*American Journal of Medical Case Reports, 2020, Vol. 8, No. 7, 197-201*
Available online at http://pubs.sciepub.com/ajmcr/8/7/10
Published by Science and Education Publishing
DOI:10.12691/ajmcr-8-7-10

# Large Left Atrial Thrombus on Amplatzer Septal Occluder Secondary to Medication Nonadherence

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*Received April 02, 2020; Revised April 17, 2020; Accepted April 22, 2020*

**Abstract** Patent foramen ovale (PFO) is a common clinical entity that is encountered in 20-34% of the general population. In most individuals, this anatomical variation is asymptomatic and goes undetected throughout their lives or is only incidentally discovered on cardiac investigations. In situations when the conduit is large enough and when the right atrial pressure exceeds the left atrial pressure, right to left interatrial flow may occur in these individuals. This creates a channel for translocation of air or thrombi from the venous to the arterial circulation, a phenomenon known as paradoxical embolism. Approximately 25-40% of strokes and transient ischemic attacks in patients less than 60 years of age are classified as cryptogenic and studies have identified a higher prevalence (60%) of PFO in young adults with strokes of unidentifiable etiology. Recent trials have demonstrated utility of PFO closure with mechanical devices for secondary prevention of recurrent strokes in patients aged <60 years of age. The general consensus of post-operative management of PFO closure has been largely drawn from randomized controlled trials and comprises use of aspirin and clopidogrel for 6 months followed by use of aspirin alone for at least 5 years. We present a case of an incidentally discovered left intra-atrial thrombus attached to a PFO closure device in a 36-year-old female with a history of cryptogenic stroke three months after implantation.

***Keywords:*** *atrial thrombus, foramen ovale, amplatzer septal occluder*

**Cite This Article:** Naseem A. Hossain, Pramod Theetha Kariyanna, Nimrah A. Hossain, Yuvraj Singh Chowdhury, Sostanie Takota Enoru, Apoorva Jayarangaiah, Moro O. Salifu, and Samy I. McFarlane, "Large Left Atrial Thrombus on Amplatzer Septal Occluder Secondary to Medication Nonadherence." *American Journal of Medical Case Reports*, vol. 8, no. 7 (2020): 197-201. doi: 10.12691/ajmcr-8-7-10.

## 1. Introduction

The foramen ovale is a communication between the right and left atria that is open during fetal development. The primum and secundum septae overlap such that when right atrial pressure exceeds the left atrial pressure, right-to-left flow through the foramen is possible. This enables fetal blood to enter the left atrium from the right atrium bypassing the fetal lungs. In about 75% of infants, the septae fuse shortly after birth. However, in about 20-34% of the population, there is failure of fusion resulting in a patent foramen ovale (PFO) that persists beyond birth [1,2]. For most individuals, this anatomical variation goes undetected throughout their lives or is only incidentally discovered on cardiac investigations.

In situations where the right atrial pressure exceeds the left atrial pressure, such as during coughing, sneezing, straining or deep-sea diving, right to left inter-atrial flow may occur in these individuals. These changes can be mimicked by asking such patients to perform and then release a Valsalva maneuver. When the conduit is large enough, this pressure gradient creates a channel for translocation of air or thrombi from the venous to the arterial circulation, a phenomenon termed as paradoxical embolism.

The first description of a PFO in a patient who had suffered a stroke dates back to 1877 when Cohnheim made the association in a young woman [3]. However, the ability to detect this conduit *in-vivo* remained difficult for many years. This changed after the advent of echocardiography and its ability to detect intra-atrial shunting with the injection of agitated saline contrast. As the use of echocardiography increased, a significant association emerged between the presence of PFO's and strokes in the young (<55 years of age) [4,5,6,7,8]. Most paradoxical emboli are likely to present as ischemic strokes and tend to occur in younger individuals.

PFO closure has emerged as a technique of secondary prevention of stroke in people with a history of cryptogenic stroke and PFO. Percutaneous transcatheter PFO closure (PTPC) is indicated in cryptogenic stroke and paradoxical systemic embolization, including myocardial infarction caused by presumed paradoxical embolism. We present a case of an incidentally discovered left intra-atrial thrombus attached to a PFO closure device (AMPLATZER) in a 36-year-old female with a history of cryptogenic stroke and an implanted septal occluder device three months after implantation.

