Idiopathic Pulmonary Fibrosis: Spectrum of High-Resolution CT Findings

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OBJECTIVE. Characteristic high-resolution CT (HRCT) findings of idiopathic pulmonary fibrosis (IPF) include reticulation, architectural distortion, and honeycombing involving mainly the lung periphery and the lower lobes. In 50% of IPF patients, HRCT is nonspecific. This article illustrates the HRCT findings of IPF correlating with the pathology.

CONCLUSION. The spectrum of HRCT manifestations varies from typical findings that allow confident diagnosis to atypical patterns mimicking other diseases, including predominance of ground-glass opacity, consolidation, nodules, and atypical distribution of lesions.

Idiopathic pulmonary fibrosis (IPF) is defined as a specific form of chronic fibrosing interstitial pneumonia of unknown cause, limited to the lungs and associated with a histologic pattern of usual interstitial pneumonia (UIP) [1, 2]. It is slightly more common in men and occurs mainly in patients over 50 years old. Clinically, IPF is characterized by the insidious onset of a nonproductive cough and dyspnea and the presence of fine end-inspiratory crackles. The prognosis is poor; the median survival from the time of diagnosis is 2.5–3.5 years [1].

The characteristic high-resolution CT (HRCT) manifestations of IPF consist of symmetric bilateral reticular opacities with associated traction bronchiectasis and honeycombing in the absence of small nodules or extensive ground-glass opacity [1–3] (Fig. 1).

Histologically, IPF is characterized by the presence of variable proportions of interstitial inflammation, fibroblastic foci, and established fibrosis and honeycombing coexisting with areas of normal lung parenchyma [1–3] (Figs. 2 and 3).

Spectrum of Manifestations of IPF
Ground-Glass Predominance

Extensive bilateral ground-glass opacity in patients with interstitial fibrosis favors the diagnosis of nonspecific interstitial pneumonia (NSIP), chronic hypersensitivity pneumonitis, or desquamative interstitial pneumonia (DIP) over IPF [1]. MacDonald et al. [4] showed that an increased proportion of ground-glass opacity in NSIP is the most important distinguishing feature from IPF (odds ratio, 1.04 for each 1% increase in the proportion of ground-glass opacity). However, in that study, approximately 33% of patients with IPF had equivalent extents of reticular and ground-glass opacity, and 12% had predominant ground-glass opacity. The authors therefore concluded that there is considerable overlap between the HRCT patterns of NSIP and IPF [4]. It should be noted that the study was biased toward patients with atypical HRCT patterns of IPF because patients with typical HRCT features seldom undergo lung biopsy.
Although the presence of predominant ground-glass opacity in patients with IPF can mimic the findings seen in NSIP and hypersensitivity pneumonitis (Figs. 4, 5, and 6), ground-glass opacity tends to be associated with an improved prognosis. In a prospective study of 38 cases of biopsy-proven IPF, Gay et al. [5] showed that the extent of ground-glass opacity on HRCT correlated with greater likelihood of response to treatment and that HRCT was superior to pulmonary function tests and open lung biopsy in predicting response to therapy.

Although ground-glass opacity may reflect the presence of potentially reversible active inflammation, it may also result from interstitial fibrosis and microscopic honeycombing below the resolution of HRCT. Ground-glass opacity should be considered as consistent with active inflammation only when there are no superimposed findings of fibrosis such as reticulation, architectural distortion, or traction bronchiectasis [6]. Other potential causes of ground-glass opacity in patients who have IPF include honeycomb cysts filled with secretions (Fig. 7), superimposed diffuse alveolar damage, or a
superimposed complication such as an infection or drug reaction.

The clinical course of IPF is characterized by gradual deterioration over several months or years, with progression of parenchymal abnormalities on serial HRCT scans (Fig. 8). A small percentage of patients develop acute exacerbation of IPF, a condition characterized by marked exacerbation of dyspnea and a decrease in arterial oxygen tension (PaO₂) of more than 10 mm Hg within 1 month in the absence of infection or heart failure. Histologi-
cally, these patients have diffuse alveolar damage superimposed on the interstitial fibrosis. Acute exacerbation is characterized on HRCT by the rapid development of multifocal bilateral areas of ground-glass opacity, consolidation, or both superimposed on a background of interstitial fibrosis (Fig. 9). In this setting, the presence of extensive areas of ground-glass opacity correlates with a poor prognosis [1].

**Consolidation and Nodules**

Consolidation and nodules are uncommon radiologic manifestations of IPF in the absence of complications such as acute exacerbation, superimposed infection, or pulmonary carcinoma [7]. In the series of 32 patients with proven IPF reported by Mac-Donald et al. [4], nodules and consolidation were not found. Risk of lung cancer is increased in patients who have IPF, thus the presence of a nodule or focal area of consolidation within areas of fibrosis should be carefully evaluated (Fig. 10).

