Running From Her Past
A Case of Rapidly Progressive Dyspnea on Exertion

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Information about a real patient is presented in stages (boldface type) to an expert clinician (Dr John R. Teerlink), who responds to the information, sharing his or her reasoning with the reader (regular type). A discussion by the authors follows.

A 51-year-old woman presented to the emergency room with progressive dyspnea on exertion. She was an avid runner, and had completed a half-marathon 2 months before presentation. Since then, she had experienced a rapid decline in exercise capacity such that, on presentation, she was unable to climb a flight of stairs without stopping to catch her breath. She had recently completed a course of azithromycin prescribed by her primary care physician without benefit. She denied chest pain, lower extremity swelling, fevers, chills, or cough. She had had stage II left breast adenocarcinoma successfully treated 2 years before with Adriamycin-containing chemotherapy, radiation to the left chest, and bilateral mastectomy. Her only medication was fexofenadine for seasonal allergies. She had no previous heart disease or cardiovascular risk factors, with the exception of a distant 10–pack-year smoking history. She had no family history of premature cardiovascular disease. There was no history of illicit substance abuse.

Dr John R. Teerlink: The differential diagnosis for rapidly progressive dyspnea on exertion includes cardiac, pulmonary, rheumatologic, and hematologic disorders. The notable aspects of the patient’s history include her dyspnea on exertion in the absence of any other symptoms and her previous vigorous exercise capacity, which suggests a rapidly progressive process. Her previous breast cancer and associated treatment raises the possibility of Adriamycin-induced cardiomyopathy, radiation-induced coronary artery disease or constrictive pericarditis, or pulmonary embolus.

On examination, the patient was comfortable but tachypneic. Her temperature was 36.6°C and her blood pressure was 112/73 mm Hg. Her heart rate was 100 bpm with a respiratory rate of 22 breaths per minute and an oxygen saturation of 94% while breathing 5 L/min oxygen via nasal cannula. The jugular venous pressure was >15 cm H2O with prominent V-waves. The Kussmaul sign was present. Her heart sounds were tachycardic with an accentuated P2 and a 2/6 early systolic murmur most prominent at the left lower sternal border with radiation to the left upper sternal border. There was a mild left parasternal heave. Breath sounds were slightly diminished at both lung bases. There was hepatomegaly to 1 cm below the costal margin, and the liver was softly pulsatile. Abdominal tenderness was noted in the right upper quadrant. Trace bilateral lower extremity edema was present.

Dr John R. Teerlink: The elevated jugular venous pressure suggests volume overload. More specifically, a positive Kussmaul sign—paradoxically increasing plethora and elevation of the jugular pulse during inspiration—is suggestive of diminished right ventricular compliance. The most common etiologies for this finding are right ventricular (RV) infarction, constrictive pericarditis, and restrictive cardiomyopathy. The systolic murmur is consistent with tricuspid regurgitation, which would explain the prominent V waves noted in the jugular pulsation. Tricuspid regurgitation, in association with diminished RV compliance, is compatible with RV infarct, RV failure, or a constrictive-restrictive process. An accentuated P2 and the presence of a RV heave, however, argue against constriction. The absence of significant pulmonary rales suggests that left heart failure is not the cause of her RV overload, although chronic left ventricular failure may be associated with absent or modest lung findings. Her hypoxia is out of proportion to the lung examination and is likely explained by an underlying pulmonary vascular or parenchymal process that is causing pulmonary hypertension and the associated right heart failure.

The white cell count was 13 000/μL with 82% neutrophils, the hematocrit was 46%, and the platelet count was 31 000/μL. A peripheral smear showed 3 to 5 schistocytes and scattered nucleated red blood cells per high-powered field, polychromasia, small to medium granular platelets,
and normal granulocytes. The creatinine was 1.15 mg/dL; the blood urea nitrogen was 28 mg/dL. The serum electrolytes were normal. The aspartate aminotransferase was 88 U/L (normal range, 16–41) and the alanine aminotransferase was 117 U/L (normal range, 11–54). The total bilirubin was 1.8 mg/dL (normal range, 0.3–1.9), and the alkaline phosphatase was 116 IU/L (normal range, 20–140). The lactate dehydrogenase was 425 IU/L (normal range, 91–185). The B-type natriuretic peptide was 430 pg/mL (normal range, <73), and the troponin was <0.02µg/L. The partial thromboplastin time was 29 seconds, and the international normalized ratio was 1.3. The chest radiograph demonstrated enlarged pulmonary arteries without intraparenchymal disease or pulmonary edema (Figure 1). The 12-lead ECG revealed sinus tachycardia, normal QRS axis, low voltages, and anteroseptal Q waves with diffuse ST-segment and T-wave abnormalities (Figure 2).

