Late onset neonatal sepsis caused by group A streptococcus

Introduction

Neonatal sepsis is defined as systemic inflammatory response syndrome in the presence of or as a result of suspected or proven infection (Goldstein et al, 2005). It includes early onset (age ≤7 days) and late onset (age 8–28 days) neonatal sepsis. Neonatal sepsis can present with a wide range of manifestations: altered behaviour or responsiveness, feeding difficulties, vomiting, abnormal heart rate and respiratory rate, hypoxia, temperature instability and signs of local infection (National Institute for Health and Care Excellence, 2012).

The incidence of all neonatal infections has been reported as 8/1000 live births and 7/1000 live births for late onset sepsis (Vergnano et al, 2011). Risk factors for neonatal sepsis include:

- Confirmed group B streptococcus infection in a previous baby
- Colonisation of group B streptococcus in maternal vaginal tract
- Bacteriuria or infection during pregnancy
- Prolonged rupture of membranes
- Preterm birth following spontaneous labour
- Intrapartum fever (temperature >38°C)
- Suspected or confirmed chorioamnionitis
- Mother had parenteral antibiotic treatment for confirmed or suspected invasive bacterial infection during labour or in the 24 hours before or after the birth
- Suspected or confirmed infection in another baby in the case of multiple pregnancy (National Institute for Health and Care Excellence, 2012).

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Vergnano et al (2011) documented 541 neonatal infections, with the most common causative organisms being group B streptococcus, *Escherichia coli*, *Staphylococcus aureus*, *Enterococcus*, *Enterobacteriaceae* and *Candida* spp.

Group A streptococcus is a common cause of bacterial tonsillitis in older children and can cause serious infections such as necrotizing fasciitis (especially with chickenpox), meningitis, sepsis, osteomyelitis, pneumonia, toxic shock syndrome and post-streptococcal complications such as scarlet fever and glomerulonephritis (Megged et al, 2006; Vallalta Morales et al, 2006). This article describes a case of late onset neonatal sepsis caused by group A streptococcus possibly contracted vertically from the mother.

Discussion

The isolate from the neonate was *Streptococcus pyogenes* emm st28.0, correlating with M-protein type, which is a bacterial protein encoded by the emm gene possibly involved in determining the virulence. A total of 111 different emm types of group A streptococcus have been identified; the most commonly detected are M1, M3, M17 and M28 (Megged et al, 2006).

Historically, neonatal sepsis caused by group A streptococcus was common. A large longitudinal US study at Yale-New Haven Hospital revealed that while group A streptococcus was the causative organism in almost 50% of cases of neonatal sepsis during the 10 years from 1933–1943, a later study (between 1988–2003) in the same hospital found no cases of neonatal sepsis caused by group A streptococcus (Bizzarro et al, 2005).

In England, Wales and Northern Ireland, the overall rate of group A streptococcus bacteraemia in 2014 was 2.4 per 100 000 (Public Health England, 2015). However, children aged <1 year had the second highest incidence (6.8/100 000), while those aged ≥75 years (9.0/100 000) accounted for the highest number of cases (Public Health England, 2015). Laboratory reports

CASE REPORT

An 11-day-old, formula-fed boy presented to the emergency department with a 3-day history of poor feeding, irritability, vomiting, loose stool and fever. He was born at 37 weeks' gestation by normal vaginal delivery without any known risk factors for sepsis (*see text*). Clinical assessment revealed a temperature of 38.1°C, heart rate 180/min, respiratory rate 62/min and central capillary refill time <2 seconds. He was unsettled but showed no signs of meningism and the rest of the systemic examination was normal. Mild erythema around the umbilicus was noted. A diagnosis of possible sepsis was made and laboratory investigations including blood, urine and CSF were sent.

He was admitted for further management and monitoring. Laboratory investigations showed white cell count 26.4 x10^9/litre, neutrophil 18.7 x10^9/litre, haemoglobin 122 g/litre, platelet 638 x10^9/litre, C-reactive protein 118 mg/litre. He was started on intravenous cefotaxime and amoxicillin, the latter was discontinued as CSF microscopy was reported as negative. Intravenous fluids were administered for the first 48 hours. Within 48 hours of starting intravenous antibiotics his condition improved.

