Annals of Clinical Case Reports

Case Report
Published: 03 Jun, 2022

An Unusual Case of Congenital Herpes Simplex Virus Type-2 (HSV-2) in an Extremely Premature Infant

*Sfurti Nath MD, Rana Alissa MD, and Renu Sharma MD**

Department of Pediatrics, Division of Neonatology, University of Florida Health Science Center, Jacksonville, USA

Abstract

We report a case of congenital infection of Herpes Simplex Virus-2 (HSV-2) in an extremely premature infant born at 25 weeks of gestation presenting in unusual manner with hydrops, atypical, extensive, hemorrhagic bullous rash, hepatosplenomegaly, coagulopathy and multi-organ failure. Placental and autopsy investigations confirmed in-utero transmission of disseminated congenital HSV-2 infection without any maternal history of HSV.

Keywords: Congenital HSV; Extreme prematurity; Hydops-fetalis

Case Presentation

An extremely premature male infant was born at 25 weeks gestation by an emergency cesarean section due to fetal distress. The mother was a 23-year-old primigravida. Her prenatal laboratory tests were negative for any sexually transmitted infection including syphilis, gonorrhea, chlamydia, human immunodeficiency virus, and group B *Streptococcus*. She was immune to rubella. She had no current or past history of genital or oral Herpes Simplex Virus (HSV) infection.

At 17 weeks of pregnancy, the mother was admitted with vaginal leakage of dark amniotic fluid followed by fever (38.9 Co). She was treated with antibiotics including ampicillin, clindamycin, and azithromycin for chorioamnionitis and threatened loss of pregnancy. Expectant management was successful as pregnancy progressed without further leakage of amniotic fluid to 25-week gestation. Mother reported decreased fetal movements during her clinic visit at 25-week of gestation. She was admitted to the hospital for fetal monitoring. She was not in preterm labor and membranes of amniotic sac were intact. Fetal biophysical profile of 3 out of total 10 (1 for heart rate, 2 for amniotic fluid), indicative of poor fetal well-being prompting delivery by an emergency cesarean section. Membranes were ruptured in operation room at delivery. Apgar scores were 1 and 3 at 1 and 5 min, respectively. Infant required resuscitation at birth with endotracheal intubation, mechanical ventilation, external cardiac compressions and administration of epinephrine.

At birth, the infant appeared hydropic with generalized body-wall edema, protuberant, firm abdomen due to severe hepatosplenomegaly with liver margin reaching 2 cm above the pelvic brim and ascites. The infant was large for gestational age with a birth weight of 1,090 gm primarily because of diffuse edema. Soon after birth, diffuse bullae developed over extensive areas of the skin covering the face, arms, chest, and abdomen that progressed to diffuse sloughing of the skin (Figure 1). These quickly became hemorrhagic. By four hours of life, the infant developed profuse bleeding from the endotracheal tube, orogastric tube and insertion sites of umbilical catheters. Laboratory tests showed disseminated coagulopathy that was treated promptly with infusions of fresh frozen plasma and cryoprecipitate followed by platelet transfusion for thrombocytopenia. Continuous infusion of dopamine and dobutamine were administered to treat hypotension. Broad spectrum antibiotics including ampicillin and gentamicin were administered for suspected sepsis. In view of infant's critical condition, empiric antiviral medication, acyclovir (15 mg/kg/dose divided every 12 h) was added despite negative maternal history for HSV. Ancillary laboratory studies revealed thrombocytopenia (platelet count = 30,000/mm^3), leukocytosis (white blood cell count =81,600/mm^3), and high concentrations of serum transaminases (Aspartate Transaminase, AST>10,000U/L, Alanine Transaminase, ALT=972 U/L). Bacterial cultures of blood and fluid specimen from dermal bullae were negative. However, HSV-2 was detected by Polymerase Chain Reaction test (PCR) in specimens obtained from blood, mouth, hemorrhagic skin bullae, rectum and placenta. Despite all supportive treatment, infant did not survive beyond the first day of life.

