Unusual presentation of more common disease/injury

Devastating coagulase-negative staphylococcal septicaemia in an extremely low birth weight infant

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Summary

In developed countries, coagulase-negative staphylococci (CoNS) are responsible for the majority of late-onset infections in very low birth weight infants undergoing neonatal intensive care. As a common skin commensal, they are often considered as mere contaminants of peripheral blood cultures or as relatively benign bacteria clinically. We present a case of invasive CoNS septicaemia in an extremely low birth weight infant which had devastating effects.

BACKGROUND

- ▶ Coagulase-negative staphylococci (CoNS) do not cause invasive infections in healthy adults or older children, yet are responsible for most episodes of late-onset infection in preterm neonates.
- ▶ Most surviving extremely low birth weight (ELBW) infants have at least one CoNS infection during hospitalisation.
- ▶ This case starkly illustrates the life-threatening devastation that coagulase-negative staphylococcal sepsis can wreak in ELBW infants.
- ▶ Despite the high incidence of CoNS in the neonatal intensive care unit (NICU), we are unaware of any similar pictorial presentation in the literature that so graphically illustrates the potential catastrophic effects of this infection in ELBW babies
- ▶ Our images and case history provide good evidence for the role and temporal relationship of postnatal CoNS infection (without preceding chorioamnionitis) in the pathogenesis of white matter brain injury in this ELBW infant.

CASE PRESENTATION

A baby girl was delivered at 26 weeks gestation by emergency caesarean section because of maternal pre-eclampsia. There was absent end-diastolic flow on umbilical arterial Doppler and the infant was growth restricted, with a birth weight of 400 g. She was born in good condition, admitted for intensive care (figure 1), and was extubated onto high-flow, high-humidity nasal cannula oxygen at age 6 h postnatal.

Placental histology showed small focal infarcts but no inflammation. Successive early cranial ultrasound scans were normal including one on day 13 (figure 2). She remained stable on the non-invasive ventilation until day 15 when she had acute onset of frequent oxygen desaturations, apnoeas and respiratory distress. She required reintubation, multiple inotropes for septic shock and was started on intravenous antibiotics (vancomycin, gentamicin and metronidazole). An abdominal x-ray showed no

features of necrotising enterocolitis. C reactive protein rose from <3 mg/l on the day prior to the sepsis episode to peak at 140 mg/l 4 days later. Total peripheral white blood cell count (WBC) rose from 8.5×10^9 to 21.0×10^9 /l, neutrophil count rose from 6.72×10^9 to 15.90×10^9 /l and platelet count fell from 207×10^9 to a nadir of 14×10^9 /l. Coagulation studies excluded disseminated intravascular coagulation. Cerebrospinal fluid (CSF) was sterile but a peripheral blood culture grew CoNS within 24 h, sensitive to vancomycin. Despite vancomycin treatment from the outset (and a satisfactory predose vancomycin concentration of 13.9 mg/l after 4 days), a further peripheral blood culture taken after 5 days also grew CoNS within 24 h, with the same antibiotic sensitivity pattern. Her percutaneous central venous catheter, in situ since postnatal day 9 for parenteral nutrition delivery, was then removed (day 21 postnatal); catheter segments and an exit site skin swab also grew CoNS on culture. Exact CoNS species in positive isolates were not defined.

OUTCOME AND FOLLOW-UP

The septicaemia caused right lower limb ischaemia and digital necrosis (figure 3). Ultimately she lost all the toes of her right foot (figure 4). Subsequent cranial scans from 4 weeks postnatal showed extensive right-sided cystic periventricular encephalomalacia (figure 5). She was discharged home aged 4 months. On follow-up aged 3 years she is a very happy interactive child, but has language delay and a dense left hemiplegia that has precluded independent walking. She stands with the assistance of a frame and supporting ankle boots. Her right boot is fleece-lined to cushion residual soft tissue thickening.

