Management of children and adolescents with pleural empyema

These guidelines should be read in conjunction with this DISCLAIMER

This guideline provides an evidence-based framework for the assessment, investigation and management of children and adolescents presenting at Princess Margaret Hospital for Children with a pleural empyema.

Definition

Pleural empyema is a parapneumonic effusion (a pleural collection in association with underlying pneumonia) that contains pus. The empyema process is a continuum, but for descriptive purposes can be divided into 3 stages[1]:

1. Exudative – clear fluid with a low white cell count
2. Fibrinopurulent – increasing white cell count with fibrin deposition leading to septation and loculation
3. Organising – thick, non-elastic peel formation

Background

The incidence of empyema is increasing worldwide[2-4]. Whilst there is limited high quality evidence to guide the management of children with empyema, the outcome is usually excellent irrespective of the initial approach, with normal Chest X-Ray and lung function at long term follow up[5-8].

There are a number of management options available[9,10]. These include antibiotics alone or in combination with chest drain insertion[11] (small or large bore, with or without intrapleural fibrinolytic therapy) and surgical approaches[12-14] (video-assisted thoracoscopic surgery (VATS), mini-thoracotomy or open decortication). However, since most patients make a complete recovery irrespective of the initial treatment modality, decisions regarding management should ideally aim to reduce short-term morbidity (e.g. time to resolution of fever, length of hospital stay, pain etc).

Aetiology

The majority of children and adolescents presenting to hospital with an empyema are previously fit and healthy and develop this secondary to acute bacterial pneumonia.

The most common pathogens causing empyema in Australia are *Streptococcus pneumoniae* and *Staphylococcus aureus* (both Methicillin susceptible *S.aureus* - MSSA and Methicillin resistant *S.aureus* - MRSA). Other organisms may include: *Group A Streptococcus, Streptococcus milleri group, Haemophilus influenzae.* Uncommon

causes are *Mycoplasma pneumonia, Chlamydia pneumonia, Pseudomonas aeruginosa*, *Burkholderia pseudomallei*, *Klebsiella* species and *Mycobacterium tuberculosis*.

In children at risk of aspiration, anaerobic organisms should be considered.

Diagnosis

History - patients usually present with symptoms of pneumonia, including cough, shortness of breath, fever, lethargy and chest or abdominal pain.

In a patient already diagnosed with pneumonia, empyema should be considered in children with persisting fever or a lack of clinical improvement after 48 hours antibiotic therapy.

Examination - pyrexia, tachypnoea, unilateral signs of decreased chest expansion, dullness to percussion and reduced/absent breath sounds suggest the presence of a pleural collection.

Imaging

- ***Chest X-Ray (CXR)*** - may merely demonstrate a loss of the costophrenic angle or a complete "white out". CXR cannot always differentiate severe consolidation/collapse from a pleural collection, but the presence of mediastinal shift away from the pathology supports the diagnosis of a pleural collection.
- ***Chest ultrasound*** - confirms the presence and can estimate the size of the pleural collection, as well as the echogenicity of fluid and the presence of loculations. There is no evidence that ultrasound findings reliably predict success or failure of conservative management (i.e. chest drain +/- fibrinolytic therapy) in children with empyema[10,15,16]. At the time of the ultrasound, the Radiologist should mark the optimum site for later drainage.
- ***CT chest scan*** - detects more parenchymal changes. CT does not provide additional benefit over ultrasound when chest drainage is being considered, but may be useful if surgical intervention (e.g. decortication) is being considered[16].

Blood tests - A blood culture and Pneumococcal PCR performed on EDTA blood should be collected in all children with empyema. Plasma albumin is often low in children and adolescents with empyema (compared to simple pneumonia), although this rarely needs specific treatment. Longitudinal measurements of inflammatory markers (CRP, WCC, platelets) may be helpful in assessing the response to therapy.

