WISCONSIN MEDICAL JOURNAL

Patent Foramen Ovale with Right to Left Shunt as a Cause of Hypoxia

Ravi K. Mareedu, MD; Juan E. Mesa, MD

ABSTRACT

Patent foramen ovale with right to left shunt as a cause of hypoxia without Eisenmengers physiology or with only moderately pulmonary artery pressures is an uncommon presentation. Initial diagnosis via transesophageal echocardiography requires detection of a shunt with either color Doppler or agitated saline contrast with or without Valsalva maneuver. This rare but diagnosable case presented was simply corrected with placement of a CardioSEAL device. Causes of right to left shunt without elevated pulmonary artery pressures are discussed.

INTRODUCTION

Patent foramen ovale (PFO) is an anatomical variant occurring in the septum separating the atrial chambers. PFO provides communication between the atrial chambers of the heart through the ostium secundum with the septum primum acting as a 1-way valve that allows flow from the right to left atria, bypassing the lungs.[1] This septum normally remains patent before birth and closes with the first breath of air a baby takes because of increased left-sided pressures. Anatomical closure usually occurs by 2 years of age. However, it remains patent in a subset of the population. Autopsy studies have shown an overall prevalence of approximately 27% in the general population, decreasing with increasing age (35% and 20% in age groups <30 years and >80 years, respectively).[2] The average size is estimated at 4.9 mm with a majority being <10 mm in size.[2] The agitated saline contrast study with transesophageal echocardiography (TEE) and the Valsalva maneuver is the gold standard test for detection of PFOs. The authors present a case report of a 58-year-old woman with an uncommon presentation of hypoxia secondary to right to left shunt (without Eisenmengers physiology and with only moderately elevated pulmonary artery pressures). A 23 mm CardioSEAL device was placed in the PFO with significant improvement in the patient's functional status at 1 month and continued stability at 6-month follow-up.

Author Affiliations: Department of General Internal Medicine, Marshfield Clinic, Marshfield, Wis (Mareedu); Department of Cardiology, Marshfield Clinic, Marshfield, Wis (Mesa).
Corresponding Author: Juan E. Mesa, MD, Department of Cardiology, Marshfield Clinic, 1000 N Oak Ave, Marshfield, WI 54449; phone 715.387.5460; fax 715.389.3808; e-mail mesa.juan@marshfieldclinic.org.

CASE REPORT

A 58-year-old woman presented with a 9-month history of shortness of breath and a 1-month history of bilateral lower extremity pedal edema with baseline oxygen saturation in the 60s to 70s. She denied orthopnea or platypnea. Pulmonary history was significant for 41 pack years of smoking and prior diagnosis of chronic obstructive pulmonary disease. Past medical history was also significant for hypertension, cervical carcinoma (28 years ago), cecal adenocarcinoma (1 year ago) stage I, earliest stage (Tis), no lymph node involvement (N0), no distant spread (M0), status post-right hemicolectomy, anal cell carcinoma (1 year ago), status post-surgical resection, and chemotherapy. The patient had an unremarkable surgical course during her hemicolectomy 1 year ago. She did not have excessive bleeding and had a hemoglobin of 12.6 g/dL. She had no problems with hypoxia. Her medications included carvedilol, furosemide, aspirin, acetaminophen with codeine, and vitamin B_{12}.

Physical examination showed the patient was afebrile with a blood pressure of 133/76 mm Hg, regular pulse of 75 beats/min and respirations at 17 beats/min. She exhibited central cyanosis and elevated jugular vein distension. Her lungs were clear to auscultation and heart sounds were regular with non-displaced apical impulse. Clinically hepatomegaly was not noted. Bilateral lower extremity pedal edema of 2-3+ was present. The remainder of the physical examination was within normal limits. The patient's oxygen (O_2) saturation measured 66% on 2 liters of O_2 and increased to

