Imaging the pleura

Pleural disease is now recognized as an important subspecialty of pulmonary medicine, with increasing provision being made for specialist services and procedures. In response, the field of pleural imaging has advanced in recent years, especially with regard to ultrasound. Salient multimodality imaging techniques are discussed.

Pleural disease is varied, manifesting in a range of ways including thickening of the pleural layers themselves or accumulation of fluid, air or pus within the pleural space. It can be more broadly subdivided into benign and malignant disease. There is considerable overlap between the investigative pathways for these two groups, so most imaging modalities have a role in both. This article outlines pleural conditions commonly encountered in hospital medicine, and describes the most appropriate radiological methods for their assessment, including plain chest X-ray, computed tomography, ultrasound, magnetic resonance imaging and positron emission tomography.

Normal pleural anatomy and imaging

The pleura are serous membranes which comprise an outer parietal layer, adherent to the thoracic wall, and an inner visceral (or pulmonary) layer, which envelops the lung. Recesses form where the visceral membrane dips into the pulmonary fissures, and at the hila where the pleura come together and descend inferiorly to form the pulmonary ligament. The movement of these layers against each other is helped by a small volume (up to 10 ml) of pleural fluid which also creates surface tension making the pleural cavity a potential space in normal circumstances.

Imaging normal pleura can be difficult, especially as their thickness is below the spatial resolution of most radiological techniques. On computed tomography scanning a 1–2 mm line called the 'intercostal stripe' may be seen between the ribs (*Figure 1*). This includes both pleural layers but is mostly made up of the innermost intercostal muscle. Computed tomography protocols may be altered to optimize the visualization of the pleura by prolonging the delay between contrast administration and image acquisition to 60–90 s, improving detection of malignant features (Raj et al, 2011). Thoracic ultrasound using a high frequency probe (>8 MHz) allows real-time visualization of the individual pleural layers, which appear as two echogenic lines sliding against each other in respiration deep to the ribs.

Dr Chloe Mortensen *is Radiology Registrar in the Department of Radiology,* **Dr Rahul Bhatnagar** *is Clinical Research Fellow in the Department of Respiratory Medicine and* **Dr Anthony J Edey** *is Consultant Thoracic Radiologist in the Department of Radiology, Southmead Hospital, Bristol BS10 5NB*

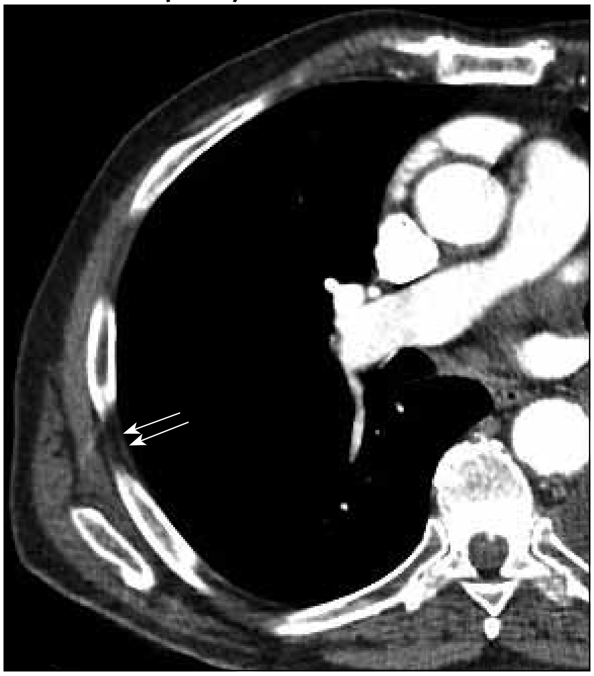
Correspondence to: Dr AJ Edey (anthony.edey@nbt.nhs.uk)

Benign pleural pathology

Pleural plaque (localized pleural thickening)

Plaques are areas of focal pleural thickening and hyaline fibrosis, primarily affecting the parietal layer. They are pathognomic of previous asbestos exposure, with a typical latency of 20–30 years before progressive calcification renders them visible on plain chest X-ray. They are often seen incidentally, and without reassurance about their benign nature can become a significant source of concern for patients. In the UK, patients with asbestos-related plaques alone are not eligible for compensation unless exposure occurred in Scotland. En face, calcified plaques appear as ill-defined opacities with irregular margins likened to a holly leaf and can occur unilaterally or bilaterally (*Figure 2*). They are visible predominantly over the lower thorax and diaphragmatic regions, tending to spare the apices and costophrenic recesses. Computed tomography is much more sensitive than chest X-ray for plaque (95% *vs* 58%) and reveals their predilection for the paravertebral recesses, underside of the ribs and diaphragm (al Jarad et al, 1991) (*Figure 3*).

