Patent Foramen Ovale With Asymmetric Pulmonary Venous Flow Reversal

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INTRODUCTION

The evaluation of pulmonary venous flow is part of a comprehensive transesophageal echocardiogram (TEE) and can provide clinical information regarding severity of mitral regurgitation (MR). We report a case of isolated right-sided pulmonary venous flow reversal in the setting of a patent foramen ovale (PFO) in a patient being evaluated for endocarditis.

CASE PRESENTATION

A 43-year-old patient with a history of *Streptococcus pyogenes* bacteremia due to lower-extremity skin and soft tissue infections presented to the emergency department (ED) for fever 5 months after their most recent hospitalization for recurrent cellulitis. The patient noted that their bilateral lower extremities are affected by chronic venous stasis dermatitis, which had developed with worsening edema, erythema, and pain over the past days.

In the ED, the patient was febrile to 101.5°F, with other vital signs being unremarkable. Initial bloodwork was notable for leukocytosis of 16,800/mm^3 on a complete blood count with 86% neutrophils. Physical examination was notable for left greater than right lower-extremity erythema, warmth, and tenderness, with areas of excoriations and associated scabs but no areas of purulence. The patient was also noted to have a furuncle on the dorsal aspect of their right hand and tenderness and restricted movement of their left shoulder.

The patient otherwise had a medical history of asthma, chronic obstructive pulmonary disease, anxiety, depression, and substance use disorder currently in remission, maintained on methadone. They had no prior surgeries.

The patient was started on intravenous antibiotics in the ED based on their known history of recurrent cellulitis complicated by bacteremia and was admitted to the hospital. Blood cultures from presentation resulted in 4/4 bottles positive for methicillin-sensitive *Staphylococcus aureus*. The patient was noted to intermittently need nasal cannula oxygen overnight, raising concern for undiagnosed obstructive sleep apnea, for which the patient was recommended to follow up for evaluation as an outpatient.

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2468-6441
https://doi.org/10.1016/j.case.2024.11.005

A transthoracic echocardiogram conducted the day after presentation did not reveal any vegetations; however, clinical suspicion for endocarditis remained high given subsequent findings of septic arthritis in the patient's left knee and left shoulder requiring washout with orthopedic surgery. Further workup with TEE was recommended by the infectious diseases consultation team.

Review of the patient's cardiac workup showed normal sinus rhythm on electrocardiogram (Figure 1). The patient's transthoracic echocardiogram demonstrated normal left ventricular systolic function with ejection fraction of 55% and normal diastolic function (left atrial [LA] volume indexed, 24 mL/m^2; medial e', 11.3 cm/sec; lateral e', 14.1 cm/sec; average E/e', 8.7 cm/sec; and tricuspid regurgitation peak velocity, 2.0 m/sec).

The patient's TEE showed normal left and right ventricular size and function, without evidence of atrial or ventricular septal defects (Figure 2, Videos 1 and 2). Examination of the patient's aortic, mitral, pulmonic, and tricuspid valves on TEE was unrevealing. In particular, only mild MR was seen (Figure 3, Videos 3 and 4).

Examination of the interatrial septum demonstrated a small PFO, with tunnel length of 1.1 cm and height of 0.2 cm (Figure 4A). It was noted that the size of the PFO significantly increased with deep inspiration, independent of the cardiac cycle (Video 5). The PFO reached a maximal size of tunnel length of 1.4 cm and height of 0.8 cm (Figure 4B) with deep inspiration. Color-flow Doppler images demonstrated eccentric flow of right-to-left shunt (Figure 4C and Video 6).

Further interrogation of the PFO demonstrated that the shunt flow was directed toward the right pulmonary veins (PVs), which are associated with systolic flow reversal in the right upper PV (Figure 5A). With expiration, systolic flow reversal in both the right upper and lower PVs appeared to improve (Figure 5B and C). Pulmonary venous flow in the left PVs was found to be normal (Figure 5D). The largest shunt was noted up to every 6 to 8 beats with deep inspiration, which matched the frequency of pulmonary venous flow reversal.

Given the patient's significant bacteremia with multiple sites of seeding, the infectious diseases team recommended treatment with 6 weeks of intravenous antibiotics. A peripherally inserted central catheter was placed prior to discharge, and the patient was recommended for close follow-up as an outpatient.

