JAMA Clinical Challenge

Increasing Hypoxemia and Dyspnea in Mild Chronic Obstructive Pulmonary Disease

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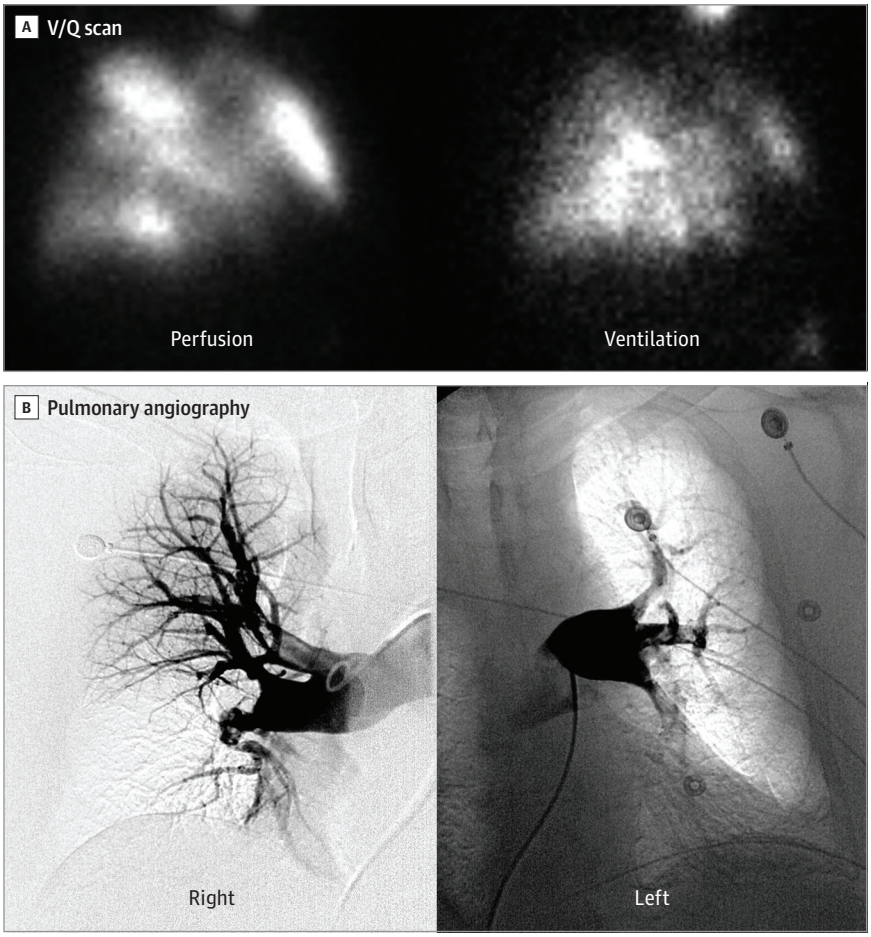

Figure. A, Ventilation/perfusion scan, right anterior oblique view. B, Pulmonary angiography.

A man with a 3-year history of chronic obstructive pulmonary disease presented with increasing dyspnea on exertion, requiring increasing flow rates of oxygen. He was a former smoker with a 50–pack-year history. He had been diagnosed with stage I low-grade prostate cancer several years previously.

Lung examination showed no wheezing. Cardiac examination showed a prominent pulmonary component (P_2) of the second heart sound. Noncontrast computed tomography of the chest was unremarkable.

An echocardiogram revealed dilated right atrium and ventricle. Spirometry showed mild airway obstruction. Duplex ultrasound showed a nonocclusive thrombus in the left femoral and popliteal veins. Catheterization of the right side of the heart showed a pulmonary arterial pressure of 79/32 mm Hg (mean, 48 mm Hg) with a normal pulmonary capillary wedge pressure. A ventilation-perfusion (V/Q) scan was obtained (**Figure**, panel A), followed by pulmonary angiography (Figure, panel B).

WHAT WOULD YOU DO NEXT?

A. Start parenteral corticosteroids and nebulized bronchodilators

B. Start heparin treatment followed by an oral anticoagulant for 6 months

C. Start anticoagulation and refer the patient for surgical embolectomy

D. Start anticoagulation and refer the patient for evaluation for pulmonary thromboendarterectomy

Diagnosis

Chronic thromboembolic pulmonary hypertension (CTEPH)

What to Do Next

D. Start anticoagulation and refer the patient for evaluation for pulmonary thromboendarterectomy

The key to the correct diagnosis is the abnormal V/Q scan findings and the presence of pulmonary hypertension. The scan shows a large mismatched defect corresponding to the superior segment of the right lower lobe (Figure, panel A). The findings of an abnormal V/Q scan combined with pulmonary hypertension support the diagnosis of CTEPH. Pulmonary angiography findings of sudden tapering of enlarged pulmonary arteries (pruning), severely decreased perfusion to the right lower lobe, and irregular vascular wall of the right lower lobe artery confirmed the diagnosis of CTEPH (Figure, panel B). Pulmonary thromboendarterectomy (PTE) is the treatment of choice.

Although parenteral corticosteroids and bronchodilators are appropriate for chronic obstructive pulmonary disease, severe pulmonary hypertension is not typical for the disorder. Anticoagulation and surgical embolectomy are accepted treatments for acute pulmonary embolism, suggested by the abnormal V/Q scan findings. However, the chronic symptoms, pulmonary angiogram findings, and severe pulmonary hypertension indicate chronicity consistent with CTEPH.

