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Case Report

CASE REPORT

PFO closure in high-risk patient with paradoxical arterial embolism, deep vein thrombosis, pulmonary embolism and factor V Leiden genetic mutation

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Abstract

Occurrence of paradoxical arterial embolism may cause the first symptoms in patients with a coexisting hypercoagulable state and patent foramen ovale (PFO). This can result in significant morbidity and mortality depending on the location of the embolism. The risks and benefits of closure of small PFOs have not been well elucidated in prior studies. We describe a patient with a history of Factor V Leiden heterozygosity who presented with left arm pain secondary to arterial embolism. The patient was a 51-year-old male who initially presented to the emergency department after awaking from sleep with progressive, severe, burning left arm pain. He had also noted intermittent shortness of breath over the 2 weeks prior to admission. Temperature was 97.4 F, pulse 86, respiratory rate 20 and blood pressure 121/87. Oxygen saturation was 94% on supplemental oxygen. He had a cool left upper extremity and the patient described subjective paresthesias in this extremity. Left radial pulse was difficult to palpate. Physical exam was otherwise unremarkable. Troponin I was mildly elevated at 0.217 ng/l. White blood cell count was 11.8 and INR 1.1. EKG showed sinus tachycardia with non-specific T abnormalities in the anterior leads. His past medical history was notable for only hypertension and hyperlipidemia. Current recommendation is for antiplatelet or anticoagulation for those with hypercoaguable states who suffer a stroke; there is currently no absolute indication for closure device. We describe the case of a 51-year-old male who had presented with left arm pain and shortness of breath. The computed tomography (CT) angiography of chest showed pulmonary emboli with heavy clot burden bilaterally. Heparin was started, but patient was found to have occlusion along large arteries of the left arm. Emergent left axillary, brachial, radial and ulnar embolectomy for acute critical arm ischemia were performed. The transthoracic echocardiogram done the next day with bubble study was positive for patent foramen ovale. Hypercoaguability showed factor V Leiden heterozygosity. Decision was made for the patient to initiate long-term anticoagulation with rivaroxaban and closure was performed. Patient was advised that closure is off label but opted to proceed with closure in light of hypercoaguable state.

Chest X-ray did not show any process that could explain the acute hypoxic episode and patient sounded clear on lung exam. Hence, computed tomography (CT) angiography of the chest was performed with higher suspicion for pulmonary embolism (PE). The CT angiography showed multiple large bilateral pulmonary emboli extending from the right and left main pulmonary arteries into the segmental and subsegmental branches with heavy clot burden bilaterally (Fig. 1). Transthoracic echocardiogram (TTE) was done showing ejection fraction of 65% and severely elevated pulmonary artery systolic pressure with right ventricular

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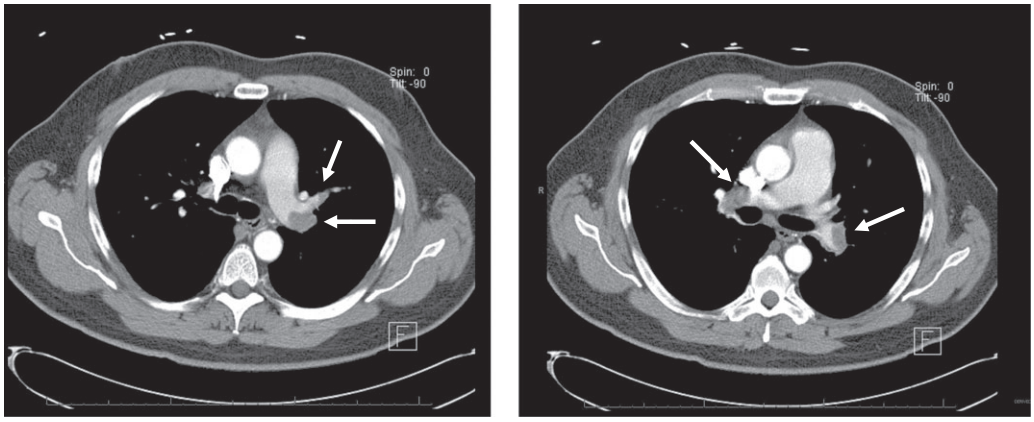

Figure 1: CT angiography of the chest was done showing multiple large bilateral pulmonary emboli extending from the right and main pulmonary arteries into the segmental and subsegmental branches with heavy clot burden bilaterally. Arrows show areas of PE.

