

Review of the management of empyemas

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An empyema is a collection of pus in the pleural cavity. It is a serious pathological condition of the pleural space and it can have high morbidity and mortality rates. The most frequent cause of empyema is infection stemming from a parapneumonic effusion. Special challenges in management arise with post-surgical empyemas and those linked to Tuberculosis. This article concentrates on addressing the management of parapneumonic effusions/empyemas.

In the initial stages of empyema, in which the fluid collection is free, antibiotic therapy alone may suffice, and drainage is seldom imperative. However, in advanced stages, a comprehensive approach involving both antibiotics and simultaneous drainage becomes essential. Various methods can be employed for drainage. Notably, thoracic surgical interventions play a pivotal role in draining empyemas.

History of managing empyemas

Empyemas were initially documented by Hippocrates in 460-370 B.C. [1]. In that historical period, the exclusive treatment for empyemas involved open drainage, a method linked with significant mortality and morbidity. Until the 19th century, there were no notable advancements in empyema management. In 1873, Playfair pioneered the use of a water seal drainage system in treating a child with empyema. Subsequently, in 1875, German physician Gotthard Bulau introduced a closed water seal drainage system as an alternative to open drainage [2].

During the influenza epidemic in 1917-1919, a closed chest tube drainage system was experimentally tested. In 1947, the first attempt at intrapleural fibrinolytic therapy was made. Closed chest tube drainage emerged as the standard treatment for empyemas in the late 1950s. Today, both open and minimally invasive thoracic surgery play crucial roles in the management of empyemas.

Causes of empyemas

The most frequent cause of empyema is an infected parapneumonic effusion resulting from pneumonia. Additionally, empyemas can arise from infection in penetrating chest injuries, undrained haemothoraces, rupture of the esophagus, and upper abdominal infections communicating with the pleural cavity. Iatrogenic factors, including repeated pleural aspirations, intercostal tube insertion, and thoracic and esophageal surgery, are also commonly identified as causes for empyemas [3].

Pathophysiology of empyema

This article will delve into the pathophysiology of parapneumonic empyemas, encompassing the broader understanding of empyema pathophysiology in general.

In pneumonia, acute inflammation triggers heightened vascular and mesothelial permeability, initially leading to a transudative pleural effusion. Inflammatory mediators, including IL-6, IL-8, Tumor Necrosis Factor- α , toxic oxygen species, and free radicals, further compromise the vascular endothelium, escalating vascular permeability.

Consequently, there is leakage of plasma proteins and cellular components such as neutrophils, transforming the effusion into an exudative state, though not yet infected.

The process advances with bacterial translocation, leading to the infection of the parapneumonic effusion.

Although free-flowing effusions can frequently respond positively to antibiotics and may resolve without drainage, infected effusions or empyemas containing frank pus require prompt and efficient drainage to avert potential complications.

In exudative effusions, plasma proteins and clotting factors including fibrinogen are present and the clotting cascade is activated in the pleural cavity. Fibrinogen is converted to fibrin and it is deposited over the visceral and parietal pleural surfaces. This is called fibrinopurulent effusion. Fibrin layers form septations, and the free flowing effusion is converted to a multiloculated effusion. Once it is loculated, it is extremely difficult to drain by simple means such as pleural aspiration or intercostal tube insertion and may need surgical drainage.

If the fibrin layer persists for an extended period, it becomes organized and fibrosis occurs. Fibrous tissue over the visceral pleura undergoes contraction resulting in an entrapped lung. Fibrous contractures over the parietal pleura narrow down the intercostal spaces leading to overcrowding of the ribs and results in a chest wall deformity. Ultimately both lung and chest wall functions are severely affected. This state is called a fibrothorax.

Pus in the pleural cavity may track down through the chest wall and this is called empyema necessitans. If pus discharges through the lung parenchyma or bronchial tree, a bronchopleural fistula will occur [3, 4].

Microbiology

Contrary to the common belief, causative organisms of empyema may be quite different from causative

organisms of the underlying pneumonia. Therefore microbiological analysis of the empyema is very important to guide antibiotic therapy.

Empyemas are caused by various organisms and it may be polymicrobial in origin. Common causative organisms include streptococcus species such as *streptococcus milleri*, *streptococcus pneumoniae*, *staphylococcus aureus*, Methicillin Resistant *Staphylococcus Aureus* (MRSA), various gram negative organisms and anaerobic bacteria. Anaerobic bacteria may occur as a component of polymicrobial infection or as the sole causative agent of the infection.

Enterobacteria, enterococci and *mycobacterium tuberculosis*, must always be considered as the cause for an empyema.

The microbiology may vary according to the location and age. For example, community acquired empyemas in adults are commonly caused by *Streptococcus milleri*; in children *Streptococcus pneumoniae* is the commonest cause. However, local epidemiological and microbiological data must be considered as guidance in managing empyemas [3, 4].

Staging of empyema

The pathophysiology of an empyema is a continuous process and its staging is rather imaginary and may be unrealistic. However, to guide the decision making process, empyemas are categorised into 3 stages.

Stage 1- Simple parapneumonic effusions. In this stage the effusion is exudative in type and is free flowing. It is usually sterile.

Stage 2- Complicated parapneumonic effusion/empyema (fibrinopurulent stage).

In this stage the effusion is infected and it may be free flowing or loculated.

Stage 3- Organized stage.

In this stage organization of fibrinous peel results in a fibrous coat and is called a fibrothorax.

As the pathological process is a continuum, these stages are sometimes indistinct and all three stages may be coexistent at any given point in time. Staging may be guided by clinical, radiological and intraoperative findings.

Clinical features

Clinical features are often vague and nonspecific and are mostly related to the underlying pneumonia. Patients often present with a recent history of lower respiratory tract infection or pneumonia. When the course of the pneumonia is prolonged and features of ongoing infection persist despite appropriate treatment for more than three days, the occurrence of an empyema should be considered. Fever, cough, purulent sputum expectoration, haemoptysis, chest pain and dyspnoea are common symptoms. On examination, dyspnoea, reduced respiratory movements in affected side, absent vocal fremitus, stony dullness to percussion and reduced breath sounds in affected side may be evident. These clinical findings are often absent or vague and a high degree of clinical suspicion is the key for early diagnosis of empyemas.

Once suspected, radiological imaging are mandatory to confirm an empyema (4). Persistently high leucocytes count and C-Reactive Protein (CRP) levels are also helpful investigations.

Radiological imaging

When an empyema is suspected clinically, it can be confirmed radiologically. There are three main imaging modalities applicable for the assessment of an empyema:

(i) Chest radiography (CXR)

This easily available, non-invasive imaging modality is extremely useful in the management of empyemas. Usually the CXR is the initial

imaging study used to confirm the presence of a pleural effusion. Postero-anterior, lateral and lateral decubitus views are helpful in assessing empyema patients, especially when other imaging studies are not available. The CXR will visualise the pleural cavity and differentiate lung consolidation, lung abscess and pleural effusion-like conditions. In a pleural effusion, blunting of the costophrenic angle indicates the presence of more than 200ml of fluid in pleural cavity. Furthermore, the CXR is advantageous to decide the need for thoracentesis and further imaging studies.

However, the CXR is unsuccessful in detecting septations, loculations and pleural thickenings which are important findings to make management decisions [4].

(ii) Ultrasound scan (US)

The US is also a non-invasive, widely available imaging technique. It is invaluable in the assessment of critically ill patients, especially in intensive care. It can detect pleural fluid volumes as low as 5 ml. Pleural thickening, septations and loculations are readily apparent in US. When thoracentesis is required it should be done under US guidance because it enhances the safety and effectiveness of the procedure. Ultrasonically empyema shows four types of changes:

1. Homogeneous anechoic (mainly transudative)
2. Complex non-septated
3. Complex septated
4. Homogeneously echogenic (containing frank pus or blood)

These sonographic types are well correlated with the pathological stages and help in management decisions [5].

- #### (iii) Contrast Enhanced Computerized Tomography (CECT) scan of the chest
- CECT scan of the chest is indicated when

surgical interventions are planned. CECT is inferior to US scan in detecting septae or loculations. However, it visualises the pleural peel, adjacent chest wall, lung parenchyma and upper abdominal structures (fig 1). Therefore, it has the added advantage of being able to detect the source of infection (such as pneumonia, upper abdominal infections), associated lung tumours, broncho-pleural fistula etc. prior to surgery. It is helpful to differentiate an empyema from a lung abscess and lung consolidation. The position of the intercostal tube can also be confirmed correctly by CT scan [4].

