CJIM | Clinical Encounters

Case Report: 44-Year-Old Male with Shortness of Breath, Cough, and Weight Loss

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Statement of Significance

Lower respiratory pathologies exhibit a broad spectrum of clinical courses ranging from self-limited to chronic and from benign to fatal. During the present COVID-19 pandemic, the prompt and proper diagnosis of respiratory disease carries even greater importance. Apart from this patient's presentation with respiratory symptoms during a respiratory pandemic, he demonstrated several concerning features for severe disease including 20 lbs of weight loss and hemoptysis. This teaching case examine the differential diagnosis, workup, clinical considerations, and management of patients presenting with severe respiratory pathology of unknown etiology.

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Case

Patient Presentation

A 44-year-old man presented to a rural emergency department in Western North Carolina with four months of worsening dyspnea, cough, night sweats, and associated 20 lb weight loss. For the past four months the patient had gradual onset of a progressively worsening cough and shortness of breath. Three months prior to presentation, the patient was evaluated by an outpatient cardiologist as he initially believed his symptoms to be cardiac in nature. Per outpatient records, he was noted to be tachycardic and tachypneic. The patient had a subsequent echocardiogram done that showed systolic heart failure with an ejection fraction of 10-15%. He subsequently had an angiogram that did not show significant coronary artery disease.

Over the past two weeks the patient's cough had become so severe that he was unable to sleep at night due to his symptoms. He also started to note that he was sweating at night and that the bedsheets were soaked upon awakening. On presentation the patient reported subjective fevers but did not check his temperature at home. He initially denied hemoptysis; however, he subsequently had an episode of small hemoptysis in the emergency department.

As his symptoms progressed, the patient was evaluated multiple times in various primary care settings and emergency departments. He had six negative covid tests and received amoxicillin, azithromycin, doxycycline, and levofloxacin, none of which provided symptom relief.

Upon presentation to the emergency department, the patient noted worsening of his cough and difficulty breathing that impeded his daily activities and ability to get around his house. He endorsed some chest soreness secondary to cough but denied chest pain, nausea, vomiting, diarrhea, and dysuria. The patient's medical history was significant only for type II diabetes and non-ischemic cardiomyopathy as described above. He

was taking sacubitril-valsartan, aldactone, aspirin, atorvastatin, carvedilol, furosemide, and glipizide. He reported no intake of alcohol, tobacco, or recreational drugs. He immigrated from Mexico to the United States twenty years previously, and at the time of presentation lived in Franklin, NC with roommates and worked as a roofer.

On examination, the temperature was 100.8, pulse was 119, respiratory rate was 24, blood pressure was 148/87, and the oxygen saturation was 93% on room air. The patient was alert and oriented but appeared to be in moderate distress and was diaphoretic. He was tachycardic but with regular rhythm and had equal pulses in all extremities. The pulmonary exam was notable for decreased breath sounds on the right and the presence of cough throughout the exam. The remainder of the physical exam was normal. Blood tests were notable for an elevated white blood cell count of 19,200 with 84% neutrophilic predominance. Platelets were elevated at 620,000 and patient had an elevated lactate of 3.22. His hemoglobin A1c was elevated to 14.6. A rapid covid antigen and covid PCR were both negative. Patient also had a negative HIV test on admission. Imaging studies were obtained.

Figure 1A-D includes the chest x-ray and chest CT scans of the patient. Imaging revealed dense infiltration of the right upper lobe of the lung. Patient also had scattered infiltrates of the right lower lobe and left lung along with prominent bilateral hilar lymphadenopathy.

Differential Diagnosis

This 44-year-old male presented to the emergency department with dyspnea, cough, night sweats, and weight loss in the setting of known non-ischemic cardiomyopathy. On evaluation, he was found to be febrile, tachycardic, and tachypneic. Laboratory studies showed significant leukocytosis and an A1c of 14.6. Imaging showed significant infiltration of the right upper lobe of the lung with scattered infiltrates and bilateral hilar lymphadenopathy.

Given the imaging findings, fever, and weight loss, this patient was immediately placed on airborne precautions out of concern for potential necrotizing pneumonia from tuberculosis. However, other etiologies of potential cough, dyspnea, and weight loss were considered including autoimmune disease, cancer, bacterial pneumonia, and other various disorders.

Tuberculosis

The initial assessment was concerning for a picture of tuberculosis given that the patient had immigrated from Mexico, even though he had not returned in 20 years. Following an initial infection of tuberculosis in Mexico, some bacteria can remain dormant and reactivate decades down the road, thus a possible reactivation of a 20-year-old infection was not unlikely.[1] When asked, patient could not identify any potential contacts of tuberculosis or remember having contracted tuberculosis as a child. Notably, the site of the patient's most significant pulmonary disease is in the apex of the right lung, as 95% of reactivated tuberculosis cases are present in the apical or posterior segments of the upper lobes.[2] Extrapulmonary manifestations of tuberculosis could also contribute to the patient's cardiac dysfunction, as cases of myocarditis and systolic heart failure have been described with tuberculosis.[3] To evaluate for the possibility of tuberculosis, an acid fast bacilli (AFB) smear and culture was obtained and a purified protein derivative for tuberculosis (PPD) was placed.

