CLINICAL VIGNETTE

A Case of Subacute Dyspnea: Pulmonary Tumor Embolism

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Introduction

Pulmonary tumor embolism is a rare cause of pulmonary hypertension (PH) and cor pulmonale. It often presents as unexplained progressive dyspnea in patients with known underlying cancer. Unfortunately, the diagnosis is often missed and has a grave prognosis.

Case Presentation

A 74-year-old male with past medical history notable for recent diagnosis of metastatic adenocarcinoma of unknown primary and atrial fibrillation presented with progressive dyspnea. He was hospitalized two weeks prior with back pain and dyspnea. At that time, he was diagnosed with atrial fibrillation with rapid ventricular rate and pericardial effusion, for which he had a pericardiocentesis and completed a 14-day colchicine course. Pericardial fluid cytology showed atypical cells, favored to be reactive, and was negative for malignant cells. For his back pain, imaging revealed mixed lytic and sclerotic thoracic spinal lesions, which were biopsied and ultimately revealed to be metastatic adenocarcinoma of unknown primary. Following discharge from the hospital, he developed progressive dyspnea with minimal exertion, as well as paroxysmal nocturnal dyspnea, weakness, anorexia and weight loss, prompting readmission.

On initial evaluation, patient was normotensive, with heart rate up to 140 requiring 4 L/min of supplemental oxygen to maintain oxygen saturations of 92 percent. Pertinent findings on physical exam included elevated jugular venous pressure, tachypnea with clear lung fields, and trace lower extremity edema. He had multiple laboratory abnormalities. White blood cell count was $12.6x10^3/\mu l$, Cr 2.12 mg/dl (baseline 0.8 mg/dl), total bilirubin was 2.5 mg/dL, AST was 928 U/L, ALT was 913 U/L, alkaline phosphatase was 224 U/L, LDH was 1090 U/L, troponin was 0.088 ng/ml, N-terminal pro-BNP was 33,289 pg/ml, D-dimer was 2,654 ng/ml, lactate was 5.6 mmol/L. Chest x-ray was negative for an acute cardiopulmonary process. Electrocardiogram (ECG) was consistent with atrial fibrillation with rapid ventricular rate (RVR), without ST or T wave changes. Right sided ECG ruled out right ventricle infarct. Transthoracic echocardiogram (TTE) was remarkable for severely dilated right ventricle with severely reduced systolic function, pulmonary artery systolic pressure of 45 mmHg, and a medium sized pericardial effusion without tamponade physiology. Left ventricular function was preserved with ejection fraction of 60 to 65 percent. Taken together, the patient had evidence of cardiogenic shock with new acute kidney injury (AKI), transaminitis, and elevated lactate on laboratory workup. These findings in the presence of new acute hypoxic respiratory failure, elevated D-dimer, N-terminal pro-BNP, and troponin, and TTE evidence of right-sided heart failure raised the concern for acute massive pulmonary embolus (PE). Due to the AKI, lower extremity venous dopplers and a ventilation-perfusion (VQ) scan were obtained to assess for PE. The dopplers ruled out deep venous thrombosis. VQ scan was negative for pulmonary embolus but showed diffuse heterogeneity throughout both lung fields.

Clinically, the patient continued to decline over a few hours and was transferred to the intensive care unit requiring increased oxygen support and vasopressin and norepinephrine for blood pressure support. He was treated with amiodarone drip for atrial fibrillation with RVR. Furosemide continuous infusion was started as well for cor pulmonale and inhaled epoprostenol for PH. Because pulmonary embolus evaluation was negative, right heart catheterization was advised with hopes of obtaining aspirate from the pulmonary wedge position for cytology as pulmonary tumor embolism was highly suspected as the cause of this presentation. RHC was consistent with cardiogenic shock due to right heart failure with cardiac index of 0.87-1.78 $L/min/m^2$. Cytology was positive for malignant cells compatible with known metastatic adenocarcinoma. A diagnosis of pulmonary tumor emboli was made. Given his clinical status and unknown primary malignancy, he was deemed not a candidate for chemotherapy. Patient and family opted for comfort care and he died shortly afterward, 48 hours after admission to the hospital.

Discussion

Pulmonary tumor embolism is a rare cause of tumoral PH and cor pulmonale and is considered an end-stage phenomenon of malignancy. This case illustrates prompt diagnosis with high clinical suspicion for pulmonary tumor embolism. This allowed for an informed discussion regarding goals of care with the patient while he was able to participate in the decision-making process.

There are two main types of tumoral PH: pulmonary tumor embolism and pulmonary tumor thrombotic microangiopathy.[1] Despite different pathophysiology, the outcomes are the same.[1] They are more commonly seen in adenocarcinomas but have

been reported in various malignancies.[1] Most case reports are identified on autopsy and are often missed antemortem.[1-5]

The presentation of pulmonary tumor embolism is typically unexplained dyspnea that is subacute and progressive in patients with malignancy.[1] Physical exam findings are consistent with PH and cor pulmonale.[1] Imaging studies are not sensitive or specific for pulmonary tumor embolism.[1] Cytology and histology are necessary to make the definitive diagnosis of pulmonary tumor embolism.[1] Options include lung biopsy such as transbronchial lung biopsy or aspiration of pulmonary artery blood in the wedge position during RHC as initial tests if imaging is nondiagnostic in patients with malignancy and unexplained dyspnea.[1] Lung biopsy is ideal for stable patients who can tolerate such a procedure, whereas RHC with aspiration is preferred in unstable patients or for those with PH.[1] Diagnosis relies on high clinical suspicion. It should be suspected when evaluation for dyspnea is negative for pulmonary embolism, but the clinical findings show evidence of PH with known malignancy. Treatment involves targeting the malignancy and supportive management until patient has response to antitumor therapy. However, this is a grave diagnosis with poor prognosis with or without antitumor therapy. In one 30-year autopsy study of patients with solid malignancy identified, only three percent with pulmonary tumor embolism.[4] Of those, with tumor embolism only 10 percent were diagnosed before death.[4] Unfortunately, minimal therapeutic information exists.

Pulmonary tumor embolism is one type of tumoral PH that should be suspected in unexplained dyspnea in patients with known malignancy. Ideally, when clinical suspicion is high and evaluation for more common causes of dyspnea is negative, specific diagnostic testing should obtain a diagnosis. Because the diagnosis is grave, informed goals of care discussions are recommended.

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