

Investigation of Pleural Effusions

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Introduction

Pleural effusion is a common medical condition which often presents on the AMU. There are more than 50 recognised causes of pleural effusion which include diseases local to the pleura or underlying lung, systemic conditions, organ dysfunction and drugs.¹ The normal pleural space contains approximately 1mL of fluid. The balance between hydrostatic and oncotic pressures in the visceral and parietal pleural vessels maintains this environment; any disorder affecting this balance will result in a pleural effusion.²

The commonest causes of pleural effusion in the UK are cardiac failure, pneumonia, malignancy, and pulmonary embolism. In view of this broad collection of pathologies a systematic approach is required to minimise complications associated with delay in diagnosis or unnecessary invasive investigations.

This article is aimed to assist Acute Physicians in the evaluation and management of pleural effusions. The reader is encouraged to think about the questions posed throughout this article (sample answers are included at the end of the text). For further information, the updated 2010 British Thoracic Society (BTS) pleural disease guidelines are strongly recommended.³

Case study

Mr. BM, a 66-year-old man, presented to the emergency department complaining of cough productive of green sputum. There was associated shortness of breath on climbing the stairs, dull chest pain on the right side, low grade fever and night sweats.

On examination he appeared unwell but was alert and orientated. He was breathless with a respiratory rate of 35 breaths per minute. His heart rate was 110 beats per minute with a blood pressure of 110/70mmHg and a temperature of 38.2°C. His jugular venous pressure was not raised and he had no heart murmurs. There were absent breath sounds and dull percussion at the right lung base. The remainder of the examination was unremarkable. His chest X-ray is shown in Figure 1.



Figure 1.

Questions

1. What further information is required from the history?
2. What does the X-ray show?

Importance of History and Clinical Examination

Dyspnoea is the most common symptom directly associated with pleural effusion. Detailed clinical assessment will provide important clues to the underlying cause of a pleural effusion in most cases. For example, dyspnoea with a raised jugular venous pressure, lower limb oedema and bilateral effusions is likely to be cardiac failure with a transudative effusion. Similarly, a short history of dyspnoea with a productive cough and fever may suggest pneumonia with an exudative effusion.

Distinguishing clinically between an exudate and a transudate helps to determine the likely cause and also the approach to further investigation. The presence of bilateral pleural effusions in the setting of cardiac failure does not require pleural aspiration unless there are atypical features or failure to resolve with treatment. Conversely, a unilateral pleural effusion on the background of pneumonia or history of weight loss, cough and/or haemoptysis will

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require early pleural aspiration to exclude empyema and malignancy respectively.

Drug history is important; a number of medications have been reported to cause exudative pleural effusions e.g. amiodarone, methotrexate and beta-blockers.³ Other examples of drugs causing pleural effusions may be found on the website www.pneumotox.com. An occupational history (including details about known or suspected asbestos exposure), tuberculosis contacts or relevant travel history should be documented. Tuberculosis is a leading cause for exudative pleural effusion in higher risk groups.

Case update

Mr. BM was previously well and active with no significant past medical history and no long term medications. His symptoms had been present for 8 days prior to admission. There was no history of smoking, no recent foreign travel and no history of contact with anyone with a chronic cough or tuberculosis. His occupation was an accountant with no history of asbestos exposure.

Questions

3. What is the differential diagnosis?
4. What is the most likely cause? Is it likely to be a transudate or exudate?
5. Does he need a chest drain immediately? What is the next step?

Investigations

Initial tests will include routine blood tests such as full blood count, biochemistry, clotting profile and C-reactive protein (CRP). Additional tests are warranted when specific aetiologies are suspected. If a pleural aspiration is planned then concurrent serum LDH and protein should be measured.

