An overview of childhood empyema

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Introduction

Normally, there is only a small amount of pleural fluid ~0.3 ml/kg present in the pleural space. Normal pleural fluid has a pH of around 7.6-7.64 with low protein content 0.1 g/l and has similar glucose content to plasma. When the amount of the fluid increases secondary to underlying pathology, a pleural effusion results. Pleural effusions are classified as either transudates or exudates. Transudates are usually bilateral and result from mechanical factors influencing the rate of formation or re-absorption of pleural fluid. The fluid collection occurs due to increased pulmonary capillary pressure as in congestive heart failure, or a decrease in colloid osmotic pressure as in renal disease. Exudates are usually unilateral and occur due to increased capillary permeability and generally of infectious etiology. Pleural fluid protein level >30 g/l or the Light’s criteria (Table 1) differentiates exudates from transudates.

The most common aetiology of a pleural effusion in the paediatric population is an underlying pneumonia, followed by congenital heart disease and less commonly, malignancy. It was said that approximately 1% of child with pneumonia had associated pleural effusions while pleural effusions were present in 40-50% adult pneumonia patients.

History

Aristotle recognised the entity of empyema and described drainage of empyema fluid with incision. Hippocrates established that death would occur if empyema did not rupture. Sir William Osler, in his 1901 text, the Principles and Practice of Medicine, stated that empyema should be treated as an ordinary abscess, “with incision and drainage”.

Terminology

Parapneumonic effusion (PPE): any effusion associated with bacterial pneumonia, lung abscess, or bronchiectasis
Complicated PPE: PPE for which tube thoracostomy is necessary for resolution
Loculated PPE: PPE that is not free flowing
Multiloculated PPE: loculated PPE with more than 1 compartment
Empyema: pus in the pleural space.

Staging of Pleural Infections

Exudative stage: pleural fluid is free flowing with low white blood cells count (WBC) and lactate dehydrogenase (LDH) (<1,000 IU/L), normal glucose (>60 mg/dl), and pH (>7.3)

Fibropurulent stage: characterised by increase inflammation, invasion of bacteria and deposition of fibrin leading to loculation. There is an increase in WBC, LDH (>1,000 IU/L), glucose (<40 mg/dl), pH (<7.2)
Organisational stage: fibroblasts infiltrate the pleural space leading to formation of thick pleural peel

One should note that the biochemical findings of the pleural fluid have not been fully validated in paediatric population.

Epidemiology

The annual incidence of PPE and empyema was 3.3 per 100,000 children. Many studies suggest that the prevalence of empyema complicating childhood pneumonia is increasing in both the USA and the U.K.
The trend is not altered despite the introduction of 7 valents pneumococcal vaccine in the USA though an earlier study by Scultz et al suggested that the prevalence may be decreasing. Empyema causes significant morbidities in childhood but rarely cause death, in contrast to adult empyema, which has an estimated mortality of 20%. Unlike adults, most children who develop empyema are previously healthy.

Microbiology

The organisms responsible for PPE are also the most frequent causes of pneumonia and sepsis. *Streptococcus pneumoniae* is the principle organism while staphylococcus is more commonly seen in age younger than 12 months and in developing world. *Haemophilus influenzae* type B is seen in 6-24 months and rare after 7 years in Western world. Group A *Streptococcus* is most commonly seen in school age children while anaerobes are commonly seen in age group younger than 2 years. Gram-negative organisms are seen in all ages. Mycoplasma pneumoniae, mycobacterium and fungus are rare causes of PPE and empyema.

Clinical Presentation

Clinical presentation of an empyema overlaps that of uncomplicated pneumonia or pleural effusion with symptoms including fever, chills, malaise, and shortness of breath, cough, pleuritic chest pain, splinting and referred pain to abdomen. Physical findings may include decreased breath sounds and chest wall excursion, crackles and friction rub on inspiration and dullness on percussion. Scoliosis toward the affect side may be detected. In addition, low blood oxygen saturation and dehydration may be present in child with severe illness.

Investigations

Radiological

Plain radiographs are the initial study of choice in diagnosis of a suspected effusion. The initial sign is blunting of the costophrenic angle and a rim of ascending fluid present in the lateral chest wall (meniscus sign) in erect film. British Thoracic Society (BTS) guidelines for management of pleural infection in children recommend PA or AP radiographs while there is no role for routine lateral radiograph. However, supine chest radiographs may only reveal diffuse hazziness in pleural effusion. Decubitus CXR allows free-flowing fluid to layer out in a dependent fashion. The amount of free flowing fluid needed to allow layering noted on lateral decubitus film is 5 to 10 mL.

Chest ultrasound is useful in identifying solid versus liquid lesions with 92% accuracy and can differentiate free from loculated fluid. It is useful to facilitate a thoracocentesis.

Computed tomography clearly visualises the underlying lung parenchyma. Loculations are also visualised with CT but not as good as chest ultrasound. It is valuable in management of complicated cases.

Blood

Blood culture should be performed in all patients with PPE. Typical laboratory findings include peripheral blood leucocytosis with a left shift with thrombocytosis. The ESR and CRP are usually markedly elevated at presentation. CRP values decrease more rapidly than the ESR and may be a useful indicator of adequate drainage and appropriate antibiotic selection. Acute and convalescent serology including ASO and anti-DNase B for *S. pyogenes* and a pneumococcal antibody panel for *Streptococcus pneumoniae* may be useful. Electrolytes should be monitored for the development of inappropriate ADH syndrome.

Pleural Fluid

The decision to do a thoracocentesis depends on the size of the effusion and the patient's symptom. Evidence-based guidelines for the evaluation of risk of complications based on pleural fluid analysis and clinical findings have been developed for adults by American College of Chest Physicians in 2000 but have not been fully evaluated in children. In adult, thoracentesis is indicated if the effusion is estimated greater than 10 mm in decubitus film. BTS guidelines recommended that biochemical analysis of pleural fluid is unnecessary in the management of uncomplicated PPE/empyema. If evaluation of pleural fluid is indicated, biochemical studies such as pH (determined using blood gas analyser), protein, LDH,
glucose should be obtained from the pleural fluid. The aspirated pleural fluid should be sent for microbiological analysis including Gram stain and bacterial culture, differential cell count, and if lymphocytosis is detected, TB and malignancy. Utine et al suggested that IL-8 concentration in the pleural fluid may be used as a marker to differentiate between uncomplicated and complicated PPE. Recent development of molecular techniques such as the polymerase chain reaction (PCR) to detect the unique sequences in bacterial 16S ribosomal DNA (rDNA) genes may become important for identifying the causative organism.

Other investigations
Expectorate sputum, if available, should be sent for bacterial culture. There is no indication of routine bronchoscopy in children.

Treatment

General
Oxygen should be given to the child if SpO2 is below 92%. Fluid therapy is indicated if the child is dehydrated or unable to drink. Antipyretics should be given to ease their discomfort in febrile children. Adequate analgesia is important to control the pleuritic pain and for management of chest drains. Chest physiotherapy is not found to be beneficial. Early mobilisation and exercise is recommended.

Specific
Effective therapy requires control of infection, resolution of the effusion and reexpansion of the lung in order to restore normal lung function. All cases should be treated with high dose intravenous antibiotics promptly and must include cover for Streptococcus pneumoniae and Staphylococcus aureus. Broader spectrum cover is required for hospital acquired infections, as well as those secondary to surgery, trauma, and aspiration. Antibiotics can later be adjusted if a particular organism is identified. Data from adults have shown that penicillin, carbenicillin, clindamycin, amikacin, and ciprofloxacin achieve adequate levels in pleural fluid as do data on cefuroxime in children. Although there are no evidence-based guidelines for the duration of antibiotic therapy, antibiotics should be intravenous till the child is afebrile and then continued orally for 1-4 weeks at discharge, but longer if there is residual disease.

Antibiotic Alone or in Combination with Simple Chest Drain
Traditionally, children with empyema have been treated with antibiotics alone or in combination with chest drainage. Those fail to improve on this regimen have gone on to an open surgical procedure.

A drain should be inserted for effusion which is enlarging or compromising respiratory function. It is also required in case of empyema. Some authors recommended placement of chest tube in complicated effusion determined by biochemical analysis of pleural fluid as loculation and further tissue damage likely resulted without a tube in this situation. However, the finding has not been validated in children. In the past, large bore chest tubes were used to drain pleural effusion because of concerns that thick pus would block the tube. More recently, small bore percutaneous catheters (8 to 12 F) have been used successfully in paediatric population. These catheters should be inserted at the optimum site suggested by the chest ultrasound. Large bore drains are preferentially placed in the mid-axillary line through the ‘safe triangle’ bordered by the anterior border of latissimus, the lateral border of the pectoralis major muscle, a line superior to the horizontal level of the nipple and an apex below the axilla. Trocar should not be used to insert a drain. The drain should be clamped for one hour once 10 ml/kg are initially removed. Jamal et al found that factors predicting failure for initial tube thoracostomy in parapneumonic collections were: an empyema rather than a simple parapneumonic collection; duration of symptoms >7 days, and a concomitant medical condition. Other authors reported that loculated collections were associated with failure of conservative treatment.

