A case of recurrent neonatal herpes skin, eye and mucosa

Neonatal herpes simplex virus infections can result in serious morbidity and mortality and can occur without any history of maternal herpes infection. Neonatal herpes skin, eye and mucosa infection is possibly an under-recognised clinical condition which can be mistaken for other benign neonatal rashes. Even though the risk of mortality is low this condition needs early recognition and antiviral therapy.

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Neonatal herpes simplex (HSV) virus infections can result in serious morbidity and mortality, especially if the disease progresses to involve the CNS or viscera. HSV is usually transmitted during delivery through an infected maternal genital tract although mothers of neonates with HSV infection often have no history or symptoms of genital infection at the time of delivery. We report the case of a neonate who presented at day 21 of life with asymptomatic herpes rashes on her forehead.

Clinical course

A female infant was born vaginally at 40 weeks' gestation with a birth weight of 3.12kg to a 26-year-old gravida 2 para 1 mother. The mother had an uncomplicated pregnancy and had a known history of genital herpes infection six years previously. Delivery occurred approximately 20 hours after rupture of membranes. There was no intrapartum fever. Apgar scores were 8 at one minute and 9 at five minutes. The infant had a normal newborn examination and was discharged home the next day.

A vesicular rash developed on the left side of her forehead on the second day of life (**FIGURE 1**). The infant was seen by three different doctors in the first 21 days of life and the mother was reassured this was a benign rash. The child remained physically well.

On day 21 of life a clinical diagnosis of neonatal herpes infection was made. There were four areas of vesicular rash on an erythematous base on the forehead. The child was systematically well.

Keywords

neonatal herpes; skin, eye and mucosa; aciclovir

Key points

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1. Neonatal HSV can present a diagnostic dilemma both in the primary and secondary healthcare services in the absence of recent documented history of maternal herpes.
2. Detailed history, clinical suspicion and early referral to paediatric services is necessary.
3. Early commencement of aciclovir therapy can prevent long-term mortality and morbidity.

The C-reactive protein was <1mg/L. Polymerase chain reaction of the vesicle fluid was HSV1 positive. The cerebrospinal fluid was normal. The child was commenced on IV aciclovir at a dose of 60mg/kg/day in three divided doses, which was given for three weeks (**FIGURE 2**). The rash resolved.

One week later the infant represented with a fresh crop of vesicles and was recommenced on IV aciclovir for two weeks. PCR for vesicle fluid was HSV1 positive. Blood and CSF cultures were negative. She was commenced on 100mg qds of oral aciclovir, this was increased to five times daily when a new vesicle appeared. The regime is to be continued for up to one year.

Discussion

Epidemiology of neonatal HSV infection

HSV 2[1] is the most common cause of genital herpes around the world, where it is responsible for 85% of cases and is the HSV type involved in 70% of neonatal herpes.

However in the UK[1], a similar incidence of neonatal HSV 1 and HSV 2 is reported, which may be explained by the high prevalence of primary genital HSV 1 infection.

The prevalence of neonatal herpes differs between countries and

FIGURE 1 At presentation

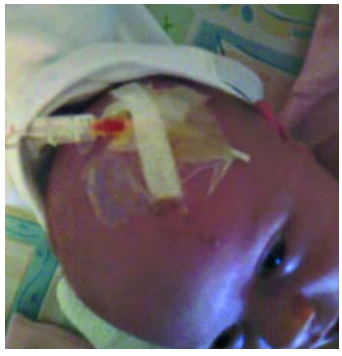

FIGURE 2 During treatment

is rarely seen in the UK[2] (estimated incidence 1.65/100000 live births), however it has a much higher incidence in the USA (estimated 20-50 per 100000 live births).

