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## Case Report

## 51 year-old male with dyspnea and hypoxia

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## A B S T R A C T

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With continued advancements in medical practice, physicians are caring for more adult patients with congenital heart diseases and their sequelae. We report a 51 year-old with obstructive sleep apnea presenting with dyspnea, hypoxia and pulmonary hypertension, found to have a congenital atrial septal defect. The patient had symptomatic improvement following percutaneous closure of his ostium secundum atrial septal defect.

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A 51-year-old man presented with 10 days of progressive dyspnea. His symptoms began as an upper respiratory infection, but had progressed to include chills and a cough productive of yellow sputum. He had also developed dyspnea at rest. Initially, moxifloxacin and bronchodilators produced some symptomatic improvement. His past medical history was significant for pulmonary hypertension, confirmed by right heart catheterization four months prior, with a mean PA pressure of 42 mmHg four months prior to admission. A recent polysomnogram had demonstrated obstructive sleep apnea (AHI 53, O<sub>2</sub> sat less than 88% for 386 min or 97% of the study), but he had not been started on therapy. He took no daily outpatient medications. Occasionally he used acetaminophen, sennakot, diphenhydramine, omeprazole, and zolpidem. He had a 20 pack-year smoking history, but quit 18 years prior. He was retired and had worked as a painter, plumber and construction laborer. He had served in the Navy, and recalled no exposure to asbestos. He had one cat and could recall no sick contacts.

His physical exam revealed an obese white male who appeared fatigued, but in no acute distress. He was able to speak in full sentences. Vital signs revealed a blood pressure of 114/76, heart rate 96 bpm, respiratory rate 22, and an oxygen saturation of 88% while breathing room air. This improved to 90% on 2 L/min by nasal cannula. Further increases in supplemental oxygen did not significantly increase his oxygen saturations. Mucous membranes were moist with no oral lesions. ENT exam demonstrated a Mallampati score was 3, no cervical adenopathy, thyromegaly or upper airway wheeze. Cardiovascular exam revealed a normal rhythm without murmurs or gallops and a prominent split and fixed S<sub>2</sub>. Neck veins were not distended. Lungs had rhonchi at the bases with good air movement bilaterally. Abdomen was soft and non-tender with

normal bowel sounds and no palpable organomegaly. Extremities revealed no clubbing, cyanosis or edema. Pulses were 2+ peripherally. Skin revealed tinea versicolor over the arms and chest, but was otherwise normal.

Labs demonstrated normal blood cell counts and differential. Chemistry was notable only for a mildly elevated creatinine at 1.2 mg/dL. BNP was 12 pg/mL, and d-dimer, cardiac markers and TSH were normal. HIV ELISA, RF, ANA and ESR were all low or negative. Room air arterial blood gas demonstrated a pH of 7.46, pCO<sub>2</sub> of 35, and a pO<sub>2</sub> of 58. CXR suggested a possible retrocardiac infiltrate and left atrial dilation (see Fig. 1). A CT scan of the chest with IV contrast showed no central pulmonary emboli, normal lung parenchyma and enlarged pulmonary arteries. Pulmonary function tests revealed an FVC 4.55 L (88%), FEV<sub>1</sub> 3.24 L (81%) and diffusing capacity adjusted for hemoglobin at 22.1 (72%). One year prior to admission, an echocardiogram showed a left ventricular ejection fraction (LVEF) of 51% with normal LV systolic function, mild dilatation of all four chambers of the heart with mild concentric left ventricular hypertrophy. Right ventricular systolic pressure was estimated at 50 mmHg. A right heart catheterization performed four months prior to admission measured pulmonary arterial pressure (PAP) at 69/30 mmHg (42), right ventricular pressure (RVP) 68/14 mmHg, pulmonary capillary wedge pressure (PCWP) 20 and pulmonary vascular resistance (PVR) was 308 dyne-sec/cm.<sup>5</sup>

Repeat contrast echocardiogram showed normal left ventricular systolic function with LVEF estimated at 49% with mild to moderate chambers dilatation. A flattened septum was noted during diastole, consistent with RV volume overload. The right ventricular systolic pressure was estimated at 65–70 mmHg and a left-to-right shunt was demonstrated at the atrial level (Fig. 2). Repeat right heart catheterization revealed: PAP 60/26 (38) mmHg, RVP 56/6 mmHg, PCWP 10 mmHg, PVR 5.4 Woods units, CO/CI 5.18/2.37 (using the Fick method). Oxygen saturations were 64% at the superior vena cava, 70% at the inferior vena cava, RA 74% in the right atrium, 71%

