Fatal late onset group B streptococcal meningitis following maternal postpartum sepsis

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Although maternal screening and the administration of prophylactic intrapartum antibiotics have decreased the incidence of early onset group B streptococcal (GBS) disease in neonates, there is still significant morbidity and mortality as a result of neonatal GBS disease.
Maternal GBS infections are not uncommon, but with appropriate therapy there is almost a uniformly good outcome. Little is written about the appropriate management of well infants born to mothers with postpartum GBS sepsis.
The question of whether well infants born to mothers with GBS puerperal sepsis should be treated empirically with antibiotics and the lack of literature concerning this issue became apparent when an untreated term infant died of late onset GBS meningitis following maternal puerperal GBS sepsis. We describe this event in the following case presentation.
With the current paucity of literature regarding the management of well infants born to mothers with postpartum GBS sepsis, it seems prudent to treat such infants empirically with antibiotics (following a full septic work-up) until this matter has been investigated further.

Key Words: *Group B streptococcus; Postpartum sepsis*

Une méningite à streptocoque de groupe B tardive fatale après une septicémie maternelle pendant la période postpartum

Bien que le dépistage maternel et l'administration d'antibiotiques prophylactiques intrapartum aient réduit l'incidence de maladie à streptocoque de groupe B (SGB) à apparition précoce chez les nouveau-nés, une morbidité et une mortalité importantes s'observent encore par suite d'une maladie à SGB néonatale.
Les infections à SGB maternelles ne sont pas rares, mais grâce à un traitement pertinent, l'issue est presque toujours positive. Il existe peu de documentation écrite sur la prise en charge des enfants en santé nés de mère présentant une septicémie à SGB pendant la période postpartum.
Le fait d'administrer ou non une antibiothérapie empirique aux nourrissons en santé nés de mères présentant une septicémie puerpérale à SGB et l'absence de documentation scientifique sur la question sont devenus apparents lorsqu'un nourrisson né à terme et non traité est décédé d'une méningite à SGB causée par une septicémie puerpérale maternelle à SGB. Nous présentons ce cas dans le présent article.
Étant donné le peu de documentation scientifique sur la prise en charge des nourrissons en santé nés de mère atteintes de SGB pendant la période postpartum, il semble prudent d'administrer des antibiotiques à ces nourrissons de manière empirique (après un bilan septique complet) jusqu'à ce que la question ait fait l'objet de recherches plus approfondies.

There is a paucity of literature on the management of well infants born to mothers with postpartum sepsis due to group B streptococcus (GBS). Before Fry's description of three cases of fatal puerperal sepsis caused by GBS in 1938 (1), the microorganism had not yet been described as a cause of puerperal sepsis. GBS infection in the postpartum woman, as in the neonate, was uncommon until the 1970s when a dramatic increase in the incidence of neonatal and maternal disease caused by GBS occurred (2). The rate of GBS puerperal sepsis was reported to be two per 1000 deliveries by Pass et al (3). Gibbs and Blanco (4) found that GBS accounted for 15% of isolates from postpartum women with bacteremia. With appropriate therapy, there is almost a uniformly good outcome in women with GBS puerperal infection (5). However, significant morbidity and mortality still exists as a result of group B streptococcal infections in neonates.

We describe a case of fatal late onset meningitis in a term neonate following maternal puerperal sepsis caused by GBS.

CASE PRESENTATION

A 35-year-old, gravida three, para two woman had no history of previous GBS infections and her two children had not suffered from GBS disease. Hepatitis B surface antigen and venereal disease research laboratory prenatal screening tests were negative and she was immune to rubella. The maternal prenatal screen for GBS was positive after 35 weeks' gestation and the administration of intrapartum antibiotic prophylaxis was planned. At 39 weeks' gestation, spontaneous labour began and artificially ruptured membranes resulted in the passage of clear amniotic fluid. This was followed 15 min later by the delivery of a female infant, weighing 3.4 kg. As a result of the precipitous nature of the

