Pneumococcal Sepsis in the Newborn - An Emerging Problem?

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Introduction

There has been increasing global interest in Streptococcus pneumoniae in recent years because of the emergence of penicillin resistance in this organism[1,2]. Although the most common manifestation of the organism is with respiratory infection, it can cause meningitis and septicemia3 Pneumococcal sepsis in the newborn period is however rare and only sporadic cases have been described from several centers in the literature[4-10]. Several of these reports have also highlighted the virulence and high mortality associated with the infection. Geelen et al[5] in a comprehensive review of 43 newborns with Pneumococcal sepsis reported between 1972 and 1990, found an overall mortality of 50-60% and a similarity of the infection in several respects to early onset group B streptococcal (GBS) sepsis.In contrast to western literature[11,12], GBS is an unusual pathogen in the developing world[13-15]. On the other hand, Streptococcus pneumoniae is ubiquitous in developing countries and although neonatal pneumoniae with this organism hasbeendescribed[16], ithasvery rarely beenreported asacause of neonatal sepsis.

As a part of a larger study of neonatal sepsis, we have pmspectively monitored the spectrum of newborn infections presenting to the AKUMC in Karachi since 1989. Of a total of 303 consecutive cases of culture-proven neontal sepsis, infection with Streptococcus pneumoniae was documented in four cases.

Case Report

Case 1

This was a term, male infant born to a 25 year old G4P3 mother after an uneventful labour. The mother had an Escherichia coli urinary tract infection in the second trimester, treated effectively with oral ampicillin. Both the mother and baby remained well for the first 36 hours afterbirth, when the mother spiked a fever and the baby was noticed to be irritable and restless. Screening blood picture in the newborn showed neutropenia (Neutrophils 800/nun3), with CSF pleocytosis (20,800 cells/mm^3), protein 2500 mg/dl, sugar 27 mg/dl and gram positive diplococci on the gram stain. The baby was placed on N cefotaxime 150 mg/dl, arnikacin 30 mg/dl and ampicillin 200 mg/dl. Cultures from the blood and CSF grew Streptococcus pneumoniae after48 hours, sensitive to penicillin, ampicillin and cefotaxime. The same organism was isolated from the maternal blood culture and high vaginal swab. Despite antibiotics and full supportive therapy including fresh plasma, dopamine, mannitol infusion and hyperventilation, the infant continued to deteriorate, developed renal failure and died at 12 days of age. The mother recovered uneventfully.

Case 2

This 25 day old neonate weighing 3.5 kg, was admitted as an emergency with aS day history ofrespimtozy distress and poor feeding. He was born at home to a 32 years old G5P3+1 lady uneventfully, after a normal antenatal period and labour. Clinical and radiological examination at the time of admission revealed a right middle and lower lobe pneumonia. Hematological investigation showed Hb 12 g/dl, WBC 17.2x109^{11}, platelets 284x10^{12}/l, PT 24 sec (control 13), PIT >120 sec (control 33 sec), normal CSF examination, electrolytes and blood gases at admission. Blood cultures and tracheal aspirates gave a pure growth of Streptococcus pneumoniae. He was initially placed on

combination of ceftizoxime (100 mg/kg/day), amikacin (30 mg/kg/day) and cloxacillin (100 mg/kg/day) and ampicillin (100 mg/kg/day) was substituted for the latter when the culture results became available. Despite full supportive therapy, the baby continued to deteriorate and developed a pneumothorax, which was drained. He died on the eighth day of admission.

