typical, and cerebral abscess is common. Rarer manifestations include meningitis, mycotic aneurysm, and cerebral granuloma (mimicking a brain tumor). Local spread from cranial sinuses also occurs. Postoperative infection develops rarely and is exacerbated by glucocorticoids, often given after neurosurgery. The presentation can be either acute or subacute, with mood changes, focal signs, seizures, and decline in mental status. MRI is the most useful immediate investigation; unenhanced CT of the brain is usually nonspecific, and contrast is often contraindicated because of poor renal function.

Endocarditis Most cases of *Aspergillus* endocarditis are prosthetic valve infections resulting from contamination during surgery. Native valve disease is reported, especially as a feature of disseminated infection and in persons using illicit IV drugs. Culture-negative endocarditis with large vegetations is the most common presentation; embolectomy occasionally reveals the diagnosis.

Cutaneous Aspergillosis Dissemination of *Aspergillus* occasionally results in cutaneous features, usually an erythematous or purplish nontender area that progresses to a necrotic eschar. Direct invasion of the skin occurs in neutropenic patients at the site of IV catheter insertion and in burn patients; such invasion may also follow trauma. Wounds may become infected with *Aspergillus* (especially *A. flavus*) after surgery.

Chronic Pulmonary Aspergillosis The hallmark of chronic cavitary pulmonary aspergillosis (also called semi-invasive aspergillosis, chronic necrotizing aspergillosis, or complex aspergilloma) (Fig. 241-1) is one or more pulmonary cavities expanding over a period of months or years in association with pulmonary symptoms and systemic manifestations such as fatigue and weight loss. (Pulmonary aspergillosis developing over <3 months is better classified as subacute invasive aspergillosis.) Often mistaken initially for tuberculosis, almost all cases occur in patients with prior pulmonary disease (e.g., tuberculosis, atypical mycobacterial infection, sarcoidosis, rheumatoid lung disease, pneumothorax, bullae) or lung surgery. The onset is insidious, and systemic features may be more prominent than pulmonary symptoms. Cavities may have a fluid level or a well-formed fungal ball, but pericavitary infiltrates and multiple cavities—with or without pleural thickening—are typical. An irregular internal cavity surface and thickened cavity walls are indicative of disease activity.

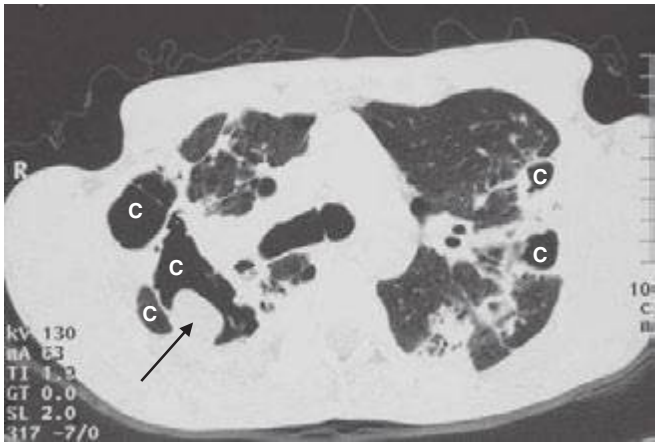

FIGURE 241-1 CT scan image of the chest in a patient with long-standing bilateral chronic cavitary pulmonary aspergillosis. This patient had a history of several bilateral pneumothoraces and had required bilateral pleurodesis in 1990. CT scan then demonstrated multiple bullae, and sputum cultures grew *A. fumigatus*. The patient had initially weakly and later strongly positive serum *Aspergillus* antibody tests (precipitins). This scan (2003) shows a mixture of thick- and thin-walled cavities in both lungs (each marked with *C*), with a probable fungal ball (*black arrow*) protruding into the large cavity on the patient's right side (*R*). There is also considerable pleural thickening bilaterally.