Discussion

CTEPH is an obliterative pulmonary arterial vasculopathy caused by organized blood clots. It has been considered rare, with prevalence among survivors of pulmonary embolism estimated at 0.1% to 0.5%.[1] However recent data suggest that CTEPH develops in as many as 5% of patients after pulmonary embolism, despite appropriate treatment.[2,3] Risk factors for CTEPH are history of previous pulmonary embolism (odds ratio [OR], 19.0), idiopathic vs provoked pulmonary embolism (OR, 5.70), large perfusion defect at the time of acute pulmonary embolism (OR, 2.22), and young age (OR, 1.79).[2]

The diagnosis of CTEPH requires evidence of pulmonary arterial hypertension (mean pulmonary arterial pressure greater than 25 mm Hg) and evidence of pulmonary thromboembolic disease.

A V/Q scan can differentiate CTEPH from other forms of pulmonary hypertension and is the diagnostic test of choice. Extensive perfusion abnormalities with multiple mismatched lobar or segmental defects are sufficient for the diagnosis in the setting of pulmonary hypertension. A normal V/Q scan excludes CTEPH.[4,5]

Pulmonary angiography may be necessary if less invasive tests do not confirm the diagnosis and helps determine the utility of PTE. The typical pulmonary angiogram findings are irregular vascular walls, eccentric filling defects, abrupt caliber decrease in distal vessels (pruning of the vessels), mosaic oligemia, pulmonary artery webs, and convex cutoff signs ("pouch" defect). In contrast, well-defined, more central emboli (polo mint sign) with smooth vessel wall and preserved vessel caliber are seen in acute embolism.

CTEPH had been considered a consequence of mechanical obstruction of the pulmonary arteries by incompletely resolved recurrent clots. However, newer evidence suggests that the age of the organized clots is quite uniform in 72% of patients with CTEPH.[6] Pathology studies have demonstrated small-vessel arteriopathy similar to changes observed in pulmonary arterial hypertension.[7] These facts suggest that pathophysiology of CTEPH is an active vascular wall remodeling process that extends beyond pure mechanical obstruction. CTEPH typically worsens without treatment, even without evidence of further thromboembolic events.[8]

Pulmonary thromboendarterectomy can result in complete symptom resolution and is the treatment of choice.[5] As opposed to embolectomy, PTE involves removing the organized clots along with the affected intima of the vessel. Mortality rate for PTE is 4% to 7%.[9] Medical therapy (eg, pulmonary vasodilators) is recommended for nonsurgical candidates.[5] Lifelong anticoagulation is indicated for all patients unless the risk of bleeding is unacceptably high. For these patients, an inferior vena cava filter is indicated.

Patient Outcomes

Patients with high pulmonary vascular resistance or pressure, poor exercise tolerance, and high surgical risk have a poorer prognosis. PTE coupled with lifelong anticoagulation is effective for 99% of patients with CTEPH.[10] Medical therapy improves the patients' exercise capacity and symptoms, but the effect on survival is unclear.

The patient underwent successful PTE. The pulmonary hypertension and hypoxemia resolved, and his exercise tolerance improved significantly.

ARTICLE INFORMATION

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Submissions: We encourage authors to submit papers for consideration as a JAMA Clinical Challenge. Please contact Dr McDermott at mdm608@northwestern.edu.

REFERENCES

1. Fedullo PF, Auger WR, Kerr KM, Rubin LJ. Chronic thromboembolic pulmonary hypertension. *N Engl J Med*. 2001;345(20):1465-1472.

2. Pengo V, Lensing AW, Prins MH, et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. *N Engl J Med*. 2004;350(22):2257-2264.

3. Guérin L, Couturaud F, Parent F, et al. Prevalence of chronic thromboembolic pulmonary hypertension after acute pulmonary embolism. *Thromb Haemost*. 2014;112(3):598-605.

4. Tunariu N, Gibbs SJ, Win Z, et al. Ventilation-perfusion scintigraphy is more sensitive than multidetector CTPA in detecting chronic thromboembolic pulmonary disease as a treatable cause of pulmonary hypertension. *J Nucl Med*. 2007;48(5):680-684.

5. Hoeper MM, Mayer E, Simonneau G, Rubin LJ. Chronic thromboembolic pulmonary hypertension. *Circulation*. 2006;113(16):2011-2020.

6. Blauwet LA, Edwards WD, Tazelaar HD, McGregor CG. Surgical pathology of pulmonary thromboendarterectomy: a study of 54 cases from 1990 to 2001. *Hum Pathol*. 2003;34(12):1290-1298.

7. Moser KM, Bloor CM. Pulmonary vascular lesions occurring in patients with chronic major vessel thromboembolic pulmonary hypertension. *Chest*. 1993;103(3):685-692.

8. Moser KM, Auger WR, Fedullo PF, Jamieson SW. Chronic thromboembolic pulmonary hypertension. *Eur Respir J*. 1992;5(3):334-342.

9. Jamieson SW, Kapelanski DP, Sakakibara N, et al. Pulmonary endarterectomy. *Ann Thorac Surg*. 2003;76(5):1457-1462.

10. Mo M, Kapelanski DP, Mitruka SN, et al. Reoperative pulmonary thromboendarterectomy. *Ann Thorac Surg*. 1999;68(5):1770-1776.