

Dyspnea due to pulmonary vessel arteritis

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Pulmonary arteritis is a rare cause of pulmonary hypertension. Causes of pulmonary arteritis can be divided into primary and secondary, as well as classified according to vessel size. Only large vessel vasculitis is associated with pulmonary hypertension; primary forms include Takayasu arteritis and giant cell arteritis. The diagnosis of pulmonary arteritis can be challenging and the associated morbidity is serious without prompt, directed treatment. The authors present a case involving a 48-year-old First Nations man presenting with a six-month history of exertional dyspnea and severe stenosis of the left pulmonary artery, who was ultimately diagnosed with pulmonary arteritis related to large vessel vasculitis.

Key Words: Arteritis; Large vessel; Pulmonary artery; Pulmonary hypertension; Pulmonary vasculitis; Stenosis

Une dyspnée causée par l'artérite des vaisseaux pulmonaires

L'artérite pulmonaire est une rare cause d'hypertension pulmonaire. On peut l'expliquer par des causes primaire ou secondaire, et la classer selon le calibre des vaisseaux. Seule la vascularite à gros vaisseaux s'associe à l'hypertension pulmonaire. Ses formes primaires sont l'artérite de Takayasu et l'artérite à cellules géantes. Le diagnostic d'artérite pulmonaire peut être difficile à poser, et la morbidité qui s'y associe est grave si elle ne fait pas l'objet d'un traitement ciblé et rapide. Les auteurs présentent le cas d'un homme des Premières nations de 48 ans qui a consulté parce qu'il faisait de la dyspnée à l'effort depuis six mois. Il avait une grave sténose de l'artère pulmonaire gauche et a fini par obtenir un diagnostic d'artérite pulmonaire liée à une vascularite à gros vaisseaux.

Learning objectives

- To develop a differential diagnosis for pulmonary arteritis.
- To develop an approach to the management of pulmonary arteritis.

CanMEDS Competency: Medical Expert

Pretest

- What are the causes of pulmonary arteritis?
- What are the appropriate investigations and initial management for pulmonary arteritis?

CASE PRESENTATION

A 48-year-old man of Cree descent presented to his family physician with a six-month history of progressive exertional dyspnea. His medical history was significant for Global Initiative for Chronic Obstructive Lung Disease class 1 chronic obstructive pulmonary disease (1) and mild obstructive sleep apnea on overnight oximetry. He had a 30 pack-year history of smoking, but had quit several months before evaluation. He described a 12 kg weight loss over one year and occasional night sweats. He reported intermittent bitemporal headaches and bright flashes in his peripheral vision. Review of systems was otherwise unremarkable.

Initial investigations included a chest x-ray revealing suprahilar fullness and decreased vascularity in the left lung. Electrocardiogram revealed right ventricular hypertrophy. Echocardiogram showed normal valves, preserved ejection fraction and possible pulmonary hypertension, with a right ventricular systolic pressure of 56 mmHg. The patient was referred to a local respirologist who documented a mild obstructive defect and a decrease in diffusing capacity for carbon monoxide on pulmonary function tests (PFTs). A subsequent contrast computed tomography (CT) scan was performed to evaluate for pulmonary embolism. This demonstrated critical stenosis of the left main pulmonary artery,

high-grade stenosis of the right main pulmonary artery and involvement of the aortic arch (Figure 1). The patient was referred to a tertiary care centre for further investigations and management.

On presentation, the patient had a heart rate of 90 beats/min and blood pressure of 130/80 mmHg, with no discrepancy between the two arms. Peripheral pulses were palpable and symmetrical, and there was no tenderness or beading to palpation of the temporal arteries. Cardiovascular examination showed a systolic murmur best heard over the pulmonic area, with radiation to his back and a supraclavicular bruit on the left. The respiratory examination revealed a respiratory rate of 16 breaths/min, good air entry bilaterally, no adventitious sounds, and no clubbing or cyanosis. The remainder of the examination was unremarkable.

