Organizing Pneumonia

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ABSTRACT: Organizing pneumonia (OP) is a histologic term characterized by patchy filling of alveoli and bronchioles by loose plugs of connective tissue. OP may be an incidental finding in lung biopsy specimens or may be found nearby areas of lung involved by other diseases. On other occasions, OP may be the primary cause for pulmonary dysfunction and/or pulmonary symptoms. OP can be either idiopathic (cryptogenic organizing pneumonia, COP) or secondary to underlying disease (secondary organizing pneumonia, SOP). COP typically presents with a prodrome of symptoms of a respiratory illness followed by the insidious onset of dyspnea weeks to months later. The radiological findings typically reveal peripheral consolidation, although ground glass infiltrates or solitary nodules may be seen. The definitive diagnosis of OP requires histology. Open lung biopsy or video assisted thoracoscopy is usually required to obtain specimens large enough for the diagnosis to be made. In some cases, transbronchial biopsy specimens may be adequate for the diagnosis. The treatment of choice for OP includes corticosteroids plus treatment of the underlying disease in cases of SOP. Relapses occur frequently, usually when treatment is withdrawn or tapered. The prognosis is good in most of the cases of COP, whereas in SOP it is dependent on the underlying cause. **KEY INDEXING TERMS:** Organizing pneumonia; Cryptogenic organizing pneumonia; Corticosteroids; therapy. **[Am J Med Sci 2008;335(1):34–39.]**

Organizing pneumonia (OP) is a clinical entity associated with a histopathologic pattern of lung repair, characterized by a patchy filling of alveoli and bronchioles by loose plugs of connective tissue. OP can be as secondary (secondary organizing pneumonia, SOP), when associated with diseases known to induce this pathologic pattern. It may present spontaneously without a known cause, which is known as cryptogenic organizing pneumonia (COP). COP is classified as an idiopathic interstitial lung disease.[1]

The term organizing pneumonia replaces the previously used term bronchiolitis obliterans organizing pneumonia (BOOP). The rationale for this nomenclature change was 2-fold. First, from the histological point of view, although the bronchiolitis obliterans pattern (which suggests obstructive histological changes of the small airways) may coexist with OP, this is not always the case. Second, the spirometric pattern seen in patients with organizing pneumonia is typically restrictive, contrary to an obstructive pattern that is common in bronchiolitis.

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Epidemiology

OP is considered to be a rare disease. A retrospective study showed that the incidence of COP was 1.10/100,000, whereas the incidence of SOP was 0.86/100,000, with an overall incidence of 1.96/100,000.[2] This study also demonstrated a significant increase in the incidence of organizing pneumonias over the last 20 years. COP is not associated with race or gender.[2,3] The mean age of onset is in the fifth to sixth decade of life,[4] although some cases have been reported in childhood.[5] There are conflicting data concerning whether there is an inverse relation between smoking and the development of COP.[6,7]

Histology

The prominent histological finding in OP is patchy involvement of the pulmonary parenchyma by fibromyxoid, polypoid plugs of granulation tissue (also known as Masson bodies) within the alveoli and occasionally within the bronchioles (in which case the term bronchiolitis obliterans organizing pneumonia may be applied) (Figure 1). There is a mild interstitial infiltrate, associated with type II epithelial cell metaplasia. Foamy macrophages (macrophages that have ingested endogenous lipoid content) may be found in alveolar spaces.[8,9] Contrary to usual interstitial pneumonia, the pathologic correlate of idiopathic pulmonary fibrosis, the pathologic lesions of OP are usually nonfibrotic and nondestructive. The lung architecture is usually pre-

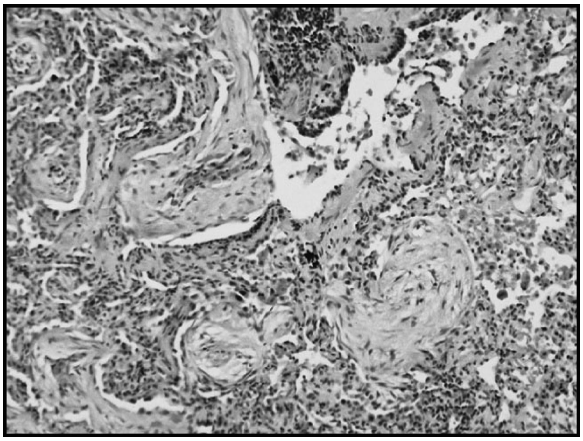

Figure 1. Organizing pneumonia: Polypoid masses of granulation tissue, filling the alveolar spaces.

