—Case Reports—

# Neonatal Case of Herpes Simplex Virus Encephalitis after Delivery from a Woman Whose Genital Herpes Simplex Virus Infection Had Been Treated with Acyclovir

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**Abstract**

A case of herpes simplex virus (HSV) encephalitis in a neonate after delivery from a woman whose genital HSV infection had been treated with acyclovir is reported. The main approach to prevent genital HSV infection in the neonate is interruption of transmission at the time of delivery. Guidelines for prophylactic therapy with acyclovir have been established, but the risk of neonatal infection remains. A fever began to develop in a male neonate delivered vaginally from a 35-year-old woman. Treatment with intravenous acyclovir was started on the basis of a diagnosis of HSV encephalitis, because polymerase chain reaction was positive for HSV in the cerebrospinal fluid. The mother had had a first genital HSV infection during the second trimester, but treatment with injected acyclovir had caused the blisters and erosion to resolve by the time of delivery. Important steps for preventing neonatal HSV infection are the appropriate treatment of mothers with a history of genital HSV infection, the assessment of delivery methods, and the appropriate treatment of neonates.
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**Key words:** herpes simplex, neonatal herpes encephalitis

## Introduction

Herpes simplex virus (HSV) infection occurs in 1 of 2,000 to 5,000 neonates[1]. Approximately 45% of these infections are confined to the skin, eyes, or mouth, whereas 30% of infections manifest as encephalitis and 25% as disseminated disease[1]. Encephalitis due to HSV has a poorer prognosis than do other types of acute encephalitis. Untreated HSV encephalitis has a mortality rate of 50% and an extremely high rate of neurological sequelae in survivors[1,2].

The main approach to preventing neonatal HSV infection is the interruption of transmission at the time of delivery. Here, we report a case of neonatal encephalitis caused by HSV transmitted from a mother who had received acyclovir treatment for

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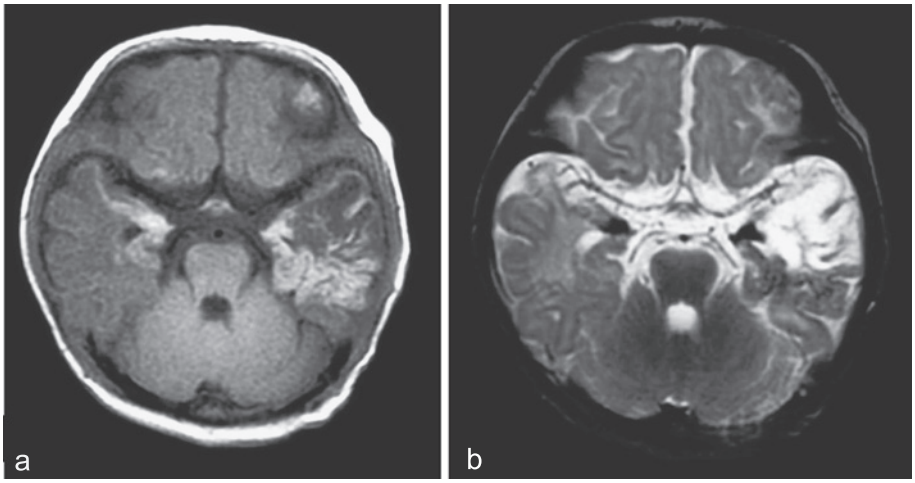


Fig. $T_1$-weighted axial images (a) and $T_2$-weighted axial images (b) obtained on the 18th day of illness. Large areas of high intensity are seen in the bilateral temporal lobes on $T_2$-weighted images. These findings are consistent with hemorrhagic infarction.

genital HSV infection before delivery.

## Case Report

A 3,656-g male neonate was delivered vaginally without asphyxia to a 35-year-old woman at 41 weeks' gestation. He had Apgar scores of 8 and 9 at 1 and 5 minutes, respectively, and was discharged successfully breastfeeding on the fifth day of life. His mother had a history of a first genital HSV infection during the second trimester. She was treated with injections of 200 mg of acyclovir for 5 days, and the genital blisters and erosion resolved. The specific immunoglobulin (IgG) against HSV was elevated to 17.0 U on immunoelectrophoresis of the serum, and neither genital blisters nor erosion was observed at 36 weeks' gestation. Therefore, suppressive acyclovir therapy from 36 weeks' gestation was not achieved.