Dual-energy CT pulmonary angiography was performed and suggested an inflammatory vasculitis involving the pulmonary arteries with more significant involvement of the left, with stranding in the perivascular space and increased iodine uptake within the perivascular thickening (Figure 2). The left pulmonary artery had a luminal diameter of 4 mm and reduced pulmonary blood flow was present within the left upper lobe (75% reduction compared with the right upper lobe) on the CT iodine maps (Figure 3A). There was also involvement of the aortic arch, distal ascending aorta, and proximal left subclavian, left carotid and left superior pulmonary veins. An echocardiogram revealed a dilated right ventricle with moderately depressed function. Resting, overnight and walking oximetry were within normal limits. PFTs demonstrated a forced expiratory volume in 1 s (FEV₁) of 113%, an FEV₁/forced vital capacity ratio of 89% and diffusing capacity of carbon monoxide of 95% of predicted. A 6 min walk test showed the patient was able to walk 411 m (71% of predicted [percentage of median walk distance for sex, unadjusted]), with a resting saturation of 94% and no exertional desaturation (2). Rheumatological work-up revealed an elevated C-reactive protein level (340 nmol/L), with negative autoimmune serology. The patient was negative for HIV, hepatitis B and hepatitis C; other bloodwork was unremarkable. A temporal artery

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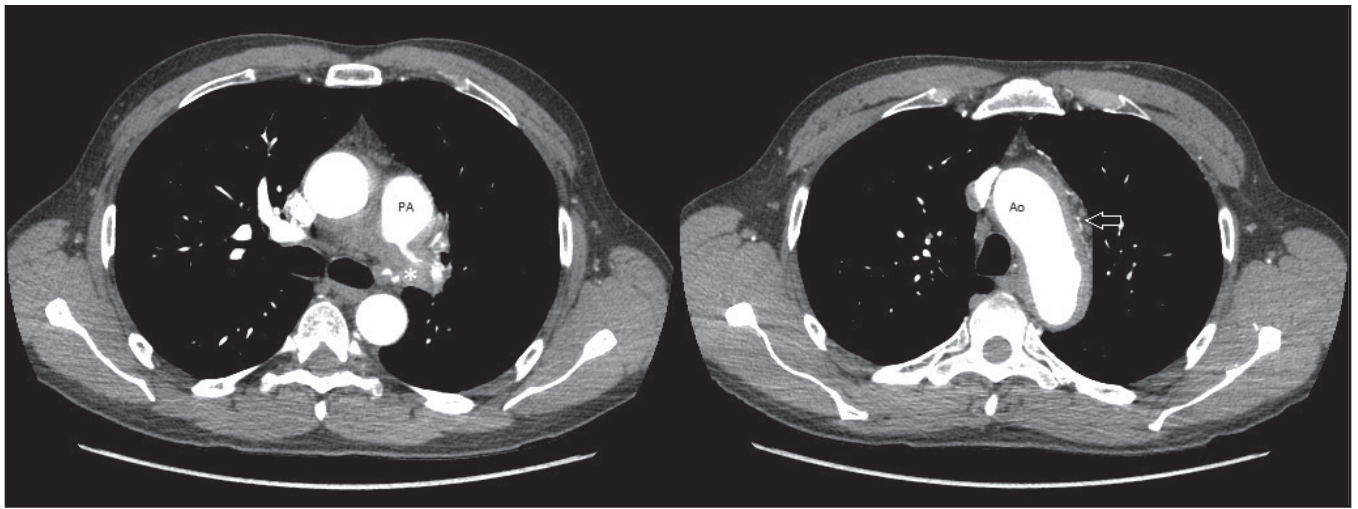


Figure 1) Contrast-enhanced computed tomography of the chest revealing significant stenosis (*) of the left pulmonary artery (PA) and thickening (arrow) of the aorta (Ao)

