a peripheral, subpleural distribution, and detection of honeycombing and traction bronchiectasis in the absence of ground-glass opacification, lymphadenopathy, and pleural disease (Fig. 17-4; E-Fig. 17-1). In the setting of a typical clinical presentation and classic HRCT findings, a lung biopsy is unnecessary. A lung biopsy may be required for confirmation in some patients.

### Diagnosis and Differential Diagnosis

IPF is diagnosed on the basis of typical clinical, radiographic (HRCT), and if available, pathologic features (e.g., biopsy showing a UIP pattern). Other potential causes of ILD, such as connective tissue disease, hypersensitivity pneumonitis, and asbestosis, must be ruled out by the history, examination, and selected laboratory testing.

HRCT of the chest should show a compatible UIP pattern, with subpleural reticulations, honeycombing, and traction bronchiectasis. If honeycombing is absent on HRCT or atypical features such as ground-glass infiltrates, lymphadenopathy, nodules, or air trapping are found, the radiographic diagnosis becomes less certain. In these cases, a lung biopsy may be needed, and it should show a UIP pattern to confirm a diagnosis of IPF. Multidisciplinary discussion during the diagnostic process, with input from experienced clinicians, radiologists, and pathologists, is ideal.

### Treatment

There is insufficient clinical evidence to suggest that any pharmacologic treatment improves survival or the quality of life for patients with IPF. A commonly used immunosuppressive combination of corticosteroids, azathioprine, and *N*-acetylcysteine was shown in a multicenter clinical trial to be more harmful than a placebo or *N*-acetylcysteine alone (level 1 evidence). *N*-acetylcysteine treatment did not show any clear advantage over placebo.

The antifibrotic drug pirfenidone has been approved in some countries based on evidence from a study showing a reduced decline in lung function with this medication, although a parallel study did not show the same results (level 2 evidence). An ongoing clinical trial of this drug showing better preserved lung function with pirfenidone compared to placebo was recently completed in the United States.

Lung transplantation should be considered for patients with IPF. Because survival of patients with IPF on the lung transplantation waiting list is worse than for patients with other indications for lung transplantation, early referral for transplantation evaluation should be initiated (level 2 evidence). Unfortunately, the 5-year survival rate for lung transplant recipients with IPF is only 40% to 50%.

Some patients with IPF experience acute respiratory deterioration in the absence of any clinically apparent cause (e.g., heart failure, pulmonary embolism, pneumonia). These episodes of idiopathic acute deterioration have been called *acute exacerbations of IPF* and are associated with a poor prognosis. HRCT findings include new ground-glass opacities and consolidation superimposed on a background reticular or honeycomb pattern consistent with UIP. Histologically, evidence of acute lung injury (i.e., diffuse alveolar damage) can be found on the background of UIP. Acute exacerbations of IPF are typically treated with high doses of corticosteroids (level 3 evidence).

### Prognosis

The prognosis for IPF is poor. The disease is progressive, ultimately leading to death from respiratory failure or other complications such as lung cancer. Median survival is often reported to be 2 to 3 years from the diagnosis, although this may be an underestimate.

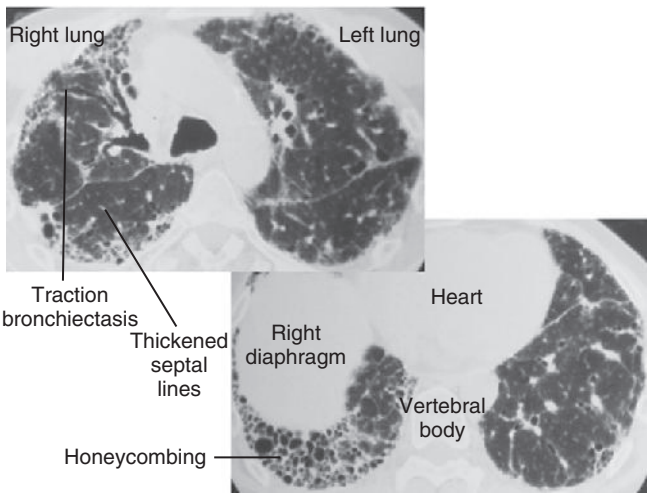


**FIGURE 17-4** Computed tomography of the chest of a patient with idiopathic pulmonary fibrosis.

## Other Idiopathic Pneumonias

The second most common IIP is NSIP. This condition exhibits a histologic picture that is nonspecific and characterized by diffuse, uniform interstitial inflammation (i.e., cellular NSIP, which is less common) with or without fibrosis (i.e., fibrotic NSIP, which is more common), as distinguished by the heterogeneous pattern seen in UIP or IPF. Patients with NSIP exhibit progressive dyspnea, cough, and bilateral interstitial infiltrates. Affected patients are middle-aged and commonly women.

Although NSIP may be idiopathic, the NSIP pathologic pattern also may occur in conditions such as connective tissue disorders (e.g., systemic lupus erythematosus, rheumatoid arthritis, polymyositis). The association with these disorders is so strong that histologic confirmation of NSIP should prompt a search for these conditions, which occasionally manifest only after the development of NSIP. The differential diagnosis also includes IPF, COP, and HP. Pulmonary function tests most commonly show a restrictive pattern. Ground-glass infiltrates, subpleural reticulation, and traction bronchiectasis are often seen by HRCT, but honeycombing is minimal or absent.

NSIP may be more responsive to immunosuppressants than IPF, and a trial period with immunosuppressive agents should be considered (level 3 evidence). Lung transplantation should be considered in these patients if they exhibit progressive disease. However, the overall prognosis is much better than for IPF, with a 5-year survival rate of more than 82% in one series.

DIP is a rare idiopathic pneumonia usually seen in younger individuals. It is associated in most cases with a history of cigarette smoking. Patients exhibit a progressive shortness of breath