Malignant Pleural Mesothelioma

Introduction and Staging

Malignant pleural mesothelioma (MPM) accounts for less than 2% of all thoracic tumors but is the most common pleural malignancy. The likelihood of contracting this disease is increased approx. 100-fold by asbestos exposure (Sohrab and Konietzko 2002). Generally a period of 20–30 years elapses between the initial asbestos exposure and manifestation of disease. In many countries the manufacture and processing of asbestos has been prohibited since the early 1990s, so it is reasonable to predict that the incidence of MPM will peak around the year 2020. By the year 2030 it is estimated that MPM will have caused approx. 250 000 deaths in Western Europe (Sohrab and Konietzko 2002). MPM has a very poor prognosis with a median survival time of 4–18 months. The average 5-year survival rate is no more than 2.5% (Bonomo et al. 2000).

MPM typically spreads within the pleural cavity. Accordingly, a hemorrhagic effusion is almost invariably present. It is also common for MPM to invade the chest wall, diaphragm, or mediastinum. Because MPM usually arises from cells of the parietal pleura, the pattern of nodal metastasis differs from that of parenchymal lung tumors. Initial nodal metastasis is usually to lymph nodes that drain the parietal pleura (TNM stage N2). Distant metastases are rare. The staging of MPM is based on the TNM classification (Rusch 1996).

The three histologic types of MPM are described as epithelial, mesenchymal, and mixed. The differentiated epithelial type is the most common and has, relatively, the best prognosis (Sugarbaker et al. 1999).

FDG PET is not useful for the T staging of MPM.

Imaging Studies

CT

The utility of PET-CT in MPM is still uncertain.

Typical findings. Typical morphologic features of MPM on CT scans are complete encasement of the lung or multiple sites of nodular pleural thickening with involvement of the interlobar septa. The tumor usually shows intense, inhomogeneous enhancement after intravenous contrast administration. Additionally, a pleural effusion is usually present, and pericardial effusion may develop in advanced cases. Often these signs are absent in the early stage, making it initially impossible to distinguish between a benign and a malignant pleural process on the basis of CT findings (Benamore et al. 2005).

In the early stage of MPM, it is often impossible to judge on the basis of CT whether the lesion is benign or malignant.

Staging. CT is the dominant imaging modality for the preoperative staging of MPM and supplies information that is essential for this purpose. Chest-wall invasion, pulmonary involvement (by lymphatic or hematogenous dissemination of tumor cells), and involvement of the pericardium and mediastinal lymph nodes can be adequately evaluated by CT. As with lung cancer, unequivocal CT signs of chest-wall or mediastinal invasion are bone destruction and/or invasion of the intercostal muscles. The obliteration of extrapleural fat planes is another manifestation of chest-wall involvement (Benamore et al. 2005). In one study, morphologic CT criteria were applied in 34 patients with MPM to correctly exclude chest-wall invasion in 93%, diaphragmatic invasion in 94%, and mediastinal invasion in 100% of the cases. The extent of chest-wall and diaphragmatic involvement was underestimated by CT, however (Patz et al. 1992).

FDG PET

Malignant pleural mesotheliomas show increased FDG uptake. Twenty-eight patients were evaluated by FDG PET imaging (Bénard et al. 1998). When a SUV cutoff of 2 was used, a sensitivity of 91% and a specificity of 100% were achieved in differentiating between malignant and benign pleural lesions. Epithelial MPM showed lower FDG uptake on average than the other types. The survival times of the seven patients who died from MPM showed a significant correlation with the mean SUV of the tumor (Bénard et al. 1999).

Other studies have also documented the contribution of FDG PET to the evaluation of pleural lesions (Carretta et al. 2000; Schneider et al. 2000). As in the case of CT, however, it is difficult to distinguish between MPM and a pleural metastasis from a nonpleural primary tumor (Carretta et al. 2000). It is essential, therefore, that the diagnosis be confirmed by biopsy before any treatment is initiated. Furthermore, FDG PET cannot provide accurate anatomic localization of increased uptake, making it unsuitable for T staging. In summary, the importance of FDG PET in the diagnosis and follow-up of MPM has not yet been fully established.

