Malignant Pleural Effusion
From Diagnostics to Therapeutics

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KEYWORDS

• Malignant pleural effusion • Malignant pleural effusion management • Dyspnea
• Pleural fluid cytology • Indwelling pleural catheter

KEY POINTS

- A large unilateral pleural effusion is suspicious for malignancy.
- Cytology-negative exudative pleural effusions should be investigated further because many turn out to be malignant.
- When pleural biopsy histology results are negative for malignancy, patients should be followed up for at least 2 years; 8.3% will turn out to be malignant.
- The main aim of management of malignant pleural effusion is symptom control.

INTRODUCTION: NATURE OF THE PROBLEM

Malignant pleural effusion (MPE) is one of the commonest causes of an exudative pleural effusion, and its incidence is increasing with increasing cancer prevalence and as more effective cancer therapy that prolongs life. It is the commonest cause of a unilateral massive pleural effusion, although 10% to 13% can be bilateral.[1,2] MPE is a common complication of malignancy, and usually indicates disseminated or advanced disease. In lung cancer, the presence of a pleural effusion upstages the cancer to stage IV, denoting a worse prognosis.[3] Median survival after a diagnosis of MPE depends on the underlying malignancy and stage at diagnosis, and varies between 3 and 12 months.[4] Most MPEs are secondary to metastases to the pleura from other sites, most commonly lung and breast, which together cause 50% to 65% of all MPE.[5]

Pleural effusion results from an imbalance between pleural fluid production and absorption. MPE likely results from a combination of impaired lymphatic outflow by parietal pleural cancer or metastases, and increased permeability of the pleural and tumor vessels, resulting in a net fluid accumulation.[6] There is an important differential diagnosis for pleural effusions in malignancy; they can be paramalignant, owing to bronchial obstruction by tumor with subsequent atelectasis and development of ipsilateral pleural effusion, or owing to pulmonary embolism, mediastinal lymphatic obstruction, thoracic duct obstruction (chylothorax), superior vena cava obstruction, malignant pericardial effusion and cardiac tamponade, hypoalbuminemia, and the side effects of chemotherapy or radiotherapy.

PATIENT HISTORY

- The mean age at presentation is 65 years.
- Most are symptomatic, although up to 15% to 25% are asymptomatic[7,8]
- Dyspnea is the commonest symptom. Patients may also present with cough, chest pain (especially in mesothelioma), and constitutional symptoms such as weight loss, malaise, and anorexia.[5]
- Symptoms of the underlying malignancy may also be present, such as hemoptysis, change in bowel habit, or passage of blood per rectum.

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PHYSICAL EXAMINATION

- Decreased air entry, dullness to percussion (typically stony dullness), decreased vocal resonance, and decreased vocal fremitus over the pleural effusion.
- Signs of underlying primary malignancy such as breast lumps or palpable lymph nodes.

IMAGING AND ADDITIONAL TESTING

Chest Radiographs

A pleural effusion of greater than 200 mL is detected on posteroanterior chest radiographs, and blunting of the posterior costophrenic angle has been reported to correlate with as little as 26 mL of pleural fluid.[9,10] MPEs are usually unilateral and large. If mediastinal shift is absent in the presence of a large MPE, there may be ipsilateral bronchial obstruction with lung collapse, for example, in lung cancer, or the mediastinum may be fixed by a malignant lymph node mass.

Thoracic Ultrasound Imaging

Increasingly, point-of-care thoracic ultrasound examination is being used in respiratory clinics and, as a result, patients have more rapid access to diagnosis and treatment. It can add valuable information about the size and depth of the pleural effusion, any contralateral pleural effusion, echogenicity, septations, loculated fluid, pleural thickening and nodularity, diaphragm position, and movement.

Pleural procedures are now often done with real-time ultrasound guidance. The use of ultrasound guidance for procedures results in a greater success rate and a reduced risk of complications, including solid organ injury; therefore, it is advocated as a best practice by national guidelines.[11] Ultrasound guidance also provides valuable information regarding accessibility of pockets of fluid in loculated pleural effusions, and the use of Doppler imaging helps to locate and, therefore, avoid intercostal vessels before pleural intervention.

Thoracic Computed Tomography Scans

A thoracic computed tomography (CT) scan, with pleural phase contrast for better definition, should be done before complete drainage of the fluid for better visualization of pleural abnormalities, and complete drainage of effusion before CT is not required to increase diagnostic sensitivity.[12] Parietal, mediastinal, and circumferential pleural thickening, and pleural nodularity indicate a likely MPE,[13,14] with a high specificity (88%–94%), but a low sensitivity (36%–51%).[13] CT scans can also provide evidence of the underlying primary tumor and evidence of metastases, although the CT scan may not show other abnormalities apart from the pleural effusion itself (Figs. 1 and 2).

MRI

Diffusion-weighted MRI distinguished benign from MPEs with 71.4% sensitivity and 87.1% accuracy in 1 study, and this finding was increased further with the use of dynamic contrast-enhanced MRI.[15] It may be useful in the assessment of treatment response, and in patients in whom contrast in contraindicated; however, access to MRI is limited.

PET–Computed Tomography

Fluorodeoxyglucose PET-CT is useful for staging pleural disease; however, its use is limited by the false-positive results obtained with infection and inflammation, including with prior talc pleurodesis. Despite this finding, 1 study showed that this modality correctly diagnosed malignancy with a sensitivity of 93% and a specificity of 68% for MPE,[16] and another reported that it correctly identified malignancy with a sensitivity of 95% to 97% and a specificity of at least 95%.[17] However, in a recent metaanalysis, the investigators concluded that PET-CT has a sensitivity of 81% and specificity of 74%, therefore, showing only moderate accuracy in differentiating malignant from benign effusions, precluding its routine recommendation.[18] The usefulness of PET scans in patients with negative biopsies to target PET-avid areas and increase diagnostic sensitivity is the subject of a currently recruiting randomized trial in the UK (Randomised controlled trial to compare the diagnostic yield of Positron Emission Tomography

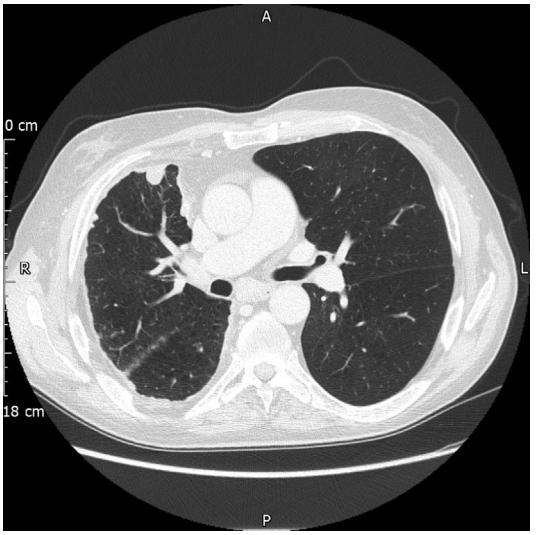

Fig. 1. CT scan image showing pleural nodularity and thickening in patient with mesothelioma.