Series Editor: Camila K. Janniger, MD

Varicella-Zoster Virus in Children Immunized With the Varicella Vaccine

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We present the case of a 4-year-old immunocompetent girl with varicella-zoster virus (VZV) that occurred 45 months after a single dose of the varicella vaccine. Varicella-zoster virus is rare in children, particularly those who have received the varicella vaccine. Our case illustrates the need for a continued high index of suspicion, even among vaccinated children with herpetiform rashes, for varicella reactivation or reinfection.

Cutis. 2012;90:114-116.

Case Report

A previously healthy 4-year-old girl presented to our dermatology clinic with a pruritic herpetiform dermatitis on her left cheek of 3 days' duration. Her parents denied other skin involvement, facial pain, visual concerns, dysphagia, fever, nausea, vomiting, or diarrhea. Additionally, her parents denied allergies, new medications, exogenous contact exposure, or trauma. Her medical history was notable for distant herpes labialis that was not medically treated, and no recent lesions or prodromal symptoms were present. The patient received a single dose of the varicella vaccine more than 3 years (45 months) prior at the age of 1 year; she also received measles-mumps-rubella, pneumococcal, and hepatitis B vaccines at that time. Her parents denied local skin reaction, fever, or adverse reactions to the vaccinations. Her mother denied history of chickenpox (varicella), breakthrough varicella, or known exposure to wild-type varicella infection.

Physical examination revealed multiple grouped small vesicles on an erythematous base on the left side of her face with several vesicles crusted over and others coalesced into plaques (Figure 1A). The involved area of her face was in the V2 dermatome of the trigeminal nerve, extending from under her left eye to the tip of her nose (Hutchinson sign). Several vesicles were noted on the ipsilateral hard palate (Figure 2). Subsequent ophthalmologic examination was unrevealing. Tzanck smear showed multinucleated giant cells. Direct fluorescence assays of both the skin and oral lesions were positive for varicella-zoster virus (VZV) antigen. Viral cultures and direct fluorescence assay were negative for herpes simplex virus types 1 and 2. A diagnosis of herpes zoster (HZ), also known as shingles, was made. A 2-week course of oral acyclovir (1440 mg daily divided every 6 hours) was prescribed with clearance of the blisters (Figure 1B). Due to her young age and low risk for postherpetic neuralgia, a tricyclic antidepressant was not prescribed. Follow-up examination 3 weeks later revealed no vesicles or residual neuropathic symptoms.

Comment

Herpes zoster arises from the reactivation of latent VZV residing in the dorsal root ganglion following a primary infection. It commonly is described in elderly and immunosuppressed populations and rarely is encountered in the pediatric population.[1,2] In the first 10 years (1995-2005) that the Advisory Committee on Immunization Practices[3] recommended routine varicella vaccination for children aged 12 to 18 months and those older children who are deemed susceptible, more than 55 million doses of the live attenuated vaccine have been distributed

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The authors report no conflict of interest.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the US Department of the Navy, US Department of the Army, US Department of Defense, or the US Government.

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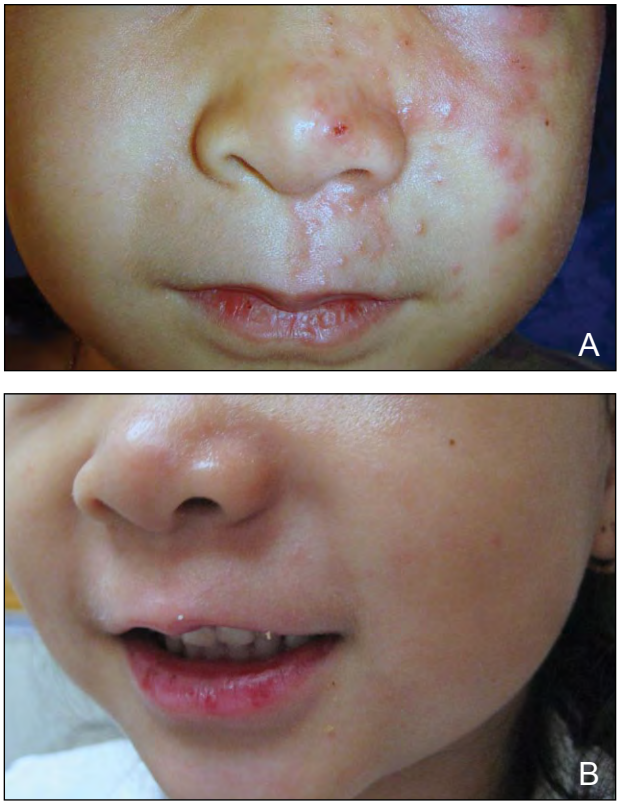

Figure 1. Multiple grouped small vesicles on an erythematous base on the left side of the face with several vesicles crusted over and others coalesced into plaques (A). The vesicles resolved following a 2-week course of oral acyclovir (B).

