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CASE REPORT

CLINICAL CASE

Carcinoid Heart Disease With Hypoxemia

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ABSTRACT

Patent foramen ovale (PFO) complicated with carcinoid heart disease (CHD) can cause severe hypoxia and worsening clinical conditions. We report the case of a patient with CHD in poor general condition with multiple severe valve regurgitations and PFO, who underwent successful percutaneous closure of the PFO. (J Am Coll Cardiol Case Rep 2024;29:102335) © 2024 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

HISTORY OF PRESENTATION

A 73-year-old man with a metastatic neuroendocrine tumor of the liver presented to our hospital with severe fatigue, refractory hypoxia on home oxygen, and unexplained syncope.

On physical examination, the patient's blood pressure was 100/55 mm Hg, his heart rate was 63 beats/min, his respiratory rate was 16 breaths/min, his temperature was 36.7 °C, and his oxygen saturation was 84% on 2 L/min of oxygen in the sitting position, which slightly improved to 95% in the supine position. He also showed peripheral edema, jugular vein distention, and a 3/6 holosystolic murmur best heard at the left lower sternal border. Severe exertional dyspnea categorized as New York Heart Association functional class IV and repeated unexplained syncope kept the patient in bed, with his physical frailty worsening to the Clinical Frailty Scale of 7.

Arterial blood gas analysis revealed oxygen tension of 60.6 mm Hg on 2 L/min oxygen. Relevant findings were as follows: hemoglobin, 12.9 g/dL; N-terminal pro-B-type natriuretic peptide, 1,242.2 ng/L; serum albumin, 2.4 g/dL; and creatinine, 1.54 mg/dL. Electrocardiography (ECG) on admission revealed a regular sinus rhythm, and no arrhythmias were observed during hospitalization.

LEARNING OBJECTIVES

- To define a diagnostic plan for CHD complicated by hypoxemia centered on PFO.
- To devise a therapeutic plan in spite of high surgical risk.

PAST MEDICAL HISTORY

The patient had undergone surgery for a primary neuroendocrine tumor of the small intestine 25 years earlier and was being followed up for postoperative liver metastasis without an indication for surgery.

DIFFERENTIAL DIAGNOSIS

On the basis of the symptoms and examination results, carcinoid heart disease (CHD) was suspected. Other differential diagnoses included infective endocarditis and rheumatic heart disease.

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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ABBREVIATIONS AND ACRONYMS