The plain chest radiograph will help confirm the presence of the effusion. The posterior anterior (PA) chest radiograph is abnormal in the presence of approximately 200 ml of pleural fluid. However, only 50 ml of pleural fluid is enough to blunt the costophrenic angle on a lateral chest radiograph.⁴ If dyspnoea is out of proportion to the size of the effusion then pulmonary embolism should be considered. Pulmonary embolism is the main cause of pleural effusion where the effusion occupies less than one-third of the hemithorax.⁵ The presence of other features on the chest x-ray such as cardiomegaly, fluid in the oblique fissure, pleural thickening or consolidation aid the diagnosis.

The 2010 BTS guidelines for the investigation of pleural effusions recommend referral to chest physicians prior to invasive investigation i.e. pleural aspiration or chest drain insertion. This is in recognition of an increase in complications associated with pleural procedures as highlighted by the National Patient Safety Agency (NPSA) report issued to the National Health Service (NHS) in 2008.⁶

Pleural Aspiration under Ultrasound guidance

The next step is pleural aspiration (thoracocentesis) and analysis of pleural fluid. This procedure is described in the BTS guidelines.⁷ Clinical decision-making information

can be gained from pleural fluid analysis in over 90% of cases, even if it is not diagnostic.⁸

Pleural aspiration should be carried out using ultrasound guidance, preferably in real time; ultrasound reduces the risk of complications (including organ puncture) and improves the chances of successfully obtaining a pleural fluid sample. Blind pleural aspiration is no longer recommended.

Studies have shown that pleural fluid can be successfully obtained using ultrasound in up to 88% of patients who have had a previously failed clinical and plain chest radiograph-guided attempt.^{9,10} Ultrasound guidance reduces the incidence of iatrogenic pneumothorax following thoracentesis and several studies have shown this effect to be independent of the size of the effusion.^{11,12,13} This value appears to be lost when the 'X marks the spot' method is employed, most probably due to differences in patient positioning between the ultrasound at the radiology department and the procedure on the ward.¹³

One prospective study compared clinical assessment and chest radiograph to ultrasound in planning a diagnostic aspiration site. The sensitivity and specificity of the clinical decision compared with the gold standard of ultrasound was 76.6% and 60.3%, respectively. Ultrasound increased the number of correct sites by 26%. The study also showed that 15% of clinically determined sites were inaccurate and could have resulted in puncture of liver, spleen or lung; although there was increasing risk with small or loculated effusions, 60% of potential organ punctures occurred in radiographically moderate to large effusions.¹⁴

The Royal College of Radiologists has published guidelines establishing the minimum standards required to achieve basic or level 1 competency in thoracic ultrasound.¹⁵ It is recommended that thoracic ultrasound training is provided for all clinicians expected to deal with and perform pleural procedures. The most recent respiratory specialist curriculum has included thoracic ultrasound in the syllabus in an attempt to deal with this issue. There is little evidence to specify the length of training required for a non-radiologist to become competent in basic thoracic ultrasound and although the guidelines state a figure on a minimum number of supervised procedures, this is a minimum and will vary according to the individual's ability.

The detailed role of thoracic ultrasound in the early investigation of pleural effusions extends beyond the scope of this article but the main importance is in improving procedural safety.

Pleural fluid analysis

Knowledge as to whether an effusion is an exudate or a transudate will narrow the differential diagnosis and direct subsequent management.

The appearance of the pleural fluid and any odour should be recorded as this may sometimes indicate the underlying cause. Pleural fluid should always be sent for protein, lactate dehydrogenase (LDH), Gram stain, cytology and microbiological culture; other tests may be required depending on the clinical circumstance.³

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Pleural Effusions			
	Common	Less Common	Rare
Transudate	Left ventricular failure Liver cirrhosis	Hypoalbuminaemia Peritoneal dialysis Hypothyroidism Nephrotic syndrome Mitral stenosis	Constrictive pericarditis Urinothorax Meigs' syndrome
Exudate	Malignancy Parapneumonic effusion Tuberculosis	Pulmonary embolism Rheumatoid arthritis Benign asbestos effusion Pancreatitis Post-myocardial infarction Post-coronary artery bypass graft	Yellow nail syndrome Drugs Fungal infections

Table 1. Causes of pleural effusions.

