Multimodality Imaging of Pulmonary Hypertension

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PULMONARY HYPERTENSION

Elevated pulmonary arterial pressures are the result of a spectrum of diseases that have been classified into 5 categories by the World Symposium on Pulmonary Hypertension.[1] The finding of pulmonary hypertension (PH) is usually the first step in a multidisciplinary workup to diagnose the underlying cause, as different etiologies have different treatment algorithms and outcomes. Diagnostic imaging plays a key role in not only the initial evaluation of a patient with PH, but also to assess disease progression or treatment response.

In trying to discover the underlying cause of PH, the diagnostic radiologist often must act as a detective. While some findings, such as varying degrees of enlargement of the pulmonary trunk and remodeling of the right heart, are ubiquitous in patients with PH, it is often the more subtle findings that can help elucidate the cause. These findings may be isolated to the lung parenchyma or may involve the pulmonary or systemic vasculature, heart, or mediastinum. The purpose of this article is to review the various findings of PH on computed tomography (CT) and ventilation/perfusion (V/Q) scans that can help one to differentiate between the various etiologies.

ASSESS THE PULMONARY VASCULATURE

When evaluating the pulmonary vasculature, there are various findings suggestive of PH that are common between the various causes. These include pulmonary artery (PA) enlargement, PA-to-aorta ratio >1, and an increased segmental artery-to-bronchus ratio (Figure 1).[2] While 3 cm is often used as a normal

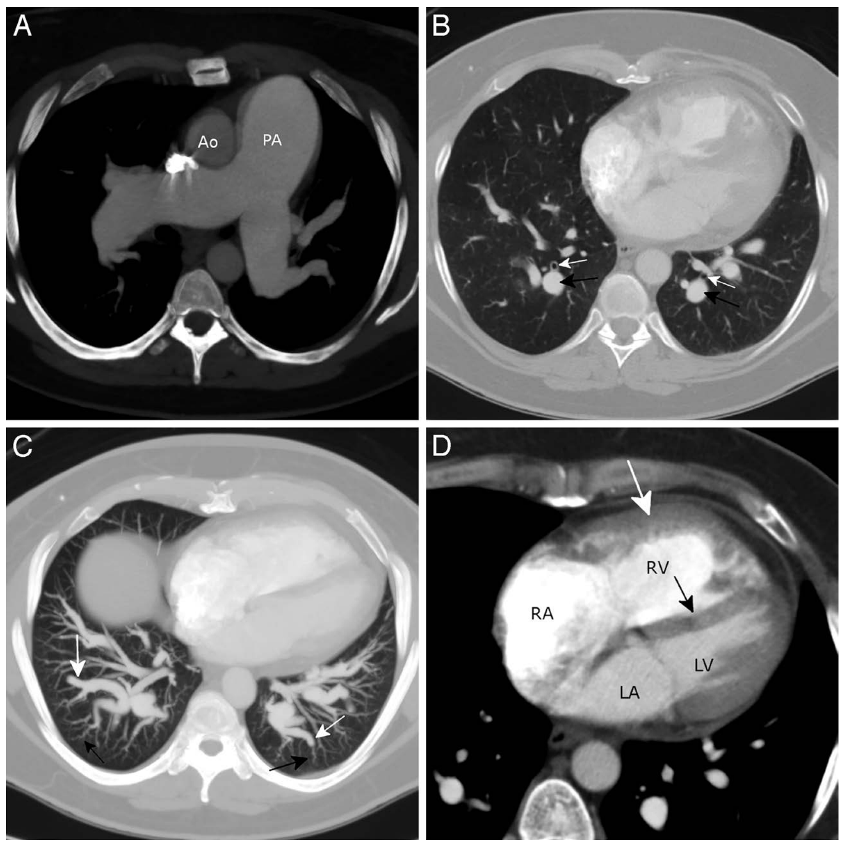

Figure 1: Idiopathic pulmonary arterial hypertension (PAH) in a 35-year-old woman. (**A**) Axial maximum intensity projection (MIP) image shows a dramatically enlarged pulmonary artery (PA) measuring 4.6 cm. This is much larger in size than the adjacent ascending aorta (Ao). (**B**) Examination of the segmental PAs (black arrows) show that they are much larger in diameter compared to the adjacent segmental bronchi (white arrows) consistent with pulmonary hypertension (PH). (**C**) Axial MIP through the lower lobes shows relatively rapid tapering of the PAs as they extend toward the periphery of the lung (white arrows). Some of the vessels have a corkscrew appearance common in cases of severe PH (black arrows). (**D**) Axial image through the heart shows pronounced thickening of the right ventricular (RV) wall (white arrow) due to RV hypertrophy. There is flattening of the interventricular septum (black arrow) toward the left ventricle (LV) due to increased RV pressures. The right atrium (RA) is also larger than the left atrium (LA) due to PH.

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Disclosure: The authors have no relevant personal financial relationships to disclose.

DOI:10.21693/1933-088X-18.4.115

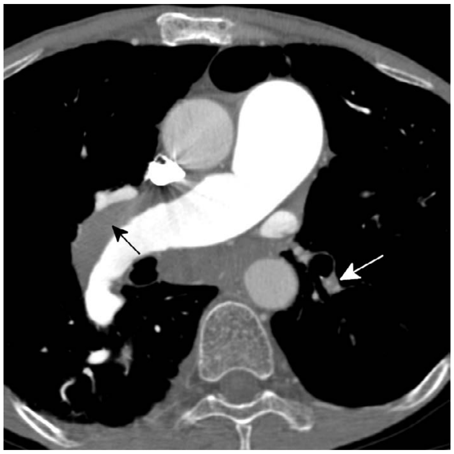

Figure 2: Axial image through the main pulmonary artery (PA) in 60-year-old man with chronic thromboembolic pulmonary hypertension shows narrowing and occlusion of the left lower lobe PA (white arrow). There is layering chronic thrombus in the right main PA (black arrow).

cutoff value for PA size, it is by no means a diagnostic finding as studies have found no direct correlation between PA diameter and mean PA pressure.[3] Multiple factors can affect PA size and include body mass index, systemic hypertension, diabetes, age, and underlying cardiovascular disease.[4] Therefore, if the main PA measures >3 cm, one should also look at size of the segmental arteries and adjacent bronchi. While a segmental PA-to-bronchi ratio greater than 1:1 is weakly correlated with elevated PA pressures,[5] the presence of both parameters has a high specificity for the diagnosis of PH.[3] An alternative and often preferred method is to assess the diameters of the main PA and the aorta. A ratio >1 is commonly associated with PH.[5,6]

It is extremely important to recognize chronic thromboembolic PH (CTEPH) as a cause of PH since invasive treatments can be curative.[7] While disease involving the central vasculature can be quite conspicuous (Figure 2), with large chronic clots layering in and sometimes obliterating the lumen of the main and lobar arteries, disease isolated to the peripheral vasculature can be quite subtle. Close inspection of the segmental and subsegmental pulmonary vasculature on pulmonary angiography CT scans can show abrupt occlusion of PAs with a "pouch" defect, luminal irregularities with eccentric wall thickening, abrupt

