

### Invasive Pneumococcal Pneumonia with Massive Empyema: A Case Report

Tin Nwe Latt, Noor Shafina Mohd Nor

Faculty of Medicine, Universiti Teknologi MARA, Selangor, Malaysia

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#### Corresponding author:

**Dr. Tin Nwe Latt,**

Lecturer,

Paediatric Department,

Women & Child Health Cluster,

Faculty of Medicine,

Sungai Buloh Campus,

Universiti Teknologi MARA (UiTM),

Sungai Buloh,

47000 Selangor,

Malaysia.

Tel: +6016-4945230

Email:

nwelatt2578@salam.uitm.edu.my

#### ABSTRACT

Although the use of appropriate antibiotics has significantly improved the outcome of pneumonia, severe complications are still encountered. We report here of a case with invasive pneumococcal pneumonia with massive empyema. A 2-year-4-month old girl presented with fever for 8 days and intermittent cough for 2 weeks. On examination, reduced air entry with dullness on percussion was noted on the left lung. Chest ultrasound revealed moderate to gross pleural effusion with septations, for which left thoraco-centesis with insertion of pigtail tube was performed. *Streptococcus pneumoniae* was detected via polymerase chain reaction (PCR) test in the pleural fluid. Intravenous (IV) benzylpenicillin and ceftriaxone were given together with one course (5 days) of intrapleural urokinase to breakdown the septations. Timely and appropriate management of pneumonia including the use of thrombolytic agent is vital to ensure optimal outcome and reduce the need of invasive procedures in cases with massive empyema. Public awareness of pneumococcal vaccination is also essential as a part of preventive measures.

**KEYWORDS:** Pneumococcal, pneumonia, empyema

#### INTRODUCTION

Worldwide estimates of the yearly incidence of pneumonia in children aged <5-years range from 120 to 160 million, with more than 99% occurring in resource-limited nations [1]. Pneumonia is one of the commonest causes of admission in children and a significant contributor to morbidity and mortality in both developed and developing countries [2]. Although the use of appropriate antibiotics has significantly reduced the number of complications arisen from bacterial pneumonias, severe invasive complications such as cavitory necrosis, abscess formation, pleural effusion or empyema are still encountered in clinical practice [3, 4].

Recently, an increasing number of invasive pneumonia cases caused by *Streptococcus pneumoniae* have been reported in children [5-6]. *Mycoplasma pneumoniae*, on the other hand, has also been reported to cause para-pneumonic effusion, and empyema in children [7]. Currently in Malaysia, nationwide exact

figures of invasive pneumonia cases in children have not been established. Nevertheless, hospital-based studies had been performed and showed that *Streptococcus pneumoniae* was the most common responsible pathogen [8, 9]. This report highlights the importance of accurate clinical management to improve the outcome in invasive pneumococcal pneumonia with massive empyema in children. It also highlights the fact that despite the availability of antibiotics, readily available treatment and prevention programmes we still encounter cases with severe complications of pneumonia. There is a need for increase public awareness of the availability of pneumococcal vaccination.

#### CASE PRESENTATION

A 2-year-4-month old Chinese girl was referred from a private medical centre with the complaints of fever for 8 days and intermittent cough for 2 weeks. Fever was high grade, ranging from 38.5 °C to 40 °C. Cough was

productive, worse at night and associated with post-tussive vomiting. Oral intake and urine output were both reduced. Both her father and babysitter had history of cough. On examination, she was slightly pale and irritable. Her weight was 10 kg (just below 3<sup>rd</sup> centile), temperature 38.4°C, pulse rate 188 beats per minutes, blood pressure 96/60 mmHg, respiratory rate 46 breaths per minutes without recessions, and blood oxygen saturation (SpO<sub>2</sub>) 100% under nasal prong oxygen 2L/min. Reduced air entry and dullness on percussion were noted over the left lung. Right lung examination was normal.

Her initial investigations revealed haemoglobin (Hb) 10.8 g/dl, total white cell count (WCC) 24.17x10<sup>9</sup>/L, (neutrophil 56.8%, lymphocyte 26.7%), and platelet 599x10<sup>9</sup>/L. C-reactive protein (CRP) was 26.20 mg/dl on admission. *Mycoplasma pneumoniae* antibody level was noted to be high with 1:320 titre via particle agglutination test. Sputum for acid fast bacilli (AFB) was negative for 3 consecutive days. Adenovirus, influenza A & B, parainfluenza 1, 2, and 3, and respiratory syncytial virus (RSV) were not detected from the naso-pharyngeal aspirate (NPA) and no growth was obtained on sputum culture. Serum glucose, renal and liver functions were all normal.