PET-CT

Available data on the utility of PET-CT in MPM are still inconclusive. Twenty-nine patients with MPM who were initially judged to be candidates for extrapulmonary pneumonectomy were evaluated by CT and FDG PET. In 11 of the patients the imaging results negated the indication for pneumonectomy. In 21 of the 29 patients the tumor was correctly staged by PET-CT (Erasmus et al. 2005). In another study, PET-CT was more accurate than PET and CT separately in establishing an indication for extrapulmonary pneumonectomy (Steinert et al. 2005).

PET-CT also provides useful information for evaluating lymph node status. Nodal status was correctly determined in 6 of 17 patients by PET-CT (Erasmus et al. 2005; **Fig. 2.30**).

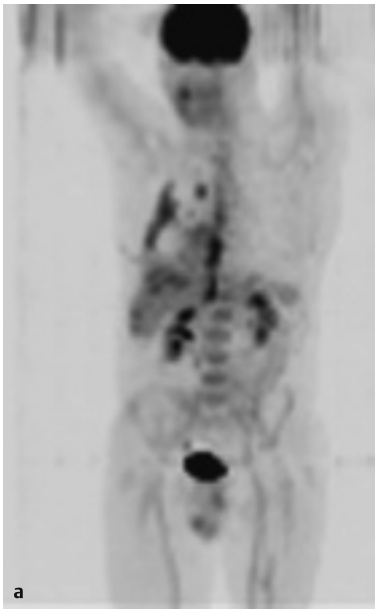
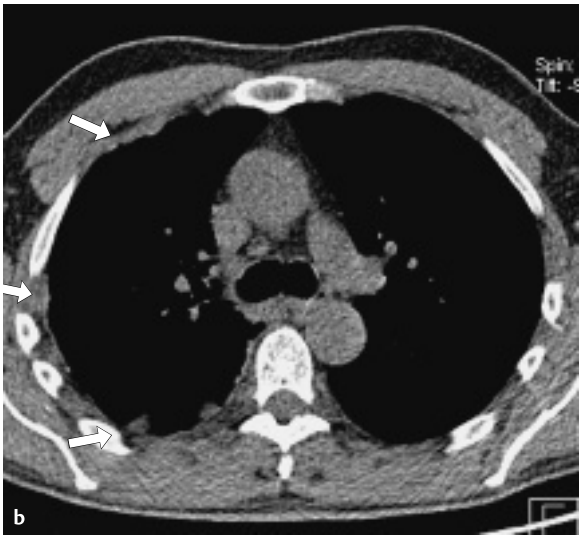


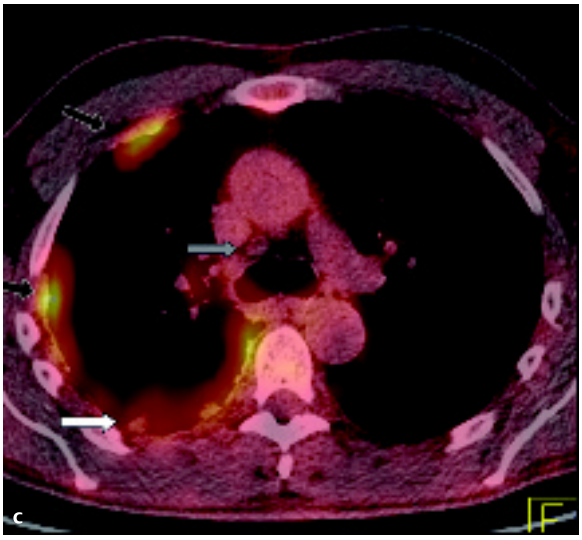
Fig. 2.30 a–g **Malignant pleural mesothelioma of the right hemithorax in a 63-year-old man.**

