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CASE REPORT

BEGINNER

CLINICAL CASE

Late Atrial Thrombus Formation After Percutaneous Patent Foramen Ovale Closure

Manjari R. Regmi, MD,[a] Odalys Estefania Lara Garcia, MD,[a] Priyanka Parajuli, MD,[a] Oswaldo Madrid, MD,[b] Abdul Moiz Hafiz, MD[a,c]

ABSTRACT

Late thrombus formation is a rare complication associated with patent foramen ovale (PFO) closure devices. We report the case of an incidental discovery of large thrombi in both atria 9 months after percutaneous PFO occlusion that required cardiac surgery for thrombi removal. (**Level of Difficulty: Beginner.**) (J Am Coll Cardiol Case Rep 2020;2:636–40)
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CASE

A 30-year-old male presented to the hospital after a mechanical fall at home from approximately 20 steps of stairs. Vital signs were stable, and examination was significant for tenderness in the right upper extremity. He had a concussion and a fracture of the left second and third proximal phalanx. Trauma protocol included performing a computed tomography (CT) scan of his chest which incidentally showed a hypodensity in the right atrium that appeared to be a thrombus or a mass. It is important to note that he had stopped all his home medications approximately 1 month previously, including aspirin.

LEARNING OBJECTIVES

- To highlight the importance of medical therapy compliance after percutaneous patent foramen ovale closure.
- To emphasize the need for further risk stratification of higher risk patients for thrombus formation who may benefit from anticoagulation or longer duration of antiplatelet therapy.

MEDICAL HISTORY. History included major depression, hypertension, left foot transmetatarsal amputation, and percutaneous patent foramen ovale (PFO) closure for arterial thromboembolism.

EVENTS LEADING TO PFO CLOSURE. More than 1 year previously, the patient presented with left lower extremity pain, absence of left dorsalis pedis pulse, and faint pulses in posterior tibial and left femoral arteries. CT angiography showed thrombus in the left common femoral artery extending 1 to 2 cm into the superficial femoral artery and the profunda femoris besides the left posterior tibial and dorsalis pedis arteries. Doppler ultrasonography showed no deep vein thrombosis, and CT showed no pulmonary

From the [a]Department of Internal Medicine, Southern Illinois University School of Medicine, Springfield, Illinois; [b]Department of Internal Medicine, Universidad Central de Venezuela, Caracas, Capital District, Venezuela; and the [c]Division of Cardiology, Southern Illinois University School of Medicine, Springfield, Illinois. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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embolism. He underwent left common femoral artery thrombectomy, endarterectomy with bovine patch angioplasty, and left popliteal/tibial thrombectomy for acute left limb ischemia, followed by left transmetatarsal amputation for constant severe rest pain in the left forefoot and significantly decreased sensation and motor function as well as presence of nonviable tissue intraoperatively (**Figure 1A**). Transthoracic echocardiography (TTE) with bubble study showed a PFO with right-to-left shunt without thrombus (**Figure 1B**), which was further confirmed by a transesophageal echocardiography (TEE) study. He was prescribed warfarin. Hypercoagulable workup was negative for factor V Leiden mutation, antiphospholipid antibody panel, prothrombin gene mutation, lupus anticoagulants, vasculitis, hepatitis, and deficiencies of proteins C and S. Negative hypercoagulability workup and a partial limb loss led to the decision to perform PFO closure. He underwent cardiac catheterization and endovascular PFO closure using Cardioform septal occluder (WL Gore & Associates, Flagstaff, Arizona) 8 months after the amputation (**Figure 1C**). After undergoing the PFO closure, he was switched from warfarin to clopidogrel and aspirin for 6 months, followed by aspirin for life. A TTE study 6 months after the procedure showed a well-seated device with no thrombus or peridevice leakage (**Figure 1D**).

DIFFERENTIAL DIAGNOSIS. Atrial mass or device-associated thrombus.

INVESTIGATIONS. Upon further evaluation for trauma, a head CT scan was negative for any acute intracranial abnormalities, and electrocardiography was unremarkable (**Figure 2**). The chest trauma CT result dictated by protocol demonstrated a large hypodensity in the right atrium measuring approximately 4 cm in the largest diameter (**Figure 3A**). TTE confirmed the presence of a 4.1- × 2.2-cm right atrial mass that was potentially a fresh thrombus prolapsing into the tricuspid valve attached to the atrial septum or PFO closure device (**Figure 3B**). TEE reconfirmed the thrombus (**Figures 3C and 3D**).

