17

Interstitial Lung Diseases

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INTRODUCTION

The interstitial lung diseases (ILDs) are a complex group of dozens of disorders with heterogeneous clinical courses and prognoses. ILDs are characterized by diffuse and typically chronic lung injury occurring in the setting of various degrees of inflammation, which often leads to lung fibrosis. These diseases are daunting for the clinician because the differential diagnosis may be broad, and the work-up required to make the appropriate diagnosis may be extensive.

Understanding of these disorders has been hampered in the past by use of confusing and nonspecific terminology, especially for the idiopathic interstitial pneumonias (IIPs). Current classifications use histopathology and clinical syndromes to categorize them in understandable groups: idiopathic interstitial pneumonitides, granulomatous disorders, connective tissue–related ILDs, drug-induced ILDs, pulmonary vasculitic disorders, and distinct entities of unknown origin that exhibit well-defined syndromes such as pulmonary Langerhans cell histiocytosis (LCH) and lymphangioleiomyomatosis.

ILD manifests with nonspecific, common clinical symptoms, including dyspnea on exertion, dry cough, and sometimes, constitutional symptoms. Pulmonary function tests usually show restriction and gas-exchange abnormalities. Imaging usually demonstrates diffuse lung disease. However, early radiographic changes may be subtle, and other clinical entities such as congestive heart failure or lymphangitic carcinomatosis may manifest with similar clinical, physiologic, and radiographic findings. The diagnosis may sometimes be delayed until other clinical entities are excluded and biopsy is undertaken. High-resolution computed tomography (HRCT) has contributed greatly to the diagnostic work-up of patients with suspected ILD because typical HRCT patterns in appropriate clinical settings may be sufficient for diagnosis.

Most ILDs, including more common entities such as idiopathic pulmonary fibrosis (IPF), manifest with chronic, progressive symptoms. However, some ILDs manifest in an acute fashion. They include acute pneumonitis due to systemic lupus erythematosus, acute hypersensitivity pneumonitis (HP), some drug reactions, and acute interstitial pneumonia. Infection often needs to be ruled out in these cases, and the diagnosis may be challenging for critically ill individuals.

When ILD is suspected in a patient with typical symptoms and diffuse lung disease on identified on imaging, the epidemiologic background, including the age, race, and sex of the patient, is helpful in formulating the diagnostic possibilities. For example, IPF typically occurs in middle-aged or elderly individuals, whereas sarcoidosis often occurs in young individuals and is most common among African Americans in the United States. Sex is also a consideration because lymphangioleiomyomatosis manifests almost exclusively in women of childbearing age, and pulmonary LCH most often occurs in young male smokers. These background data can help to focus the initial differential diagnosis.

The history can further narrow the differential diagnosis for suspected ILD. Important factors to elicit are rash, dysphagia, arthritis, and Raynaud's phenomenon, which may suggest an underlying connective tissue disorder. If the patient has a diagnosis of connective tissue disease, the work-up may be limited if imaging findings are typical of the pulmonary manifestations of that disease. A history of severe or poorly controlled asthma for a patient with radiographic infiltrates and constitutional symptoms should lead to consideration of Churg-Strauss syndrome, whereas a history of severe sinus disease should raise the possibility of granulomatosis with polyangiitis (formerly called *Wegener's granulomatosis*).

Drug-induced ILD should be considered for all patients with diffuse lung disease seen on imaging, and a careful evaluation of medication use is critical. The smoking history is important because several ILDs are associated with cigarette smoking, including respiratory bronchiolitis–associated interstitial lung disease, desquamative interstitial pneumonitis, and pulmonary LCH.

Environmental exposures should be elicited. For example, an exposure to pet birds or hot tubs may suggest HP. Home visits can be informative, and the occupational history is important. Although the pneumoconioses due to asbestos and silica exposure are becoming much less common with modern safeguards and restrictions, these diseases continue to manifest long after exposure. High-technology manufacturing has particular hazards, such as beryllium exposure leading to berylliosis in susceptible individuals. Nonindustrial professions also carry occupational risks. For example, outbreaks of granulomatous pneumonitis have been described in indoor lifeguards exposed to molds.

The physical examination may reveal only oxygen desaturation with exertion in early ILD. Patients may have evidence of decreased chest expansion during inspection. Auscultation of the lungs typically reveals Velcro-like crackles at the lung bases. The patient may have clubbing. Skin rashes, arthritis with joint deformities, Raynaud's phenomenon, and dysphagia may point to a connective tissue–related ILD such as dermatomyositis or polymyositis, progressive systemic sclerosis, or mixed connective tissue disorder. Evidence of right ventricular heart failure with jugular vein distention, a cardiac gallop, a loud P_2 sound, and leg