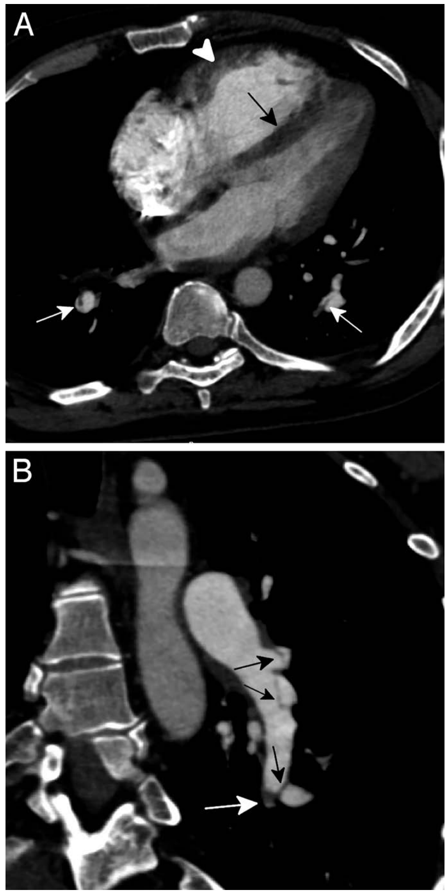

Figure 3: 45-year-old woman with chronic thromboembolic pulmonary hypertension. (**A**) 4-chamber reconstruction shows flattening of the interventricular septum (black arrow) due to elevated right heart pressures and right ventricular hypertrophy (white arrow). Nonocclusive webs are seen in the posterior segmental arteries in the lower lobes (white arrows). (**B**) Coronal oblique reconstruction through the right lower lobe pulmonary artery shows proximal segmental webs (black arrows). In addition, there is occlusion of the posterior segment (white arrow) with a pouchlike appearance.

caliber change (often due to recanalization), and webs or bands (Figure 3).[8–10]

Pulmonary arterial hypertension (PAH, Group 1) includes idiopathic PAH, heritable PAH, drug/toxin-induced PAH, and PAH associated with connective tissue disease, human immunodeficiency virus (HIV) infection, portal hypertension, congenital heart disease, and schistosomiasis.[1] In severe longstanding PAH, in situ thrombus and calcified atherosclerosis along the walls of the PAs may develop due to extremely high pressures (Figure 4). Even among experts, these findings can

Figure 4: In situ thrombus in a 34-year-old woman with pulmonary arterial hypertension (PAH). (**A**) Coronal computed tomography scan shows calcified and noncalcified layering thrombus in the right main pulmonary artery (white arrow). Extensive layering thrombus was also present on the left, a portion of which is seen in a segmental left upper lobe artery (white arrowhead). (**B**) Ventilation/perfusion scan in this patient shows heterogeneous perfusion throughout the lungs common in PAH. However, there are no mismatched defects to suggest chronic thromboembolic pulmonary hypertension.

be mistaken for CTEPH, and given the differences in treatment, this distinction is quite important. One method to distinguish is to evaluate the morphology of the more peripheral vessels. While both can give rise to "corkscrew" appearing vessels and/or peripheral pruning of the vasculature, in PAH the findings are diffuse (Figure 1), while in CTEPH there are often discrete areas of lobar, segmental, and subsegmental obliteration (Figure 2). V/Q scan or dual-energy CT angiography can often help differentiate. In PAH, one will see heterogeneous regional perfusion without mismatch on V/Q scan or occlusive filling defects on CT scan (Figure 4). In CTEPH, V/Q mismatches correspond to vascular territories, and

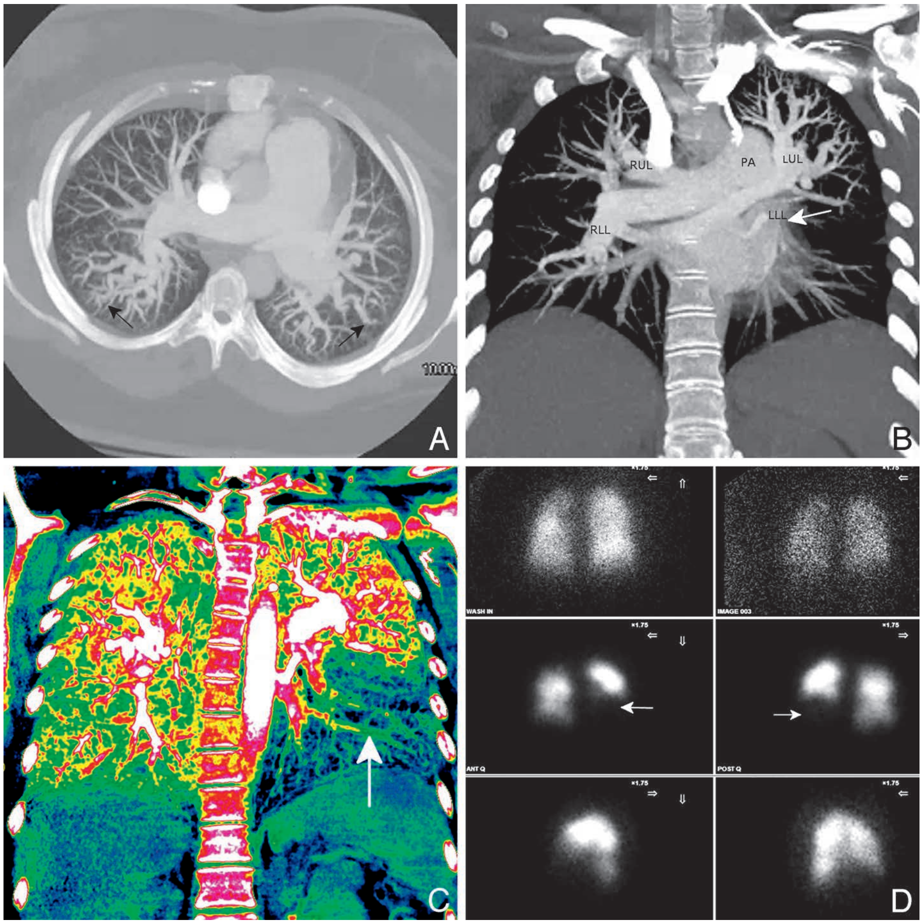

Figure 5: Chronic thromboembolic pulmonary hypertension in a 45-year-old woman. (**A**) Axial maximum intensity projection (MIP) image shows an enlarged pulmonary artery (PA) and multiple corkscrew-shaped vessels due to pulmonary hypertension (PH). (**B**) Coronal MIP shows complete occlusion of the left lower lobe PA due to chronic thrombus (white arrow). There is no associated arterial perfusion to the left lower lobe (LLL). The visualized vessels in the LLL represent pulmonary veins. Due to this occlusion, there is compensatory engorgement of the PAs in the left upper lobe (LUL) when compared to the relatively normal branches in the right upper lobe (RUL) and right lower lobe (RLL). The main PA is enlarged. (**C**) Associated coronal image from a dual-energy computed tomograpy scan shows lack of perfusion to the LLL (white arrow) corresponding to findings on (**D**) ventilation/perfusion scan (white arrows).