MANAGEMENT. The patient was started on heparin infusion and underwent urgent cardiac surgery for thrombus removal. Intraoperative findings included a large right atrial thrombus and a left atrial white thrombus attached to the device. The biatrial thrombi and the PFO occluder device, along with segments of the atrial septum, were explanted, followed by closure with a pericardial patch. After the procedure, he was discharged on warfarin for life. Microscopic examination of the specimen revealed organizing thrombus and the pale white membranous device which was well endothelialized (**Figure 3E**). A follow-up CT (**Figure 3F**) and TTE 4 months later revealed no thrombus.

DISCUSSION

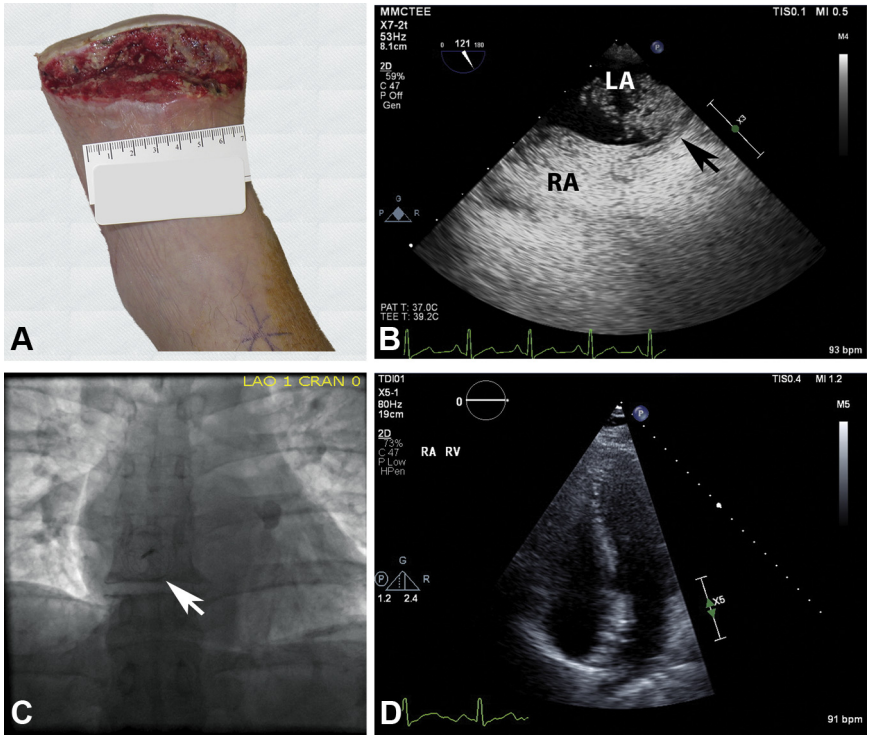
Percutaneous closure of the PFO by using an occluder device has become standard of care for secondary prevention of cryptogenic strokes. Long-term outcome data (1–3) support device therapy in patients who experience cryptogenic strokes and undergo device implantation compared to those who undergo only medical therapy. PFO occlusion has also been performed, although less often, off-label for patients with migraines and peripheral vascular embolism. The present patient had significant, acute limb ischemia with an embolic phenomenon which was thought to be caused by the paradoxical emboli, which prompted the closure of the PFO. Generally, venous thrombosis is identified by doppler ultrasonography in patients with paradoxical emboli. However, there are many cases of embolism with negative Doppler results (4). The adverse effects associated with percutaneous device closure are transient ischemic attack or stroke, malposition, device embolization, erosions, transient atrial fibrillation, vascular complications, and infective endocarditis. Late biatrial thrombus formation is a rare but life-threatening complication. Risk factors associated with thrombus formation are age, female sex, hypercoagulable disorders, hypertension, hyperlipidemia, shorter duration since the procedure, thrombogenic nature of the device, coronary artery disease, diabetes, atrial fibrillation, residual shunt, persistent atrial septal aneurysms, and nonadherence to medication therapy (5).