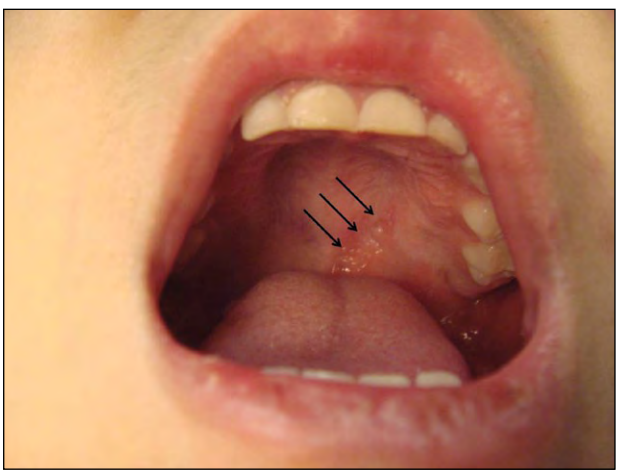

Figure 2. Vesicles on the hard palate (arrows).

in the United States alone.[4] The side-effect profile of the vaccination has been well-studied and VZV rarely has been reported among vaccinated children; however, we report a case of a child who experienced VZV more than 3 years after receiving the varicella vaccine, which illustrates the potential for reactivation in immunocompetent children.

Adverse events associated with the varicella vaccine occurred in 52.7 cases per 100,000 doses administered and most commonly included rash (17.3/100,000 doses), fever (11.4/100,000 doses), injection-site reactions (6.9/100,000 doses), and urticaria (2.2/100,000 doses).[5] Other rarely reported adverse effects included HZ, encephalitis, meningitis, erythema multiforme, ataxia, anaphylaxis, thrombocytopenia, and secondary transmission.[6] Serious adverse events were reported in 2.6 cases per 100,000 doses administered.[5] Localized skin infections were the most common adverse reactions, with 62% (836/1349) occurring within the first 2 weeks after vaccination and 86% (1160/1349) occurring within the first 3 weeks.[6] Breakthrough varicella, defined as varicella occurring more than 42 days following vaccination, has been reported to occur in 15% to 20% of vaccinated patients[6,7] and occurred a mean of 28 months after vaccination in one study.[8] When compared with varicella in nonvaccinated individuals, the clinical course of breakthrough varicella typically is characterized by fewer lesions and a milder systemic illness.[9]

Herpes zoster has an overall incidence of 42 cases per 100,000 person-years and is most commonly reported in elderly and immunosuppressed populations. Among children who have received the varicella vaccine, the incidence of HZ has been reported to be 14 cases per 100,000 person-years[10]; however, more recent population-based studies reported the incidence of HZ between 19.2 and 33.3 cases per 100,000 person-years.[11,12] The incidence of varicella in nonvaccinated children is reported to be between 2.14 and 4.05 cases per 1000 person-years. Similar to the wild-type infection, the live attenuated form of VZV can produce latent infection in the sensory neurons, which may later reactivate into a zoster that is clinically indistinguishable from zoster arising from the wild-type infection.[13]

The identification of HZ as secondary to vaccination or wild-type infection may be made based on analysis of viral DNA obtained from the zoster itself. In one study, 22 of 32 cases of HZ in vaccinated hosts were found to be vaccine-type cases, with 10 cases arising from wild-type infection. This study indicated that although the majority of cases of HZ in vaccinated children arose due to reactivation of vaccine-strain virus, wild-type infection predating immunization can only be ruled out with DNA analysis.[8] Regardless of type, the risk for HZ in vaccinated children younger than 10 years was estimated to be 4 to 12 times lower than nonvaccinated children, and the clinical course was shorter and associated with less pain and fewer systemic symptoms. Vaccinated children with HZ typically

are younger than those who have had natural disease (median age, 5 vs 8 years) and are more likely to involve lumbar or sacral regions.[12] The location and prominence of vesicles on the V2 dermatome of the trigeminal nerve in our patient, features that are more commonly associated with wild-type disease, illustrate the broad presenting features that may accompany vaccine-associated HZ.

Among vaccinated children who subsequently develop HZ, immunosuppression is a known risk factor.[8] Disseminated HZ in an immunized child has been described as an AIDS-defining illness.[14] Other risk factors for HZ among vaccinated children include corticosteroid use; depression; stress; infection with viruses such as cytomegalovirus or Epstein-Barr virus, which impact cell-mediated immunity responses; and trauma to a dermatome.[11] Other risks for HZ include prior varicella-related rash due to either wild-type infection or a vaccine, including breakthrough varicella. Skin break in these cases is hypothesized to allow infection of sensory neurons associated with the infected skin.[13] Wild-type infection before 1 year of age also is a known risk factor for HZ in childhood[15]; these children have been shown to have a 9-fold increased risk for childhood HZ compared with children who acquired VZV after 1 year of age.[11] Children vaccinated after 5 years of age have been shown to have increased rates of HZ in childhood. This finding may reflect a higher incidence of subclinical wild-type infection, which itself confers a higher risk for HZ than vaccine-type VZV.[11] No statistically significant differences in HZ rates have been shown among children immunized with the varicella vaccine alone compared with children who received the vaccine in conjunction with other vaccines, such as the measles-mumps-rubella vaccine.[5]

Conclusion

We report a case of VZV occurring in a 4-year-old girl 45 months after receiving the varicella vaccine. This case illustrates the possibility of HZ development in immunocompetent children with no recognized course of prior VZV infection or breakthrough varicella. The impact of the 2-dose vaccination schedule on HZ remains to be seen and continued physician monitoring is required to ensure HZ is appropriately diagnosed, treated, and reported.

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