Late-Onset Group B Streptococcal Cellulitis in a Premature Infant

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Case Report

A 828 g male infant was born to a healthy 37-year-old mother at 25 weeks' gestational age. Mother was admitted three days before delivery for ruptured membranes and loin pain. High vagina swab on admission grew *Streptococcus agalactiae* (Group B Streptococcus, GBS) and became sterile after peripartum antibiotics. After birth, baby received systemic penicillin and gentamicin for risk of sepsis. Initial blood culture showed no bacterial growth. Placenta histology revealed acute chorioamnionitis while all surface as well as placental swabs were negative for bacterial culture which was likely the result of maternal antibiotic treatment. Chest X-ray did not show evidence of respiratory distress syndrome or perinatal pneumonia. Initial urine detection of early-antigen fluorescent foci (DEAFF) test for Cytomegalovirus (CMV) was negative. He however remained ventilator dependent because of insufficient ventilatory effort and recurrent apnoea. On day 27 of life, systemic Amphotericin B was commenced for a persistent candida growth from urine culture. Blood for fungal culture was negative. A 39-day course of antifungal therapy was given. His respiratory condition was further complicated by acquired CMV pneumonitis on day 46 of life. Urine and saliva DEAFF tests for CMV were positive. In view of the clinical deterioration, a 14-day course of systemic Ganciclovir was started empirically, and subsequent urine culture was CMV free. All along he was fed on expressed breast milk (EBM) which was not tested for CMV or GBS. There was no neutropaenia after the course of systemic Ganciclovir. He had been on mechanical ventilation with a high setting of maximum FiO₂ 1.0. Later his respiratory condition progressed into chronic lung disease (CLD). Inhaled nitric oxide (iNO) was attempted on day 55 of life for pulmonary hypertension secondary to CLD although echocardiogram did not demonstrate supra-systemic pulmonary pressure. iNO treatment did demonstrate a good clinical response with marked reduction in ventilator setting and oxygen requirement. He was subsequently extubated to non-invasive ventilation on day 100 of life. Surgical ligation of patent ductus arteriosus was performed on day 89 of life. There were repeated episodes of Klebsiella pneumonia which were treated with...
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intravenous antibiotic accordingly. Mechanical ventilation was subsequently not required since four months of age.

On day 112 of life, he developed high fever 39°C and tender erythematous rash over pubic and perineal area. The involved skin was swollen and triangular in shape up to the level of umbilicus (Figure 1). There was also scrotal erythema with induration and oedema. Abdomen was soft but mildly distended. Clinical picture was cellulitis with possible intra-abdominal sepsis. Paediatric surgeon was consulted and agreed that gastrointestinal pathology was unlikely. Investigations revealed a low peripheral white blood cell count 3.9 x 10⁹/L with 28% neutrophils; C-reactive protein serum concentration was elevated at 149 mg/L. Abdominal X-ray showed dilated bowel shadows. Computerised tomography of abdomen and pelvis revealed soft tissue swelling around both groin region with no intra-abdominal collection or ascites. X-ray hips did not reveal any bony changes. After blood culture was obtained, intravenous Ampicillin, Gentamicin and Metronidazole were started empirically. GBS was isolated from the blood culture. Cerebral spinal fluid (CSF) culture was negative. Fever came down after two days of antibiotic treatment. The erythematous cellulitis over diaper area resolved clinically a few days after initiation of antibiotic treatment. Repeat blood culture after 48 hours of treatment showed no bacterial growth. A 14-day course of intravenous antibiotic was completed and there was no recurrence of cellulitis. There was no outbreak of GBS infection during the same period of time in the Neonatal Intensive Care Unit.

Discussion

*Streptococcus agalactiae* is the species designation for Lancefield group B streptococci. Despite great progress in perinatal care, GBS remains an important cause of invasive disease in neonates. These premature infants account for 25% of the cases of GBS disease among neonates. They are also at greatest risk of an adverse outcome from GBS infection.

Clinically GBS disease can be classified into early-onset disease, which presents at <7 days of age, and late-onset disease, which presents at 7 days of age or later. The epidemiology of early-onset GBS disease in neonates suggests that maternal colonization with GBS, followed by the infant's acquisition during passage through the birth canal, accounts for most infections. Late-onset disease can result from both vertical and horizontal sources. Spreading of the organism occurs from colonized to uncolonized infants via hands of hospital staff or by direct contact from colonized personnel. Careful hand-washing will hence minimise the risk of spread in both types of infection. In this case, mother had been colonized with GBS and hence vertical transmission was a possibility. It was also reported that breast feeding was associated with late-onset GBS submandibular cellulitis in a premature infant as the same GBS serotype was isolated in mother's milk. Unfortunately we did not culture breast milk. Although some infants with late-onset GBS disease acquire the organism from non-maternal source, studies for concordance of serotypes suggest that the vertical route of acquisition is still the major determinant of risk for late-onset infection which accounts from one half to two thirds of cases. Additional risk factors for late-onset disease are African-American origin, gestational age of less than 34 weeks and the need for prolonged hospitalisation. Our patient had late-onset GBS disease, with prematurity and prolonged hospital stay as risk factors. As prompt and appropriate treatment was given, there was no complication afterwards.

