Rare Coexistence of Major Lung Pathologies

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Presentation: A 40-year-old African American female with past history of congenital heart murmurs of unknown etiology, iron deficiency anemia, and intellectual disability secondary to newborn shaken baby syndrome presented to the emergency department with worsening dyspnea, cough, sore throat, and fatigue. Family history was significant for Wegener's granulomatosis and lung cancer. Social history was negative for tobacco, alcohol, or illicit drug use. She lives at home with her sister as her legal caregiver. Workup revealed tachycardia, III/VI holosystolic murmur, right axis deviation on electrocardiogram (EKG), and respiratory alkalosis on arterial blood gas (ABG). She was found to have bilateral upper lobe infiltrates and hilar lymphadenopathy as well as an enlarged pulmonary artery on computed tomography (CT) scan (Figure 1). She was admitted and treated empirically for pneumonia with antibiotics without clinical improvement. She was then referred to the pulmonary clinic for further clinical workup and evaluation of radiographic changes.

Assessment: A pulmonary function test at her outpatient workup indicated a mild restrictive pattern with a total lung capacity of 74% and FEV1/FVC at 84%. Bronchoscopy was performed and analysis of the bronchoscopic lavage was negative for all cultures and flow cytometry. Endobronchial ultrasound-guided fine-needle aspiration noted noncaseating granuloma (Figure 2). Gallium scan showed uptake in both hilar regions and bilateral upper lobes (Figure 3). Echocardiogram revealed severe tricuspid regurgitation and an enlarged right ventricular (RV) cavity with hypokinesis of the RV free wall and severely reduced RV systolic function. A follow-up dobutamine stress test was negative for any evidence of ischemia. Her blood work indicated a slightly elevated ACE level at 68, but ESR, CRP, PT/PTT, HIV, RF, and ANA were within normal limits. Right heart catheterization (RHC) noted severe pulmonary arterial hypertension (PAH) (Table 1, Figure 4a).

Therapy and Follow-up: The patient was diagnosed with sarcoidosis-associated pulmonary hypertension (SAPH) and stage II sarcoidosis due to hilar lymphadenopathy and minor parenchymal involvement as noted on the radiographic imaging. Treatment was initiated with prednisone and bosentan. At her 3-month follow-up she was noted to have a favorable response to the therapy, as evidenced by a drop in ACE level, improvement in cough, and an improvement in her 6-minute walk test (6MWT) from 113 m to 153 m. However, 6 months later, her condition deteriorated with worsening dyspnea, and she was subsequently hospitalized for a repeat evaluation. A ventilation-perfusion (V/Q) scan revealed multiple wedge-shaped defects suggestive of pulmonary thromboembolism, which prompted further evaluation with a CT angiogram (CTA) (Figure 5). The CTA noted mediastinal fibrosis with compressive effects, peripheral pruning, and central pulmonary arterial enlargement with no clear emboli. A repeat RHC showed deteriorating PAH (Table 1, Figure 4b). The patient's sarcoidosis alone could not account for the severity of the PAH; therefore, a pulmonary angiogram was performed. It revealed focal subsegmental stenosis of 70% to 80% in the right upper, right lower, and left lower arterioles (Figure 6). Following the findings on the pulmonary angiogram and CTA, she was diagnosed with PAH secondary to peripheral pulmonary artery stenosis (PPS).

The patient was nonresponsive to vasodilator challenge (epoprostenol) and was subsequently started on inhaled treprostinil and sildenafil. This provided mild symptomatic relief while surgical treatments were explored. She was evaluated at multiple transplant centers for lung transplantation, but did not qualify due to intellectual disability. At this point, pulmonary artery stenting to relieve PAH secondary to PPS was considered. Following placement of the pulmonary artery stents, she was noted to have decreased dyspnea on exertion. A pulmonary angiogram revealed significant improvement in her hemodynamics

