

## Case Report

### DISSEMINATED HERPES ZOSTER IN A 9-MONTH-OLD INFANT

Adelia Martalova. AJ<sup>1</sup>, Lidya Alexandra<sup>1</sup>, Tjokorda Dalem Pemayun<sup>2</sup>

<sup>1</sup>General Practitioner, Wangaya Regional General Hospital, Denpasar, Bali, Indonesia

<sup>2</sup>Dermato-venereologist, Department of Dermatovenereology, Wangaya Regional General Hospital, Denpasar, Bali, Indonesia

**Article Info:** Received 22 August 2019; Accepted 14 September. 2019

**DOI:** <https://doi.org/10.32553/ijmbs.v3i9.522>

**Address for Correspondence:** Adelia Martalova. AJ, General Practitioner, Wangaya Regional General Hospital, Denpasar, Bali, Indonesia

**Conflict of interest:** No conflict of interest.

#### Abstract

Herpes Zoster (HZ) or shingles is a clinical manifestation caused by the reactivation of varicella-zoster virus (VZV). HZ is rarely happening in children, and its incidence increases with age. We report a 9-month-old baby boy with disseminated HZ. There were grouped vesicles on an erythematous base scattered in several dermatomes with dominant lesions in C5-C7 dermatomes. Complete blood counts were within the normal limits. Human immunodeficiency virus (HIV) serology was negative both in mother and baby. Patient was treated with 150 mg oral acyclovir 4 times a day for 5 days. The infant experienced significant improvement and recovered completely without sequelae.

**Keywords:** disseminated, herpes zoster, infant, shingles, *varicella-zoster virus*

#### INTRODUCTION

Herpes Zoster (HZ) or shingles is a form of reactivation after primary infection of the *varicella-zoster virus* (VZV).<sup>1-3</sup> The word derived from the Latin *cingulum* which means a belt.<sup>4</sup> After the primary varicella infection, the virus will be dormant,<sup>2</sup> as the characteristic of  $\alpha$ -herpes virus,<sup>5</sup> in the dorsal nerve root. Lesions in HZ are generally grouped vesicles on an erythematous base which are localized to certain dermatome and accompanied by pain.<sup>2</sup> Each year, it is estimated that there are more than 1.7 million new cases of HZ in the world.<sup>6</sup> HZ incidence in the United Kingdom ranges from 1.85-3.9 cases per 1000 population, which increases with age.<sup>2</sup> In the United States of America, 33.33% of the population experiences HZ in their lifetime.<sup>7</sup> Based on data obtained by the Indonesian Herpes Study Group, there were 2232 HZ patients in 13 teaching hospitals in Indonesia for 3 years of observation, with the most cases (37.95%) occur in the age group between 45-64 years and the lowest number (0.49%) occur in the age group under 5 years.<sup>8</sup> Every person who had been infected with varicella had the potential to suffer from HZ. Vulnerability will increase with age or the conditions or medications that trigger the immune system suppression.<sup>2,9</sup>

#### Case Report

A 9-month-old baby boy presented in the Emergency Department of the Wangaya Regional General Hospital with a 4 days history of vesicular eruption. Initially, there was a reddish rash on the thumb of the right hand and then it was followed by the spread of vesicular eruption over the right hand and lateral side of the arm, right shoulder, left thigh, left calf, abdomen, and head. New lesions still appear until day 5 after the first rash appears. Patient had a history of common cold and decreased appetite. Other constitutional symptoms were denied. History of previous varicella was unclear, but the patient had a fever accompanied by small fluid-filled blisters when he was 6 months old. There was no history of varicella in his mother during pregnancy. The history of long-term drug consumption, malignancy, surgery, transfusion, diabetes mellitus (DM), transplantation, trauma, seizures, spasms, and others that can disrupt the immune system were denied. The patient was born at fullterm and got breast-fed until 4 months old. The rest of the growth and development was normal.

On examination, the patient was irritable with 8.3 kg body weight. In the lateral, the right upper extremity and hand, right shoulder, both lower extremities, abdomen, and frontalis region appeared grouped

vesicles on an erythematous base. No other abnormalities were noted. Complete blood cell count were within normal limits. Human immunodeficiency virus (HIV) serological tests was negative both in mother and baby. Other supporting tests were not carried out. The diagnosis was made based on typical clinical manifestations.

During treatment, the patient received oral acyclovir therapy 150 mg, four times per day, for 5 days. Supportive therapy and education about the patient's condition were also provided. The patient experienced significant improvement and there were no new lesions after the therapy began. He was discharged after 5 days hospitalization.



**Figure 1: Lesions in patients based on the location sequentially on the 5<sup>th</sup> day, 7<sup>th</sup> day, and 9<sup>th</sup> day after the onset of the rash. A. Head; B. Right arm and right hand; C. Left leg; D. Abdomen**



**Figure 2: Lesions on the patient's right foot on the 7<sup>th</sup> day, 8<sup>th</sup> day, and 9<sup>th</sup> day after the onset of the rash**

## Discussion

In primary infections, the VZV is transmitted through droplets which will cause varicella.<sup>6</sup> 1 of the 5 children aged 2-4 years who are exposed to a varicella patient will experience varicella primary infection. It is estimated that only 0.1% of individuals will experience post-exposure varicella with HZ patients. However, HZ will be the main source of varicella transmission when the immunization program can eliminate the varicella primary infection.<sup>6,9</sup> Primary infection creates long-term immunity against varicella. The virus will become latent which can last a lifetime,<sup>9</sup> in the dorsal nerve root and reactivate when the immune system declines.

Many things which are related to the decline in the our defense system, especially the cellular immune system that can trigger HZ, including aging (immunosenescence),<sup>6,9</sup> malnutrition, emotional stress, physical trauma, fatigue,<sup>4</sup> malignancies, the use of immunosuppressive drugs (such as corticosteroids, chemotherapy),<sup>9,10</sup> DM, transplants, HIV infection, and systemic lupus erythematosus.<sup>6</sup> Viruses in HZ are transmitted through direct contact with lesions in the vesicular phase to individuals who do not have immunity to this virus so it triggers the occurrence of varicella.<sup>2,11</sup>

Varicella occurs in children in medium temperate regions and in older age groups in the tropical region.<sup>9</sup> HZ is rarely happening in children.<sup>10</sup> Generally, HZ in children has a mild severity compared to older people, and it rarely causes severe and prolonged acute pain.<sup>9</sup> HZ incidence is not affected by seasons with a tendency to increase at the age above 50 years, including in immunocompetent individuals.<sup>4</sup> HZ only occurs once in a lifetime. Recurrent episodes of HZ are rarely happening in immunocompetent individuals. This is because the HZ episode will increase immunity and prevent the reactivation of symptomatic VZV.<sup>9</sup>

Risk factor that is known to cause HZ in children is a history of maternal varicella during pregnancy or a history of primary varicella in the first year of life, which is assumed occur due to weak specific immune memory to VZV during the primary exposure to VZV in childhood.<sup>9</sup> In women with primary varicella infection during pregnancy, about 20% of fetuses with primary VZV<sup>12</sup> infection will develop neonatal or infantile HZ,<sup>5,12</sup> which is virus reactivation after primary intrauterine infection. The short latent

period is caused by an immature cellular immune response. Transmission of the virus to the fetus from mother with HZ is rare. This is due to the presence of maternal antibodies against previous VZV and a lower degree of viremia compared to the primary infection. Therefore, the risk of VZV transmission in primary infection is higher than HZ.<sup>12</sup>

In our case, the baby was not immunodeficient, no intrauterine exposure was found and the previous history of varicella was doubtful. However, the signs and symptoms found in the patient are in accordance with typical representation of HZ and based on the distribution of lesions, it can be said to be disseminated HZ. Generally, a diagnosis of HZ can be made based on typical clinical symptoms,<sup>2,4</sup> which is grouped vesicles with the distribution according to the dermatome involved and does not cross the midline of the body. The course of the disease can be preceded by prodromal symptoms accompanied by burning sensation for 2-3 days, then erythematous macules will appear, followed by grouped vesicular lesions in the ganglion dermatome which involved in 1-2 days. In immune-competent patients, it usually involves only one dermatome. Vesicles will become pustules within 1 week after the onset of redness, followed by ulceration and crust formation in 3-5 days later. Resolution occurs within 2-4 weeks.<sup>2,9</sup> The appearance of new vesicles after 1 week of onset leads to suspicion of an underlying immune system defect.<sup>9</sup> A number of 20% of patients may experience systemic symptoms such as fever, headache, malaise, or fatigue. In HZ, the presence of lesions outside or near the primary dermatome involved is uncommon.<sup>2,9</sup>

In immunodeficiency conditions, for example in immune-senescence, vesicles or skin symptoms associated with viremia at a distant location with the dermatome are involved, which is referred to as cutaneous dissemination.<sup>9</sup> If there are more than 20 vesicles outside the main or adjacent dermatome, it can be categorized as disseminated HZ.<sup>4</sup> A number of 1.7% of HZ cases are disseminated<sup>2</sup> HZ cases and are found in about 1 in 10 of immunocompromised patients.<sup>4</sup> Polymerase chain reaction (PCR) examination with a sample of lesions can be useful for differentiating genital HZ from herpes simplex or for diagnosis of HZ by typical pain without rash (blood PCR).<sup>2</sup> In severe immunocompromised conditions, HZ patients can suffer viremia with life-threatening internal organ involvement.



The goal of HZ management are to treat pain, to promote skin lesion healing, to minimize complications,<sup>4</sup> and to stop viral replication.<sup>9</sup> Systemic anti-virus is the first-line therapy for HZ.<sup>9</sup> The usual oral dose of acyclovir is 20 mg/kg body weight/dose every 6 hours<sup>13,14</sup> or 40-60 mg/kg body weight/day which is divided into 4 doses.<sup>15,16</sup> Acyclovir can be given for 5-10 days or until 2 days after no new lesions appear.<sup>6,9,13,15-17</sup> Antiviral administration is recommended in 72 hours after the appearance of the lesion. However, sometimes it is difficult to apply because of the patient's delay in coming to the doctor.<sup>6,9</sup>

Our patient started oral antiviral therapy at the usual recommended dose on day 5 after the first rash appeared. Until the therapy started, new lesions still appeared. There are no data yet describing the effectiveness of antiviral treatment that starts more than 72 hours after the onset of the rash. Although HZ treatment should ideally begin within 72 hours of the appearance of the rash, treatment can still be done after 72 hours to prevent complications. If there are new vesicles or HZ complications, it can be said that viral replication is still ongoing and antiviral therapy may be of benefit. Therefore, in this condition, antiviral systemic therapy can be started. Many factors are considered in the selection of antivirals for HZ, including the effectiveness of the drug, side effects of the drug, price, route and method of administration. Acyclovir is the first antiviral developed for HZ therapy and has been shown to reduce viral replication and the emergence of new lesions and accelerate rash healing, even though blood acyclovir levels and the activity are not as good as brivudin, famciclovir and valaciclovir. Acyclovir is available in generic preparations, so the price is cheaper. However, the frequency of administration of acyclovir is 4-5 times daily orally to achieve optimal effects which sometimes makes patients uncomfortable. Meanwhile, topical antiviral does not provide benefits for HZ, so it is not recommended. The presence of barriers that make antiviral agents in the blood difficult to enter the tissues and lower VZV sensitivity compared to HSV against antiviral agents causes VZV require higher doses.<sup>9</sup>

In this case, the patient had never received varicella vaccination before because the Centers for Disease Control and Prevention (CDC) recommends giving 2 doses of varicella vaccine to children. The first dose was given at 12-15 months of age and the repeat

dose was at 4-6 years of age. Varicella vaccine does not need to be given to individuals who already have immunity to VZV.<sup>18</sup> Therefore, patients who have experienced HZ are considered to have immunity against VZV, so varicella vaccination is not needed. However, patients can still get the HZ vaccine when they are  $\geq 60$  years old. The HZ vaccine is recommended for all people aged  $\geq 60$  years regardless of the history of varicella or HZ and previous varicella or HZ vaccination status, unless there are contraindications.<sup>19</sup>

## Conclusion

HZ in infants is a rare case. A history of maternal varicella and primary varicella infection in infancy are the main risk factors. Although HZ is a self-limiting disease, evaluation of the presence of other underlying diseases, especially in disseminated HZ, is still needed.

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