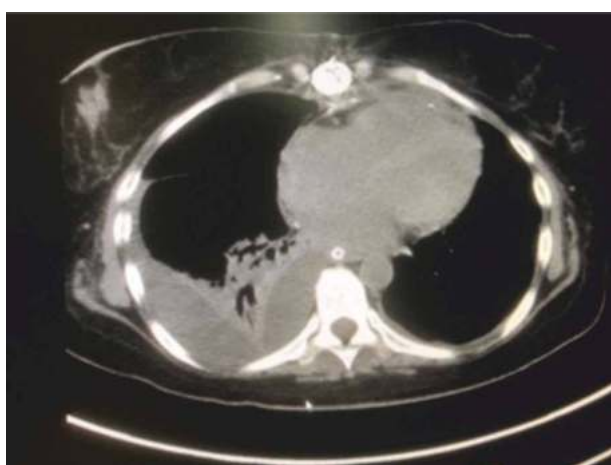


Fig 1 : CECT of a loculated empyema

Imaging studies are valuable to predict the response to treatment. For example, free flowing non-loculated anechoic pleural effusions are much more responsive to antibiotics therapy and drainage than complex loculated effusions or empyemas [6].

Pleural fluid sampling

Pleural effusions associated with pneumonia or sepsis require diagnostic pleural fluid sampling. Pleural fluid characteristics remain the most reliable diagnostic test to guide management. Once a pleural effusion is confirmed radiologically, pleural fluid sampling is done by thoracentesis, preferably under ultrasound guidance. If the aspirated fluid is frankly purulent, it is diagnostic of empyema. If it is not purulent, further analysis should be done.

The sample is analysed for:

- White blood cell counts with differential counts: Neutrophil predominance indicates bacterial infections and lymphocytes predominance indicate tuberculosis (TB)
- Protein
- Lactate dehydrogenase (LDH)
- Glucose levels
- Microbiological analysis - Gram stain, Culture/antibiotic sensitivity test (ABST), Acid-Fast Bacilli (AFB) stain, TB culture, Fungal studies
- Pleural fluid pH
- Cytology (if malignancy is suspected)

Pleural fluid PH <7.2 is the most reliable indication for IC tube insertion and drainage of an empyema. If the PH levels are unavailable, pleural fluid LDH (>1000IU/l) and Glucose level (<3.4 mmol/l) can be used as an indication for IC tube insertion and drainage [4].

Other than the neutrophil leucocytosis and increased C-reactive protein (CRP) that indicate an on-going infection, no specific blood test can confirm an empyema. However, these investigations are helpful to assess the response to treatment.

Treatment of empyemas

The aims of treating an empyema are to control of infection/ sepsis and drain the infected fluid/pus from the pleural cavity. To control pleural infection, intravenous antibiotics according to local microbiological guidance is mandatory. The treatment of an empyema is also guided by the three stages of the disease:

Treatment of stage 1 empyemas

Stage 1 parapneumonic effusions are free flowing and may be sterile. The aim of their management is the early diagnosis of infected pleural effusions and the prevention of its progression to advanced stages in which serious complications are common.

Small to moderate (<10mm thick) stage 1

parapneumonic effusions are treated with antibiotics and drainage is usually not required. Small to moderate parapneumonic effusions with negative microbiological results and pH more than 7.2 respond well to antibiotics alone.

If the pleural effusion is large (>40% of the hemithorax) and the patient is symptomatic (e.g. dyspnoeic) drainage should be considered. Drainage can be achieved by thoracentesis or intercostal tube (ICT) insertion. If repeated pleural aspirations are required for symptomatic relief, intercostal tube (ICT) insertion and drainage should be considered [4, 6].

Stage 1 empyemas can be drained either by pleural aspirations or by inserting an ICT [6]. Indications for ICT insertion are:

- A pleural aspiration yielding frank pus
- Microbiological evidence of infected pleural effusion such as positive Gram stain or culture
- Radiological evidence of a large effusion with loculations and pleural thickening
- Pleural fluid pH <7.2 [4,6].

Delay in drainage of established empyemas may lead to progression of the disease to its more advanced stages. Drainage is more difficult in the advanced stages and complications are common. The need of surgical interventions for drainage, prolonged hospital stay, and an increase in morbidity and mortality occur in such advanced stages.

Size of the ICT

The size of the ICT is a much debated topic. If there is frank pus with thick consistency, the tube may be blocked frequently and the purpose of the tube is lost. Small tubes have a higher tendency to block than large tubes. However, a large tube will cause pain and discomfort. Therefore, the size of the tube must be judged on an individual basis. If thick pus is present, a large bore tube is advisable. If intercostal spaces are narrow and the patient is of small contour, a small tube can be inserted and frequent flushed to keep the tube patent.

