

extremities due to impaired venous return. Despite its aesthetic and prognostic implications, its involvement typically does not represent a medical emergency.

The physical examination may be normal or may reveal changes in the lung, such as crackles (e.g., postobstructive pneumonia) (E-Fig. 23-7), inspiratory wheeze suggesting airway obstruction, or dullness to percussion as a result of underlying pleural effusion. Lymph node enlargement in the neck or axillary areas suggests metastatic disease (E-Fig. 23-8).

Lung cancers that occur in the apex of the chest and invade apical chest wall structures are known as *superior sulcus* or *Pancoast tumors* (E-Fig. 23-9). The classic description involves a syndrome of radicular-type pain or paresthesias radiating down the arm due to tumor erosion into the brachial plexus. Tumor erosion into the cervical sympathetic chain can result in Horner's syndrome, which is characterized by a triad of physical findings: ptosis, miosis, and anhidrosis over the face and forehead.

Paraneoplastic syndromes are usually neurologic syndromes that are rare and are elicited by a patient's own immune response to neoplastic processes, often originating in the lung. Neurologic symptoms develop over weeks and may include difficulties in walking or swallowing, loss of muscle tone, loss of fine motor coordination, slurred speech, memory loss, vision problems, dementia, sleep disturbances, seizures, and vertigo. Neurologic paraneoplastic syndromes include stiff-person syndrome, encephalomyelitis, cerebellar degeneration, neuromyotonia, and sensory neuropathy. Neuromuscular junction disorders can occur, as observed in the Lambert-Eaton myasthenic syndrome. Myopathies, electrolyte disturbances, and certain visual loss syndromes can also be manifestations of a paraneoplastic syndrome.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Non–Small Cell Lung Carcinomas

Between 60% and 80% of squamous cell carcinomas tend to be located in central airways (E-Fig. 23-10). The airway lumen may become obstructed, leading to collapse of the lung (i.e., atelectasis) or postobstructive pneumonia. Although necrosis and cavity formation may occur in any lung tumor, this feature is more common with squamous cell carcinomas. Because of their slow rate of growth, these tumors have the lowest propensity for metastasis of all types of lung cancer.

Adenocarcinomas represent the most common type of lung cancer and the most common type in nonsmokers (almost 20% of cases). Adenocarcinomas are most often found in the periphery of the lung (75%) (E-Fig. 23-11). This tumor is frequently associated with malignant pleural effusions (60%) and has a high propensity for distant metastasis.

Previously called *bronchoalveolar cell carcinomas*, it is now understood that these more insidious forms of adenocarcinoma likely exist as a spectrum of disease. In its most benign form, atypical adenomatous hyperplasia (AAH) exhibits mild to moderate nuclear atypia without stromal invasion. A stepwise progression of classification, including adenocarcinoma in situ (AIS), minimally invasive adenocarcinoma, and lepidic pattern adenocarcinoma, describes a gradual progression of invasion. This is the most common form of lung cancer found in

nonsmokers and young patients. It can develop as a lung infiltrate or as a solitary nodule, and it can be accompanied by excessive production of secretions.

Large cell carcinomas (giant cell and clear cell subtypes) frequently develop as a peripheral lesion and may be associated with pneumonitis and hilar adenopathy. Patients usually have cough and weight loss. Given the aggressive nature of these tumors, symptoms (e.g., bone pain) are often the consequence of metastatic disease.

Small Cell Lung Carcinomas

SCLC is strongly associated with cigarette smoking. SCLCs typically are found in perihilar locations, frequently originating in the main bronchi, and they often have associated lymphadenopathy (E-Fig. 23-12). These tumors metastasize rapidly, most commonly to the thoracic lymph nodes, bones, liver, adrenal glands, and brain. Approximately 70% of patients have metastatic disease at the time of clinical presentation.

Diagnostic Evaluation

Because lung cancer typically is diagnosed at an advanced stage, when cure is not possible, an effective strategy for detection of lung cancer at an early stage is desirable. Results from the National Lung Screening Trial, sponsored by the National Cancer Institute, have started to support the formation of lung cancer screening guidelines. This was a randomized trial that compared two ways of detecting lung cancer in smokers: low-dose helical computed tomography (CT) and standard chest radiography. More than 50,000 patients were enrolled in this study over a period of 2 years, with a follow-up time of 5 years. Subjects enrolled were between 55 and 74 years old and smoked for a minimum of 30 pack-years. Former smokers enrolled in this study had quit within the preceding 15 years. There was a 20% relative reduction in mortality from lung cancer with low-dose helical CT screening. However, formal recommendations have not been made for the application of these data to larger cohorts given the rate of false positives and concurrent increased rate of invasive procedures (with potential negative outcomes).

When a suspected lung cancer is identified, a tissue diagnosis is essential for most patients. If imaging reveals sites of suspected metastasis, the site of biopsy should be chosen to determine the greatest extent of spread or highest stage of the tumor to prevent patients from undergoing multiple invasive procedures. If the apparent tumor is confined to the chest, bronchoscopy (potentially with endoscopic ultrasound-guided lymph node biopsies) is appropriate for central masses, whereas transthoracic needle aspiration can be performed for more peripheral lesions. An identified pleural effusion should be sampled to assess for malignant cells. In some cases, if the pretest probability is very high that the lung lesion is a primary lung cancer and there is no imaging evidence of disease spread, direct referral for surgical resection may be appropriate. In these cases, equivocal biopsy results should not hamper attempts to remove the lesion. If patients are too debilitated to undergo treatment or insightfully refuse interventions, tissue diagnosis may be deferred with the intention of palliative measures.

After a lung cancer is diagnosed, staging is necessary to determine the treatment and prognosis. For NSCLCs, staging can