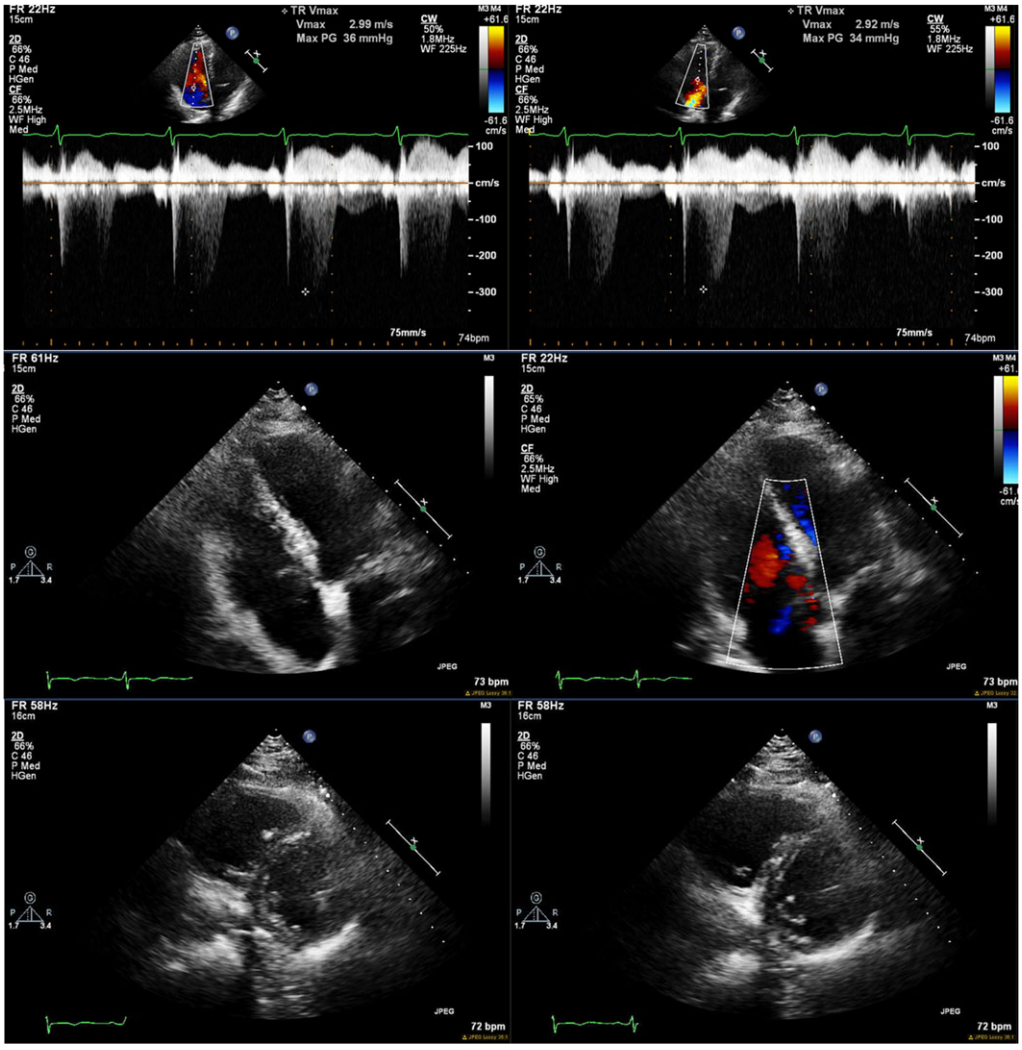

Figure 2: TTE was done showing ejection fraction of 65% and improved pulmonary artery systolic pressure with RVSP of 46 mmHg after 3 days of therapy.

systolic pressure (RVSP) of 72 mmHg (Fig. 2). There was no free-floating cardiac thrombi detected, and echo did not show concomitant septal flattening; moreover, McConnell's sign was not present Workup thus far was discussed with pulmonology and the patient was not felt to be a candidate for thrombectomy since he was not showing hemodynamic instability characteristic of massive PE, so therapeutic heparin drip was initiated and the patient was admitted to the intensive care unit for submassive PE.