DISCUSSION

Thorough inspection of the PVs is an essential part of a comprehensive TEE examination. Systolic flow reversal has a high specificity (>80%) for severe MR even when the regurgitant flow is not directed into the PV images,[1,2] with prior studies reporting 82% to 100% specificity.[2-7] In normal physiology, pulmonary venous flow is pulsatile and comprises biphasic or triphasic forward flow in systole and diastole, while in MR, systolic blunting, late systolic flow

VIDEO HIGHLIGHTS

Video 1: Two-dimensional TEE, midesophageal orthogonal biplane (15° and 90°) views, demonstrates normal left ventricular size and global systolic function.

Video 2: Two-dimensional TEE, midesophageal orthogonal biplane (15° and 140°) views, demonstrates normal left ventricular size and global systolic function.

Video 3: Two-dimensional TEE, midesophageal 4-chamber (30°) zoom view with color-flow Doppler, demonstrates mild MR.

Video 4: Two-dimensional TEE, midesophageal long-axis (60°) zoom view with color-flow Doppler, demonstrates no MR.

Video 5: Two-dimensional TEE, midesophageal long-axis (120°) view after administration of agitated saline bubbles, demonstrates variation in the size of the PFO with respiration.

Video 6: Two-dimensional TEE, midesophageal long axis (119°) view with color-flow Doppler, demonstrates variation in the size of the PFO with respiration and right-to-left shunting.

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reversal, and, finally, pansystolic flow reversal occur with worsening degrees of regurgitation.[2,3]

The mechanism of PV systolic flow reversal is thought to be due to an increase in LA pressure and has been described in the setting of restrictive cardiomyopathy, left ventricular diastolic dysfunction, and atrial fibrillation in addition to MR.[2,8,9] Other causes of abnormal pulmonary venous flow patterns include hemodynamically significant left-to-right shunts such as atrial and ventricular septal defects.[10,11]

Severe MR can lead to an increase in LA pressure and subsequently PV flow reversal. However, another mechanism that could result from an increase in LA pressure is a right-to-left shunt. In our patient, who was undergoing examination for possible valvular involvement of methicillin-sensitive *Staphylococcus aureus*, the finding of pulmonary venous systolic flow reversal initially prompted a reexamination of the mitral valve in case mitral valve endocarditis leading to MR was missed. However, no mitral pathology was seen, which brought our focus to the patient's PFO.

The patient's interatrial septum was interrogated, and no atrial septal defect (ASD) was appreciated. Prior studies have also shown that in large uncomplicated ASD, there is an absence of distinct systolic and diastolic PV spectral Doppler displays and that instead there is a continuous antegrade spectral Doppler profile.[10] The spectral Doppler pattern in our patient had distinct systolic and diastolic components of the spectral profile.

Patent foramen ovales are common and are present in almost 1 in 4 adults.[12] In postnatal development, the septum primum, which had previously created a flap valve over the foramen ovale, fuses with the septum secundum. The cause of PFO is still unclear; however, there appears to be an association with anatomical features such as Chiari networks and persistent Eustachian valves.[12]

In our patient, PFO flow was minimal at baseline but increased dramatically during deep inspiration, exaggerating systolic flow reversal in the right PVs. The mechanism of this intermittent deep respiration is likely undiagnosed obstructive sleep apnea as the patient had been noted to intermittently require nasal cannula oxygen overnight during the admission. During inspiration, intrathoracic pressure decreases, augmenting venous blood return for right-sided filling.[13,14] This subsequent elevation in right atrial pressure increases the pressure difference between the left and right atria, leading to the

