BENIGN AND MALIGNANT MESOTHELIAL PROLIFERATION

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KEYWORDS

• Mesothelial proliferations • Malignant mesothelioma • Metastatic carcinoma • Pleural effusion

ABSTRACT

Malignant mesothelioma (MM) is a rare primary malignant tumor of the surface serosal cells. The diagnosis of MM is challenging with a broad differential diagnosis. For many decades, studies have focused on distinguishing MM from other types of cancer; however, benign mesothelial cell hyperplasia, especially in small biopsies, has emerged as a major problem. The features of pleural lesions are somewhat different from peritoneal diseases, and this article primarily focuses on pleural diseases. Thorough interpretation and correlation of clinical, radiologic, and pathologic findings are essential for a correct diagnosis.

Mesothelial cells lining the pleural, pericardial, and peritoneal cavities are specialized coelomic epithelial cells and are, therefore, mesodermal in origin. Embryonic mesothelial cells contribute to the coronary and intestinal vasculature by differentiating into endothelial cells, vascular smooth muscle cells, and pericytes. This differentiation process is an epithelial-mesenchymal transition.[1] Embryonic and adult lungs are both covered by a thin layer of mesothelial cells. During development, the mesothelium plays an important role in regulating the overall size and morphology of the lung through interactions with submesothelial mesenchyma.[2] Adult mesothelial cells in the pleura perform vital functions, such as contributing a smooth and lubricated surface, initiating and resolving inflammation, repairing tissue, and secreting and reabsorbing electrolytes and pleural fluid.[3]

Malignant mesothelioma (MM) is a tumor of mesothelial cells that is predominantly associated with asbestos exposure. The diagnosis of this rare tumor is challenging in most instances and should be supported by clinical and radiologic information. In contrast, reactive mesothelial cells can mimic a variety of malignancies, including MM and other types of cancer, in cytologic specimens and pleural biopsies. During the past few decades, several histologic criteria as well as many immunohistochemical markers have been proposed in differentiating the diagnosis of MM from benign mesothelial hyperplasia and metastatic adenocarcinomas of various sites.[4,5]

GROSS FEATURES

Macroscopically, MM is observed as a dense thickening of the pleura with firm white-yellow tissue (**Fig. 1**). Sometimes, it may show cystic areas containing mucoid material. The tumor often invades the diaphragm, fissures, and underlying atelectatic lung and, in advanced cases, mediastinal and pericardial involvement can be seen. It is also associated with pleural effusion. MM may present as

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Key Features
Malignant Mesothelioma

- Mesothelial cell proliferation and many malignant and benign tumors may mimic pleural MM.
- Benign mesothelial proliferation, simple or atypical, primarily occurs as a result of infection, collagen vascular disease, pulmonary infarct, drug reaction, pneumothorax, subpleural lung carcinoma, surgery, or trauma.
- Well-differentiated papillary mesothelioma (WDPM) is a localized lesion with a good prognosis. It is composed of fibrovascular papillary projections covered by a single layer of bland mesothelial cells.
- MM presents as firm, gray-white thickening of the pleura; however, nodular and localized gross features can be observed.
- MM can be divided into 3 basic histologic types: epithelial, biphasic, and sarcomatous. Several uncommon histologic subtypes have been noted, including deciduoid, small cell, clear cell, and signet ring cell variants of epithelioid MM and desmoplastic and lymphohistiocytic variants of sarcomatous MM. The desmoplastic histologic variant can also exhibit epithelial features focally.
- Sarcomatous mesothelioma is primarily composed of fibroblast-like spindle cells; however, it may exhibit highly anaplastic features. Pleural fluid examination is not diagnostic for sarcomatous mesothelioma because the tumor cells are never shed into the pleural cavity.
- Immunohistochemistry is a useful tool in the diagnosis of MM; however, none of the mesothelial cell markers is 100% specific and highly sensitive. The most commonly used mesothelial cell markers are calretinin, keratin 5/6, WT1, HBME-1, thrombomodulin, mesothelin, and podoplanin (D2-40). Caveolin-1 and tenascin-X recently have been proposed.
- Epithelial histology and extrapleural pneumonectomy are independent predictors of prolonged survival. Homozygous deletion of 9p21 and loss of p16 immunoreactivity are also associated with shorter survival.

multiple tumor nodules or, occasionally, as a solid and localized mass (localized MM). The parietal pleura is often more extensively involved. The majority of MM cases are unicavitary; however, simultaneous involvement of the pleura and peritoneum can occur.[6] At autopsy, distant metastases are identified in up to 50% of all cases.

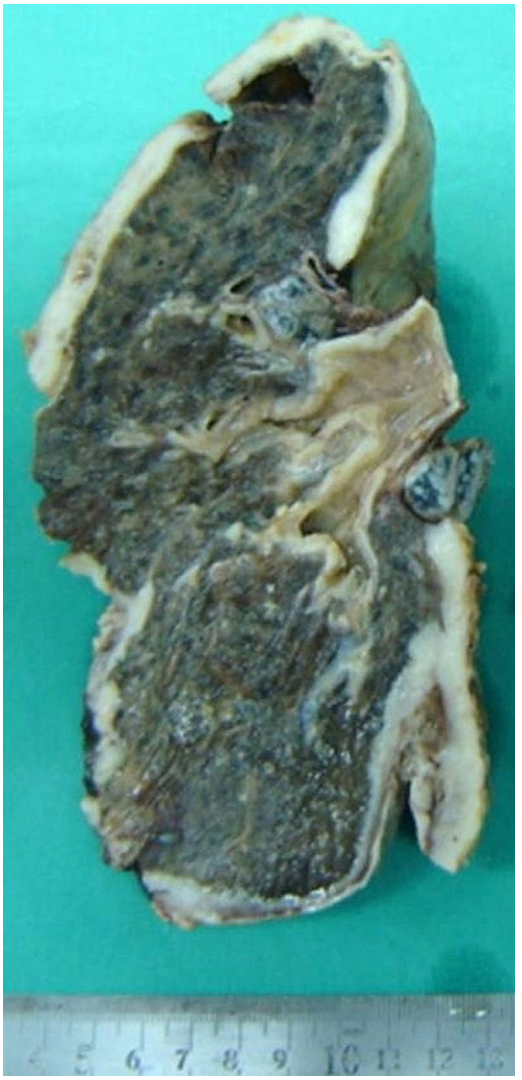

Fig. 1. Firm thickening of the pleura by MM.

Diffuse serosal growth is not a specific feature of MM. Nonmesothelioma neoplasms, so-called pseudomesotheliomas, demonstrating a diffuse growth pattern have been described. Pulmonary and nonpulmonary carcinomas, sarcomas, and lymphomas may demonstrate this growth pattern.[7] A diffuse pleural growth pattern is not a consistent feature of MM, however. In localized MM, the tumor appears as a circumscribed pleural-based mass, with a size of 2.2 to 15 cm, without any evidence of pleural spread.[8] WDPM is a distinct mesothelial tumor with a good outcome. Its presentation consists of unilateral pleural effusion and superficial spreading of stout papillary formations with myxoid cores. It can also present with only pleural effusion and without any nodularity or mass lesion. Galateau-Salle and colleagues[9] detected thin, focal pleural thickening in 9 of 24 cases (37.5%).

Local spread, primarily through the chest wall, lungs, and mediastinum, is a more common feature of MM. Distant metastases are rare in