Case 008: An older woman complains of dry cough and shortness of breath.

Authors: Thomas YK Chan MD, PhD, FRCP  
               David C Chung MD, FRCP  
Affiliation: The Chinese University of Hong Kong

A 67 year-old woman presented to the clinic for the first time with insidious onset of dry non-productive cough and progressive shortness of breath over the past 12 months. Her exercise capacity has degenerated to half a flight of stairs because of dyspnea. She never smoked and was not on any regular medications except an herbal tea once a week prescribed by a Chinese herbalist to clear “lung heat”. She used to be a shop assistant in a department store until she retired at age 55. There was no history of allergies.

Examination revealed a somewhat underweight patient looking older than her age. She was not in respiratory distress but was obviously tachypneic with a respiratory rate of 24 breaths/min. There was mild finger clubbing but no central or peripheral cyanosis. Chest expansion was decreased bilaterally. Auscultation revealed fine inspiratory crackles over the lung bases. The jugular venous pressure (JVP) was judged normal and there was no dependent edema.

1. What is the differential diagnosis?

   The differential diagnosis includes all causes of dyspnea that is progressive in onset over months to years:
   
   o Chronic lung disease of any cause, including chronic obstructive pulmonary disease (COPD), connective tissue disease (e.g. rheumatoid arthritis), pulmonary fibrosis, sarcoidosis, pneumonconiosis.
   o Chronic heart failure from any cause.
   o Restriction of chest wall movement (e.g. deformities, ankylosing spondylitis).
   o Anemia.
   o Neuromuscular disease.

2. What laboratory tests would you order as a first step in the investigation of this patient?

   Besides general blood tests, the following investigations would be helpful:
   
   o Chest x-ray.
   o Pulmonary function tests.
   o Arterial blood gases when breathing room air.

Blood test results were normal and her chest x-ray appears below:
The x-ray showed contracted lung volumes bilaterally with reticular interstitial shadows most prominent in the lower zones. There were also honeycomb-like patterns in the periphery.

Pulmonary function tests showed restrictive lung disease with reduced vital capacity and total lung capacity. There was no obstructive component. Carbon monoxide diffusion capacity (DLCO) was also reduced.

Arterial blood gas results were: pH 7.36, pCO2 44 mmHg, pO2 91 mmHg, Base excess -2 mmol/L. (Reference range: pH 7.35 to 7.45, pCO2 35 to 45 mmHg or 4.6 to 6 kPa, pO2 90 to 100 mmHg or 12 to 13 kPa, base excess -2 to 2 mmol/L).

3. What other investigations are helpful?
   - High resolution CT scan of the lungs.
   - Lung biopsy.

The CT scan (not shown) showed subpleural reticular abnormalities (especially in the lung bases), peripheral patches with ground glass appearance, and honeycomb-like cystic structures.

Based on these findings, diagnosis of idiopathic pulmonary fibrosis (cryptogenic fibrosing alveolitis) was made and lung biopsy was deemed not necessary.
4. What is idiopathic pulmonary fibrosis?

Idiopathic pulmonary fibrosis is a relatively rare condition in which there is diffuse fibrosis of the lung parenchyma with lower lobe predominance. The etiology of the disease is unknown. Cigarette smoking, inhalation of metal or wood dust, infectious causes and chronic aspiration may play a role in pathogenesis but these factors are not always present. Some patients show features of autoimmunity and familial preponderance. It was thought previously that chronic inflammation in response to lung injuries is the cause of fibrosis. The current concept is fibroblastic proliferation, with little evidence of inflammation, is responsible for pathogenesis of the disease.

Clinical presentation of the disease in our patient is typical:
- It strikes patients of all races typically between the age of 40 and 70 years. More men than women are affected.
- Onset is insidious. May start with general malaise, easy fatigability, weight loss, muscle aches, joint pains, and shortness of breath. Non-productive coughs, resting tachypnea, and exertional dyspnea are prominent features.
- Clubbing may or may not be present.
- Auscultation of the lungs reveals fine crackles that are most prominent during the second half of inspiration. These crackles start at the base of both lungs and move up the lungs as the disease progresses.
- Pulmonary function tests and imaging results seen in our patient are typical.
- ABG results are normal and patients are free of cyanosis in the early stage. Cyanosis, pulmonary hypertension, cor pulmonale, and right heart failure are prominent features in the terminal stage.

5. When is lung biopsy indicated?

In the hands of experienced clinicians, diagnosis can be made based on clinical features, pulmonary function tests, and imaging results. Lung biopsy is considered only if there is suspicion that the underlying condition may be another treatable disease or when lung transplant is contemplated (see following section).

6. What is the treatment for idiopathic pulmonary fibrosis?

- Treatment is entirely of an empirical nature.
- Administration of influenza and pneumococcal vaccines is advised to prevent intercurrent infection.
- Supportive treatment should be administered to patients who are hypoxemic and have heart failure.
- Based on previous belief that inflammation is the cause of fibrosis, specific treatment relies heavily on anti-inflammatory medications, usually prednisone combined with azathioprine or cyclosporaphamide. However, there is no evidence that these medications improve survival or quality of life.
- Based on the current concept that fibrosis rather than inflammation is the cause of the disease, antifibrotic drugs (e.g. colchicines, pirfenidone) combined with steroids have been tried. A study using interferon \( \gamma \)1b in addition to prednisone is showing promise.
Lung transplantation may be offered to younger productive individuals where surgical facility permits.

7. What is our patient’s prognosis?

There is no cure for idiopathic pulmonary fibrosis; spontaneous remission does not occur; and the clinical course is invariably downhill. Patients who have a salutary response and stable disease 3 to 6 months after a course of corticosteroid therapy have better prognosis but five year survival is only between 30 and 50%.

Further Readings