Figure 1. Axial contrast-enhanced computed tomography scan showing the 'intercostal stripe' comprising normal pleura and intercostal muscle (arrows).



Diffuse pleural thickening

Diffuse areas of thickening may be caused by exposure to more generalized pleural insults such as rheumatoid arthritis, empyema, tuberculosis or post-surgical reactions (*Figure 4*). Inflammation tends to affect the visceral pleural layer and can occasionally result in aggressive fibrous deposition. The resultant 'fibrothorax' may lead to significant restrictive ventilatory impairment, with or without associated symptoms. Asbestos exposure may also be implicated but, because appearances are often non-specific, other radiological markers of asbestos exposure, such as calcified plaques, and a clear history of exposure are needed to confirm this diagnosis.

Both chest X-ray and computed tomography may be used to identify diffuse pleural thickening, although definitions vary. In the context of asbestos exposure, the International Labour Office (2011) revised guidelines apply the following diagnostic criteria for diffuse pleural thickening:

1. Obliteration of the costophrenic angle
2. Bilateral thickening involving at least 25% of the chest or 50% if unilateral
3. Pleural thickness greater than 5 mm at any site.

Using computed tomography, the definition of what constitutes relevant pleural thickening can be more contentious, but examples include:

1. Thickening extending 8 cm in the craniocaudal direction and 5 cm laterally with a thickness of more than 3 mm (Aberle et al, 1988)
2. Areas of pleural thickening with tapering (rather than shouldered) margins (Copley et al, 2001).

Regardless of the modality used, and separate to ruling asbestos exposure in or out, imaging can help identify potential causes of benign pleural thickening. When located in the apical regions, changes may indicate either preceding tuberculosis infection or age-related pleural thickening ('apical cap'). Unilateral sheet-like calcification with thickening of the extra pleural fat and the presence of marked volume loss are further classical features of previous tuberculosis, and healed rib fractures with preserved underlying lung may point to previous haemothorax or surgery. Alternatively, the 'talc sandwich' appearance may be seen following pleurodesis, and is seen as pleural thickening covering a high-density layer of talc, with a deeper layer of thickened visceral pleura.

Diffuse pleural thickening usually forms an irregular interface with adjacent lung and, in up to 90% of cases (Gevenois et al, 1998), is associated with underlying parenchymal band formation or regions of folded lung, which result from distortion caused by fibrotic inflam-

Figure 2. Chest X-ray showing florid asbestos-related calcific pleural and diaphragmatic plaques. Note the classic 'holly leaf' appearance on the right.

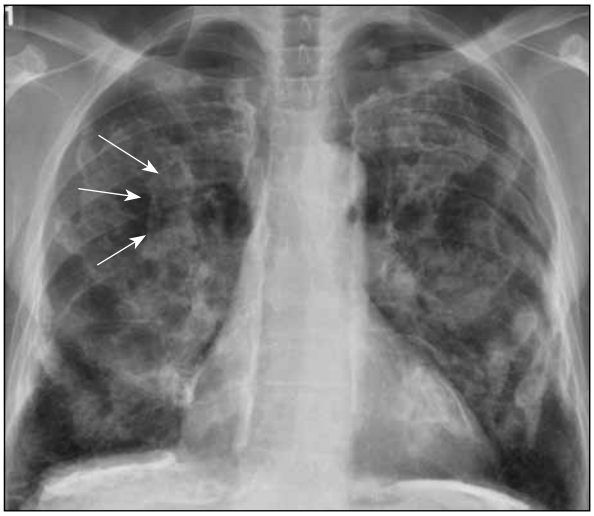


Figure 3. Axial computed tomography scan showing widespread calcific asbestos-related pleural plaques characterized by their focal, shouldered configuration, with a paravertebral (arrowheads) and subcostal (arrows) predilection. There are also calcific pericardial plaques, which are relatively uncommon (dashed arrows).

