

Pulmonary Artery Sarcoma Misdiagnosed as Chronic Thromboembolic Pulmonary Hypertension

ERIC WIDERA, M.D.¹, AND ROXANA SULICA, M.D.²

Abstract

Pulmonary artery sarcomas are rare neoplasms of the pulmonary artery that are often confused with chronic thromboembolic disease, as both diseases have similar presentations. In patients with presumed chronic thromboembolic pulmonary hypertension, certain clinical and imaging characteristics may suggest the alternative diagnosis of pulmonary artery sarcoma. In this article we present a case of a man initially diagnosed with chronic thromboembolic pulmonary hypertension, but who was later found to have pulmonary artery sarcoma. We review the distinguishing characteristics of the two diseases and discuss possible treatment strategies.

Key Words: Pulmonary artery sarcoma, chronic thromboembolic pulmonary hypertension, ventilation-perfusion scan, computed tomographic angiogram.

Case Report

A 66-YEAR-OLD MAN with a history of mild chronic obstructive pulmonary disease and heavy tobacco use was initially admitted to an outside hospital with a 3-month history of dyspnea and cough. He was placed on heparin for a presumptive diagnosis of pulmonary embolism based on a computed tomographic (CT) scan of the chest, which showed a “filling defect” in the main pulmonary artery extending into and completely occluding the left pulmonary artery. A ventilation-perfusion scan showed normal ventilation with complete lack of perfusion to the left lung and entirely normal perfusion of the right lung. The work-up for hypercoagulable state was negative. The patient subsequently received warfarin anti-

coagulation and Greenfield filter placement, and was discharged home.

One month later he developed small amounts of hemoptysis. A repeat CT scan revealed an increase in the size of the “filling defect” in the pulmonary artery. Transthoracic echocardiography showed elevated right ventricular systolic pressure (RVSP) of 65 mm Hg and mild right ventricular dysfunction. The patient was referred to the Mount Sinai Pulmonary Hypertension Program for further management, still complaining of chronic dry cough and intermittent hemoptysis, and having lost 25 pounds over a 3-month period. On physical examination the patient’s blood pressure was 135/75 mm Hg, with a heart rate of 85 beats/min, and oxygen saturation of 97% in room air. Fine rales were audible at the left lung base, while the cardiovascular examination was normal. The chest radiographic examination was significant for prominence of the main pulmonary artery and an ill-defined nodular density in the left mid-lung field. Ventilation-perfusion scanning again demonstrated complete lack of perfusion to the left lung with normal ventilation (Fig. 1). A repeat chest CT angiogram showed further interval increase in the pulmonary artery “filling defect,” with total occlusion and invasion of the wall of the left pulmonary

¹Resident and ²Assistant Professor of Medicine, Cardiovascular Institute, Department of Medicine, Mount Sinai School of Medicine, New York, NY.

Address all correspondence to Roxana Sulica, M.D., Mount Sinai Pulmonary Hypertension Program, Box 1030, One East 100th Street, New York, NY 10029; email: Roxana.Sulica@mounsinai.org

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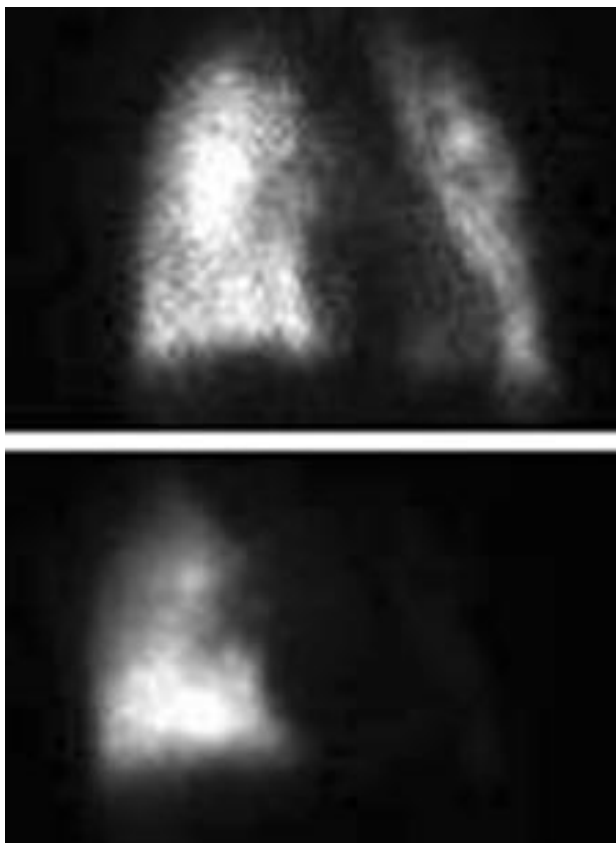


