

CASE REPORT OPEN ACCESS

Neonatal Varicella, Treated With Oral Acyclovir: A Rare and Challenging Case Report in a Limited-Resource Country Like Cambodia

Chariya Chap¹  | Sakviseth Bin^{2,3} ¹Neonatal Ward, National Pediatric Hospital, Phnom Penh, Cambodia | ²University of Health Sciences, Phnom Penh, Cambodia | ³Neonatal Intensive Care Unit, Calmette Hospital, Phnom Penh, Cambodia**Correspondence:** Sakviseth Bin (sakviseth_bin@yahoo.com)**Received:** 27 August 2024 | **Revised:** 21 October 2024 | **Accepted:** 27 October 2024**Funding:** The authors received no specific funding for this work.**Keywords:** acyclovir | developing countries | neonatal sepsis | newborn | varicella-zoster virus

ABSTRACT

Varicella-zoster virus can be transmitted transplacentally to a fetus from symptomatic mothers developing skin lesions between 5 days before and 2 days after delivery. The diagnosis is clinical. Its management is challenging in limited-resource countries, namely Cambodia, due to the lack of varicella zoster immune globulin and intravenous acyclovir.

Taxonomy Classification: Perinatal Medicine, Paediatrics and Adolescent Medicine, Infectious Diseases

1 | Introduction

Varicella-zoster virus (VZV), also known as human herpesvirus 3 (HHV-3), is responsible for varicella (chickenpox) and herpes zoster (shingles). It can spread easily from infected individuals to unimmunized ones either by direct (e.g., contact with body lesions) or indirect (e.g., contact with infected respiratory droplets) contact. Mother-to-child-transmission during pregnancy is also possible [1, 2]. Maternal infection during the first and second trimester of pregnancy can lead to congenital varicella syndrome (CVS) with distinct clinical features including stillbirth, low birth weight (LBW), aplasia cutis congenita, eye defects, limb deformity, or central nervous system defects [3]. Maternal infection during the last 3 weeks of pregnancy, on the other hand, can cause neonatal varicella, with a transmission rate of 50%. The severe form during the neonatal period (the first month of life) is commonly associated with maternal symptoms appearing between 5 days before and 2 days after delivery, which may be due to exposure to high viral loads and the lack of sufficient time for acquiring the maternal antibodies. VZV can cause systemic life-threatening diseases during the first 2 weeks of life in about

20%–50% of cases, and the mortality rate is approximately 20% in the absence of a prophylactic therapy by varicella zoster immune globulin (VZIG) in conjunction with a curative treatment with intravenous acyclovir [4, 5]. In what follows, we report a case of severe neonatal varicella, in a resource-restricting setting, in a 15-day-old boy who did not receive VZIG at birth and who was treated successfully with oral acyclovir.

2 | Case Presentation

A male infant was admitted to the neonatal ward on Day 15 of life for generalized skin lesions since Day 7 of life, accompanied by fever and poor feeding. On arrival, he had a toxic appearance, lethargy, and fever with an axillary temperature of 38.5°C, heart rate of 110/min, respiratory rate of 40/min, and SpO₂ of 93% on room air. On physical examination, he had hypotonia and poor sucking. Generalized vesicular eruptions occurred on the face, scalps, and extremities. Some crusted lesions and peri-oral ulcerations were also found and treated with gentian violet (Figure 1). There were no oro-mucosal

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FIGURE 1 | Vesicular rash with some crusted lesions at admission.

lesions or conjunctivitis. He also had signs of dehydration including a weight loss of 100 g, depressed fontanelle, sunken eyes, and dry mouth.

3 | Methods (Differential Diagnosis, Investigations, and Treatment)

In light of the clinical severity and local guidelines of late-onset neonatal sepsis, large-spectrum antibiotics (cloxacillin and ceftriaxone) were prescribed in tandem with intravenous rehydration, enteral nutrition via oro-gastric tube, and respiratory support with oxygen cannula. Common differential diagnosis included varicella, herpes simplex virus (HSV) infection, hand, foot, and mouth disease (HFMD), impetigo, and congenital syphilis. Given the skin manifestations, the lesions did not affect the eyes and oral cavity, and the pattern was neither clustered nor localized; therefore, HSV infection, HFMD, and impetigo were ruled out; a negative paired serology later ruled out congenital syphilis as well. An interview with the parents revealed that the mother had been diagnosed with varicella exhibiting generalized vesicular lesions 3 days prior to delivery. At a local center, the newborn was observed at the nursery, and after discharge, the baby was isolated at home as per the local neonatologist's advice to prevent possible post-natal transmission. Based on the perinatal history and clinical presentation, he was diagnosed with severe neonatal varicella. The laboratory studies prior to the administration of antibiotics showed increased leucocytes of $22 \times 10^9/L$ ($4-9 \times 10^9/L$), increased absolute neutrophil count of $12 \times 10^9/L$, increased aspartate aminotransferase (AST)



FIGURE 2 | Generalized crusted lesions on Day 3 of hospitalization.

of 102 UI/L (<32 UI/L), and increased alanine aminotransferase (ALT) of 89 UI/L (<32 UI/L). C-reactive protein (CRP) of 1.3 mg/L was within normal range. The blood culture and cerebrospinal fluid (CSF) revealed negative results. The polymerase chain reaction (PCR) of CSF for herpes was not available in our setting. Because intravenous acyclovir therapy, though indicated, is not available in the country, we decided to give oral acyclovir with the dosage of 20 mg/kg every 8 h.

