The keys to diagnosing interstitial lung disease: Part 2

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Abstract: Many patients with sarcoidosis are asymptomatic at presentation and have bilateral hilar adenopathy on a chest radiograph obtained for other reasons. Symptomatic patients usually present with chronic cough, dyspnea, or noncardiac chest pain. Extrapulmonary organ involvement is not uncommon. Lung biopsy shows well-formed noncaseating granulomas in a bronchovascular distribution. Interstitial lung disease also may result from collagen vascular disease, such as systemic lupus erythematosus and Sjögren syndrome. In patients with acute hypersensitivity pneumonitis, cough, dyspnea, and flu-like symptoms occur within 12 hours of exposure to the inciting antigen, such as pigeon stool or moldy hay. Some patients have a subacute or chronic course, probably as a result of continued exposure to the offending antigen. In acute hypersensitivity pneumonitis, the chest radiograph may show diffuse small nodules, whereas in chronic disease, reticular lines or fibrosis may be seen. (J Respir Dis. 2005;26(10):443-448)

Interstitial lung disease (ILD) includes a large group of entities, the most common of which is idiopathic pulmonary fibrosis (IPF). In the September 2005 issue of The Journal of Respiratory Diseases, we reviewed the classification of these diseases and discussed the pre-sentation and diagnosis of IPF and the other idiopathic interstitial pneumonias.

In this article, we will focus on other forms of ILD, including sarcoidosis, the ILDs associated with collagen vascular diseases, hypersensitivity pneumonitis, asbestosis, and silicosis. In a subsequent article, we will present our approach to the diagnosis. Sarcoidosis

This granulomatous ILD has no known cause. Genetically susceptible persons are thought to have an abnormally polarized helper T lymphocyte type 1 immune response to an unknown antigen(s) that causes granuloma formation and may lead to pulmonary fibrosis. Proposed causes include mycobacterial antigens and Propionobacterium acnes. Sarcoidosis has a worldwide distribution, with considerable geographic and ethnic variation; the highest incidence is in Scandinavians and African Americans. The diagnosis is usually made in persons younger than 40 years, although incident cases are frequently observed in older persons and, occasionally, in children.

Nearly 50% of patients with sarcoidosis have no symptoms at presentation. In most of these patients, stage I radiographic disease (bilateral hilar adenopathy) is found when a chest radiograph is obtained for other reasons. Over two thirds of these patients have spontaneous disease remission and normalization of chest radiographic findings within 2 years of diagnosis. Patients younger than 40 years, those with stage I or II disease (bilateral hilar adenopathy and upper lobe infiltrates), Scandinavians, and those who present acutely with either Lofgren syndrome (stage I disease, arthritis that usually affects the ankles or knees, and erythema nodosum) or Heerfordt disease are more likely to have spontaneous remission.

Symptomatic persons usually present with chronic cough, dyspnea, or noncardiac chest pain. Extrapulmonary organ involvement is common and can include any organ system. The most frequently involved extrapulmonary sites are skin, peripheral lymph nodes, and eyes (anterior uveitis).

Lung biopsy shows well-formed noncaseating granulomas in a bronchovascular distribution. The characteristic high-resolution CT (HRCT) findings include bilateral hilar adenopathy, right paratracheal adenopathy, subpleural small nodules, nodules along bronchovascular bundles, and interlobar- lar septal thickening. These findings tend to be in a mid to upper lung zone distribution. HRCT findings also may include fibrosis and honeycombing in end-stage sarcoidosis, diffuse micronodules mimicking miliary tuberculosis, diffuse ground-glass opacities, or consolidation. Despite the diversity of findings, HRCT can strongly support the diagnosis of sarcoidosis, especially when the diagnosis is not readily discerned from the clinical and chest radiographic presentation. However, when the clinical presentation and chest radiographic findings are typical for sarcoidosis, the diagnosis usually can be made on the basis of these findings and CT is not needed.

Sarcoidosis has a good prognosis overall, with a mortality rate that is considerably lower than that
for usual interstitial pneumonia. Adverse prognostic factors include age greater than 40 years, splenomegaly, African American race, extrapulmonary disease, lupus pernio, disease duration of more than 2 years, and stage IV (fibrotic) disease. Collagen vascular disease
ILD that results from collagen vascular disease is most commonly associated with systemic lupus erythematosus, scleroderma, Sjögren syndrome, rheumatoid arthritis, and pyomyositis/dermatomyositis. The clinical presentations are diverse (Table). Hypersensitivity pneumonitis
This can be incited by a large number of known organic particles smaller than 5 mm, such as those in animal products, fungal elements, or thermophilic actinomyces. Through repeated inhalation of these antigens, persons can become sensitized and an inflammatory pneumonitis with large numbers of infiltrating suppressor T lymphocytes may develop, involving the alveoli and terminal bronchioles.

The histopathology changes as the disease progresses. The initial stage is characterized by neutrophilic infiltrates, the subsequent stage by suppressor T-cell infiltrates, a later chronic stage by the appearance of loosely formed epithelial noncaseating granulomas, and the final stage by fibrosis. Subacute hypersensitivity pneumonitis shows both lymphocytic and granulomatous inflammation.

The most common forms of hypersensitivity pneumonitis in the United States are farmer's lung and pigeon breeder's lung. Patients with hypersensitivity pneumonitis usually present with dyspnea and cough, but fevers, chills, chest tightness, and weight loss are also common. The acute and subacute forms of hypersensitivity pneumonitis are associated with their own clinicoradiographic presentations.