CSF, urine and stool samples did not reveal any bacterial organisms. Blood culture revealed β-haemolytic group A streptococcus within 24 hours, which was later confirmed to be sensitive to penicillin and clindamycin. Following a discussion with microbiology, he was treated with intravenous cefotaxime for 1 week. A significant improvement in his clinical condition and normalization of blood results (C-reactive protein 20 mg/litre, white cell count 17.9 x10^9/litre) were noted within 7 days of starting cefotaxime therapy.

At discharge he was feeding well. His parents were advised to give a further 2 weeks of oral amoxicillin, and the signs of deterioration were explained to them. Two weeks later, the Public Health England laboratory confirmed the organism to be *Streptococcus pyogenes* emm st28.0, correlating with M-protein type. The infant is currently reported to be doing well.

confirmed a total of 811 cases of invasive group A streptococcus disease in England over a 24-week period in 2015–16 which is much higher than the average for the previous 5 years (n=618); 17% of infections were reported in children aged <10 years (Public Health England, 2016). The direct financial costs of hospital care in England for management of invasive group A streptococcus infections (n = 3696) ranged from £1984 to £2212 per case (Hughes et al, 2015).

Centers for Disease Control and Prevention's (2016) surveillance across 10 states in the United States reported 17 cases/100 000 of group A streptococcus disease in children aged <1 year in 2014. Patients with group A streptococcus meningitis can develop neurological sequelae and hearing impairment.

Multiple studies have reported that group A streptococcus isolates from blood cultures were sensitive to penicillin and vancomycin (Megged et al, 2006; Vallalta Morales et al, 2006; Knowles et al, 2015). Interim UK guidelines recommend chemoprophylaxis if either mother or neonate develops invasive group A streptococcus disease in the neonatal period (first 28 days of life) (Health Protection Agency and Group A Streptococcus Working Group, 2004). Oral penicillin-V is the drug of choice for chemoprophylaxis; azithromycin is a suitable alternative for individuals allergic to penicillin. Although anecdotal, the authors' practice is to treat otherwise well neonates with oral amoxicillin or penicillin-V for 14 days in cases where the mother's high vaginal swab or urine grew group A streptococcus.

Maternal invasive group A streptococcus infection, skin infection or colonization in the vagina is considered to be the route of transmission to neonates although an environmental source may also be responsible (Martic et al, 2010). A prospective study between 2005 and 2012, involving 150 043 mothers, found 272 laboratory-confirmed cases of sepsis in pregnancy and the puerperal period. Group A streptococcus bacteraemia accounted for 12 of the 272 cases (4.4%); three out of 12 mothers required intensive care unit admission (Knowles et al, 2015).

Maternal deaths from rapidly deteriorating disseminated intravascular coagulation secondary to group A streptococcus sepsis have been reported (Acharya et al, 1988). In high-income countries the incidence of maternal morbidity from puerperal sepsis is 0.1–0.6 per 1000 deliveries with group A streptococcus the most common causative microorganism (van Dillen et al, 2010; Anderson, 2014). Caesarean section was the single most important risk factor for postpartum infection and prophylactic antibiotics administered during the procedure substantially reduced the infection risk (van Dillen et al 2010). The clinical presentation in mothers with puerperal group A streptococcus infections is often atypical with extremes of temperature, unusual and vague pain, and pain in extremities. Endometrial aspiration in addition to blood cultures is a useful rapid diagnostic tool (Anderson, 2014). A combination of penicillin and clindamycin is the optimal antibiotic regimen in puerperal sepsis caused by group A streptococcus (Anderson, 2014).

Conclusions

Neonatal group A streptococcus sepsis is uncommon but potentially fatal. A full septic screen and treatment with broad-spectrum antibiotics is suggested. Group A streptococcus is the leading cause of puerperal sepsis and manifestation can often be atypical. Early recognition and initiation of antibiotic therapy is likely to have a better outcome. Chemoprophylaxis is suggested for neonates or mothers who develop invasive group A streptococcus disease in the neonatal period. There is a need for updated evidence-based guidelines for treatment and chemoprophylaxis of neonatal group A streptococcus infections. **BJHM**

LEARNING POINTS

- Neonatal sepsis caused by group A streptococcus, although uncommon, can lead to serious morbidity and mortality.
- Transmission to neonates generally occurs vertically from the maternal vaginal tract.
- Identifying neonates at increased risk and early intervention is associated with improved prognosis.
- Chemoprophylaxis is suggested to mother or neonate where one had developed invasive group A streptococcus disease.

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