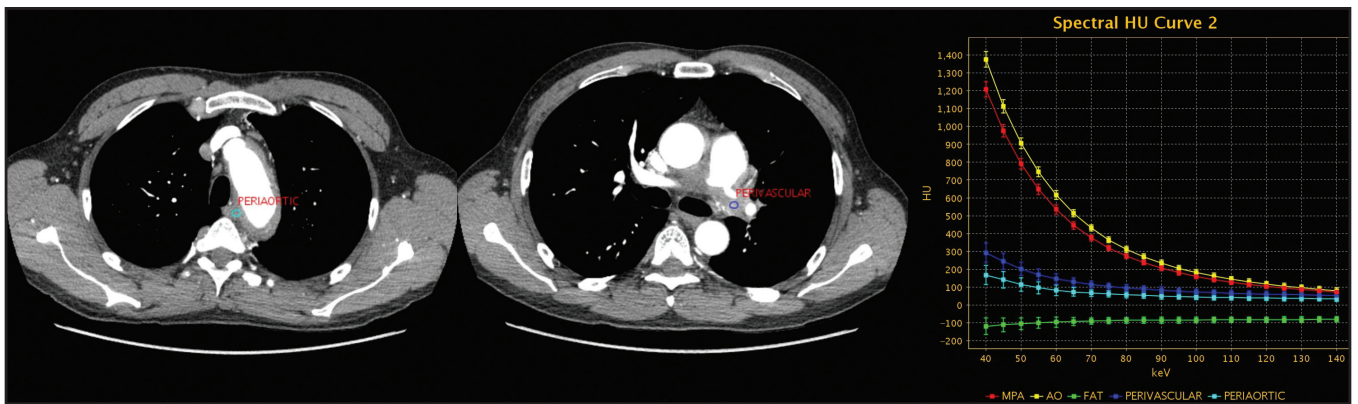


Figure 2) Representative axial sections from computed tomography showing periaortic and perivascular markers. The monochromatic energy levels are plotted on the x axis and Hounsfield unit (HU) attenuation on the y-axis. Note the marked upslope of the spectral HU curve for vascular structures containing iodine such as the main pulmonary artery (MPA) and aorta (Ao) (red and yellow curves), but also the upslope of the spectral HU curve for the perivascular and periaortic soft tissue (turquoise and blue curves), suggesting the presence of iodine. Importantly, these curves would be expected to be flat if this were bland thrombus without iodine enhancement

biopsy was performed, which showed no inflammation of the artery, no giant cells and an intact elastic lamina. The patient was diagnosed with large vessel vasculitis and was started on prednisone 1 mg/kg per day and methotrexate 15 mg per week.

At six-week follow-up, the patient did not indicate significant symptomatic improvement. 6 min walk (428 m, 74% of predicted [percentage of median walk distance for sex, unadjusted]) and PFTs showed no significant change. Ventilation and perfusion nuclear scans of the lung showed the left lung receiving 8% of total perfusion with normal ventilation (Figure 4). An echocardiogram demonstrated normal right ventricular systolic function, abnormal septal motion consistent with abnormal right ventricular dynamics and a dilated right atrium. Right pulmonary artery stenosis was present at the bifurcation of the main pulmonary artery, with a peak gradient of 82 mmHg. Repeat dual-energy CT pulmonary angiography scan showed reduction in the degree of soft tissue thickening surrounding the aorta and pulmonary arteries, particularly at the level of the aortic arch and the left main pulmonary artery. However, there was persistent narrowing of the left main pulmonary artery, with minimal increase in calibre of the left upper lobe and left lower lobe pulmonary arteries.

On six-month follow-up, the patient reported improvement in exertional dyspnea. His echocardiogram remained unchanged, but his dual-energy CT pulmonary angiography demonstrated further reduction in perivascular inflammatory tissue and near symmetrical iodine uptake of the right and left upper lung zones (Figure 3B). We suspect

there were several contributors to our patient's persistent dyspnea. Increased dead space ventilation, activation of mechanical receptors from the dilated right atrium and poor peripheral oxygen delivery from right ventricular dysfunction have played a role and have not been fully reversed on treatment.

DISCUSSION

Primary causes of pulmonary arteritis are rare and are classified based on the Chapel Hill nomenclature of vasculitides according to blood vessel size (3). Primary large vessel vasculitides include Takayasu arteritis (TA) and giant cell arteritis (GCA). Secondary causes of pulmonary vasculitides include infectious diseases, connective tissue disease, sarcoid, inflammatory bowel disease and hypersensitivity disorders (4,5). Primary large vessel pulmonary vasculitides are rare disorders, with 20 to 100 cases per million reported (4). Moreover, the diagnosis can be challenging because the signs and symptoms are nonspecific and have significant overlap with secondary causes of pulmonary arteritis. Diagnosis can be established based on high clinical suspicion coupled with appropriate clinical history, physical examination, laboratory results and radiologic patterns.

TA is an idiopathic vascular disorder that can involve the aorta and its branches. TA is more common in Asia and more frequently found in women <40 years of age. Symptoms are nonspecific and include chest pain, dyspnea, palpitations and left ventricular dysfunction (5). Constitutional symptoms, such as fever, weight loss, arthralgias,

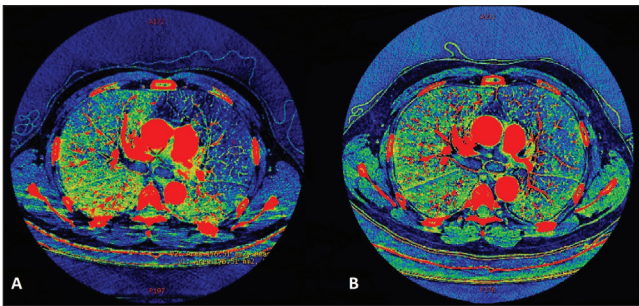


Figure 3) Representative axial sections from dual-energy computed tomography (CT) pulmonary angiography showing narrowing of the left pulmonary artery and reduced pulmonary blood flow within the left upper lobe on the CT iodine map as noted by the asymmetry with region mapped in blue reflecting a reduction in iodine distribution. **A** Baseline imaging. Following six months of treatment, follow-up dual-energy CT examination shows an improvement in pulmonary flow and iodine distribution as noted by less asymmetry with the right lung and a lesser area of blue on the colour perfusion maps than noted before treatment (**B**)

myalgias and malaise, may be present. On physical examination, patients can have absent or diminished pulses, limb claudication and discrepancy in blood pressures. Histologically, TA is characterized by granulomatous inflammation of the arterial wall with proliferation and fibrosis of the vessel (4). TA can be complicated by pulmonary hypertension, a serious and life-threatening manifestation (5).