CHD = carcinoid heart disease

CT = computed tomography

ECG = electrocardiography

PFO = patent foramen ovale

RLS = right-to-left shunt

TEE = transesophageal echocardiography

TR = tricuspid regurgitation

TTE = transthoracic echocardiography

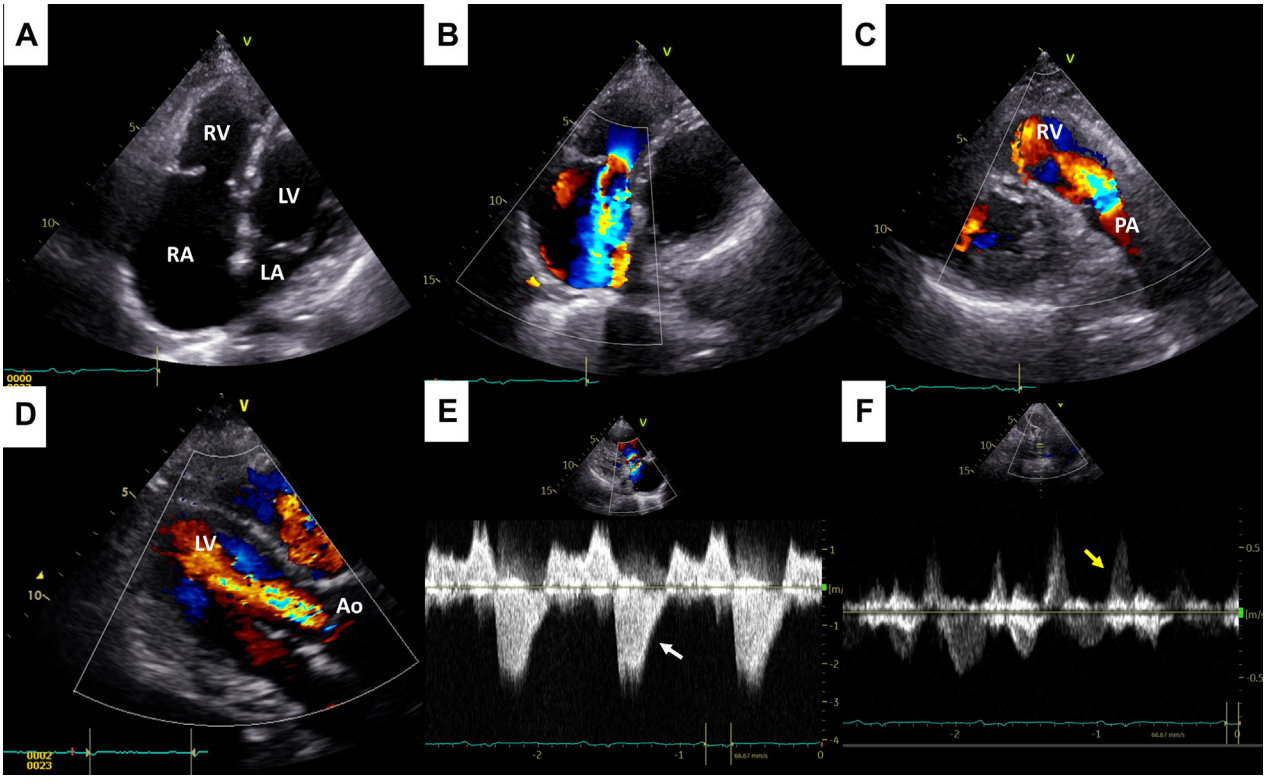
INVESTIGATIONS

Transthoracic echocardiography (TTE) revealed torrential tricuspid regurgitation (TR), severe pulmonary regurgitation with a dilated right ventricle, and moderate aortic regurgitation (**Figures 1A to 1D**, Videos 1A and 1B, 2, and 3). The tricuspid and pulmonary valves appeared rigid and restricted in their motion, resulting in severe regurgitations with the cut-off sign of the TR velocity profile using continuous-wave Doppler (**Figure 1E**). TR led to dilation of the inferior vena cava and flow reversal in the hepatic veins (**Figure 1F**). Bubble contrast TTE revealed a patent foramen ovale (PFO) with a grade 4 right-to-left shunt (RLS) at rest (Video 4). Transesophageal echocardiography (TEE) was attempted using conscious sedation; however, the procedure had to be discontinued because of a decrease in the patient's oxygen saturation. Therefore, ECG-gated cardiac computed tomography (CT) was alternatively performed to evaluate valvular heart disease. The tricuspid and pulmonary valves were thickened and shortened, thereby causing coaptation loss of leaflets with a large regurgitant orifice area (**Figures 2A to 2C**, Videos 5 and 6). Moreover, cardiac CT confirmed the presence of a PFO (**Figure 2D**). Chest and abdominal CT revealed multiple liver metastases (**Figure 2E**) without pulmonary embolism or thoracic disease.