Dr John R. Teerlink: The most notable laboratory finding is the marked thrombocytopenia, which may be related to sequestration, destruction, or impaired production of platelets. There were no signs of bleeding on examination. Chronic hepatic congestion from right heart failure can cause cirrhosis (“cardiac cirrhosis”) and portal hypertension with hypersplenism, but this degree of thrombocytopenia would be unusual. The physical examination did not report an evaluation for an enlarged spleen, and this should be revisited. The peripheral smear does not have the enlarged platelets with otherwise normal cell lines that are characteristic of idiopathic thrombocytopenic purpura; the normal hematocrit and creatinine with only moderately elevated lactate dehydrogenase make thrombotic thrombocytopenic purpura less likely. The low platelets could be explained by malignant bone marrow infiltration or a chronic (compensated) disseminated intravascular coagulation process sometimes seen in advanced malignancies. The B-type natriuretic peptide >400 is suggestive of ventricular volume and/or pressure overload, remembering, however, that failure of either the left or right ventricle can produce elevated circulating B-type natriuretic peptide concentrations. An elevated troponin would not have been surprising in this clinical presentation.

Enlarged pulmonary arteries seen on chest radiograph in combination with the evidence of right heart failure raise the
suspicion for pulmonary hypertension. The chest radiograph does not suggest an underlying pulmonary disorder, such as obstructive or interstitial lung disease. The ECG is consistent with previous silent infarction, and the lack of right axis deviation suggests that there may not be significant RV hypertrophy.

A transthoracic echocardiogram demonstrated a small left ventricle (LV) with hyperdynamic function (ejection fraction, 70%) and no wall motion abnormalities. There was severe right atrial enlargement. The RV was severely enlarged, with normal wall thickness and severely reduced systolic function. There was flattening of the intraventricular septum throughout systole and diastole, suggesting both pressure and volume overload of the RV (Figure 3 and Movie I in the online-only Data Supplement). Severe tricuspid regurgitation was present, and the pulmonary artery systolic pressure was estimated to be 75 mm Hg based on a right atrial pressure of 15 mm Hg (as evidenced by the degree of plethora of the inferior vena cava). The mitral and aortic valves were anatomically and physiologically normal. With agitated saline, there were scant bubbles shunting right-to-left during Valsalva consistent with a small patent foramen ovale.

Dr John R. Teerlink: The echo suggests that the LV preload is diminished because of pulmonary hypertension. The lack of RV hypertrophy corroborates the rapid time course suggested by the patient’s history. The previously noted anterosespal Q waves and low precordial voltages on the ECG probably reflect posterior displacement of the LV because of RV enlargement. The lack of right axis deviation on the ECG is consistent with RV enlargement without significant hypertrophy, as seen on the transthoracic echocardiogram. There is no significant right-to-left shunt by bubble study on transthoracic echocardiogram, suggesting that a congenital shunt is not the cause of the patient’s pulmonary hypertension, but a formal assessment with an oxygen saturation run will be necessary.

At this point, the patient requires a workup for the etiology of her pulmonary hypertension as well as a complete hemodynamic assessment with a right heart catheterization. The World Health Organization has divided pulmonary hypertension (PH) into 5 groups. Group 1 includes pulmonary arterial hypertension from a multitude of causes, including idiopathic, familial, congenital, connective tissue, HIV, drugs/toxins, pulmonary veno-occlusive disease, and pulmonary capillary hemangiomatosis; group 2 PH is related to left heart disease; group 3 PH is associated with parenchymal lung disease and/or hypoxia; group 4 is chronic thromboembolic PH; and group 5 consists of several forms of PH for which the pathogenesis is unclear or multifactorial, including disorders of hematologic (eg, myeloproliferative disorders), systemic (eg, sarcoidosis), metabolic (eg, Gaucher, thyrotoxicosis), and anatomic (eg, tumor obstruction, fibrosing mediastinitis) origin.