## 2. Case Presentation

The patient is a 36-year-old African American female with a past medical history of diabetes mellitus, ethanol abuse, cryptogenic stroke and PFO repair with an atrial septal occlude device placed 3 months prior to her presentation. She presented to the emergency department with complaints of two days of palpitations, shortness of breath, nausea, vomiting and generalized weakness. Vital signs revealed a blood pressure of 94/65 mm of Hg, heart rate of 129 beats per minute, temperature of $97.7^0$F and a respiratory rate of 18 per minute. Physical examination revealed a woman in moderate distress with epigastric tenderness. Her cardiac exam was pertinent for tachycardia, regular low volume equal pulses and no murmurs on auscultation. Electrocardiogram (ECG) was significant for sinus tachycardia at a rate of 130 bpm. Laboratory investigations demonstrated an anion gap of 51, potassium of 6.8 mEq/L, chloride of 83 mEq/L, $CO_2$ of 5 mEq/L, creatinine of 1.45 mg/dL and a serum glucose of 731 mg/dL. A venous blood gas showed a pH of 7.08, and point of care lactate of 5.3 mmol/L. The patient was given metoclopramide, ondansetron, intravenous fluids, and started on an insulin drip. The patient was admitted to the medical intensive care unit for the management of her diabetic ketoacidosis. Once her serum glucose levels improved, acidosis resolved and the anion gap normalized, she was transitioned to subcutaneous insulin and was restarted on her oral dual antiplatelet therapy comprising of aspirin 81 mg and clopidogrel 75 mg. On admission, the patient reported poor compliance to all of her medications including dual antiplatelet therapy. Bedside ultrasonography during rounds incidentally showed a mobile mass in the left atrium. Complete 2D transthoracic echocardiography confirmed a large mass in the left atrium and also demonstrated the atrial septal occluder device on the interatrial septum (Amplatzer) [Figure 1, Figure 2, and Figure 3]. She was continued on her dual antiplatelet therapy with aspirin and clopidogrel, started on a heparin drip and transferred to a tertiary care hospital for surgical thrombectomy, as she was at a high risk of thromboembolic events.

