Dyspnea and Chest Pain in a 45-Year-Old Woman

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From the Case Records of the Alpert Medical School of Brown University Residency in Emergency Medicine

DR. JONATHAN AMELI: Today's patient is a 45-year-old woman who presents with difficulty breathing and chest pressure. Her chest discomfort has been constant since the morning. She had mild chest pain the day before, but ignored it due to fear of visiting the emergency department (ED).

The patient has a history of bipolar disorder, morbid obesity, and chronic obstructive pulmonary disease (COPD). She smokes tobacco, occasional marijuana, and has a long-standing cough. She is on aripiprazole, bronchodilators and inhaled steroids for COPD.

DR. FRANCESCA BEAUDOIN: Can you describe her physical exam?

DR. AMELI: The patient is a morbidly obese woman in no distress. She is afebrile. Her pulse is 120 bpm and regular, respiratory rate is 20, blood pressure is normal at 123/70 mmHg, and she has an oxygen saturation of 85% on room air. She has minimal wheezing on lung exam and her heart is tachycardic with regular rhythm and no murmur. Her abdomen is soft and non-tender, and she has bilateral edema in her lower extremities. Her right calf is slightly larger than the left and she has mild erythema overlying the skin bilaterally.

DR. SARAH GAINES: The patient is tachycardic and hypoxic. What were your initial concerns and were you able to make a diagnosis?

DR. AMELI: Our initial concerns included acute coronary syndrome, as well as pulmonary embolism (PE). Other disorders on our differential diagnosis included COPD exacerbation, congestive heart failure, acute aortic dissection, and pneumonia. An electrocardiogram was obtained within 10 minutes of the patient's arrival and she was found to have a sinus tachycardia without significant ST abnormalities. A portable chest xray demonstrated a poor inspiratory effort and non-specific bilateral air space disease. Laboratory studies revealed a WBC count of 18,000 mm3, an unremarkable chemistry panel, and a normal beta natriuretic peptide (BNP) and troponin. A d-dimer was elevated at 2,777 ng/ml. A bedside echocardiogram showed no pericardial effusion, and the patient was stable enough to obtain a pulmonary embolism protocol CT scan. The CT demonstrated a large pulmonary embolus at the right main pulmonary artery as well as multiple left sided segmental and subsegmental pulmonary emboli (**figure 1**). She also had likely pulmonary infarcts seen as ground-glass opacities bilaterally (**figure 2**).

Figure 1. Pulmonary Embolus at Right Main Pulmonary Artery

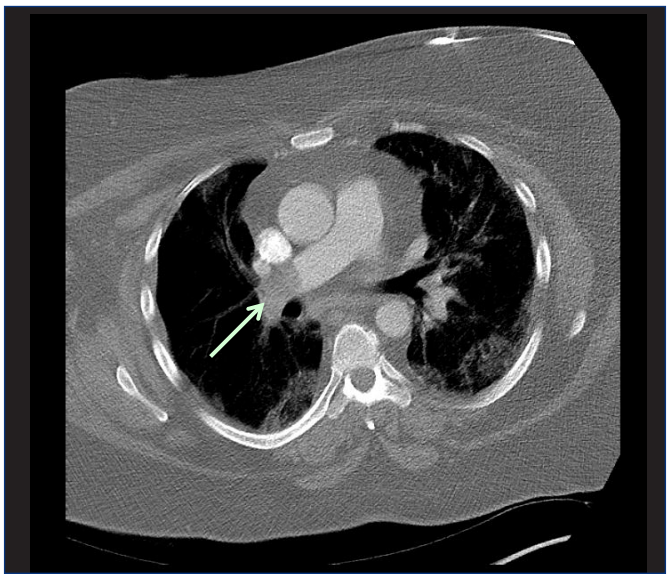
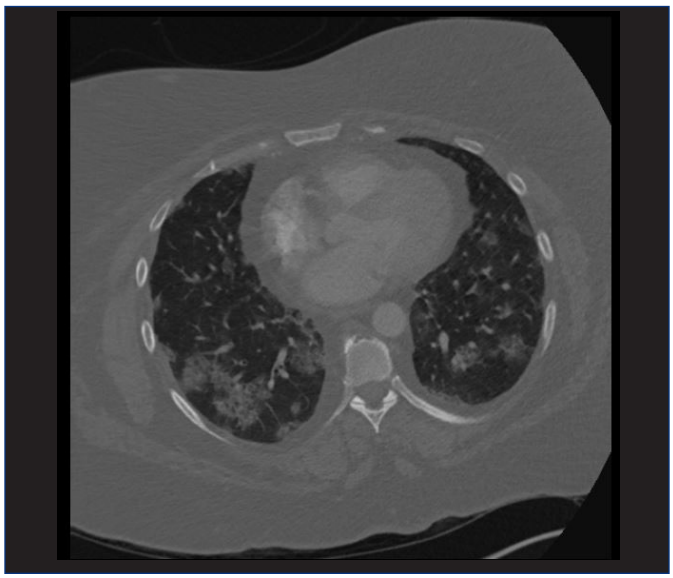