Fig. 1: Upper image: ventilation scan. Lower image: perfusion scan. Anterior views, showing lack of perfusion and normal ventilation on the left.

artery and extension into the right upper lobe anterior segment associated with a left upper lobe cavitary mass with surrounding infiltrate (Fig. 2). Echocardiography showed mild right ventricular dilatation with probable normal function, but RVSP could not be estimated due to insufficient tricuspid regurgitation. The patient was restarted on heparin and received antibiotics for possible community-acquired pneumonia. Three induced-sputum specimens failed to disclose acid-fast bacilli.

Given the progression of the pulmonary arterial “filling defect” despite long-term anticoagulation, the pulmonary artery mass extension into the vascular wall, and the unilateral character of the lung perfusion defect in a patient with symptoms of chronic disease, the possibility of a pulmonary artery sarcoma was entertained. The patient was referred for surgical consultation. Preoperatively, pulmonary function tests were significant only for mild obstructive flow pattern, and left heart catheterization showed evidence of non-obstructive coronary artery disease. The patient underwent surgery with partial resection of

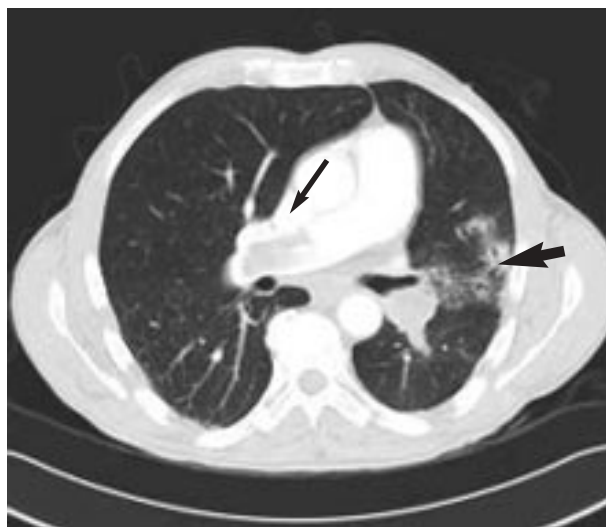


Fig. 2: CT chest examination showing large pulmonary arterial mass (thin arrow), mediastinal lymphadenopathy and left upper lobe infiltrate (thick arrow).

a bilateral pulmonary artery tumor. There were no complications from the procedure. Pathology revealed high-grade spindle cell sarcoma consistent with leiomyosarcoma. There was no evidence of lung metastasis, and the nodular left upper lobe mass proved to be a lung infarct. The patient was discharged from the hospital 6 days after surgery, but no chemotherapy was instituted, in accordance with the patient’s preference. Eighteen months after surgery the patient is alive and well.

Discussion

As this case exemplifies, the preoperative diagnosis of pulmonary artery sarcoma is difficult and frequently delayed, as it is often confused with chronic thromboembolic disease. In the initial evaluation of patients with presumed chronic thromboembolic pulmonary hypertension (CTEPH), certain presenting aspects may suggest an alternative diagnosis of a pulmonary artery neoplasm. We will briefly review the diagnostic criteria and the work-up of CTEPH and discuss those diagnostic clues that should alert physicians to the uncommon entity of pulmonary artery sarcoma. For both conditions, surgery is the only treatment modality with curative potential. A presumptive preoperative diagnosis of a pulmonary artery neoplasm rather than chronic thromboembolic disease may influence the operative technique. The long-term prognosis is better for chronic thromboembolic disease compared to pulmonary artery sarcoma, even if complete resection is feasible.