MANAGEMENT

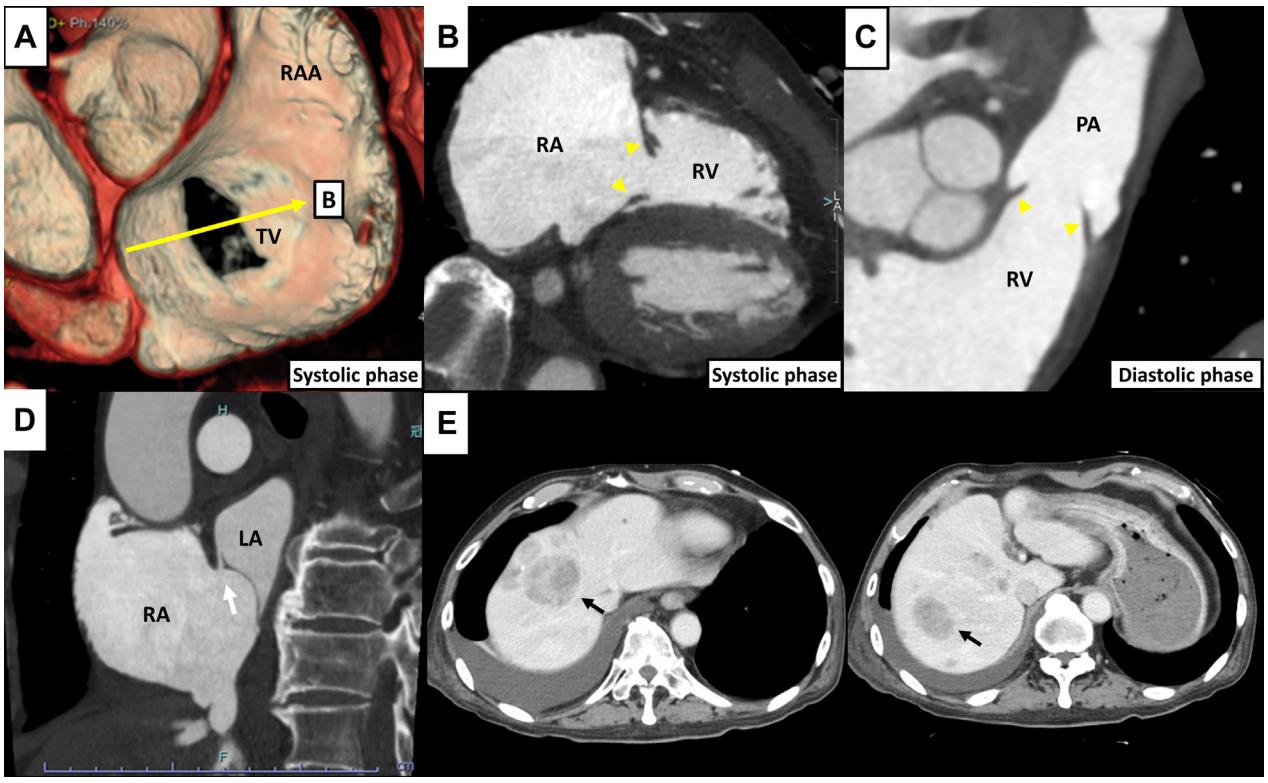
Carcinoid syndrome was confirmed with an elevated 24-hour urinary 5-hydroxyindoleacetic acid value of 69 mg/24 h (normal range: 2-9 mg/24 h). Our heart team concluded that although the patient had an indication for treatment of valve lesions and RLS, he was considered inoperable because of his severe frailty. Therefore, the patient began treatment with subcutaneous octreotide (300 μg daily); however, the patient's symptoms did not improve with the medical

FIGURE 1 Transthoracic Echocardiography



Transthoracic echocardiography showing (A and B) torrential tricuspid regurgitation with the coaptation loss of leaflets, (C) severe pulmonary regurgitation, (D) moderate aortic regurgitation, (E) tricuspid regurgitation velocity profile using continuous-wave Doppler (white arrow), and (F) flow reversal in the hepatic veins (yellow arrow). Ao = aorta; LA = left atrium; LV = left ventricle; PA = pulmonary artery; RA = right atrium; RV = right ventricle.