Fibrinolytics
The use of fibrinolytic agents in loculated pleural effusions has been shown to be effective therapy in
The mechanism of action is to decrease fibrinous strands in loculations and thereby clear the lymphatic pores. Effective filtration and reabsorption of the pleural fluid can then be established to restore the normal dynamics of pleural fluid circulation. Three different fibrinolytic agents are used: streptokinase, urokinase, and alteplase (also called tissue plasminogen activator, or tPA). There have been 16 paediatric case series and 3 randomised, controlled trials (RCTs) reviewed by Cremonesini et al with total 686 patients. The overall success rate (discharge without surgery) was 84.5% and failure was highest in the two Turkish studies. There was one multicentre randomised placebo trial in 60 children which shown a significant better outcome for the urokinase-treated group in terms of length of stay (7.4 vs 9.5 d). However another prospective trial by Singh et al in 40 patients did not find a substantial benefits of fibrinolysis (Streptokinase). Moreover a large, double blind trial in adults MIST1 did not show benefit for streptokinase verse placebo for both proportion of patient who died or needed surgery at 3 months. Also a metaanalysis and Cochrane review both failed to support the routine of fibrinolytic therapy. The recent BTS guidelines recommended to use either urokinase 40,000 units in 40 ml 0.9% saline given twice daily for 3 days to children aged 1 year above or 10,000 units in 10 ml saline if under 1 year. Urokinase 25000-100000 units (mean 3100 units/kg/day) and alteplase 0.1 mg/kg once daily with 1 hour dwell time appear effective and safe treatment. The adult findings are of questioning relevance in children as there are differences in mortality or need for surgery, comorbidity, nutrition, bacteriology and healing.

Others suggest that streptokinase and urokinase are less than ideal because of short half lives and lack of specificity for fibrin. They are unable to decrease viscosity of intrapleural pus to enhance chest tube drainage. MIST2 is currently undergone to assess the possible benefits of combined DNase and alteplase in adult patients

**Surgery**

Patient who fails to get a clinical and radiological response after 7 days of medical treatment (antibiotics, chest tube drainage and fibrinolytic) or has persistent sepsis with pleural effusion despite medical treatment should be considered for surgery. The surgical options are minithoracotomy, open decorticication and video-assisted thoracoscopic surgery (VATS). Formal thoracotomy and decortication is indicated in symptomatic child with organised empyema. In recent years, VATS has been advocated in the management of empyema at any stage in children. VATS allows visual inspection of the lung and pleura, optimal placement of chest tubes and immediate fibrinolysis and decortication if needed. Gates in 2004 published a limited systemic review of the literature on empyema management and found that thoracotomy (9.9 days) and VATS (10.5 days) had a significantly lower mean postoperative length of stay than chest tube alone (16.4 days) or in combination with fibrinolytics (18.9 days). A recent meta-analysis by Avansino et al compared operative and nonoperative management of paediatric empyema and suggested primary operative therapy was associated with lower mortality, reintervention, and length of hospitalisation, time of chest tube drainage, and time on antibiotic. Sonnappa et al directly compared fibrinolytic therapy (urokinase) with VATS in 60 children found no difference in total hospital stay, failure rate or radiological outcomes at 6 months. Moreover, VATS is 25% more expensive than intrapleural urokinase in their centre.

**Conclusion**

The prevalence of childhood empyema continues to rise and cause significant morbidities. The optimal
treatment of paediatric empyema remains controversial, awaiting larger randomised trials to be conducted. However, fibrinolytics and VATS are effective and enable patients for early discharge from hospital. A small flexible drain placed under sedation is less invasive and less painful than any operative procedure. Therefore, it is reasonable to use antibiotics plus fibrinolysis through a small bore chest tube under ultrasound guidance as initial management in children with empyemas. Also long term outcomes on these children are good following current treatment approach.

References

7. The genuine works of Hippocrates translated from the Greek with a preliminary discourse and annotation by Frances Adams. LDL 1849.