Figure 2. Bilateral ground-glass opacities



DR. JEFF FEDEN: The patient did not have any known risk factors for pulmonary embolism. How common is this disorder?

DR. AMELI: Approximately 5%-8% of the US population has one of several genetic risk factors leading to an increasing risk of venous thromboembolism.[1] Additionally, our patient had minor risk factors (relative risk = 2 – 4) including obesity and chronic obstructive pulmonary disease, as well as tobacco use. Incidence of PE at age 45 is less than 0.2% annually but rises significantly with age.[2] There are greater than 250,000 people hospitalized for PE per year.[3] In the United States, approximately 100,000 deaths per year are related to PE, with many cases not being diagnosed until autopsy, and 15% of all in-hospital deaths can be attributed to venous thromboembolism.[4,5]

DR. JOHN FOGGLE: This patient appeared to be hemodynamically (HD) compromised. What is the pathophysiology of an acute PE that would cause her symptoms?

DR. WILLIAM BINDER: The proximal portion of a lower extremity deep venous thrombosis can break off spontaneously, travel the venous system to the right ventricle, and then lodge in the pulmonary arteries. This obstruction can cause an increase in dead space in the alveoli, leading to high ventilation, low perfusion, and hypoxemia.

In a patient without prior cardiac or pulmonary disease, obstruction of 30–50% of the pulmonary bed will lead to the development of pulmonary hypertension. The sudden higher pressures, in turn, leads to an increase in right ventricular (RV) afterload, followed by RV dilatation and right-sided heart failure.[5,6] If pulmonary vascular resistance rises above a level the RV can tolerate, sudden death through pulseless electrical activity or asystole can occur. In submassive PE, a decrease in RV output causes diminished left ventricular (LV) filling, and interventricular septal bulging. Decreased outflow leads to decreased blood pressure and syncope, or even cardiogenic shock. Other complications include diminished coronary flow and subendocardial RV ischemia and infarction, which may be amplified by underlying coronary artery atherosclerosis. Because of dual pulmonary circulation arising from the pulmonary and bronchial arteries, pulmonary infarction usually does not occur although it is certainly a well known complication of pulmonary embolism.[5] Compensatory mechanisms countering right-sided failure include activation of the sympathetic nervous system and increased inotropy and chronotropy, which help preserve pulmonary artery flow and maintain systemic circulation.[5-7]

DR. LISA MERCK: How do we risk-stratify PE once we have the diagnosis?

DR. AMELI: Risk stratification has important management implications in pulmonary embolism, and is based on the clinical presentation in combination with biomarkers, ECG findings, and echocardiogram abnormalities. Clot burden measured on CT has not been shown to be directly related to clinical manifestations and outcome – a morphologically extensive PE can present as a hemodynamically minor injury, while conversely a small PE can have significant hemodynamic consequences in patient's with impaired cardiovascular status and reserve.[8,9] The American Heart Association (AHA) has defined 3 major risk categories in PE: massive, submassive, and low risk.[3]

Massive PE can be defined as sustained hypotension (systolic blood pressure <90 for at least 15 minutes), pulselessness, or sustained bradycardia (HR <40) with signs of shock, and not due to another cause such as septic or hypovolemic shock.[3] It is a morbid diagnosis. In the International Cooperative Pulmonary Embolism Registry (ICOPER) trial, about half of the patients with acute PE and SBP<90 at presentation died, and 15% of the remainder also succumbed during their hospital stay. Additionally, having right ventricular (RV) hypokinesis, as measured by echocardiogram, doubled mortality.[10] In the Management Strategies and Prognosis of Pulmonary Embolism (MAPPET) trial, which included 1,001 patients, mortality during hospital stay occurred in 25% of patients with acute PE and HD instability, and in 65% of those requiring any form of CPR.[11]

Low-risk PE patients have HD stability on presentation, normal biomarkers such as troponin and BNP, and no signs of RV dysfunction or strain on echocardiogram.[3]