Seven hours after initial presentation, the patient continued having severe left arm pain. It was initially thought that the pain was musculoskeletal in nature; however, after discovery of multiple coagulation events, prospect for embolism was endorsed. He was sent for ultrasound of upper and lower extremities. Ultrasound of bilateral lower extremities revealed acute deep venous thrombosis within the left posterior tibial and peroneal veins. Venous ultrasound of the upper extremities showed no evidence of clot. Arterial ultrasound of the left upper extremity showed occlusion of the left proximal to mid-brachial artery with reconstitution of flow at the level of the distal brachial artery. Vascular surgery was consulted and the patient underwent emergent left axillary, brachial, radial and ulnar embolectomy for acute critical arm ischemia (Fig. 3).

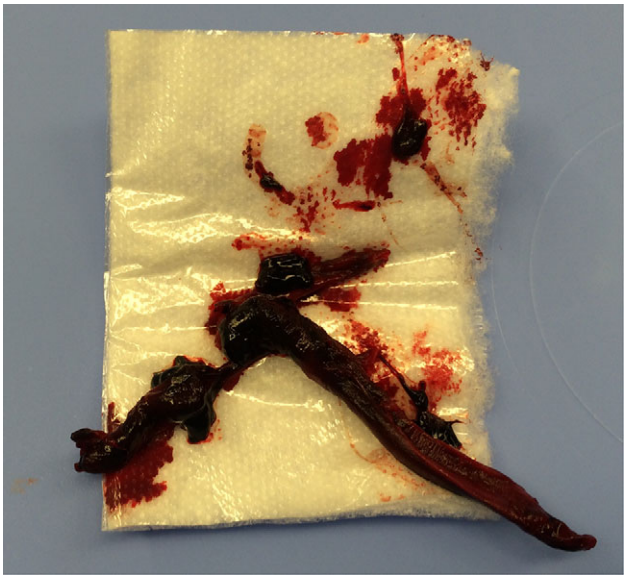

Figure 3: Patient underwent emergent left axillary, brachial, radial and ulnar embolectomy for acute critical arm ischemia and sample of clot is shown.

TREATMENT

A repeat TTE was done the next day and bubble study was positive for a patent foramen ovale (PFO). Cardiology and cardiothoracic surgery were consulted regarding the need for open heart surgery versus percutaneous closure of the PFO. It was decided that the patient initiate long-term anticoagulation and that percutaneous closure could be performed at a later date. Hematology was consulted and the patient underwent a hypercoagulability workup which later was remarkable for Factor V Leiden heterozygosity. The patient opted for treatment with rivaroxaban over warfarin, and therefore rivaroxaban 15 mg twice daily was started with plans to adjust dosing to 20 mg daily in three weeks. Another TTE was done on admission Day 3 showing improvement of pulmonary artery systolic pressure