	Specific Tests	Amount of fluid needed / mls
Biochemistry	Protein LDH +/- Glucose +/- Amylase	1-2
Microbiology	Gram stain Culture & Sensitivity Acid Fast Bacilli	5
pH	When infection is suspected and fluid is non-purulent	5
Cytology		10-20

Table 2. Pleural fluid analysis.

Historically, a pleural fluid protein >30g/L has been used as a cut off to indicate an exudate and <30 g/L a transudate. This cut off point is not accurate when the serum protein is abnormal or when the pleural fluid protein concentration is close to 30 g/L. The application of Light's criteria is recommended in such cases.¹⁶ In order to apply Light's criteria, the total protein and lactate dehydrogenase (LDH) should be measured in both blood and pleural fluid simultaneously.

Lights Criteria

According to Light's criteria, the pleural fluid is an exudate if one or more of the following criteria are met:

- pleural fluid protein divided by serum protein is >0.5
- pleural fluid LDH divided by serum LDH is >0.6
- pleural fluid LDH >2/3 the upper limits of laboratory normal value for serum LDH

Another parameter which has considerable value is the pleural fluid pH. This is used in cases of suspected pleural infection where the fluid is not frankly purulent. A pH value of <7.2 indicates that resolution without drainage is unlikely and chest tube drainage should be carried out as soon as it is safe to do so. A meta-analysis, examining pleural pH and the need for chest tube drainage in surgical

patients with a parapneumonic effusion found that a pH <7.2 was the most specific predictor of complicated pleural infection.^{17, 18}

Case Update

Mr.BM was consented for pleural aspiration; this was done under ultrasound guidance. The pleural fluid was straw-coloured and not frankly purulent. The pleural fluid biochemistry showed protein 44g/L and LDH of 487 IU/L. Divided by serum value, the ratio was 1.3 for protein and 1.6 for LDH, confirming an exudate. The gram stain was negative but with a pH of 7.1.

Chest Drain – To drain or not to drain?

Chest drains (including the new smaller Seldinger drains) are associated with a high rate of complications. All doctors likely to need to insert chest drains should be aware of these complications, be suitably trained and familiar with the drainage equipment.

Before inserting a chest drain you should ask yourself the following:

- Do I need to do this?
- Does it need to be done as an emergency or can it wait?
- Do I have enough training to feel confident to do this? Are senior staff to hand?
- Am I familiar with this equipment?
- Is ultrasound available, with trained staff, to position it safely?⁶

Pleural procedures should not take place out of hours except in an emergency, and the majority of cases can wait. Written consent should be obtained and all pleural aspirations and chest drains should be inserted in a clean area using full aseptic technique. The use of large-bore drains should be avoided. Small-bore chest drains are less painful and have a lower complication rate.^{19- 27}

Fluid should be drained at a controlled rate of no more than 1.5 l in the first 1 hour to avoid the risk of re-expansion pulmonary oedema.

In emergency areas, doctors may be more familiar with the ATLS technique for chest drainage in trauma cases where drains are set to evacuate blood quickly. This

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technique is not safe or appropriate for medical causes of pleural effusion where the fluid has usually been present for some time and the physiological effects of rapid evacuation can be life-threatening.

It is important to carry out a chest radiograph following insertion of a chest drain to look for complications such as pneumothorax and correct positioning of the drain. Chest drains should be managed in a ward with trained nursing staff and clear instructions should be given to nursing staff and the patient regarding care of the drain.