Chest radiograph (CXR) on admission, which revealed homogeneous opacity on the left with obliteration of left costophrenic angle and mediastinal shift, was shown in Figure 1.

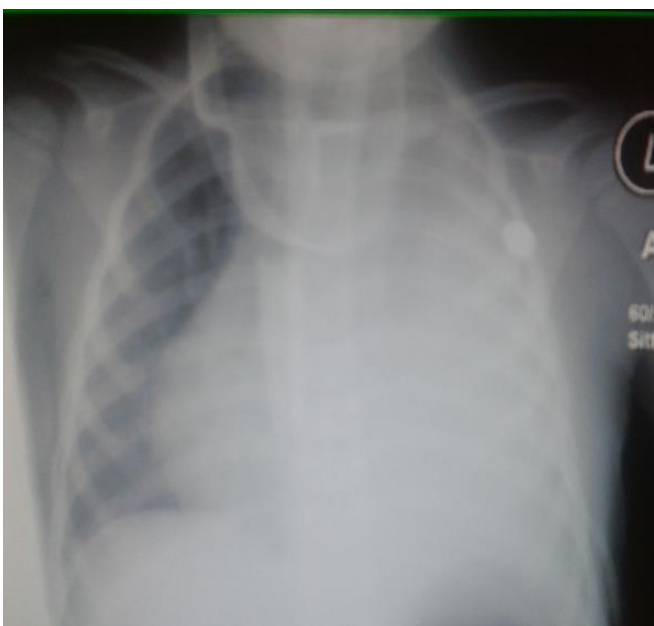


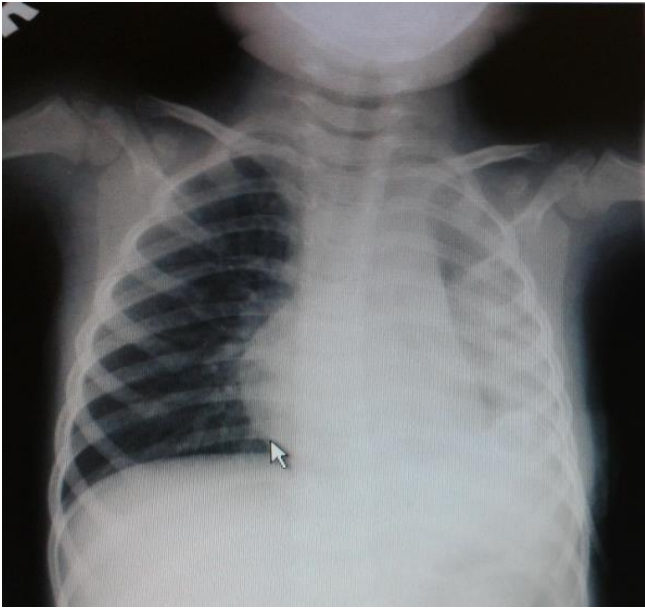
Figure 1 Chest x-ray on admission

She was started on IV benzylpenicillin 100,000 U (100,000U/kg/dose) 6 hourly and IV ceftriaxone 500mg (50mg/kg/dose) 12 hourly to ensure adequate gram positive as well as gram negative coverage. Chest ultrasound revealed moderate to gross pleural effusion with septations on the left lung, for which left thoraco-centesis with pigtail tube insertion was performed. A total of 150ml pus was drained on the first day, and continuously draining for the next 12 days. The exudative fluid was macroscopically cloudy with occasional pus cells under microscope; however, no organism was seen on gram stain. Cell count showed RBC: 10 cell/mm<sup>3</sup>, WBC: 20 cell/mm<sup>3</sup> (predominantly: polymorphs) with no growth on culture. Pleural fluid cytology showed inflammatory cells with neutrophils predominant and no atypical cells. *Streptococcus pneumoniae* was detected via polymerase chain reaction (PCR) test for *Streptococcus pneumoniae* genome in the pleural fluid.