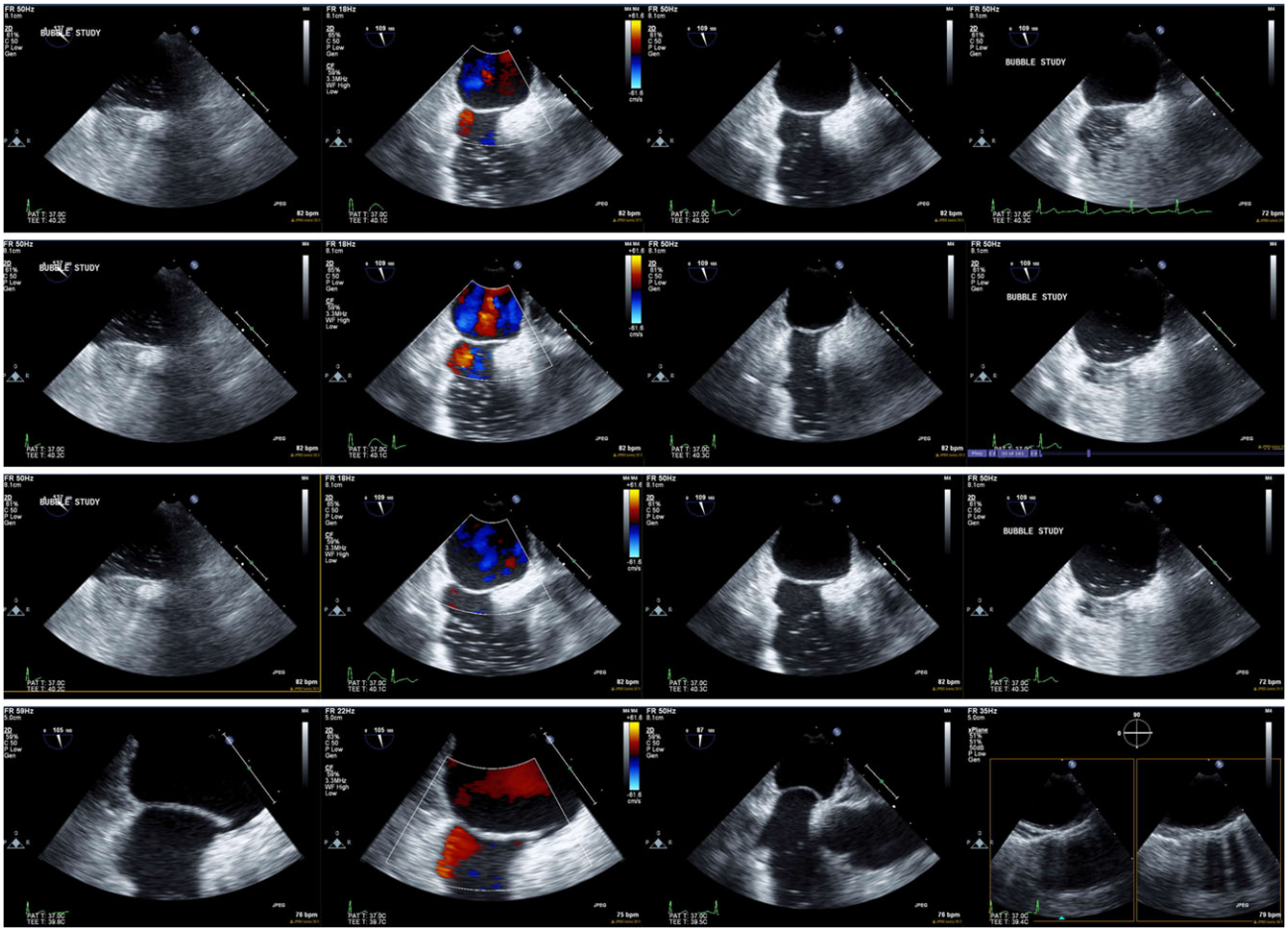

Figure 4: One week after discharge, the patient underwent further evaluation with TEE showing a very large PFO with right to left shunt by bubble study.

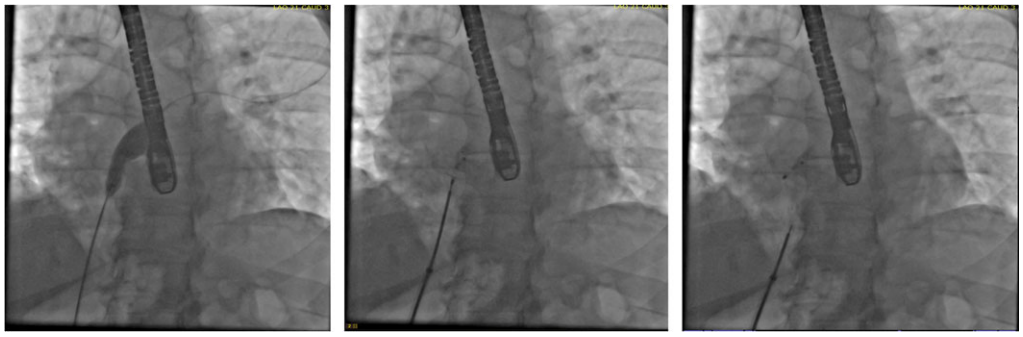

Figure 5: A balloon was placed across the PFO for size measurement and the decision made to deploy a 25 mm cribriform Amplatzer PFO occluder device.

