Stepwise Progression of Right-to-Left Atrial Shunting

through a Combination of Patent
Foramen Ovale and Tricuspid Regurgitation

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Patent foramen ovale is a common clinical finding that generally becomes a concern in the presence of transient ischemic attack or stroke. Rarely, patent foramen ovale is associated with hypoxemia in the presence of substantial right-to-left atrial shunting.

We present the case of an 86-year-old woman with a pacemaker, who was initially asymptomatic notwithstanding a patent foramen ovale. Over 1.5 years, her symptoms progressed in a stepwise fashion, in the setting of progressive pacemaker-associated tricuspid regurgitation. Ultimately, the patient's symptoms and her hypoxemia resolved after percutaneous closure of her patent foramen ovale with use of a 25-mm "Cribiform" occluder device.

This case highlights the fact that clinically significant right-to-left shunting requires an anatomic lesion, such as patent foramen ovale, together with elevated right atrial pressure, which in this case was contributed by severe tricuspid regurgitation. (Tex Heart Inst J 2016;43(2):171-4)

Key words: Echocardiography, transesophageal; echocardiography, transthoracic; foramen ovale, patent/complications/physiopathology/therapy; heart septal defects, atrial; pacemaker, dual-chamber; septal occluder device; tricuspid regurgitation

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Patent foramen ovale (PFO) is a common clinical finding by transthoracic echocardiography (TTE), for it occurs in 25% of the adult population.¹ Although most patients with PFO are asymptomatic, PFO has been associated with serious complications, including stroke due to paradoxical embolism, and migraine headaches.^{2,3} In rare cases, hypoxemia associated with PFO's right-to-left shunting can lead to symptoms. We present a case of a patient with a PFO that became clinically significant in the presence of progressive pacemaker-associated tricuspid regurgitation (TR), and resolved after closure of the shunt with an occluder device.

Case Report

In October 2012, an 86-year-old woman presented at our clinic for evaluation of intermittent dyspnea on exertion. She had a medical history significant for percutaneous coronary intervention to the right coronary artery (14 years earlier) and dual-chamber pacemaker placement for brady-tachy syndrome (8 years earlier). Transthoracic echocardiography, performed 2 years earlier, had shown normal left ventricular function, mild-to-moderate mitral and tricuspid regurgitation, and a PFO.

At this visit, the patient reported dyspnea on exertion that had worsened over several weeks. Physical examination revealed elevated jugular venous pressure, a right ventricular (RV) lift, and a grade 3/6 systolic murmur consistent with TR, although no peripheral edema was present. Repeat TTE showed normal left ventricular function with moderate-to-severe TR caused by impingement of the RV pacemaker lead on the septal leaflet of the tricuspid valve (Fig. 1), and once again the presence of a PFO. A transesophageal echocardiogram (TEE) showed the PFO in color-flow Doppler mode with right-to-left shunting evident upon agitated-saline injection (Fig. 2), and moderate TR. The patient showed clinical improvement after she was started on 20 mg/d of furosemide.

Ten months later, she presented at the hospital with progressive malaise and fatigue, experienced while ballroom dancing. Results of resting and ambulatory oximetry included normal saturation at rest (96%), but hypoxemia with ambulation (81%). Transthoracic echocardiography showed moderate TR, with evidence of right-to-left

Fig. 1 Transthoracic echocardiogram (apical 4-chamber view with right ventricle on the right) shows incomplete coaptation of the tricuspid valve due to impingement of the pacemaker lead on the septal leaflet.

Supplemental motion image is available for [Figure 1](#).

Fig. 2 Transesophageal echocardiogram (bicaval view, with zoom of the interatrial septum and simultaneous biplane view) shows right-to-left shunting upon injection of agitated saline.

Supplemental motion image is available for [Figure 2](#).

shunting in color-flow Doppler mode, but not during agitated-saline injection. Pulmonary evaluation included computed tomography of the lungs, which was negative for pulmonary embolism or parenchymal disease. Pulmonary function testing showed mild obstructive lung disease and decreased diffusion capacity for carbon monoxide. After her hypoxemia resolved, she was discharged for additional evaluation as an outpatient.

During supine bicycle TTE, she developed hypoxemia after 2 minutes of exercise (oxygen saturation, 78%) and showed right-to-left shunting upon agitated-saline injection both at rest and during exercise. As a result of this study, she was referred for right- and left-sided heart catheterization. Right-sided catheterization was performed with an oximetry analysis (Table I), which revealed a mean right atrial pressure of 10 mmHg with a V wave to 16 mmHg; a mean left atrial pressure of 12

TABLE I. Hemodynamic Measurements and Oximetry Values at First Right-Sided Heart Catheterization

Chamber	Pressure (mmHg)	Oxygen Saturation (%)
Inferior vena cava	—	54.5
Superior vena cava	—	57.3
Right atrium (mean)	10	54.6
Right ventricle (systolic/end-diastolic)	27/10	54.5
Pulmonary artery (mean)	16	54.3
Left atrium (mean)	12	93.5

mmHg; and systolic, diastolic, and mean pulmonary artery (PA) pressures of 27, 9, and 16 mmHg, respectively. Cardiac output (Fick method) was depressed at 1.8 L/min in the presence of elevated systemic vascular resistance (3,900 dyn•s/cm⁵). Left-sided catheterization revealed a dominant right coronary artery containing a patent stent as well as minor luminal irregularities of the left anterior descending and right coronary arteries. Given mean right atrial pressure less than left atrial pressure, normal PA pressures, and the absence of hypoxemia in the presence of an alternative explanation for her symptoms (obstructive lung disease and heart failure with preserved ejection fraction), it was decided that there was not definite evidence to support closure of the PFO at that time.