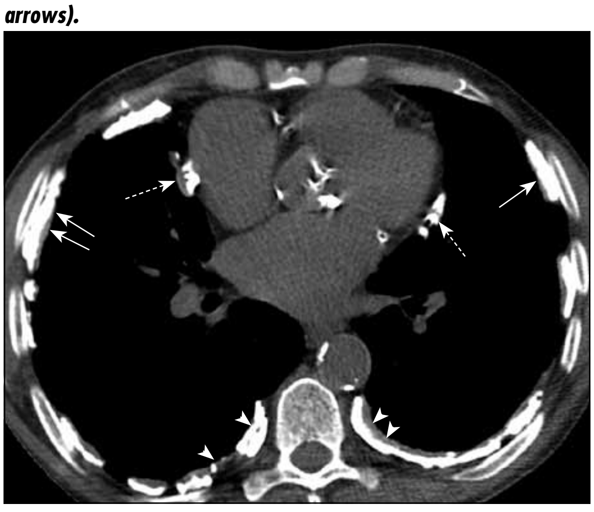
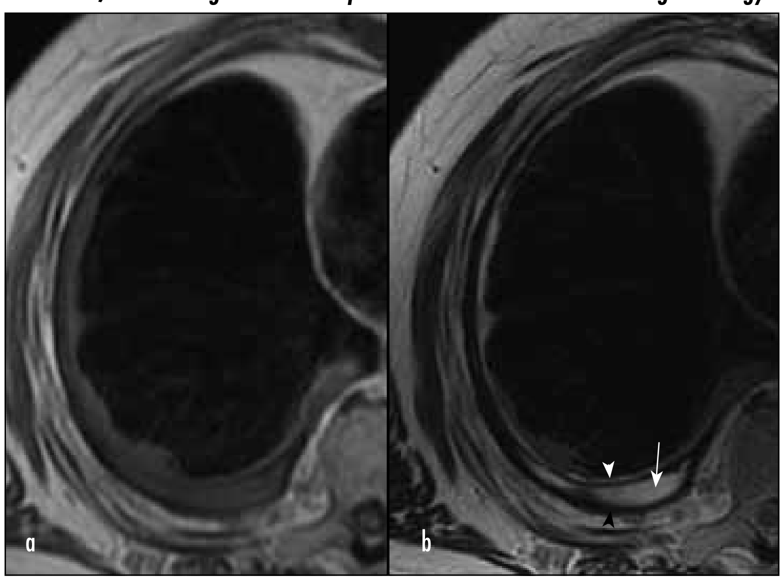


Figure 4. a. Axial T1 and (b) T2 weighted images showing pleural thickening as a result of inflammation with a small chronic effusion (arrow), as a result of underlying rheumatoid disease. The pleura (visceral = white arrowhead, parietal = black arrowhead) is of low signal on both sequences which is indicative of a benign aetiology.



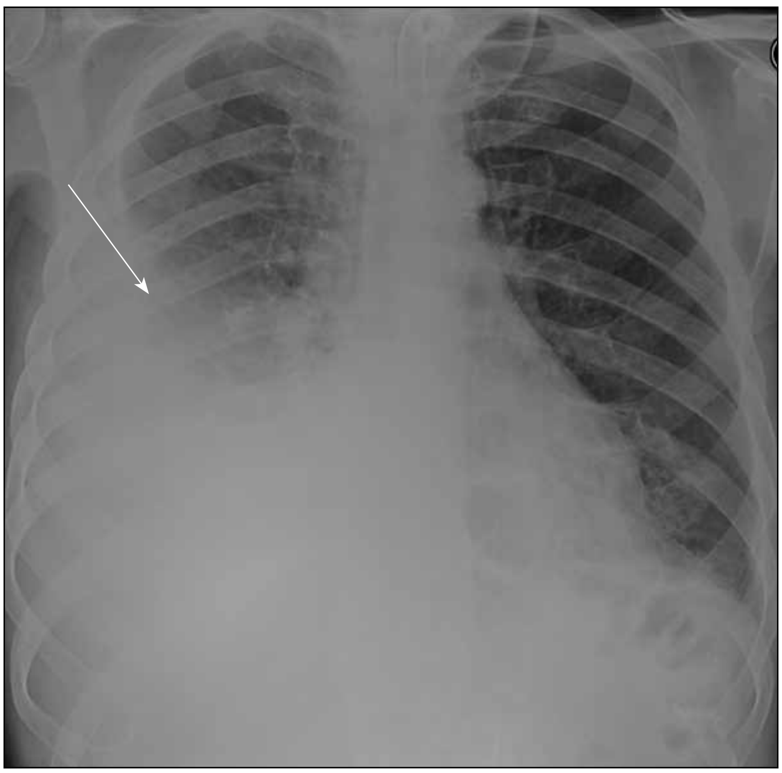
mation of the overlying visceral pleura. This is typically visible on computed tomography which, unsurprisingly, is more sensitive than plain radiographs for the detection of diffuse pleural thickening. This was shown by Qureshi and Gleeson (2006) who demonstrated a 'normal' chest X-ray in 20% of patients who had pleural thickening evident on computed tomography. A further advantage is that computed tomography can more firmly establish the extent and distribution of disease, as well as highlight areas of possible malignant disease more easily. For patients in whom there is a high index of suspicion for malignancy despite benign appearances on computed tomography, or following inconclusive biopsy, magnetic resonance imaging may be suitable to further the diagnosis.

Ultrasound compares favourably with computed tomography in the diagnosis of malignant *vs* benign disease, with one study showing an overall sensitivity of 73% and specificity of 100% (computed tomography 89%), concluding that pleural thickening >1 cm, pleural nodularity and diaphragmatic thickening of >7 mm were highly suggestive of malignant disease (Qureshi et al, 2009). Ultrasound, however, tends to be used more in the assessment of pleural effusions.

Benign pleural effusions

Pleural effusions are a common finding in hospital practice. Plain chest radiography is typically the initial investigation of choice, with postero-anterior chest X-ray able to show as little as 200 ml of pleural fluid causing blunting of the costophrenic angle. The nature of fluid (e.g. blood, pus, serous) can never be shown directly using X-ray, although certain inferences regarding aetiology can sometimes be made based upon fluid distribution. Although there are exceptions, bilateral effusions tend to be associated with benign conditions such as heart or hepatic failure and are often managed medically. Unilateral effusions raise more suspicion, especially in the absence of clear trauma or infective symptoms, and almost always need further investigation.

Figure 5. Chest X-ray showing a large right-sided loculated pleural effusion. Note the biconvex shape to the lateral aspect of the effusion (arrow) that is consistent with loculation.



Chest X-rays have significant limitations and can be 'normal' despite the presence of surprisingly large effusions. Greater accuracy can be gained by performing a lateral projection, as this can demonstrate as little as 50 ml but in practice this is rarely performed (Blackmore et al, 1996). Particular care should be taken when assessing supine films, a common situation in sick patients, as effusions are more difficult to detect as a result of posterior pooling in the dependent pleural space. Effusions in the supine patient can manifest as a generalized increase in the opacity of the hemithorax with preserved vascular shadows, haziness of the hemidiaphragm or as an apical cap. Fluid may also track along the fissures, mimicking thickening (Ruskin et al, 1987), or become encysted, which can have the appearance of a pulmonary mass. Loculation of pleural fluid, which typically results in a biconvex, pleurally based opacity, raises the possibility of underlying empyema (*Figure 5*). A subpulmonic effusion is the presence of fluid between the diaphragmatic surface of the lung and the diaphragm, and can also be easily missed on chest X-ray. Elevation and lateral displacement of the peak of the hemidiaphragm, simulating eventration, is the most obvious clue to its presence (Hansell et al, 2009).

Following chest X-ray, thoracic ultrasound is often the next imaging modality used. Usually readily available at the bedside, it comes into its own when more detailed information regarding effusions is required. Anechoic fluid is more likely to represent a transudative process while echogenic fluid, in which proteinaceous 'swirling' may sometimes be seen, raises the suspicion of exudative fluid, pus or blood. However, the definitive clinical distinction of effusions into transudates or exudates can only be done by fluid sampling. Ultrasound also shows internal fibrous septations and loculations better than computed tomography (Kearney et al, 2000) (*Figure 6*).