Pleural fluid - A sample of pleural fluid should be obtained as early as possible, to maximise the chances of identifying the causative organism. In most instances, the sample of pleural fluid can be obtained at the time of chest drain insertion. A fine needle aspiration of pleural fluid, obtained under ultrasound guidance, should be considered in some circumstances:

- Individuals with a small amount of pleural fluid and minimal respiratory distress, who are going to be managed with antibiotics alone and no formal drainage
- If there is any suggestion that the effusion is not infective, obtain a sample for cytological analysis.

Pleural fluid should be collected into a sterile yellow top container. In addition, pleural fluid should be inoculated into a BACTEC™ PEDS PLUS™ blood culture bottle (1-5ml) and an EDTA blood tube (1-3ml)

The following tests should be requested:

- Cell count, Gram stain and culture
- Pneumococcus and *Staphylococcus aureus* PCR

Other investigations:

Sputum - send for microscopy, culture and sensitivity (MC&S).

Nasopharyngeal aspirate or throat swab – send for respiratory virus detection.

Pleural fluid for mycobacterial culture and Adenosine Deaminase (ADA) - the following investigations should be considered If pleural tuberculosis is being considered (birth or travel to high-incidence country, exposure to index case or subacute presentation), consider the following investigations:

Additional respiratory specimens for AFB stain, mycobacterial culture, mycobacterial PCR and ADA should be requested.

Isolation in a negative pressure room is required if tuberculosis is being considered.

Management

Supportive - children should receive oxygen supplementation if hypoxic (oxygen saturation <93%), fluid therapy if dehydrated and adequate analgesia.

<u>Empiric Antibiotics</u>

In children with empyema IV Ceftriaxone 50mg/kg (to a maximum of 2grams) daily AND IV Vancomycin 15mg/kg (to a maximum initial dose of 750mg) 6 hourly is recommended. This will provide empiric cover against the common organisms including *Streptococcus pneumoniae*, *Staphylococcus aureus* (both Methicillin susceptible and resistant *S. aureus*), *Group A Streptococcus, Streptococcus milleri group and Haemophilus influenzae,*

If there is a history suggestive of aspiration, add IV Clindamycin (10mg/kg) 8 hourly to Ceftriaxone instead of Vancomycin

If the child resides in the far north of Western Australia, consideration should be given to melioidosis (*Burkholderia pseudomallei*) or *Acinetobacter* infection, although *Streptococcus pneumoniae*, *Staphylococcus aureus* will still be the most likely pathogens. If there is a significant history of allergy to beta-lactams or vancomycin, alternative antibiotics will be required. For very ill children, the additional anti-Staphylococcal antibiotics (eg flucloxacillin, clindamycin, linezolid) cover should be considered. Discuss these situations with an Infectious Diseases Physician or Clinical Microbiologist.

NB: If an organism is cultured and sensitivities are known, the choice of intravenous and oral antibiotics should be reviewed.

Pathogen-directed antibiotics

Antibiotics should be reviewed in all children after microbiological results are available. Antibiotics should be modified based upon:

- Results of blood culture, pleural culture and blood/pleural PCR
- Clinical response

Most children with pneumococcal empyema can be treated with IV penicillin (60mg/kg 6 hourly to a maximum of 2.4g qid) and then oral Amoxycillin (30mg/kg three times daily, maximum 1g tds). IV Ceftriaxone may be used if reduced susceptibility to penicillin is identified or to facilitate outpatient IV treatment.

Most children with Methicillin-sensitive *Staphylococcus aureus* empyema can be treated with IV Flucloxacillin (50mg/kg 6 hourly to a maximum of 2g qid) and then either oral cephalexin (25mg/kg/dose 4 times daily, maximum of 1g qid) or amoxycillin/clavulanic acid (25mg/kg/dose of the amoxycillin component twice daily, maximum of 875mg per dose)

Children with Methicillin-resistant *Staphylococcus aureus* empyema should be discussed with an Infectious Diseases Physician or Clinical Microbiologist as sensitivity of individual pathogens may vary.