Chronic Thromboembolic Pulmonary Hypertension

Chronic obstruction of the main pulmonary arteries due to unresolved thromboembolic disease is an often underdiagnosed but potentially correctable cause of pulmonary hypertension, and a relatively common and serious complication of pulmonary embolism. In a recent prospective case series, the cumulative incidence of pulmonary hypertension after one episode of an adequately treated acute pulmonary embolism in patients without a history of prior venous thromboembolism was 1% at 6 months, 3.1% at 1 years, and 3.8% at 2 years (1). However, in clinical practice most patients present late in the course of the disease, as many patients may remain asymptomatic for months or even years.

The pathogenesis of pulmonary hypertension in chronic thromboembolic disease is multifactorial. In the majority of patients, more than 40% of the pulmonary vascular bed is obstructed by organized thrombi (2), but other factors, such as recurrent thromboembolism, in-situ pulmonary artery thrombosis, and pulmonary vascular remodeling with the development of a hypertensive pulmonary arteriopathy, play a significant role in the hemodynamic progression of the disease (3, 4).

The clinical signs and symptoms of chronic thromboembolic pulmonary hypertension, such as progressive exertional dyspnea and decreased exercise tolerance, mimic those of other forms of pulmonary hypertension. As the disease progresses, chest pain on exertion, presyncope, or syncope may occur. Findings on physical examination include an accentuation of the pulmonic component of the second heart sound. In some patients, a bruit over the lung fields may be heard; it originates from turbulent pulmonary blood flow through partially occluded pulmonary arteries by recanalized thrombi (5).

As with pulmonary hypertension of all types, the diagnostic work-up includes determination of the disease severity, assessment of right ventricular function and a thorough search for other conditions known to be associated with pulmonary hypertension. When CTEPH is suspected, certain imaging modalities are employed to establish the proximal extent and location of the thromboembolic material; these variables are the most important determinants of the operative candidacy (2). Transthoracic echocardiography often demonstrates impaired right ventricular systolic function with enlargement of the right atrium and right ventricle and moderate-to-severe tricuspid regurgitation (6). Ventilation-perfusion scanning should be per-

formed in all patients with pulmonary hypertension to screen for the presence of chronic thromboembolic disease. Any mismatched, segmental or larger perfusion defects would help to differentiate chronic thromboembolic pulmonary hypertension from pulmonary arterial hypertension, as there should be no large perfusion defects in the latter (7). Lower extremity Doppler examination may also be performed, but evidence of prior deep vein thrombosis is only seen in 35–45% of patients with CTEPH (8, 9). Findings on chest CT examination include presence of chronic thromboembolic material located in an eccentric position within the central pulmonary arteries, bronchial artery collateral flow, parenchymal abnormalities consistent with prior infarcts, and mosaic attenuation of the pulmonary parenchyma (2).

Pulmonary angiography is the definitive test to characterize the surgical operability of CTEPH; it is recommended for all patients with suggestive ventilation-perfusion scans. Pulmonary angiographic findings in CTEPH include “pouching” defects, webs or bands, abrupt vascular narrowing, complete vascular obstruction, and intimal irregularities. The latter finding is in contrast to the well-defined intraluminal defects seen in acute embolisms (10). In specialized centers, direct visualization of the intimal changes of the pulmonary artery may be done at angiосcopy (2). Right heart catheterization is performed in all patients with unexplained dyspnea, large mismatched perfusion defects and evidence of pulmonary hypertension and right ventricular dysfunction (2), since hemodynamic parameters, particularly the calculated pulmonary vascular resistance, are important factors in the preoperative evaluation.