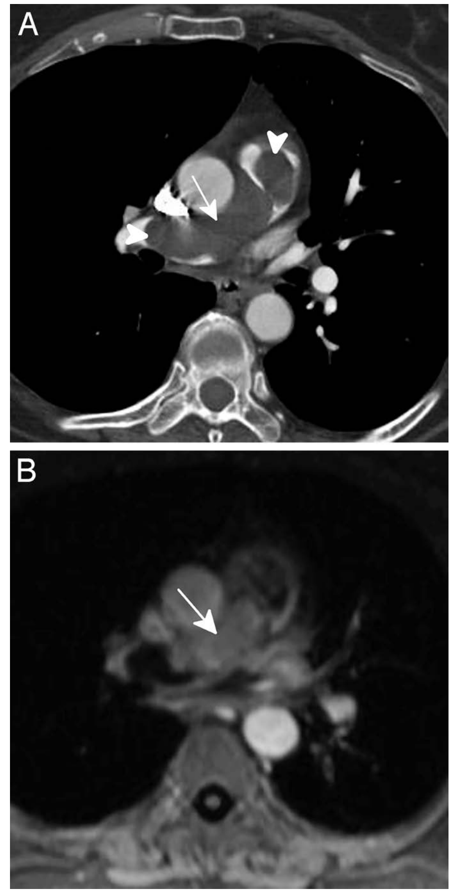

Figure 6: Pulmonary artery (PA) sarcoma in a 68-year-old man. (**A**) Axial computed tomography scan shows a large mass filling the right PA (white arrow) and extending proximally toward the right ventricular outflow track (white arrowhead). The edges of the mass are curvilinear which is common with PA sarcomas. The patient was initially treated with anticoagulation without effect. (**B**) Axial magnetic resonance image through the same level shows intense enhancement in the center of the mass (white arrow) consistent with a sarcoma. A thrombus would not be expected to enhance.

discrete occlusive lobar, segmental, and subsegmental filling defects can often be seen on CT (Figure 5). Another method of differentiation is the evaluation of the pulmonary parenchyma, as discussed below, which show distinct changes associated with the underlying pathophysiology.

Another less common mimic of CTEPH is a PA sarcoma. Differentiation between these two entities can be difficult, which is highlighted by the fact that most PA sarcomas are initially misinterpreted as intravascular thrombus.[11,12] However, certain findings, if present, are suggestive of a sarcoma, including a soft tissue mass nearly filling and potentially expanding the lumen of the pulmonary trunk, left PA, or right PA with protrusion of the proximal end of this mass towards the right ventricular (RV) outflow tract (Figure 6).[11] The ends of the soft tissue mass are often curvilinear. The mass can demonstrate enhancement on portal-venous phase of imaging. Positron emission tomography-CT and magnetic resonance imaging may need to be performed to differentiate in complex cases.

EVALUATE THE HEART AND SYSTEMIC VASCULATURE

In addition to remodeling the PAs, chronically elevated pulmonary pressures cause remodeling of the right heart. Findings such as RV hypertrophy (free wall thickness >4 mm), RV dilatation (>1:1 ratio between RV and left ventricle diameter on axial images), and flattening or leftward deviation of the interventricular septum[13] are associated with increased pulmonary pressures (Figures 1 and 2). PH can lead to RV failure, which is often associated with dilation of the inferior vena cava with reflux of contrast into the hepatic veins (Figure 7). Prolonged hepatic congestion can lead to cirrhosis.[14]

The presence of a dilated right heart (with or without hypertrophy) should always prompt a careful search for an undiagnosed intracardiac or extracardiac

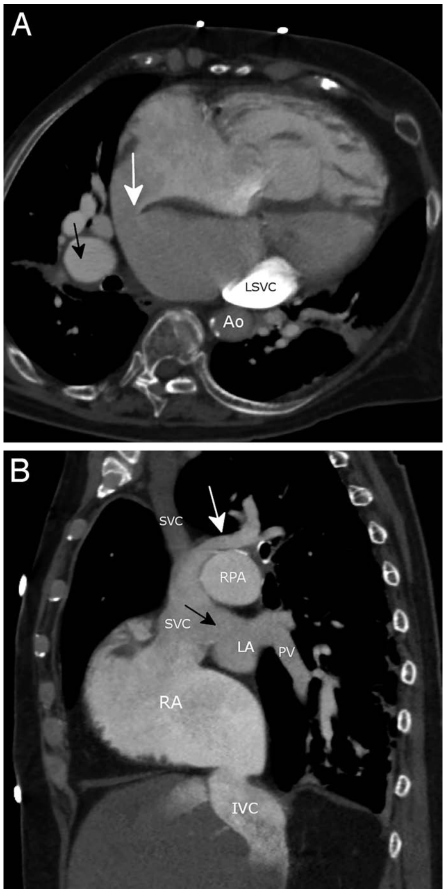

Figure 7: 67-year-old woman presenting to the emergency department with shortness of breath. (**A**) 4-chamber image through the heart from a pulmonary embolism computed tomography angiography shows a dilated right heart and right lobe pulmonary artery (black arrow) consistent with pulmonary hypertension. A defect is present in the superolateral and posterior aspect of the interventricular septum consistent with a sinus venosus atrial septal defect (SV-ASD). Incidental note is made of a left-sided superior vena cava (LSVC). (**B**) Sagittal oblique image through the heart shows a dilated right atrium (RA) and reflux of contrast into a distended inferior vena cava (IVC) due to elevated right heart pressures. The right-sided superior vena cava (SVC) is mildly enlarged centrally. An SV-ASD (black arrow) is present along the inferior aspect of the SVC near its junction with the RA allowing for communication between the right heart and the left atrium (LA). The right inferior pulmonary vein (PV) drains into the LA. The right superior pulmonary vein (white arrows) anomalously drains into the SVC (white arrow) consistent with a partial anomalous pulmonary venous return. The 2 anomalies coexist in the majority of cases of a SV-ASD.

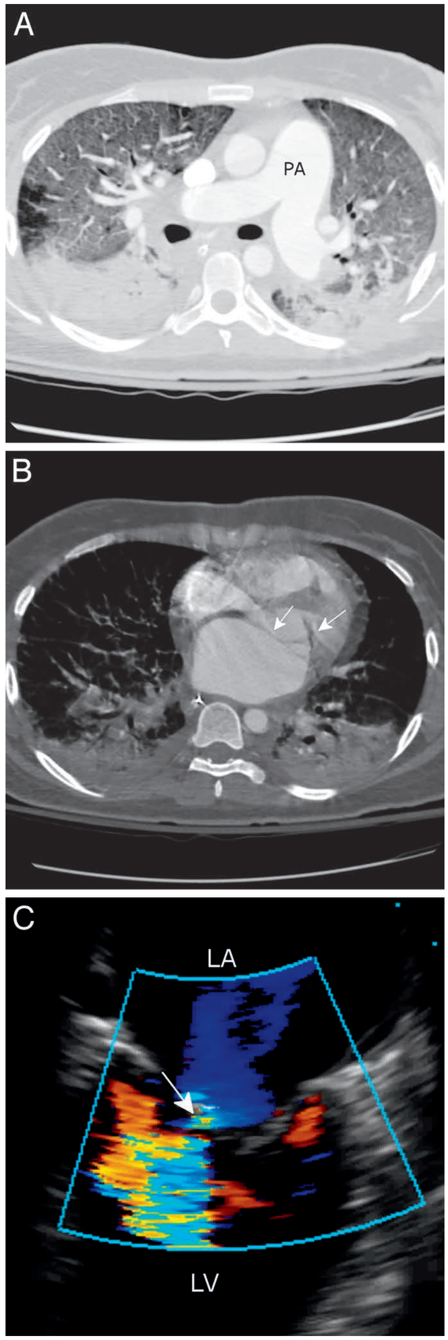

Figure 8: Longstanding mitral stenosis (MS) leading to pulmonary hypertension in a 70-year-old woman. (**A**) Axial computed tomography image shows a dilated main pulmonary artery (PA). There is diffuse ground glass opacity with septal thickening due to pulmonary edema. (**B**) Axial image through the heart shows a dilated left atrium with thickening of the mitral valve leaflets (white arrows). (**C**) Doppler image from an echocardiogram shows a high velocity jet flowing from the left atrium (LA) into the left ventricle (LV) through a severely stenotic mitral valve with a markedly reduced opening area (white arrow).

