

# Fatal Early-Onset Neonatal Sepsis Due to *Streptococcus pneumoniae*

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## Summary

Two cases of invasive early-onset neonatal pneumococcal sepsis are reported. One neonate was born at term with no risk factors and the other preterm at 35 weeks. Sepsis was not detected at birth for either of these babies and diagnosis was made at the stage of severe sepsis. A fatal outcome resulted despite treatment. Pneumococcal sepsis was confirmed after death in both these cases. Although maternal carriage was not documented in either case, the ages at presentation and progression suggested perinatal acquisition of infection. Early onset neonatal pneumococcal sepsis presents similarly as early onset neonatal Group B streptococcal (GBS) sepsis. Vaginal carriage of pneumococcus is rare but the micro-organism may have a higher invasion to colonisation ratio (attack rate) than GBS. Risk factors for invasive disease are similar to GBS.

**Key Words:** *Streptococcus pneumoniae*, Pneumococcus, Neonate, Early-onset sepsis

## Introduction

Invasive pneumococcal infections are being reported to be increasing<sup>1</sup>. *Streptococcus pneumoniae* has been variously described to account for 1.5-5% of all neonatal sepsis<sup>2</sup> and this rate may be increasing as well. Clinical features of neonatal sepsis due to this micro-organism are strikingly similar to those due to Group B streptococcus<sup>2</sup>. Two cases of early onset neonatal pneumococcal sepsis seen at this hospital over a period of 2 years are described.

## Case Reports

### Case 1

A 32 year old woman, gravida 5, delivered vaginally at this hospital, a 2440 g term baby girl with Apgar scores of 8 at 1 minute and 9 at 5 minutes. Membranes were ruptured less than 18 hours before delivery and there was no maternal fever. Pregnancy was uneventful. Mother and baby were discharged 10 hours after birth. However even before discharge, the baby was noted by the mother to be lethargic and feeding poorly. While at

home, she remained inactive, fed poorly and on the morning of admission had vomited. At 30 hours of life she developed a cyanotic episode. The baby was then brought to hospital and admitted to the neonatal intensive care (NICU) at 33 hours of life. On admission, the infant was in poor condition, comatose and flaccid. She was cyanosed and had gasping respiration. The peripheral pulses were weak, blood pressure by Dinamap was 77/41 with pulse rate of 136. The extremities were cold with capillary refill of 3 seconds. Axillary temperature was 36.7°C and capillary blood sugar was 1.4 mmol L<sup>-1</sup>. The abdomen was distended with no organomegaly. Resuscitation was commenced with intubation, ventilation and crystalloid and inotrope infusion. Hypoglycaemia was corrected with glucose bolus and subsequent infusion. Blood culture was taken. High dose of intravenous (iv) penicillin G (120 mg/kg/day) and iv gentamicin (5 mg/kg/day) were commenced. The white cell count was  $3.5 \times 10^9 \text{ L}^{-1}$  (differential not available). Blood urea nitrogen was 11.7 mmol L<sup>-1</sup>, serum calcium was <1.4 mmol L<sup>-1</sup>. Chest radiograph showed widespread diffuse consolidation and cardiomegaly. The infant did

not show any improvement with resuscitative measures and continued to deteriorate rapidly. Soon after admission, the peripheral pulses were not palpable and despite continued cardiorespiratory support, she failed to respond and died 3 hours after admission. Cerebrospinal fluid (CSF) was obtained at postmortem. Latex agglutination (bioMerieux®) on CSF was positive for *Streptococcus pneumoniae*. Blood and CSF cultures grew *Streptococcus pneumoniae*. Susceptibility was done by comparative disc diffusion test using known susceptible *Staphylococcus aureus* (NCTC 6571) as the control organism. Susceptibility to the isolate was reported as sensitive to penicillin, erythromycin, tetracycline and cefotaxime. Oxacillin was not tested. Minimum inhibitory concentration (MIC) and serotyping were not done. The mother was called back for cervical and vaginal swabs for culture but she defaulted.