Previous investigators have reported cases with PFO closure-associated thrombus formation. A European group (6) investigated 1,000 cases (PFO and atrial septal defect) and found 11 cases had left atrial thrombus, 6 had right atrial thrombus, and 3 had both. Of these, 14 patients were found within 4 weeks, 3 in 6 months, 2 in 1 year, and 1 in 5 years. The incidence was 7.1% using the CardioSEAL (NMT Medical, Boston, Massachusetts), 5.7% using the StarFLEX (StarFLEX, Lowell, Massachusetts), 6.6% using the PFO-star device (Cardiastar, Medical Company, Golden Valley, Minnesota), 3.6% using the ASDOS device (Osypka Corp., Grenzach-Wyhlen, Germany), and 0% using the Amplatzer device (Abbott, Santa Clara, California). Although most of these devices are no longer marketed in the United States, except for the Amplatzer device, none of the cases used the Cardioform device (Gore) implanted in

ABBREVIATIONS AND ACRONYMS

CT = computed tomography
PE = pulmonary embolism
PFO = patent foramen ovale
TEE = transesophageal echocardiogram
TTE = transthoracic echocardiogram

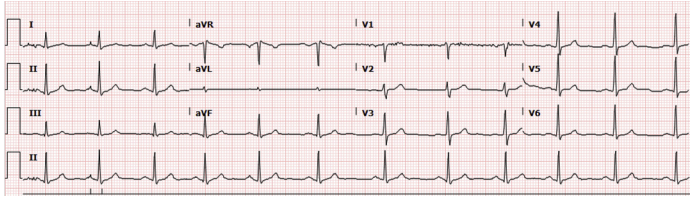
FIGURE 1 Transmetatarsal Amputation, PFO on Bubble Study, PFO Closure Device, and TTE 6 Months Post-Procedure



(A) Transmetatarsal amputation; **(B)** PFO on bubble study; **(C)** PFO closure device; **(D)** TTE 6 months post-procedure. PFO = patent foramen ovale; TTE = transthoracic echocardiogram.

the present patient. The sizes of the thrombi ranged from 0.5 to 3.0 cm. Another European study (7) specifically investigated 150 PFO closure cases using the Cardioform (Gore) device and reported the first case of thrombus formation within 6 months. A Korean study (8) reported no case of thrombus formation in 6 months' follow-up after PFO closure of 267 studied cases. Seventeen cases used the Cardioform device. Another study (9) from Detroit, Michigan, reported 1 patient experiencing a stroke 5 years after PFO closure using the Amplatzer (Abbott) septal occluder device when subsequent echocardiography showed a thrombus measuring 0.5 to 1.2 cm. To the best of the authors' knowledge, the size of the thrombus in the present patient (4.1 cm × 2.2 cm) by TTE is the largest reported thrombus after percutaneous PFO closure, to date. The present case is also the second case to date reporting thrombus formation using the Cardioform device.