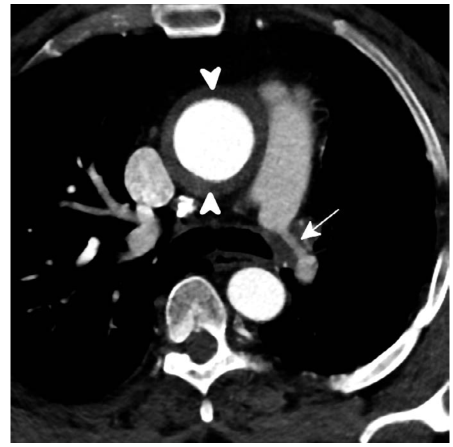

Figure 9: Axial computed tomography in a 20-year-old woman with Takayasu's arteritis shows marked narrowing of the left pulmonary artery (white arrow) due to vasculitis. The right pulmonary artery was also narrowed. Circumferential thickening of the wall of the aorta (white arrowheads) helps make the diagnosis of a large vessel vasculitis.

shunt as the cause of PH (Figure 7). Evaluation of the cardiac valves, even on a study performed without cardiac electrocardiogram gating, should be performed. Mitral stenosis, which manifests as thickening and calcification of the valve leaflets with severe left atrial dilation, can lead to PH (Figure 8). The aorta and branch vessels should also be assessed for irregularities, such as areas of stenosis and aneurysmal dilation, that may signify an underlying vasculitis as the cause of the PH (Figure 9).

ASSESS THE PARENCHYMA

Interlobular Septal Thickening

Interlobular septal thickening is most often seen in PH due to left heart failure. Smooth septal thickening represents the increased interstitial congestion/edema of the pulmonary veins and lymphatics related to increased left atrial pressures (Figure 8). Ultimately, the passive backward transmission of increased left atrial filling pressures leads to the pulmonary vascular remodeling and right heart failure associated with PH. Irregular septal thickening can be seen along with reticulation with fibrosis, and nodular septal thickening can be seen with sarcoidosis and lymphangitic disease.[15]

In the absence of left heart failure/enlargement, interlobular septal thickening associated with PAH is the hallmark of postcapillary congestion seen in patients with pulmonary veno-occlusive disease (PVOD). PVOD is characterized by intimal fibrosis, which leads to the occlusion and narrowing of pulmonary veins from the postcapillary level and beyond. As a consequence, the lymphatic channels within the interlobular septa dilate and become edematous, leading to the

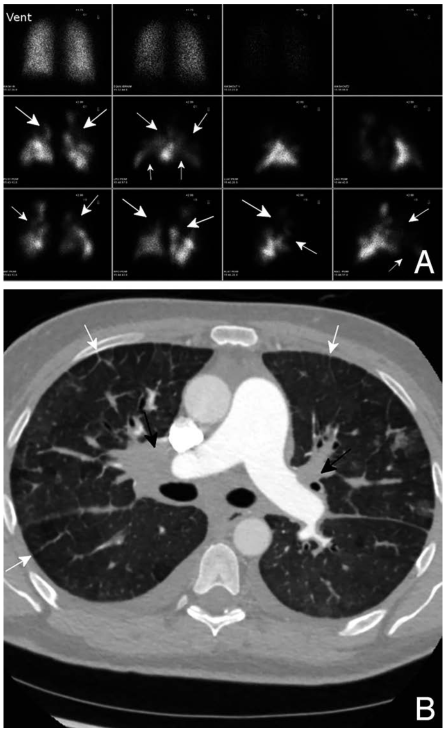

Figure 10: Pulmonary veno-occlusive disease (PVOD) in a 34-year-old woman. (**A**) Ventilation/perfusion scan shows multiple areas of mismatch leading to a high-probability diagnosis of pulmonary emboli. (**B**) Subsequent computed tomography pulmonary angiography shows an enlarged main pulmonary artery but no acute or chronic pulmonary emboli. However, there is diffuse septal thickening (white arrows), bilateral enlarged hilar lymph nodes (black arrows), and a few scattered areas of ground glass opacity. The findings were highly suggestive of PVOD, which was confirmed on biopsy.

smooth interlobular septal thickening classically seen on CT (Figure 10) and the septal thickening (Kerley B lines) seen on radiographs.[16,17] In PVOD, smooth interlobular septal thickening is often associated with scattered ground glass opacities, pleural effusions, and mediastinal lymphadenopathy.[16–18] V/Q scans are regarded as nonspecific for PVOD and can have a wide range of interpretations ranging from normal to findings of "high probability" with mismatched perfusion defects.[16,19]

PVOD can be classified as idiopathic or associated to other conditions, including systemic sclerosis, HIV infection, pulmonary Langerhans histiocytosis, and sarcoidosis. PVOD is likely underestimated in sarcoid-associated PH (SAPH) and radiographically seen as smooth interlobular septal thickening with associated patchy areas of ground

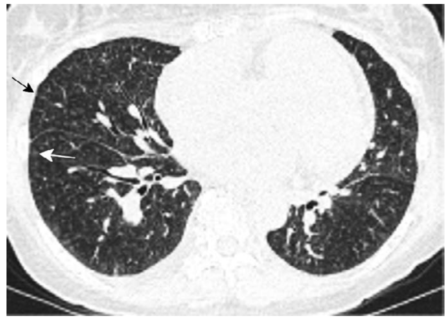

Figure 11: Axial computed tomography image in a 59-year-old woman with dyspnea demonstrates diffuse centrilobular nodularity (white arrow) due to pulmonary capillary hemangiomatosis (PCH). Associated septal thickening is seen but to a lesser extent than in most cases of pulmonary veno-occlusive disease (PVOD). Given that PCH/PVOD share similar hemodynamic, clinical, and radiographic findings, revised guidelines recommend that PVOD and PCH be combined into a single diagnosis called "PAH with overt features of venous/capillaries (PVOD/PCH) involvement."

glass and/or venous infarcts.[20] The pathophysiology of SAPH is complex and often multifactorial with 40% to 60% of patients with SAPH having no radiographic evidence of fibrosis.[20]

Nodules

In an untreated patient with PAH, the presence of hazy centrilobular nodularity should raise the possibility for pulmonary capillary hemangiomatosis (PCH; Figure 11). These nodules are often diffuse in nature, involve all lobes, and spare the lung periphery.[16,21] Although the distinction between PCH and PVOD on imaging can be difficult, septal thickening and pleural effusions are less common in PCH.[21] In PCH, they represent the capillary proliferation within the alveolar walls; however, in PVOD these nodules represent the looplike capillary engorgement seen secondary to pulmonary venous narrowing and stenosis.[16] Given that PCH/PVOD share similar hemodynamic, clinical, and radiographic findings, revised guidelines recommend that PAH with PVOD/PCH belong to a subgroup of Group 1 PH (subgroup 1.6) for the spectrum of pulmonary vascular disease known as "PAH with overt features of venous/capillaries (PVOD/PCH) involvement," as opposed to two distinct entities.[22]

