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The Management of Paediatric Empyema

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Abstract Empyema is a recognised complication of bacterial pneumonia in children. It is a very different disease compared to that seen in adults as mortality is very rare, but it is associated with significant morbidity. The management of empyema in children is largely dependent on local centre expertise and physician bias as there are limited studies to guide best management. Recent properly controlled studies have attempted to address this. Fortunately, whichever treatment approach a physician chooses, the clinical outcome is usually excellent. This review summarises the causes, diagnostic issues and different management options available for a child with empyema.

Key words Empyema; Fibrinolytics; Parapneumonic effusion; Video-assisted thoracoscopic surgery

Introduction

Empyema is an important complication of pneumonia and is a significant cause of morbidity in children. It is estimated that 0.6% of pneumonias progress to empyema in children affecting about 3.3 per 100,000 children.[1] Recent studies from countries such as USA[2-4] and the United Kingdom[5-11] suggest that the incidence of empyema is increasing. The definite cause of this increase in incidence of childhood empyema is unknown but is thought to be related to several reasons such as: the change in antibiotic prescription pattern; late referral to an appropriate centre; or as a direct effect of the introduction of pneumococcal vaccination resulting in replacement disease with serotypes not covered in the vaccine.[2,3,12-15] However, the increase in incidence in empyema has also been seen in England[6,7] and Scotland[5] prior to the introduction of pneumococcal vaccination.[16,17] Empyema is a very different disease compared to that seen in the adult population in which there is 20% mortality[4] and therefore it is inappropriate to extrapolate studies from adults to children where death fortunately rarely occurs.

Defining Empyema

The pleural space usually contains 0.3 ml of pleural fluid per kilogram of body weight. This fluid is usually sterile and prevents friction between the visceral and parietal pleura .There is a continuous circulation of pleural fluid within the pleural space and drainage is facilitated by lymphatic stomata. A disruption of this normal pleural fluid circulation either by an increased production, decreased reabsorption or increase in vascular permeability, will result in accumulation of pleural fluid.[18]

Empyema is defined as having purulent pleural collection in association with an underlying pneumonia. The American

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Thoracic Society has classified the empyema process into three distinct stages:[19]

1. Exudative: also known as simple parapneumonic effusion which is the result of accumulation of clear fluid with a low cellular count in response to the inflammatory process associated with the underlying pneumonia. In adults this stage is characterised by a normal pleural fluid pH and a lactate dehydrogenase (LDH) less than 1,000 IU.[20]
2. Fibrinopurulent (complicated parapneumonic effusion): frank pus is present with thicker fluid and deposition of fibrin in the pleural space leading to septation and loculation. Fluid microscopy usually shows increased white cells particularly neutrophils and degenerated cells. In adults the pleural pH is <7.2 and LDH >1,000.[20]
3. Organising: fibroblasts infiltrate the pleural cavity and transform the thin intrapleural fibrin membranes into thick and non-elastic peels which may prevent the lung's ability to re-expand and impairs gas exchange.[16,17]

Aetiology

Effusions are usually unilateral when associated with bacterial infections; bilateral effusions are less common and may indicate tuberculosis or may also be secondary to other underlying conditions such as malignancy, heart failure, renal disease, connective tissue disease or post trauma.[21-23]

The bacterial cause of empyema varies depending on the commonest cause of community-acquired pneumonia in that geographical location. *Streptococcus pneumoniae* is the most common cause in the developed world while *Staphylococcus aureus* is the commonest cause in the developing world.[17,24] The reported rates of identifying an infectious cause from pleural fluid vary from between 8 and 76%.[21-23] Pleural fluid is usually sterile due to the widespread early use of antibiotics prior to obtaining the sample for culture.[16] New molecular techniques utilise polymerase chain reaction (PCR) for example, to detect the unique sequences in bacterial 16S ribosomal DNA genes and therefore increase the likelihood of identifying a causative organism in conjunction with bacterial culture.[25]

In a study from Newcastle, UK *Streptococcus pneumoniae* was detected by PCR in 75% of culture negative pleural fluid samples.[9] Other bacterial causes of empyema include *Streptococcus pyogenes*, *Haemophilus influenzae*, Mycobacterium species, *Pseudomonas aeruginosa,* anaerobes, *Methicillin resistant staphylococcus aureus* and *Mycoplasma pneumonia*. Extremely rarely fungi may be a cause which tends to be nosocomial in origin with Candida species being the commonest cause.[18] The contribution of viruses to the development of empyema is not accurately known, as only a few studies have addressed this.[16]

Diagnosis

Clinical Presentation

Classically a patient with empyema presents with symptoms of pneumonia with persistent fever, malaise and lethargy early in the disease. Cough and tachypnoea subsequently develop due to progression of the underlying pneumonic process and children become more unwell as the effusion develops. Pleural pain and referred abdominal pain may be a feature especially in older children. Scoliosis toward the affected side is not uncommon.[26] Examination usually reveals an ill looking tachypnoeic child with reduced or absent breath sounds, crepitations and dull percussion on the affected side. Children often prefer to lie on their affected side.