GCA is a vasculitis primarily affecting individuals >50 years of age. The predominant manifestations are involvement of the extracranial carotid branches and the aorta. Signs and symptoms include swollen temporal arteries, temporal headache, jaw claudication and visual loss (4). From sporadic case reports, it is less frequently associated with pulmonary hypertension (6).

There is significant clinical overlap between TA and GCA, making definitive diagnosis challenging. On CT, both can appear similar, with evidence of arterial wall thickening, stenosis and thrombosis (6). In the present case describing our 48-year-old man, the clinical features and symptomatology did not clearly point to one diagnosis over the other. His age was between the diagnostic criteria for TA and GCA, his ethnic background was not one commonly associated with either disorder and his sex was not supportive of TA. Therefore, once secondary causes were ruled out, he was diagnosed with large vessel vasculitis.

Both TA and GCA can be treated with high-dose glucocorticoids and a steroid-sparing agent such as methotrexate or azathioprine. This induces remission in the majority of cases. Cyclophosphamide and anti-tumour necrosis factor agents have been used in TA for individuals resistant to glucocorticoids (5). In patients unresponsive to medical therapy, balloon angioplasty with stent placement can be used (7,8). Pulmonary hypertension is a serious and life-threatening condition that should be treated aggressively with pharmacological and/or invasive approaches. Early diagnosis and treatment allows for better outcomes, and prevention of irreversible stenotic and fibrotic changes (5). The morbidity from pulmonary arteritis can be significant and, therefore, an aggressive approach coupled with close follow-up is essential.

Dual-energy CT is an exciting new technique that enables physicians to acquire an image of a patient at two different energy spectrums (80 kVp and 140 kVp) simultaneously. These low and high kVp projections are processed such that the attenuation measurements from the projections are mathematically transformed into the density of two basis materials that would be needed to produce the measured attenuation. This allows for differentiation of various material pairs including iodine, calcium and water, as well as the quantification of the material (eg, iodine) content in the different tissues. These material basis-pair images, in turn, allow for the generation of monochromatic CT images at any arbitrary energy level between 40 keV and 140 keV. Because the attenuation value of iodine rapidly increases

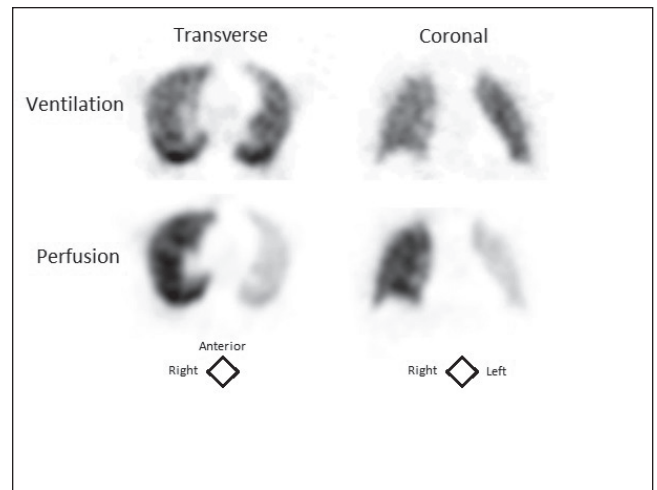


Figure 4) Ventilation and perfusion scans demonstrating decreased perfusion to the left lung. Representative of transverse and coronal views

with decreasing photon energy, images reconstructed at varying energy levels (keV) also allows for the quantification and subtraction of iodine. Iodine can then be mapped to quantify perfusion within the lung (Figure 4). Moreover, it can be applied to detect areas of increased iodine in tissue, suggesting active inflammation, as in the present case (Figure 3). The varied interaction of commonly found materials in patients undergoing evaluation with CT with photons of different energy levels allows for the isolation not only of iodine but also other commonly found materials such as calcium and water. The ability to detect active inflammation and quantify regional lung blood flow made this modality a useful tool in both the initial diagnosis and follow-up of this patient. Additionally, compared with traditional CT pulmonary angiography, dual-energy CT enables reduced contrast exposure, similar radiation dose and higher signal intensity of the pulmonary arteries at the expense of a slight reduction in image quality and increased image noise (9). The opportunity for material separation represents a significant improvement over traditional CT angiography but may also be additive to gadolinium-enhanced magnetic resonance imaging. Magnetic resonance imaging offers inherently higher contrast resolution than CT but remains limited by the complexity and time required for image acquisition.