Obtaining pleural fluid samples calls for radiological guidance, although this was not the case historically. More recent series have shown that ultrasound-guided pleural aspirations are not only safer, but are more likely to result in a successful aspiration when compared to clinical examination in conjunction with chest X-ray (Diacon et al, 2003). In 2010 the British Thoracic Society formalized this by advocating the routine use of ultrasound guidance to aid in pleural aspiration and drain insertion (Hooper et al, 2010). Ultrasound guidance should ideally be provided immediately before or at the same time as needle insertion, with the patient in the same position throughout. The practice of 'X-marking' in a radiology department is unable to guarantee safe aspirations and can, in many instances, create a false sense of security for practitioners.

Computed tomography has a valuable role in assessing patients with an effusion. The British Thoracic Society now recommends performing computed tomography in all undiagnosed exudative pleural effusions, as well as for complicated pleural infection when initial tube drainage has been unsuccessful and surgery is to be considered (Hooper et al, 2010). Viewed on computed tomography, free fluid in the pleural space collects in dependent regions and typically appears as a low density sickle-shaped opacity. Blebs of gas are more readily seen on computed tomography than with other modalities, and may be an indicator of recent instrumentation or gas-forming organisms in pleural infection. In empyema, pleural enhancement surrounding a lenticular-shaped fluid collection (the 'split pleura' sign) may also be seen along with pleural thickening and thickening of the adjacent extra pleural fat (Qureshi et al, 2009) (*Figure 7*). Finally, computed tomography is the best method for confirming placement following drain insertion, especially into small or complicated collections, although in most uncomplicated cases a chest X-ray will suffice.

Benign pleural masses

Pleural masses appear on chest X-ray as localized opacities with a well-defined lateral margin, but fade at the internal boundary. Localized tumours of the pleura are uncommon, the most prevalent being solitary fibrous tumour of the pleura which has had a variety of names in the past including localized mesothelioma and pleural fibroma. Approximately 10% exhibit malignant behaviour but this distinction is histological rather than radiological. Solitary fibrous tumour of the pleura presents in middle age, and tends to induce cough, breathlessness and chest pain (Theros and Feigin, 1977). Unsurprisingly, larger lesions are more likely to cause symptoms. Tumours may be large (up to 20 cm) and pedunculated, thus their orientation may vary with positioning or respiration. Heterogeneity of larger lesions may be caused by internal necrosis or haemorrhage, with focal pleural tumours tending to be vascular, causing intense enhancement following intravenous contrast administration. Punctate calcification is a more unusual feature predominantly seen in larger lesions (Ferretti et al, 1997).

Cross-sectional imaging can also be used to identify other, rarer types of pleural mass including lipomas, which are typically benign and asymptomatic, or liposarcomas, which tend to be large, infiltrative and symptomatic.

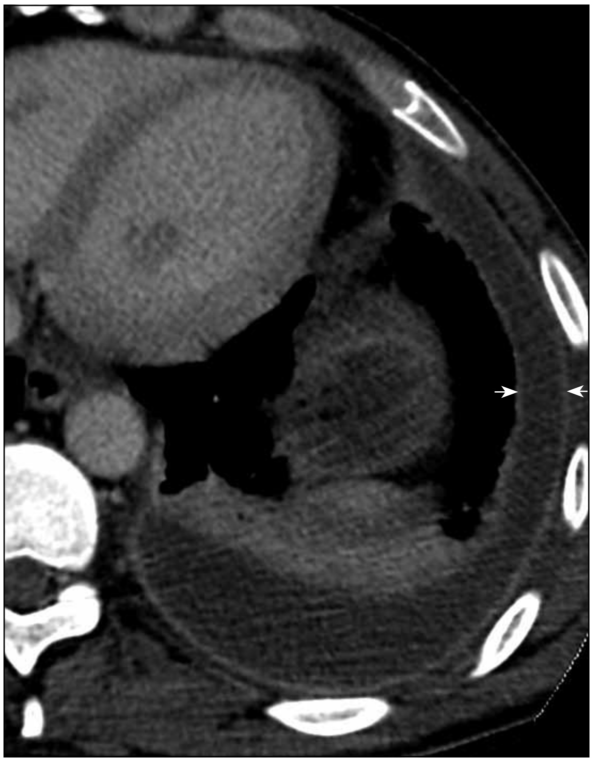
Malignant pleural pathology

Three mechanisms typically lead to malignant pleural involvement: direct invasion from adjacent tumour, disease which has metastasized to the pleura from a distant tumour, or primary malignant transformation in the pleura, known as malignant pleural mesothelioma. These can manifest as either pleural thickening and/or a malignant pleural effusion.