Pneumonia and bacteraemia are common presenting symptoms in early-onset GBS sepsis. Late-onset disease commonly manifests as occult bacteraemia or meningitis. Other focal infections such as osteomyelitis, septic arthritis, and pneumonia can occur. However, in a recent article, Prieto et al reported that fever (70.8%), irritability (54.1%) and cellulitis-adenitis syndrome (20.8%) were the major presentations in a cohort of infants with late-onset GBS infection. Neonatal GBS infections with a focus are more common in late-onset than in early-onset infections, but
Pathogenesis probably involves GBS mucous membrane colonization, with subsequent bacteraemia and seeding of the soft tissues. Cellulitis may also result from breaks in skin integrity with direct organism inoculation at the site. Diaper region is an area prone to trivial trauma or local skin abrasion where colonized bacteria can enter into body causing local and systemic infection. Cellulitis in young infants less than three months is commonly caused by GBS, and GBS cellulitis may be associated with bacteraemia. The submandibular region has been reported to be the most common site for cellulitis. Other sites of involvement include facial, submaxillary and retropharyngeal areas. Cellulitis over perineum or lower abdomen is rare and has been misdiagnosed as septic arthritis of hips or diaper rash. In our case, there was diaper-like rash of cellulitis over the perineum and lower abdominal region. Investigations for the hips, abdomen and pelvis further confirmed that there was no septic arthritis or intra-abdominal lesion.

GBS cellulitis has been associated with bacteraemia in up to 90% and meningitis in 25% of cases. Young infant (<3 months) with GBS cellulitis requires full laboratory evaluation including blood culture and lumbar puncture. Our patient had GBS septicaemia while the CSF culture had no bacterial growth. If initial CSF shows positive growth, we recommend repeating lumbar puncture at least 48 hours after initiation of antibiotic therapy to ensure treatment response as central nervous system infection carries significant morbidity and that lumbar puncture is a safe procedure.

Differentials for an erythematous lesion over diaper area include simple diaper rash, diaper rash with secondary bacterial infection (commonly caused by Streptococcus pyogenes), perineal candidiasis, chemical burns or dermatitis from topical therapy, septic arthritis of hips, necrotising fasciitis (commonly caused by Clostridium, Streptococcus or Staphylococcus), and rarely Fournier's gangrene which is a form of necrotising fasciitis affecting male genitalia. Although Fournier's gangrene affects primarily adults, there are reports of infants suffering from this rare but serious disease. Predisposing factors are prematurity and diaper rash, and therefore a high index of suspicion, prompt diagnosis and multidisciplinary approach are the mainstay of management in paediatric Fournier's gangrene.

Recent recommendations stated that antibiotic after delivery was not effective to prevent perinatal GBS vertical transmission or reduce late GBS disease. This may be due to horizontal infections from maternal sources, community or cross infections. Local infection after disruption of skin integrity or seeding of the soft tissue from bacteraemia in a carrier of GBS might be the pathogenesis of GBS cellulitis although the origin of bloodstream infection could not be clearly elucidated. As in our case, early antibiotic therapy could not prevent the development of late-onset GBS bacteraemia and cellulitis.

Treatment with appropriate intravenous antibiotic for 7 to 10 days is required for infants with GBS bacteraemia or pneumonia, whereas a 14-day minimal duration is recommended for the soft tissue infection or meningitis. The initial use of Ampicillin or Penicillin together with Aminoglycoside for suspected neonatal GBS sepsis is based on their in vitro synergy for these organisms. Once the diagnosis is established and a clinical response is documented, treatment can be completed with Penicillin alone. We chose the combination of Ampicillin and Gentamicin to cover the possible organisms which might cause neonatal sepsis. Metronidazole was also included for the possibility of intra-abdominal sepsis as the initial presentation was erythema and tenderness over lower abdominal region. We had given the baby a 14-day course of all these antibiotics. There was no growth from the repeated blood culture and no residual change was noted over the involved skin of the perineum and lower abdomen.

Conclusion

GBS should be considered as an etiological agent in an infant presenting with signs of systemic infection and localised lymphadenitis or cellulitis. This case reminds us that large diaper rash-like dermatologic sign in a hospitalised premature infant is rare and it warrants prompt investigation and treatment. Underlying bacteraemia is common and has to be ruled out. It is important to maintain high clinical suspicion of late GBS infection and start early antibiotic treatment.

References
2. Bertini G, Dani C. Group B streptococcal late-onset sepsis with