Key Words—arterial stenosis, dyspnea, mediastinal fibrosis, pulmonary angiogram, sarcoidosis
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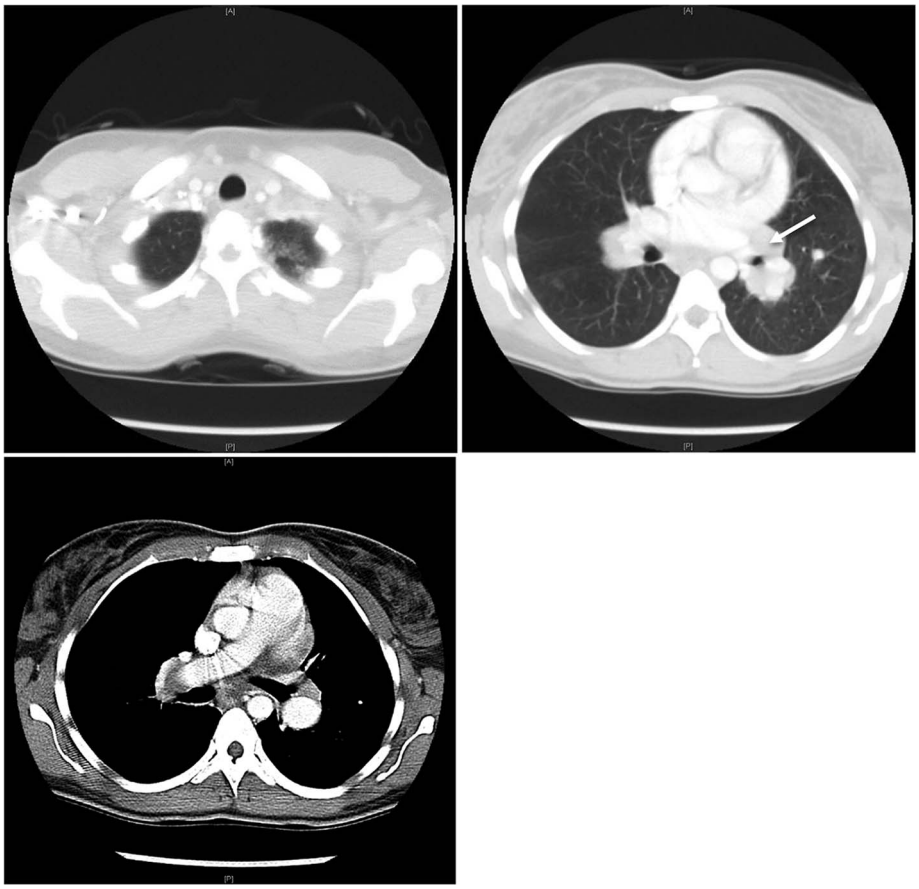

Figure 1: CT scan at initial presentation showing upper lobe infiltrates, hilar lymphadenopathy, and enlarged pulmonary artery.

and pulmonary arterial flow (Figure 7). She was able to walk 356 m on her 6MWT as compared to 153 m before stenting. She was weaned off the inhaled treprostinil but continued on sildenafil and bosentan. At 1-year follow-up, her sister reported substantial improvement in quality of life with consistent maintenance of her 6MWT, and she was able to go back to her daily living activities, including swimming in the Special Olympics.

Discussion: This is a rare case of acquired PPS from sarcoidosis-mediated mediastinal fibrosis, as noted by the compressive effects on the CT scan. However, it is believed that a stage II sarcoidosis with minor parenchymal involvement and hilar lymphadenopathy is not significant enough to cause her suprasystemic right ventricular systolic pressure (RVSP). With her history of congenital heart murmur, it is hypothesized that she most likely had undiagnosed congenital PPS with mild hemodynamic effects. Her preexisting congenital PPS was worsened by the acquired PPS from sarcoidosis in adulthood, resulting in severe PAH and right-sided heart failure.

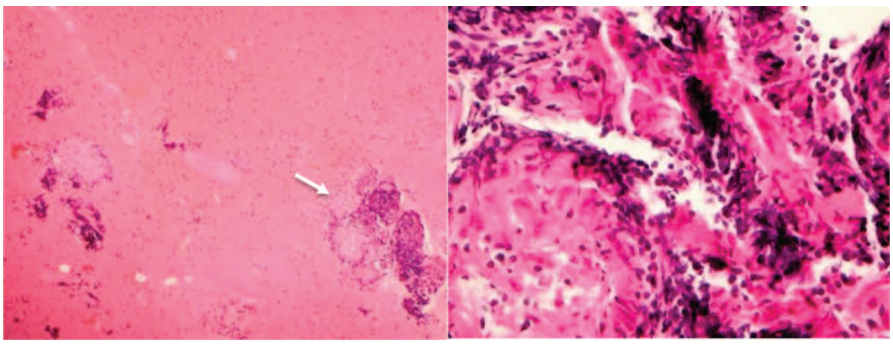

Figure 2: Pathologic specimen from endobronchial biopsy showing noncaseating granulomas.

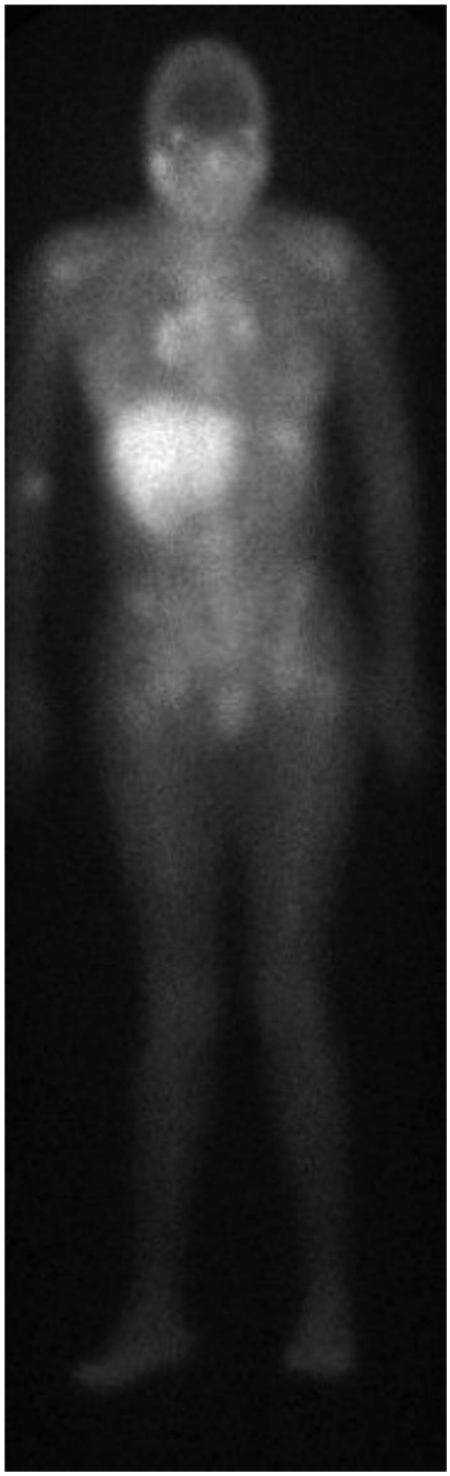

Figure 3: Gallium scan showing uptake in hilar regions and bilateral upper lobes.

PAH is a fatal syndrome with a median life expectancy of 2.8 years without treatment, but early detection and intervention is key for an optimal outcome.[1] SAPH is an important complication in advanced sarcoidosis that can

Table 1. Catheterization data

	Initial RHC	Second RHC	Reference range
Right atrial pressure	4	8	<5 mm Hg
RV pressure	125/8	139/3	<25/5 mm Hg
Pulmonary artery pressure	120/34/64	136/43/75	<25/10/15 mm Hg
Pulmonary capillary wedge pressure	4	9	<12 mm Hg
Pulmonary vascular resistance	11.11 WU	18 WU	<1.6 Wood units
Fick cardiac index	2.37	2.57	

result in significant morbidity and mortality.[2] Sarcoidosis is a multiorgan noncaseating granulomatous disorder with lung involvement in 90% to 95% of patients.[3] There are multiple pathophysiologies considered in SAPH. These include obliteration of pulmonary vascular bed from chronic hypoxemia and parenchymal lung destruction; granulomatous invasion of pulmonary vessel walls resulting in destruction, remodeling, and subsequent pulmonary veno-occlusive disease-like physiology; vascular remodeling and vasoconstriction from endothelin-induced proliferation of smooth muscle cells and fibroblasts; and physical compression of pulmonary arteries by mediastinal fibrosis or enlarged hilar lymph nodes.[2,3] With a high degree of clinical suspicion, the confirmatory diagnostic test of choice is RHC, which helps characterize the condition and exclude pulmonary venous hypertension.[3] In addition to treatment of the PAH, treatment of underlying sarcoidosis is required for improved prognosis. PPS is defined as >50% obstruction of tertiary branches from pulmonary trunk. Congenital PPS has been well described in children and is typically associated with a congenital syndrome or heart defect.[4] However, in cases of mild hemodynamic effects, patients don't present until suprasystemic RVSP.[4] Acquired PPS is a rare disorder, which is often a diagnostic and thera-

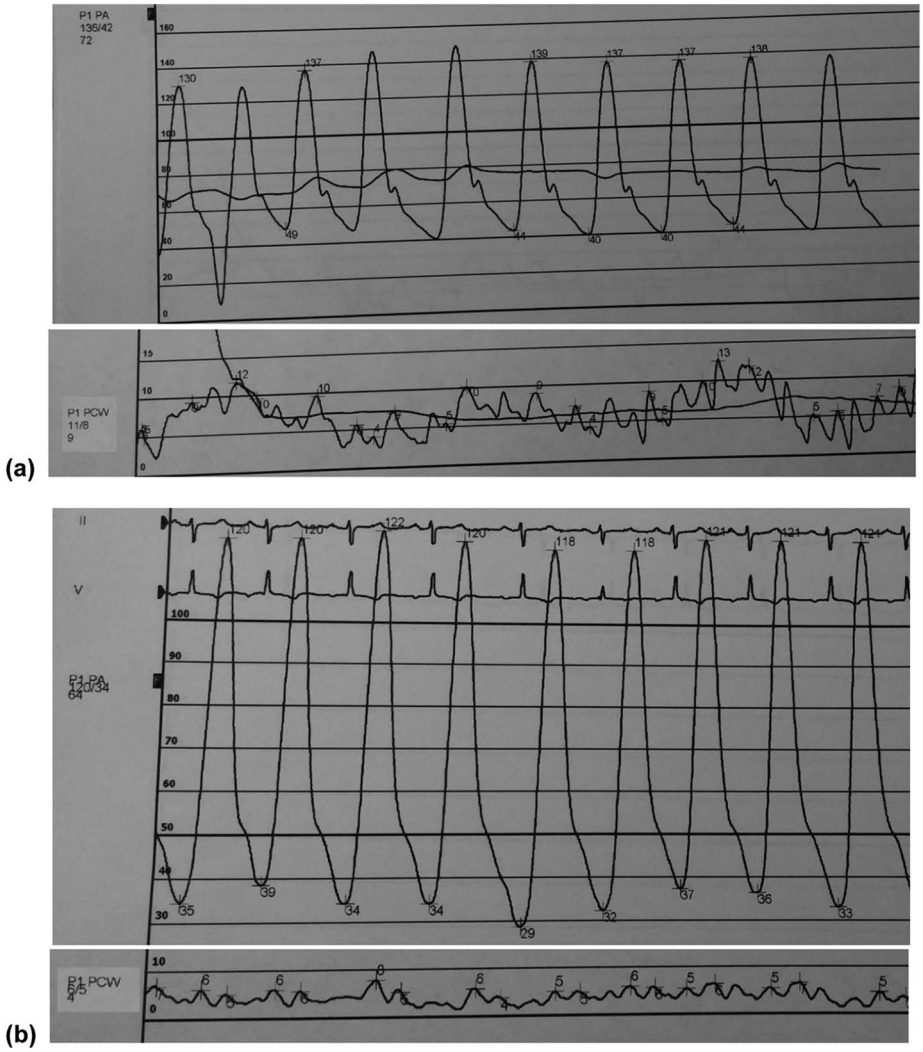

Figure 4: Cardiac catheterization waveforms. Initial RHC (a); follow-up RHC (b).

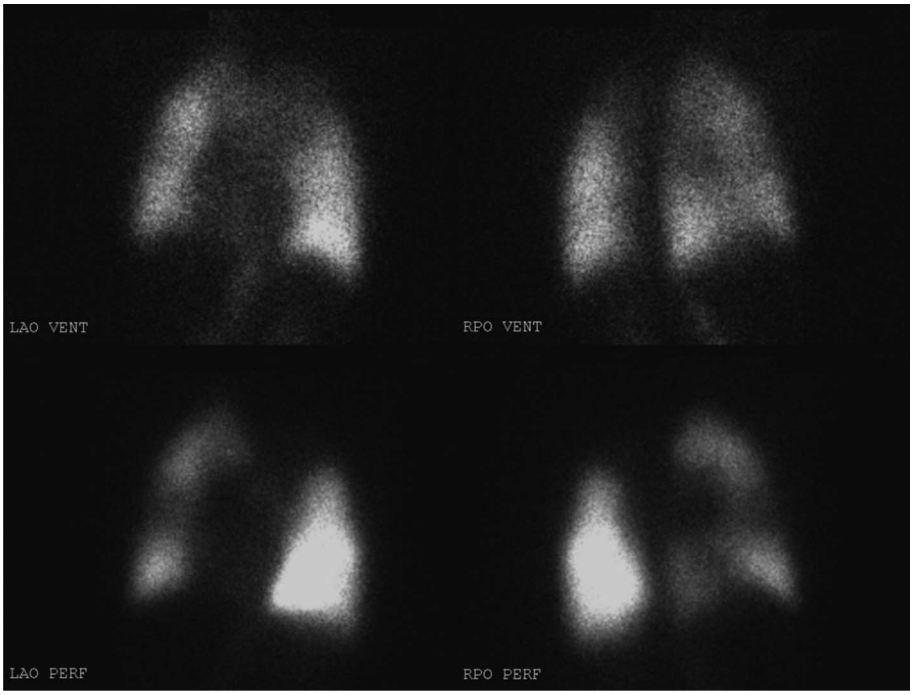

Figure 5: V/Q scan with multiple wedge-shaped defects.

peutic challenge. In cases of primary lung disorder with secondary PAH, PPS should be ruled out with a pulmonary angiogram or V/Q scan. PPS pattern on a V/Q scan appears similar to chronic thromboembolic disorders with unmatched segmental defects. However, pulmonary angiogram is the gold standard for diagnosis of PPS, which can also localize the stenosed arteries. Percutaneous angioplasty and stenting are currently the nonsurgical modality of choice in PPS and have shown good prognosis in children.[5] Postsurgical complications include in-stent stenosis occurring years after initial stenting, and stent embolization in cases with severe pulmonary regurgitation.[6] Without considerable reported data or guidelines for adult variant of congenital PPS and acquired PPS, close clinical surveillance is key for positive long-term prognosis and investigation of innovative preventative strategies are warranted.