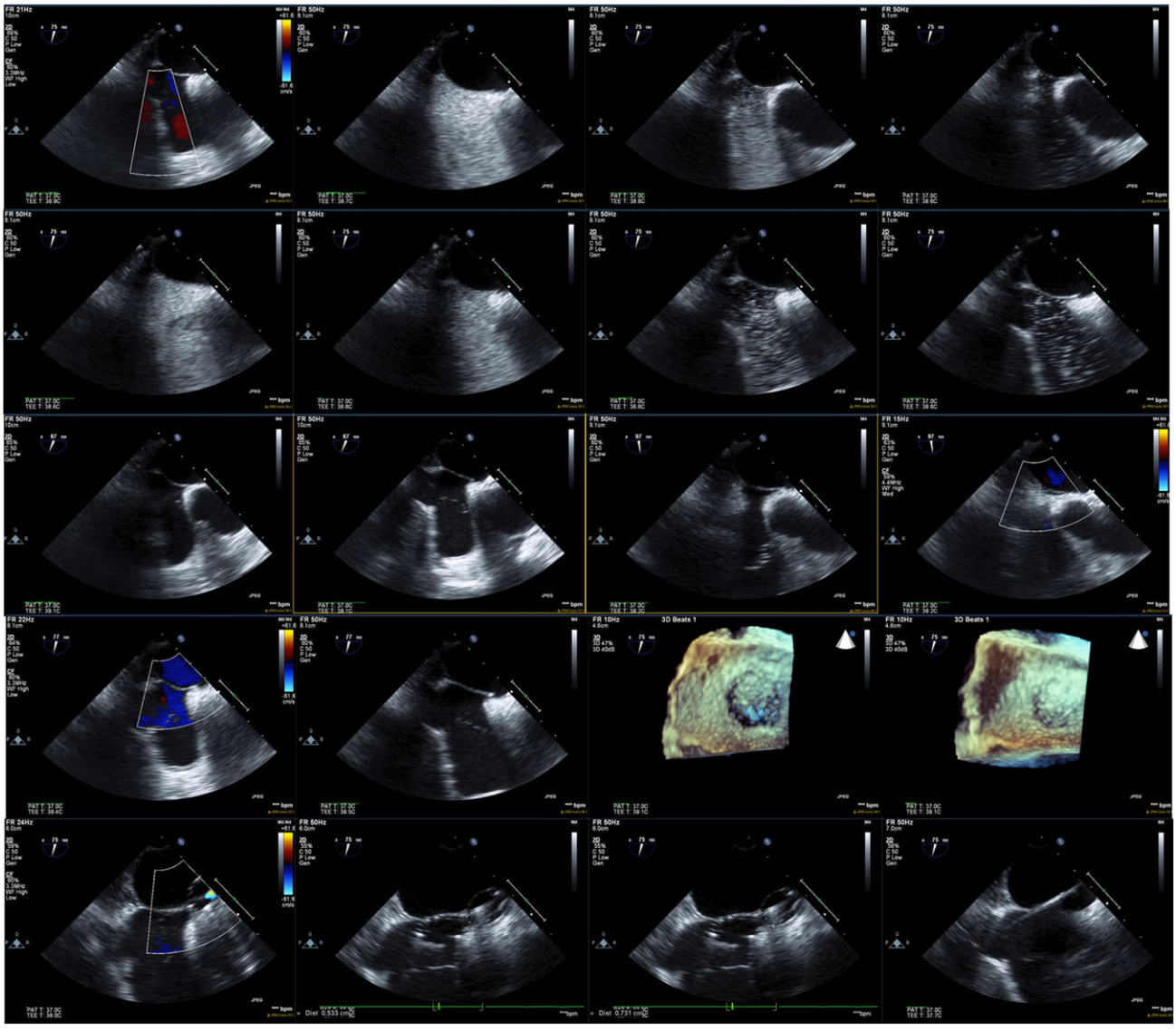

Figure 6: Placement was confirmed by TEE showing negative bubble study.

with RVSP of 46 mmHg. Pulmonology recommended against inferior vena cava filter placement as patient had rapid clinical improvement with systemic anticoagulation. After 2 more days of observation and treatment, the patient was discharged from the hospital with plans for outpatient follow-up.