A submassive PE is defined as a PE in a HD stable patient with evidence of RV dysfunction as seen on ECG, biomarker levels, CT scan, or echocardiogram.[3] On ECG, RV strain can be seen as the S1Q3T3 pattern, but more commonly, as a right bundle branch block, or t-wave inversions in leads V1-4.[12] Biomarkers can be used to measure RV dysfunction caused by increased pulmonary vascular resistance. Micro-infarctions and shear stress on the RV lead to elevations in cardiac troponin and BNP. If a patient has normal biomarkers, and they are HD stable, it can be argued that an echocardiogram is not needed to assess for RV dysfunction.[13]

If biomarkers are elevated with a confirmed PE, an echocardiogram is indicated for further risk stratification. RV dysfunction on echocardiogram can be appreciated as dilatation of the right ventricle (RV > LV more than 1:1), paradoxical septal motion (RV bows toward the LV via the interventricular septum), tricuspid regurgitation, or McConnell's sign (RV free wall hypokinesis).[14] The CT PE scan itself can be used to predict RV dysfunction by showing a right to left ventricular ratio of >0.9.[15] Findings of RV dysfunction in combination with acute PE have been shown to be predictive of a higher odds-ratio of short-term mortality.[16]

All three categories of confirmed or highly suspected pulmonary embolism should be treated with supportive care, airway management, and in most cases, intravenous fluids to increase preload. In addition, anticoagulation should be started as soon as possible. Thrombolysis, in addition to

heparin, should be used for all massive PE (SBP<90, HR<40, cardiac arrest with high suspicion). Surgical embolectomy is considered in massive PE when there are absolute contraindications to thrombolysis.[5]

DR. FRANZ GIBBS: Are thrombolytics indicated in submassive pulmonary embolism?

DR. AMELI: The decision to administer thrombolytics in submassive PE is controversial. Short-term mortality in submassive PE is approximately 3%, and development of pulmonary hypertension occurs in 0.1 – 3.8% of patients. Consequently, many studies are not sufficiently powered to evaluate composite endpoints.[9] While the Pulmonary Embolism Thrombolysis (PEITHO) trial demonstrated improvement in HD in submassive PE through fibrinolysis with tenecteplase, the risk of major bleeding was significant.[17] The Tenecteplase or Placebo: Cardiopulmonary Outcomes at Three Months (TOPCOAT) trial showed that treatment with tenecteplase in combination with heparin in submassive PE was associated with positive self-assessment of health (such as exertional dyspnea, exercise tolerance) at 90 days by the surviving patients as compared to those that received heparin alone. Limitations to this trial include an early termination, and a small sample size.[18] The Moderate Pulmonary Embolism Treated with Thrombolysis (MOPETT) trial showed half-dose tPA in combination with enoxaparin for submassive PE was effective in decreasing pulmonary hypertension and recurrent PE at 28 months in comparison to enoxaparin alone. However, limitations of this study included lack of blinding among other issues.[19]

Catheter-directed embolectomy is another alternative method designed to reduce the systemic effects of thrombolysis. While it has been shown to increase RV function in submassive PE, it has not yet demonstrated efficacy in decreasing ICU length of stay, or improving patient outcomes. [20,21]

There still does not exist a single, large trial that shows thrombolysis, in addition to standard anticoagulation for submassive PE, is beneficial in terms of all-cause mortality, although a meta-analysis in JAMA has shown some benefit.[22] The AHA has consistently recommended thrombolytics to be used only for massive PE.[3] The most recent American College of Emergency Physicians (ACEP) clinical policy from 2011 states that thrombolytics should only be used in massive PE, or HD unstable patients with confirmed pulmonary embolism (level B recommendation), or massive PE with high suspicion (level C recommendation).[23]

DR. ERIC GOLDLUST: What was the patient's clinical course and outcome?

DR. AMELI: In the ED, she was immediately started on a heparin drip, and admitted to the medical intensive care unit (MICU). After a very brief stay in the MICU, the patient was transferred to the medical floor, but she suddenly worsened and required intubation for hypoxic, hypercarbic respiratory failure. She had a bronchoscopy that did not show evidence of infection. Her repeat echocardiogram showed mild RV dysfunction. Her biomarkers showed a small increase in troponin and BNP. Thrombolytics were not used. After several days on the ventilator, she was extubated, and had an uneventful course thereafter. She was again transferred to the floor, and gradually weaned off oxygen. Her heparin drip was bridged to warfarin, and she was discharged successfully a few days later.

DIAGNOSIS: Submassive PE in an obese patient with COPD.

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