A 57-year-old white woman presented with a 3-month history of progressive shortness of breath. Although she attributed her initial subtle symptoms of mild dyspnea as a result of exertion during exercise to "getting older," she sought evaluation 1 month before presentation because of the onset of a cough productive of purulent sputum. A chest radiograph demonstrated a consolidation in the right lower lobe, prompting treatment for community-acquired pneumonia with oral levofloxacin for 10 days. The patient’s cough resolved, but her shortness of breath relentlessly progressed to symptomatic dyspnea at rest. Dyspnea was exacerbated while upright and improved in the recumbent position.

Further history revealed episodes of recurrent epistaxis since childhood, a spontaneous right hemothorax at age 21 during the third trimester of pregnancy, an ischemic stroke at age 25, and hypothyroidism. She has smoked 1 pack of cigarettes per day for the past 30 years and occasionally drinks alcohol. Family history was remarkable for recurrent epistaxis in her brother and son.

During examination, oxygen saturation on room air was 83% when upright and 91% lying down. She had clubbing in all fingers (Figure 1), and multiple pinpoint telangiectasias were noted on the tongue (Figure 2) and mucosal surface of the lips. Auscultation revealed normal S1 and S2 without any murmurs, normal breath sounds, and a loud, continuous murmur posteriorly over the left lung base, which intensified with inspiration. Routine laboratory data were unremarkable. Arterial blood gas analysis showed a partial pressure of oxygen of 61 mm Hg, with an inspired oxygen fraction of 44% producing an alveolar-arteriolar gradient of 192. ECG

Figure 1. Evidence of clubbing with an increase in nail bed angle and convexity.

Figure 2. Multiple pinpoint telangiectasias seen on the surface of the tongue.

Figure 3. Posteroanterior chest radiograph shows hyperinflated lung fields and a subtle opacity in the left lower lobe, marked by blue arrows.
was normal, and chest radiograph showed a subtle density in the lower lobe of the left lung (Figure 3). Transthoracic echocardiography showed normal ejection fractions and valve architecture. A computed tomography angiogram with 3-dimensional reconstruction showed a single large pulmonary arteriovenous malformation (AVM) in the left lower lobe, with aneurysmal dilation of the venous sac measuring 4 cm (Figures 4A, 4B, and 5). A transcutaneous pulmonary angiogram confirmed a large AVM in the left lower lobe with a single feeding artery measuring 10.6 mm in diameter. A 14-mm Amplatzer vascular plug was deployed within the feeding artery, and follow-up angiograms revealed no residual flow in the AVM (Figures 6A and 6B and online-only Data Supplement Movies I and II). After the procedure, oxygen saturation increased from 86% to 97% and platypnea resolved. The patient was doing well at follow-up 3 weeks after discharge.

Discussion

Hereditary hemorrhagic telangiectasia (HHT), also known as the triple eponym Osler-Rendu-Weber syndrome, is a group of related disorders inherited in an autosomal-dominant pattern with variable penetrance. Its prevalence is greater than previously thought and currently is estimated at 1 in 5000 individuals.1,2

HHT is a monogenic disorder. Mutations in the genes endoglin, ACVRL1/ALK1, and SMAD4 are known to cause the disease phenotype. These genes code for crucial proteins involved in the signal transduction pathway of the transforming growth factor β family of receptors. The exact pathogenesis of HHT is not completely understood. However, current evidence indicates that defective signal transduction in the transforming growth factor β superfamily of receptors results in an aberrant response to normal angiogenic stimuli, such as tissue injury from mechanical trauma, inflammation, and oxidative stress, leading to the formation of telangiectasias and AVMs with increasing age.2

HHT is a clinical diagnosis based on the Curacao criteria, which include epistaxis, telangiectasias, visceral AVMs, and appropriate family history. Diagnosis is definite in the presence of 3 of the 4 criteria.1 On the basis of her history of epistaxis, findings of telangiectasias and visceral AVMs, and an appropriate family history, our patient met all 4 Curacao criteria for the diagnosis of HHT.1 Genetic testing is most helpful during childhood and adolescence, when the disease may not yet fully manifest clinically.1 The most common clinical feature is epistaxis, which usually begins during childhood and almost always is present by the fourth decade of life.1 Telangiectasias involving the mucosal surfaces of the mouth and facial skin are common.1,2 AVMs may involve multiple vascular beds, including the gastrointestinal, hepatic, pulmonary, and cerebral circulation. Chronic blood loss due
to epistaxis and gastrointestinal bleeding can cause profound iron deficiency anemia.²

Pulmonary AVMs (PAVMs) occur in HHT with an incidence of approximately 15% to 50%.¹⁻⁴ and ≈70% of all PAVMs are associated with HHT.³ Platypnea-orthodeoxia occurs because of positional changes in blood flow through the PAVM and is relatively common among symptomatic patients.³ PAVM is a major risk factor for ischemic strokes through paradoxical embolism as well as for cerebral abscesses because the PAVM functions to bypass the filter of the pulmonary circulation.² Antibiotic prophylaxis is, therefore, indicated before any procedure that may cause bacteremia.¹ As in this case, most patients who have suffered ischemic strokes due to PAVMs are not diagnosed with HHT at first presentation.² An ischemic stroke in a young patient should prompt consideration of paradoxical embolism as a possible mechanism of the stroke. PAVMs, when identified, should raise clinical suspicion for HHT; in addition, all patients with known HHT should be screened for PAVMs using contrast echocardiography.¹ Left untreated, persistent right-to-left shunt causes chronic hypoxemia and may cause high-output heart failure and pulmonary hypertension. PAVMs can also lead to hemorrhagic complications such as spontaneous hemothorax, which are seen more frequently during pregnancy.¹⁻²

Transcatheter embolization using stainless steel or platinum coils compatible with magnetic resonance now is recommended for treatment of PAVMs, with a feeding artery >3 mm in adults and all symptomatic children.¹⁻⁴ In high-flow vessels supplying large PAVMs, multiple coils usually are required to occlude the vessel, increasing the risk of embolization. In a large case series by Hart et al.¹ the Amplatzer vascular plug (AGA Medical, Plymouth, MN) was used successfully and showed a statistically significant increase in oxygen saturation after the procedure. There were no instances of PAVM-related complications or recanalization at a mean follow-up of 9.6 months.⁴ Given the large size of the PAVM in our patient, an Amplatzer vascular plug was chosen for embolotherapy.

This case illustrates the classic findings associated with a complex and fascinating disorder. We demonstrate the successful use of a vascular occlusion device for closure of a large PAVM associated with HHT.

Disclosures

None.

References


Figure 6. Large pulmonary arteriovenous malformation in the left lower lobe with a supplying artery measuring 10.6 mm in maximal diameter. The pulmonary arteriovenous malformation subsequently was successfully occluded using a 14-mm Amplatzer vascular plug device. No residual flow was seen.
Platypnea-Orthodeoxia Syndrome as a Presentation of Hereditary Hemorrhagic Telangiectasia
Nilay Kumar, Ryan R. Kraemer, Rajini K. Murthy and Jason R. Hartig

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