FIGURE 2 **Electrocardiogram-Gated Cardiac Computed Tomography**



(A) Three-dimensional and (B) cross-sectional e-dimensional computed tomography images showing a thickened and retracted tricuspid valve (TV) in the late systolic phase (yellow arrowheads). (C) The thickened and retracted pulmonary valves in the diastole phase (yellow arrowheads). (D) Patent foramen ovale (white arrow). (E) Abdominal computed tomography showing multiple liver metastases (black arrows). RAA = right atrial appendage;; other abbreviations as in Figure 1.

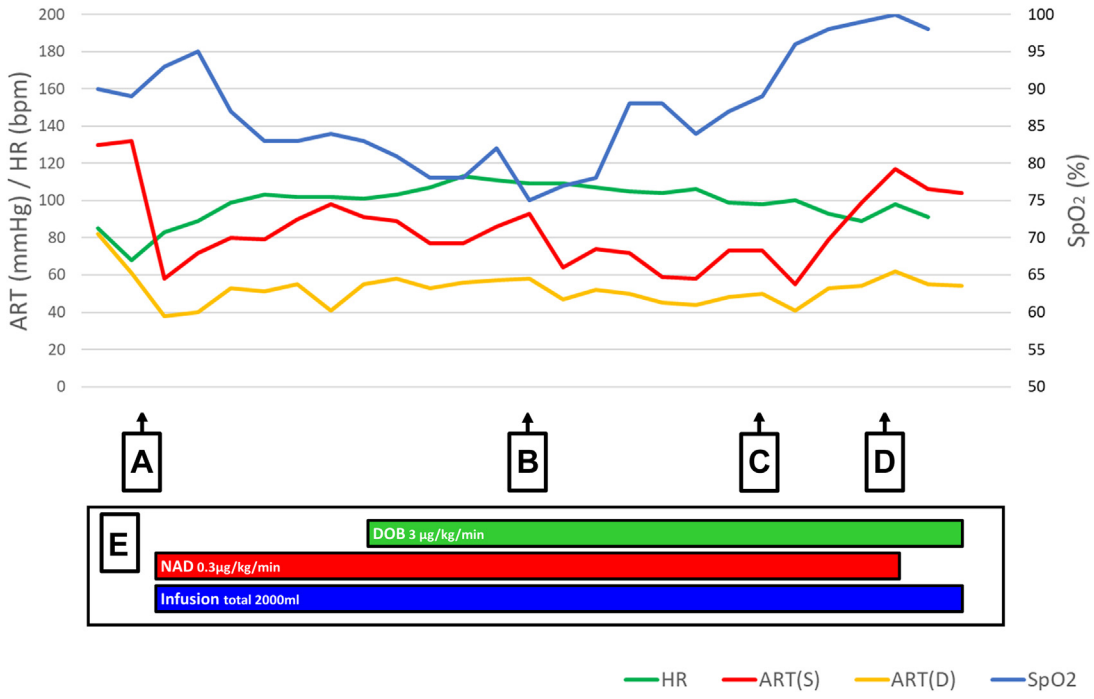
treatment only. We considered the possibility that minimizing the RLS by percutaneous closure of the PFO could improve the patient's quality of life. PFO closure was performed using general anesthesia and with TEE guidance because there was concern about decreased oxygenation of the patient during the procedure using conscious sedation. However, after the induction of general anesthesia and the initiation of positive pressure ventilation, the patient's blood pressure dropped markedly, and his arterial oxygen saturation decreased from 95% to 76%. These changes were attributed to systemic vasodilation and increased RLS caused by increased right atrial pressure after the initiation of positive pressure ventilation because the patient responded to intravenous volume replacement and administration of norepinephrine (Figures 3A and 3E). After deployment of a 25-mm Amplatzer PFO Occluder (Abbott Vascular), his oxygen saturation gradually improved from 76% to 85% (Figure 3B), although bubble contrast TEE revealed some residual RLS, which was expected to disappear gradually with endothelialization of the device in several months. Furthermore, despite initiating dobutamine infusion in advance, cardiac output decreased because of reduced RLS after device implantation, thus resulting in a rapid decrease of systolic blood pressure from 90 to 58 mm Hg, which improved with additional fluid loading and continuous dobutamine administration (Figures 3B and 3E). After weaning from mechanical ventilation (Figures 3C and 3D), the patient's arterial oxygen saturation improved and was maintained at >90% of room air.

