Unusual presentation of more common disease/injury

Varicella infection in a neonate with subsequent staphylococcal scalded skin syndrome and fatal shock

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Summary

A male term neonate, at day 23 of life, presented with vesicular lesions over the trunk, which spread to all over the body on the next day. Five days later, he started developing blistering of the skin over the trunk and extremities, which subsequently ruptured, leaving erythematous, tender raw areas with peeling of the skin. The mother had vesicular eruptions, which started on the second day of delivery and progressed over the next 3 days. Subsequently, similar eruptions were noticed in two of the siblings before affecting the neonate. On the basis of the exposure history and clinical picture, a diagnosis was made of varicella infection with staphylococcal scalded skin syndrome (SSSS). The blood culture and the wound surface culture grew *Staphylococcus aureus*. Treatment included intravenous fluid, antibiotics, acyclovir and wound care. However, after 72 h of hospitalisation, the neonate first developed shock, refractory to fluid boluses, vasopressors and catecholamine along with other supports; and he then succumbed. In all neonates, staphylococcal infection with varicella can be fatal due to SSSS, the toxic shock syndrome or septicæmia.

BACKGROUND

Although varicella infection is uncommon in neonates, neonates are at a high risk of developing severe disease with a fatal outcome in 20–31% of the cases.^{1 2} The risk is maximum if the mother develops rashes 5 days antepartum or 2 days postpartum.³ Indeed, a mild secondary bacterial infection of the skin, of little significance, is the most common varicella complication. There have been reports of severe bacterial infection during or following varicella.^{4 5} The occurrence of a varicella infection complicated by the development of the staphylococcal scalded skin syndrome (SSSS) is very rare.^{6 7} To the best of our knowledge, such a complication has not been reported so far in neonates. We report a case of a term neonate with onset of vesicular lesions of varicella on day 23 of life, who subsequently developed SSSS, septicæmia and shock and could not survive despite treatment.

CASE PRESENTATION

This male neonate was delivered at 37 weeks 5 days gestation to a 29-year-old, gravida 3, para 2 mother by lower segment caesarean section at a private hospital. The indication for caesarean section was a previous caesarean with the presence of obstructed labour. The mother undergone a regular antenatal checkup but it was uneventful. There was no prolonged rupture of the membrane, and the amniotic fluid was clear of meconium. The baby cried soon after birth and did not require resuscitation. His birth weight was 3620 g, length 47 cm and head circumference 35 cm, all of which were within the normal range for a term baby. Vital parameters were also normal and there were no apparent congenital malformations. General and systemic examinations did not reveal any abnormality and he was initiated on breast feeding. He ran an otherwise normal initial postnatal course. On the second day of delivery, the mother developed vesicular eruptions

starting from the trunk and spreading over the face and extremities over 3 days, and this was associated with low-grade fever and body ache. She was diagnosed to have varicella infection, was isolated, and given acyclovir, and she started recovering after the 5th day and was discharged from the hospital on the 8th day of delivery. The baby did not receive any prophylaxis, but was isolated from the mother and was put on replacement feeding for 5 days. Six days after the maternal illness, the younger sibling also contracted the infection and developed similar eruptions. The older sibling also acquired the infection 3 days after the illness of younger sibling started. Both the siblings used to visit the mother when she was in hospital. Both sibs did not get acyclovir for the illness and recovered in a week. On the 23th postnatal day, the mother noticed similar vesicular lesions in the baby, over the skin of the face and the trunk, which progressed to involve most parts of the body over the next two days. This was followed by the development of blistering lesions of the skin with massive peeling and desquamation of the skin after 5 days of onset of rash. With this condition, the baby got admitted on day 28 of life in our neonatal intensive care unit. Vital signs were stable at admission but the baby appeared to be very irritable. There was diffuse superficial peeling of the skin involving most parts of the body except tender, erythematous, denuded raw areas (figure 1). Some vesiculo-pustular lesions were also visible over the face (figure 2). There was no involvement of mucosa. The axillary temperature was 36.2°C, the heartbeat was 154/min, the respiratory rate was 56/min, and the capillary refill time was <3 s. Systemic examination was normal. Considering the classical history of infectious contact with siblings and the mother, a diagnosis of postnatal varicella with SSSS was made on clinical grounds. His haemoglobin count, white blood cell count and platelet count were normal. Serum

