Herpes Zoster Following Varicella Vaccination in Children

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PRACTICE **POINTS**

- Most children with herpes zoster are immunocompromised, have a history of varicella, or were exposed to varicella in utero.
- Herpes zoster has been reported in immunocompetent children due to either wild-type or vaccine-strain varicella-zoster virus.

Herpes zoster (HZ), or shingles, is commonly seen in older adults but does occur in children. Routine administration of the varicella vaccine started in 1995 in the United States; since then, the incidence of varicella and HZ has declined. We report a case of HZ in an otherwise healthy 19-month-old boy who had been vaccinated at 13 months of age and recovered fully after acyclovir treatment. We review previously reported cases of HZ in healthy vaccinated children.

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Varicella-zoster virus (VZV) causes varicella as a primary infection. It is a highly contagious disease characterized by a widespread papulovesicular eruption with fever and malaise.[1,2] After the primary infection, the virus remains latent within the sensory dorsal root ganglia and can reactivate as herpes zoster (HZ).[1-5] Herpes zoster is characterized by unilateral radicular pain and a vesicular rash in a dermatomal pattern.[1,2] It is most common in adults, especially elderly and immunocompromised patients, but rarely occurs in children. Herpes zoster is most often seen in individuals previously infected with VZV, but it also has occurred in individuals without known varicella infection,[1-17] possibly because these individuals had a prior subclinical VZV infection.

A live attenuated VZV vaccine was created after isolation of the virus from a child in Japan.[2] Since the introduction of the vaccine in 1995 in the United States, the incidence of VZV and HZ has declined.[5] Herpes zoster rates after vaccination vary from 14 to 19 per 100,000 individuals.[3,5] Breakthrough disease with the wild-type strain does occur in vaccinated children, but vaccine-strain HZ also has been reported.[1-5] The risk for HZ caused by reactivated VZV vaccine in healthy children is unknown. We present a case of HZ in an otherwise healthy 19-month-old boy with no known varicella exposure who received the VZV vaccine at 13 months of age.

Case Report

An otherwise healthy 19-month-old boy presented to the dermatology clinic with a rash that began 2 days prior on the right groin and spread to the right leg. The patient's mother denied that the child had been febrile and noted that the rash did not appear to bother him in any way. The patient was up-to-date on his vaccinations and received the first dose of the varicella series 6 months prior to presentation. He had no personal history of varicella, no exposure to

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sick contacts with varicella, and no known exposure to the virus. He was otherwise completely healthy with no signs or symptoms of immunocompromise.

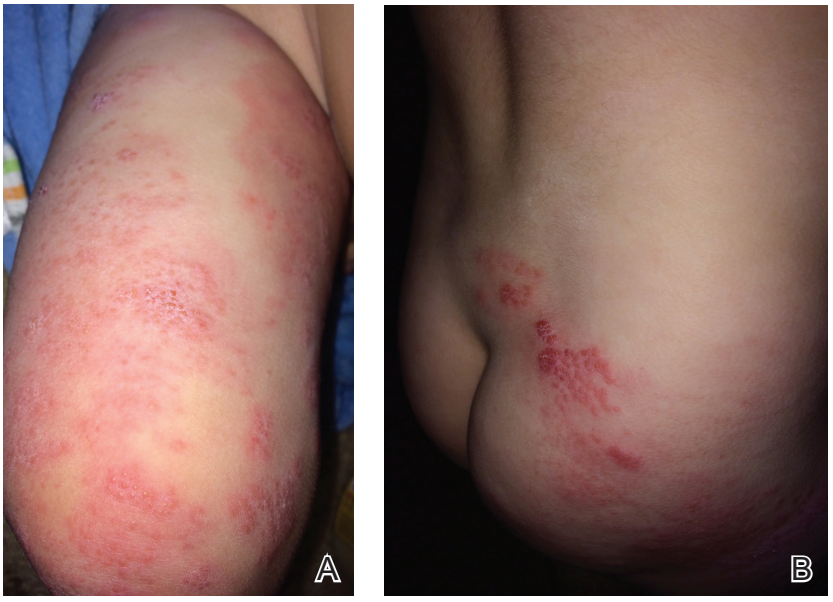
Physical examination revealed grouped vesicles on an erythematous base on the right thigh, right sacrum, and lower abdomen that did not cross the midline (Figure). There were no other pertinent physical examination findings. The eruption was most consistent with HZ but concern remained for herpes simplex virus (HSV) or impetigo. A bacterial culture and polymerase chain reaction assay for VZV and HSV from skin swabs was ordered. The patient was prescribed acyclovir 20 mg/kg every 6 hours for 5 days. Laboratory testing revealed a positive result for VZV on polymerase chain reaction and a negative result for HSV. The majority of the patient's lesions had crusted after 2 days of treatment with acyclovir, and the rash had nearly resolved 1 week after presentation. Subsequent evaluation with a complete blood cell count with differential and basic metabolic profile was normal. Levels of IgG, IgA, and IgM also were normal; IgE was slightly elevated.

Comment

Herpes zoster in children is an uncommon clinical entity. Most children with HZ are immunocompromised, have a history of varicella, or were exposed to varicella during gestation.[8] With the introduction of the live VZV vaccine, the incidence of HZ has declined, but reactivation of the live vaccine leading to HZ infection is possible. The vaccine is 90% effective, and breakthrough varicella has been reported in 15% to 20% of vaccinated patients.[1-17] The cause of HZ in vaccinated children is unclear due to the potential for either wild-type or vaccine-strain VZV to induce HZ.