In patients with PAH not related to PVOD/PCH, hazy ground glass centrilobular nodules can occur and can mimic findings seen in PCH (Figure 12).[23] While the nodules in PCH represent

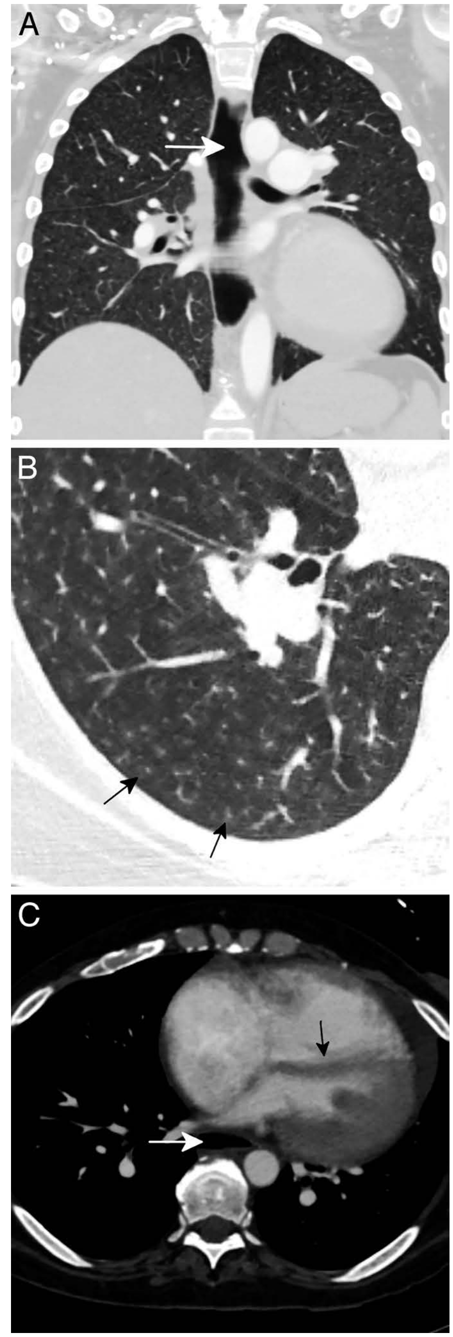

Figure 12: Pulmonary arterial hypertension with ground glass nodules in a 52-year-old woman with scleroderma. (**A**) Coronal image shows a diffusely dilated esophagus (white arrow). (**B**) Innumerable small ground glass centrilobular nodules are present, which are better seen on a coned down image through the right lower lobe (black arrows). (**C**) Axial image through the heart shows marked dilated and hypertrophy of the right ventricle with flattening of the interventicular septum (black arrow). The dilated esophagus (white arrow) helps suggest the diagnosis of scleroderma.

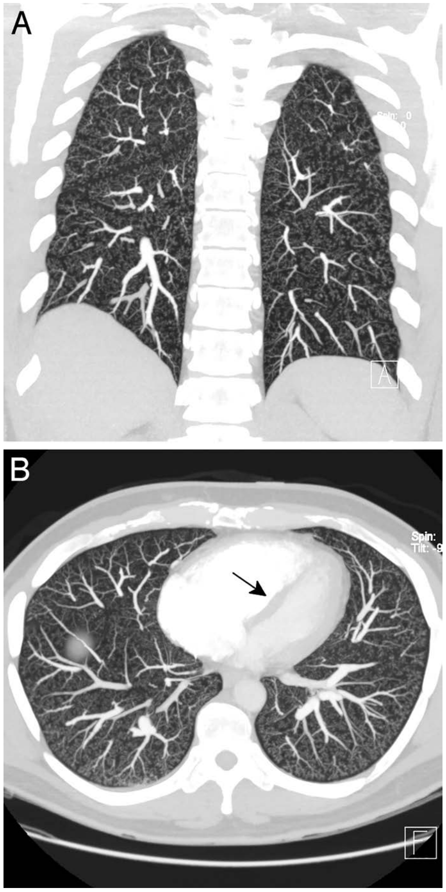

Figure 13: Excipient lung disease in a 25-year-old man who injected crushed OxyContin tablets. (**A**) Coronal maximum intensity projection (MIP) image shows innumerable well-defined centrilobular nodules throughout the entire lung. There is conspicuous sparing of the fissures due to the centrilobular distribution. These nodules are due to microemboli of excipient fragments into the pulmonary arterioles leading to a granulomatous reaction. Unlike the centrilobular nodules seen in pulmonary arterial hypertension, these tend to be more well defined. (**B**) Axial MIP through the heart shows marked dilated and hypertrophy of the right ventricle with flattening of the interventicular septum (black arrow). Innumerable well-defined centrilobular nodules are again seen.

capillary proliferation in the alveolar walls, this finding in PAH has been attributed to periarteriolar cholesterol granulomas, large plexogenic arterial lesions, or small systemic collateral arteries.[24,25] Distinction between the two can be difficult and may require biopsy. However, hazy centrilobular ground glass nodules are uncommon in other causes of PH.[13]

Excipient lung disease is another rare cause of centrilobular nodules in the setting of PH. This is secondary to the intravenous injection of crushed oral tablets, usually narcotic pain killers. Excipients, including talc, microcrystalline cellulose, crospovidone, and starch, are insoluble inert filler materials that bind and protect the active drug.[26] When the drug is injected, this material embolizes into the pulmonary arterioles, inciting a granulomatous reaction in and around the vessel. As the pulmonary arteriole is in the center of the pulmonary lobule, this granulomatous reaction leads to diffuse ground glass nodules which involve the entire lung from the apices to the bases. In comparison to the centrilobular nodules seen in PAH and PCH, these nodules tend to be small and well defined (Figure 13).

Sarcoidosis is a multisystem disease characterized by noncaseating granulomatous inflammation which often manifests along and within the pulmonary vessels and airways as well as the subpleural interstitium. This inflammation creates small nodules in a perilympathic distribution which are distinct from the centrilobular nodules seen on PAH and PCH (Figure 14). As discussed below, symmetric mediastinal and hilar lymphadenopathy and perihilar conglomerate fibrotic masses may develop over time. Sarcoidosis may contribute to PH via capillary destruction and alveolar hypoxia/hypoxic pulmonary vasoconstriction in the setting of fibrosis in late-stage (class 4) disease; however, the degree of PH in these patients is out of proportion to the degree of fibrosis in many patients, implicating additional mechanisms of SAPH including pulmonary vascular infiltration/obliteration by granulomatous inflammation, altered flow dynamics due to lymphadenopathy, and cardiac/extracardiac disease.[27,28]

Mosaicism

Specific patterns of a mosaic attenuation, defined as regional heterogeneity in pulmonary parenchymal attenuation, are characteristic for certain types of PH. Although any cause of PH can lead to a mosaic attenuation, PAH and CTEPH are the most common.[29] Mosaic attenuation, also referred to as "mosaic perfusion," reflects regional difference in lung perfusion in patients with PH.[30] In PAH, mosaicism often manifests as