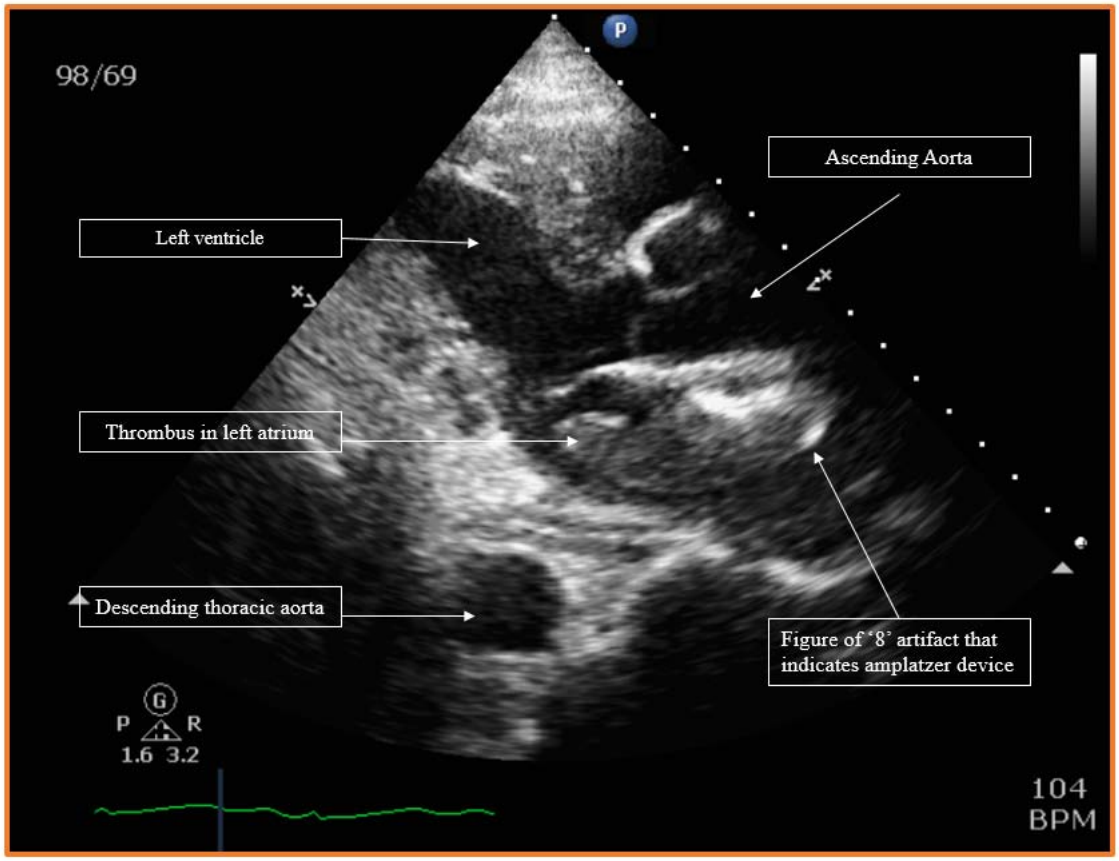


**Figure 1.** Parasternal long axis view of the transthoracic echocardiography which revealed huge thrombus in the left atrium attached to the amplatzer septal occluder

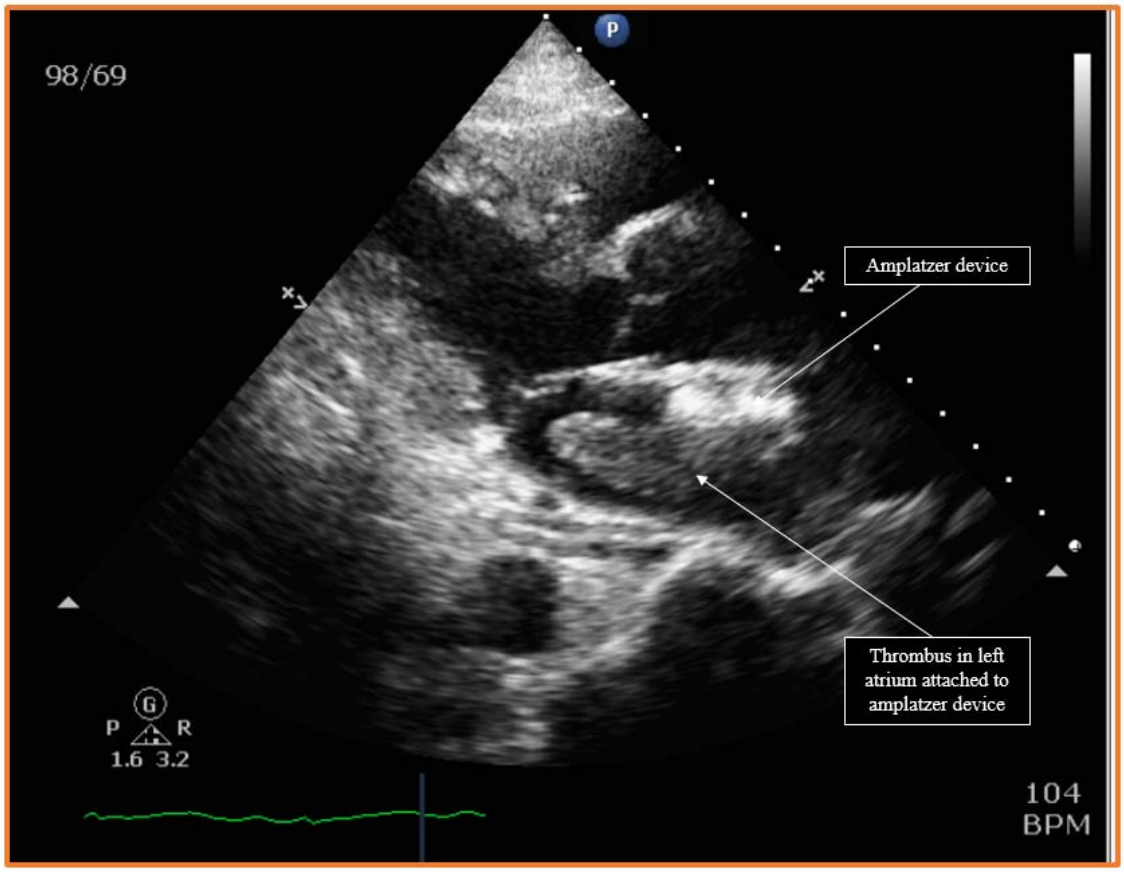


**Figure 2.** Parasternal long axis view of the transthoracic echocardiography which revealed huge thrombus in the left atrium attached to the amplatzer septal occluder