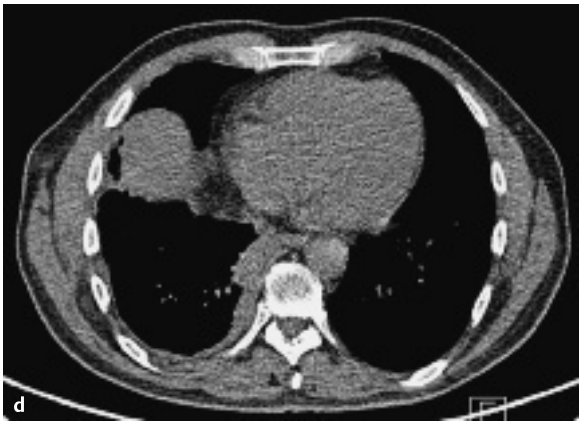
a FDG PET (MIP).

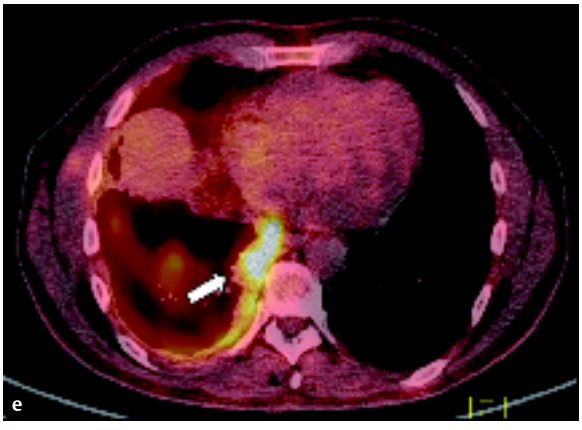
b–e PET-CT (**c, e**) with corresponding unenhanced low-dose CT scans (**b, d**). Nodular foci of pleural thickening show a combination of low FDG uptake (**c**, white arrow) and higher uptake (**c**, black arrow; **e**, white arrow). PET-CT is more accurate in determining the exact location of a hypermetabolic lesion for percutaneous biopsy. Enlarged mediastinal lymph node with a fatty hilum (**c**, gray arrow). Absence of FDG uptake indicates an inflammatory-reactive pathogenesis.

f, g Coronal reformations of FDG PET (**f**) and PET-CT (**g**). Accurate image fusion is technically difficult for lesions near the diaphragm (**g**, black and white arrows) but is easy for lesions distant from the diaphragm (**g**, gray arrow).