In children in whom no pathogen is identified, empiric intravenous therapy (IV Ceftriaxone and Vancomycin) should be maintained until clinical improvement. Amoxycillin/clavulanic acid (25mg/kg/dose of the amoxycillin component twice daily, maximum of 875mg per dose) is the preferred oral agent.

Children who are known to be colonised with MRSA should be discussed with an Infectious Diseases Physician or Clinical Microbiologist.

Length of antibiotics - children should receive intravenous antibiotics at least until afebrile for 24 hours. If a child is having a chest drain inserted under general anaesthesia or sedation, consideration should be given to inserting a PICC line at the same time, to avoid issues with venous access. Oral antibiotics should be given after discharge for a period of 1-4 weeks, or longer if necessary. The length of treatment depends on factors including the severity of the disease, causative organism and complications.

No chest drain versus chest drain - Children with a small pleural effusion and minimal respiratory distress may respond to antibiotics alone, whereas those with a moderate-large sized pleural effusion and/or moderate-severe respiratory distress will require drainage.

NB: Some children with a small pleural effusion, who are being appropriately managed with antibiotics alone, will progress to develop a moderate to large sized pleural effusion requiring drainage. If no improvement after 48 hours of signs of clinical deterioration, consider a repeat chest ultrasound and/or consultation with Respiratory Medicine.

Chest drain insertion versus early surgery - there are two prospective random control trials that have compared the outcomes of children with pleural empyema managed by chest drain plus fibrinolysis versus VATS[12,13]. Neither study demonstrated any evidence to support a better clinical outcome (short or long term) from VATS compared to a chest drain plus fibrinolysis in children with empyema. Thus, the decision to proceed with a chest drain or VATS should be based on the availability to proceed to drainage of the pleural collection without undue delay.

Currently at PMH, a chest drain can be inserted on ICU with minimal delay, meaning that a chest drain plus fibrinolysis should be first option for children/adolescents with a pleural empyema requiring drainage, unless specific circumstances dictate otherwise

Chest drain - a pigtail catheter should be inserted with appropriate analgesia and sedation either in ICU or theatre. There is no evidence that large bore drains confer any advantage, so small pigtail catheters are preferred to minimise discomfort. Once 10mls/kg pleural fluid has been removed, clamp the drain for 1 hour (to reduce the very small risk of re-expansion pulmonary oedema)[9]. The chest drain should be aspirated every 4 hours and then re-clamped. There is no evidence to suggest that chest drains placed under suction confer any advantage.

Fibrinolytics - intrapleural Alteplase (tissue type plasminogen activator, tPA) should be instilled if the pleural fluid obtained is turbid or if there is evidence of loculations on ultrasound [9,17.]

Dose:

- For patients >10 kg, instil Alteplase 0.1mg/kg (maximum 6mg) in 1ml/kg 0.9% saline (maximum volume 50mls) and clamp the drain for 1 hour[11,13]. Give once daily for 3 days only.
- For patients <10 kg, instil Alteplase 0.1mg/kg in 10mls 0.9% saline and clamp the drain for 1 hour[11,13.] Give once daily for 3 days only.

Minor side effects reported following treatment with intrapleural fibrinolytics include transient chest pain during instillation and transient blood staining of the pleural fluid. Intrapleural bupivicaine 0.25% can be instilled (0.5-1.0mls/kg) at the same time as tPA if significant discomfort[9].

Rare cases of immediate hypersensitivity reaction and cases of bleeding have been reported in adults.

If the clinical status of the child deteriorates at any time (eg: increased shortness of breath or chest pain), examine the patient, **UNCLAMP CHEST DRAIN IMMEDIATELY** and consider an urgent portable CXR.

Chest drain removal – The timing of chest drain removal is a clinical decision that should be based on a number of factors, including the amount of fluid draining and the clinical status of the child. It is not necessary to await complete cessation of drainage and the chest drain can generally be removed if drainage is less than 1-2ml/kg/24h. It may be useful to get a repeat ultrasound to confirm the absence of a significant amount of fluid when nothing is draining, to ensure the fluid is not simply loculated or the drain blocked. The chest drain should be removed either while the child performs a Valsalva manoeuvre or during expiration, with a brisk firm movement. A chest x-ray should be taken shortly afterwards to ensure a pneumothorax has not developed during removal.