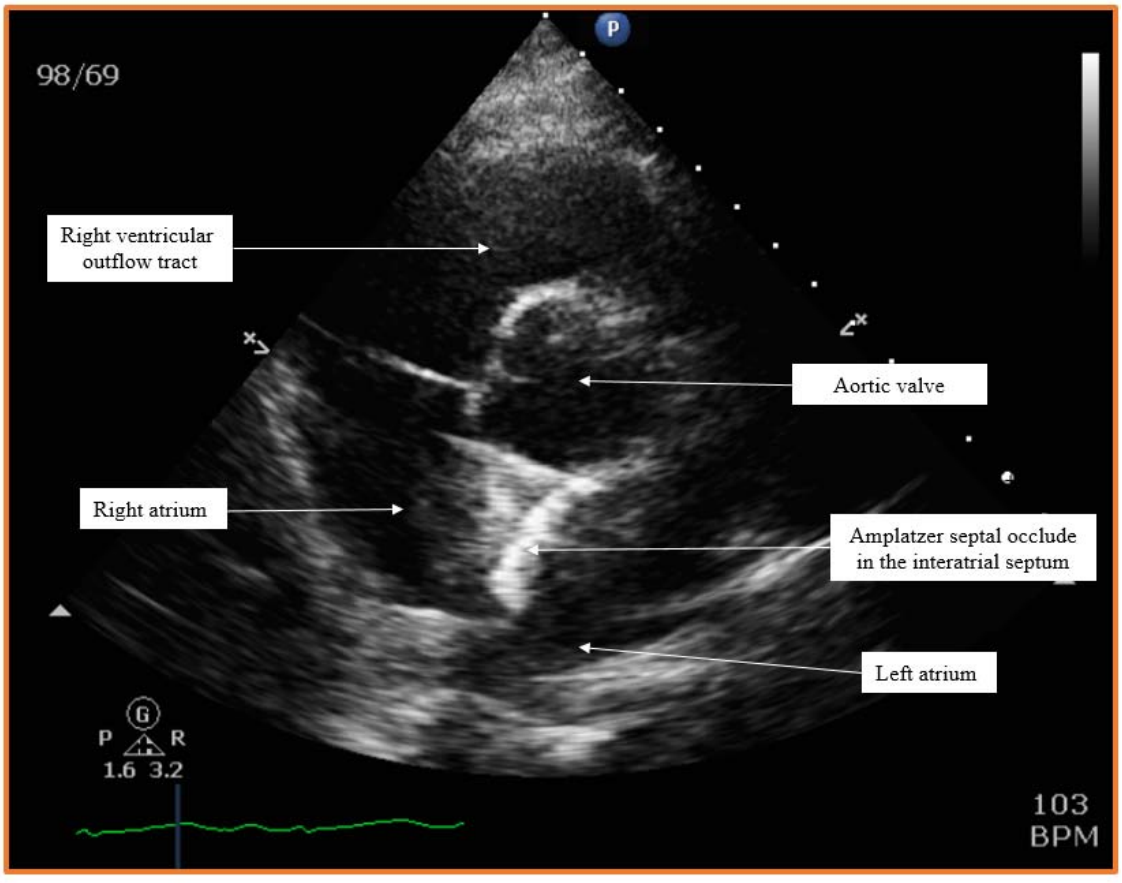


**Figure 3.** Parasternal short axis view at the level of aortic valve in transthoracic echocardiography. Note amplatzer device in interatrial septum

## 3. Discussion

Embolic strokes, when encounter in patients with PFOs have long been considered potentially causal especially in populations that are younger than the typical stroke patients [4,5,6,7,8]. Approximately 25-40% of strokes and transient ischemic attacks in patients less than 60 years of age are classified as cryptogenic [3]. Studies have identified a higher prevalence (60%) of PFO in young adults with strokes of unidentifiable etiology [9,10]. An atrial septal aneurysm when associated with a PFO has been found to increase the risk of initial [odds ratio of 4.96] and recurrent strokes (odds ratio of 23.9). This is because the atrial septal aneurysm may open the PFO with the cardiac cycle and facilitate a right to left inter-atrial shunt [11]. Recent trials have demonstrated utility of PFO closure for secondary prevention of recurrent stroke in patients aged <60 years of age.