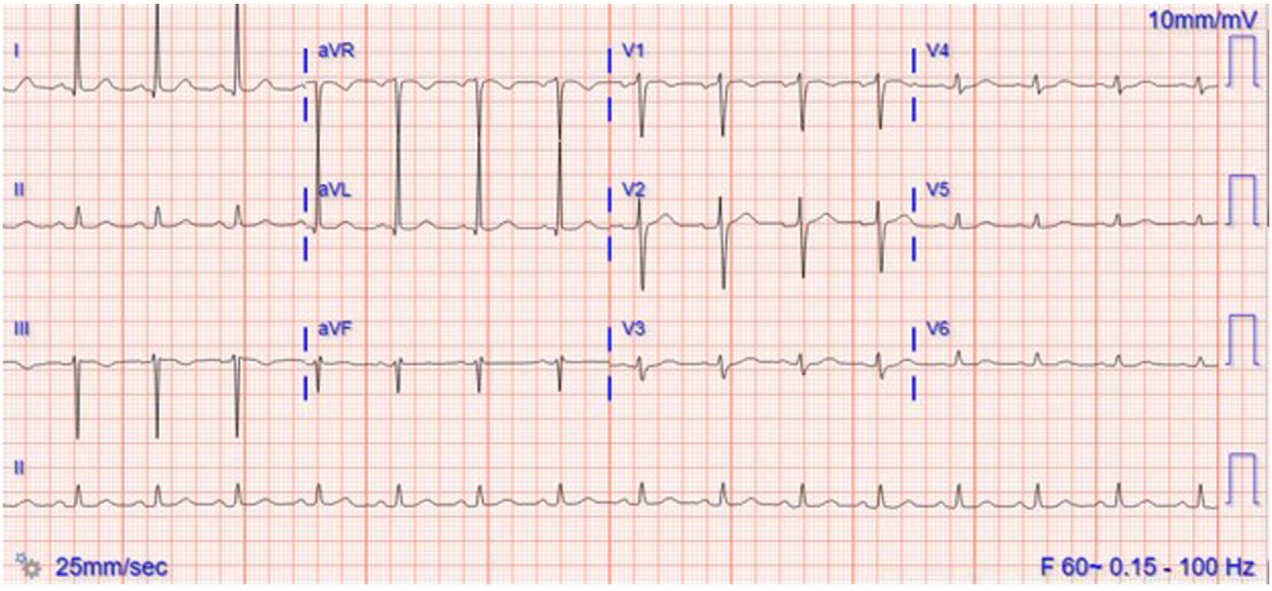

Figure 1 Twelve-lead electrocardiogram (prior to the TEE) demonstrates normal sinus rhythm without significant abnormal finding.

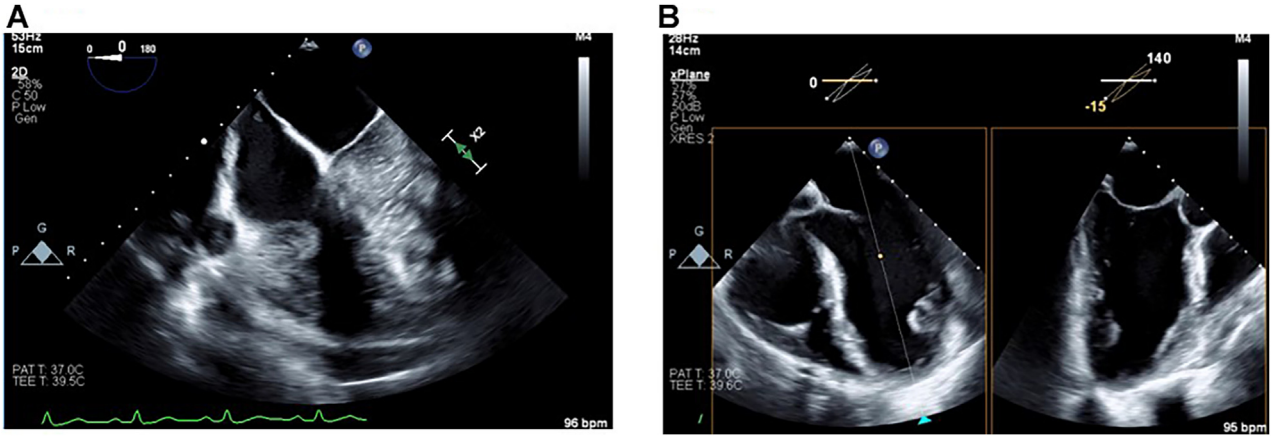

Figure 2 Two-dimensional TEE, midesophageal 4-chamber diastolic view (0°) rotated rightward **(A)**, demonstrates normal right heart dimensions; orthogonal biplane (15° and 140°) diastolic views **(B)** demonstrate normal left ventricular size.