DISCUSSION

CoNS are ubiquitous skin commensals that do not cause invasive infection in well adults and older children. Yet in ELBW (<1000 g) infants, CoNS are responsible for most late-onset infections during hospitalisation^{1 2} and can be devastating. The peak age of onset is 2–4 weeks postnatal.^{2 3} CoNS infections increase duration of

Figure 1 Normal right foot on postnatal day 1.

hospitalisation, need for antibiotics, invasive procedures and ventilation, and costs of medical care.⁴ Clinical features of CoNS sepsis can range from subtle to overt signs of overwhelming sepsis. Signs include apnoea, increased ventilatory support, bradycardia, temperature instability, metabolic acidosis, feed intolerance, abdominal distension and hypotension. Investigations may show raised or depressed WBC, thrombocytopenia, hyperglycaemia and raised C reactive protein. Morbidity may include

Figure 2 Normal ultrasound head (right parasagittal view) on postnatal day 13.

pneumonia, meningitis, osteomyelitis, septic arthritis and parenchymal brain injury.⁵ Incidence, recurrence rates, associated mortality (9% overall for ELBW infants¹), and morbidity are all highest in the lightest, most premature infants.¹

Preterm infants are at higher risk of nosocomial CoNS infection than more mature infants because of immaturity of immune systems and host defences, including humoral, cellular and innate immune systems, thinner skin and a relatively poor gut mucosal barrier. Intravascular catheters, parenteral nutrition infusion (especially lipid infusion), and mechanical ventilation are additional major risk factors for CoNS infection.¹ Staphylococcal colonisation of catheters from skin insertion sites is a well-recognised route of acquired bloodstream infection in ELBW infants. Recent studies examining postnatal evolution of the microbiome indicate that staphylococci often colonise the gut of extremely preterm infants within weeks of birth.^{6,7} Infants developing late-onset staphylococcal sepsis show less diversity of early microfloral succession and predominant acquisition of staphylococci in their microbiome.⁷ The gut may yet emerge as the significant reservoir of staphylococci in ELBW infants, and intestinal translocation may be the source of many CoNS infections.

CoNS infections in ELBW infants are usually treated with vancomycin or teicoplanin. These are glycopeptide

Figure 3 Ischaemic right foot on postnatal day 18.

Figure 4 Necrotic toes right foot, day 41.

Figure 5 Ultrasound head (right parasagittal view) showing extensive encephalomalacia (arrow) on postnatal day 34.

antibiotics with bactericidal activity against aerobic and anaerobic Gram-positive bacteria including multiresistant staphylococci. The present patient had persistent CoNS bacteraemia. Despite prompt therapy with vancomycin and an adequate therapeutic drug level, she nevertheless sustained significant injury. Advances in the prophylaxis and treatment of CoNS infections in high-risk infants are required to improve outcomes. Unfortunately, studies administering specific monoclonal antistaphylococcal antibodies to ELBW infants to prevent staphylococcal sepsis have so far yielded disappointing results.

Bloodstream CoNS infections markedly increase the risk of cerebral palsy and adverse neurodevelopmental outcome.⁸ Postnatal infection, even without a positive culture, can cause widespread abnormalities of brain metabolic and microstructural development in preterm infants: 27 of 36 culture-positive infections associated with white matter injury as reported by Chau *et al*⁹ in preterm infants <32 weeks gestation were CoNS isolates (Chau V, written personal communication, February 2012). The pathogenesis of cerebral white matter damage with sepsis is multifactorial and includes ischaemia-reperfusion injury, and the direct neurotoxicity of proinflammatory cytokines and free radicals on vulnerable oligodendrocyte precursors.^{8–10}

CoNS infections have previously been considered to be relatively benign.³ The resultant cerebral palsy in the present case and the recent literature illustrate that for ELBW infants they can be life-threatening and can cause serious, life-long morbidity.

Learning points

- ▶ Coagulase-negative staphylococci (CoNS) are often considered as relatively benign pathogens or as contaminants of blood cultures from small babies.
- ▶ In extremely low birth weight (ELBW) preterm infants CoNS can be a cause of significant morbidity.
- ▶ CoNS sepsis can cause white matter brain injury in ELBW premature infants with potentially devastating lifelong effects.
- ▶ Advances in the prophylaxis and treatment of CoNS infections are required to improve the outcomes for ELBW infants.

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Competing interests None.

Patient consent Obtained.

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