served, although occasionally scarring and remodeling may be seen.[8]

Clinical Symptoms and Findings

The disease usually develops after a prodrome of a flu-like syndrome associated with fever, fatigue, nonproductive cough (70%), mild dyspnea (65%), and weight loss (60%), which lasts for several weeks. Radiographs typically show alveolar infiltrates (Figure 2). Antibiotic administration for a presumptive infectious pneumonia is ineffective. The diagnosis is typically not suspected for at least 4 to 10 weeks.[10] Although many of the prodromal symptoms resolve, dyspnea worsens and usually becomes the major complaint. COP is usually not associated with hemoptysis, chest pain, or wheezing,[4,7] although in the secondary forms, symptoms depend on the underlying disease. Fever may be absent in half of the patients; this clue suggests the diagnosis, in contrast to bacterial pneumonia.[7]

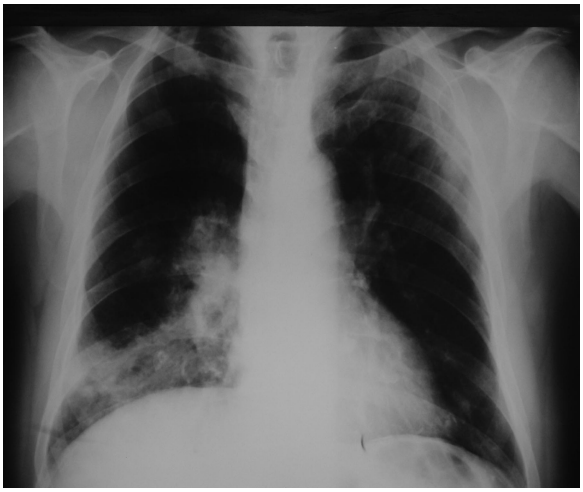

Figure 2. Typical chest radiograph with OP showing a localized alveolar opacity suggesting infectious pneumonia.

The physical examination is nonspecific. Inspiratory crackles are present in two-thirds of the patients and are more common in patients with SOP.[11] Clubbing is rare. Twenty-five percent of the patients have a normal physical examination.[12]

Occasionally, the disease may present with in more aggressive, rapidly progressing form with acute respiratory failure and is occasionally a cause of acute respiratory distress syndrome.[13,14] This is an important point, as this form of acute respiratory distress syndrome is often corticosteroid-responsive (see treatment section below). Rarely, organizing pneumonia may present as a pneumothorax.[15] Some patients may have a completely asymptomatic course, and the disease is discovered on the basis of an abnormal screening chest radiograph.

The laboratory findings are nonspecific, showing leukocytosis and neutrophilia in half of the patients, an increased C-reactive protein in 70% to 80% and an increased sedimentation rate (84%).[16] The presence of antinuclear antibodies is rare (<5%).[17] An increase of γ-glutamate transferase and alkaline phosphatase may be associated with multiple relapses.[6]

Spirometry usually shows a mild restrictive pattern. In contrast to isolated bronchiolitis obliterans without OP, an obstructive pattern is rare with OP and is usually seen in patients with an underlying obstructive lung disease. The diffusing capacity for carbon monoxide is usually decreased.[7,16] Arterial hypoxemia, recognized by an increased alveolar-arterial gradient at rest and during exercise, is common and usually mild.[7]

Radiological Findings

There are 3 radiological patterns of OP, each associated with different clinical presentation.[18,19] The most common radiological pattern of COP is peripheral, bilateral, diffuse alveolar opacities. This pattern is often confused with infectious pneumonia. These opacities are usually located in the lower lung lobes, and they may be recurrent and migratory in up to 50% of the cases. High-resolution computed tomography (CT) detects such abnormalities in more than 90% of cases. Their density ranges from consolidation (Figure 3) to ground-glass opacities (Figure 4). Air bronchograms and bronchial dilatation are often observed.[1,4,16,20,21]

The second radiological pattern is a solitary pulmonary nodule (10% to 15% of patients).[17] These lesions may occasionally cavitate.[3,22] Patients with this radiologic pattern may have the clinical syndrome of OP or be asymptomatic. The diagnosis usually requires surgical excision of the lesion, since, even if transbronchial biopsy specimens show organizing pneumonia, this is inadequate to exclude