The salient points of this patient’s history that need to be considered to narrow the differential for her PH include the rapidity of her decline, the marked hypoxia, her history of cancer (and subsequent therapies), and her thrombocytopenia. A preliminary differential diagnosis for this patient would include chronic thromboembolic disease (ie, group 4 PH) given her history of cancer; postirradiation pulmonary fibrosis (group 3 PH), a complication that typically occurs 6 to 24 months after radiation exposure; pulmonary veno-occlusive disease; tumor-related causes (group 5) such as sarcoma, carcinomatosis, or tumor emboli; or group 1 idiopathic pulmonary arterial hypertension, a diagnosis of exclusion, which typically does not evolve this rapidly. At this point, there is no evidence for occult drug abuse, right-to-left shunts, obstructive sleep apnea, or left heart disease attributed to anthracycline toxicity or irradiation.

High-resolution computed tomography and computed tomography angiogram of the chest showed no acute pulmonary emboli, interlobular septal thickening, nodules, masses, or significant adenopathy. The pulmonary arteries were enlarged. There were small bilateral effusions and only minimal anterior lung fibrosis consistent with previous radiation therapy. To exclude chronic thromboembolic PH, a ventilation/perfusion (V/Q) lung scan was performed, which was interpreted as intermediate probability for chronic pulmonary thromboembolic disease on the basis of a normal ventilation, and a nondiagnostic, but atypical, perfusion pattern. There were no segmental or subsegmental mismatched perfusion defects. Lower extremity Doppler ultrasound showed no deep venous thrombosis. Laboratory testing for antinuclear antibodies and rheumatoid factor was negative, as were serologies for HIV and hepatitis B and C. Further questioning revealed no history of weight loss supplements or illicit substance abuse.

Dr John R. Teerlink: Interlobular septal thickening, a sign of pulmonary edema, was not identified and argues against significant left heart disease or pulmonary veno-occlusive disease as the cause of this patient’s clinical condition. The lack of masses and adenopathy argue against recurrent breast

Figure 3. Transthoracic echocardiogram images. A, An apical 4-chamber view demonstrating a severely enlarged right atrium and ventricle with a small left ventricular cavity. B, A parasternal short-axis view demonstrating a severely enlarged RV with flattening of the intraventricular septum. RA indicates right atrium; RV, right ventricle; LV, left ventricle.
cancer or a secondary malignancy. Pleural effusions in the absence of pulmonary edema suggest that the pulmonary arterial pressures may be elevated in the absence of elevated pulmonary venous pressures. Venous drainage for the lung parenchyma and the visceral pleura returns through the pulmonary veins and ultimately enters the left atrium (in this case, a low-pressure system), whereas the parietal pleura’s venous drainage typically returns through the inferior vena cava or brachiocephalic trunk to the right atrium (a high-pressure system in this patient).

Although there is no large acute pulmonary embolism by computed tomography angiogram, chronic pulmonary emboli (small vessel) remain on the differential given the abnormal results of the V/Q scan, the rapidity of the patient’s symptoms, the degree of hypoxemia, and the history of cancer.

Anticoagulation was considered for empiric treatment of possible chronic pulmonary emboli but the persistent, marked thrombocytopenia and a lack of definitive diagnosis, in addition to planned cardiac catheterization and bone marrow biopsy procedures, factored into the decision to withhold heparin. Despite initial stabilization, the patient’s oxygen saturation continued to decline. She was transferred to the coronary care unit on high-flow oxygen by nasal cannula at 20 L/min on hospital day 2. Her subsequent arterial blood gas demonstrated a pH of 7.46, a pCO₂ of 36, and a pO₂ of 82. The blood pressure at the time of transfer was 88/55 mm Hg, and the heart rate was 100 bpm. On examination, the extremities were cool to the touch. The patient was started on continuous dobutamine infusion at 3 μg · kg⁻¹ · min⁻¹.

Hemodynamic assessment by right heart catheterization demonstrated a mean right atrial pressure of 9 mm Hg, a RV systolic pressure of 75 mm Hg, and a pulmonary artery pressure of 75/37 mm Hg (mean, 49 mm Hg). Serial pulmonary capillary wedge pressure (PCWP) tracings from multiple positions in both right and left lungs showed a mean pressure of 35 mm Hg with a normal-appearing waveform (Figure 4). Blood sampling for oximetry could not be obtained from the pulmonary capillary wedge position. The elevated PCWP and possible premature timing of the V wave relative to the ECG T wave—suggesting an incompletely wedged position—prompted a left heart catheterization. The epicardial coronary arteries were angiographically normal. Systemic and LV systolic pressures were 96 mm Hg. There was exaggerated respirophasic variation in the aortic pressure tracing consistent with 16 mm Hg of pulsus paradoxus. The left ventricular end-diastolic pressure (LVEDP) was 3 mm Hg. The remainder of the right heart catheterization demonstrated a pulmonary arterial oxygen saturation of 36% without evidence of left to right shunting by oxygen saturation assessment. The cardiac output was 2.0 L/min by the Fick equation. The pulmonary vascular resistance was 1840 dynes · s⁻¹ · cm⁻⁵ (based on the LVEDP) and systemic vascular resistance was 2720 dynes · s⁻¹ · cm⁻⁵. Pulmonary angiography was not performed.