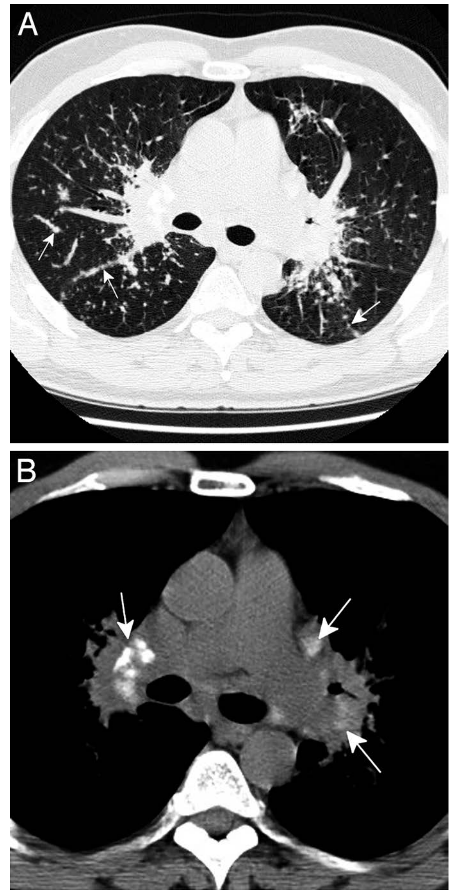

Figure 14: Pulmonary hypertension in a 49-year-old man with sarcoidosis. (**A**) Axial computed tomography in lung windows shows conglomerate perihilar soft tissue with extensive nodularity along the perilymphatic interstitial (white arrows). (**B**) Soft tissue window at the same level shows extensive symmetric mediastinal and hilar lymphadenopathy (white arrows). Many of the lymph nodes are calcified.

focal perivascular ground glass opacities, or small, scattered areas of increased attenuation often confined to center of the secondary pulmonary lobule[31] (Figure 15). In some instances, the perivascular hyperattenuation can appear as subtle ground glass centrilobular nodules as discussed above.

Compared to the mosaic pattern seen in PAH, the pattern in CTEPH often manifests as larger, regional areas of decreased attenuation that correspond to a vascular territory with associated narrowing or occlusion of the supplying vessel (Figure 15).[32,33] In severe cases of CTEPH, in addition to areas of hypoperfusion, segmental or subsegmental areas of hyperperfusion and increased attenuation can be present and reflect

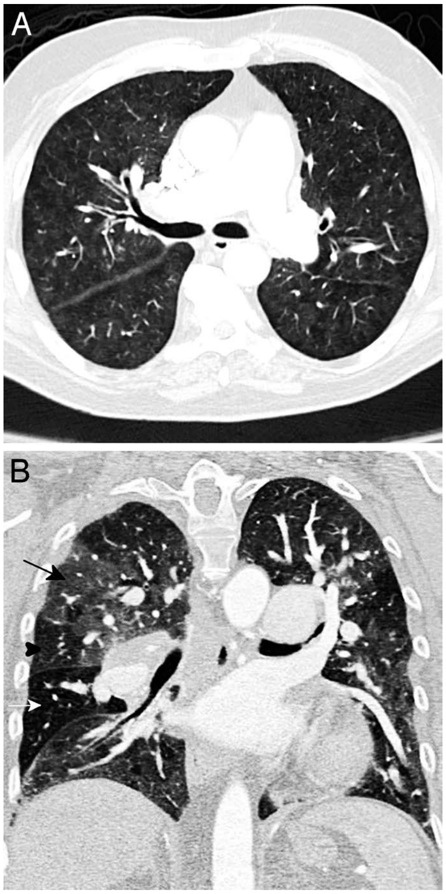

Figure 15: Comparison of mosaic attenuation. (**A**) 33-year-old man with pulmonary arterial hypertension shows lobular areas of ground glass opacity directly adjacent to more lucent lung creating a mosaic attenuation. (**B**) In comparison, in chronic thromboembolic pulmonary hypertension, the mosaicism tends to be more well defined and corresponds to vascular distributions. An area of normal attenuation (black arrowhead) lies directly adjacent to an area of lobar, segmental, or subsegmental hypoperfusion (white arrow) inferiorly and hyperperfusion (black arrow), due to compensatory increased flow, superiorly.

shunting of blood to these nonoccluded regions. Within these areas of hyperperfusion, the corresponding vasculature is often engorged and increased in size compared to the adjacent bronchus reflecting increased blood flow (Figure 5).

PH due to left heart disease and PH due to lung disease and/or hypoxia are less likely to lead to a mosaic pattern.[8] These can usually be distinguished on imaging by the presence of ancillary findings, for example, dilated left atrium in the setting of mitral valve disease, presence of severe emphysema, fibrosis, or other lung disease, as discussed below. Therefore, the combination of PA enlargement and mosaic attenuation should prompt a careful search for ancillary findings to help narrow the differential diagnosis.

Emphysema

The prevalence of PH in chronic obstructive pulmonary disease (COPD) varies from 50% in mild disease to 70% to 90% in severe disease.[34] The pathogenesis of PH in emphysema is multifactorial, resulting from destruction of the pulmonary vascular bed, vascular remodeling, endothelial dysfunction, and thrombosis.[34,35] The presence of PH is a poor prognostic indicator, and the 5-year survival rate was 36% for patients with a mean pulmonary arterial pressure >25 mm Hg in one series.[36] Over time, PH in patients with emphysema can lead to cor pulmonale and subsequent right heart failure[37] (Figure 16).

As emphysema is smoking related, findings are generally upper-lobe predominant. On CT, emphysema can be identified by abnormal lucency with a density less than −950 Hounsfield Units (HU), compared with a normal range −770 to −885 HU for lung parenchyma. The predominant finding of centrilobular emphysema is abnormal lucency in the central portion of secondary pulmonary lobules without a visible wall separating abnormal from normal lung parenchyma; the absence of a surrounding wall differentiates centrilobular emphysema from cystic lung disease. In severe disease, these spaces become extensive and confluent. Paraseptal emphysema typically involves the distal airways and is recognized by its involvement of the subpleural lung. Unlike centrilobular emphysema, the area of focal lucency may be surrounded by a thin wall. An area of paraseptal emphysema >1 cm is termed a bulla. Finally, in panlobular emphysema, there is uniform destruction of the pulmonary lobule; unlike other types of emphysema, panlobular emphysema tends to affect the entire lung uniformly or may be more basal predominant.