Blood

Initial full blood count may show leukocytosis, thrombocytosis and anaemia. Acute phase reactants are usually elevated, but are unable to distinguish between viral and bacterial infections. White blood count and C-reactive protein are useful in monitoring progress. Delber et al found that C-reactive protein was a sensitive marker in making the diagnosis and in the follow up of treatment response in children with empyema.[27] However, repeated phlebotomy should not be done routinely, particularly if children are improving clinically. Blood cultures should be performed in all patients with parapneumonic effusion.[16] The serum may also be sent for molecular techniques to detect organisms, if available.

Imaging

Chest X-rays should be done on all patients with signs of pleural effusion to confirm the diagnosis (Figure 1). They cannot differentiate whether an effusion is infected or not. Lateral X-rays rarely add anything extra to the diagnosis and should not be done routinely.[16,28]

Chest ultrasound remains the gold standard method to determine accumulation of fluid in the pleural cavity (Figure 2). It helps differentiate extensive consolidation from overlying

pleural fluid in a case of a complete "white out" on the chest X-ray. It also detects loculations, fibrin strands and estimates the size of the collection and may guide chest drain insertion if needed.

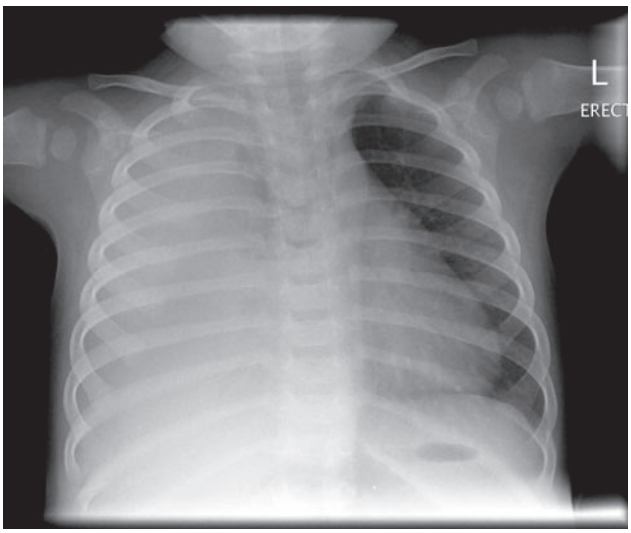

Figure 1 Chest X-ray showing a complete "white out" of the right side.

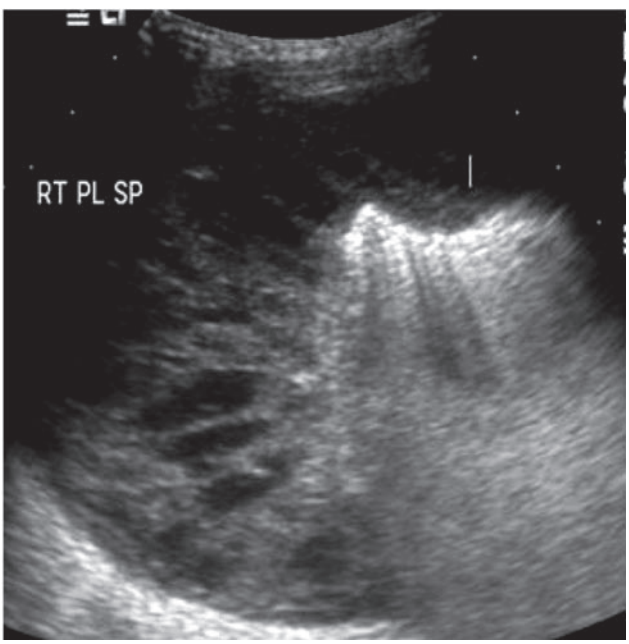

Figure 2 An ultrasound of the chest showing a semi-solid right pleural collection that is hypoechoic and multiple thin septations within it.

