Pulmonary Embolism in the Patient with Chronic Obstructive Pulmonary Disease*  
A Diagnostic Dilemma

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It is often difficult to distinguish pulmonary embolism from worsening underlying disease in the setting of severe chronic obstructive lung disease. We describe three patients with severe COPD and angiographically documented pulmonary emboli to stress that standard clinical and radioisotopic studies of little value in establishing a diagnosis. All patients had acute increases in alveolar ventilation immediately following the embolus with a reduction in previously elevated levels of PaCO₂, as well as hypoxemia. Such changes in arterial blood gases in the patient with severe COPD should suggest pulmonary embolus rather than increased obstruction.

The diagnosis of pulmonary embolism is difficult despite extensive literature on the subject and clinical experience. This is especially true in patients with severe chronic obstructive lung disease (COLD) in whom the increased dyspnea, cough, hemoptysis, fever, and signs of increasing right heart failure may just as likely result from worsening of their underlying illness as from pulmonary embolus. In addition, although chronic lung disease is often included as a major risk factor in pulmonary embolism, the degree and etiology of this increased risk is poorly defined. We report three cases in which documented pulmonary embolism developed in the setting of severe obstructive lung disease to analyze the features in their presentation that allow for appropriate evaluation and management. We also review the literature concerning the risk and identification of pulmonary embolism in this clinical setting.

CASE REPORTS

CASE 1

A 62-year-old man was admitted because of profound dyspnea. He had a smoking history and severe obstructive lung disease (FEV₁/FVC 26 percent) that had progressed over the last ten years. His activity at home had been limited to one half block of level walking, and he had been receiving continuous low-flow oxygen to treat mild right heart failure. Aminophylline, isethionate, and prednisone were given as therapy for bronchospasm. There was no past history of thrombophlebitis or coagulopathy.

Acute symptoms began four days before admission with sudden increase in dyspnea and reduction of the patient's exercise tolerance to two or three steps. There was no associated syncope, chest pain, or hemoptysis (Table 1). His temperature was 37.6°C, and blood pressure was 180/100 mm Hg. His respiratory rate was 32 breaths/min. The pulse rate was 130 beats/min.

On examination the patient was in acute respiratory distress (Table 1) with bilateral wheezing and hyperinflation. Heart sounds were distant without increased prominence of P₂ or murmurs. The abdomen was obese but otherwise normal. There was no cyanosis, clubbing, edema, or tenderness of the extremities.

Significant laboratory studies are reported in Table 2. Of note is the great increase in alveolar ventilation, with a decline in his usual PaCO₂ from 47 mm Hg to 35 mm Hg. Chest roentgenogram (Fig 1) showed hyperinflation and prominence of the left pulmonary artery, which was unchanged from past films. Radionuclide ventilation-perfusion lung scan (Fig 2) showed unmatched multiple bilateral segmental perfusion defects, and pulmonary angiography showed occlusion of the main right pulmonary artery as well as segmental vessels in the lower lobes, lingula, and right upper lobe (Fig 3). Doppler studies of the lower extremities revealed obstruction to venous flow on the left side.

The patient was given a continuous heparin infusion for seven days followed by orally administered warfarin. His dyspnea gradually abated and his exercise tolerance im-

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<td>36</td>
<td>Warm right calf</td>
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Figure 1. PA chest roentgenogram in case 1 at the time of acute symptoms. The left pulmonary artery is prominent but unchanged from previous examination.

proved. A repeated perfusion lung scan done ten days after admission (Fig 4) showed marked resolution.

Comment

This patient's presentation showed the difficulty that arises in evaluating an exacerbation of dyspnea in a patient with chronic obstructive airway disease. Major clues to the diagnosis of pulmonary embolism were the sudden worsening of dyspnea, decrease in exercise tolerance, and the association of increased hypoxemia and hypocarbia in a previously hypercapneic patient. His plasma DNA level was significantly elevated.