Thirteen days after birth, the neonate presented with a fever of 39.5℃. He did not have any skin lesions, and blood counts and biochemical data were within their normal ranges. A full screening for sepsis was performed and included lumbar puncture. Analysis of the cerebrospinal fluid (CSF) showed mild mononuclear cell-dominant pleocytosis with protein elevation; 608/3 white blood cells/μL and 68 mg/dL protein on the 13th day, and 871/3 cells/μL (87% mononuclear cells) with no obvious glucose decrease (47 mg/dL) on the 14th day. Because viral meningitis was suspected, treatment with intravenous antibiotics was started while the results of bacterial culture were pending.

Although the neonate had not been exposed to anyone with clinical evidence of oral herpes, we started an infusion of acyclovir (30 mg/kg/day) and immunoglobulin, considering that his mother was seropositive for HSV and had had an HSV infection during the second trimester. On the second day of treatment, seizures developed and required treatment with phenobarbital. Computed tomography on the third day confirmed normal density. However, analysis of the CSF now showed an elevated level of total protein, and $T_2$-weighted magnetic resonance images (MRI) on the 18th day revealed high-intensity areas around the bilateral temporal lobes **(Fig.)**.

In the absence of evidence of bacterial infection or severe hypoxic ischemic insult, the most likely cause for such extensive changes on MRI in this age group is HSV encephalitis. Polymerase chain reaction (PCR) for HSV in the CSF was positive on the 4th day. Moreover, specific IgG and IgM against HSV in serum was negative on day 2, but IgG and IgM had increased to 12.2 U and 8.86 U, respectively, by day 21.

We increased the dosage of infused acyclovir to 60 mg/kg/day and continued administration for 3 weeks. Because the patient was asymptomatic and

feeding well, he was discharged from the nursery on the 47th day. At 11 months, he was able to walk with one hand held, and seizures were prevented with phenobarbital.

## Discussion

Neonatal HSV encephalitis results in significant morbidity and mortality. Infections with HSV acquired in the peripartum period are most often caused by maternal transmission. The major mode of HSV infection is thought to be direct contact of the fetus with virion-infected vaginal secretions during delivery[2]. Brown et al. have reported that cesarean section significantly reduces the risk of neonatal HSV infection when maternal HSV infection is diagnosed during labor. However, because most HSV-infected women lack histories suggesting genital HSV infection, cesarean section will not eliminate neonatal HSV disease[3]. The American Congress of Obstetricians and Gynecologists (ACOG) issued practice guidelines in 1988 that included elimination of weekly antenatal genital cultures and recommended that cesarean delivery be performed only if genital herpes lesions were present when parturition was imminent[1]. The ACOG guidelines simplified treatment and significantly reduced the need for cesarean delivery without causing neonatal infections[1]. Both the ACOG guidelines and European guidelines from 2010 recommend either oral or intravenous acyclovir in standard doses for maternal HSV infection acquired during the first or second trimester and recommend daily suppressive acyclovir treatment (400 mg, 3 times daily) starting at 36 weeks' gestation to women with once or more genital HSV to prevent neonatal HSV infection[2,4].

In the present case, vaginal delivery was performed because the genital herpes lesions had resolved with medication, genital lesions were not observed, and the mother became seropositive for HSV only at delivery. However, HSV encephalitis still developed in the neonate.

The symptoms in the present case included only fever but no loss of appetite. Neonates with fever are usually screened for bacterial meningitis and urinary tract infection. However, distinguishing bacterial infection from HSV infection can be difficult in the early neonatal period because the symptoms are nonspecific. Antibodies against HSV appear late, approximately 2 to 12 weeks after infection, and cannot be used to diagnose acute infection[2]. The results of ultrasonography, computed tomography, and conventional MRI are normal in the early stage of HSV encephalitis[3].

In many laboratories, detection of viral DNA in the CSF with PCR is the most sensitive and, usually, the most rapid method. In the present case, HSV encephalitis due to monocyte-dominant pleocytosis with protein elevation was suspected and was diagnosed with PCR. We examined specific IgG and IgM against HSV in serum and performed computed tomography on admission, but the findings were unremarkable.

Neonates with fever are treated empirically while culture results are pending. However, Benson et al. have reported that encephalitis is regularly treated empirically with antibiotics but not with acyclovir[5]. We started empirical treatment with acyclovir but at a dose that was not effective. A recent report has shown that high-dose acyclovir (20 mg/kg every 8 hours) for 21 days significantly reduces mortality for infants with either encephalitis or disseminated disease[6].

Pediatricians must closely monitor neonates for signs and symptoms of HSV infection, particularly when they are born to mothers with a history of HSV infection. In an era of rapid HSV diagnosis and effective therapy, HSV infection should be aggressively pursued and empirically treated.

**Conflict of Interest:** None of the authors have any conflicts of interest associated with this paper.

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