## Case 2

A 19 year old primigravida gave birth at home, vaginally to a 2320 g baby boy at 35 weeks gestation. Apgar scores were 8 at 1 minute and 9 at 5 minutes. Duration of membrane rupture was not known. There was no maternal fever and pregnancy had been uneventful. The baby was admitted to this hospital's NICU for prematurity and tachypnoea. On admission at 2 hours of life, the baby was noted to be active and pink with oxygen saturation by pulse oximetry of 88-90% on room air. There was slight grunting with mild tachypnoea, respiratory rate of 50 per minute and minimal subcostal recession. Axillary temperature was 36.8°C. Systems examination revealed no other abnormalities. Hypoglycaemia was noted on admission with capillary blood sugar of 1.8 mmol L<sup>-1</sup>. The baby was incubator nursed and kept nil by mouth. Hypoglycaemia was corrected with glucose bolus and maintained with infusion. Vital signs and oxygen saturation were monitored. Over the next 24 hours he remained stable, active and well oxygenated on room air. He remained mildly tachypnoeic with respiratory rates between 50 and 60 per minute. At 36 hours of life the infant suddenly developed a severe apnoeic episode with cyanosis. This responded to stimulation but he developed moderate respiratory distress with subcostal recession and grunting, requiring oxygen via head-box of FiO<sub>2</sub> 0.4 to maintain adequate saturation. A septic workup was carried out including lumbar puncture and

antibiotics were commenced which were iv penicillin G (60 mg/kg/day) and gentamicin (3.5 mg/kg/day). An hour and a half later however, he developed another severe apnoea this time requiring face mask oxygen and subsequent intubation and ventilatory support. He appeared ill, off colour and inactive. Investigations revealed a marked metabolic acidosis with pH of 6.95, base deficit of 10.4 mmol L<sup>-1</sup>. Haemoglobin was 15.2 g L<sup>-1</sup>, with white cell count of 1.5 x 10<sup>9</sup> L<sup>-1</sup> (40% neutrophils) and platelets 126 x 10<sup>9</sup> L<sup>-1</sup>. Capillary blood sugar was 5.6 mmol L<sup>-1</sup>. Blood urea nitrogen was 10.2 mmol<sup>-1</sup>, sodium 124 mmol L<sup>-1</sup> and potassium 4.9 mmol L<sup>-1</sup>. The chest radiograph showed generalised diffuse opacities. The dose for penicillin was doubled and cefotaxime was substituted for gentamicin as the blood urea nitrogen was elevated. The infant continued to deteriorate. He became mottled, with poor perfusion and despite ventilatory and circulatory support the baby died at about 50 hours of life (14 hours after acute deterioration). Blood culture grew *Streptococcus pneumoniae* while CSF was sterile. CSF biochemistry and microscopy were not done as there was insufficient specimen. Antibiotic susceptibility test was carried out as for the first case with the report of susceptibility of the isolate to penicillin, erythromycin and cefotaxime. Oxacillin was not tested. MIC and serotyping were not done. Follow-up of the mother and cervical and vaginal swabs for culture could not be done as she defaulted.

## Discussion

Pneumococcal puerperal and neonatal infections were common in the pre-antibiotic era and have become rare since the introduction of penicillin. Neonatal sepsis due to *Streptococcus pneumoniae* has not been previously reported in Malaysia. However, worldwide, over the last 25 years several reports of maternal and neonatal and even foetal pneumococcal sepsis have been reported (2). A review of the literature of neonatal pneumococcal sepsis by Geelen et al in 1990 summarised 43 documented cases together with 7 of their own since 1972 (2). Of those where information was available, 50% occurred in preterms, 43% had rupture of membranes more than 24 hours. 90% of the cases presented within 48 hours of birth and mortality was 50-60%. The same authors noted that of the 25 for whom maternal vaginal and cervical swab culture results

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were available, 80% were positive and serotyping analysis demonstrated 100% concordance with those isolated from the infants. Eleven serotypes were identified, most frequent being serotypes 3 and 19. The authors stated that epidemiological data suggest that the majority of infants are colonised at birth because most were born vaginally, almost half had prolonged rupture of membranes and in most the onset was within 48 hours of birth and there was 100% concordance in pneumococcal serotype distribution of maternal-infant cultures. Other routes of infection include haematogenous transplacental transmission and nosocomial transmission. The early onset of infection in both our cases before 48 hours, suggests perinatal acquisition.