Other Pneumonias

Although the patient had not responded to outpatient antibiotic therapy, other infectious etiologies of necrotizing pneumonia had to be considered. Patient's A1c at time of admission was noted to be 14.6. Diabetes is an immunocompromising disease and can increase the risk of developing pneumococcal pneumonia and other immunocompromising infections.[4] In addition, the patient

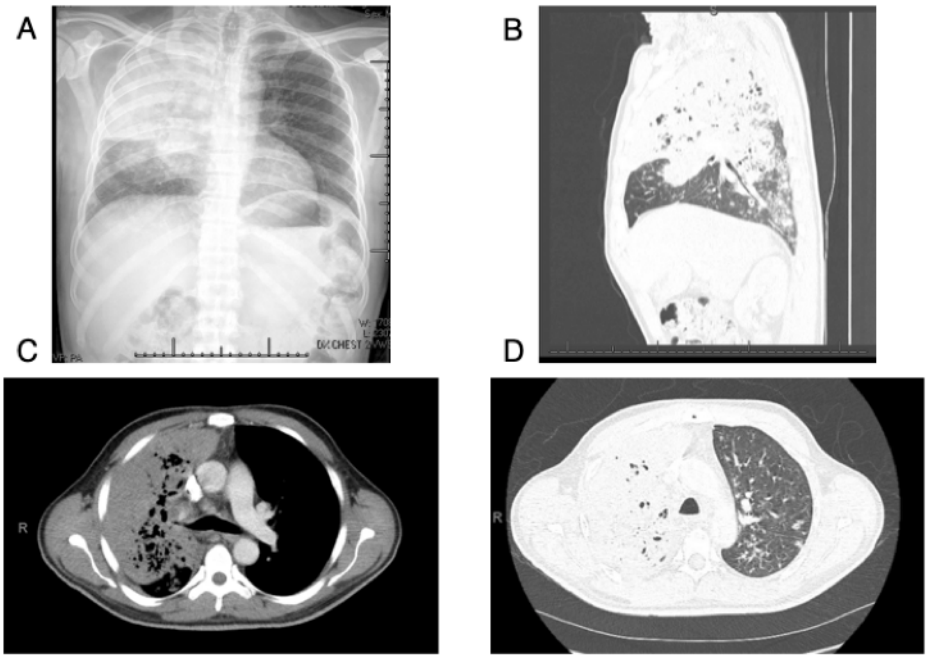

Figure 1. **A.** Patient's chest x-ray on admission to the hospital showing dense infiltration of the right lung. **B**. Sagittal view of chest CT with and without contrast performed on admission to the hospital showing dense infiltration of the right upper lobe of the lung and scattered infiltrates of the right lower lobe of the lung. **C & D**. Axial views of chest CT with and without contrast further demonstrating lung consolidation.

resided in western North Carolina where both histoplasmosis and blastomycosis are endemic.,[5,6] Histoplasmosis is well-known for mimicking the presentation of tuberculosis and can cause extrapulmonary manifestations including effects on cardiac tissue.[7] Blastomycosis is also a fungal cause of pneumonia and causes extrapulmonary manifestations of the skin and bones.[6] To evaluate for other infectious etiologies, blood cultures were obtained, and a sputum sample was obtained.

Autoimmune Diseases

Although less common than other etiologies described, cryptogenic organizing pneumonia is characterized by autoimmune inflammatory reaction to lung tissue that causes fatigue, fever, cough, shortness of breath and consolidation on imaging.[8] Organizing pneumonia is frequently initially mistaken for infectious pneumonia and many patients are prescribed multiple rounds of antibiotics prior to diagnosis[8]. Definitive diagnosis requires a lung biopsy. We planned to obtain a lung biopsy and hilar lymph node biopsy if no definitive diagnosis was made with sputum sample and blood cultures.

Cancer

Lung cancer is a possible cause of dyspnea, cough, shortness of breath, and weight loss. Cancer was lower on our differential given the rapid progression of the patient's symptoms, his lack of smoking history, and his relatively young age. Although smoking does contribute to a considerable portion of primary lung cancers, patients who are younger and non-smokers can develop adenocarcinomas of the lung due to genetic predisposition.[9] To assess for this possibility, we intended to perform a hilar lymph node biopsy if no etiology was established on sputum study.

Management and Follow Up

AFB smear and culture returned negative, and patient did not have a positive PPD. Gram stain of sputum showed multiple broad budding yeasts consistent with blastomycosis. Serum blastomycosis antigen was elevated to 14.7 ng/mL (reference: <0.2 ng/mL). The patient was started on liposomal amphotericin B with marked improvement in symptoms and vital signs within two weeks. He also had an echocardiography performed prior to discharge that showed improvement of his ejection fraction to 55-60%. Patient was seen for follow up by infectious disease two months after his hospitalization with significant improvement in his cough and respiratory symptoms.

Learning Points

Blastomycosis is a fungal infection that is endemic to the Ohio River Valley of the United States. Most cases of blastomycosis involve the lung but skin, bone, genitourinary, and CNS involvement can also be present.[10] Diagnosis of blastomycosis infection requires visualization and growth from a specimen. Blastomycosis is not a contaminant, and it is never an asymptomatic colonizer, thus pathologic identification of the organism is sufficient for diagnosis.[11] Blastomycosis diagnosis is often delayed, and many patients receive multiple rounds of antibiotics prior to diagnosis.

Our patient's most likely exposure to blastomycosis occurred in his job as a roofer. Cardiac manifestations of blastomycosis is thought to be rare and difficult to diagnose as most biopsy proven endocarditis cases have negative blood cultures.[12] Most cardiac manifestations of blastomycosis are diagnosed via pathology and a case series from the American Journal of Pathology in 1937 describes two cases of blastomycosis that caused systolic heat failure and endocardial damage.[13] A recent case report from the European Journal of Case Reports in Internal Medicine identified a case of blastomycosis that presented with spontaneous coronary artery dissection, although the patient in question had a normal left ventricular ejection fraction.[12] Notably, there is a dearth of literature describing cardiac manifestations and outcomes of patients with blastomycosis.

ARTICLE INFORMATION

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