Patients with IPF are also at increased risk for tuberculosis, which may also present as a solitary nodule [8]. Another cause of nodules in IPF is pulmonary ossification, a rare condition in which mature bone, often containing
marrow, is formed in the lung parenchyma. HRCT shows sharply defined small calcified nodular opacities typically confined to areas of fibrosis [9] (Fig. 11).

**Distribution of Abnormalities**

The characteristic basal and peripheral predominance of the abnormalities on HRCT scans is an important clue to the diagnosis of IPF [1]. It is important to realize, however, that the fibrosis tends to involve all lobes. In a recent study by Hunninghake et al. [3], 85% of patients (45/53) with IPF...
had reticulation in the upper lobes, whereas only 31% (11/36) with other interstitial pneumonias presented with this finding. The results of this study showed that, although more extensive and severe in the lower zones, the presence of fibrosis in the upper lobes is an important predictor of IPF and increases the specificity of HRCT in the diagnosis.

Fig. 8 (continued)—57-year-old man with biopsy-proven idiopathic pulmonary fibrosis.
C, HRCT at same approximate level as A, 3 years later, shows extensive reticular opacities, traction bronchiectasis, and honeycombing in areas previously involved by ground-glass opacities.
D, Gross pathologic specimen from autopsy shows predominantly lower lobe, peripheral, and subpleural fibrotic lesions that alternate with areas of normal lung (asterisks). Honeycombing cysts are seen in subpleural regions (arrow).

Fig. 9—Accelerated idiopathic pulmonary fibrosis (IPF) in 62-year-old man.
A, High-resolution CT (HRCT) shows patchy bilateral ground-glass opacities and subpleural reticulation.
B, HRCT obtained 10 days later shows extensive areas of ground-glass opacity and patchy consolidation involving both lungs. (Fig. 9 continues on next page)
Some authors have suggested that familial IPF, a rare condition defined as the presence of IPF in at least two family members, should be considered separately from nonfamilial IPF [1]. Although the clinical presentation of familial IPF is similar to sporadic IPF, the long-term prognosis is better. The findings on HRCT are similar to those described in the nonfamilial condition except for a lower prevalence of predominant basal distribution and honeycombing [10].

**Diseases Mimicking IPF**

There is considerable overlap between the HRCT findings of IPF and those of NSIP [11, 12]. MacDonald et al. [4], in a comparative study between 21 patients with histologic diagnosis of IPF and 32 with NSIP, found that HRCT had an accuracy of 66% for discrimination between NSIP and IPF. The sensitivity of CT for the diagnosis of IPF was 63% and the specificity was 70% for IPF with a corresponding sensitivity of 70% and specificity of 63% for NSIP. Predominance of ground-glass opacity was seen more commonly in patients with NSIP and predominance of reticulation was seen more commonly in patients with IPF [4].
Fig. 11—74 year-old-man with idiopathic pulmonary fibrosis and pulmonary ossification.  
A. High-resolution CT (HRCT) shows subpleural reticulation and mild ground-glass opacity.  
B. HRCT image photographed using soft-tissue windows at same level as A shows bilateral small calcified nodules (curved arrows) within areas of fibrosis.

Fig. 12—63-year-old man with biopsy-proven desquamative interstitial pneumonia (DIP).  
A. High-resolution CT (HRCT) shows patchy bilateral areas of ground-glass opacity and mild reticulation.  
B. Photomicrograph of histopathologic specimen obtained by surgical biopsy shows mild thickening of alveolar septa and extensive airspace filling by macrophages (arrow). (H and E, ×100) Inset: Higher-power view shows airspace macrophages and chronic interstitial inflammatory infiltrate (arrow). (H and E, ×250) Findings are characteristic of DIP.  
C. HRCT scan at same approximate level as A 13 years later shows extensive fibrotic changes with irregular reticular opacities, traction bronchiectasis, and subpleural honeycombing (arrows). Findings are those of end-stage fibrosis and mimic those of idiopathic pulmonary fibrosis.
Idiopathic Pulmonary Fibrosis on CT

The other forms of idiopathic interstitial pneumonias seldom mimic the HRCT findings of IPF [1]. DIP is characterized by extensive bilateral ground-glass opacities and minimal or no fibrosis [1]. The majority of patients improve or the condition resolves with treatment. However, severe fibrosis mimicking IPF may be seen in patients with long-standing disease (Fig. 12).

HRCT manifestations of IPF may be identical to those seen in UIP associated with collagen-vascular diseases, particularly rheumatoid arthritis and asbestosis [1]. Presence of pleural plaques and parenchymal bands and visualization of ferruginous asbestos bodies on biopsy allow a correct diagnosis of asbestosis [1, 13]. Chronic hypersensitivity pneumonitis, sarcoidosis, and certain drug-induced lung reactions can also occasionally result in a pattern of fibrosis indistinguishable from IPF. In such cases, correct diagnosis requires clinical, serologic, and histologic correlation [1].

References