CLINICAL VIGNETTE

Platypnea-Orthodeoxia Syndrome in a 46-Year-Old Woman

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Case Presentation

A 46-year-old female with well-controlled type 2 diabetes mellitus, hypothyroidism, and endometriosis presented to the hospital with severe fatigue with exertion. She was previously a dancer, but for the last 12 years experienced intense fatigue, palpitations and near syncope with simple activities. She reports her symptoms to be triggered when standing up to reach for something. Her fatigue became debilitating. She reports not showering for up to 2 weeks because showering required too much effort. She was evaluated by a cardiologist with a Zio Patch, transthoracic echocardiogram, and tilt table test that were unrevealing. She obtained an over-the-counter pulse oximeter and measured her pulse and oxygen saturation during these episodes. With standing and ambulation, her pulse would increase to the 140s-150s, and room air oxygen saturation would drop to 87%-88%. Given the finding of hypoxia with exertion, her cardiologist referred her to the hospital for further evaluation.

On admission, she was afebrile and her with normal vital signs. Physical exam was not notable for any abnormalities, including cardiopulmonary and neurologic exams. Initial laboratory testing included CBC, BMP, troponin, D-dimer and TSH were unremarkable. Chest X-ray and CT chest with contrast did not show any acute pathology. While monitored, several maneuvers were performed. At rest, her heart rate was in the 90s, with room air oxygen saturation between 95%-98%. With standing, her heart rate increased to the 120s-130s, and her room air oxygen saturation decreased slightly to 94%-96%. With ambulation, her heart rate climbed further to 140s-150s, and her oxygen saturation decreased to 88% with an adequate waveform. While continuing to stand, she was placed on up to 8 liters of nasal oxygen supplementation without improvement in hypoxia. However, when lying supine, her oxygen saturation returned to 98% on room air within 30 seconds, and her heart rate decreased to the 110s within 1 minute. Given concerns for a possible shunt, a transthoracic echocardiogram with bubble study was completed. This revealed significant right-to-left shunting through a likely patent foramen ovale (PFO). Given her significant symptoms and vital sign abnormalities she referred for PFO closure.

Discussion

Platypnea-orthodeoxia syndrome is an exceedingly rare clinical condition characterized by difficulty breathing and hypoxia induced by being in the upright position and resolved with returning to the supine position. The orthodeoxia is specifically defined as a drop in PaO2 > 4 mmHg or a drop in oxygen saturation greater than 5% from the supine to upright position. It was first described by Burchell et al in 1949.[1] Since that time, only a few hundred cases have been reported.

The most common cause of platypnea-orthodeoxia syndrome is an intracardiac shunt. Up to 87% of cases are due to intracardiac communication between the right and left atria. Patent foramen ovale (PFO) is the most common, though platypnea-orthodeoxia has also been reported with shunts from atrial septal defects (ASD), atrial septal aneurysms (ASA), and other abnormalities. However, not every patient with a PFO develops platypnea-orthodeoxia syndrome. Approximately 24% of the general population has a PFO,[2] and patients with platypnea-orthodeoxia syndrome also have a secondary anatomic or functional factor that predisposes to shunting through the intracardiac shunt. The most common secondary factor is aortic pathology (i.e. dilation or aneurysm), but was also includes other conditions that can cause either preferential blood flow across the shunt, or elevated right atrial pressures. These include: aortic valve repair, severe kyphosis, paraesophageal hernia, and pulmonary hypertension. Although intracardiac shunt is the most commonly associated condition with platypnea-orthodeoxia syndrome, it has also been reported with extracardiac pathologies. These include causes of intrapulmonary shunt (such as pulmonary arterio-venous malformation (AVM) or hepato-pulmonary syndrome), and often conditions such as diabetic neuropathy and ileus.[3] In hepatopulmonary syndrome, pulmonary microvascular endothelial changes develop due to increased hepatic production of endothelin 1 and pulmonary endothelin B from ongoing stress. This causes increased nitric oxide production and subsequent vasodilation. Vasodilation and increased angiogenesis in the pulmonary vasculature lead to AV shunt formation due to increased blood flow without a concomitant increase in alveolar ventilation, and a ventilation-perfusion mismatch.[4]

After platypnea-orthodeoxia is determined, evaluation is adjusted to identify the underlying cause. The most common cause is intracardiac shunt, and transthoracic echocardiogram with bubble study should be completed in both supine and upright positions. If echocardiogram is nondiagnostic, but high clinical suspicion remains, transesophageal echocardiogram can be performed for clearer assessment of cardiac defects. Cardiac MRI also can define cardiac anatomy. If intracardiac

shunt is not found, testing should continue with evaluation for intrapulmonary shunt. CT angiography can identify pulmonary AVMs and pulmonary perfusion evaluated with a ventilation/perfusion (V/Q) scan or perfusion scan scintigraphy.

Treatment of platypnea-orthodeoxia syndrome depends on the underlying cause. With intracardiac shunts, PFO closure or ASD need repair. Generally, PFO closure or ASD repair is recommended in patients with right atrial and right ventricular enlargement, or if associated with platypnea-orthodeoxia syndrome or paradoxical emboli. This is increasingly performed percutaneously using septal occluding devices. Agarwal, et al reported greater than 95% of patients had symptoms resolve after shunt repair.[3] Treatments are also available for patients with extracardiac causes of platypnea-orthodeoxia syndrome. Those with pulmonary AVMs can be treated with embolization. However, patients with advanced disease such as diffuse pulmonary AVMs or hepatopulmonary syndrome may require lung or liver transplant for definitive therapy.

Our patient experienced symptoms for many years before diagnosis. Dyspnea and fatigue with standing upright should prompt an evaluation for platypnea-orthodeoxia syndrome. Initially measuring her supine and upright oxygen saturation can be done in the office. Basic cardiac evaluation with transthoracic echocardiogram with bubble study can assess possible intracardiac shunt. This case highlights nonspecific, positional symptoms warrant systematic evaluation for timely diagnosis and treatment.

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