Computed tomography (CT) scans detects more lung parenchymal changes than chest X-rays (Figure 3), however, the additional information does not alter management and is unable to predict clinical outcome, and therefore, its routine use in children is not recommended.[29] Coren et al found that CT scans were least useful in the preoperative assessment of empyema.[7,30] Chest CT has a role in complicated cases where children are not clinically improving or if malignancy is suspected. Surgeons may request a chest CT before surgery as a 'road-map' for the procedure if undertaking video-assisted thoracoscopic surgery; however, this is not the practice of all surgeons.[31]

Pleural Fluid

Frank pus or a turbid pleural fluid sample is diagnostic of empyema. Fluid should be sent for gram stain, culture and differential cell count when a chest drain is inserted or surgery is performed. A predominance of lymphocytes in the fluid should raise the possibility of malignancy or tuberculosis, for which cytological examination and staining for acid fast bacilli should be performed. In adults, diagnostic thoracocentesis is performed routinely and pleural markers such as pH are used to guide therapy, including chest drain insertion. There is little evidence that the biochemical markers in the pleural fluid of children have any role in guiding management of empyema. Chiu

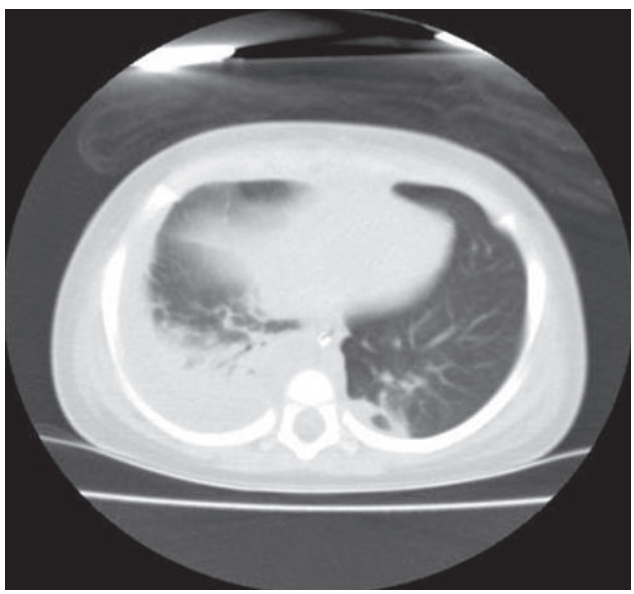

Figure 3 CT of the chest showing an area of consolidation with an associated moderate sized pleural effusion in the right hemi-thorax.

et al[32] demonstrated that the increased release of proinflammatory cytokines, such as tumour necrosis factor-α (TNF-α), interleukin-1β (IL-1β) and IL-6 caused by bacteria as the disease progresses, resulted in an imbalance of the fibrinolytic system enzymes, tissue-plasminogen activator (tPA) and plasminogen activator inhibitor type 1 (PAI-1) which subsequently led to fibrin deposition. The study found that a decrease in pleural pH and glucose values and an increase in the pleural lactate dehydrogenase concentration were correlated with the progression of the parapneumonic effusions as previously reported.[33,34] They also found that IL-β, PAI-1 and pH were the most reliable pleural markers to predict severity of pleural infection and subsequent need for interventions. Future studies are required to confirm that these markers are useful in guiding intervention. However, the utility of biochemical markers in the pleural fluid in children is limited as diagnostic thoracocentesis is not recommended in children as it is invasive.

Lower Respiratory Tract Secretions

Culture of the lower respiratory tract secretions should be sent if possible to rationalise antibiotics. Bronchoscopy is not routinely indicated although bronchoalveolar lavage may isolate an organism but this is usually unnecessary if pleural fluid is available.

Management

The treatment a child receives for empyema is usually affected by several factors including local practice guidelines, physician bias and expertise, availability of medication, instruments and family preference. The aim of treatment of empyema is to eradicate the infection, restore normal pleural fluid circulation, re-expand the lungs and return to normal respiratory function. Initial therapy consists of oxygen when needed, fluid therapy in cases of dehydration, antipyretics, analgesics and antibiotics. Physiotherapy is usually not beneficial apart from encouraging the child to mobilise and cough.[16]

Specific treatment for empyema ranges from conservative management to a number of different surgical approaches. Despite these differences, the management outcome in paediatric empyema is considerably good compared to adults, irrespective to the method of treatment a child receives.[16,17,35,36]

