TREATMENT MANAGEMENT ISSUES IN PATIENTS WITH IPF

Untreated patients with IPF show continued progression of their disease and have a high mortality rate. There is no effective therapy for IPF. Thalidomide appears to improve cough in patients with IPF. Chronic microaspiration secondary to gastroesophageal reflux may play a role in the pathogenesis and natural history of IPF. Gastroesophageal reflux (GER) therapy may be of benefit in IPF. In patients with IPF, treatment with the three-drug regimen of prednisone, azathioprine, and *N*-acetylcysteine (NAC) or warfarin (in IPF patients who lacked other indications for anticoagulation) has been shown to increase the risks of hospitalization and death.

Patients with IPF and coexisting emphysema (combined pulmonary fibrosis and emphysema [CPFE]) are more likely to require long-term oxygen therapy and develop pulmonary hypertension and may have a more dismal outcome than those without emphysema.

Patients with IPF may have acute deterioration secondary to infections, pulmonary embolism, or pneumothorax. Heart failure and ischemic heart disease are common problems in patients with IPF, accounting for nearly one-third of deaths. These patients also commonly experience an accelerated phase of rapid clinical decline that is associated with a poor prognosis (so-called acute exacerbations of IPF). These acute exacerbations are defined by worsening of dyspnea within a few days to 4 weeks; newly developing diffuse ground-glass abnormality and/or consolidation superimposed on a background reticular or honeycomb pattern consistent with the UIP pattern; worsening hypoxemia; and absence of infectious pneumonia, heart failure, and sepsis. The rate of these acute exacerbations ranges from 10–57%, apparently depending on the length of follow-up. During these episodes, the histopathologic pattern of diffuse alveolar damage is often found on the background of UIP. No therapy has been found to be effective in the management of acute exacerbations of IPF. Often mechanical ventilation is required, but it is usually not successful, with a hospital mortality rate of up to three-fourths of patients. In those who survive, a recurrence of acute exacerbation is common and usually results in death at those times.

Patients should be referred early for lung transplant because of the unpredictability of disease progression (e.g., acute exacerbations) **(Chap. 320e)**.

NONSPECIFIC INTERSTITIAL PNEUMONIA

This condition defines a subgroup of the idiopathic interstitial pneumonias that can be distinguished clinically and pathologically from UIP, DIP, AIP, and COP. Importantly, many cases with this histopathologic pattern occur in the context of an underlying disorder, such as a CTD, drug-induced ILD, or chronic hypersensitivity pneumonitis.

Clinical Manifestations Patients with idiopathic NSIP have clinical, serologic, radiographic, and pathologic characteristics highly suggestive of autoimmune disease and meet the criteria for undifferentiated CTD. Idiopathic NSIP is a subacute restrictive process with a presentation similar to that of IPF but usually at a younger age, most commonly in women who have never smoked. It is often associated with a febrile illness. HRCT shows bilateral, subpleural ground-glass opacities, often associated with lower lobe volume loss **(Fig. 315-3)**. Patchy areas of airspace consolidation and reticular abnormalities may be present, but honeycombing is unusual.

Histologic Findings The key histopathologic feature of NSIP is the uniformity of interstitial involvement across the biopsy section, and this may be predominantly cellular or fibrosing. There is less temporal and spatial heterogeneity than in UIP, and little or no honeycombing is found. The cellular variant is rare.

Treatment The majority of patients with NSIP have a good prognosis (5-year mortality rate estimated at <15%), with most showing improvement after treatment with glucocorticoids, often used in combination with azathioprine or mycophenolate mofetil.

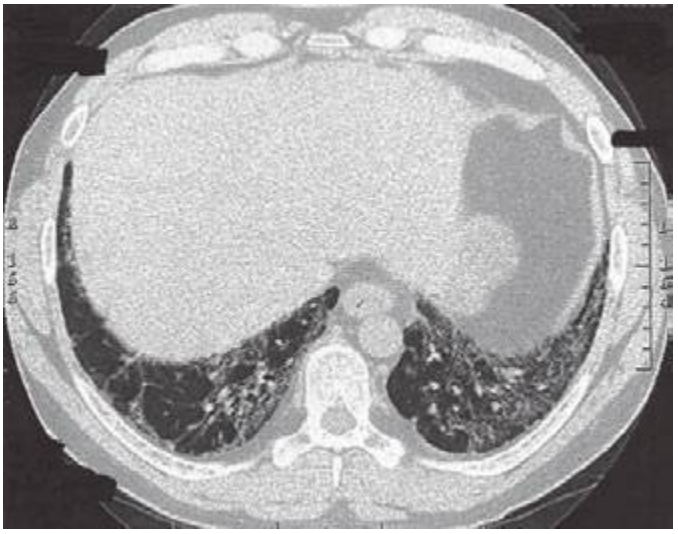

FIGURE 315-3 Nonspecific interstitial pneumonia. High-resolution computed tomography through the lower lung shows volume loss with extensive ground-glass abnormality, reticular abnormality, and traction bronchiectasis. There is sparing on the lung immediately adjacent to the pleura. Histology showed a combination of inflammation and mild fibrosis.

ACUTE INTERSTITIAL PNEUMONIA (HAMMAN-RICH SYNDROME)

Clinical Manifestations AIP is a rare, fulminant form of lung injury characterized histologically by diffuse alveolar damage on lung biopsy. Most patients are older than 40 years. AIP is similar in presentation to the acute respiratory distress syndrome (ARDS) **(Chap. 322)** and probably corresponds to the subset of cases of idiopathic ARDS. The onset is usually abrupt in a previously healthy individual. A prodromal illness, usually lasting 7–14 days before presentation, is common. Fever, cough, and dyspnea are common manifestations at presentation. Diffuse, bilateral, air-space opacification is present on the chest radiograph. HRCT scans show bilateral, patchy, symmetric areas of ground-glass attenuation. Bilateral areas of air-space consolidation also may be present. A predominantly subpleural distribution may be seen.

Histologic Findings The diagnosis of AIP requires the presence of a clinical syndrome of idiopathic ARDS and pathologic confirmation of organizing diffuse alveolar damage. Therefore, lung biopsy is required to confirm the diagnosis.

Treatment Most patients have moderate to severe hypoxemia and develop respiratory failure. Mechanical ventilation is often required. The mortality rate is high (>60%), with most patients dying within 6 months of presentation. Recurrences have been reported. However, those who recover often have substantial improvement in lung function. The main treatment is supportive. It is not clear that glucocorticoid therapy is effective.

CRYPTOGENIC ORGANIZING PNEUMONIA

Clinical Manifestations COP is a clinicopathologic syndrome of unknown etiology. The onset is usually in the fifth and sixth decades. The presentation may be of a flulike illness with cough, fever, malaise, fatigue, and weight loss. Inspiratory crackles are frequently present on examination. Pulmonary function is usually impaired, with a restrictive defect and arterial hypoxemia being most common. The roentgenographic manifestations are distinctive, revealing bilateral, patchy, or diffuse alveolar opacities in the presence of normal lung volume. Recurrent and migratory pulmonary opacities are common. HRCT shows areas of air-space consolidation, ground-glass opacities, small nodular opacities, and bronchial wall thickening and dilation. These changes occur more frequently in the periphery of the lung and in the lower lung zone.