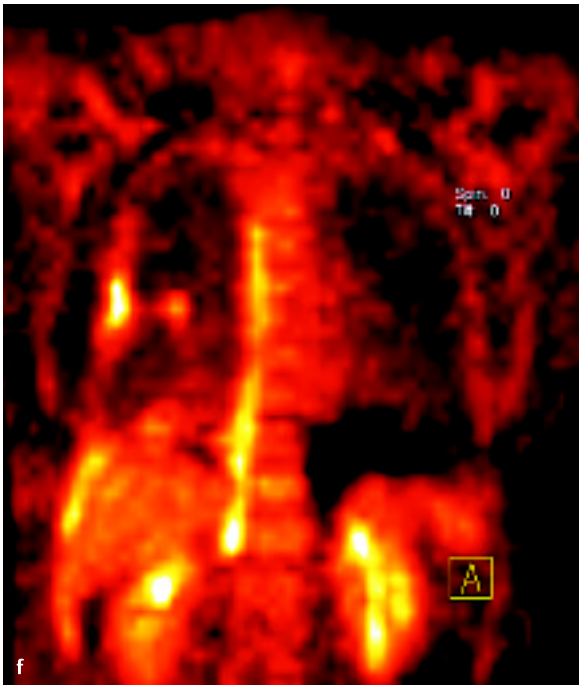








Continued →



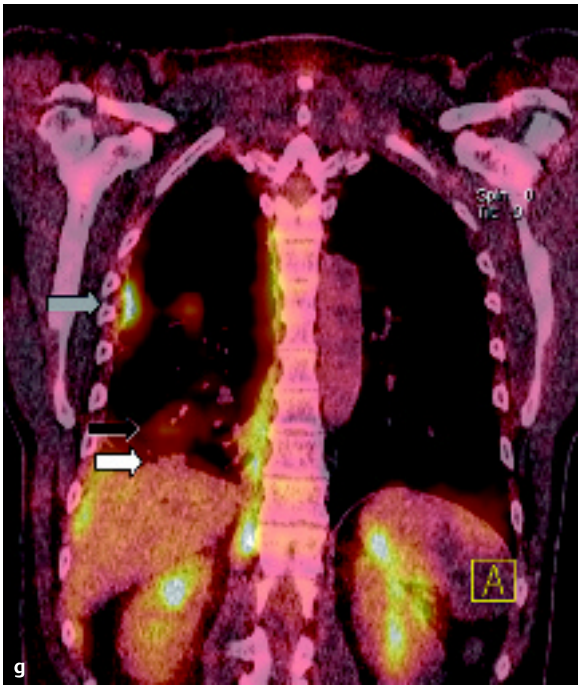


Fig. 2.30 a–g **Continued** (see legend on p. 115)

To date there have been no systematic studies on the accuracy of PET-CT for TNM staging compared with CT or FDG PET alone.

The combination of anatomic (CT) and metabolic (PET) information can also improve the accuracy of percutaneous biopsy (**Fig. 2.30**). This has clinical relevance because the cytologic evaluation of a pleural effusion or the histologic examination of a suspect lesion does not always yield definitive results, creating a need for multiple biopsies that may cause iatrogenic tumor cell dissemination (Boutin et al. 1995).

The respiratory movements of the diaphragm mean that there is a natural limit on the detection of diaphragmatic invasion by PET-CT. Early tumor involvement may be completely obscured by respiratory motion. In addition, variations in respiratory excursions may hamper the coregistration of FDG PET and CT images (**Fig. 2.30**).

Even CT may fail to detect a diaphragmatic tumor, because of the respiratory movements of the diaphragm.

Pulmonary Metastases

The lung is the most frequent target site for hematogenous metastasis from extrapulmonary malignancies. The tumors that most commonly metastasize to the lung are carcinomas of the thyroid gland, breast, and prostate, bone and soft-tissue sarcomas, and tumors of the testes, kidneys, adrenal glands, uterus, ovaries, and nasopharynx. Metastases account for the highest percentage of malignant pulmonary nodules.

CT

CT is the modality of choice for diagnosing pulmonary metastases, although lesions less than 6 mm in diameter are notoriously difficult to detect. A study on the detection of histologically confirmed pulmonary metastases by CT indicated an overall sensitivity of 77% for lesions of all sizes. The sensitivity was 94% for metastases 6–10 mm in size but 100% for metastases larger than 10 mm (Diederich et al. 1999).

Moreover, CT cannot positively distinguish between metastases and pulmonary nodules due to other causes. The size of a pulmonary nodule is of only limited value for determining whether or not it is malignant. The same is true of other morphologic parameters (Diederich et al. 2005). The pulmonary nodules detected by CT are frequently benign, even in patients with a known neoplastic disease (Kronawitter et al. 1999; Picci et al. 2001).

The accuracy of CT for identifying malignancy of a lesion can be increased by conducting follow-ups (analyzing changes over time) or by using CT with complementary modalities such as FDG PET.

FDG PET

The ability of FDG PET to detect pulmonary metastases has not yet been investigated for all primary tumor types. Nevertheless, studies to date indicate that FDG PET can detect pulmonary metastases from numerous primary extrapulmonary malignancies such as colon and breast cancer, malignant melanoma, and soft-tissue sarcomas