4 | Outcome and Follow-Up

He was weaned off oxygen on Day 3 of hospitalization, and he started to suck well with the bottle. Antibiotics were used for 5 days until the results of hemoculture showed negativity. After 10 days of treatment with oral acyclovir, all vesicular lesions became crusted (Figure 2). The baby regained the birth weight with normal activities and reflexes, without neurological or respiratory complications. The complete blood count and liver functions on Day 9 normalized. The boy was discharged, and after 14 days of treatment and at the first follow-up, he was healthy and gained weight well (Figure 3).

5 | Discussion

Neonatal varicella can occur when the mother is infected by VZV within the last 3 weeks of pregnancy. If symptoms appear within the first 10 days after birth, it is most likely due to a prenatal infection, given that the typical incubation period



FIGURE 3 | Varicella scars at the follow-up.

of varicella is between 10 and 20 days [5, 6]. The severe form during the neonatal period is reported in children whose maternal skin lesions appear between 5 days before and 2 days after delivery. This observation might be due to exposure to high viral loads and the lack of time to create maternal antibodies. Development of life-threatening disseminated diseases during the first 10 days of life occurs in 20%–50% of severe cases, and the fatality rate is high (20%) without on-time and aggressive treatment. However, there was no neonatal fatality case reported in a mother contracting chickenpox between 6 and 20 days prior to delivery [4, 5, 7].

The diagnosis of neonatal varicella is clinically based in that physicians rely on the findings of skin lesions at different stages (e.g., papular, vesicular, or crusted) in an infant born to a mother having been exposed to VZV or developed the symptoms close to the delivery. Starting as pruritic macules, the lesions rapidly develop into papules before becoming vesicles. These vesicles subsequently evolve into pustules, which later become crusts. These lesions appear firstly on the head and then spread all over the body with healing within 7–10 days. Moreover, varicella in newborns can disseminate to other viscera, causing pneumonia, hepatitis, or meningoencephalitis [8, 9]. In case of uncertain or severe cases, the confirmatory tests rely on the PCR of VZV from a swab of vesicular content, a scrap of crusted lesions, or CSF [10].

The management of neonatal varicella is still controversial because of the uncertain and severe nature of the infection and the lack of consensus. Regarding prophylaxis, Centers for Disease Control and Prevention (CDC) and the Advisory Committee on Immunization Practices (ACIP) recommend intramuscular VZIG as soon as possible during the first 10 days of life, to newborns whose mothers having developed symptoms of varicella from 5 days before to 2 days after delivery. The recommended dosage is 125 units/10 kg and 62.5 units in neonates with birth weight below or equal to 2 kg. The isolation from the mother is also recommended until she is no longer infectious. If the specific VZIG is not available, IVIG (immune globulin intravenous) could be used with the dosage of 400 mg/kg [10].

The treatment of varicella in severe form is intravenous acyclovir with a dosage of 20 mg/kg/8 h for 7–10 days [7, 8, 11]. If the intravenous lines cannot be placed to give intravenous acyclovir after several attempts, the oral acyclovir should be used with the dosage of 900 mg/m²/day (60 mg/kg/day) [7, 10, 12, 13]. The antiviral must be introduced as soon as possible because most viruses stop replicating within 72 h of the appearance of skin lesions [14]. However, it is of note that a case report of varicella in a 21-day-old-male baby acquired from the mother who recovered from zoster after 10 days of treatment, and treated at Day 5 of skin lesions, with intravenous acyclovir with the dosage of 20 mg/kg/8 h [15]. If the baby has a high-grade fever ($\geq 38.5^{\circ}\text{C}$) or altered status, the microbiological workup, including lumbar puncture, is warranted. Broad intravenous antibiotics should be given in addition to acyclovir to cover superimposed bacterial infection and can de-escalate to a narrow spectrum if any source is identified [7].

In our case, the newborn was isolated from his mother immediately after birth, the prophylaxis with IVIG or VZIG is not available in our setting. Having developed a skin rash around one week of life, the newborn was later admitted at the second week. He was initially treated with broad-spectrum antibiotics due to fever, altered consciousness, and dehydration. Then oral acyclovir was added due to the severity of the disease and the maternal history of varicella during pregnancy.

To conclude, in low-income countries such as Cambodia, managing severe neonatal varicella is not optimal. It is challenging due to the lack of neonatal-specific guidelines, the unavailability of VZIV and intravenous acyclovir, and the scarcity and high cost of IVIG. Additionally, in tropical countries, this disease is often deemed mild and self-limiting in older children or adults; hence, the need for intravenous acyclovir is often underestimated. In our report, despite early precautionous mother-newborn separation, the baby still got infected. Oral acyclovir was effective in our case. However, further studies are needed to study the benefit/risk ratio in the neonatal population, particularly in restricted-resources settings.

Author Contributions

Chariya Chap: data curation, investigation, writing – original draft, writing – review and editing. **Sakviseth Bin:** conceptualization, supervision, writing – original draft, writing – review and editing.

Acknowledgments

We would like express our gratitude to Prof. Kim Ang for his support and encouragement.

Ethics Statement

The authors have nothing to report.

Consent

Written informed consent was obtained from the patient's parents and is available for review upon request.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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