*Streptococcus pneumoniae* is not part of the resident vaginal flora. However, rare carriage has been documented. Because *Streptococcus pneumoniae* is a commensal of the upper respiratory tract, it has been suggested that pneumococcal colonisation or infection of the female genital tract may be caused by oral-genital contact. An alternate route of infection may be via the gastrointestinal tract. Serious maternal infections can occur and include endometritis, salpingitis, pelvic inflammatory disease, diffuse peritonitis, septicaemia and meningitis. Predisposing factors for maternal infections are thought to be intrauterine devices, recent birth and gynaecologic surgery.

GBS maternal carriage has been described at between 5-40% of pregnant women. Colonisation of baby is usual with rates varying between 29-85% but the incidence of invasive disease is low with a colonisation to invasive disease of about 100 : 1. However the attack rate for *Streptococcus pneumoniae* may be high considering the rarity of maternal carriage. Thus when screening reveals maternal pneumococcal carriage and the baby is found to be colonised but asymptomatic at birth, it may be advisable for these babies to be presumptively treated. Risk factors for neonatal pneumococcal sepsis are similar to GBS and include genital inoculum, premature onset of labour, prolonged rupture of membranes (more than 18 hours). An important common risk factor for GBS infections is maternal and thus neonatal absence of GBS-specific immunoglobulin G particularly of the IgG<sub>2</sub> subclass.

In both our babies, diagnosis was made late. In the first case, the baby was born at term with no risk factors. Early signs of sepsis were probably missed until the baby presented at 33 hours of life in septic shock. The second case, born at home, had risk factors, being preterm and unwell at birth. However this was attributed to prematurity and early signs of sepsis were also probably missed. Detection of maternal carriage before birth and appropriate treatment of mother during labour together with screening and monitoring of baby after birth may have prevented an adverse outcome. Screening of pregnant mothers for carriage of GBS could also include *Streptococcus pneumoniae* and thus help characterise the epidemiology and predisposing factors in neonatal disease. As with early onset GBS sepsis, the subsequent pregnancies of mothers of infants affected by early-onset pneumococcal sepsis should be monitored carefully and intrapartum penicillin given if carriage is documented or when risk factors are present. Vaccination may be considered in such cases where maternal pneumococcal antibody levels are shown to be low.

Invasive pneumococcal infections are reported to be increasing worldwide together with reports of increasing resistance to penicillin and multiple antibiotics. A recent article<sup>3</sup> outlining a few local studies has reported a similar trend of increasing penicillin resistance of pneumococcal isolates in Malaysia by minimum inhibitory concentration (MIC) values, sensitive being  $\geq 0.06$  mg L<sup>-1</sup>, intermediate 0.1 - 1 mg L<sup>-1</sup> and high level resistance being  $\geq 2$  mg L<sup>-1</sup>. Resistance was reported as 4.7% of 104 isolates from hospitalised patients in 1988 and 7.8% of 273 isolates in 1996. In one study of 86 isolates in 1995, 7 (8%) were found to be penicillin resistant, 2 isolates (2.3%) being of high level resistance. These resistant strains belonged to serotypes 14, 19, and 32<sup>3</sup>.

Pneumococcal isolates can be screened for penicillin resistance by the use of oxacillin discs in disc diffusion tests as this is more sensitive than the use of penicillin discs. Isolates exhibiting diminished zone sizes (defined as  $\leq 19$  mm for 1  $\mu$ g oxacillin disc on Mueller-Hinton-sheep blood agar according to USA based National Committee for Clinical Laboratory Standards) should be considered as presumptive resistant and confirmed by MIC estimations. In both our cases, the isolates were

reported to be susceptible by disc diffusion tests to penicillin but oxacillin was not tested.

A systematic surveillance of important isolates in Malaysia may help us understand the burden and types of pneumococcal infections in our country. This could

be done by submitting all significant isolates from peripheral hospitals to a central reference laboratory for MIC values and serotyping. Significant isolates may include those from invasive infections (blood and CSF) and those exhibiting resistance to oxacillin on disc diffusion.

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### References

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