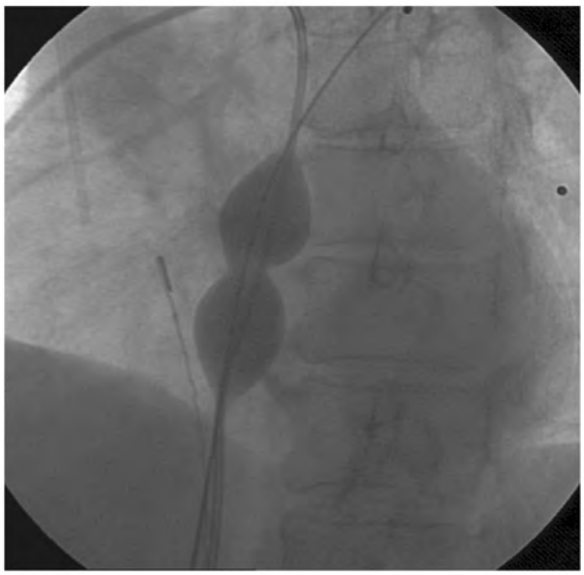

Figure 1. Sizing balloon showing the diameter of the PFO.

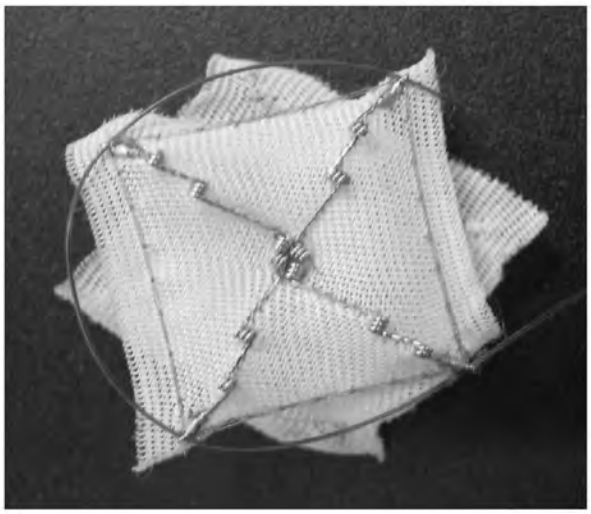

Figure 2. CardioSEAL device.

73% on 5 liters of O_2. Laboratory studies showed an elevated red blood cell count (5.83 x 10^6/µl), an elevated hematocrit (47.8%), an elevated D-Dimer (3.94 µg/ml), an elevated B-type natriuretic peptide (1180 pg/ml), and arterial blood gases demonstrating respiratory alkalosis (pH 7.46, pCO_2 29 mm Hg, pO_2 42 mm Hg, FiO_2 10 liters). A computed tomography (CT) angiogram did not show any evidence of pulmonary embolus, and pulmonary function tests showed mild to moderate obstructive ventilatory defect. CT of the abdomen showed hepatomegaly at 17 cm.

Electrocardiogram showed sinus rhythm with T-wave abnormality in antero-inferior leads, long QT interval, and left posterior hemi-fascicular block. Echocardiogram (ECHO) showed evidence of a severely enlarged right atrium and right ventricle, depressed right ventricular systolic function, normal left ventricular systolic function, and continuous flow to left atrium from an unknown source. A systolic pulmonary artery pressure was estimated to be at 40-45 mm Hg from a tricuspid regurgitation jet. A pulmonary regurgitation jet was not identified. TEE showed marked right heart enlargement and presence of a defect in atrial septum with the presence of a flap valve formed due to overlapping layers of foramen ovale with the blood flowing from the right atrium to the left atrium under this flap, consistent with a PFO.

Catheterization confirmed presence of low femoral artery saturation (82%) with normal saturation in the left upper pulmonary vein (100%). There was a 9 mm Hg pressure gradient across the interatrial septum with mean pressure in the right atrial of 20 mm Hg and mean pressure in the left atrial of 11 mm Hg. Pulmonary artery trunk pressure was moderately elevated at 40/20/28 mm Hg with normal capillary wedge pressure at 8 mm Hg. To evaluate for tolerance of right heart after closure, temporary occlusion of the PFO with the sizing balloon was attempted (Figure 1), and the femoral artery O_2 saturation increased from a value of 75% O_2 saturation to a value of 94% O_2 saturation at 10 minutes, and to a value of 95% O_2 saturation at 30 minutes. The size of the PFO was measured at 10 mm. Pulmonary artery trunk pressures (baseline 48/27/34 mm Hg, 37 minutes after occlusion 52/25/37 mm Hg) and aortic pressures (baseline 145/90 mm Hg, 37 minutes after occlusion 157/94 mm Hg) remained stable after temporary occlusion of PFO. A 23 mm CardioSEAL device (Figure 2) was subsequently placed in the PFO without complications. An ECHO obtained the next day documented successful PFO closure with minimal residual shunting. The patient's O_2 saturation ranged between 85%-93% on 5-6 liters of oxygen in the first 24 hours. At 1 month follow-up, the patient showed significant improvement in functional status with O_2 saturations of 82% on room air. She continued to be stable at 6 months post-procedure.