Genital herpes – an under recognised condition

Interestingly 60-80% of babies[1,2] who develop neonatal HSV infection are born to mothers without a history of neonatal herpes. This may be due to the non-specific nature of the presentation or lesions high in the birth canal. Also women who have a previous history of genital herpes may be asymptomatic with no recurrences, but continue to shed herpes viruses. Prospective mothers may pick up infection from oral and genital lesions in a partner via intimate relationship during the pregnancy thus putting the unborn baby at risk.

Even though a cervical smear screening test[3] for herpes virus culture is available it is not recommended. It is advisable that all women should be questioned about recent symptoms and examined carefully for clinical evidence of genital HSV infection on admission for delivery; and all newborn infants whose mothers have genital lesions or a history of infection should be examined/observed.

In other studies[1,2,4] because of aciclovir's safety record in pregnancy along with a desire to decrease neonatal HSV disease and reduce the number of caesarean deliveries performed for herpes indication, the use of oral aciclovir from about 36 weeks onwards is becoming a common clinical practice.

Herpes SEM infection in neonates

SEM (skin, eye and mucosa) disease[1,5,6] typically presents with erythematous rash and vesicular lesions in the first or second week of life. It is the most easily recognised form of neonatal HSV infection. The vesicular lesions may occur singly or in clusters anywhere on the body, but typically occur on the presenting part or on traumatised sites such as the fetal scalp monitoring sites. Prolonged rupture of membrane[1,7] (ie longer than six hours) appears to increase the risk of fetal infection, probably as a result of the ascending infection in the cervix.

Transplacental maternal neutralising and antibody-dependent cell-mediated cytotoxic (ADCC) antibodies[1] have an ameliorative effect on the acquisition and severity of infection in babies exposed to HSV. The higher the ADCC antibody titre the milder is the clinical presentation which explains why HSV infections acquired late in pregnancy are associated with increased risk of transmission and severity and may benefit from caesarean section delivery.

SEM disease is associated with little or no mortality as long as the disease does not progress to involve the CNS or viscera. Infants with SEM disease experience skin recurrences in 90% of cases. Even without CNS involvement, 20% of infants who have three or four recurrences in the first six months of life will have developmental delay. The risk of neurologic sequelae appears to be greater with HSV 2 infections.

Other types of HSV infection in neonates

Central nervous system[1,8] infections usually present in the second or third week of life with fever, irritability, focal or generalised seizures, poor feeding, bulging fontanelle, pyramidal tract signs and they sometimes also have skin lesions.

Disseminated herpes infections[1,8] are usually more serious, less common than the other types of neonatal herpes, and typically present between 9 and 11 days of life. Earlier presentation in the first few days of life can occur with symptoms of fever, respiratory distress, seizures, lethargy, jaundice, bleeding diasthesis and irritability and is frequently fatal.

Management of herpes SEM infection

In the absence of antiviral therapy 75% of children with SEM infection progress to either CNS or disseminated disease. Prospective multicentre analyses[1] showed mortality was much higher in disseminated disease than either isolated CNS or SEM infection (57% versus 15% and 0% respectively).

Studies[1,9] have supported using a dose of 60mg/kg/day of IV aciclovir for three weeks, but transient neutropaenia has been observed. It is advised that children on prolonged oral aciclovir therapy should have monitoring of neutrophil count and if absolute neutrophil count falls below 500/mm^3, decreasing the dose of aciclovir or administering GCSF (granulocyte colony stimulating factor) should be considered. Monitoring should also be carried out for hyperkalaemia. Further recurrences on oral aciclovir can be managed with increase in dose of aciclovir.

The use of prolonged viral suppressive therapy with aciclovir for SEM disease is advocated by many authorities. The rationale for this is largely because there is a correlation between the frequency of cutaneous recurrences and the development of neurological impairment. It is unclear for how long such viral suppressive therapy should continue, but treatment for six to 12 months is common.

Conclusion

This case illustrates the importance of considering neonatal SEM in an infant with a vesicular rash who is systemically well in a primary care setup and also the need to elicit a thorough history about possible maternal genital herpes infection.

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