Surgical closure of PFOs have paved the way for percutaneous closure of these defects. John Gibbon in 1953 was the first surgeon to perform an ASD repair using a cardiopulmonary bypass machine [12]. In 1975, the first percutaneous repair was performed using a 35-mm King–Mills Cardiac Umbrella and this paved the way for the current-day FDA approved ASD closure devices - Amplatzer PFO Occluder and the Gore Cardioform Septal Occluder [13].

Advances and data from recent trials in structural cardiology have accelerated the use of PFO closure in place of anticoagulation. These trials have shown benefit with closure devices when compared to anticoagulation alone. A meta-analysis of patient-level data from CLOSURE I, PC and RESPECT trials found PFO closure superior to medical therapy for the prevention of recurrent ischemic stroke (adjusted hazard ratio 0.58; 95% CI, 0.34-0.99) [14,15,16,17].

The general consensus of post-operative management of PFO closure has been derived based on the results of randomized controlled trials (CLOSE, RESPECT, CLOSURE I, DEFENSE-PFO) [14,15,18,19] and comprise use of aspirin and clopidogrel for 6 months followed by use of aspirin alone continued for at least 5 years unless the patients has other indications for the use of anticoagulation (such as atrial fibrillation, venous thromboembolism, *et cetera*) [20].

One of the complications noted from early trials of PFO occluding devices was thrombus formation after device placement. The current incidence of device related thrombus formation ranges from 0.7-1% [21]. Thrombus formation during implantation of closure devices has also been documented [22]. Post-procedurally, thrombus formation has been noted to occur at any phase after placement, ranging from 6 months to 8 years [23,24,25]. It is most commonly seen 4 weeks after device placement [26]. Thrombus formation due to occluding devices is usually treated by anticoagulation (usually with heparin or warfarin) although there have been reports of the use of recombinant tissue plasminogen activator with glycoprotein IIb/IIIa inhibitors as well [27]. Of all cases of device related thrombosis, over 80% of cases have been treated with medical management [20]. Current observations suggest that device related thrombosis resolves within 4 weeks to 6 months after starting treatment [28]. Surgical thrombectomy has been required in select cases due to thrombus size, friability or device failure [25,29,30]. Theorized mechanisms for thrombus formation are centered around an impaired coagulation cascade, poor epithelialization of the device and foreign body reaction [31,32,33].

The risk of PFO closure device thrombosis may be under-reported as there is no established guideline for surveillance of thrombi. Sherman *et al* suggest that all patients should have echocardiographic surveillance within the first 3 months of device implantation [34]. Studies have suggested routine transesophageal echocardiograms (TEE) at intervals of 4 weeks, 6 months and 12 months for early detection of thrombi and surveillance of the device [28]. However, no current consensus exists regarding surveillance TEE after PFO closure. Management od PFO associated with interatrial septal aneurysm has been discussed elsewhere [35].

PFO closure is performed to reduce the risk of thromboembolic events, in particular, prevent paradoxical emboli in the systemic circulation. Our patient developed a large left atrial thrombus emanating from the PFO closure device due to poor compliance with anti-platelet therapy consisting of aspirin and clopidogrel. Although the thrombus found was not believed to have embolized to the systemic circulation, it raises the question of the presence of thrombi formation from these devices and whether short to long term surveillance with transesophageal echocardiography is warranted.

## 4. Conclusion

Our case of device related thrombosis 3 months after poor compliance with dual antiplatelet therapy highlights the need stringent adherence to dual antiplatelet therapy. We believe that development and institution of a standardized protocol for surveillance and developing strategies to further minimize the risk of device related thrombus formation and systemic embolization will be beneficial. More studies regarding the efficacy of dual antiplatelet therapy after PFO closure will be helpful for our management of these patients.

## Acknowledgements

This work is supported, in part, by the efforts of Dr. Moro O. Salifu M.D., M.P.H., M.B.A., M.A.C.P., Professor and Chairman of Medicine through NIH Grant number S21MD012474.

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