V/Q scintigraphy typically demonstrates in homogenous but matched upper lobe ventilation and perfusion

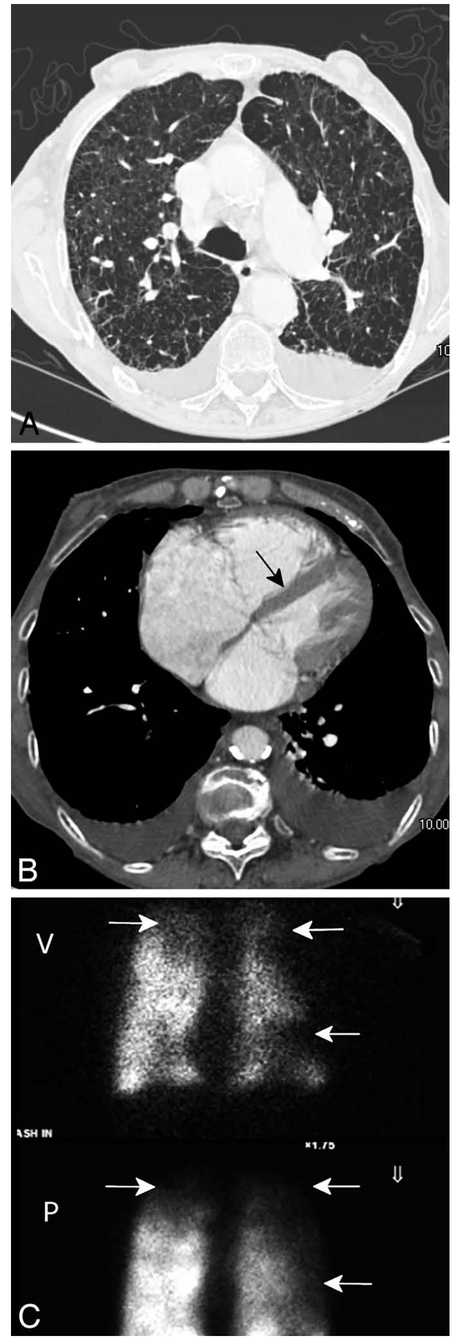

Figure 16: Pulmonary hypertension and cor pulmonale in a 75-year-old man with severe emphysema. (**A**) Axial computed tomography in lung windows shows extensive centrilobular emphysema. (**B**) Axial image through the heart shows right ventricular hypertrophy and dilation with flattening of the interventricular septum. The right atrium is also enlarged. (**C**) Ventilation/perfusion scan shows hyperinflated lungs with matched ventilation (V) and perfusion (P) defects, most notably in the upper lobes (white arrows) where the emphysema is most severe.

corresponding to areas of emphysema.[38] In some cases, a “stripe sign” may be seen, with centrally decreased perfusion and peripherally preserved perfusion, which is specific for centrilobular emphysema in COPD patients.[39]

Fibrosis

Fibrosis is the common terminal stage in multiple interstitial lung diseases. Mechanisms of fibrosis related to growth factor release, fibroblast activation, and alterations to the endothelin system appear to be shared with the pathogenesis of PH.[40] While nearly any fibrotic lung disease can be associated with PH, those most commonly associated with PH include collagen vascular disease (particularly systemic sclerosis and rheumatoid arthritis), idiopathic pulmonary fibrosis, and sarcoidosis.[40]

On both chest x-ray and high-resolution CT, fibrosis usually presents as areas of peripheral reticulation with associated volume loss. More severe fibrosis results in pronounced architectural distortion and widening of the airways, known as traction bronchiectasis. Severe fibrosis also results in honeycombing, represented by multilayered 3 mm to 2 cm cysts in a subpleural location. Two specific histologic patterns of lung disease which demonstrate some of these findings are usual interstitial pneumonia (UIP) and nonspecific interstitial pneumonia (NSIP).

A UIP pattern is seen in idiopathic pulmonary fibrosis (Figure 17) in addition to collagen vascular diseases, especially rheumatoid arthritis and scleroderma. This pattern is characterized by subpleural lower-lobe predominant peripheral reticulation, traction bronchiectasis, honeycombing, and extensive volume loss.[41] NSIP, which is the most common pattern of fibrotic lung disease seen in patients with collagen vascular diseases, usually demonstrates symmetric lower-lobe predominant peribronchiolar ground glass opacity extending toward the periphery with associated reticulation and traction bronchiectasis.[42] A characteristic feature of NSIP is the presence of subpleural sparing, distinguishing it from a UIP pattern (Figure 17). Differentiation between these two patterns can be difficult even for the most experienced radiologist.

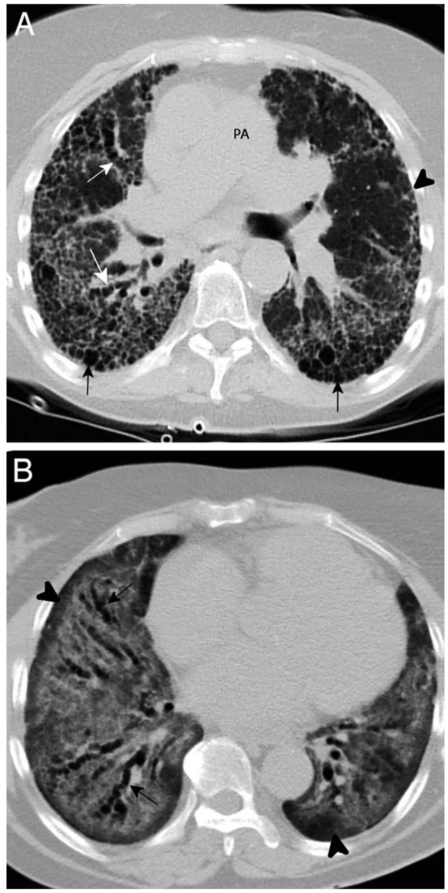

Figure 17: Pulmonary hypertension associated with fibrosis. (**A**) Axial oblique image in a 63-year-old woman with idiopathic pulmonary fibrosis shows an enlarged pulmonary artery (PA) and a typical usual interstitial pneumonia pattern with lower lobe and subpleural predominant fibrosis as indicated by the presence reticulation (black arrowhead), traction bronchiectasis (white arrows), and honeycombing (black arrows). (**B**) Axial image in a 40-year-old woman with mixed connective tissue disease shows perihilar ground glass opacity with traction bronchiectasis (black arrows) and subpleural sparing (black arrowheads) characteristic of a nonspecific interstitial pneumonia pattern.

Compared to the lower-lobe predominant fibrosis seen in UIP and NSIP, the fibrosis in sarcoid is usually perihilar and upper lobe predominant (Figure 18). Perilymphatic nodules may be visualized in areas adjacent to the fibrosis. Less common parenchymal findings include fibrocystic lesions, which manifest as irregular bronchiectatic and cystic changes with an upper lobe predominance. Pulmonary V/Q scintigraphy is usually noncontributory in these patients, and on occasion, vascular narrowing or occlusion due to surrounding lymphadenopathy or perihilar fibrosis can mimic findings in CTEPH (Figure 18). Gallium single photon emission computed tomography imaging may also play a role in diagnosing sarcoidosis but is beyond the scope of this article.

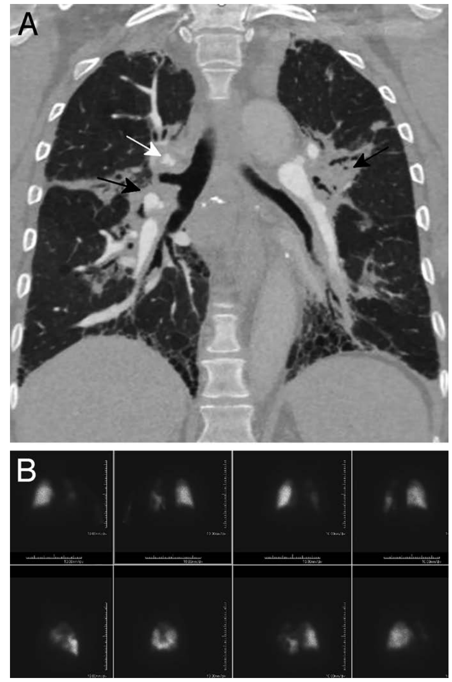

Figure 18: Pulmonary hypertension in fibrotic sarcoid. (**A**) Coronal image in a 57-year-old man with sarcoid shows extensive perihilar fibrotic changes (black arrows) with conglomerate soft tissue and traction bronchiectasis. In certain areas, the pulmonary artery branches are narrowed by the surrounding fibrosis (white arrow). No pulmonary emboli were present. (**B**) These areas of vascular compression led to multiple areas of ventilation/perfusion (V/Q) mismatch on V/Q scan which was interpreted as a high probability for pulmonary emboli.