A confident diagnosis of pleural malignancy can only be made on chest X-ray in advanced disease, when it is

Figure 6. Ultrasound showing a loculated pleural effusion – there are multiple septations (arrowheads) forming numerous contained locules with fluid of varying echogenicity, highly suggestive of an infective aetiology, confirmed on aspiration. Underlying compressive atelectasis is clearly visible (arrows).

Figure 7. Axial contrast-enhanced computed tomography scan with altered windowing to optimize visibility of the abnormally thickened, enhancing pleura surrounding an effusion ('split pleura' sign = arrowheads) typical of an empyema.



usually associated with a pleural effusion. Radiographic findings are of lobulated circumferential pleural thickening with signs of volume loss in the affected hemithorax (*Figure 8*). A useful rule of thumb is that very large unilateral effusions are highly likely to be the result of malignancy (*Figure 9*). Contrast-enhanced computed tomography is the imaging modality of choice to differentiate benign from malignant disease, and in metastatic pleural disease may also detect a primary tumour (*Figure 10*). Leung et al (1990) describe four features on pleural computed tomography which indicate a malignant rather than a benign process:

1. Circumferential pleural thickening
2. Nodular pleural thickening
3. Parietal pleural thickening greater than 1 cm
4. Mediastinal pleural involvement.

Magnetic resonance imaging may be of value in indeterminate cases where clinical suspicion is high, or when iodinated contrast media are contraindicated.

Figure 8. Typical radiographic appearance of malignant mesothelioma with nodular, circumferential thickening of the pleura and a small right basal effusion (arrow).

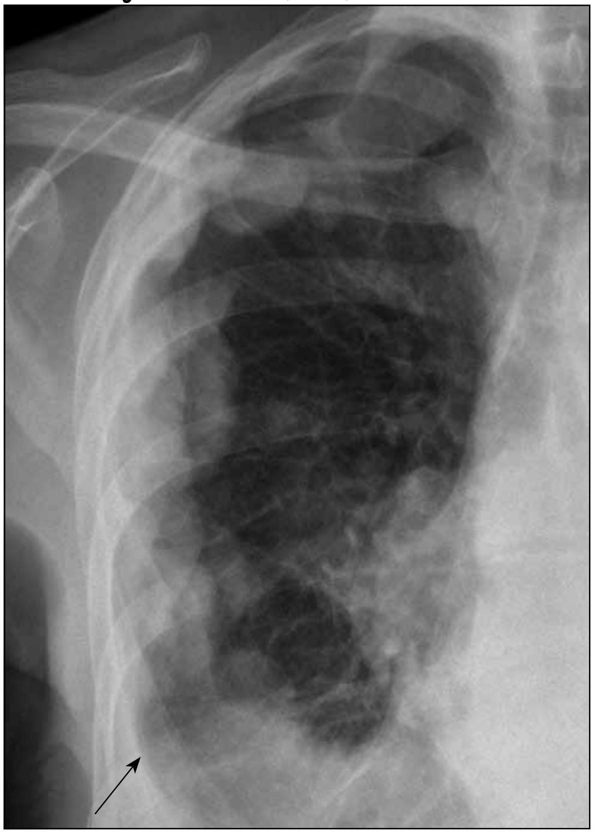


Figure 9. Massive right-sided effusion shifting the mediastinum to the left. Malignancy is the most common cause of very large unilateral effusions.

Malignant pleural mesothelioma

Three major histological subtypes of malignant pleural mesothelioma have been defined: epithelioid, biphasic and sarcomatoid, with epithelioid having a better prognosis (Kao et al, 2011). Malignant pleural mesothelioma is strongly associated with asbestos, with a typical latency of around 30–40 years following exposure, but occurs in a minority of at-risk individuals (between 5 and 7%) (Ferretti et al, 1997). Imaging of mesothelioma is challenging given its anatomical location and unusual growth pattern. On chest X-ray malignant pleural mesothelioma may appear as irregular pleural thickening, and may or may not be accompanied by a pleural effusion and/or volume loss. These features in themselves are indistinguishable from metastatic pleural disease, although identification of features of previous asbestos exposure suggests malignant pleural mesothelioma.