IgG antibodies (usually precipitating) to *Aspergillus* are almost always detectable in blood, and levels fall slowly with successful therapy. Some patients have concurrent infections—even without a fungal ball—with atypical mycobacteria and/or other bacterial pathogens. One or more *Aspergillus* nodules that resemble early lung carcinoma and may cavitate have been recognized. If untreated, chronic pulmonary aspergillosis typically progresses (sometimes relatively rapidly) to unilateral or upper-lobe fibrosis. This end-stage entity is termed *chronic fibrosing pulmonary aspergillosis*.

Aspergilloma Aspergilloma (fungal ball) occurs in up to 20% of residual pulmonary cavities ≥2.5 cm in diameter. Signs and symptoms associated with single (simple) aspergillomas are minor, including cough (sometimes productive), hemoptysis, wheezing, and mild fatigue. More significant signs and symptoms are associated with chronic cavitary pulmonary aspergillosis and should be treated as such. The vast majority of fungal balls are caused by *A. fumigatus*, but *A. niger* has been implicated, particularly in diabetic patients; aspergillomas due to *A. niger* can lead to oxalosis with renal dysfunction. The most significant complication of aspergilloma is life-threatening hemoptysis, which may be the presenting manifestation. Some fungal balls resolve spontaneously, but the cavity may still be infected.

Chronic *Aspergillus* Sinusitis Three entities are subsumed under this broad designation: fungal ball of the sinus, chronic invasive sinusitis, and chronic granulomatous sinusitis. *Fungal ball of the sinus* is limited to the maxillary sinus (except in rare cases involving the sphenoid sinus) and consists of a chronic saprophytic entity in which the sinus cavity is filled with a fungal ball. Maxillary disease is associated with prior upper-jaw root canal work and chronic (bacterial) sinusitis. About 90% of CT scans show focal hyperattenuation related to concretions; on MRI scans, the T2-weighted signal is decreased, whereas it is increased in bacterial sinusitis. Removal of the fungal ball is curative. No tissue invasion is demonstrable histologically or radiologically.

In contrast, *chronic invasive sinusitis* is a slowly destructive process that most commonly affects the ethmoid and sphenoid sinuses but can involve any sinus. Patients are usually but not always immunocompromised to some degree (e.g., as a result of diabetes or HIV infection). Imaging of the cranial sinuses shows opacification of one or more sinuses, local bone destruction, and invasion of local structures. The differential diagnosis is wide, including infections caused by numerous other fungi; sphenoid sinusitis is often caused by bacteria. Apart from a history of chronic nasal discharge and blockage, loss of the sense of smell, and persistent headache, the usual presenting features are related to local involvement of critical structures. The orbital apex syndrome (blindness and proptosis) is characteristic. Facial swelling, cavernous sinus thrombosis, carotid artery occlusion, pituitary fossa, and brain and skull base invasion have been described.

Chronic granulomatous sinusitis due to *Aspergillus* is most commonly seen in the Middle East and India and is often caused by *A. flavus*. It typically presents late, with facial swelling and unilateral proptosis. The prominent granulomatous reaction histologically distinguishes this disease from chronic invasive sinusitis, in which tissue necrosis with a low-grade mixed-cell infiltrate is typical. IgG antibodies to *A. flavus* are usually detectable.

Allergic Bronchopulmonary Aspergillosis In almost all cases, ABPA represents a hypersensitivity reaction to *A. fumigatus*; rare cases are due to other aspergilli and other fungi. ABPA occurs in ~2.5% of patients with asthma who are referred to secondary care and in up to 15% of adults with cystic fibrosis. Episodes of bronchial obstruction with mucous plugs leading to coughing fits, "pneumonia," consolidation, and breathlessness are typical. Many patients report coughing up thick sputum casts. Eosinophilia commonly develops before systemic glucocorticoids are given. The cardinal diagnostic tests include an elevated serum level of total IgE (usually >1000 IU/mL), a positive skin-prick test in response to *A. fumigatus* extract, or detection of *Aspergillus*-specific IgE and IgG antibodies. The presence of hyperattenuated mucus in airways is highly specific. Central bronchiectasis is characteristic, and some patients develop chronic cavitary pulmonary aspergillosis.