## Case Report

# Invasive Pneumococcal Disease; Current Management Challenges in a case of severe infection

Gulati Raj Rani, Adly Victor, Rajaram Usha
Department of Pediatrics, Al Jahra Hospital, Kuwait

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**ABSTRACT**

An increase in invasive pneumococcal disease (IPD) requiring intensive care admissions has been reported recently. This increasing prevalence of pneumococci with decreased susceptibility to penicillin and to cefotaxime or ceftriaxone has complicated the management of pneumococcal invasive disease including meningitis. *Streptococcus pneumoniae* is the leading cause of bacterial meningitis in children beyond the neonatal period. Although the use of third generation cephalosporins as initial empiric therapy for suspected pneumococcal meningitis is currently recommended, the failure of this treatment is frequently reported. Due to its excellent penetration into the cerebrospinal fluid, vancomycin is now being recommended in the treatment of meningitis by the Infectious Disease Academy. We report a case of a healthy Kuwaiti infant who had pneumococcal meningitis and septicemia, with a rapid progressive deterioration, in spite of initiating therapy within 24 hours of the onset of symptoms and signs of meningitis.

KEYWORDS: disseminated intravascular coagulation, invasive pneumococcal disease, meningitis

## INTRODUCTION

An increase in invasive pneumococcal disease (IPD) requiring intensive care admission has been reported recently[1,2]. Increasing prevalence of pneumococci with decreased susceptibility to penicillin and to cefotaxime or cefriaxone has complicated the management of pneumococcal meningitis and invasive pneumococcal disease[3,4,5]. *Streptococcus pneumoniae* is the leading cause of bacterial meningitis in children beyond the neonatal period[6]. Herein, we report a case of an infant presenting with IPD, who rapidly developed complications of disseminated intravascular coagulation (DIC) ascites, pericardial effusion, multi-organ failure, and brain abscess resulting in a fatal outcome.

## CLINICAL PICTURE

A 2-month-old Kuwaiti infant presented with high fever of 39 °C, irritability, vomiting, bulging anterior fontanelle and pallor within two hours of receiving her first dose of diphtheria-pertusis-tetanus, oral polio and *haemophillus influenza* vaccine. Before immunization, she was said to be perfectly healthy. There was no history of trauma or ear discharge. No other family member was sick at home. During examination, she developed generalized seizures with central cyanosis. She was immediately intubated. After stabilization, she was shifted to the pediatric intensive care unit isolation room. Neurologically, she was at modified Glasgow Coma Scale 9/15. Her convulsions stopped after rectal diazepam. A complete septic work up was done including cerebrospinal fluid (CSF) examination. Therapy with intravenous cefotaxime (200 mg/kg/day), vancomycin (60mg/kg/day) and dexamethasone (0.6mg/kg/day) was initiated. Her CSF was turbid. Gram stain smear revealed gram-positive diplococci. CSF slidex was positive for pneumococci. CSF and blood cultures were positive for *Streptococcus pneumoniae* and sensitive to penicillin, cefotaxime and vancomycin. Her blood serology was negative for viruses. Hematologically, she showed leucocytosis with toxic granulations inside neutrophils. Her initial metabolic screen included normal liver and kidney functions, ammonia and lactic acid levels. Immunological assay showed borderline low levels of IgA, IgG, and IgM. Her initial bedside cranial ultrasound was normal. Urgent plain CT Head showed widened subarachanoid spaces (Fig. 1).