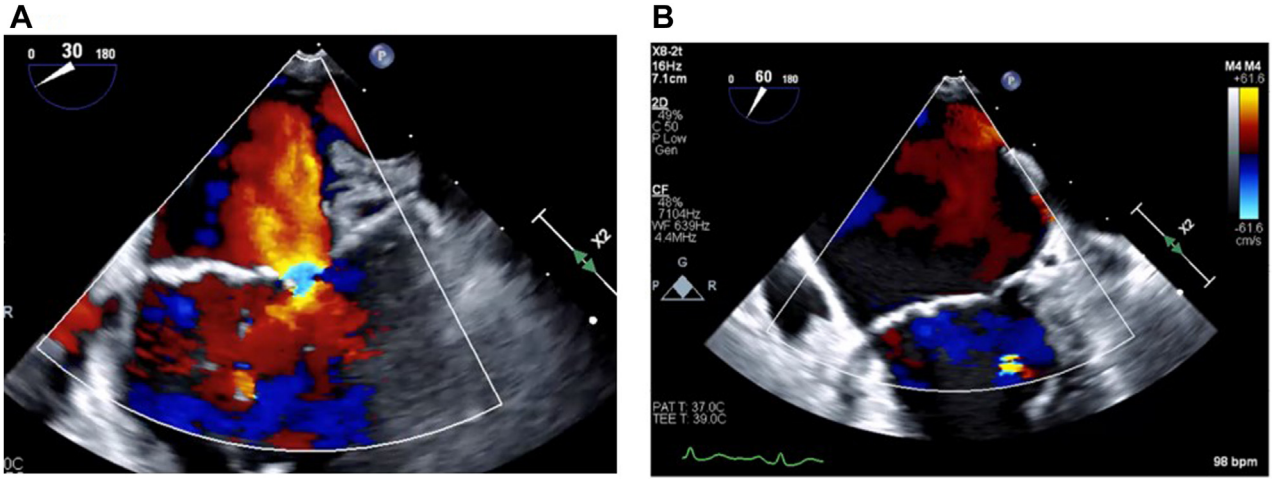

Figure 3 Two-dimensional TEE, midesophageal 4-chamber (**A**: 30°) and (**B**: 60°) systolic zoom views with color-flow Doppler, demonstrates mild MR.

enlargement of the patient's PFO, and increases the volume and velocity of the right-to-left shunt. The patient's right-to-left shunt does not appear to be hemodynamically significant given lack of cyanosis and no reported limitations in exercise tolerance.

CONCLUSION

Pulmonary vein systolic flow reversal has a high specificity for severe MR. We observed PV systolic flow reversal in the absence of significant MR or ASD in the setting of a PFO with significant size variation with respiration, independent of the cardiac cycle. We proposed that this is a result of exaggerated right-to-left shunting through the PFO with deep inspiration, leading to intermittent increases in LA volume and pressure.

ETHICS STATEMENT

The authors declare that the work described has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans.

CONSENT STATEMENT

The authors declare that since this was a non-interventional, retrospective, observational study utilizing de-identified data, informed consent was not required from the patient under an IRB exemption status.

FUNDING STATEMENT

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

DISCLOSURE STATEMENT

The authors report no conflict of interest.

SUPPLEMENTARY DATA

Supplementary data related to this article can be found at https://doi.org/10.1016/j.case.2024.11.005.