Treatment of stage 2 empyemas

Stage 2 is characterized by a fibrinopurulent effusion. Fibrinous septa divide the empyema into loculations. These empyemas range from free flowing, infected effusions to multiloculated collections of thick pus.

Treatment options available for this stage include:

- Intercostal tube insertion

When multiloculated, the empyema may not drain successfully by pleural aspiration or intercostal tube insertion. However, intercostal tubes may be inserted to the largest loculated collection under radiological guidance and this may suffice to drain adequately in some patients. ICT alone as a method of drainage for Stage 2 empyemas has a high failure rate because of the thick pus in multiple loculations that cannot be drained adequately by ICT alone. To increase the success rate, an ICT should be placed in the largest loculation under ultrasound guidance followed by guided aspiration of the other loculi. Alternatively, insertion of a second ICT may be needed to drain other loculations.

- Intrapleural fibrinolytic therapy

Drainage of fibrinopurulent empyemas can be enhanced by intrapleural fibrinolytic therapy. Intrapleural fibrinolytics were first introduced in the late 1940s. Partially purified streptococcal concentrates containing streptokinase and streptococcal DNase were instilled into the pleural cavity of fibrinopurulent empyema patients with variable results. Resurgence of interest in this therapy occurred in the 1980s following the report of several successful case series [6]. Fibrinolytic agents such as streptokinase, tissue plasminogen activator (TPA) and urokinase can be instilled into the pleural cavity to liquefy fibrinous material and facilitate free drainage of purulent material via an ICT.

Efficacy of intrapleural fibrinolytics as a treatment for empyema is controversial. According to a meta-analysis of 761 patients treated with intrapleural

fibrinolytics it demonstrably reduce the necessity for surgical intervention and hospital stay [6]. However, other randomised controlled trials showed that it had no remarkable benefit in the management of empyemas [7].

Compared to surgical drainage and debridement, fibrinolytics demonstrate higher failure rates. Nevertheless, it is beneficial for patients who are unfit for general anaesthesia or surgery due to comorbidities.

- Surgical drainage and debridement

If a Stage 2 empyema is drained inadequately in spite of an ICT insertion or sepsis is continuing despite an ICT, surgical drainage and debridement must be considered [4].

Surgical drainage and debridement is performed as an open procedure through a thoracotomy or as a minimally invasive procedure – i.e. Video Assisted Thoracoscopic Surgery (VATS).

In 2000, the American College of Chest Physicians reviewed Stage 2 empyema patients treated with no drain, thoracentesis, ICT, Intrapleural fibrinolytic therapy, thoracotomy and VATS.

They reported a failure rates of 40% for ICT alone, 15% for ICT with intrapleural fibrinolytics, 10% for thoracotomy and none for VATS [8]. Currently VATS drainage and debridement is regarded as the procedure of choice for stage 2 empyema due to its overwhelming advantages compared to open drainage and debridement.

Treatment of stage 3 empyema

Stage 3 empyemas typically occur four to six weeks after the parapneumonic effusion. It is characterized by the presence of a fibrous layer over the visceral and parietal pleural surfaces and over the diaphragm giving the name “fibrothorax”.

Contraction of this thick fibrous tissue layer leads to lung entrapment which in turn leads to atelectasis

and chest wall deformity. Fibrothorax ultimately causes a restrictive ventilator syndrome characterised by ventilation–perfusion mismatch and dyspnoea.

At this stage drainage of pus and control of infection can be achieved by parenteral antibiotic therapy and insertion of an intercostal tube.

However to rectify respiratory impairment, it is required to remove the fibrous coat over the lung and chest wall to re-establish pulmonary and chest wall functions. In a Stage 3 empyema, the underlying lung parenchyma is infected and consolidated and therefore the lung is overwhelmingly fragile and excessive bleeding, air leak and bacteraemia can occur during surgery. This leads to increased morbidity following surgery. In Stage 3 empyemas, the lung parenchyma tends to heal gradually. Once the lung is healthy, it can withstand surgical trauma to a greater extent and bleeding, air leak and bacteraemia become minimal during surgery. Therefore timing of surgery is an important issue in managing Stage 3 empyemas.

In 2015, the European Association of Cardiothoracic Surgery issued a consensus statement that VATS has an important role in the management of pleural empyema because of its safety and effectiveness both in Stage 2 and Stage 3 empyemas, but that thoracotomy plays a key role for lung re-expansion in the presence of an entrapped lung [9].

