactivates as HZ in the same area after a latent period.¹² Only 46% of HZ due to VZV vaccines occur in the same area of vaccination and the remaining cases show HZ at the different sites of the vaccination due to viremia of the vaccine strain.¹¹ If the vaccine strain became latent in the dorsal root ganglia and presented as HZ in our case, the duration of the latent period may be as short as 60 days. This is because the retrograde and anterograde velocity of VZV in human axons were reported to be 1.4 and 1.5 $\mu\text{m/s}$, respectively. The total distance from the site of vaccination to the area of the HZ via the dorsal root ganglia was approximately 30 cm, and it took approximately 3 days for VZV to travel.^{13,14}

Reporting cases of HZ due to VZV vaccines is crucial to ensure the safety of VZV vaccines. In addition, early recognition of an undiagnosed underlying immunocompromised status may improve the course of the illness.

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