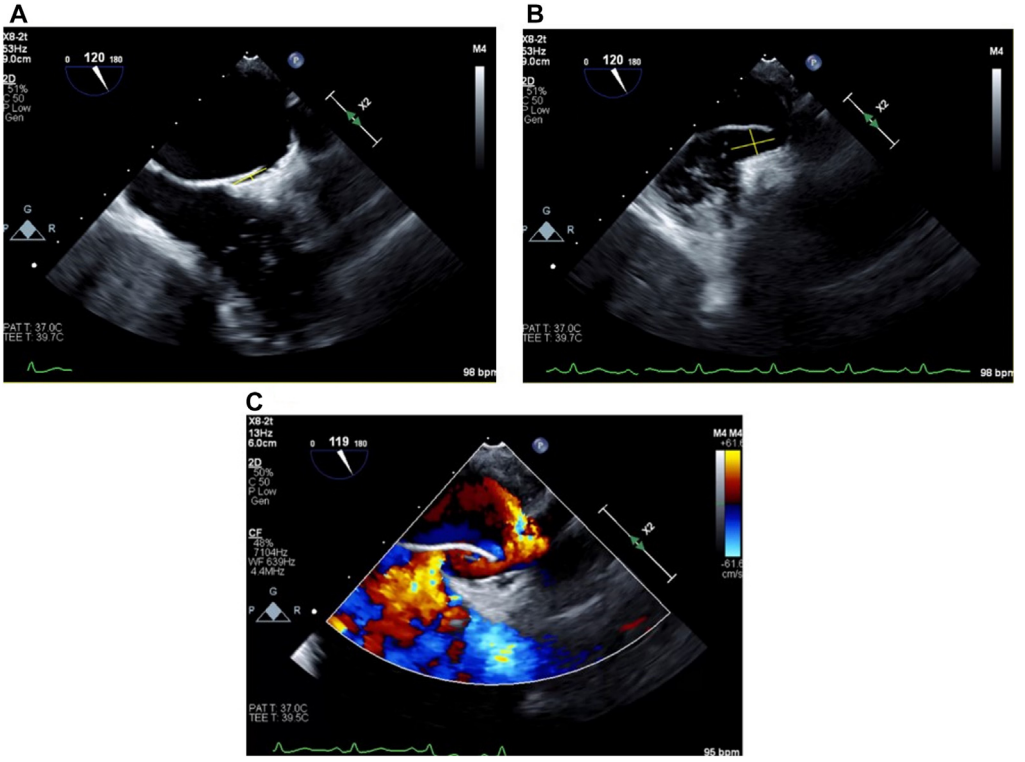

Figure 4 Two-dimensional TEE, midesophageal level long-axis (120°) view, demonstrates **(A)** the PFO at baseline (tunnel length, 1.13 cm; height, 0.19 cm) and **(B)** the PFO with deep inspiration (tunnel length, 1.35 cm; height, 0.8 cm) and with color-flow Doppler (119°), which demonstrates the right-to-left shunt **(C)**.

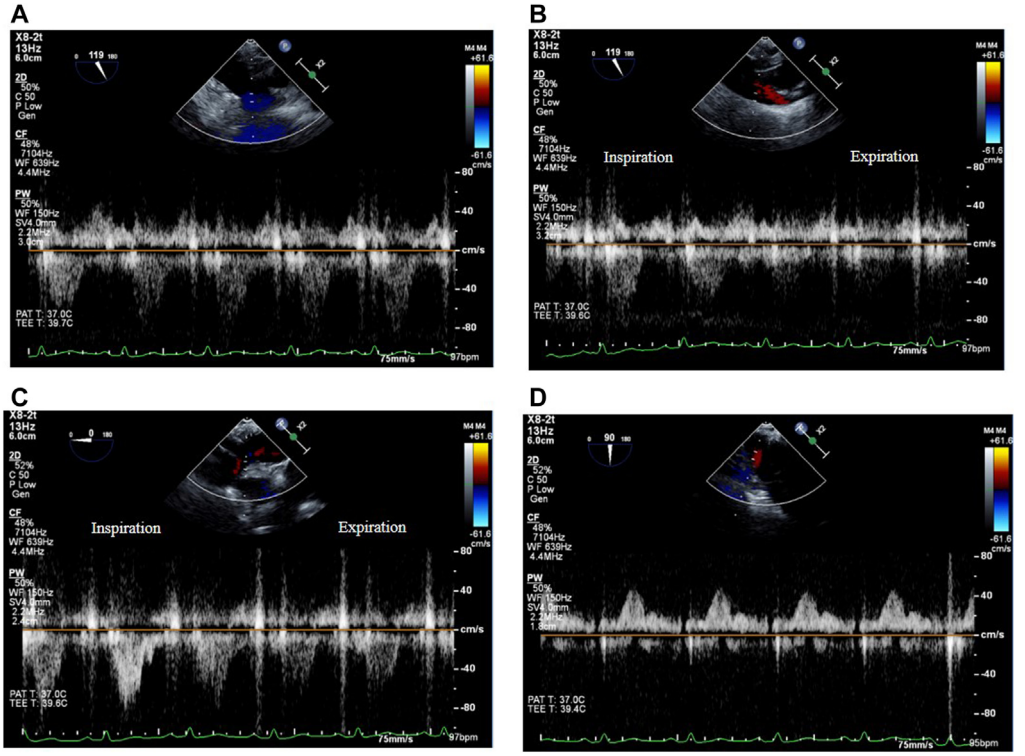

Figure 5 Two-dimensional TEE, midesophageal long-axis (119°) view with color-flow Doppler-guided pulsed-wave Doppler, demonstrates **(A)** systolic flow reversal in the right upper PV spectral Doppler display that changes during respiration and is mostly seen during inspiration **(B)**; long-axis (0° and 90°) views demonstrate inspiratory systolic flow reversal in the right lower PV **(C)** and normal antegrade systolic flow **(D)** in the left upper PV.

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