**Dr John R. Teerlink:** The patient had been adequately diuresed before catheterization (suggested by the right atrial pressure of 9 mm Hg). However, in the presence of severe pulmonary vascular disease and a failing RV, the LV preload and subsequent cardiac output were severely diminished, leading to profound cardiogenic shock despite what appears to be a normally functioning LV. Consistent with cardiogenic shock physiology, her tissue perfusion pressures were maintained by robust augmentation of her systemic vascular resistance.

In the presence of RV failure, RV preload should be optimized. However, this can often be a very delicate balancing act with too much diuresis leading to inadequate RV preload and reduced RV stroke volume on one hand, and inadequate diuresis leading to RV volume overload that can also compromise stroke volume due to compromise of ventricular function by relative ischemia from disproportionate increases in wall stress and afterload mismatch on the other. A target right atrial pressure of 8 to 12 mm Hg is probably optimal in this situation. If LV preload and cardiac output remain low despite optimization of right-sided filling pressures, then inotropic support for the RV is indicated. Current
evidence suggests that low-dose dobutamine is the inotropic agent of choice for RV failure and should be titrated between 2 and 6 \( \mu \text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1} \) as needed.\(^1\)

Discordance between the PCWP and LVEDP, as seen in this case, is most commonly due to difficulty fully wedging the pulmonary artery (PA) catheter. Such difficulties can arise because of structural changes in pulmonary arteries that are exposed to elevated pressures. An incompletely wedged PA catheter allows some antegrade flow into the arteriole bed, which will augment the observed pressure measurement. Antegrade venous blood will also dilute the oxygen saturation of blood aspirated from the wedged position, thus oxygen saturation assessment is typically the best way to confirm the position of the PA catheter. Morphology and timing of the PCWP waveform can also provide some clues. An unusual-appearing PCWP tracing should certainly raise one’s suspicion for an incompletely wedged position. Severe mitral regurgitation will create large V waves on the PCWP tracing, which can mimic a PA pressure tracing, or an incompletely wedged position. Therefore, the pressure tracing alone cannot always be relied on to confirm the adequacy of the wedged position. As an additional clue, the V wave of the PCWP tracing should arise between the electrocardiographic T wave and P wave in the absence of QT prolongation. This can be difficult to accurately determine when patients are quite tachycardic, but a V wave that appears premature relative to the electrocardiographic T wave suggests an incompletely wedged position, because antegrade flow will arrive at the pressure transducer sooner than retrograde flow reflected from the left atrium.

In the absence of evidence for an incompletely wedged position, the differential diagnosis for discordant PCWP and LVEDP includes mitral stenosis, cor triatriatum, left atrial myxoma, and positive pressure ventilation. Perhaps more speculatively, ventricular interdependence, aortic regurgitation (from premature mitral valve closure), and anatomic obstruction, eg, tumor microemboli and carcinomatosis, have been implicated. Interestingly, pulmonary veno-occlusive disease is typically thought to lack a PCWP-to-LVEDP gradient despite anatomic obstruction between the pulmonary capillaries and left atrium.\(^2\)

This patient currently needs aggressive therapy for PH, irrespective of its pathogenesis. Options for PH therapy are limited by the patient’s hypoxia and large alveolar-arterial gradient as well as her hypotension and low platelet count. First, all prostacyclin analogues, but especially epoprostenol, are known to cause platelet dysfunction. Second, pulmonary vasodilators given systemically, especially epoprostenol, may vasodilate the entire pulmonary arterial bed and can increase perfusion to poorly ventilated lung regions, exacerbating V/Q mismatch and worsening hypoxemia. In contrast, inhaled nitric oxide is a selective pulmonary vasodilator that can be administered in the intensive care unit setting, and it may enhance V/Q matching. However, it is very expensive and cannot be used chronically.