Although our patient improved radiographically and symptomatically, his echocardiogram showed persistent changes, suggesting that pulmonary artery stenting or bypass surgery may need to be considered in the event of deterioration.

Post-test

- What are the causes of pulmonary arteritis?

Pulmonary arteritis can be caused by primary and secondary conditions. Primary causes are based on the Chapel Hill nomenclature of vasculitides according to blood vessel size, with large vessel including TA and GCA (3). Secondary causes include infectious disease, connective tissue disease, sarcoid, inflammatory bowel disease and hypersensitivity disorders.

- What are the appropriate investigations and initial management for pulmonary arteritis?

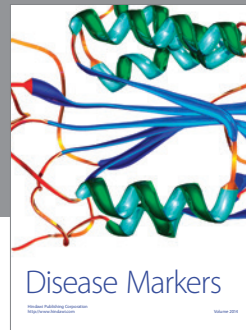
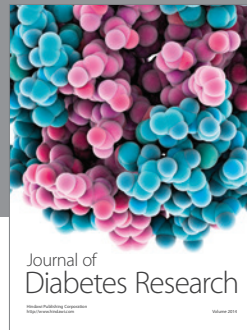
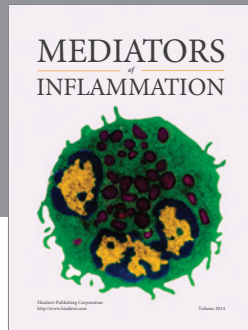
Diagnosis can be challenging because signs and symptoms may be nonspecific. It is imperative to exclude other causes of pulmonary artery stenosis and/or V/Q mismatches. Such mimics include, but are not limited to: pulmonary emboli, chronic thromboembolic pulmonary hypertension, congenital stenosis and extrinsic compression. Once identified, workup should be focused on differentiating primary from secondary causes of pulmonary arteritis. Blood

work focusing on connective tissue diseases and infectious causes of vasculitis should be initiated. Clinical history and imaging should include screens for inflammatory bowel disease and sarcoid. Other testing should include basic chest x-rays, PFTs, 6 min walk test, echocardiogram and CT pulmonary angiography. Dual-energy CT is especially helpful because it can help differentiate between extrinsic and intrinsic causes of stenosis. Treatment for both forms of primary large vessel vasculitis is similar and includes corticosteroids and immunosuppressive agents such as methotrexate or azathioprine. Pulmonary hypertension should be identified and managed. Invasive approaches may be used if there is partial or no response to pharmacological approaches.

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REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease. 2013. <www.goldcopd.org/uploads/users/files/GOLD_Report_2013_Feb20.pdf> (Accessed May 24, 2013).
2. Enright PL, Duan SL. Reference equations for the six-minute walk in healthy adults. *Am J Respir Crit Care Med* 1998;158:1384-7.
3. Jennette JC, Falk RJ, Andrassy K, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. *Arthritis Rheum* 1994;37:187-92.
4. Castander E, Alguersuari A, Gallardo X, et al. When to suspect pulmonary vasculitis: Radiologic and clinical clues. *Radiographics* 2010;30:33-53.
5. Toledano K, Guralnik L, Lorber A, et al. Pulmonary arteries involvement in Takayasu's arteritis: Two cases and literature review. *Semin Arthritis Rheum* 2011;41:461-70.
6. Marten K, Schnyder P, Schirg E, et al. Pattern-based differential diagnosis in pulmonary vasculitis using volumetric CT. *Am J Roentgenol* 2004;184:720-33.
7. Ramsey J, Amari M, Kantrow S. Pulmonary vasculitis: Clinical presentation, differential diagnosis, and management. *Curr Rheumatol Rep* 2010;12:420-8.
8. Borg FA, Dasgupta B. Treatment and outcomes of large vessel arteritis. *Best Pract Res Clin Rheumatol* 2009;23:325-37.
9. Yuan R, Shuman W, Earls J, et al. Reduced iodine load at CT pulmonary angiography with dual-energy monochromatic imaging: Comparison with standard CT pulmonary angiography – a prospective randomized trial. *Radiology* 2012;262:290-7.



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