MEDIASTINUM

Careful evaluation of the mediastinum is important in patients undergoing imaging workup for PH, as mediastinal abnormalities may implicate alternative, multifactorial diagnoses. Fibrosing mediastinitis (FM) is a rare but serious—and sometimes fatal—disease with focal granulomatous and diffuse nongranulomatous subtypes; diffuse disease is characterized by florid inflammation and fibrous proliferation within the mediastinum, which results in encasement and extrinsic compression of mediastinal structures including airways and vascular structures.[43–45] Vascular manifestations most commonly involve the superior

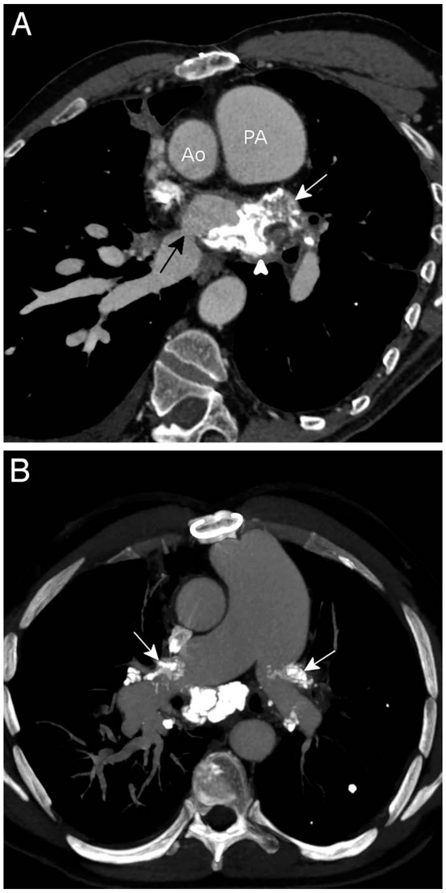

Figure 19: Pulmonary hypertension in fibrosing mediastinitis (FM). (**A**) Axial oblique image through the left atrium shows a confluent, predominantly calcified soft tissue mass surrounding and compressing the left atrium due to FM. The ostia of the left superior (white arrow), left inferior (white arrowhead), and right superior (not shown) pulmonary veins were completely obstructed by FM. The ostium of the right inferior pulmonary vein is severely narrowed but patent (black arrow). The pronounced pulmonary venous obstruction was the cause of the patient's severe pulmonary hypertension as evidenced by the markedly enlarged main pulmonary artery (PA) which is much larger than the adjacent ascending aorta (Ao). (**B**) Axial oblique maximum intensity projection image shows a markedly enlarged main PA. Confluent predominantly calcified soft tissue fills the mediastinum with mild narrowing of the left and right main PAs (white arrows). The patient died a few months after the exam.

vena cava (SVC) which may result in SVC syndrome. Pulmonary arterial/venous stenoses or even occlusions can be seen in these patients, which can lead to precapillary and/or postcapillary forms of PH (Figure 19).[44]

Focal/granulomatous FM is most often associated with *Histoplasma* or tuberculosis infection, with rupture of the encapsulated granuloma thought to trigger an intense fibroinflammatory response in some patients, but diffuse disease can be secondary to myriad causes including trauma, prior radiation therapy, autoimmune disease (eg, rheumatoid arthritis and systemic lupus erythematosus), sarcoidosis, Behçet Disease, sclerosing neoplasm, or may be idiopathic.[45]

Classically, CT will demonstrate an infiltrative middle mediastinal soft tissue mass with encasement of adjacent structures (Figure 19). Pulmonary arterial abnormalities are typically central in distribution (ie, main, lobar, or segmental) with architectural distortion secondary to fibrosis, inducing irregular arterial narrowing and peripheral soft tissue thickening. Pulmonary venous involvement may be characterized by soft tissue encasement of central pulmonary veins, juxta-ostial or perivenous masslike tissue resulting in stenosis or occlusion, and can be quite dramatic with a pronounced, abrupt "shoulder." Findings of pulmonary edema, including interlobular septal/peribronchial thickening and centrilobular ground-glass opacities, are common in these patients and, when due to PA or vein stenosis, may be geographic depending on the level of obstruction.[44] Secondary pulmonary venous infarcts manifest like pulmonary infarcts associated with acute pulmonary embolism, as peripheral, wedge-shaped opacities that may demonstrate central clearing. Scarring secondary to chronic infarcts often demonstrates an atypical distribution with parenchymal bands and peripheral/subpleural reticulation.[46] Other CT findings associated with FM include diffuse mediastinal fat stranding/inflammatory change, calcified mediastinal/hilar lymph nodes, and pleural and/or pericardial effusions.

FM can mimic both CTEPH and vasculitis. The geographic areas of perfusion abnormality seen in FM may mimic CTEPH on V/Q scintigraphy, yet this distinction is crucial. While peripheral lobar thrombus in CTEPH may demonstrate a similar appearance, the other characteristic CTEPH findings of weblike filling defects and segmental and subsegmental occlusions will be absent in FM. There is no adequate medical treatment for FM, and currently favored treatment modalities include endovascular angioplasty and/or stenting versus meticulous surgical dissection; however, attempted surgical dissection of the fibrotic rind seen in FM can be extremely difficult and is associated with high perioperative morbidity/mortality.[45] If these patients are misdiagnosed as having CTEPH, attempted pulmonary thromboendarterectomy can have devastating consequences. Distinguishing FM from vasculitis is also important, and the presence of alternating tapering/dilation of vessels and/or extrapulmonary vascular structures are highly suggestive of a vasculitis.

Mediastinal involvement with sarcoidosis most typically manifests as relatively symmetric enlargement of hilar and mediastinal lymph nodes with or without concomitant pulmonary parenchymal findings depending on the stage of the disease (Figure 14). Hilar and mediastinal lymphadenopathy is also a common finding in PVOD and is secondary to lymphatic congestion and vascular transformation of the sinuses, intrasinusal hemorrhage, and lymphoid follicular hyperplasia[47] (Figure 10). However, PVOD and sarcoid can usually be distinguished from one another through associated parenchymal findings as discussed above.

Finally, specific attention should be given to the esophagus. As mentioned above, FM may result in esophageal compression and upstream dilation. Alternatively, a patulous/dilated esophagus may be seen in the setting of scleroderma, a rare multisystem autoimmune disease that includes PAH in approximately 13% of patients (Figure 12). Interestingly, while patients with PAH related to scleroderma typically have slightly lower mean pulmonary arterial pressure compared to patients with idiopathic PAH, they have higher morbidity/mortality, poorer response to therapy, and worse outcomes than patients with idiopathic PAH, though the pathophysiology and mechanisms underlying these differences have not been entirely elucidated.[48]

CONCLUSION

The diagnosis of PH should initiate a multidisciplinary workup to elucidate an underlying cause. Imaging, especially CT, plays an integral part in the initial evaluation. Careful assessment of the pulmonary and systemic vasculature, heart, lungs, and mediastinum allows for one to piece together various clues and make the correct diagnosis, optimizing patient care.

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