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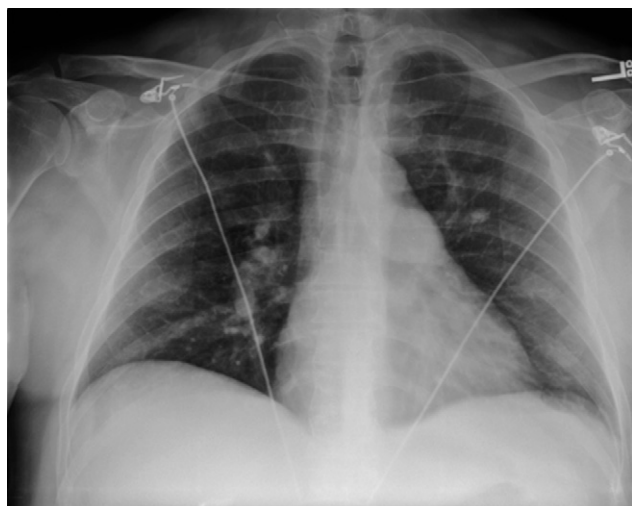


Fig. 1. CXR showing sign of left atrial dilation.

in the right ventricle and 91 % in the pulmonary artery. The Qp/Qs (pulmonary to systemic flow ratio) was 1.23, although this was felt to be decreased from the actual value due to a bidirectional shunt at the atrial level.

## 2. Diagnosis

Congenital atrial septal defect (ASD) and obstructive sleep apnea diagnosed in an adult manifest as pulmonary hypertension, hypoxia, and right-to-left shunt.

Pulmonary hypertension is common and its incidence probably underappreciated. It is often found concomitantly with other cardiopulmonary diseases and the differential for its etiology is wide (Table 1).<sup>11</sup> Pulmonary hypertension is found in 17–52% of patients with OSA.<sup>6</sup> Nocturnal hypoxia acutely causes pulmonary vasoconstriction, and it is believed that recurrent hypoxic episodes in patients with obstructive sleep apnea cause vascular remodeling and subsequent pulmonary hypertension. Our patient had

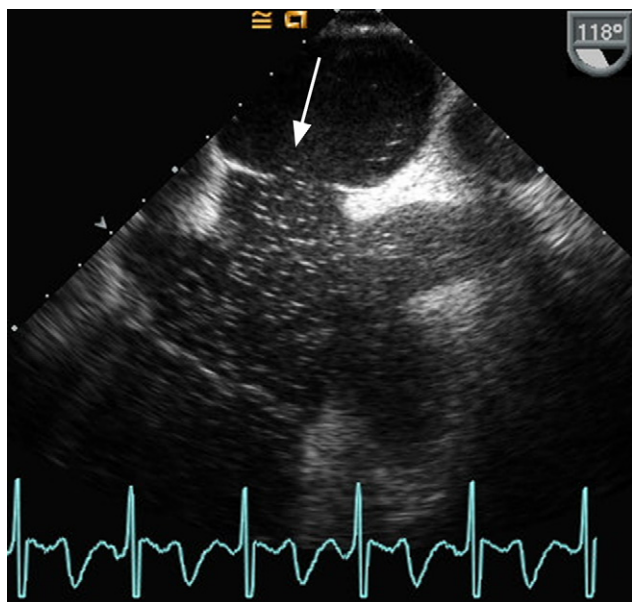


Fig. 2. Trans-esophageal echocardiographic images showing agitated saline bubbles crossing from the right to the left atrium through the ASD (arrowhead).

Table 1

Differential diagnosis of pulmonary hypertension.

### WHO Class 1 (PAH)

- Idiopathic
- Familial
- Collagen vascular disease
- Congenital systemic to pulmonary shunts
- Portal hypertension
- HIV
- Drugs or toxins
- Veno-occlusive disease
- Capillary hemangiomatosis
- Persistent pulmonary hypertension of the newborn
- Other: Thyroid disease, Glycogen storage disease, Gaucher disease, Hereditary hemorrhagic telangiectasias, Hemoglobinopathies, Splenectomy, Myeloproliferative disease

### WHO Class 2 (Pulmonary Venous Hypertension)

- Left-sided atrial or ventricular disease
- Left-sided valvular disease
- Extrinsic compression of pulmonary veins

### WHO Class 3 (Disorders of the Respiratory System or Hypoxemia)

- COPD
- Interstitial lung disease
- Sleep disordered breathing/OSA
- Hypoventilation disorders
- Chronic exposure to high-altitude
- Developmental abnormalities

### WHO Class 4 (Thromboembolic Diseases)

### WHO Class 5 (Miscellaneous)

- Sarcoidosis
- Langerhans cell histiocytosis
- Extrinsic compression of pulmonary vessels
- Lymphangiomatosis

Recreated based on Table 1 in: Diagnosis and Treatment of Secondary (Non Category 1) Pulmonary Hypertension. Rich, Stewart and Marlene Rabinovitch. Circulation 2008; 118: 2190–2199.

