Cryptogenic Organizing Pneumonia

Tajender S. Vasu, MD

QUESTIONS

1. A 50-year-old woman who has been experiencing cough and shortness of breath with intermittent fever for the past 2 months is referred to a pulmonary medicine physician by her primary care physician for evaluation. The patient has received 2 courses of antibiotics from her primary care physician without improvement. On examination, her vital signs are stable with a temperature of 100.4°F, and auscultation reveals bilateral crackles. The physician suspects organizing pneumonia as a possible diagnosis and orders computed tomography scan of the chest. Which of the following is the most likely radiologic finding in a patient with organizing pneumonia?
   (A) Bilateral patchy consolidation  
   (B) Honeycombing  
   (C) Multiple cavity lesions  
   (D) Pleural effusion

2. What is the next step for establishing a diagnosis of organizing pneumonia in this patient?
   (A) Bronchoalveolar lavage  
   (B) Lung biopsy  
   (C) Magnetic resonance imaging of the chest  
   (D) Pulmonary function testing

3. The patient undergoes video-assisted thoracoscopic lung biopsy, and histopathologic evaluation of a specimen demonstrates organizing pneumonia. What are the characteristic histopathologic features of organizing pneumonia?
   (A) Deposition of granulation tissue plugs (Masson bodies) within the lumens of small airways  
   (B) Fibroblastic foci  
   (C) Formation of hyaline membrane  
   (D) Prominent accumulation of alveolar macrophages

4. Further history reveals that the patient works in a microwave popcorn production plant. Exposure to which chemical has been shown to be associated with cases of bronchiolitis in employees of a microwave popcorn factory?
   (A) Acramin-FWN  
   (B) Diacetyl  
   (C) Diisocyanate  
   (D) Nitrogen dioxide

5. Which of the following method has recently been shown to distinguish cryptogenic organizing pneumonia (COP) from secondary organizing pneumonia on lung biopsy?
   (A) CD34 staining  
   (B) CD1a staining  
   (C) HMB-45 staining  
   (D) Periodic acid–Schiff reaction

6. A 55-year-old woman presents to a pulmonary medicine physician with cough, fever, and dyspnea for the past 3 weeks. Chest radiology shows bilateral patchy consolidation. She had received a course of antibiotic therapy without any improvement. The patient undergoes lung biopsy, which shows findings consistent with organizing pneumonia. Further work-up does not reveal an underlying cause of organizing pneumonia. What is the first treatment of choice for this patient?
   (A) Cyclophosphamide  
   (B) Macrolide antibiotics  
   (C) Methotrexate  
   (D) Prednisone

Dr. Vasu is a fellow, Division of Pulmonary and Critical Care Medicine, Thomas Jefferson University Hospital, Philadelphia, PA.


**ANSWERS**

1. **The correct answer is (A), bilateral patchy consolidation.** Patients with organizing pneumonia most commonly have bilateral patchy consolidation on chest imaging.\(^\text{1,2}\) Consolidation may be seen in up to 70% to 80% of patients,\(^\text{3–5}\) while pleural effusion, honeycombing, and multiple cavitary lesions are extremely rare. Other findings suggestive of organizing pneumonia include a focal lesion and diffuse interstitial infiltrate.\(^\text{6}\) An unusual feature on computed tomography associated with COP is reversed halo sign (seen in 19% of patients\(^\text{2}\)), which is characterized by crescentic or ring-shaped opacities surrounding areas of ground-glass opacification.

**References**


2. **The correct answer is (B), lung biopsy.** At this point in the evaluation, lung biopsy with histopathologic evaluation demonstrating the distinct pathologic pattern of organizing pneumonia is necessary to pursue a diagnosis of organizing pneumonia.\(^\text{1}\) In a patient with organizing pneumonia, pulmonary function testing commonly reveals a restrictive defect, although mixed, obstructive, or normal studies have also been reported.\(^\text{1,2}\) Bronchoalveolar lavage findings in patients with organizing pneumonia include increased lymphocyte counts.\(^\text{3}\) However, neither bronchoalveolar lavage or pulmonary function tests can be used to make a definitive diagnosis of organizing pneumonia. There is no role for magnetic resonance imaging of the chest in the evaluation of COP.

**References**


3. **The correct answer is (A), deposition of granulation tissue plugs (Masson bodies) within the lumens of small airways.** Organizing pneumonia is characterized by the formation of granulation tissue plugs (Masson bodies) within the lumens of small airways, alveolar ducts, and alveoli with preserved alveolar architecture.\(^\text{1}\) Hyaline membranes are seen in diffuse alveolar damage. Usual interstitial pneumonitis is characterized by formation of fibroblastic foci. Diffuse accumulation of alveolar macrophages is seen in patients with desquamative interstitial pneumonitis.\(^\text{2}\) It is important to note, however, that the organizing pneumonia histologic pattern is not specific to organizing pneumonia as it is seen in various lung diseases, such as pulmonary infarcts and neoplasms. Thus, the clinical context must be considered along with the pathologic findings before conferring a diagnosis of obstructive pulmonary disease. In addition, the diagnosis of COP requires that secondary causes and associated disorders be excluded.

**References**


4. **The correct answer is (B), diacetyl.** Inhalational agents including fumes, gases, mists, mineral dusts, or organic material may lead to the development of bronchiolitis and are among the secondary causes of organizing pneumonia. Inhalation of diacetyl, a butter-flavoring agent, has been linked to cases of bronchiolitis among workers at a microwave-popcorn...
factory. Exposure to nitrogen dioxide from silage may cause extensive lung injury that manifests with cough, dyspnea, and progressive hypoxemia. The histopathology of silo filler’s disease shows bronchiolitis. Occupational asthma can be caused by exposure to diisocyanate. Inhalation of Acramin-FWN from aerosolized paint has been reported to cause cases of bronchiolitis among workers in the textile industry in Spain. Other secondary causes of organizing pneumonia include infections, drugs, connective tissue disorders, transplantation, and radiation exposure.

References

5. The correct answer is (A), CD34. The intraluminal plug in patients with secondary organizing pneumonia is strongly positive for immunohistochemical stains for CD34, an endothelial marker, as well as alpha-smooth muscle cell actin. Both have been shown to distinguish COP from secondary organizing pneumonia. Langerhans cells react with immunohistochemical stains for CD1a and S-100 as seen in patients with pulmonary Langerhans cell histiocytosis. HMB-45 stain is positive in patients with lymphangioleiomyomatosis. Pulmonary alveolar proteinosis is characterized by deposition of granular extracellular material composed of protein and lipids within the air spaces that is periodic acid–Schiff-positive.

References

6. The correct answer is (D), prednisone. Systemic steroid therapy is the treatment of choice for COP. The prognosis of COP is usually good, and more than 70% of patients have rapid clinical and radiologic improvement with administration of steroids. The addition of cyclophosphamide, azathioprine, or methotrexate may be considered in patients who continue to deteriorate despite being on corticosteroids. Macrolide antibiotics have been used as an alternative therapy because of their anti-inflammatory and immunomodulatory effects.

References