During the next 48 hours, she continued to be febrile (39 °C), her pupils became non-reactive and neurologically she deteriorated to modified GCS 6/15. She needed continuous ventilatory support. However, her cardiovascular status was stable. Prolonged bleeding was seen at puncture sites. Repeat CT head showed intracerebral hemorrhages in the left frontoparietal and right frontal lobe with surrounding edema (Fig. 2). There was 1.5 cm midline shift to the right with compression of the left lateral and third ventricle. A second CSF examination was deferred by the neurosurgeon. Fibrinogen degradation products in her blood were

*Address correspondence to:*
*Dr. Raj Rani Gulati, Al-Jahra Hospital, P.O.Box 40206, Pin Code 01753, Kuwait. Tel: (O)4581678/4577213, Email: rajrani11@hotmail.com*

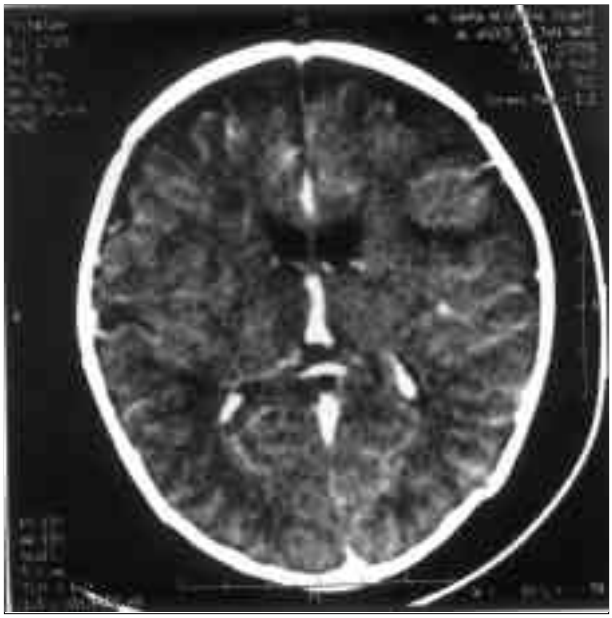

Fig. 1: Plain CT Head shows widened subarachanoid spaces.

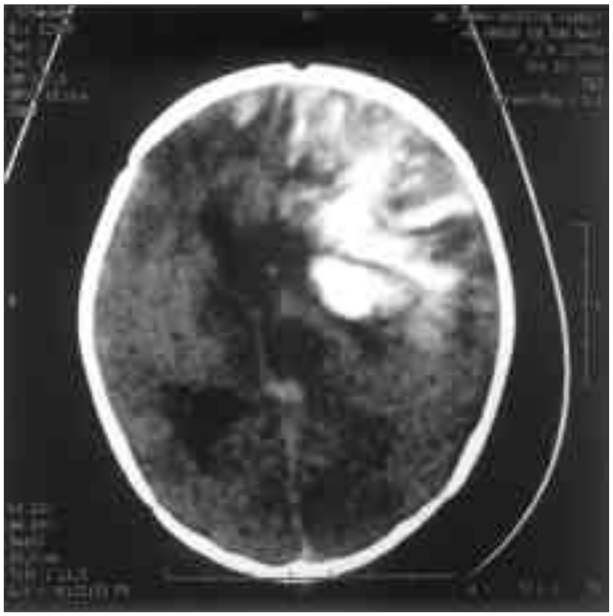

Fig. 2: CT Head showing intracerebral hemorrhages in left frontoparietal and right frontal lobe 48 hours after admission.

raised upto 16000 nanograms / ml (D-Dimer normal range < 500 nanogram / ml). She was given intensive supportive therapy with fresh frozen plasma, fresh whole blood, and intravenous immunoglobulins. Pediatric neurologist and neurosurgeon anticipated her poor outcome clinically and suggested to continue our management.

No clinical improvement was noted. Over next 72 hours her clinical course was complicated by generalized tonic-clonic seizures and development of petechiae around puncture sites. She developed increasing degree of generalized edema, more prominent on her neck. Neurologically she was now at modified GCS 3 / 15. Bed side Doppler study ruled out any obstruction of the superior vena cava. Cranial ultrasound revealed multiple areas of liquefaction in the left frontal and temporal lobes. Clinically and radiologically, she had developed signs of pericardial effusion and ascites during the second week. Neurologically no improvement was noted. Her brain perfusion scan showed only tiny areas of perfusion in the posterior aspect of parietal and temporal lobes. She finally died of multi-organ failure despite receiving full intensive supportive therapy from day one.