Twenty-two cases of HZ in healthy children after vaccination were identified with a PubMed search of articles indexed for MEDLINE using the search terms *herpes zoster infection after vaccination* and *herpes zoster infection AND immunocompetent AND vaccination* in separate searches for all English-language studies (Table). The search was limited to immunocompetent children and adolescents who were 18 years or younger with no history of varicella or exposure to varicella during gestation.

The mean age for HZ infection was 5.3 years. The average time between vaccination and HZ infection was 3.3 years. There was a spread of dermatomal patterns with cases in the first division of the trigeminal nerve, cervical, thoracic, lumbar, and sacral distributions. Of the 22 cases of HZ we reviewed, 16 underwent genotype testing to determine the source of the infection. The Oka vaccine strain virus was identified in 8 (50%) cases, while wild-type virus was found in 8 (50%) cases.[1,2,4,5,7,8,10,11,13,14,16] Twelve cases were treated with acyclovir.[2,3,5,6,9-12,14-17] The method of delivery, either oral or intravenous, and the length of treatment depended on the severity of the disease. Patients with meningoencephalitis and HZ ophthalmicus received intravenous acyclovir more often



Grouped vesicles on an erythematous base with secondary crusting along the L4 dermatome of the right thigh on day 2 of the eruption (A) and right sacrum on day 3 of the eruption (B).

Reports of HZ in Children Vaccinated for VZV

Reference (Year)	Age, mo	No. of Months Since VZV Vaccination	Dermatomal Pattern of HZ	Wild-Type Vaccine Strain	Oka Vaccine Strain	Treatment	Symptoms
Matsubara et al[6] (1995)	60	40	V1	Not tested	Not tested	Systemic and topical acyclovir (dosing unknown)	Febrile, painful, HZ ophthalmicus
Na[1] (1997)	58	34	Sacral	1	0	NA	NR
	37	20	Sacral	1	0	NA	NR
	65	24	Thoracic	1	0	NA	NR
	30	18	Thoracic	1	0	NA	NR
	45	15	Lumbar	1	0	NA	NR
	50	22	Sacral	1	0	NA	NR
Liang et al[5] (1998)	19	4	Thoracic	0	1	Acyclovir 20 mg/kg (unknown route) 4 times daily for 2 wk	Afebrile, painful
Kohl et al[7] (1999)	72	0.4	Thoracic	1	0	Prochlorperazine for nausea	Afebrile, painful
Uebe et al[2] (2002)	27	16	Cervical	0	1	IV acyclovir 10 mg/kg 3 times daily for 7 d	Afebrile, painless
Feder and Hoss[8] (2004)	60	45	Sacral	1	0	No treatment	Afebrile, painful
Binder et al[9] (2005)	96	84	V1	Not tested	Not tested	IV acyclovir for 4 days, then oral acyclovir 400 mg 3 times daily for 1 week; ciprofloxacin ointment 4 times daily and cyclopentolate opthalmic solution 1% 3 times daily for 4 d	HZ ophthalmicus

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Table. (continued)

Reference (Year)	Age, mo	No. of Months Since VZV Vaccination	Dermatomal Pattern of HZ	Wild-Type Vaccine Strain	Oka Vaccine Strain	Treatment	Symptoms
Levin et al[10] (2008)	96	84	Thoracic	0	1	IV acyclovir 15 mg/kg 3 times daily for 2 d	Meningoencephalitis
Obieta and Jacinto[3] (2008)	15	2	Sacral	Not tested	Not tested	Acyclovir 30 mg/kg (unknown route) for 14 d	Afebrile
Ota et al[4] (2008)	28	3	Thoracic	0	1	No antiretroviral	Afebrile, painful
Iyer et al[11] (2009)	108	96	Cervical	0	1	IV acyclovir 500 mg/m^2 3 times daily for 10 d	Meningoencephalitis
Lin et al[12] (2009)	192	106	V1	Not tested	Not tested	Oral acyclovir 800 mg 5 times daily for 14 d with prednisolone acetate 1% ophthalmic drops	Afebrile, HZ ophthalmicus
Chouliaras et al[13] (2010)	42	20	V1	0	1	NA	Encephalitis, HZ ophthalmicus
Han et al[14] (2011)	84	72	Cervical	0	1	IV acyclovir 10 mg/kg 3 times daily for 21 d	Afebrile, painful
Ryu et al[15] (2014)	156	144	Cervical	Not tested	Not tested	IV acyclovir 250 mg 3 times daily for 7 d + oral prednisone 25 mg daily for 2 wk	No history of varicella; HZ ophthalmicus and isolated trochlear nerve palsy
Iwasaki et al[16] (2016)	27	10	V1	0	1	IV acyclovir 10 mg/kg 3 times daily for 7 d	Afebrile
Peterson et al[17] (2016)	15	3	V1	Not tested	Not tested	Oral acyclovir 200 mg 4 times daily for 7 d	HZ ophthalmicus
Current case	19	13	Sacral	Not tested	Not tested	Oral acyclovir 20 mg/kg 4 times daily for 7 d	Febrile

Abbreviations: HZ, herpes zoster; VZV, varicella-zoster virus; V1, first division of the trigeminal nerve; NA, not available; NR, not reported; IV, intravenous.

and also had a longer course of acyclovir compared to those individuals with involvement limited to the skin.

This review found HZ occurs from reactivation of wild-type or Oka vaccine-strain VZV in immunocompetent children.[1-17] It shows that subclinical varicella infection is not the only explanation for HZ in a healthy vaccinated child. It is currently not clear why some healthy children experience HZ from vaccine-strain VZV. When HZ presents in a vaccinated immunocompetent child without a history of varicella infection or exposure, the possibility for vaccine strain–induced HZ should be considered.

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