FIGURE 2 Electrocardiography

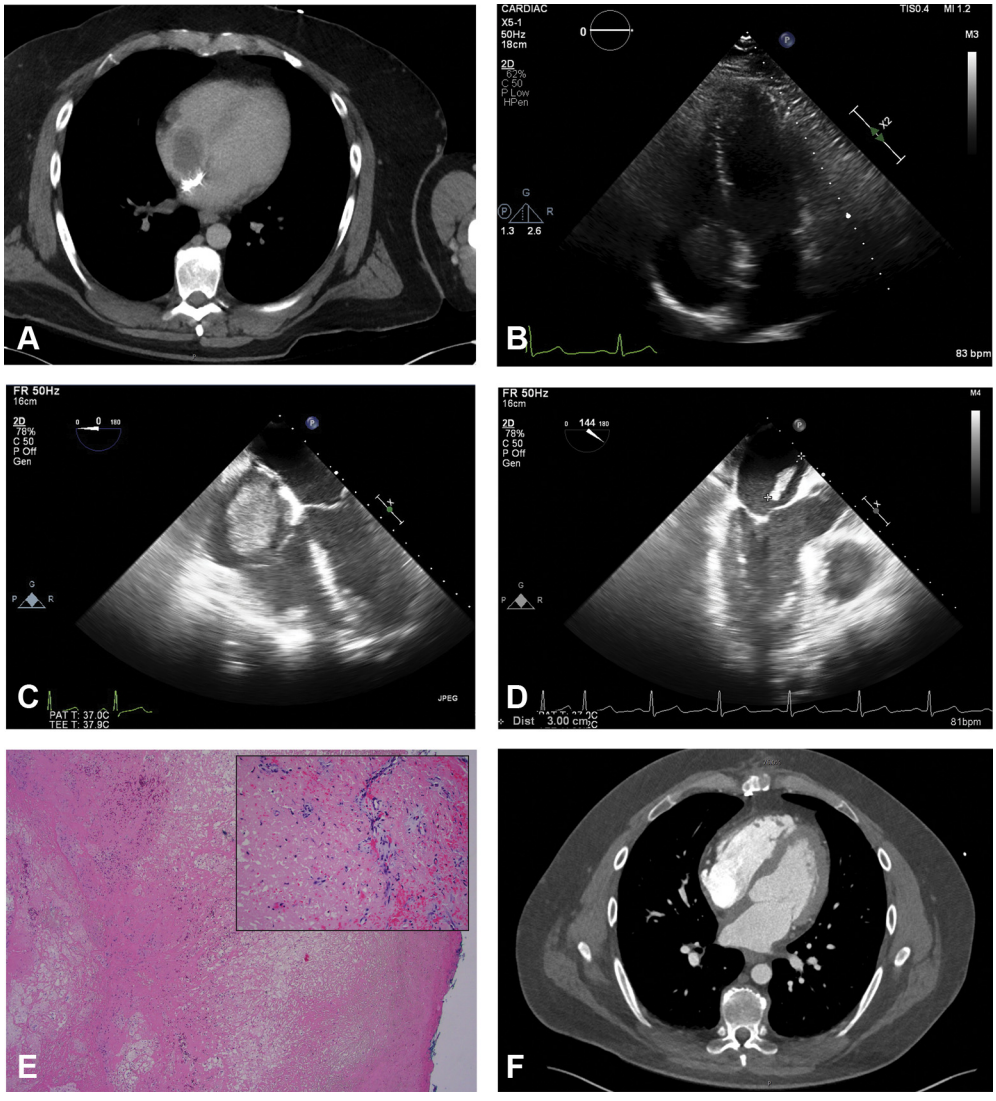


Currently, no clear guidelines exist for the duration of antiplatelet or anticoagulation therapy post-procedure in the absence of clinical trial data. However, some investigators (6) have suggested the administration of antithrombotic therapy for at least 6 months after the procedure. This is because re-endothelialization is thought to be completed by 6 months after the procedure (5). In the present patient, it is likely that the cause of this complication was nonadherence to antiplatelet therapy, as he reported medication noncompliance.

CONCLUSIONS

PFO closure is indicated for patients at high risk for recurrent cryptogenic embolic strokes. Off-label use has been reported in patients with migraine and

FIGURE 3 **CT Chest, TTE Right Atrial Thrombus, TEE Bi-Atrial Thrombus, Microscopic Examination of Specimen, CT 4 Months After Surgery**



(A) CT chest, right atrial hypodensity. **(B)** TTE, 4.1- × 2.2-cm right atrial thrombus. **(C) and (D)** TEE biatrial thrombus. **(E)** Microscopic examination of the specimen. **(F)** CT 4 months after surgery. CT = computed tomography; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram.

vascular embolic phenomena. Current standard of care is dual antiplatelet therapy for 6 months post-procedure. Our case raises several important questions: could nonadherence to antiplatelet therapy possibly be the only factor associated with thrombus formation in our patient? Similarly, is there a need for longer antiplatelet or anticoagulant therapy after PFO closure procedure to avoid late device thrombus formation? And finally, is there a better way to risk stratify certain patients who would be at risk for device thrombosis? In the opinion of the present authors, dedicated larger studies are required to answer such questions as the uptake and use of PFO closure devices are likely going to increase in the near future.

ADDRESS FOR CORRESPONDENCE: Dr. Manjari Rani Regmi, Internal Medicine, Southern Illinois University School of Medicine, 701 North First Street, Springfield, Illinois 62702. E-mail: mregmi81@siumed.edu.

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