The postoperative course was uneventful. The patient no longer had unexplained syncope, and he had markedly improved shortness of breath on exertion.

DISCUSSION

Carcinoid syndrome occurs in 30% to 40% of patients with neuroendocrine tumors, with an incidence rate ranging from 2.5 to 5 cases per 10,0000 population.

FIGURE 3 Intraprocedural Hemodynamic Changes



(A) Induction of general anesthesia and initiation of positive pressure ventilation. (B) Deployment of a 25-mm Amplatzer PFO Occluder (Abbott Vascular). (C) Reversal of neuromuscular blockage with sugammadex. (D) Weaning from ventilator management. (E) The patient was treated with intravenous volume replacement with 2,000 mL and administration of norepinephrine of 0.3 μg/kg/min and dobutamine of 3 μg/kg/min. ART(D) = diastolic arterial blood pressure; ART(S) = systolic arterial blood pressure; DOB = dobutamine; HR = heart rate; NAD = norepinephrine; NIBP = noninvasive blood pressure; Spo_2 = oxygen saturation.

This syndrome is associated with liver metastases, with consequent release of vasoactive substances into the systemic circulation through the hepatic vein. CHD frequently occurs in carcinoid syndrome and is accountable for substantial morbidity and mortality.[1] CHD typically affects the right-sided heart valves more than left-sided heart valves because of the inactivation of serotonin by the lung. Right-sided CHD may cause exertional dyspnea, fatigue, peripheral edema, and right-sided heart failure. PFO, which complicates 40% of CHD cases, is mainly involved in the pathologic features of the left-sided heart valves and causes severe hypoxia secondary to RLS.[2]

Surgical valve replacement is the curative treatment for symptomatic carcinoid valve disease; however, because of the overall mortality risk, surgery is often deemed impossible in patients in severely impaired physical condition. Percutaneous closure of the PFO is considered useful as a palliative treatment for hypoxic symptoms of RLS; however, its efficacy in inoperable patients with severe CHD is unknown.[2,3] Actually, in our case, progression of right-sided heart failure and constant RLS through the PFO caused severe dyspnea and hypoxia. Our patient required combined surgery for the tricuspid valve, pulmonary valve, and PFO but was considered inoperable because of severe frailty. Only PFO closure was performed to alleviate his symptoms, and his general condition improved. Subsequent vigorous rehabilitation should be recommended for the patient in case progression of heart failure symptoms refractory to medication occurs in the future.

Nevertheless, several aspects should be considered even when treating only PFO in patients with CHD. First, the induction of general anesthesia and mechanical ventilation may cause hemodynamic compromise. Severe CHD can lead to severe hypotension secondary to systemic vasodilation caused by

general anesthesia. Furthermore, a PFO can cause severe hypoxia because of an increase in RLS caused by increased right atrial pressure after the initiation of positive pressure ventilation. Second, in patients with a large RLS volume, the reduction in shunt volume when a PFO closure device is implanted may decrease cardiac output and lead to cardiogenic shock. To the best of our knowledge, only 2 cases of hemodynamic deterioration during percutaneous closure of the PFO using general anesthesia have been reported (Supplemental Table 1).[3,4] Less invasive local anesthesia may be preferable when performing this procedure in severely ill patients.

FOLLOW-UP

Seven months after the procedure, the patient was living independently at home without apparent worsening of heart failure.

CONCLUSIONS

Closing the PFO percutaneously could serve as a secure and efficient choice to alleviate symptoms and address hypoxia when managing CHD characterized by severe hypoxia and a compromised general condition.

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The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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KEY WORDS carcinoid heart disease, patent foramen ovale

APPENDIX For a supplemental table and supplemental videos, please see the online version of this paper.