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CASE REPORT

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Percutaneous closure of patent foramen ovale for treatment of hypoxemia: A case series and physiology review

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Abstract

Intracardiac right-to-left shunt (RTLS) mediated hypoxemia is a rare complication of patent foramen ovale (PFO). The process may be potentiated by reversal of the usual trans-atrial pressure gradient, or from alteration of intracardiac geometry such that venous flow is preferentially directed toward the PFO. We describe a series of four patients who presented with hypoxemia, detailing the diagnostic evaluation which led to the ascertainment of intracardiac RTLS across PFO as the culprit pathology. All underwent successful percutaneous closure with rapid resolution of hypoxemia. Particular attention is given to the underlying anatomic and physiologic derangements facilitating the intracardiac RTLS.

KEYWORDS
intracardiac shunt, platypnea-orthodeoxia syndrome

1 | INTRODUCTION

Intracardiac right-to-left shunt (RTLS) driven hypoxemia is a well-known phenomenon but remains an often-delayed diagnosis. The pathophysiology necessitates both anomalous structural communication and functional perturbation. The former is most commonly a patent foramen ovale (PFO).[1,2] The prevalence of PFO in adults is estimated to be 20%–30% and in the vast majority remains clinically insignificant.[3] Under normal physiological parameters, left atrial pressure is generally 5–8 mmHg higher than right atrial pressure, which results in functional closure of an existing PFO.[2] Both transient and chronic physiologic conditions that raise right-sided cardiac pressures can reverse this gradient, promoting RTLS with resultant hypoxemia. Intracardiac RTLS across a PFO also occurs in the setting of normal right-sided cardiac pressures when congenital or acquired distortions of the cardiopulmonary anatomy alter the geometric relationship between the interatrial septum and vena cava blood flow, resulting in preferential streaming of deoxygenated venous blood across the PFO.[4–9] The same process may also ensure from a tricuspid regurgitant jet. This physiology is often accentuated in the upright position, leading to presentation with platypnea-orthodeoxia syndrome.[5,10] When intracardiac RTLS across PFO is determined to be driving hypoxemia, percutaneous closure has been demonstrated to be highly efficacious.[10–13]

1.1 | Case series

1.1.1 | Case 1

An 82-year-old woman with no known cardiopulmonary history was admitted for subacute progressive dyspnea and hypoxemia. Symptoms worsened when standing, alleviated with recumbency, and had not improved despite bronchodilators, antibiotics, and corticosteroids. Arterial oxygen saturation (SaO_2) was 92% when supine and 73% with

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standing, with minimal improvement despite treatment with high fraction of inspired oxygen (FiO_2). Chest X-ray was notable for elevated right hemidiaphragm. Computerized tomography with angiography (CTA) of the chest was negative for pulmonary embolism. Transthoracic echocardiography (TTE) with saline bubble study revealed an intracardiac shunt across a PFO. Cardiac magnetic resonance imaging (CMR) confirmed a PFO with an aneurysmal interatrial septum, and a pulmonary-to-systemic blood flow ratio of 0.86. Subsequent right heart catheterization (RHC) with intracardiac echocardiography (ICE) demonstrated predominately RTLS across the PFO despite normal right-sided heart pressures (right atrial pressure 5 mmHg, pulmonary artery mean pressure 19 mmHg). The patient underwent successful PFO closure with a 30 mm GORE® CARDIOFORM Septal Occluder (GCSO; Gore Medical) which resulted in immediate and complete resolution of hypoxemia (preprocedure SaO_2 88% on 15 L/min high flow oxygen; postprocedure SaO_2 98% on room air). Diaphragmatic fluoroscopy with sniff testing confirmed right hemidiaphragmatic paralysis with paradoxical elevation during inspiration (Figure 1), the chronicity and etiology of which remain unknown. At 1-year follow-up, she continued to do well without any oxygen requirement.

1.1.2 | Case 2

A 69-year-old man with a history of ascending aortic aneurysm status post open repair with a 32 mm Dacron graft a decade prior, known PFO, paroxysmal atrial fibrillation, previous ischemic stroke, chronic obstructive pulmonary disease, and Parkinson's disease with recurrent falls and recent traumatic subdural hemorrhage precluding anticoagulation presented for evaluation of left atrial appendage occlusion (LAAO) device, as well as dyspnea with increased baseline oxygen requirement from 2- to 5 L/min over the preceding year despite stable pulmonary function testing. Previous TTE's from years prior had shown apical displacement of the tricuspid valve (TV) annulus relative to the mitral valve, raising suspicion of Ebstein anomaly, though only mild to moderate tricuspid regurgitation (TR). Evaluation proceeded with RHC and ICE, revealing ventricularly displaced TV, severe TR, highly mobile interatrial septum, significant RTLS across a large PFO, elevated right atrial pressure of 20 mmHg, right ventricular pressure of 34/17 mmHg, and pulmonary artery pressure of 34/20 mmHg. Oximetry measured pulmonary vein saturation at 98.6% with simultaneous systemic saturation of 90%, further confirming intracardiac RTLS. He was deemed at prohibitive risk for open surgical repair of his TV. Subsequent transesophageal echocardiography, performed during deployment of a WATCHMAN® (Boston Scientific) LAAO device, confirmed Ebstein anomaly variant with apically and anteriorly displaced TV (Figure 2), and restricted mobility of the TV septal leaflet due to abnormal adherence to myocardium causing malcoaptation and severe TR, with the jet oriented toward his PFO. One month later, he underwent successful PFO closure with a 30 mm GCSO device with immediate improvement in oxygen saturation from 88% to 98%, and with no residual shunt seen across the interatrial septum. At 6-month follow-up, he was not requiring any supplemental oxygen.

1.1.3 | Case 3

An 83-year-old woman underwent four-vessel coronary artery bypass grafting (CABG) during which the right atrium was noted to be

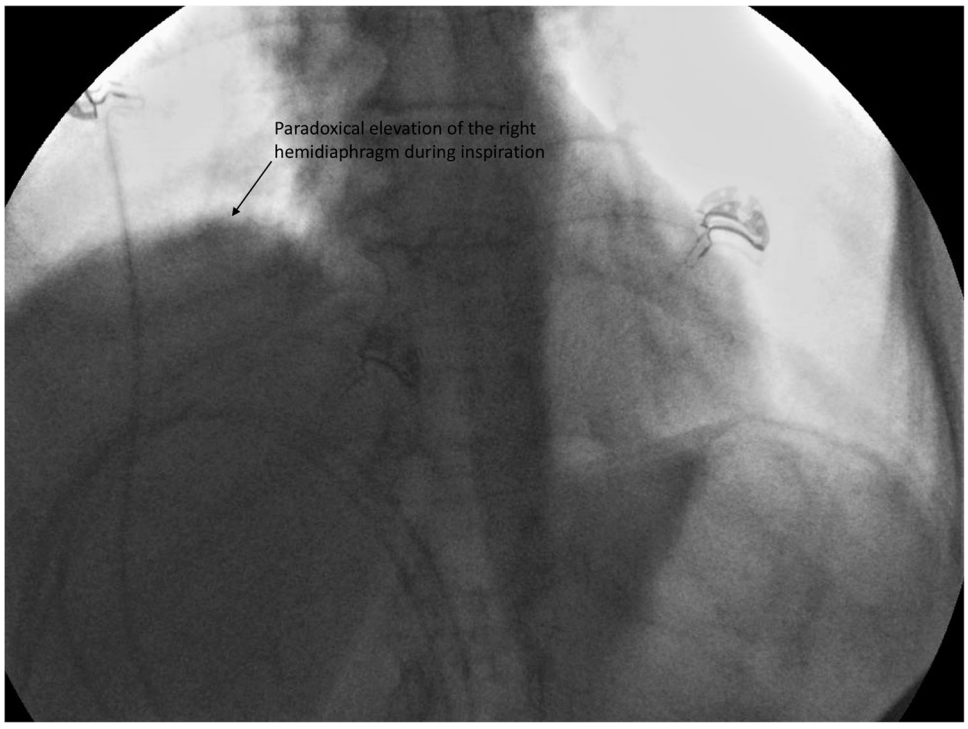

FIGURE 1 Diaphragmatic fluoroscopy demonstrating paradoxical elevation of the right hemidiaphragm during inspiration.

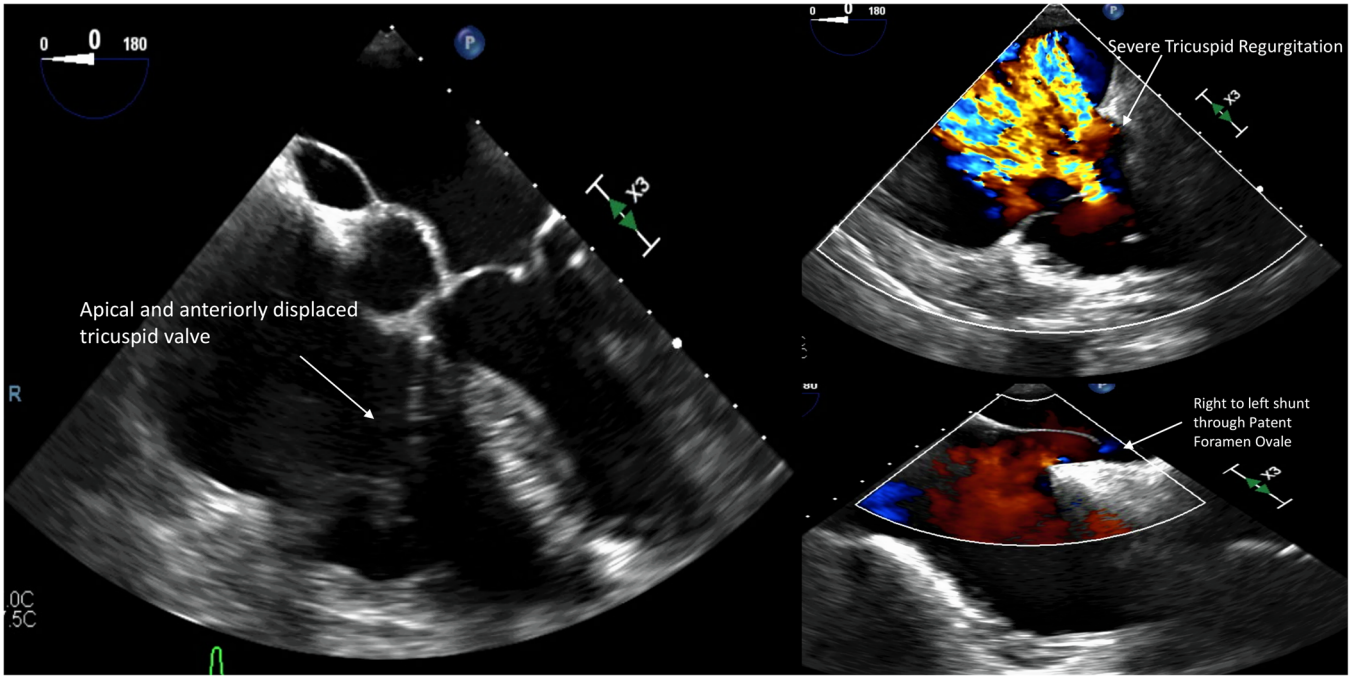

FIGURE 2 Transesophageal echocardiogram with color doppler showing structurally abnormal tricuspid valve, severe tricuspid regurgitation, and right-to-left shunt across a patent foramen ovale. [Color figure can be viewed at wileyonlinelibrary.com]

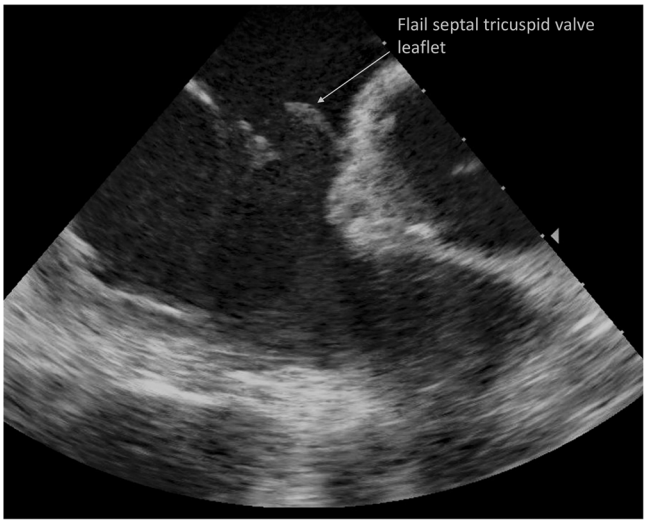

FIGURE 3 Intracardiac echocardiography showing flail septal tricuspid valve leaflet.

exceptionally fragile during cannulation and required multiple suture reinforcement. Preoperative TTE had shown no significant valvular disease with only mild mitral regurgitation. Postoperatively, she became persistently hypoxemic, requiring high-flow nasal cannula with no less than 50% FiO_2 for over a month despite vigorous diuresis. A chest CTA showed no pulmonary embolism or significant pulmonary pathology. She was transferred for further evaluation and TTE with bubble study was consistent with intracardiac RTLS. ICE demonstrated severe TR with flail septal leaflet (Figure 3), a hypermobile interatrial septum, and a large gap PFO with significant RTLS. Heart catheterization revealed normal right- and left-sided pressures (right atrial pressure 7 mmHg, right ventricular pressure 21/8 mmHg, pulmonary artery mean pressure 12 mmHg, left atrial pressure 6 mmHg), with 100% pulmonary vein saturation despite continued systemic hypoxemia. During fluoroscopy, her right hemidiaphragm was noted to be elevated with reduced excursion. The patient elected to proceed with percutaneous PFO closure and a 30 mm GCSO device was successfully deployed. Her hypoxemia rapidly resolved, and she was weaned to room air by the following day.

1.1.4 | Case 4

An 83-year-old man with history of bioprosthetic aortic valve replacement and four-vessel CABG 5 years prior was transferred for management of severe bioprosthetic aortic insufficiency driving decompensated heart failure with severe hypoxemic respiratory failure necessitating mechanical ventilation. Following extensive diuresis, pulmonary capillary wedge pressure was 15 mmHg, and he was able to be extubated to high flow noninvasive ventilation. After being deemed prohibitively high risk for re-do surgery, the patient underwent successful valve-in-valve transcatheter aortic valve replacement (TAVR) with a 29 mm CoreValve (Medtronic), with immediate reduction of left ventricular end-diastolic pressure from 34 to 8 mmHg. Concomitant angiography showed patent grafts. Despite radiographically alleviated pulmonary edema, the patient continued to have ongoing hypoxemia. Though initially attributed to aspiration pneumonitis and later pneumonia, he failed to improve despite antibiotics and time. As his course progressed, he was

observed to have sudden oxygen desaturations with standing. A TTE with bubble study revealed RTLS through PFO only occurring with Valsalva and standing, consistent with platypnea-orthodeoxia syndrome. There had been no aortic aneurysm, nor any cardiac or pulmonary artery compressive lesion seen on pre-TAVR CTs. Heart catheterization revealed normal right- and left-sided pressures (right atrial pressure 2 mmHg, pulmonary artery mean pressure 15 mmHg, left atrial pressure 6 mmHg). The patient underwent successful PFO closure with a 30 mm GCSO device with complete resolution of hypoxemia. At 1-month follow-up, the patient had no evidence of desaturation with 6-min walk test.

2 | DISCUSSION

With the onset of ventilation following birth, pulmonary vascular resistance rapidly falls, promoting opposition of the flap-like septum primum against the septum secundum with resulting functional closure of the foramen ovale. Subsequent fusion of these tissues results in an intact atrial septum with the formation of the remnant fossa ovalis. In an estimated 20%–30% of the population, this fusion remains incomplete, giving rise to a PFO.[1,3] While the vast majority remain clinically silent, given a promoting physiologic milieu, transient or sustained interatrial blood flow can occur. Such trans-atrial RTLS provides opportunity for paradoxical embolization which is the most common complication of PFO. In an even smaller subset, such shunting occurs with sufficient severity to manifest systemic hypoxemia.[1,11] In addition to interatrial communication, which can also be provided by an ASD, this process further requires a functional aberration. Intuitively, conditions that raise right-sided intracardiac pressures may provide the impetus for RTLS. However, this process can also be facilitated in the setting of normal right atrial pressure when an anatomical distortion alters the usual interface between the interatrial septum and either vena caval flow or, if present, a tricuspid regurgitant jet, resulting in preferential streaming of blood directed at and through an existing PFO.[4–9] In particular, horizontal displacement of the interatrial septum is more likely to result in the PFO being aligned with inferior vena cava (IVC) flow.[14] Predisposing variants include the presence of a prominent Eustachian valve or an atrial septal aneurysm (ASA).[7,8] The Eustachian valve is a crest of tissue located at the junction of the IVC and the right atrium and is a remnant of the embryonic right valve of the sinus venosus which serves the in-utero function of redirecting IVC blood flow through the foramen ovale. This structure involutes to a varying degree after birth.[15] An ASA results in the dynamic application of tension to an existing PFO, widening the defect and promoting RTLS.[11]

Each of the four described cases demonstrated unique underlying anatomic and physiologic derangements mediating intracardiac RTLS across a PFO. The first patient had right hemidiaphragmatic paralysis with resulting distortion of anatomy aligning inferior caval flow through a stretched PFO. The second case involved a variant of Ebstein anomaly with a structurally abnormal TV who had late-developing TR with regurgitant jet oriented toward the PFO, along with elevated right atrial pressure. An aneurysmal atrial septum and previous ascending aortic aneurysm repair also likely contributed. The third patient's shunt was also driven by a TR jet streaming at the PFO, this time from flail leaflet that arose as surgical complication, with additional anatomic predisposition from a hypermobile interatrial septum and iatrogenic right phrenic-nerve palsy. The final patient had undergone valve-in-valve TAVR, and we speculate that consequent reduction in previously elevated left atrial pressure was then enabling RTLS in anatomy predisposed to shunting. Several other anatomic changes incurred with age or surgery have also been shown capable of inducing this phenomenon, in particular any structural alteration of the aortic root or arch.[2,6] The degree of these geometric distortions is frequently amplified in the upright posture as the accompanying decline in right atrial filling applies additional tension to the atrial septum.[5,10] Accordingly, presentation with platypnea-orthodeoxia syndrome is not uncommon.

When PFO-mediated RTLS is established as the etiology of hypoxemia, percutaneous closure has been consistently demonstrated to be efficacious with low complication rates and is the accepted standard of care.[4,10–13] Indeed, as evidenced by these cases, dramatic and rapid resolution of hypoxemia can be achieved. Procedural success is contingent, however, upon confirming the hypoxemia is principally resultant of intracardiac RTLS rather than any concomitant pulmonary pathology.[4] While the gold standard remains confirming the presence of a step-down in oxygen gradient between the pulmonary vein and left atrium, contemporary imaging technologies including ICE and CMR can also provide substantial evidence.[1,4,6] Temporary occlusion of the PFO by inflation of a sizing balloon provides a definitive demonstration of hypoxemia amelioration, while simultaneously affording assessment of the changes in right-sided cardiac pressures before proceeding with the deployment of the permanent device.[12] The latter is particularly important when concern exists for right ventricular dysfunction or pulmonary hypertension, as the closure of a PFO that is functioning as a pressure release valve can result in acute right ventricular failure.[1,11]

3 | CONCLUSION

In a minority of patients with PFO, promoting conditions can generate RTLS with resulting systemic hypoxemia. Intuitively, elevated right-sided cardiac pressures can provide the impetus; however, acquired anatomical distortions in the geometric relationship between venous flow and the interatrial septum can also facilitate this process. This case series contributes to the existing body of evidence that when intracardiac RTLS is determined to be driving hypoxemia, percutaneous closure of PFO provides a safe and effective treatment.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this case series.

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