Figure 1 Generalised staphylococcal scalded skin syndrome in a varicella-infected neonate showing characteristic superficial exfoliation with areas of sparing.

urea, creatinine and blood glucose levels were normal. Chest x-ray was essentially normal. However, the serum sodium level was low (115 mmol/l), which was corrected slowly (139 mmol/l, after 30 h of admission). Cerebrospinal fluid examination could not be performed due to skin lesion over the back. Sepsis screen was positive; the blood culture and the wound surface culture grew *Staphylococcus aureus*. There being no facilities at hand, demonstration of exfoliative toxin was not possible. Albeit rare, infants with staphylococcal septicaemia are at risk of developing endocarditis, and so echocardiography should be done. However, echocardiography could not be performed for this patient. Our patient is less likely to have developed this complication as he deteriorated rapidly, without showing any sign of congestive cardiac failure, murmur or thrombocytopaenia that are common with endocarditis.

DIFFERENTIAL DIAGNOSIS

The main differential diagnosis of SSSS includes bullous impetigo, characterised by fragile bullae surrounded by normal skin and lack of systemic signs; and toxic epidermal necrolysis (TEN), which usually presents with mucosal lesions, shows different histological features and is most often drug related. This was ruled out in the absence of any mucosal lesion in this patient and in the absence of drug history.

Figure 2 A few vesiculo-pustular stage varicella rashes over the forehead and eyelids are seen.

TREATMENT

The baby received intravenous fluids, which was increased owing to evaporative loss through the raw surface; injection vancomycin, ceftazidime and acyclovir. Sodium correction was done on the day of admission, and monitored subsequently. Vaseline and mupirocin ointments were applied on the raw skin surface. On detection of shock, the baby received two normal saline boluses, followed by vasopressors (dopamine, dobutamine and later epinephrine), and ventilatory assistance along with other supportive measures.

OUTCOME AND FOLLOW-UP

Desquamation continued to progress on the day of admission. However, the baby seemed stable on the second and third days of admission with normal vitals, perfusion, saturation, electrolytes, blood glucose, and urine output; and was partly on oral feed. The illness ran a fairly downhill course after 72 h of hospitalisation. The baby had multiple episodes of vomiting, was found to be lethargic, having poor perfusion, tachycardia, tachypnoea and desaturation, suggesting shock; and was managed accordingly. However, within an hour, his sensorium deteriorated further, and shock was non-responsive to fluid boluses. At this point of time, the serum electrolytes were found to be normal; however, arterial blood gas analysis revealed hypoxaemia and severe metabolic acidosis. The patient continued to deteriorate further despite suitable measures, could not recover from shock, and succumbed after about 10 h of detection of shock. The cause of death was attributed to staphylococcal septicaemia and/or toxic shock syndrome (TSS) following varicella infection. Autopsy was not possible in this case because this is not a routine at our institution and it is difficult to obtain consent for the same.

DISCUSSION

Neonatal varicella is different from the congenital varicella syndrome, which occurs when the mother gets varicella infection in the first or second trimester.⁸ Neonatal varicella is usually acquired perinatally, and has two presentations. If the mother gets the infection from 5 days before to 2 days post delivery, the baby is at the highest risk of getting severe infection, because antibodies are not transferred to the baby in this time period.³ In the other group, the mother has the infection at least 5 days before delivery. Here, adequate antibodies are transferred and the infection is less severe. Neonatal varicella usually manifests within 2–12 days of postnatal age. The incubation period from exposure to appearance of rash varies from 10 to 23 days with an average of 14 days.⁹ Any infection in neonates beyond 14 days is usually acquired postnatally (postnatal varicella). In our patient, the infection was probably acquired postnatally from other siblings or the mother, since the baby became symptomatic only at day 23 of life.

The diagnosis of neonatal varicella is usually based on the typical clinical picture. There was no doubt about clinical diagnosis in the present case as the history of the mother and two siblings getting affected was classical, and no serological investigation was deemed necessary to prove the same. Although detection of viral DNA by

PCR in the clinical specimen is believed to be very sensitive and specific, this facility was not available at our centre.

