characterized by a proliferation of perivascular epithelioid cells that express markers of both melanocytes and smooth muscle cells. The proliferation distorts the involved lung, leading to cystic, emphysema-like dilation of terminal airspaces, thickening of the interstitium, and obstruction of lymphatic vessels. The lesional epithelioid cells appear to frequently harbor loss of function mutations in the tumor suppressor *TSC2*, one of the loci linked to tuberous sclerosis (Chapter 28). You will recall that the protein encoded by *TSC2*, tuberin, is a negative regulator of mTOR, a key regulator of cellular metabolism. While *TSC2* mutations points to increased mTOR activity as a contributing factor, the disorder remains poorly understood. The strong tendency to affect young women suggests that estrogen contributes to the proliferation of perivascular epithelioid cells, which often express estrogen receptors. Patients most commonly present with dyspnea or spontaneous pneumothorax, the latter related to the emphysematous changes. The disease tends to be slowly progressive over a period of several decades. mTOR inhibitors are being tested in clinical trials, but lung transplantation is the only definitive treatment available currently.

Inflammatory myofibroblastic tumor, though rare, is more common in children, with an equal male-to-female ratio. Presenting symptoms include fever, cough, chest pain, and hemoptysis. It may also be asymptomatic. Imaging studies show a single (rarely multiple) round, well-defined, usually peripheral mass with calcium deposits in about a quarter of cases. Grossly, the lesion is firm, 3 to 10 cm in diameter, and grayish white. Microscopically, there is proliferation of spindle-shaped fibroblasts and myofibroblasts, lymphocytes, plasma cells, and peripheral fibrosis. Some of these tumors have activating rearrangements of the anaplastic lymphoma kinase (*ALK*) gene, located on 2p23, and treatment with ALK kinase inhibitors have produced sustained responses in such cases.

Tumors in the mediastinum either may arise in mediastinal structures or may be metastatic from the lung or other organs. They may also invade or compress the lungs. Table 15-12 lists the most common tumors in the various compartments of the mediastinum. Specific tumor types are discussed in appropriate sections of this book.

Table 15-12 Mediastinal Tumors and Other Masses

Anterior Mediastinum
Thymoma
Teratoma
Lymphoma
Thyroid lesions
Parathyroid tumors
Metastatic carcinoma
Posterior Mediastinum
Neurogenic tumors (schwannoma, neurofibroma)
Lymphoma
Metastatic tumor (most are from the lung)
Bronchogenic cyst
Gastroenteric hernia
Middle Mediastinum
Bronchogenic cyst
Pericardial cyst
Lymphoma

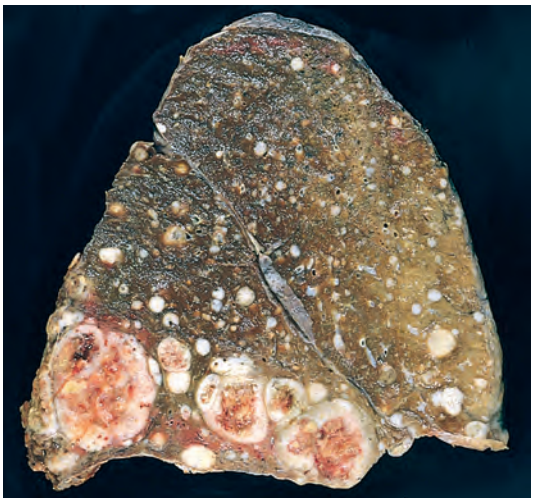

Figure 15-49 Numerous metastases to lung from a renal cell carcinoma. (Courtesy Dr. Michelle Mantel, Brigham and Women's Hospital, Boston, Mass.)

Metastatic Tumors

The lung is the most common site of metastatic neoplasms. Both carcinomas and sarcomas arising anywhere in the body may spread to the lungs via the blood or lymphatics or by direct continuity. Growth of contiguous tumors into the lungs occurs most often with esophageal carcinomas and mediastinal lymphomas.

MORPHOLOGY

The pattern of metastatic growth within the lungs is quite variable. In the usual case, multiple discrete nodules (cannonball lesions) are scattered throughout all lobes, more being at the periphery (Fig. 15-49). Other patterns include solitary nodule, endobronchial, pleural, pneumonic consolidation, and combinations of these. Foci of lepidic growth similar to adenocarcinoma in situ are seen occasionally with metastatic carcinomas and may be associated with any of the listed patterns.

Pleura

Pathologic involvement of the pleura is, most often, a secondary complication of some underlying disease. Secondary infections and pleural adhesions are particularly common findings at autopsy. Important primary disorders include (1) primary intrapleural bacterial infections that imply seeding of this space as an isolated focus in the course of a transient bacteremia and (2) a primary neoplasm of the pleura: mesothelioma (discussed later).

Pleural Effusion

Pleural effusion is a common manifestation of both primary and secondary pleural diseases, which may be inflammatory or noninflammatory. Normally, no more than 15 mL of serous, relatively acellular, clear fluid lubricates the pleural surface. Accumulation of pleural fluid occurs in the following settings: