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MINI-FOCUS ISSUE: CLINICAL CARDIOLOGY

BEGINNER

CASE REPORT: CLINICAL CASE

Beyond the Diagnosis of Group IV Pulmonary Hypertension

Chronic Thromboembolic Pulmonary Hypertension Mimickers

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ABSTRACT

We present 3 patients with similar clinical presentation of group IV pulmonary hypertension but with totally different diagnoses. This case series highlights the need to keep a broad differential diagnosis and to utilize more diverse imaging modalities for the diagnosis of group IV pulmonary hypertension. (**Level of Difficulty: Beginner.**)
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Pulmonary hypertension (PH) has different etiologies that could all share the same presentation and diagnostic imaging. The World Health Organization identifies 5 distinct groups of PH based on pathogenesis and etiology. Among these, group IV is PH secondary to chronic thromboembolic pulmonary hypertension (CTEPH) (1). With improving diagnostic modalities, the incidence and prevalence of CTEPH are increasing. However, CTEPH can cause a diagnostic dilemma in many cases because any disease that causes pulmonary artery occlusion can mimic and easily be mistaken for CTEPH (2,3). Here we present a case series of patients who presented similarly but had vastly different diagnoses.

LEARNING OBJECTIVES

- To differentiate between multiple etiologies causing pulmonary artery obstruction.
- To understand the importance of imaging modalities and noninvasive testing in establishing the etiology.
- To understand the importance of a multidisciplinary approach to diagnosis and management of patients with group IV PH.

CASE DESCRIPTIONS

CASE 1. A 72-year-old man presented with progressively worsening dyspnea, lower extremity edema, and abdominal swelling. Pertinent history includes pulmonary embolism diagnosed the year before presentation, permanent atrial fibrillation, and prostate cancer post-resection. On examination, the patient had an irregularly irregular rhythm, with jugular venous distension and bilateral lower extremity edema.

Computed tomography angiography (CTA) of the chest revealed failure to opacify the right middle and lower lobe branches of the right pulmonary artery, possibly secondary to occlusion from a right hilar mass with middle lobe pulmonary emboli. Due to the patient's severe orthopnea, he was unable to undergo

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ABBREVIATIONS AND ACRONYMS

CTEPH = chronic thromboembolic pulmonary hypertension

MRA = magnetic resonance angiogram

PET = positron emission tomography

PH = pulmonary hypertension

RV = right ventricular

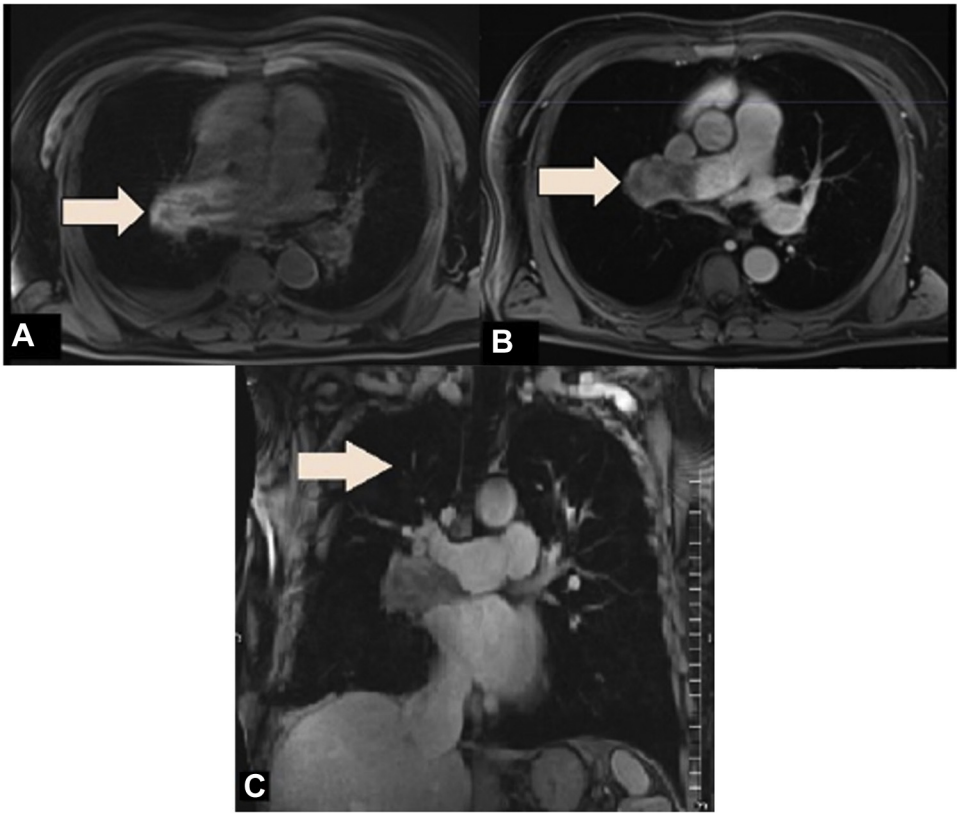
V/Q = ventilation/perfusion scan

a right heart catheterization or biopsy of the mass. Magnetic resonance angiogram (MRA) of the chest was performed and showed a large nonenhancing mass-like filling defect involving the right main, interlobar, middle, and lower lobe pulmonary arteries with signal characteristics consistent with bland thrombus and no evidence of extension outside the lumen (Figures 1). A pulmonary ventilation/perfusion (V/Q) scan confirmed numerous mismatch perfusion defects. Echocardiography was performed given the suspicion of PH, and it showed a dilated right ventricle with severely depressed right ventricular (RV) systolic function; RV pressure was consistent with severe PH.

After aggressive diuresis, the patient improved clinically and was able to undergo pulmonary endarterectomy, with good results (Figure 1C). Pulmonary pressures taken intraoperatively (Table 1) confirmed CTEPH.

CASE 2. A 37-year-old woman presented for chronic exertional dyspnea and lower extremity edema. Pertinent medical history includes nonischemic cardiomyopathy with recovered ejection fraction, papillary thyroid carcinoma post-partial thyroidectomy, and iatrogenic hypothyroidism. On examination, she had an accentuated P2, parasternal heave, jugular venous distention, and mild bilateral pitting lower-limb edema. Echocardiography showed a mildly dilated right ventricle with normal RV systolic function; however, Doppler findings suggested PH.

FIGURE 1 A 72-Year-Old Man With Chronic Thromboembolic Pulmonary Hypertension



(A) Magnetic resonance angiogram (MRA) of the chest without contrast showing a large mass-like filling defect **(arrow)** involving the right main pulmonary artery. **(B)** MRA of the chest with contrast showing a nonenhancing filling defect **(arrow)** in the right main pulmonary artery, consistent with a bland thrombus rather than mass. **(C)** Pulmonary MRA with filling defects in the branches of the right pulmonary artery **(arrow)**.

TABLE 1 Comparison Between Study Cases of CTEPH, Spindle Cell Sarcoma, and Takayasu Arteritis

	CTEPH	Spindle Cell Sarcoma	Takayasu Arteritis
Age (yrs)	72	37	32
Clinical presentation	Dyspnea, lower extremity edema, chest pain, history of PE, or deep venous thrombosis	Dyspnea, lower extremity edema, profound weight loss and cachexia, and hemoptysis	Arm and leg pain from limb claudication, peripheral cyanosis, weight loss, low-grade fever, fatigue, arthralgias, progressive dyspnea, and chest pain
TTE	Dilated right ventricle with severely depressed RV systolic function; RV pressure was consistent with severe PH	Echocardiography showed mildly dilated right ventricle with normal RV systolic function; however, Doppler findings suggested PH	Echocardiography did not show PH
CT chest scan with and without intravenous contrast	Filling defects in the pulmonary arteries consistent with chronic emboli	Filling defects in the pulmonary arteries with irregularities of the arterial wall, features of local invasion or systemic metastasis	Filling defects in the pulmonary arteries consistent with chronic emboli with mural wall thickening that can also be seen in other arterial vasculature (e.g., the aorta)
Hemodynamic parameters	RAP: unable to estimate Peak PAP: 95 mm Hg POD1 systolic/diastolic (mean): 42/21 (30) mm Hg PCWP (mean): 20 mm Hg PVR: 2.11 Wood units	RAP systolic/diastolic (mean): 12/8 (7) mm Hg PAP systolic/diastolic (mean): 30/10 (20) mm Hg PCWP systolic/diastolic (mean): 22/17 (15) mm Hg PVR: 1.00 Wood units	RAP systolic/diastolic (mean): 5/2 (4) mm Hg PAP systolic/diastolic (mean): 43/13 (26) mm Hg PCWP systolic/diastolic (mean): 12/10 (8) mm Hg PVR: 4.50 Wood units
Pathology	Arterial wall and organizing thrombus	Biopsy results positive for spindle cell sarcoma	Was not performed during right heart catheterization
Treatment	Surgical endarterectomy/balloon pulmonary angioplasty, medical therapy	Surgical resection and chemotherapy	High-dose steroids

CT = computed tomography; PAP = pulmonary artery pressure; PCWP = pulmonary capillary wedge pressure; PE = pulmonary embolism; PH = pulmonary hypertension; POD1 = post-operative day 1; PVR = pulmonary vascular resistance; RAP = right atrial pressure; RV = right ventricular; TTE = transthoracic echocardiogram.

Given the patient's persistent symptoms, CTA of the chest (Figure 2A) was performed, revealing chronic central pulmonary thrombus with increasingly irregular margins. This was concerning for an underlying mass at the site of thrombosis. Subsequently, magnetic resonance imaging of the chest (Figures 2C and 2D) with and without contrast revealed an infiltrative enhancing mass extending into the left and right main pulmonary artery system with intravascular extension. This imaging was followed by a whole-body positron emission tomography (PET) scan (Figure 2B). This scan showed a hypermetabolic mass involving the heart: the main pulmonary arteries extending into the left lobar arteries and veins, narrowing the left main stem and lobar bronchi and mediastinal lymphadenopathy. Fine needle aspiration of the mediastinal lymph nodes showed spindle cell sarcoma, and the patient was started on chemotherapy followed by immunotherapy with decreasing disease burden on follow-up.

CASE 3. A 32-year-old woman presented to our hospital with a 2-month history of progressive dyspnea and chest pain. She was previously being seen for recurrent pericarditis, Raynaud's phenomenon, arthralgias, and syncope with a working diagnosis of mixed connective tissue disease. She was taking hydroxychloroquine and methotrexate.

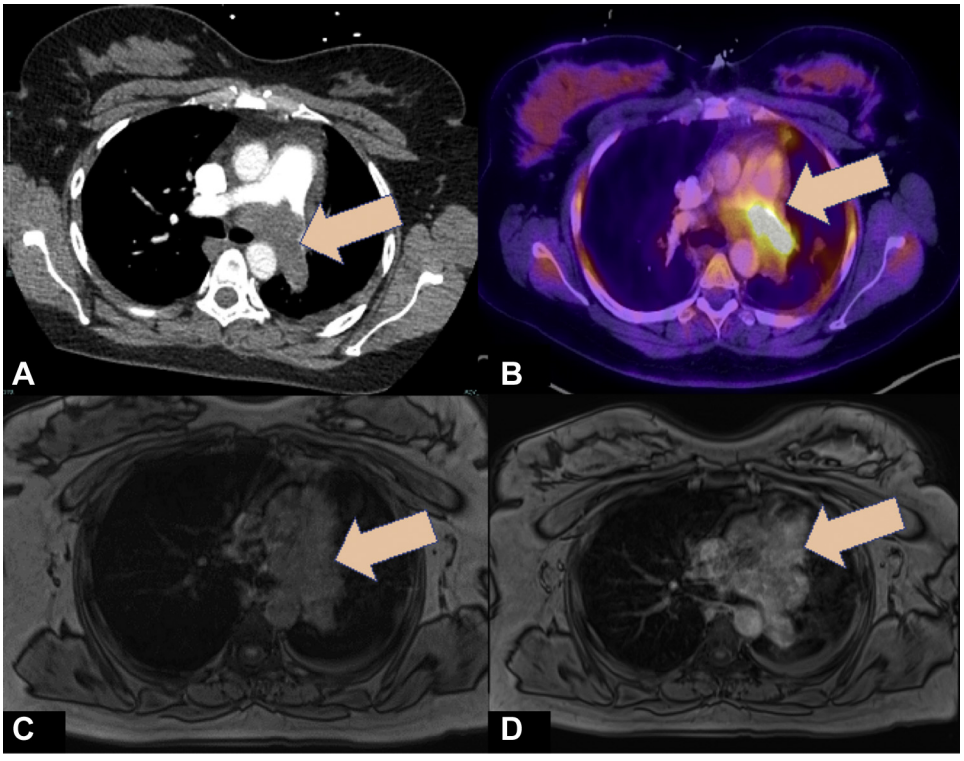
On examination, the patient had a mildly accentuated P2 with an II/VI systolic murmur at the right upper sternal border. Her erythrocyte sedimentation rate was 67 mm/h, and C-reactive protein was 86 mg/l.

Computed tomography scan of the patient's chest showed peripheral bilateral lower lobe pulmonary artery filling defects with wedge-shaped peripheral parenchymal densities in the right middle and lower lobes. The peripheral distribution was suggestive that these may be resolving or chronic (Figure 3A). V/Q scan showed multiple peripheral wedge-shaped perfusion defects bilaterally, with the right worse than the left. The patient was referred for evaluation of PH and consideration for pulmonary endarterectomy. Echocardiography did not show PH, and she was discharged home with rivaroxaban and outpatient hypercoagulable evaluation, which was only positive for heterozygous Factor V Leiden.

The patient was later seen in the heart failure clinic for worsening dyspnea. A right heart catheterization showed moderate PH (Table 1). Pre-admission testing for pulmonary endarterectomy was ordered, including a carotid ultrasound that showed bilateral carotid occlusions. Given the patient's age, previous symptoms, atypical presentation, and the findings of her carotid ultrasound, a whole-body PET scan (Figure 3B) along with MRA of carotids, chest (Figures 3C and 3D), and abdomen were ordered.

MRA showed complete bilateral common carotid artery occlusion with subtle mural thickening of the

FIGURE 2 A 37-Year-Old Woman With Spindle Cell Sarcoma of the Pulmonary Arteries



(A) Computed tomography angiogram of the chest showing saddle pulmonary embolism **(arrow)**. **(B)** Positron emission tomography of the chest showing hypermetabolic mass involving the main pulmonary arteries **(arrow)**. **(C)** Magnetic resonance imaging of the chest without contrast showing an infiltrative mass extending into the left and right main pulmonary arteries **(arrow)**. **(D)** Magnetic resonance imaging of the chest after contrast showing enhancement **(arrow)** of the infiltrating mass with visible intravascular extension.

thoracic aorta suggestive of Takayasu arteritis. This was confirmed on whole-body PET scan.

The patient's condition improved with steroids.

DISCUSSION

Following the 6th World Symposium of PH in 2019, the *European Respiratory Journal* updated the clinical classification and now recommends that group IV be defined as PH due to pulmonary artery obstructions (4). Application of this definition broadens our differential to include obstructive diseases other than CTEPH.

CTEPH, spindle cell sarcoma, and Takayasu arteritis can all be mistaken for the other (5) when causing pulmonary artery occlusion. All 3 study cases presented with exertional dyspnea, peripheral edema, perfusion mismatch on V/Q scan, and filling defects on imaging. However, their management was dictated by the underlying etiology. One patient underwent pulmonary endarterectomy, the second received chemotherapy, and the third required immunosuppression.

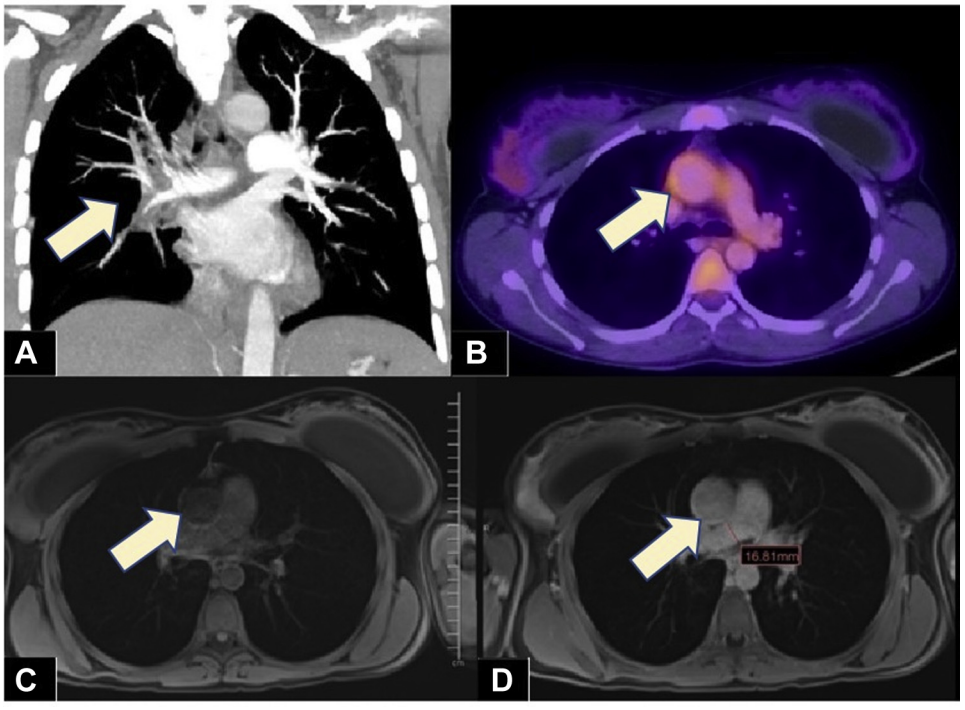
Table 1 highlights the similarities and differences between these diseases.

Many other mimickers also exist such as pulmonary cement embolism after kyphoplasty, and thoughtful evaluation with a multidisciplinary approach involving an experienced radiologist is paramount. Certainty of the diagnosis is crucial as taking the patient to the operating room without the correct diagnosis can lead to significant morbidity and mortality (6).

CONCLUSIONS

Compared with CTEPH, spindle cell sarcomas and Takayasu arteritis are rarer diagnoses with atypical presentations that include PH (2,7). Therefore, while evaluating patients for signs of right heart failure, the index of suspicion for these diseases should be high, especially if there is concern of refractory or worsening obstructive burden while on anticoagulation. Timely diagnosis can help reduce significant morbidity and mortality.

FIGURE 3 **A 32-Year-Old Woman With Takayasu Arteritis**



(A) Computed tomography angiogram of the chest showing a peripheral filling defect in the lower lobe pulmonary artery branches **(arrow)**. **(B)** Positron emission tomography scan of the chest showing hypermetabolic activity **(arrow)** site of mural thickening of the aorta. **(C)** Magnetic resonance angiogram of the chest without contrast showing subtle mural thickening **(arrow)** in the thoracic aorta. **(D)** Magnetic resonance angiogram of the chest after contrast with minimal mural enhancement **(arrow)**.

AUTHOR RELATIONSHIP WITH INDUSTRY

The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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