## DISCUSSION

An increase in IPD requiring intensive care admission has been reported recently[1-2]. The antibiotic resistance to pneumococcal infections is also being reported increasingly[3-6]. Over the last decade, the percentage of pneumococcal strains isolated from children with invasive infections that are non-susceptible to penicillin and cephalosporins has increased dramatically, leading to recommendations that vancomycin should be included in the empiric antibiotic coverage for children with suspected bacterial meningitis[7,8]. We initiated therapy with an appropriate synergistic combination of third generation cephalosporins and vancomyin on admission. Our patient did not show any clinical improvement. We postulate that her poor outcome could be due to tolerance of the organism to vancomycin. Recently, strains of *S. pneumoniae* tolerant to vancomycin have been characterized[9]. Such tolerant strains are more difficult to eradicate[10]. It has been suggested that tolerance may be a precursor to the development of drug resistance. Clinical failure in our case inspite of attaining peak serum concentration of vancomycin (30-40 microgram / ml), could be due to drug resistance. This fact could not be verified due to lack of second CSF examination. More sensitive tests such as detection of pneumococcal DNA by PCR could determine the tolerance and / or resistance to vancomycin[11]. It could be argued that the poor clinical outcome in our baby reflected possibly the inherent severity of the disease rather than pure ineffectiveness of the synergistic combination of vancomyin and cefotaxime. However, the early initiation of recommended double drug therapy with vancomycin and cefotaxime did not produce the anticipated clinical response.

The role of adjunctive corticosteroid therapy in pneumococcal meningitis is controversial[12]. In an uncontrolled study, Steven C *et al*[12], found that trends are towards decreased rates of hearing loss

and other neurological deficit among patients who received dexamethasone (starting within one hour after initiation of intravenous antibiotics and continuing for at least two days). In another study, Arditi M *et al*[13] reported that children with pneumococcal meningitis, who were treated with dexamethasone demonstrated increased rate of neurological deficit and hearing loss. The use of dexamethasone resulted in delayed clearance of *S. pneumoniae* from CSF and abolished the synergistic effect of vancomyin and cefotaxime[14]. We initiated dexamethasone therapy with the first dose of antibiotics and our baby deteriorated progressively despite treatment with third generation cephalosporins and vancomycin with a peak serum concentration of 30 microgram / ml. The adjunctive use of steroids in our case may have invoked a possible cause of variable penetration and net adverse outcome. Additional data are necessary to determine the true effects of dexamethasone in IPD.

Deaths due to IPD may be underestimated[11]. Thayyil *et al* have reported sudden infant death due to disseminated pneumococcal infection[15]. Appearance of extensive intracerebral hemorrhages with midline shift on second CT at 48 hours of admission reflected her poor outcome. In our case, evidence of cerebritis was seen in the left frontal and temporal lobe. Same authors described focal areas of necrosis and inflammation in the brain substance earlier. Her clinical course deteriorated rapidly with a picture of generalized edema, mucosal bleeds, ascites, and pericardial effusion. Since the edema was more prominent on the neck, bedside Doppler study ruled out superior vena cava obstruction. Extensive inflammatory infiltrates over the pericardium, focal abscesses in the myocardium and thymus have been described earlier by Sharief *et al*[16]. Disseminated pneumococcal infection involving the meninges, brain substance, pleura pericardium, myocardium and soft tissue of the neck was also reported earlier by Thayyil *et al*. Extensive fatty changes in the liver can occur due to disseminated pneumococcal infection leading to DIC.

The developmental of DIC leading to multiorgan failure probably indicates a more virulent strain. In our case, the clinical presentation and the hospital course was not influenced by the susceptibility of the pneumococcal isolate, since our pneumococcal isolate was sensitive to all antibiotics. A second sample of CSF for determination of the strains' tolerance and resistance to the antibiotics used was not possible because of intracranial events leading to danger of brain herniation.

## CONCLUSION

IPD results in a high degree of morbidity and mortality. Pediatric health care workers must be made aware of this fact. Routine pneumococcal immunization in Kuwait is suggested to prevent this disease.

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