The most common complication of varicella is bacterial skin and soft tissue infection. In a series of 26 cases of neonatal varicella (12 perinatal varicella and 14 postnatal varicella), Singalavanija *et al*¹⁰ have reported pyoderma in 9 (35%) patients, clinical sepsis in 8 (30%) cases, pneumonia in 7 (26%) cases and hepatitis in 1 (0.4%) case, as a complication. They did not find any difference between the complications of perinatal and postnatal groups. Another study, comprised of seven cases of neonatal varicella (all prenatal infection), has reported hepatitis in three, pneumonia in two cases, pyoderma in one case and sepsis in one case, as a complication.¹¹ None of the five patients having postnatal infection in their series had any of these complications. For prophylaxis, varicella zoster immunoglobulin (VZIG) administration should be considered for susceptible pregnant women within 72–96 h of exposure and for neonates whose mothers have signs and symptoms of varicella 5–7 days before or 2–3 days after delivery.² However, VZIG does not always prevent disease in the newborn; rather it may modify the clinical course by prolonging the incubation period, decreasing the severity and appearance of atypical rashes. Therefore, following treatment, these newborns should be under vigilance for an extended period of 30 days and on development of any sort of rash intravenous acyclovir should be considered.^{2 12} Prophylactic intravenous acyclovir can prevent neonatal varicella or reduce disease severity; however, further evidence is required.^{13 14}

In patients with varicella, bacterial superinfection is facilitated by skin barrier disruption and possibly by transient virus-induced alteration of local immunity. *S aureus* and group A streptococcus are very often responsible for skin and soft tissue infection and invasive infections, sometimes involving toxins production, mainly TSS— toxin 1 and superantigenic toxins, manifest as TSS, and exfoliative toxins A and B, manifest as bullous impetigo and SSSS.^{15–17} Streptococcal septicæmia following primary chickenpox infection has been reported in young children, with fatal outcome in one out of two children.⁴ Pollard *et al*,⁵ in a series of 13 children aged between 1½ months and 84 months that had invasive bacterial infection following 2–14 days of varicella rash, have reported TSS in eight patients, one of which died; the isolates were *S aureus* and *Streptococcus*. Our patient developed SSSS together with septicæmia and deteriorated rapidly after 72 h of admission, possibly because of TSS or septic shock. Young age is the main risk factor for SSSS due to dissemination of exfoliative toxins, because of the decreased renal clearance of these toxins in them, whereas immunosuppression and consumptive infectious disease are the risk factors in the older for acquiring this disorder.^{7 18} The diagnosis of SSSS is usually based on clinical grounds and/or histology. Bacterial studies and genotyping are sometimes confusing because the skin of these patients is sterile and blood culture is often negative,¹⁹ although blood culture grew *S aureus* in our patient, suggestive of bacteraemia. The treatment of SSSS includes prompt initiation of antibiotics targeting *S aureus*, and supportive skin care. Clindamycin may prove beneficial for treating infection with susceptible

strains, as it decreases toxin production.²⁰ Secondary bacterial infections and fluid and electrolyte imbalance are other possible complications that need to be monitored. This patient had hyponatraemia on the day of admission, and this was corrected. Our patient was at a high risk of contracting severe varicella infection, as the mother had onset of varicella rash on the second day of delivery, and the baby remained exposed to multiple household cases with varicella. Despite this fact, he could not receive specific immunoglobulin or acyclovir prophylaxis, probably because of wrong notions about the disease or a lack of awareness about severe complications, which could have otherwise protected the baby or ameliorated the disease.

Learning points

- Postnatal varicella is not always benign, and one should monitor the development of rare but potentially fatal bacterial complications such as staphylococcal scalded skin syndrome (SSSS), toxic shock syndrome and septic shock.
- SSSS usually affects neonates at 3–16 days of life, but may manifest in the late neonatal period.
- SSSS can be associated with underlying bacteraemia and sepsis.
- Patients with staphylococcal infection can develop multiple toxin-related manifestations, such as SSSS and toxic shock syndrome.
- Neonates exposed to varicella should be considered for specific immunoglobulin or acyclovir prophylaxis.

Competing interests None.

Patient consent Obtained.

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