Timing of surgery

The transition from the fibrinopurulent stage to fibrothorax is not very clear radiologically. Due to the thick exudate deposited over the visceral pleura, it is difficult to identify a fibrous cortex by imaging. In such circumstances, formation of a fibrothorax can be identified only during surgical exploration. Surgical exploration is preferably done by VATS.

During VATS exploration if the empyema is purely in fibrinopurulent stage (Stage 2) drainage and debridement is done at the same sitting.

If there is an associated fibrothorax, the surgeon has to decide whether to proceed to decortication either by VATS or open thoracotomy. Alternatively, the procedure can be limited to simple debridement and drainage and definitive decortication can be performed at a later stage when the underlying lung is adequately healed.

The lung and chest wall have the ability to remodel naturally by resolving the fibrous cortex to a certain extent. Therefore, when an established Stage 3 disease is encountered preoperatively or if it is diagnosed during VATS, it is prudent to withhold the procedure until the lung is healthy. Definitive decortication can be attempted when underlying lung is healed. In such a situation, continuation of antibiotics according to microbiological advice, chest physiotherapy and mobilization is mandatory to achieve good results.

If it is not resolved after a reasonable period (i.e. three to six months) of conservative management, decortication has to be done [4].

Decortication

Decortication is the removal of the fibrous coat from the surfaces of the lung and chest wall to release lung entrapment and correct chest wall deformity. Decortication can be performed as an open thoracotomy and decortication or as a VATS decortication.

Traditionally, decortication was done as an open procedure. With the development of minimally invasive surgery, VATS Decortication also become a surgical option [10,11, 12]. Initially VATS drainage and debridement was done for Stage 2 (fibrinopurulent) empyema but when Stage 3 empyema was encountered, the procedure was converted to open decortication. With increasing experience, VATS decortication became a safe option and today its success rate is equal to that of open decortication. Currently VATS Decortication is considered safe and effective. Its benefits include minimal surgical trauma, low blood loss with reduced need for blood transfusions, reduced

incidence of prolonged air leak, magnified view during surgery that help meticulous dissection, less postoperative pain that helps to give vigorous chest physiotherapy and early mobilization in the postoperative period, minimal hospital stay, reduced duration of ICT, minimal wound complications and more cosmetically acceptable incisions. On occasion, VATS decortications may need to be converted to open thoracotomy and decortication. Reasons for conversion are usually excessive intraoperative bleeding, an unhealthy underlying lung with high risk for lung damage and air leak.

VATS decortication demands a higher level of surgical expertise and needs progression through a learning curve. If the operating surgeon does not have adequate experience for VATS decortication, it is prudent to convert to open decortication when Stage 3 empyema is encountered during surgery [4].

In contemporary minimally invasive thoracic surgery, Uniportal VATS (U-VATS) can be regarded as the final frontier of its kind. Drainage and debridement of stage 2 empyema, lung biopsy, pleural biopsy, surgical procedures for pneumothorax and anatomical lung resections were performed as U-VATS. With increasing experience U-VATS decortication is also being performed successfully. Although a complex and tedious procedure, U-VATS decortication demonstrates similar efficacy and safety as compared to open and VATS Decortication [5].

Open window thoracostomy

If all treatment options have failed and the patient is unfit for further surgery, either open or VATS, open window thoracostomy may be an option. In this procedure, a vertical incision is made through the chest wall with a rib resected at the inferior border of the empyema cavity allowing drainage of empyema directly through the chest wall. Alternatively, a wide-bore ICT can be placed at the most dependant part of the empyema cavity. The empyema is drained through the ICT and the tube may be connect to a drainage bag. The tube is gradually advanced outward as the tract is closed with granulation tissue.

This process is less invasive than open or VATS Decortication but it takes two to three months to complete the procedure.

Conclusion

Pleural empyemas are best managed according to their stage. Staging is done by radiological studies, especially ultrasonography as well as intraoperative findings. Free flowing empyemas can be effectively treated by antibiotics and drainage. Drainage can be done either by thoracentesis or thoracostomy tube. Once it is septated and loculated, effective drainage can only be done by open or VATS surgery. Fibrothorax needs open or VATS decortication to re-establish pulmonary and chest wall function. Successful management of empyemas depend on correct timing of surgical intervention and therefore early thoracic surgical referral is beneficial for all patients with empyemas.

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