Chapter 1
Approaching the Diagnosis of Diffuse Malignant Mesothelioma

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For most pathologists, diffuse malignant mesothelioma (DMM) is a disease for which its rarity renders it unfamiliar, its histologic diversity diagnostically challenging, and its medical–legal implications overly stressful. Because DMM has a dismal prognosis and very limited treatment options compared to its much more common mimics, accurate diagnosis is paramount.

The World Health Organization's classifications of tumors of the pleura [1] and peritoneum [2] include DMM; however, as the vast majority of DMM is pleural, it is pleural tumor upon which this book focuses. DMM is the most common primary malignant neoplasm arising within the pleura. The WHO's classification also recognizes four DMM histologic subtypes: epithelial, sarcomatous, biphasic, and desmoplastic; however, the designation of desmoplastic DMM—generally considered a variant of sarcomatous DMM—as a separate histologic subtype is controversial. Although desmoplastic DMM is strongly mimicked by chronic fibrous pleuritic, and has an especially bad prognosis, neither of these features warrants the stature of independent subtyping.

In order to render an accurate diagnosis, a biopsy sample must provide adequate diagnosable tissue. For the diagnosis of DMM, such a biopsy sample typically is obtained from open procedures such as thoroscopy. Pleural needle biopsies have the benefit of low morbidity and cost; however, those efficiencies often come at the high cost of diagnostic compromise [3, 4]. Once determined adequately, a tissue sample must then be assessed to determine whether it contains reactive or neoplastic tissue, and if neoplastic, whether the tumor is DMM or another, likely metastatic, neoplasm. The differential diagnosis and workup are guided by the histology, specifically by the presence of an epithelioid cellular proliferation or a spindle cell proliferation. In these cases, even with ample tissue available for examination, histology alone is typically insufficient to allow a definitive DMM diagnosis to be rendered, and im-

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munostains are a necessary next step in the diagnostic workup. Yet immunostains themselves also have significant limitations; for example, their use in determining reactive versus neoplastic tissue is very restricted, and their utility with spindle cell proliferations is also narrow. Further, it must be remembered that both neoplastic and reactive proliferations may be present in a single biopsy. *En face* sectioning might also show sheet-like collections of mesothelial cells suggesting the presence of a solid tumor. Also, nuclear atypia involving reactive proliferations may be so marked as to mimic malignancy, while DMM may present with generally bland-appearing nuclear features. In the end, numerous potential diagnostic pitfalls must be avoided. Ultimately, biopsy findings must be correlated with clinical and radiologic findings to best ensure accurate diagnosis.

DMM is frequently associated with prior occupational exposure to asbestos; however, asbestos exposure history is irrelevant to the histologic diagnosis of DMM, or its exclusion from a differential diagnosis, and should not be used as a factor in the histologic diagnosis of DMM. A misdiagnosis may yield substantial medical–legal consequences.

Because DMM diagnosis—and often even its mere clinical speculation—initiates legal proceedings, pathologists—subject to resultant diagnostic pressure—must maintain the highest level of professionalism and diagnostic accuracy. It must be remembered that the vast majority of cases for which DMM is clinically entertained in the end are either reactive proliferations or metastases. To best serve the patient, consultation with a pulmonary pathologist with expertise in DMM diagnosis is recommended in all but the most straightforward of DMM cases. One should reasonably assume that the pathologist's DMM diagnosis will be carefully scrutinized in the legal arena.

References

1. Travis WD, Brambilla E, Muller-Hermelink HW, et al. Pathology and genetics of tumors of the lungs, pleura, mediastinum and heart. Lyon: IARCPress; 2004.
2. Tavassoli FA, Devilee P. Pathology and genetics of tumours of the breast and female genital organs. Lyon: IARCPress; 2003.
3. Boutin C, Rey F. Thoracoscopy in pleural malignant mesothelioma: a prospective study of 188 consecutive patients. Cancer. 1993;72:389–3.
4. Attanoos RL, Gibbs AR. The comparative accuracy of different pleural biopsy techniques in the diagnosis of malignant mesothelioma. Histopathology. 2008;53:340–4.