Case 2

A 75-year-old woman was admitted because of progressive fatigue and dyspnea. The patient had been a heavy smoker and had severe COLD (FEV₁/FVC 30 percent), which had been treated with theophylline. Continuous low-flow oxygen was administered because of severe hypoxemia and previous right heart failure.

Figure 2. Posterior view of perfusion lung scan obtained in case 1 showing multiple bilateral perfusion defects (arrows). Ventilation sign, not reproduced, showed unmatched defects.

Figure 3. Anterior view of pulmonary arteriogram (case 1) showing large filling defect in right main pulmonary artery (arrow).

Figure 4. Posterior view of perfusion lung scan obtained ten days after institution of heparin therapy. Significant resolution of filling defect is demonstrated.
Her current symptoms began subacutely over five days with increasing dyspnea and weakness leading to a severe reduction in her already limited exercise capacity. Clinical data is presented in Table 1.

The patient’s temperature was 36°C. The pulse was 112 beats/min, and respirations were 28 breaths/min. Her blood pressure was 100/70 mm Hg. On examination she appeared chronically ill and acutely short of breath. Jugular venous distention was present with diffuse wheezing throughout her chest. Heart sounds were distant without accentuated \( P_2 \). There was no edema, cyanosis, or calf tenderness.

Laboratory evaluation is presented in Table 2. The chest roentgenogram was unchanged from previous films and showed reduced vascularity and hyperinflation. A radio-nucleotide ventilation-perfusion scan showed bilateral, irregular but matched ventilation and perfusion defects. A pulmonary angiogram demonstrated occlusion of segmental arteries to lingular and right lower lobes; the mean pulmonary artery (PA) pressure was 24 cm of water. Continuous heparin infusion was instituted for ten days, after which therapy was begun with warfarin given orally. A repeated perfusion study done two weeks later demonstrated resolution of the defects, which correlated with improvement in symptoms.

**Comment**

Only increased dyspnea and acute hypoxemia and hypocarbia in a previously hypercarbic patient suggested the diagnosis of pulmonary embolism. Leukocytosis and sinus tachycardia were not specific and suggested a typical exacerbation of obstructive airway disease. Again, the plasma DNA level was elevated.

**Case 3**

A 65-year-old man was admitted because of cough and fever (temperature, 38.8 °C). The patient had a 15-year history of severe obstructive lung disease (FEV1/FVC 24 percent), with hypercapnea and secondary erythrocytosis. A chest roentgenogram confirmed the diagnosis of right upper-lobe pneumonia, and Gram stain and culture indicated a pneumococcal etiology.

The patient was improving clinically four days into a course of penicillin therapy, when he had a sudden and transient syncopal episode. On regaining consciousness he complained of severe dyspnea but had no chest pain or hemoptysis. The patient had been at bed rest during his hospitalization. Blood pressure was 100/90 mm Hg. The pulse was 140 beats/min. The respiratory rate was 40 breaths/min. Examination of the chest showed hyperinflation and bronchovesicular breath sounds over the right upper lobe. There were no pleural friction rubs and no increase in \( P_2 \). There was mild cyanosis of the extremities, and the left calf was warmer than the right. No edema, pain, or tenderness of either extremity was noted (Table 1).

Results of laboratory studies are noted in Table 2. The chest roentgenogram showed dense right upper-lobe consolidation. Pulmonary angiography was performed and showed an embolus occluding the artery to the left lower lobe. Mean PA pressure was 40 cm of water.

The patient was given continuous infusion of heparin followed by warfarin administered orally. By day 2 the dyspnea had improved to the previous baseline levels.

**Comment**

The diagnosis of pulmonary emboli was confused by the patient’s underlying pneumonia. The syncope and the acute-ness of the dyspnea while in the recovery phase of his pneumonia suggested pulmonary embolus. Arterial blood gases once again showed hypoxemia and relative hypocarbia.

Physical examination was not useful in separating worsening airway obstruction or cardiac arrhythmia from acute embolism. While ECG, WBC count, and transaminase determinations were abnormal, they were not specific for pulmonary embolism.