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delivery, prophylactic intrapartum antibiotics were not administered. During the intrapartum period, the mother was afebrile and the fetus was not tachycardic. In the immediate postpartum period, the infant was stable and resuscitation was not required. Specifically, the infant was normothermic and there were no signs of respiratory distress or tachycardia. The infant was deemed to be at low risk for the development of sepsis and an observation period of 48 h was planned. A blood culture and complete blood count were not obtained from the infant. Breast feeding was commenced immediately postpartum. At 36 h postpartum, the infant was well, but the mother had developed fever, chills and rigors without localizing findings or signs of mastitis. GBS was cultured from the maternal urine and blood. The mother was given intravenous penicillin for four days and then switched to cephalexin. The infant continued to breast feed and remained well without antibiotic therapy. On day 6 postpartum, the mother and child were well and were discharged home. On the 10th day of life, the infant was seen by her paediatrician for a routine newborn check-up and was found to be growing and feeding well, with an unremarkable physical examination. Early on the 11th day of life, the child became lethargic with decreased feeding and poor colour, and was taken to the emergency department. She was febrile (rectal temperature of 38.7°C), lethargic, groaning and had delayed capillary refill. Results of the lumbar puncture showed a white blood cell count of 1225×10^9/L (80% polymorphonuclear cells), red blood cell count of 400×10^{12}/L, protein greater than 6 g/L, glucose less than 1.1 mmol/L, and Gram-positive cocci on the Gram stain. The complete blood count showed a white blood cell count of 3.5×10^9/L (with 1.62×10^9/L polymophonuclear cells and 0.17×10^9/L bands), hemoglobin of 141 g/L, and a platelet count of 363×10^9/L. The chest radiograph was unremarkable. GBS (serotype III, penicillin sensitive) was cultured from the infant's blood and cerebrospinal fluid. Intravenous ampicillin and cefotaxime were given at the age-appropriate meningitic doses and frequencies. The infant's status rapidly deteriorated over the following 24 h with the development of seizures, cerebral edema and increased intracranial pressure. Brain stem reflexes and activity eventually ceased, and life-supporting mechanisms were withdrawn.

DISCUSSION

Faro (5) described a series of 40 women with endometritis or endoparametritis caused by GBS. One-third of these women had concomitant GBS bacteremia. The onset of fever was characteristically in the early postpartum period (average onset of fever was 11.7 h postpartum) and maternal recovery was uniform after the administration of an antimicrobial to which GBS was susceptible. Of the 45 infants born to these mothers, six (13.3%) developed GBS septicemia and the infections were fatal in three cases. Faro (5) concluded that febrile morbidity in a mother may be the single early clue of bacteremic infection in her neonate and thus the infants of such women should be carefully evaluated.

The pathogenesis of late onset (seven days to 12 weeks of age) group B streptococcal infection is not well defined. Acquisition of the organism occurs during passage through the birth canal, or less likely from an external source in either the community or hospital. Serotype III strains are isolated from 90% of infants with meningitis and 75% to 80% of infants with late onset disease, regardless of the focus of infection (6). It does not appear that type III strains of GBS have an advantage over other serotypes, with respect to acquisition or duration of asymptomatic mucous membrane infection (2,7). Duration of asymptomatic infection in colonized infants may be weeks or months irrespective of the serotype of the infecting strain (7). However, the spectrum of late onset disease severity produced by type III strains of group B streptococci, from asymptomatic bacteremia to rapidly fatal meningitis, suggest strain differences in virulence.

In fulminant cases, several other factors could be involved. Boyer et al (8) found that vertical transmission rates were substantially higher in women who had heavy compared with light colonization, and that infants born to heavily colonized mothers were more likely to be colonized at multiple sites and to develop early onset disease. Boyer and Gotoff (9) showed that maternal intrapartum prophylaxis with ampicillin significantly reduces infant GBS colonization (9% of infants born to treated mothers versus 51% of infants born to untreated mothers, $P<0.001$). Intrapartum prophylaxis has reduced the risk of early onset neonatal GBS disease, however it has not been shown to reduce the incidence of late onset GBS disease (10).

Baker and colleagues detected low levels (less than 2 µg/mL) of antibodies to type III capsular polysaccharide in acute sera from 28 infants with late onset bacteremia and 51 with meningitis (11). These low levels of capsular-specific antibodies in term infants with late onset type III GBS infection correlated with low maternal levels at delivery (11).

Special consideration has been given to the management of the unaffected sibling of a twin with group B streptococcal disease. Pass et al (12) suggest that the second twin is at an extremely high risk for development of invasive group B streptococcal infection if the first twin is affected. Because of high morbidity and mortality associated with these infections, Edwards and colleagues (13) recommend an empirical approach for the observation and treatment of the apparently uninfected sibling of a twin with invasive group B streptococcal infection.

The efficacy of empirical therapy in preventing GBS disease in the apparently unaffected sibling of a twin with GBS infection has been questioned. Rubin and McDonald (14) described late-onset GBS disease in the sibling of a twin with early onset disease. The initially unaffected twin had negative blood and cerebrospinal fluid cultures and received empiric therapy for 72 h at the time of the first twin's illness.

As attempts were made to manage the fulminant case described above appropriately, it became evident that little is written about such events. Specifically, whether empiri-

cal treatment of well infants born to septic mothers should be the current recommendation? With a lack of literature regarding management of such cases and the existing parallels to GBS disease in twins of a similar context, it seems prudent to complete a full septic work-up and treat empirically well infants of mothers presenting with GBS sepsis during the 48-h observation period.

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