Nitric oxide can also be tested in the catheterization laboratory to assess pulmonary vasoreactivity, because its onset of action is very rapid. Classically, a nitric oxide challenge is considered positive if there is a decrease in mean PA pressure of \(\geq 10\) mm Hg without decrement in cardiac output and/or a reduction in pulmonary vascular resistance of \(\geq 25\%\) after 5 minutes of therapy. Such positive results are only seen in approximately a fifth of all patients with PH, but typically portend both a better overall prognosis as well as likely responsiveness to oral calcium channel blocker therapy. Formal nitric oxide challenge was not performed in this case, and oral calcium channel blockers are clearly not the therapy of choice in such an acute situation.

Prostacyclin analogues given via the inhalational route, such as iloprost and treprostinil, are felt to be less likely to worsen V/Q mismatching than a systemically administered agent. Endothelin receptor antagonists do not generally have rapid onset of action and would not be expected to reverse the life-threatening course of her illness acutely. Phosphodiesterase type-5A inhibitors, such as sildenafil or tadalafil, despite being given systemically, generally have the lowest-risk profile for causing worsened V/Q mismatch and hypoxemia, because of the markedly increased density of phosphodiesterase type-5A in the pulmonary vasculature, and they have a rapid onset of action. Careful attention for the development of pulmonary edema with any pulmonary vasodilator therapy is necessary given the continued concern that this patient could still have pulmonary veno-occlusive disease. Increasing pulmonary arterial flow in the setting of an anatomically fixed venous obstruction can cause fluid extravasation and rapid pulmonary edema.

After returning to the Coronary Care Unit following cardiac catheterization, the patient was started on high-flow oxygen by face mask with 20 ppm inhaled nitric oxide. The inhaled nitric oxide was tolerated without signs or symptoms of pulmonary edema, and the patient was then treated with sildenafil 25 mg 3 times daily. She tolerated sildenafil without worsening systemic hypotension, and subsequently intravenous treprostinil was added. With these therapies, her pulmonary pressures remained near-systemic, but the ventricular filling pressures and cardiac output normalized. Unfortunately, she did not demonstrate significant clinical improvement, and remained severely dyspneic and hypoxic with increasing oxygen requirements. She was deemed not to be a candidate for lung transplantation because of her relatively recent history of cancer. On hospital day 6, she had a bradycardic arrest from which she could not be resuscitated.
a leftward shift of the pressure volume relationship such that small volume increases are more directly manifest as increased pressure. This does not address the patient’s refractory hypoxia.

Despite a thorough evaluation, there is no evidence of LV dysfunction, pulmonary parenchymal disease, right-to-left shunting, or underlying conditions commonly associated with PH. Although we were unable to demonstrate it, there must have been some process that rapidly and microscopically progressed in the pulmonary vasculature that impeded both blood flow and oxygenation. The intermediate probability V/Q scan leaves pulmonary emboli as a distinct possibility. However, the final diagnosis would ideally also explain the severe and persistent thrombocytopenia. Recurrence of her breast cancer—either through bone marrow infiltration or a chronic compensated disseminated intravascular coagulation—could do so. We suspected that she must have had progressive and microscopic emboli (either tumor or fibrin clot) distributed throughout her pulmonary vasculature, likely heralding the recurrence of her breast cancer.

An autopsy was performed. Gross evaluation of the cardiopulmonary system demonstrated severe right atrial and RV dilation with an RV thickness of 0.3 cm. There were no significant intracardiac shunts. The left heart was anatomically normal as were all the valves. The lung parenchyma was anatomically normal, and there were no macrovascular thromboemboli or gross obstruction of the vasculature. Microscopic examination of the lungs revealed organizing thromboemboli containing metastatic carcinoma involving the arterioles and lymphovascular structures of the lung without parenchymal involvement (Figure 5). The tumor emboli were histologically consistent with a primary breast cancer. Islands of tumor were also found in the pituitary and bone marrow. No metastatic tumors were identified elsewhere.

Discussion

The seminal diagnostic features of this case were a rapidly progressive form of PH, unremitting hypoxia, marked thrombocytopenia, and an incongruity between a very elevated PCWP and a low LVEDP. Initially, the difference in PCWP and LVEDP was ascribed to technical difficulty in achieving a truly wedged position with the PA catheter. Technical challenges during right heart catheterization are not infrequent and are undoubtedly more common than the presence of pulmonary arteriole or venous obstruction. Additional clues to the patient’s ultimate diagnosis of pulmonary tumor thrombotic microangiopathy (PTTM) included her history of breast cancer and her profound, unexplained thrombocytopenia.