Treatment Options

1. Antibiotics alone or with chest drain insertion

As soon as a child is diagnosed with empyema intravenous antibiotics should be commenced according to the local guidelines. Generally broad spectrum antibiotics are used to cover the most common organisms causing community acquired pneumonia in the geographical region from which the child comes. Antibiotics alone usually have a role in small effusions when the child has no respiratory compromise. This method of treatment should be reconsidered if there is no improvement within 48-72 hours from initiating therapy, or if there is evidence of an enlarging effusion at which stage the effusion may need to be drained. Adequately trained personnel should insert drains under ultrasound guidance with adequate sedation and analgesia or general anaesthesia. The size of the chest drain is still controversial; small drains are more tolerable and comfortable for children and easier to insert allowing for mobilisation and coughing. However they are prone to blocking with fibrinous material if fibrinolytics are not instilled regularly. Intravenous antibiotics are usually continued for 24 hours after drain removal and the patient is afebrile. While conservative treatment with antibiotics and chest tube drainage is usually effective in 60-80% of cases, it is associated with a prolonged hospital stay (14-24 days) when compared with other interventions.[35,36] Repeated thoracocentesis should not be performed to limit repeated trauma to a child.

2. Fibrinolytics

The intrapleural use of fibrinolytics has become standard therapy in many countries. Fibrinolytics are instilled into the pleural cavity through the chest drain to lyse fibrinous strands and clear lymphatic pores thus overcoming chest tube occlusion by debris, facilitate better drainage and re-establish pleural circulation. Several studies using fibrinolytics in paediatric empyema have been published.[37-40] Comparisons between the studies are difficult as they used different protocols and fibrinolytics such as streptokinase, urokinase, alteplase or (tPA). The success rate in these series was approximately 80-90% with the major side effect being pain during administration. They all concluded that the use of fibrinolytics in children is safe. There are no randomised controlled studies in children comparing different fibrinolytic agents. In a British multicentre study, Thomson et al[40] demonstrated that using Urokinase at a dose of 40000 units diluted in 40 ml normal saline (10000 units diluted in

10 ml saline if less than 1 year of age) shortened the hospital stay significantly compared to instilling normal saline. Those children in whom a smaller percutaneous drain was used had a shorter hospital stay compared to large bore drains. It is unknown if this is the optimal dose of Urokinase for use in children, but it is a protocol adopted by many centres.

3. Surgery

There are no evidence-based criteria to guide the optimal timing of surgical intervention in empyema management. The surgical options are mini-thoracotomy, open decortication and video-assisted thoracoscopic surgery (VATS).

Open decortication involves the removal of thickened pleural rind and irrigation of the pleural cavity through a large posterolateral incision. It is a long and complicated procedure leaving a large scar. A prospective study compared 30 children who were randomised to receive either open thoracotomy or chest tube insertion demonstrated shorter hospital stay in the thoracotomy group.[41]

Mini-thoracotomy is a debridement procedure performed through a small incision similar to VATS but it is an open procedure, which leaves a small linear scar along the rib lines.[42]

VATS is a less invasive method of decortication suitable in children who will tolerate single lung ventilation during anaesthesia. It achieves debridement of fibrinous pyogenic material, breakdown of loculations and drainage of pus from the pleural cavity under direct vision through 2-3 small incisions.[43]

The choice of surgical intervention is mainly dependent on access to a specific service, local surgical experience and expertise. No studies have directly compared open thoracotomy to VATS. Kurt et al compared VATS with chest drains alone in 18 patients and found that VATS had significantly shorter hospital stay, less days with chest tube and less narcotic use.[37] In a prospective randomised study, Sonnappa et al compared VATS to small percutaneous chest drain and 3 days of intrapleural urokinase in a group of 60 children and concluded that there was no difference in the clinical outcomes of both.[39] However, importantly VATS was a more expensive option and required the availability of appropriate equipment and suitably trained surgeons. These studies suggest that urokinase and percutaneous drainage may be the most cost effective strategy for treating children with empyema.[44]

Conclusion

While we are in an era of evidence based practice, the British Thoracic Society guidelines on the management of empyema in children highlight the lack of available Grade A recommendations.[16] Since its publication in 2005, some properly conducted studies have been carried out to answer some of these questions. Nevertheless, irrespective of the treatment modality a child receives, the clinical outcome is excellent. Properly designed studies are required to answer many questions in this field which will help to identify the best practice in the diagnosis and management of childhood empyema.

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