The above two antibiotics were continued for 2 weeks and then changed to syrup cefuroxime for another 4 weeks (a total of 6 weeks antibiotic treatment). Syrup clarithromycin 75mg (7.5mg/kg/dose) twice a day was also given for 1 week, started from day 3 of admission, after obtaining the positive serology result of *Mycoplasma pneumoniae*. One course (5 days) of intrapleural urokinase 40,000 units in 40 ml of normal saline 12 hourly was also administered to breakdown the septations. She was also prescribed syrup multivitamin 2.5ml OD, folic acid 250mcg (2.5ml) OD, and ferrous ammonium citrate 3ml OD in view of low Hb level, and hypochromic microcytic anaemia with pencil shaped cells seen on peripheral blood films. Low serum iron level with high total iron binding capacity was also suggestive of iron deficiency anaemia.

Repeated chest ultrasound on day 10 of hospitalization revealed residual left pleural fluid collection measuring 0.5cm x 0.9cm in maximal depth, with echogenic debris and strands within it. CXR on day 10 post treatment showed improvement with residual left pleural effusion (Figure 2). The repeated CRP and WCC also showed marked reduction. The pigtail tube was hence removed on day 12 of admission and she was discharged with oral antibiotics. She was regularly followed up in our

outpatient clinic and was last seen 2 months ago with full recovery and no residual findings.



**Figure 2** Chest x-ray on day 10 of treatment

## DISCUSSION

Invasive pneumococcal disease (IPD) is defined as an acute and a serious communicable infection confirmed by the isolation of *Streptococcus pneumoniae* from a normally sterile sites (eg, blood, cerebrospinal fluid, pleural fluid, joint fluid or pericardial fluid)[10]. Children with IPD present severely ill as a consequence of pneumonia, septicaemia and meningitis. The commonest pathogen to cause community-acquired bacterial pneumonia in children is *Streptococcus pneumoniae*. A recognised and common complication of pneumococcal pneumonia is pleural effusion and empyema[11]. Our patient showed evidence of the presence of *Streptococcus pneumoniae* antigen in her pleural fluid which fulfilled the criteria for invasive pneumococcal pneumonia, complicated by empyema.

An increase in complications of pneumonia has recently been recorded in children's population, with *Streptococcus pneumoniae* being the predominant cause[5,8,12,13]. However, there was a recent case report on a large pleural effusion with empyema caused by *Mycoplasma pneumoniae* requiring chest tube drainage for more than a week[14]. Clinicians should be aware of the potential complications of these causal organisms while treating children with

pneumonia, so that early diagnosis and appropriate therapy can be instituted. Typically, the clinicians should alert the possible complications of pneumonia such as pleural effusion and empyema if there is a persistent fever after 48 hours of proper antibiotics, together with a change in physical signs. In our case, patient had high fever with productive cough for more than 1 week and had received treatment in a private medical centre. However, her condition did not improve necessitating suspicion of the presence of complications. Therefore, appropriate investigations including blood investigations, CXR and chest ultrasound are warranted, as early as possible, to confirm the possibility of developing parapneumonic effusion and empyema.

Parapneumonic effusions are more frequent compared to true empyema. Parapneumonic effusions could be under-diagnosed and empyema can occur within 7 days of the initial fluid collection[15]. Empyema is, by definition, the collection of pus in the pleural space. According to American Thoracic Society, it has been divided into 3 stages. They are: (1) Exudative – in which a sterile exudate accumulates in the pleural space with low white cells; (2) Fibrinopurulent - where pus is present with an increase in cellular counts; and (3) Organised - in which the pleural space is filled by a thick exudate with heavy sediment and there is a formation of thick peel due to fibroblast proliferation[16,17].

Investigations, at initial cannulation, should include white cell counts, CRP levels, serological testing for mycoplasma and blood culture for any gram positive as well as gram negative organisms. Repeated blood testing should be considered for cases with persistent fever, or if there is a concern of patient not responding to appropriate treatment. Pleural fluid should be sent for microscopy, culture including *Mycobacterium tuberculosis*, PCR test of suspected organisms such as *Streptococcus pneumoniae* and cytology. Chest ultrasound is the investigation of choice to be performed for all children with doubtful para-pneumonic effusion and empyema. A computerised tomography (CT scan) of thorax should be considered for cases; if children have failed to respond to proper treatment, or if there is any doubt of different pathologies[18].

Choice of antibiotics should also adhere with the national guidelines and hospital policy. According to Infectious Diseases Society of American (IDSA) guidelines, benzylpenicillin is the drug of choice for *Streptococcus pneumoniae* with minimal inhibitory concentrations (MIC) for penicillin  $\leq 2.0$  ug/mL and ceftriaxone or cefotaxime should be given for those with MIC  $\geq 4.0$  ug/ml and resistant to penicillin[19]. According to Paediatric Protocols for Malaysian Hospitals, benzylpenicillin is to be given as a first line drug in hospitalised cases with pneumonia and cefuroxime or cefotaxime as a second line antibiotic[20].