PTTM is a rare, but underappreciated, cause of rapidly progressive PH and cor pulmonale marked by diffuse occlusion of the small pulmonary arterioles with metastatic tumor cells. These tumor emboli engender an obliterator fibrointimal hyperplasia and in situ thrombosis of the pulmonary vasculature, thus further diminishing the aggregate patent pulmonary vascular bed and worsening the PH. This process of embolization and hyperplasia also disrupts the retrograde transmission of reflected left atrial pressure to the pulmonary arterial catheter in the wedged position resulting in discordant PCWP and LVEDP measurements, one of the harbingers of the diagnosis in our case. Interestingly, in the cardiac catheterization laboratory, it was noted that the V wave of the PCWP tracing might have arisen early relative to the standard electrocardiographic landmarks. It is possible this was due to a fraction of the retrograde pressure wave reflecting from obstructed arterioles, which are anatomically more proximal to the PA catheter than the left atrium. Although also speculative, the arteriole hyperplasia of PTTM may also explain the patient’s marked alveolar-arterial gradient. Measurement of carbon monoxide diffusion capacity on pulmonary function tests may have shed further light on this finding, although pulmonary function tests are rarely possible in the setting of critical illness.

A formal diagnosis of PH is defined by a mean pulmonary artery pressure >25 mm Hg at rest (pressures of 21–24 mm Hg are abnormal but of indeterminate significance). Invasive hemodynamic assessment with right heart catheterization is required to establish the diagnosis but is rarely the first diagnostic test for suspected PH given the relative ease and safety of assessing pulmonary artery pressures via trans-thoracic echocardiography.

New-onset PH is often misdiagnosed initially, as was true of this case. The most common presenting symptom of PH is exertional dyspnea, as was also seen in this case. Atypical chest pain is commonly present, and presyncope, syncope, orthopnea, hemoptysis, and even voice hoarseness (Ortner syndrome from compression of the left recurrent laryngeal nerve by engorgement of the pulmonary artery) are also
possible symptoms. Physical examination findings are most often related to RV sequelae—either hypertrophy, enlargement, or failure, depending on the acuity and degree of progression of the disease—although systolic pulsations over the second left intercostal space suggest dilation of the pulmonary artery itself. Evidence of LV failure may also be present in World Health Organization group 2 PH patients.

The rate of progression of PH is related to the underlying pathogenesis of the disease. Acute-onset PH does not allow for hypertrophy of the RV. In such cases, the RV can rarely generate a pressure >60 mm Hg and will quickly begin to fail. Treatment of RV failure from any cause can be extremely challenging and has recently been reviewed in the literature. Key elements to the treatment of isolated RV failure, as was required in this case, include volume status optimization, avoidance of both mechanical ventilation and hypoxia whenever possible to limit their deleterious effects on RV afterload, supportive care with inotropes as necessary, and identification of any underlying etiology for targeted therapies.

In the case of RV failure from PH, the treatment plan requires a thorough diagnostic workup, which may be tailored based on a careful history and physical examination. In the absence of any clear, reversible cause of the PH, such as left heart failure or pulmonary embolus, empirical therapies targeting reduction of the pulmonary vascular resistance and RV afterload are necessary.

In our case, the underlying diagnosis remained speculative during the clinical course. PTTM is an elusive antemortem diagnosis, especially if a primary neoplasm is occult or felt to be successfully treated. The diagnosis of PTTM depends on the acuteness and degree of progression of the disease—although systolic pulsations over the second left intercostal space suggest dilation of the pulmonary artery itself. Evidence of LV failure may also be present in World Health Organization group 2 PH patients. PTTM is an elusive antemortem diagnosis, especially if a primary neoplasm is occult or felt to be successfully treated. The diagnosis of PTTM depends on the acuteness and degree of progression of the disease—although systolic pulsations over the second left intercostal space suggest dilation of the pulmonary artery itself. Evidence of LV failure may also be present in World Health Organization group 2 PH patients. The rate of progression of PH is related to the underlying pathogenesis of the disease. Acute-onset PH does not allow for hypertrophy of the RV. In such cases, the RV can rarely generate a pressure >60 mm Hg and will quickly begin to fail. Treatment of RV failure from any cause can be extremely challenging and has recently been reviewed in the literature. Key elements to the treatment of isolated RV failure, as was required in this case, include volume status optimization, avoidance of both mechanical ventilation and hypoxia whenever possible to limit their deleterious effects on RV afterload, supportive care with inotropes as necessary, and identification of any underlying etiology for targeted therapies.

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