Chronic thromboembolic pulmonary hypertension is a clot you cannot swat

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ABSTRACT

A 49-year-old man with progressive dyspnea on exertion and a remote history of syncope presented with hypotension and acute right ventricular failure, and was ultimately diagnosed with acute pulmonary embolism. Laboratory data revealed a prolonged activated partial thromboplastin time, which confounded treatment options. He was ultimately diagnosed with anti-phospholipid syndrome and factor XII deficiency, and underwent a thromboendarterectomy procedure with resolution of right ventricular failure and symptoms. Careful attention to history, initial physical examination manifestations, and clinical data often permit a timely diagnosis of and treatment for chronic thromboembolic pulmonary hypertension. (J Vasc Surg Cases and Innovative Techniques 2019;5:402-5.)

Keywords: Thrombus; Pulmonary embolism; Pulmonary hypertension; CTEPH

CASE REPORT

A 49-year-old Caucasian man with some vascular risk factors presented to the office of a cardiologist who initially felt his symptoms were concerning for angina. Prestress echocardiographic imaging revealed a severely dilated and hypokinetic right ventricle (RV). He was then referred to the emergency department. The patient described dyspnea in the preceding months, which became profound after walking several feet. His medical history was significant for dyslipidemia and hypothyroidism, as well as syncope—which was attributed to a vasovagal event. Family history was negative for thrombophilia, but significant for autoimmune disease.

The patient’s physical examination in the emergency department included the following: blood pressure of 92/62 mm Hg, pulse of 104 beats/min, respiratory rate of 16 breaths/min, and an oxygen saturation of 95% on room air. The patient had an RV heave and a prominent second heart sound. The 12-lead electrocardiogram revealed sinus tachycardia, diffuse repolarization abnormalities, and deep precordial lead T wave inversions suggestive of RV strain (Fig 1). Laboratory data included: N-terminal prohormone of brain natriuretic peptide of 2059 pg/mL (reference range, 0-450), cardiac troponin T of less than 0.01 ng/mL (reference, < .03), platelet count of 111 × 10^3/μL (reference range, 150-330 × 10^3/μL), prothrombin time of 13.2 seconds (reference range, 10.0-12.9 seconds), activated partial thromboplastin time (aPTT) of 61.5 seconds (reference range, 15.8-37.9 seconds). To further explore the abnormal aPTT, a coagulopathy investigation revealed antiphospholipid antibodies and a positive lupus anticoagulant study. The patient’s pretest probability for pulmonary embolism (PE) using the Wells scoring system was 4.5 (moderate probability for PE), resulting in computed tomography angiography (CTA) imaging, which revealed a large thrombus in the right as well as in the left pulmonary artery (PA; Fig 2), determined to be a ‘submassive’ PE owing to the presence of RV dysfunction as demonstrated on CTA, echocardiography, and elevated cardiac biomarkers. This triggered evaluation by the Pulmonary Embolism Response Team and the patient was admitted to the coronary care unit. Thrombus along with positive lupus anticoagulant suggested antiphospholipid syndrome (aPL).

The patient was anticoagulated parenterally with unfractionated heparin (UFH) before becoming hypoxic, raising concern for imminent respiratory failure. Therapy beyond anticoagulation alone, including catheter-directed thrombolysis (CDT), was considered. CDT was unsuccessful after failure to pass a guidewire beyond the thrombus in the PA. Widespread thromboembolic disease with distal pruning of the vasculature was observed, consistent with a diagnosis of chronic thromboembolic pulmonary hypertension (CTEPH; Fig 3, A). The patient was discharged on the fifth hospital day on low-molecular-weight heparin and warfarin until a goal international normalized ratio of 2 to 3 was achieved. He was evaluated in the pulmonary hypertension clinic then referred to a surgeon with experience in performing pulmonary endarterectomy (PEA) 4 months after the initial presentation (Fig 3, B). After median sternotomy, PEA occurred with circulatory arrest. The ascending aorta and right atrium were cannulated, and he was placed on...
The right PA was opened and thrombus was removed before closing with 4-0 Prolene sutures. The left PA was dissected and obliterative clot was removed, then closed with 4-0 Prolene suture. Overall, 14 minutes of circulatory arrest and 109 minutes of clamp time were required. After rewarming to 35°C, the PA pressure improved from 60/15 mm Hg to 30/19 mm Hg postoperatively.