Case Update

Mr. BM consented to chest drain insertion after the risks and benefits of the procedure were explained to him. A small bore chest drain was inserted under ultrasound guidance by a trained doctor. He was monitored by nursing staff familiar with chest drain care and a patient leaflet was given to Mr. BM. Analgesia and regular drain saline flushes were prescribed. The drain was monitored daily and after two days there was a marked improvement in his clinical condition with no more fluid draining. A chest radiograph showed resolution of the effusion and the chest drain was removed. He was discharged from hospital and a follow up appointment was arranged.

Further Advanced Investigations

If the cause of a pleural effusion remains unclear, then further tests may be carried out depending on local availability and suspected aetiology. A chest specialist will guide the most appropriate sequence of investigations at this stage which may include:

Computed tomography (CT): CT scan with contrast enhancement may show pleural thickening, malignancy, pulmonary emboli or other underlying causes. It may help guide a drain for complex loculated effusions or the site of pleural biopsy. In the case of large effusions, aspiration is recommended before a scan to remove some fluid so the underlying lung may expand enough to demonstrate underlying pathology. Drainage to dryness is not recommended however as this would delay subsequent thoracoscopic examination if required.

Magnetic resonance imaging (MRI): Although MRI distinguishes accurately between benign and malignant pleural effusions via differences in signal intensity on T2-weighted images,²⁸ it does not have a place in the routine investigation of pleural effusions currently, except in patients in whom contrast is contraindicated.

Positron emission tomography -CT imaging (PET-CT) While the uptake of 18-fluorodeoxyglucose (FDG) is increased in malignant pleural effusions, the value of PET-CT imaging in distinguishing between benign and malignant pleural disease is limited due to the false positives in patients with pleural inflammation.^{29,30}

Percutaneous pleural biopsy This is the procedure of choice when faced with an undiagnosed effusion where malignancy is suspected and areas of pleural nodularity are shown on contrast-enhanced CT. This is usually done with CT guidance. Blind closed pleural biopsies are no longer recommended except in areas of high TB incidence where expertise still exists.

Thoracoscopy When malignancy is suspected and pleural aspiration is inconclusive, either medical thoracoscopy (local anaesthetic thoracoscopy) or surgical video assisted thoracoscopy (VATS) is recommended. Where this is readily available it may be the preferred initial investigation.

Non-specific Pleuritis

'Non-specific pleuritis' is a term given where no diagnosis has been achieved, even though all appropriate investigations have been performed. The majority of patients with non-specific pleuritis (91.7%) follow a benign course, with spontaneous resolution of the effusion in 81.8% of cases; watchful waiting might be the most suitable option in such patients.³¹

TAKE HOME POINTS

- Thorough clinical assessment will aid a swift diagnosis and the appropriate management of a patient presenting with pleural effusion.
- Refer patients with pleural effusions to chest physicians at an early stage.
- Always perform pleural aspiration under ultrasound guidance.
- Send pleural fluid samples for biochemistry (protein, LDH), microbiology (gram stain, culture, acid fast bacilli) and cytology.
- Send paired blood samples for total protein and LDH
- Pleural fluid pH should be assessed only in non-purulent effusions when pleural infection is suspected. A pH of <7.2 or purulent fluid will require a chest drain as soon as it is safe to do so.
- Use small chest drains, avoid chest drain insertion out of hours and seek specialist help when not sure.

Answers to Questions

1. A more detailed and comprehensive history is required including onset of symptoms, duration, associated symptoms including cough, pain and haemoptysis, past medical history, drug history occupational exposures (asbestos) and smoking history.
2. Right-sided pleural effusion.
3. See Table 1.
4. In view of the acute presentation with no smoking history and symptoms suggestive of pneumonia, this is likely to be an exudate (parapneumonic effusion or empyema).
5. Referral to a chest physician with a view to initial pleural aspiration under ultrasound guidance. When pleural aspiration confirms the presence of an exudative pleural effusion and developing empyema with pH 7.1 then a chest drain is indicated. Whilst this needs to be done promptly, it can usually wait until a doctor competent in chest drain insertion under ultrasound guidance is available 'in hours'.

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