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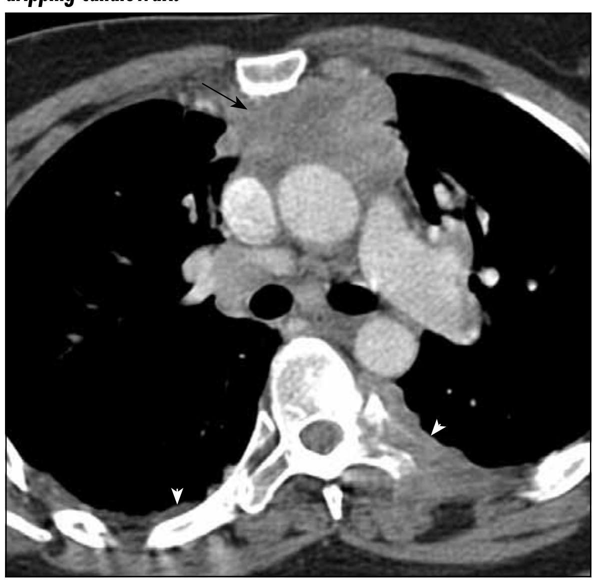
Figure 10. Axial contrast-enhanced computed tomography scan showing an invasive thymoma (black arrow) with pleural metastases (arrowheads), the appearance of which is likened to dripping candlewax.



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Computed tomography is the most widely used modality for the diagnosis of malignant pleural mesothelioma. Nodular pleural thickening is common, predominantly in the lower zones, with diaphragmatic thickening, fissural involvement and effusions also prevalent findings (*Figure 11*). Unusual appearances such as a localized calcified pleural mass may be seen, as well as remote isolated nodules representing multifocal disease. Computed tomography is also used to assess response of disease to treatment although modified criteria have to be applied because of malignant pleural mesothelioma's unique circumferential growth pattern (Byrne and Nowak, 2004).

Positron emission tomography also has an emerging role in assessing the stage, prognosis and response to treatment of malignant pleural mesothelioma. It differentiates between benign and malignant pleural disease, as well as being highly sensitive in the detection of distant metastases (Plathow et al, 2008). Positron emission tomography may also have a role in defining appropriate biopsy sites as a second-line modality in patients with a degree of suspicion for malignancy but a negative first biopsy (Mavi et al, 2009), and may even offer improvements in prognostication (Nowak et al, 2010). Currently, because most queries can be addressed using simpler modalities, positron emission tomography is generally only used in the investigation of malignant pleural mesothelioma on a case-by-case basis. There may also be a niche group of mesothelioma patients in whom magnetic resonance imaging is useful, such as those being considered for radical resection although because of the late presentation in most cases, magnetic resonance imaging is not usually indicated as it adds no further value in advanced (i.e. inoperable) stage 4 disease.