As a general guideline, benzylpenicillin and ceftriaxone are not often combined but our aim of using ceftriaxone in this case was to cover for other gram negative organisms although it can also be used for *Streptococcus pneumoniae*. There are other reports in the literature where this combination has been used to treat complicated pneumonia with effusion and empyema [21,22]. In severe cases of pneumonia, parenteral therapy combining second or third generation cephalosporins and macrolides should be administered[20,23]. The mortality was lower (p 0.004) for those who received a  $\beta$ -lactam-containing combination regimen as compared for those who received a  $\beta$ -lactam as monotherapy among critically ill patients with bacteraemic pneumococcal illness [23].

A high index of suspicion for *Staphylococcal* infection is also required due to rapid deterioration and significant risk of mortality. If radiological features such as multilobar consolidations, pneumatoceles and spontaneous pneumothorax are present, high dose of cloxacillin (200 mg/kg/day) for a longer period should be given to cover for *Staphylococcal aureus*[20]. Upgrading to second or third line antibiotics needs to be considered especially in cases with no signs of recovery, and patients remain ill with spiking temperature after 48 - 72 hours of initial treatment[20].

All children with empyema should be ideally managed by, or in discussion with, respiratory paediatricians together with paediatric surgeons and transferred to a tertiary paediatric centre, if feasible. The infusion of intrapleural fibrinolytics such as urokinase or tissue plasminogen activator through chest

drains can shorten the hospital stay in comparison with chest drain alone[24].

Fibrinolytics act by breaking down fibrin bands causing loculation of the empyema; and hence, drainage of the infected material is improved through the chest tube and thereby pleural circulation can be re-established[24]. Our case markedly improved by pigtail chest tube drain together with intrapleural fibrinolytic therapy using urokinase and prolonged use of appropriate antibiotics. She did not require any invasive surgery like open thoracotomy or video assisted thoracoscopic surgery (VATS) which should be considered if no clinical improvement.

Several interventions to reduce community acquired pneumonia include frequent hand-washing, promoting breastfeeding, reducing exposure to other children, avoiding tobacco smoke, and immunization[25]. The widespread use of pneumococcal immunization has reduced the incidence of IPD[26]. Currently, three types of conjugate vaccine are available, such as 7-valent Pneumococcal Conjugate Vaccine (PCV7), PCV 10 (Synflorix) and PCV 13 (Prevenar 13). PCV7 can prevent the seven different serotypes 14, 6B, 19 F, 23 F, 18 C, 4, 9V. Synflorix (PCV10) constitutes the seven serotypes in PCV7 plus the serotypes 1, 5 and 7F, whereas, Prevenar 13 (PCV13) includes the serotypes of PCV10 in addition to serotypes 3, 6A, and 19 A.

In Malaysia, 19F is the most common serotypes of *Streptococcus pneumoniae* causing IPD followed by 19A, 14 and 6B [9,27,28,29]. Hence, pneumococcal vaccination, by using these vaccines, can reduce the risk of developing IPD cases in Malaysia. These vaccines are available in the private medical centres and have not been introduced in the national immunisation schedule to date. However, discussion to add this vaccine into the national immunisation programme is currently ongoing. In many developed countries, pneumococcal vaccines have already been included in the national immunization schedule to reduce the incidence of IPD in infants and children [30, 31, 32, 33, 34]. Our patient did not receive the pneumococcal vaccine due to the lack of awareness of availability of the vaccine although recommendations for pneumococcal vaccination, even in children without underlying

medical illnesses, are usually made to parents to reduce such complications.

## CONCLUSIONS

In conclusion, although the use of appropriate antibiotics has significantly improved the outcome of pneumonia, severe complications such as massive empyema are still encountered. Timely and accurate management including the use of thrombolytic agent is vital to ensure the optimal outcome and reduce the need of invasive procedures if it has developed. Public awareness of pneumococcal vaccination in infants and children is also essential to reduce such complications.

## Conflict of Interest

Authors declare none.

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## Authors' contribution

TNL initiated the idea for the paper and wrote the initial draft, and both authors (TNL & NSMN) were involved in editing and finalising the paper.

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