At the 6-month follow-up visit, the patient reported significant improvement in symptoms with a decrease in RV pressure from 106 mm Hg before the endarterectomy to 26 mm Hg after (Fig 4). The decision was made to continue anticoagulation indefinitely with warfarin and a goal international normalized ratio of 2 to 3 given his acquired thrombophilia. The patient agrees to publish their case details and images.
DISCUSSION

CTEPH manifests as World Health Organization class IV pulmonary hypertension and can be a source of RV failure from obstructive shock. Progressive dyspnea and exercise intolerance are two common presenting symptoms for CTEPH, which often evades clinicians, although patients often recall episodes of pleuritic chest pain, lower extremity discomfort even years before presentation. CTEPH commonly manifests with diffuse repolarization abnormalities and right axis deviation on the electrocardiogram. Echocardiographic or catheterization assessment of RV pressure of greater than 100 mm Hg frequently points to a diagnosis of CTEPH, because the failing RV from acute PE usually presents with normal or only slightly elevated RV pressure.

A prolonged aPTT suggestive of therapeutic anticoagulation or coagulopathy was later confirmed to be aPL by serology. In addition, the patient was confirmed to have factor XII deficiency. The combination of aPL and factor XII deficiency created a prothrombotic environment, likely predisposing the patient to CTEPH. A meta-analysis by Cheng et al found the presence of antiphospholipid antibodies to be common in patients ultimately diagnosed with CTEPH. A family history of autoimmune disease and therefore a genetic predisposition of thrombosis may—at least in part—explain why an otherwise healthy individual developed aPL. Managing aPL with acute PE simultaneously was a therapeutic challenge. Although the PEITHO trial demonstrated a hemodynamic benefit from treating intermediate risk (submassive) PE with systemic thrombolytic agents, PEITHO II showed no long-term mortality benefit if this practice is routinely used. Neither studies included patients with aPL. The prolonged aPTT on initial presentation created pause when considering the administration of systemic thrombolysis, although it should be recalled that aPL is highly thrombogenic and a prolonged aPTT is a feature of the laboratory assay and not evidence of therapeutic anticoagulation. Using low-molecular-weight heparin allows for earlier therapeutic anticoagulation compared with UFH and removes the confounding need for aPTT monitoring for UFH. Life-long therapeutic anticoagulation for unprovoked venous thromboembolism is consistent with established guidelines.

Another therapeutic option gaining attention for submassive PE treatment is CDT. There remains, however, a paucity of literature outlining specific indications and effectiveness of this procedure and, although the recent OPTALYSE PE trial demonstrated an improvement in RV pressure.
function in patients with submassive PE, the study ultimately failed to show mortality benefit.9

Once CTEPH is suspected, a V/Q scan is preferred over CTA for surveillance after anticoagulation; right heart catheterization and pulmonary angiography better define anatomy and hemodynamics.10 PEA is a technically challenging procedure, although often curative for CTEPH and only available at a few centers.11 Ideal surgical candidates have primarily proximal thrombotic disease with an increased pulmonary vascular resistance.12 The goal of PEA surgery is to decrease pulmonary vascular resistance to improve RV function.

Circulatory arrest permits dissection down to the level of PA subsegmental branches. Each lung is limited to 20 minutes of circulatory arrest. Major complications vary by center and include reperfusion lung injury (9.6%) and neurologic injury (11.2%). In-hospital mortality ranges from 2.2% to 4.7% and varies based on center expertise.11 Vasodilator therapy or PA balloon angioplasty are alternatives to surgery, but remain generally reserved for inoperable disease or distal pulmonary vascular thrombosis.13

CONCLUSIONS

A diagnosis of aPL is uncommon in males and should be considered if prolonged aPTT is a feature of laboratory data. Concomitant factor XII deficiency is exceedingly rare and may have predisposed the patient to CTEPH. In the context of superimposed acute PE, CTEPH is difficult to diagnose and inappropriate treatment with systemic or CDT is common. CTEPH substantially remodels the vessel wall and can precipitate RV failure from pressure overload and eventually obstructive shock. Recalling the physical exam manifestations and performing the appropriate imaging studies allows for an efficient diagnosis of CTEPH, then potentially treatment by PEA.

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