**Discussion**

The diagnosis of pulmonary embolus in the patient with COPD is a clinical dilemma that prompts two questions: (1) Are patients with COPD at greater risk for pulmonary embolism than the general hospital population? If so, what is the source of this risk? (2) Can the presentation of pulmonary thromboembolism be differentiated from worsening airway obstruction?

Our patients represented 18 percent of a population of patients with emphysema admitted with dyspnea that had become more severe over a three-month period. Although this is lower than the 20 to 60 percent incidence reported previously, it is clear that pulmonary embolus represents a significant complication in this population. The source of this risk is not well defined, but probably relates to inactivity and right heart failure. Our patients were clearly inactive owing to greatly impaired exercise tolerance, though only one patient was bedridden.
All had clinical evidence of cor pulmonale, which has been sited as a major risk factor in pulmonary embolus. Ryan noted that 23/26 patients with emphysema and pulmonary emboli had right heart failure, and 7/26 patients had mural thrombi of the right ventricle. Severe polycythemia, which increases blood viscosity, was not associated with increased thromboembolic risk.

The major clinical features suggesting pulmonary embolism in our patients were profound dyspnea unresponsive to bronchodilator therapy and hypoxemia with relative hypocapnia in a previously hypercapnic patient. The mean increase in A-a gradient was 20 ± 13 mm Hg (mean ± SD), and the mean fall in Pco2 was 10 ± 4.7 mm Hg. As indicated in Table 1, none of the typical clinical findings of pulmonary embolism were present. While the WBC count and ECG were abnormal, neither of these results is specific. Perfusion lung scan was abnormal in the two patients in whom it was performed, but such abnormalities may be present in chronic airway obstruction without emboli.

In addition, xenon ventilation scanning in one patient showed only matched defects. This confirms studies by Wagner, who found that the addition of xenon ventilation scanning has not substantially increased the accuracy of diagnosing pulmonary embolism in patients with COPD. In all of our patients pulmonary angiography was required for confirmation.

Baum reported a 30 percent incidence of emboli in patients with emphysema and suggested that emboli must be considered when patients fail to respond to the usual therapy for COPD. The development of worsening hypoxemia and dyspnea in the absence of infection or other obvious cause in patients with COPD should suggest the diagnosis of emboli. Increased alveolar ventilation reflected by decreased PCO2 in a previously hypercapnic patient should also suggest pulmonary emboli. Though the mechanism is unknown, it has previously been found that the discharge from medullary respiratory neurons increases after experimental pulmonary embolism, thereby increasing ventilation and activity of respiratory muscles. Hypoxemia and apprehension may also contribute to the increase in alveolar ventilation. This ventilatory response suggests that central rather than mechanical factors were mainly responsible for the baseline hypercarbia in our patients.

Sipes et al have proposed plasma-free DNA as a highly sensitive and specific method for the diagnosis of pulmonary embolism. In their series plasma DNA was detected in 19/23 patients with pulmonary emboli diagnosed by radioisotopic or angio-

graphic methods, but in 0/49 patients with other diagnoses including myocardial infarction, thrombo- phlebitis, and pneumonia. In both of our patients tested plasma-free DNA was detectable and elevated at the time of diagnosis of pulmonary embolism. If further studies support the specificity and sensitivity of this determination, it will be of particular use in the patient with COPD whose clinical signs are often equivocal.

In summary, we recommend the following guidelines for the diagnosis of pulmonary embolism in the emphysema patient:

1. Pulmonary embolism should be suspected in any patient with COPD and cor pulmonale whose dyspnea worsens precipitously and is unresponsive to conventional bronchodilator regimen.

2. The diagnosis of pulmonary embolism is supported by a reduction in the PaCO2 in a previously hypercarbic patient.

3. Clinical signs and radioisotopic studies are not useful in differentiating pulmonary embolism from worsening obstruction.

4. Angiography must be undertaken to confirm the diagnosis of pulmonary embolism in the patient with severe obstructive lung disease.

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