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Correspondence:
Renu Sharma, Professor of Pediatrics, Division of Neonatology, University of Florida Health Science, 655 W 8th Street, Jacksonville, Florida, 32209, USA, Tel: 904-244- 3508; Fax: 904-244-4301;
E-mail: renu.sharma@jax.u l.edu

Received Date: *12 May 2022*
Accepted Date: *31 May 2022*
Published Date: *03 Jun 2022*

Citation:
Nath S, Alissa R, Sharma R. An Unusual Case of Congenital Herpes Simplex Virus Type-2 (HSV-2) in an Extremely Premature Infant. Ann Clin Case Rep. 2022; 7: 2208.

ISSN: 2474-1655

Figure 1: Atypical diffuse hemorrhagic vesicobullous lesions in a critical hydropic premature infant born at 25-week gestation with hepatosplenomegaly.

Discussion

HSV infection in neonates has devastating consequences with high mortality and morbidity despite treatment with acyclovir [1]. Advances in medicine have reduced neonatal mortality rates in disseminated HSV infection from 85% to 29% and in isolated central nervous system disease, from 50% to 4% [1]. Primary infection during pregnancy is more severe than in the non-pregnant state with a greater risk of infecting fetus (50%) with primary infection than with recurrent infection (<3%).

Vertical transmission from mother to the neonate can occur in-utero (5%), during perinatal (85%) or during postnatal period (10%) [1]. Ascending infection along the birth canal in the presence of rupture of membranes from active genital lesions is an important mode of transmission [1]. Mother in our case did not experience any genital lesions during the pregnancy or around the time of birth. The epidemiological data do support that 70% of congenital HSV infection cases present with no preceding maternal history of HSV. Furthermore, congenital HSV in extreme premature infants, as in our case, can present in non-classical manner with atypical presentation [1-3].

It was unusual in our case that although there was vaginal leakage of two-day duration at 17 wk. of gestation, subsequent fetal ultrasounds indicated that ruptured membranes had sealed with re-accumulation of amniotic fluid. Amniotic membranes remained intact from 17 wk. onwards until they were ruptured artificially during cesarean section. Amniotic fluid was light yellowish to dark brown in color reflecting in-utero infection. As is usual practice, in most of these cases, including ours, appropriate antibiotics were administered to mother following prolonged vaginal leakage of amniotic fluid at 17 wk. of gestation but she was not screened for HSV at that time. Clearly antibiotics can only be beneficial if the intrauterine infection is of bacterial origin. As reported recently, microbial invasion of the amniotic cavity can occur due to microorganisms other than bacteria where viral infection can play a role in pregnancy loss or early neonatal death [4]. We believe that in our case, HSV was inoculated into feto-placental unit at 17-wk. of age when the mother experienced amniotic fluid leakage. Although pregnancy progressed subsequently in asymptomatic manner, congenital viral infection reactivated when the mother began experiencing decreased fetal movements. As described in literature [5], this assertion is further supported by the placental pathology in our case which showed areas of focal opacification with degradation of amniotic membranes and chorionic villi and necrotizing inflammation with stromal cell necrosis of umbilical cord and fetal surface. The HSV DNA PCR was also positive for HSV-2 from placenta that was trans-abdominally delivered in sterile manner trans-abdominally during Cesarean section [5].

While congenital HSV infection presents most commonly as either Skin, Eyes and Mucosal disease (SEM) or CNS infection [1-3], our case presented with the least common variant, as the disseminated disease with hepatosplenomegaly and hydrops. As in our case, HSV infections can have atypical presentation in premature infants attributable to an immature immunologic response to the virus [3]. Typically, cutaneous HSV is described as vesicular or pustular eruptions with erythematous base [2]. Our case rapidly developed diffuse, large hemorrhagic bullous lesions coalescing together within a matter of few hours of birth, progressing rapidly with sloughing of skin (Figure). This was highly unusual and unique presentation. The lesions appeared somewhat similar to infants presenting with scalded skin syndrome, aplasia cutis congenital or congenital bullous dermal disorders [2]. A somewhat similar case of vesiculobullous lesions in a 27-week-gestation preterm neonate with HSV has been reported before but unlike our case, active recurrent genital lesions of HSV were present in the mother prior to delivery in that case [2,3]. The findings of leukocytosis and hydrops with severe hepatosplenomegaly in our case were also consistent with previous rare reports of neonatal HSV disease and with in-utero transmission [1,3].