DISCUSSION

Clinical manifestations of PFO include stroke, platypnoea-orthodeoxia, decompression sickness, right to left shunt, and migraine headaches. Hypoxia secondary to right to left shunt (without Eisenmengers physiology or significantly elevated pulmonary artery pressures) is an uncommon presentation. Initial diagnosis via TEE requires detection of a shunt with either color Doppler

or agitated saline contrast with or without Valsalva maneuver. The agitated saline contrast study with TEE and the Valsalva maneuver is the gold standard test for detection of PFOs.

Pathophysiology

Right to left shunt via PFO is commonly seen secondary to chronically increased right side pressures including tetralogy of Fallot, pulmonary stenosis, right heart tumors, tricuspid atresia, tricuspid stenosis, ventricular septal defects, and atrial septal defects. There is another subset of patients wherein acute right to left shunting occurs secondary to increased right side pressures with recurrent pulmonary emboli, right ventricular infarction, pulmonary hypertension secondary to pneumonectomies or lobectomies, asthma, low atmospheric pressure, and pericardial tamponade.[3-8]

It is sometimes simple to find the trigger for right to left shunt, but in patients whose pulmonary artery trunk pressure was only moderately elevated, there is no easily identifiable single cause. Multiple theories have been postulated to explain severe shunting that can lead to hypoxia. One theory is the transient elevation of right atrial pressure in each cardiac cycle. The presence of sino-atrial node causes earlier depolarization of the right atrium leading to higher pressure in the right atrium compared to the left, thus leading to the right to left shunt.[9] This transient elevation of right-sided pressures is exacerbated in a variety of physiological conditions like respiratory cycles (inspiration), Valsalva maneuver, posture (underlying mechanism for platypnea-orthodeoxia syndrome), etc. A second theory that may explain this phenomenon is the flow of blood from the inferior vena cava preferentially toward the PFO (and inter-atrial septum), similar to the circulatory pattern in the fetus.[10-11] This flow is secondary to the anatomical remodeling of the right atrium, positioning the fossa ovalis in the direction of the blood flow from the inferior vena cava, with the Eustachean valve contributing significantly to the flow phenomenon into fossa ovalis.[11] A third theory proposes the decreased compliance of the right ventricle in comparison to the left ventricle as the mechanism of cause.[12]

Diagnosis and Treatment

The gold standard for diagnosing PFO is TEE with agitated saline contrast and Valsalva maneuver. Typically initial screening is performed with TTE with agitated saline contrast.[13] Because of the preferential blood flow from the inferior vena cava toward the atrial septum, contrast administration from the femoral vein has shown higher sensitivity for detection of PFOs compared to the ante-cubital vein approach.[13-14] Common respiratory conditions and thromboembolic events as a cause of hypoxia should be ruled out initially. Correction of hypoxia with temporary occlusion of the PFO during catheterization will provide clear evidence of PFO with right to left shunt as the etiology of hypoxia, as demonstrated in this patient.

Mechanical closure is clearly indicated in significantly hypoxic patients. In recent years, with advancement of percutaneous techniques, transcatheter closure of the PFO has yielded positive results without accompanying surgical morbidity and mortality.[15] Most studies regarding the effectiveness of closure devices in patients with PFOs were performed in patients with cryptogenic strokes.[16-17] Complications arising from percutaneous closure include thrombus formation on the closure device, pericardial effusion, or fracture of the device. One case series reported thrombus formation on the closure device in only 20 of 1000 patients who had device placement.[18]

In summary, this case illustrates the pathophysiological mechanisms underlying a left to right shunt across PFO with only moderately elevation of the pulmonary artery trunk pressures. This is a rare but identifiable cause of hypoxia, which can be simply corrected.

Acknowledgments/Funding/Support: The authors thank Marshfield Clinic Research Foundation for its support through the assistance of Anne Nikolai, Linda Weis, and Alice Stargardt in the preparation of this manuscript.
Financial Disclosures: None declared.