obstructive sleep apnea, which was initially felt to be a cause of his pulmonary hypertension. Patients with obstructive sleep apnea also often have an elevated wedge pressure during exercise. This implies that exercise-induced pulmonary hypertension seen in this subset of patients may be due to a post-capillary cause of pulmonary hypertension related to left ventricular diastolic dysfunction. Supplemental oxygen, tracheotomy and CPAP have been shown to lower pulmonary artery pressures in patients with obstructive sleep apnea.<sup>6</sup> Pulmonary hypertension attributed to obstructive sleep apnea is almost always mild when not associated with an underlying lung disease.<sup>9,12,13</sup>

Given the degree of pulmonary hypertension in this patient, it is most likely that his pulmonary hypertension was caused primarily by his atrial septal defect. Adults with congenital heart disease now outnumber children, present in more than one million adults in the United States with many shunt lesions are diagnosed later in life. The incidence of ASD is 4 in 100,000 live births. The most common type of ASD is the ostium secundum defect. Symptoms of an ASD include exercise intolerance and arrhythmias. Physical exam signs include those indicative of right heart failure: right ventricular heave, a systolic ejection murmur in the left upper sternal border, and a persistently split second heart sound. These patients can have a diastolic murmur due to tricuspid stenosis and eventually can develop hypoxemia relatively refractory to oxygen supplementation. Pulmonary hypertension develops in approximately 15% of patients with an ASD.<sup>15</sup>

Atrial septal defects are considered appropriate for closure if the patient has symptoms related to the shunt, including exercise intolerance, fatigue, dyspnea, heart failure, paroxysmal embolism or platypnoea-orthodeoxia syndrome.<sup>15</sup> A high pulmonary-to-

systemic flow ratio (Qp/Qs) is considered appropriate for shunt closure, although the level at which to consider closure is debated: the AHA recommends closure for flow ratios  $>1.5:1$  in children, recommendations are not as well established in adults.<sup>4</sup> Closure is generally avoided in severe pulmonary hypertension or those with pulmonary vascular resistances greater than 15 Woods units (1200 dynes). This value comes from a large retrospective observational study of 702 patients with ASD from 1953–1972. 40 (6%) of these patients had pulmonary hypertension. 26 received surgical closure and of these, and 22 patients were alive at follow-up. All patients alive at follow-up had PVR  $<15$  Woods' units. All 4 with PVR  $>15$  Woods' units who had received surgical closure did not survive to follow-up. Of the 14 who received medical management, 6 of 9 with PVR of 15 or greater were alive at follow-up.<sup>16</sup>

Surgical intervention should be considered in those with secundum ASD without severe pulmonary hypertension. A randomized controlled trial evaluated the outcomes of surgical versus medical treatment in 473 patients with an ASD greater than 40 years-old with mPAP  $<70$  and Qp/Qs  $>1.5:1$ . The medical management group had an overall higher risk of major cardiovascular events and a trend towards increased mortality when compared to the surgical intervention group.<sup>1</sup>

An increasing number of patients are being considered for percutaneous closure of secundum ASDs. A percutaneous catheter-based closure can be used in these patients when there is adequate rim tissue surrounding the defect, the defect is not too large for percutaneous closure devices, and there is no other significant cardiac abnormality that precludes percutaneous closure. Complications of percutaneous closure are rare and include residual shunt, malpositioning, arrhythmias, device erosion, and thrombus formation with or without cerebral embolization. After closure, a TEE is performed to ensure adequate repair. The patient should continue on aspirin and clopidogrel for at least six months to prevent thrombus formation.<sup>10</sup> These patients are generally placed on antibiotic prophylaxis to prevent endocarditis for the first six months post-closure.<sup>17</sup>

Although severe pulmonary hypertension is still generally considered a contraindication to ASD closure, there are now studies supporting safe and successful closure of ASD associated with pulmonary hypertension using percutaneous closure devices.<sup>3</sup> Pulmonary arterial pressures improve following ASD closure, although less than 50% result in normalization of the PAP.<sup>2</sup> There are several case reports outlining successful closure of ASDs in patients with severe pulmonary hypertension with concomitant use of IV epoprostenol, bosentan or both.<sup>5,7,8,14</sup>

### 3. Outcome

In this patient, a 30 mm Amplatzer septal device was placed percutaneously. The patient was continued on aspirin for life, and Plavix and antibiotics for the next 6 months. He is tolerating CPAP. Repeated echocardiograms performed after ASD closure showed resolution of shunt physiology with appropriate placement of the inter-atrial septal device. The patient still has right atrial and ventricular dilation, with pulmonary artery pressures still estimated as being elevated by echocardiogram. He is symptomatically improved and off of supplemental oxygen, with most recent room air oxygen saturation of 96%.

### Conflict of interest

The authors have no competing interests to declare. The manuscript has been reviewed and approved by all authors.

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