Analgesia – Pleuritic pain as well as the discomfort of a chest drain may reduce deep breathing and affect the child's willingness to cough, so adequate analgesia should be provided to keep the child comfortable.

Physiotherapy - to assist in early mobilisation only. Chest physiotherapy is not beneficial.

Follow up

Children and adolescents should be followed up as an outpatient until they have fully recovered and the CXR has returned to normal. Most radiographs return to near normal within 3-6 months[9].

Routine immune function tests are not necessary, but may be considered in selected cases[9]. In young infants with a pleural empyema secondary to *Staphylococcus aureus* or *Pseudomonas aeruginosa* consider a sweat test to exclude cystic fibrosis.

Related policies, procedures, protocols and guidelines

Children's Antimicrobial Management Program (ChAMP)

References

1.Hamm H, Light RW. Parapneumonic effusion and empyema. *Eur Respir J* 1997;10:1150-6.

2. Byington CL, Spencer LY, Johnson TA, *et al*. An epidemiological investigation of a sustained high rate of pediatric parapneumonic empyema: risk factors and microbiological associations. *Clin Infect Dis* 2002;34:434-40.

3. Spencer DA, Iqbal SM, Hasan A, *et al*. Empyema thoracis is still increasing in UK children. *BMJ* 2006;332:1333.

4. Gupta R, Crowley S. Increasing paediatric empyema admissions. *Thorax* 2006;61:179.

5. Satish B, Bunker M, Seddon P. Management of thoracic empyema in childhood: does the pleural thickening matter? *Arch Dis Child* 2003;88:918-921.

6. McLaughlin FJ, Goldmann DA, Rosenbaum DM, *et al*. Empyema in children: clinical course and long-term follow-up. *Pediatrics* 1984;73:587-93.

7. Redding GJ, Walund L, Walund D, *et al*. Lung function in children following empyema. *Am J Dis Child* 1990;144:1337-42.

8. Kohn GL, Walston C, Feldstein J, *et al*. Persistent abnormal lung function after childhood empyema. *Am J Respir Med* 2002;1(6):441-5.

9. Balfour-Lynn IM, Abrahamson E, Cohen G, *et al*. BTS guidelines for the management of pleural infection in children. *Thorax* 2005;60 (Suppl 1):i1-21.

10. Paediatric Empyema: Recommendations for Management. Position statement from the Thoracic Society of Australia and New Zealand 2010.

11. Thomson AH, Hull J, Kumar MR, *et al*. Randomised trial of intrapleural urokinase in the treatment of childhood empyema. *Thorax* 2002;57:343-7.

12. Sonnappa S, Cohen G, Owens CM, *et al*. Comparison of urokinase and video-assisted thoracoscopic surgery for treatment of childhood empyema. *Am J Respir Crit Care Med* 2006;174:221-7.

13. St. Peter SD, Tsao K, Harrison C, *et al*. Thoracoscopic decortication vs tube thoracostomy with fibrinolysis for empyema in children: a prospective, randomised trial. *J Pediatr Surg* 2009;44:106-111.

14. Carey JA, Hamilton JR, Spencer DA, *et al*. Empyema thoracis: a role for open thoracotomy and decortication. *Arch Dis Child* 1998;79:510-13.
15. Kalfa N, Allal H, Lopez M, *et al*. Thoracoscopy in pediatric pleural empyema: a prospective study of prognostic factors. *J Pediatr Surg* 2006;41:1732-7.
16. Jaffe A, Calder AD, Owens CM *et al*. Role of routine computed tomography in paediatric pleural empyema. *Thorax* 2008;63:897-902.
17. Wells RG, Havens PL. Intrapleural fibrinolysis for parapneumonic effusion and empyema in children. *Radiology* 2003;228(2):370-78.

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