REFERENCES

1. Gill EA Jr. Definitions and pathophysiology of the patent foramen ovale: broad overview. *Cardiol Clin.* 2005;23:1-6.
2. Hagen PT, Scholz DG, Edwards WD. Incidence and size of patent foramen ovale during the first 10 decades of life: an autopsy study of 965 normal hearts. *Mayo Clin Proc.* 1984;59:17-20.
3. Estagnasie P, Djedaini K, Le Bourdelles G, Coste F, Dreyfuss D. Atrial septal aneurysm plus a patent foramen ovale. a predisposing factor for paradoxical embolism and refractory hypoxemia during pulmonary embolism. *Chest.* 1996;110:846-848.
4. Laham RJ, Ho KK, Douglas PS, et al. Right ventricular infarction complicated by acute right-to-left shunting. *Am J Cardiol.* 1994;74:824-826.
5. van Rossum P, Plokker HW, Ascoop CA. Breathlessness and hypoxaemia in the upright position after right pneumonectomy. *Eur Heart J.* 1988;9:1230-1233.
6. Robert R, Ferrandis J, Malin F, Herpin D, Pourrat O. Enhancement of hypoxemia by right-to-left atrial shunting in severe asthma. *Intensive Care Med.* 1994;20:585-587.
7. Levine BD, Grayburn PA, Voyles WF, Greene ER, Roach RC, Hackett PH. Intracardiac shunting across a patent foramen ovale may exacerbate hypoxemia in high-altitude pulmonary edema. *Ann Intern Med.* 1991;114:569-570.

8. Klepper JI, Seifert F, Lawson WE, et al. Intracardiac right-to-left shunting following cardiac surgery. *Am Heart J.* 1988;116:189-192.
9. Maraj R, Ahmed O, Fraifeld M, Jacobs LE, Yazdanfar S, Kotler MN. Hypoxia due to patent foramen ovale in the absence of pulmonary hypertension. *Tex Heart Inst J.* 1999;26:306-308.
10. Gallaher ME, Sperling DR, Gwinn JL, Meyer BW, Fyler DC. Functional drainage of the inferior vena cava into the left atrium—3 cases. *Am J Cardiol*. 1963;12:561-566.
11. Zanchetta M, Rigatelli G, Ho SY. A mystery featuring right-to-left shunting despite normal intracardiac pressure. *Chest.* 2005;128:998-1002.
12. Schoevaerdts D, Gonzalez M, Evrard P, Buche M, Installe E. Patent foramen ovale: a cause of significant post-coronary artery bypass grafting morbidity. *Cardiovasc Surg.* 2002;10:615-617.
13. Gill EA Jr, Quaife RA. The echocardiographer and the diagnosis of patent foramen ovale. *Cardiol Clin.* 2005;23:47-52.
14. Woods TD, Patel A. A critical review of patent foramen ovale detection using saline contrast echocardiography: when bubbles lie. *J Am Soc Echocardiography.* 2006;19:215-222.
15. Dearani JA, Ugurlu BS, Danielson GK, et al. Surgical patent foramen ovale closure for prevention of paradoxical embolism-related cerebrovascular ischemic events. *Circulation.* 1999;100:II171-II175.
16. Schrader R. Indication and techniques of transcatheter closure of patent foramen ovale. *J Interv Cardiol.* 2003;16:543-551.
17. Bridges ND, Hellenbrand W, Latson L, Filiano J, Newburger JW, Lock JE. Transcatheter closure of patent foramen ovale after presumed paradoxical embolism. *Circulation.* 1992;86:1902-1908.
18. Krumsdorf U, Ostermayer S, Billinger K, et al. Incidence and clinical course of thrombus formation on atrial septal defect and patient foramen ovale closure devices in 1000 consecutive patients. *J Am Coll Cardiol.* 2004;43:302-309.

advancing the art & science of medicine in the midwest

WMJ

WMJ (ISSN 1098-1861) is published through a collaboration between The Medical College of Wisconsin and The University of Wisconsin School of Medicine and Public Health. The mission of *WMJ* is to provide an opportunity to publish original research, case reports, review articles, and essays about current medical and public health issues.

Visit www.wmjonline.org to learn more.