Five months later, the patient presented at the hospital after several days of confusion and dyspnea. Physical examination revealed markedly elevated jugular venous pulsation and lower-extremity edema. Her serum sodium level was 111 mmol/L. Pacemaker interrogation revealed normal device function with no high-rate episodes. While hospitalized, she was witnessed to have multiple episodes of acute hypoxemia while recumbent, during which her pulse oximetry level fell to as low as 60%. The transient hypoxemia was refractory to pure oxygen supplementation but improved with upright positioning. Repeat TTE revealed severe TR (Fig. 3), as supported by findings of a V-shaped Doppler signal (Fig. 4) and systolic reversal of the hepatic vein flow by Doppler. In addition, there was substantial right-to-left flow across the PFO in color-flow Doppler mode (Fig. 5). Results of a transcranial Doppler study confirmed a right-to-left shunt, present both at rest and with the Valsalva maneuver.

The patient again underwent right-sided heart catheterization. At the time of the procedure, there was systemic hypoxemia at rest (oxygen saturation, 87%). Hemodynamic measurements included a mean right atrial pressure of 16 mmHg; a mean left atrial pressure of 15 mmHg; and systolic, diastolic, and mean PA pres-

Fig. 3 Transthoracic echocardiogram with color-flow Doppler (apical 4-chamber view with right ventricle on the right) shows severe tricuspid regurgitation.

Supplemental motion image is available for [Figure 3](#).

Fig. 4 Continuous-wave Doppler interrogation of the tricuspid regurgitation jet shows a dense, early-peaking, V-shaped signal consistent with severe tricuspid regurgitation.

Fig. 5 Transthoracic echocardiogram with color-flow Doppler (apical 4-chamber view with zoom of the interatrial septum and right atrium on the right) shows right-to-left flow across the patent foramen ovale.

Supplemental motion image is available for [Figure 5](#).

tures of 39, 15, and 23 mmHg, respectively. Her pulse oximetry level fell from 90% to 80% when the catheter wire was passed through the PFO. A 25-mm “Crib-riform” septal occluder device (St. Jude Medical, Inc.; St. Paul, Minn) was then deployed under intracardiac echocardiographic guidance without complications.

After PFO closure, the patient did well. The severe TR was well managed with careful diuretic use. She had experienced no further hypoxic events in the 1.5 years since the procedure, and had returned to her pastime of ballroom dancing.

Discussion

Patent foramen ovale usually becomes a clinical concern only when patients experience a transient ischemic attack or stroke. Even in these cases, the benefit of PFO closure remains debatable.⁴ An important, although unusual, clinical consequence of PFO is the development of hypoxemia via right-to-left shunting. Hypoxemia was the indication for PFO closure in only 18 of 800 patients (2%) in a series reported by Inglessis and colleagues.⁵

Right-to-left shunting occurs when the normally low (<5-mmHg) right atrial pressure is elevated because of substantial RV dysfunction or severe TR. The resulting elevation of right atrial pressure, exceeding that of the left atrium, favors right-to-left shunting. Multiple causes of RV dysfunction have been associated with right-to-left shunting, including RV infarction, carcinoid syndrome, cardiomyopathy, and TR.⁶⁻⁹

Our patient had a known PFO and developed pacemaker-related TR. She initially presented with mild symptoms due predominantly to volume overload from the TR, but her symptoms progressed and she presented with upright hypoxemia (platypnea-orthodeoxia).¹⁰ We postulate that, as the severity of her pacemaker-mediated TR worsened, so too did the severity of her right-to-left shunting, and she ultimately presented with severe recumbent hypoxemia that improved after percutaneous closure of her PFO.

Whereas TTE typically identifies the presence of PFO, right-to-left shunting is not well detected by contrast TTE: a recent meta-analysis showed an overall sensitivity of 46%.¹¹ However, TEE has an overall sensitivity of 89%.¹² Transcranial Doppler has the highest sensitivity and specificity for the diagnosis of right-to-left shunting, but might not be widely available.¹³ Given the dynamic nature of symptoms in patients who present with right-to-left shunting, a comprehensive imaging evaluation is of the utmost importance.

The factors that affect the clinical presentation of patients with right-to-left shunting are unclear, but our case report highlights the contributions of increased right atrial pressure and body position. Notably, we failed to definitively identify right-to-left atrial shunting during

the first right-sided heart catheterization. One possible explanation for this is that hypovolemia caused by pre-procedural fasting might have decreased right-to-left shunting. Indeed, Afonso and colleagues found that the detection rate for PFO increased from 11% to 26% after saline loading.¹⁴ Saline loading can easily be performed in future cases to improve sensitivity for the detection of right-to-left atrial shunting during right-sided heart catheterization. In addition, body position might have played a role. In 2015, Moses and colleagues showed that PFO recruitment was higher in the upright position than in the supine.¹⁵ Consequently, a second possible explanation for our failure to definitively identify right-to-left atrial shunting at the initial catheterization is that the supine position required for the procedure might have decreased right-to-left shunting.

Once the right-to-left shunting was identified, we pursued percutaneous closure of the PFO, which led to complete resolution of the patient's symptoms. Transcatheter closure of PFO has been shown to be both safe and effective.⁵ Furthermore, percutaneous closure of PFO for hypoxemia has resulted in improvements in right-to-left shunting, in functional class, and in oxygen requirements.¹⁶

Our case highlights the importance of maintaining high suspicion of right-to-left shunting as a cause of hypoxemia in patients who have the anatomic and functional substrate; the diagnosis can be challenging in patients who have multiple or otherwise complex cardiopulmonary comorbidities.

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