Teaching Points

1. PPS is typically a congenital disorder that presents in childhood with a congenital murmur and significant PAH.
2. Adult-variant PPS presents itself when the hemodynamic effects from congenital PPS are mild until RVSP is suprasystemic in adulthood. Another pathophysiology for adult-variant PPS involves primary lung pathology causing arterial stenosis.
3. PPS should be considered in adults with insidious onset of dyspnea and chronic thromboembolic pattern on a V/Q scan without hypercoagulable risk factors. This should be carefully worked up given the marked differences in therapy for these disease processes.
4. Pulmonary angiogram is the diagnostic test of choice for PPS.
5. Percutaneous angioplasty and stenting are the nonsurgical treatments of choice for PPS, which require long-term monitoring due to complications of in-stent stenosis and stent embolization.
6. SAPH is an important complication of advanced sarcoidosis with significant morbidity and mortality; treatment should be aimed at both sarcoidosis and PAH.

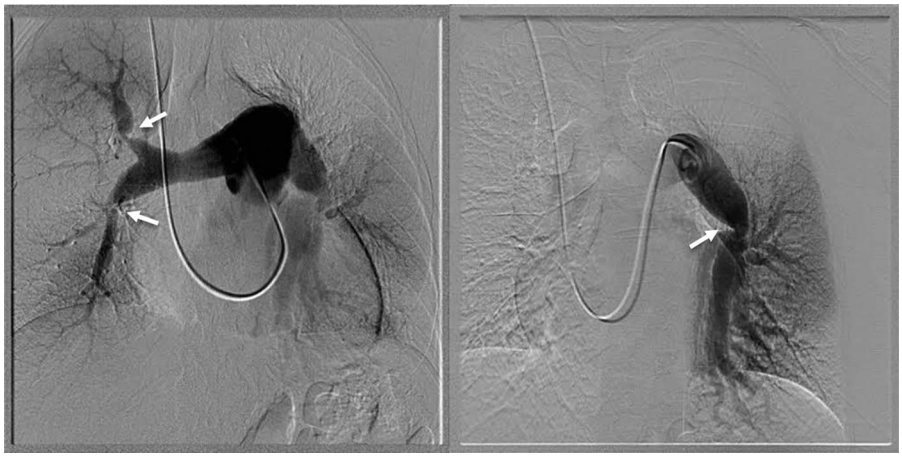

Figure 6: Pulmonary angiogram showing peripheral pulmonary arterial stenosis in right upper and lower lobe and left lower lobe.

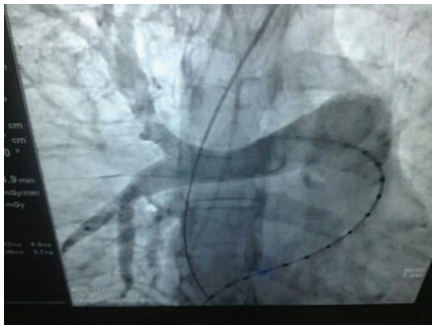

Figure 7: Post-stent angiogram of right upper and lower lobe.

References

1. Galiè N, Manes A, Branzi A. [New insights on pulmonary arterial hypertension]. *Rev Esp Cardiol*. 2004;57(7):603-607.
2. Palmero V, Sulica R. Management of Sarcoidosis-Associated Pulmonary Hypertension. *CML: Pulmonary Hypertension*. 2012;3(3):69-76.
3. Ryu JH, Krowka MJ, Pellikka PA, Swanson KL, McGoon MD. Pulmonary hypertension in patients with interstitial lung diseases. *Mayo Clin Proc*. 2007; 82(3):342-350.
4. Kreutzer J, Landzberg MJ, Preminger TJ, et al. Isolated peripheral pulmonary artery stenoses in the adult. *Circulation*. 1996;93(7):1417-1423.
5. Kushner T, Halperin JL, Nair AP, Fuster V, Love BA. Peripheral pulmonary artery stenosis masquerading as pulmonary hypertension: a diagnostic and therapeutic challenge. *Vasc Med*. 2012; 17(4):235-238.
6. Hallbergson A, Lock JE, Marshall AC. Frequency and risk of in-stent stenosis following pulmonary artery stenting. *Am J Cardiol*. 2014: 113(3):541-545.