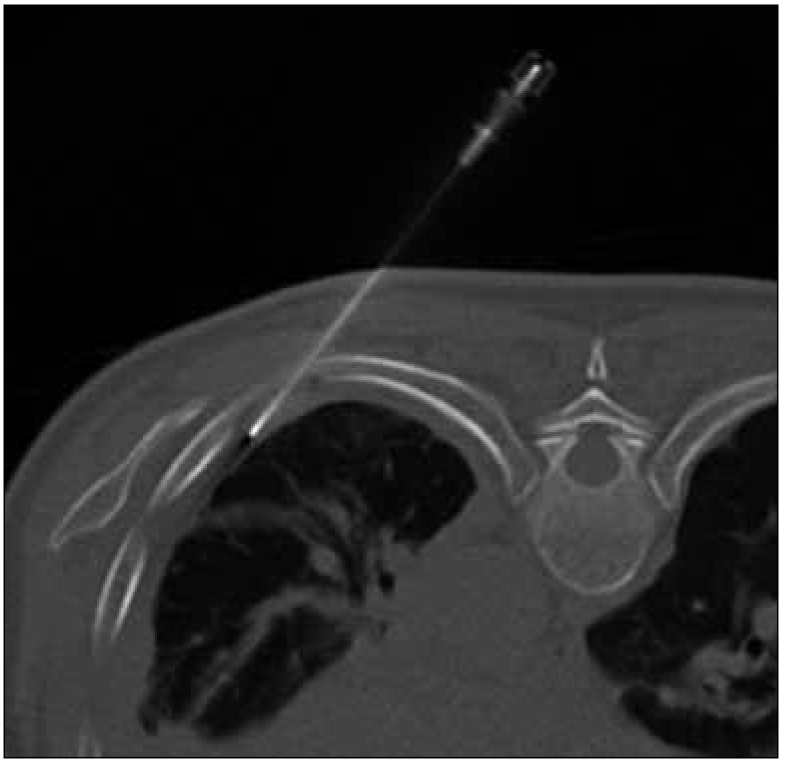
Radiologically-guided pleural biopsy

In certain patients, especially those who are frail or not keen for intervention, radiological suspicion of malignancy alone may be sufficient to form a management plan. However, for the majority, biopsy for histological evaluation of pleural abnormalities should be considered where there is a suspicion of malignancy.

A range of invasive techniques are available for tissue sampling in those patients with an effusion and suspicious pleural appearances, including percutaneous image-guided procedures, medical thoracoscopy and surgical sampling, most commonly using video-assisted thoracoscopic surgery. Blind Abrams needle biopsies, which were the historical norm, have a relatively poor diagnostic rate of only 57% for malignancy (Tomlinson, 1987), along with significant complication rates. By using contrast-enhanced computed tomography, focal areas of pleural thickening can be visualized and biopsied in a targeted manner (*Figure 12*), with prospective and retrospective studies showing this to be an extremely sensitive (86–88%) and specific (100%) method (Adams and Gleeson, 2001; Maskell et al, 2003). British Thoracic Society guidelines now recommend that when investigating an undiagnosed effusion where malignancy is sus-

Figure 11. Axial contrast-enhanced computed tomography scan showing marked circumferential, nodular pleural thickening >1 cm and involving the mediastinal surface, thus fulfilling all computed tomography criteria for pleural malignancy (mesothelioma).

Figure 12. Axial prone computed tomography showing a co-axial 18G core biopsy introducer in situ for targeted pleural biopsy.



pected, and where there are areas of pleural nodularity on contrast-enhanced computed tomography, an image-guided cutting needle is the percutaneous pleural biopsy method of choice (Hooper et al, 2010).

For those patients who present with possibly malignant pleural thickening without associated fluid, computed tomography-guided biopsy offers a potentially diagnostic option without resorting to surgery. Radiological biopsy may also find a role if other methods are unable to provide a diagnosis, for example if medical thoracoscopy has failed, or if patients are too frail or have other contraindications to such a procedure.

Conclusions

The pleura can be assessed using a wide range of imaging modalities, although the clinical question being asked must be carefully considered when choosing which images to obtain. Plain radiography is usually indicated in the first instance, with conditions such as pleural plaque or proven benign thickening often requiring little else in terms of follow up. Unenhanced computed tomography remains the workhorse of pleural imaging as it yields excellent image definition and resolution in most pleural abnormalities. Ultrasound is an increasingly key modality which has found a place in assessing both the nature of an effusion, and in facilitating bedside image guidance for pleural procedures. Contrast-enhanced computed tomography is now the mode of choice for assessing pleural disease suspicious for malignancy, and when image-guided biopsy is performed. Magnetic resonance imaging and positron emission tomography currently have a limited role in pleural imaging, but each undoubtedly has a role in the few circumstances when other modalities are unable to provide adequate information, as may be the case in the diagnosis or management of malignant pleural disease. BJHM

Conflict of interest: none.

KEY POINTS

- Malignancy is the most common cause of a large unilateral pleural effusion.
- Contrast-enhanced computed tomography can frequently differentiate between benign and malignant pleural thickening, and can greatly assist in identifying potential causes.
- Ultrasound is an excellent modality for assessing the presence and nature of pleural effusions. The routine use of ultrasound guidance to aid in pleural aspiration and drain insertion is advocated – 'X-marking' does not guarantee safe or effective aspiration.
- In all undiagnosed exudative pleural effusions, as well as for complicated pleural infection when initial tube drainage has been unsuccessful and surgery is to be considered, imaging with computed tomography is recommended.
- When investigating an undiagnosed effusion where malignancy is suspected, in the presence of pleural nodularity on contrast-enhanced computed tomography, image-guided pleural biopsy is the method of choice.

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