Case 3

This 4 day old newborn infant was transferred from another hospital for management of intractable seizures and sepsis. He was born at term to a 34 years old G5P3+1 mother, who had recurrent respiratory infections during pregnancy and received several courses of antibiotics. The baby weighed 2.04 kg at birth and there were no obvious problems. Breast feeding was attempted but the baby had a weak suck. On the third day, the baby was noticed to be icteric and lethargic. A sepsis screen was done and the baby was placed on IV cefotaxime. A CSFexaminationwas not performed. The baby developed fever and seizures the next day and was transferred to AKUMC. At admission the baby was in an extremely poor condition and hypotensive. Investigations revealed Hb 12.3 g/dl, WCC 3.2xlO9fl (neutrophils 47%), platelets 377xl0^{12}/l, PT 16 sec (control 11 sec), PTT 44 sec (control 28 sec), creatinine 1.5 mg/dI, normal electrolytes, calcium 6.6 mg/dl. CSF examination revealed 2600 cells/mm3 (predominantly neutrophils), protein 232 mg/dl, glucose 6 mg/dl and a negative gram stain. A part from supportive therapy and IV phenytoin, the baby was placed on IV cefotaxime (150 mg/kg/day) and amikacin (30 mg/kg/day). However, the seizures persisted and the blood and CSF cultures grew Streptococcus pneumoniae at 48 hours, with intermediate sensitivity on disc diffusion testing to chloramphenicol and erythromycin. Ampicillin (200 mg/kg/day) was added to the antibiotic regime. Maternal high vaginal swab, pbatyngeal swab and blood cultures were negative. The seizures persisted despite combination anticonvulsants (Phenytoin, phenobarbitone and paraldehyde infusion), IV mannitol and hyperventilation. There was evidence of generalized bleeding by day 3 and deterioration in hematological parameters, platelets 22x10^{12}/l, PT >120 sec (control 12 sec), PTT >120 sec (control 28 see). In view of signs of brain stem death, in consultation with the parents, life support systems were switched off on the 7th day of admission.

Case 4

This 5 day old female child was referred from another facility with a history of feeding difficulty and lethargy. The mother, a 24 years old primigravida had an uneventful antenatal period and delivered a 3.1 kg infant at term. She developed a fever and vaginal discharge on day 3, around which time the baby stopped breast feeding. The CSF examination was normal. At admission, the baby was hypothermic, poorly perfused and in respiratory distress. The baby's blood culture and maternal high vaginal swab grew Streptococcus pneumoniae after 48 hours. The initial antibiotic combination of cefotaxime, amikacin and ampicillin was continued, alongwith supportive therapy. The baby recovered, was given a ten day course of therapy in all and is doing well on follow-up to date.

Comments

Pneumococcal infections accounted for 1.3% of all documented neonatal infections for this period and the prevalence among AKUMC births was 0.1 per thousand births over this duration. The overall mortality of 75% in our experience highlights the virulence of this infection and supports the observations of Primhak et al that pneumococcal infections carry a greater invasion to colonization ration than GBS[10]. The virulence of infection in all of our patients canbe gauged from the observation that despite prompt initiation of therapy in atleast two infants, the progress of the septicemia and associated multi- organ dysfuncion was inexorable. Although we used ampicillin in combination in all cases, once the bacteriology and sensitivity results were available, the reported high prevalence of penicillin resistance among pneumococcal isolates in Pakistan, poses problems in terms of appropriate choice of antibiotics in suspected pneumococcal disease. Prompt institution of antibiotic therapy is

important, the only survivor of pneumococcai sepsis in our experience was Case 4, ampicillin was added to the regime on clinical suspicion, before culture results became available.

Although, the chief means of infection appears to be the genital tract, the possibility of transpiacental infection cannot be excluded in some cases[7,8]. It is also likely that given exposure to pneumococci in the environment, the newborn may acquire the organism postnatally. Shakunthala et al[16] isolated Streptococcus pneumoniae from a large number of lung aspirates in neonates presenting with pneumoniae and although a subsequent study has failed to confirm their fmding[17], the possibility of late acquisition of pneumococcal sepsis by some newborns cannot be ignored. Case 2 in our experience acquired pneumococcal sepsis and pneumonia after the third week and no evidence of maternal disease was found.

It does appear that pneumococcal sepsis is a particularly virulent infection in the newborn. Certainly this organism, though rare, has had the highest organism-specific mortality in our experience in Karachi. In view of the similarities between pneumococcal disease and early onset GBS[4,6,7], pneumococcal sepsis is a clinical curio in Pakistan, as GBS infections are extemely rare and inourexperience, less virulent. The precise reasons for this increased virulence of pneuinococcal disease in the newborn is unclear and requires further studies including estimation of the cytokine responsiveness of effected patients in comparison with other types of sepsis[18,19].

It is also important to study other contributoiy factors to invasive pneumococcal infection in the newborn. A defect in the opsonic defence system against pneumococci has been described[20], but to date, there are no studies on the mucosal immunity and adherence of the organism to the genital tract epithelium[6]. Until the pathogenesis of pneumococcal colonization or maternal/newborn infection becomes clear, we believe that prompt antibiotic therapy should be instituted if there is evidence of maternal or newborn colonization.

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