The presence of fever with premature prolonged rupture of membrane as in our case without any evidence of a bacterial infection highlights the need to investigate an alternative infectious etiology. It is prudent to have a high index of suspicion for HSV in such cases and to screen mothers for HSV-2 in addition to screening for bacterial infection. Although the American Academy of Pediatrics has provided guidelines for the management of neonatal HSV among those with maternal history of HSV and for those with primary and recurrent exposure, screening for HSV during pregnancy is not yet routine practice in the United States specifically in the absence of positive maternal history of HSV infection or in the absence of perinatal exposure. As most cases of neonatal HSV infection occur following cervical viral shedding without any clinically detectable genital lesion, universal maternal screening for HSV serology is warranted [1]. The epidemiologic data suggesting a rise in the prevalence of neonatal HSV infection because more HSV-1 sero-negative individuals are entering sexually active age group combined with the changing sexual practices, the need for universal maternal screening is even more important. In addition, continued adherence to measures preventing vertical transmission from mother to neonate in the presence of known maternal history, including maternal treatment and prophylaxis with acyclovir, may check potential future increase in neonatal herpes infections. Trans-placental passage of acyclovir has been shown to offer protection to the fetus against maternal viremia; however, justification of its use in preventing neonatal HSV in the absence of documented maternal HSV infection remains unclear [1-3]. Additionally, various prototypes for both therapeutic and prophylactic vaccines are being developed but none has yet been proven effective for mass use. Continued investigations to analyze cost-based efficacy of vaccines against genital herpes maybe justifiable [1].

Conclusion

In-utero transmission of HSV-2 with absence of maternal history of HSV and with absence of premature perinatal rupture of membrane as in our case is rare. Our case highlights the importance of considering HSV infection in pregnant women presenting with intra-partum fever without a clear bacterial etiology, and screening all mothers for HSV even in the absence of history or in the absence of active genital lesions. Congenital HSV infection continues to exert high mortality and morbidity in neonates. The outcome is even more severe among extremely premature infants often resulting in loss of pregnancy during first or second trimester. Our case also highlights the rare form of cutaneous, systemic presentation with hydrops in extreme premature infants. Empiric and early treatment with acyclovir should be considered particularly in a sick premature infant with unique vesicobullous lesions even in the absence of maternal history and in the absence of history of exposure to HSV because of very high mortality. There is a need for continuing research on identifying newer strategies for screening and treatment of HSV during pregnancy so that in-utero HSV transmission to the fetus can be prevented even in asymptomatic women with subclinical infection.

References

1. Anzivino E, Fioriti D, Mischitelli M, Bellizzi A, Barucca V, Chiarini F, et al. Herpes simplex virus infection in pregnancy and in neonate: State of art of epidemiology, diagnosis, therapy and prevention. Virol J. 2009;6:40:1-11.
2. Harris HH, Foucar E, Andersen, RD, Ray TL. Intrauterine herpes simplex infection resembling mechanobullous disease in a newborn infant J Am Acad Dermatol. 1986;15:1148-55.
3. O'Riordan DP, Golden WC, Aucott SW. Herpes simplex virus infections in preterm infants. Pediatrics. 2006;118:e1612-20.
4. Romero R, Miranda J, Chaiworapongsa T, Chaemsaithong P, Gotsch F, Dong Z, et al. A novel molecular microbiologic technique for the rapid diagnosis of microbial invasion of the amniotic cavity and intra-amniotic infection in preterm labor with intact membranes. Am J Reprod Immunol. 2014;71:330-58.
5. Smith AE, McKenney A, Rabinowitz L, Das A. Diagnosis of neonatal herpes simplex infection from the placenta. Case Rep Pediatr. 2020;20:1-4.