Cough, dyspnea, and flu-like symptoms occur within 12 hours of exposure to the antigen (pigeon stool, moldy hay) in acute disease. Symptoms often resolve spontaneously within a few days. However, some patients have a subacute or chronic course in which recurrent, low-grade acute episodes occur, probably as a result of continued exposure to the offending antigen. The chronic form of disease is caused by continuous low-level exposure to the antigen.

In acute hypersensitivity pneumonitis, the chest radiograph may show diffuse small nodules, whereas in chronic disease, reticular lines or fibrosis may be seen. In contrast to IPF, fibrotic changes of chronic hypersensitivity pneumonitis tend to be in upper lung zones. It is important to remember, however, that the findings on plain chest radiography can be normal, in between acute episodes.

HRCT generally shows centrilobular nodules, with ground-glass opacities and mosaic attenuation resulting from the bronchiolar involvement. This pattern is not specific for hypersensitivity pneumonitis and can be associated with other disorders that have bronchiolar involvement, such as respiratory bronchiolitis with ILD.

Pulmonary function testing often shows a restrictive ventilatory defect and reduced carbon monoxide-diffusing capacity (DICO). Proven or suspected exposure to antigens, proof of sensitization to an antigen (positive serum precipitants or bronchoalveolar lavage [BAL] lymphocytosis), and typical findings on a chest radiograph or HRCT scan are required to make a confident diagnosis of hypersensitivity pneumonitis. Silicosis/asbestosis
Silicosis and asbestosis are the most common pneumoconioses diagnosed in the United States. Pneumoconiosis is caused by long-term, sustained inhalation of inorganic dust particles, combined with a pulmonary response thought to be initially characterized by injury and inflammation that eventually progress to fibrosis.

Silica is the most abundant mineral in the earth's crust, and persons whose occupation involves disturbing the earth's crust (mining, tunneling, quarrying, stonework), sandblasting, or foundry work are at increased risk for silica-induced lung disease. The most common form of silicosis is a chronic variant that is caused by long-term inhalation of silicates.

There is a latency of more than 20 years. Patients may present with chronic dyspnea and cough. More often, however, they are initially asymptomatic and the abnormalities on chest radiography are discovered incidentally.

Lung histopathology shows silicotic nodules in the peribronchiolar regions. This finding corresponds to the appearance on CT scans of multiple subcentimeter nodules that predominate in the upper lung zone. Mediastinal adenopathy with eggshell calcification of lymph nodes may be present. Nodules may coalesce into conglomerate nodules and eventually progress to massive fibrosis.

Once conglomerate nodules form, patients are at 3-fold greater risk for tuberculosis. Thus, any cavitation of conglomerate nodules should be worrisome. A high level of silica exposure over months may cause diffuse alveolar opacities (acute silicosis), with a histopathology similar to that of pulmonary alveolar proteinosis.

Asbestosis is caused by long-term inhalation of asbestos fibers that leads to lung inflammation and...
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scarring. The alveolar macrophages attempt to ingest asbestos fibers but undergo apoptosis and necrosis ("frustrated phagocytosis"). The fibrosis initially centers around the walls of the respiratory bronchioles but can eventually involve the alveoli and lead to honeycombing of the lungs. Asbestos fibers are known for their tensile strength and resistance to heat and acid. As a result, these fibers have been used widely in industries such as brake fiber manufacturing, pipefitting, insulation, and shipbuilding. With the recognition of asbestos-induced lung disease caused by exposure to asbestos fibers, most westernized countries have not allowed the use of asbestos in manufacturing since the 1970s. Therefore, persons with potential asbestos exposure may have been exposed in the past, or they may have current exposure because of occupations that involve liberation of asbestos fibers, such as building demolition, building maintenance, and insulation removal.

Asbestos classically results from prolonged exposure to inhaled asbestos fibers; amphibole fibers are the most fibrogenic because of their length and poor clearance by alveolar macrophages. Patients have usually been exposed for more than 10 to 20 years, but exposure can rarely be as short as several months if it is high-intensity (such as ship "mothballing"). Patients often present with chronic dyspnea or cough, and pulmonary function testing shows a restrictive ventilatory defect with reduced DlCO. However, a mixed pattern of restriction and obstruction may be seen. The obstruction is usually caused by cigarette smoking, but nonsmokers may have asbestos-related small-airway disease.

The chest radiograph often demonstrates bibasilar opacities, including irregular lines, septal thickening, and a shaggy heart border. However, chest radiography is less sensitive than HRCT for detecting fibrosis. HRCT can detect up to one third of cases of asbestosis that were not identified on chest radiography. HRCT features of asbestosis include honeycombing, thickening of interlobular septae, and evidence of diffuse fibrosis involving the visceral pleura (diffuse pleural thickening, parenchymal bands, rounded atelectasis). Hilar or mediastinal adenopathy is not a feature of asbestosis, and its presence suggests an alternative diagnosis, such as silicosis or fibrotic sarcoidosis. Advanced IPF can have a similar appearance to asbestosis, but CT signs of visceral pleural involvement are typically absent in IPF, and patients with IPF tend to have a more rapid clinical course. Asbestosis is invariably progressive and can eventually lead to hypoxemic respiratory failure. Therefore, the diagnosis is important not only for medical decision making but also for medicolegal reasons and patient compensation. The American Thoracic Society has proposed diagnostic criteria, which include:

Evidence of structural lung pathology consistent with asbestosis that can be documented by imaging or histology.

Evidence of causation by asbestos that is documented by a reliable occupational history; presence of pleural plaques; or presence of asbestos bodies in lung tissue, BAL fluid, or sputum specimens.

Exclusion of the various alternative diagnoses.

References: REFERENCES


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