The prognosis of patients with CTEPH is poor without intervention and depends on the degree of pulmonary hypertension at the time of diagnosis. The five-year survival rate is reported to be 30% if pulmonary artery pressure is greater than 40 mm Hg and only 10% if pulmonary artery pressure is above 50 mm Hg (8). Definitive treatment includes the use of lifelong anticoagulation, inferior vena cava filter placement and the use of pulmonary thromboendarterectomy in selected symptomatic patients with hemodynamic or ventilatory impairment at rest or with exercise. Pulmonary thromboendarterectomy is a true endarterectomy that involves removal of the organized fibrotic material in the large pulmonary vessels. The procedure is performed through median sternotomy, with cardiopulmonary bypass under deep hypothermia and periods of hypothermic circulatory arrest (11). Both short- and long-term surgical results are excellent in specialized centers with large operative

volume, with reported mortality for thromboendarterectomy as low as 4.5% (12). These results compare favorably with outcomes from lung transplantation, which is the only surgical alternative. For CTEPH patients with inoperable disease, chronic administration of pulmonary vasodilators commonly used for pulmonary arterial hypertension may offer symptomatic and functional benefit, but, to date, no large-scale studies have been performed with such patients (13, 14).

Pulmonary Artery Sarcoma

Pulmonary artery sarcomas are rare tumors. The first such case was reported in 1923 (15), and since then, approximately 150 primary sarcomas of the pulmonary artery have been described (16). Most pulmonary artery sarcomas are classified as undifferentiated spindle cell sarcomas or leiomyosarcomas, but the histological classification does not appear useful prognostically or clinically (17). The usual duration of symptoms before presentation is around 3–12 months. Clinical presentation includes dyspnea, chest or back pain, cough, and hemoptysis, as well as signs and symptoms of pulmonary hypertension and right ventricular dysfunction. These clinical findings may mimic those of chronic thromboembolic pulmonary hypertension, but a history of weight loss, clubbing, low-grade fever, anemia and an elevated ESR should raise suspicion of malignancy (17). Other warning signs include lack of prior history of deep vein thrombosis or pulmonary embolisms, a negative work-up for a procoagulant state, and no response to anticoagulation over several weeks (17).

Pulmonary artery sarcomas and chronic thromboembolic pulmonary hypertension are easily confused by CT scan findings because both diseases have intraluminal filling defects and pulmonary arterial dilation, but there are radiographic criteria that may help differentiate the two entities. CT findings consistent with malignancy include filling defects occupying the entire luminal diameter of the main or proximal pulmonary arteries, expansion of the involved pulmonary artery with the filling defect, and extraluminal extension of the tumor (18). In addition, pulmonary artery sarcomas may be indicated by areas of inhomogeneous high or low attenuation representing hemorrhage or necrosis, soft tissue density in pulmonary arteries, or enhancement after administration of gadopentetate dimeglumine on magnetic resonance imaging examination (19). A unilateral central pulmonary embolus is relatively uncommon and suggests the possibility of malignancy.

Ventilation/perfusion scans may demonstrate perfusion defects of varying size in one or both lungs with pulmonary artery sarcomas. Predominantly unilateral perfusion defects are rare in CTEPH and suggest malignancy. Otherwise, the perfusion defects are indistinguishable from pulmonary embolism, but serial scans will show no resolution despite anticoagulation, as seen in the case presentation. Pulmonary angiography may show intraluminal masses and lung perfusion abnormalities with a smooth tapering of pulmonary arteries and “to-and-fro” motion of pedunculated or lobulated lesions (17).

The prognosis of pulmonary artery sarcomas is extremely poor. The median survival of untreated patients is as short as one and a half months, with decompensated heart failure as the primary cause of death (20–22). Metastases are primarily to the lung, while distant extrathoracic metastases develop in 16% of cases. Treatment with aggressive resection lengthens median survival time to 10 months, with rare reports of patients remaining tumor-free 5 years after the initial surgery (21, 22). Adjuvant chemotherapy or radiation may improve the patient’s prognosis, but there is insufficient confirmatory data.

Conclusion

Chronic thromboembolic pulmonary disease is one of the few potentially curable causes of pulmonary hypertension. With careful preoperative evaluation and postoperative care, an excellent long-term prognosis can be achieved in highly specialized centers. However, a broad differential remains important during the work-up. The alternative diagnosis of pulmonary artery sarcoma should be suggested for patients with no predisposing factors for embolism, inadequate relief of symptoms with anticoagulation, or with distinctly abnormal perfusion studies or CT scans.

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