OUTCOME AND FOLLOW-UP

One week after discharge, the patient underwent further evaluation with transesophageal echocardiogram (TEE) showing a very large PFO with right to left shunt by bubble study (Fig. 4).

During outpatient cardiology follow-up, there was a discussion with the patient regarding the very large PFO/atrial septal defect (ASD) and his high risk of further embolic event. He was advised that closure is off-label and that the latest trials did not show superiority with closure versus anticoagulation. Given his high risk of embolic event, and because he was a scuba diver with increased risk for the decompression sickness, he opted to proceed with closure.

Three weeks later, patient underwent percutaneous closure of the PFO with intraoperative fluoroscopy guidance. A balloon was placed across the PFO for size measurement and the decision made to deploy a 25 mm cribriform Amplatzer PFO occluder device (Fig. 5). This device consists of two disks, the first deployed on the left side of the PFO and then the second along the right side of the PFO. Placement was confirmed by TEE (Fig. 6). Patient was started on dual antiplatelet therapy with aspirin and plavix for 3 months and advised to continue systemic anticoagulation with rivaroxaban.

DISCUSSION

This patient was found to have a hypercoagulable state from Factor V Leiden heterozygosity. This predisposed him to the development of lower extremity deep vein thrombosis and large bilateral PE [1]. The development of arterial embolus to the left arm was made possible by a large PFO and has been cited several times in the literature [2].

Paradoxical arterial embolism has been associated with PFO, atrial septal aneurysm (ASA), and ostium secundum ASD. Recommended therapy differs depending on the type of anomaly present and its characteristics that can predispose the patient to increased risk of arterial embolism events. PFO occurs in 25–30% of the general population. It is thought to be an innocent bystander in many patients with stroke; however, in the younger population (<55 years of age), it could be the underlying etiology for recurrent arterial embolus events, such as cryptogenic stroke or peripheral embolism [3].

Currently, the usefulness of percutaneous closure of PFO versus surgical closure or medical therapy alone remains unclear. Further complicating factors to decide on treatment include hypercoaguable states that were not part of inclusion criteria when evaluating for efficacy. The current recommendation is for antiplatelet or anticoagulation for those with hypercoaguable states who suffer a stroke [4]. Three studies (CLOSURE I trial, PC trial and RESPECT trial) have failed to demonstrate that percutaneous PFO closure relates significant reduction in primary endpoint (stroke, TIA, peripheral embolism, etc.) outcomes [5–7]. However, extended data from the RESPECT trial after 10 years have shown some benefit to closure with 54% relative risk reduction for recurrent cryptogenic stroke versus those assigned to medical management of anticoagulation. Moreover, two more recent trials have shown some benefit to closure of PFO closure with aspirin in those with a true cryptogenic stroke: REDUCE and CLOSE [8, 9]. Additional randomized trial data are still needed to determine the effectiveness of percutaneous PFO closure as compared to other treatment modalities before considering a widespread use.

LEARNING POINTS

In summary, paradoxical arterial embolism via PFO should be determined to be a possibility in a patient presenting with deep venous thrombosis and/or PE who also have evidence of an arterial embolic event. Testing may include CT angiogram, venous/arterial ultrasound and echocardiography with bubble study. Treatment options include systemic anticoagulation, IVC filter placement, percutaneous closure of PFO, surgical closure of PFO or no closure of PFO depending on the patient's presentation, history, and consideration of indications/contraindications. Pending further randomized trial data, percutaneous PFO closure may be considered as for prevention of paradoxical arterial embolism.

CONFLICT OF INTEREST STATEMENT

None declared.

CONSENT

Written consent was obtained from the patient for publication of this article.

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