Fatal newborn varicella despite varicella zoster immunoglobulin prophylaxis

Sir,

Neonatal varicella is expected in babies of mothers who develop chickenpox during the last 3 weeks of pregnancy. Infection is usually transmitted from the mother to child by (1) trans-placental route, (2) ascending infection during delivery or (3) by postnatal contact (respiratory droplet/direct).[1] An infant whose mother develops chickenpox rash 4 days antepartum to 2 days postpartum, may develop disseminated neonatal varicella with extensive cutaneous and visceral involvement resulting in a fatal outcome.[2] Varicella zoster immunoglobulin (VZIG) prophylaxis has been used in babies with perinatal exposure to prevent severe infection and mortality.[2] However, though extremely rare, fatal neonatal varicella has been reported despite VZIG prophylaxis. We describe one such neonate who died of fulminant varicella despite VZIG prophylaxis.

A 9-day-old newborn presented to us with fever, non-acceptance of feeds and respiratory distress since 1 day. He had an extensive erythematous, vesicular rash on the whole body at admission [Figure 1]. He was a term,

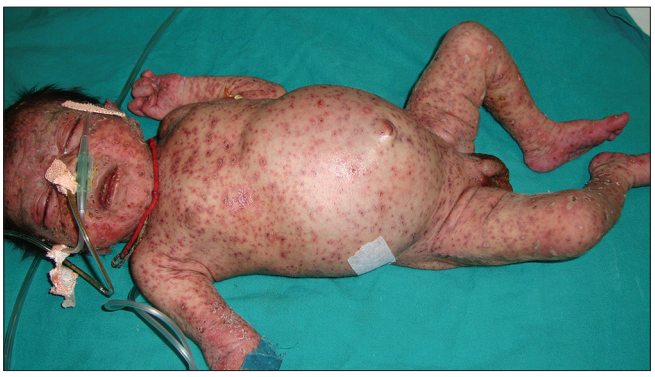

Figure 1: Newborn with extensive varicella rash

3.0 kg, male born of a non-consanguineous marriage at a private hospital. The baby cried immediately and had no skin lesions or congenital malformations at birth. Three days before delivery, his mother had a rash typical of varicella: It was pruritic and erythematous, localized to face and neck initially, which later progressed to a maculopapular and vesicular form spreading to the whole body. She had a positive varicella contact with her nephew about 2 weeks before. The baby received 125 I.U of VZIG intramuscularly at 12 h of life and was asymptomatic when discharged on day 2 of life. The child re-visited the private practitioner for poor feeding, irritability and a few erythematous skin lesions on the face on day 6 and 7 of life. The practitioner diagnosed it as an innocuous newborn rash and reassured the parents in view of VZIG prophylaxis. The child, however, deteriorated and was referred to us on day 9 of life in a critical condition with respiratory distress and shock. He developed repeated generalized convulsions on day 2 of admission. He was isolated and treated with intravenous acyclovir (15 mg/kg l 8 h), antibiotics, phenobarbital and phenytoin, inotropes and mechanical ventilation. The child, however, continued to deteriorate and expired on day 15 of life. Investigations revealed positive serum varicella zoster immunoglobulin M antibody test (test value - 1.32 Immune Status Ratio [ISR]; positive >0.90 ISR), lumbar puncture suggestive of viral encephalitis (cerebrospinal fluid protein - 175 mg%, sugar - 68 mg% [blood sugar - 102 mg%], cells - 200/mm^3, 70% were lymphocytes). Blood picture showed positive C-reactive protein. Repeated blood cultures sent during the neonate's hospital stay were sterile. Chest X-ray showed bilateral infiltrates suggestive of varicella pneumonia. The characteristic clinical picture of mother and child (confirmed subsequently by laboratory work-up) established the diagnosis of disseminated neonatal varicella in a newborn. Differential diagnosis considered were other intrauterine infections such as herpes virus, cytomegalovirus, rubella and toxoplasmosis, but ruled out in view of the absence of clinical features and negative antibody titers. A limitation of the study was that no skin biopsy and confirmation of diagnosis could be performed due to resource constraints.

The severity of varicella in a newborn is determined by the timing of the mother's illness in relation to childbirth. In mothers who develop chickenpox 4 days before to 2 days after delivery, fulminant neonatal varicella and fatal outcome is a distinct possibility. This, in turn, is due to lack of transfer of protecting maternal immunoglobulin G antibodies and a deficient cell mediated immunity of the neonate unable to prevent hematogenous dissemination of varicella zoster virus after its trans-placental spread.[3,4] VZIG prophylaxis in such babies helps to modify the clinical course and prevent severe disease. However, previous reports indicate it does not actually prevent infection and the risk of death, though reduced, is not completely eliminated.[5] Such babies are born well, but may become sick over the next 1-2 weeks, therefore, they should be kept under close surveillance in the hospital for 2 weeks (i.e. incubation period of disease).[5] Timely initiation of treatment with intravenous acyclovir is known to help decrease the severity of neonatal varicella.[6] In our case, the child was discharged early (on day 2) without any concurrent advice to parents regarding persistent possibility of varicella infection in the baby. Furthermore, when the child returned to the primary physician with early signs of varicella, immediate admission and treatment with intravenous acyclovir was warranted. This unfortunately was not carried out thereby leading to a delay in starting antiviral therapy and hence a fatal outcome. The treating pediatrician's misplaced confidence in VZIG and the reassurance given to parents in this regard was perhaps due to lack of knowledge on the issue.

Severe neonatal varicella leading to death may occur despite appropriate VZIG prophylaxis at birth. Therefore, newborn babies at high risk of varicella should be kept under hospital surveillance for a minimum of 2 weeks (i.e., until the incubation period of disease ends) after receiving VZIG.[2] Even, if discharged early, parents should be appropriately counseled regarding further care and quick hospital review if the newborn appears unwell or shows any signs of varicella. Appropriate treatment guidelines for doctors and clear discharge instructions to parents (preferably written) in this regard would help prevent unnecessary morbidity and mortality and constitute correct medical practice.

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