Introduction

Atrial fibrillation (AF) is a common disease associated with developing strokes. The mainstay therapy for this condition is chronic oral anticoagulation, however, in patients with a high bleeding risk profile or prior life-threatening bleed, conventional therapy may not be ideal. New advanced technologies such as transcatheter closure of the left atrial (LA) appendage (LAA) provides clinicians an alternative therapy to reduce the stroke risk in patients with contraindications to chronic oral anticoagulation. One of the most feared complications is device related thrombus formation. We present a 66-year-old male with chronic AF who developed a life-threatening intracranial bleed on oral anticoagulation. He subsequently underwent LAA closure using an Amplatzer muscular ventricular septal defect closure device for stroke prevention. However, he was found to have a large thrombus attached to the device a year later. We present a review of the various LAA closure devices, importance of periodic surveillance via echocardiography and management options to prevent this complication. Also, the case highlights the importance of contrast-enhance echocardiography in diagnosis of LAA closure device thrombus.

Case

A 66-year-old male with an extensive past medical history including hypertension, hyperlipidemia, diabetes, metastatic prostate cancer treated with prostatectomy along with radiation and chemotherapy, previous ischemic stroke, known severe 3-vessel coronary artery disease with coronary bypass grafting surgery after myocardial infarction, preserved ejection fraction of 50%, and chronic AF on anti-coagulation with warfarin. The patient suffered a fall resulting in left cerebellar hemorrhage, left temporal lobe subarachnoid hemorrhage as well as encephalomalacia of posterior right frontal lobe due to intraparenchymal hemorrhage. Due to his inability to tolerate long-term anticoagulation and high CHADS2 score of 5, he underwent percutaneous LAA closure using a 16 mm Amplatzer muscular ventricular septal defect closure device (AGA Medical Corp., Plymouth, MN, USA). He was not a candidate for Lariat device (SentreHEART, Redwood City, CA, USA) due to prior cardiac surgery. The device was deployed with no complications and no residual flow. The patient was placed on lifelong daily aspirin 81 mg and a three-month course of clopidogrel 75 mg.

Transthoracic 2D-echocardiogram performed post procedure, 45 days, and at 6 month follow-up was unremarkable for device complications. However, the 1 year follow-up transthoracic 2D-echocardiogram revealed a spherical echo dense structure measuring 2.38 × 1.42 cm suggestive of clot in the left atrium (Fig. 1, 2, and 3, Supplementary movie 1 and 2).
Transesophageal echocardiogram demonstrated a bilobed echo dense mass in the LA, the smaller being $1.53 \times 1.87$ cm and the larger mass being $2.45 \times 2.33$ cm (Fig. 4 and 5, Supplementary movie 3). The mass was found to be attached to the closure device. The patient had no coagulation abnormalities. The patient was bridged to warfarin with heparin and anticoagulation was resumed. There were no early complications as a result of the treatment. Repeat transthoracic echocardiogram six months later did not reveal any evidence of residual thrombus on contrast imaging. His warfarin was subsequently discontinued and he has been maintained on daily 81 mg aspirin. He has remained asymptomatic from a cardiac and neurological standpoint and is regularly followed by cardiology.

**Discussion**

AF is the most common sustained cardiac arrhythmia and increases the risk for stroke. LAA is the site of around 75–90% of thrombus formation in non-valvular AF, and thus obliteration or exclusion of this structure, at least in theory, should lead to stroke risk reduction. Three devices have been specifically designed for LAA occlusion: the percutaneous left atrial appendage transcatheter occlusion (PLAATO), the Watchman (Atritech, Boston Scientific, Natick, MA, USA) LAA system, and the Amplatzer Cardiac Plug (ACP) (AGA, St. Jude Medical, Minneapolis, MN, USA). The PLAATO device has been discontinued for commercial reasons. The embolic protection in patients with atrial fibrillation trial compared closure of the LAA with the Watchman device with long-term warfarin therapy and found it was non-inferior to standard anticoagulant therapy for stroke prophylaxis in high-risk AF patients. Recently, the ASA Plavix Feasibility Study With Watchman Left Atrial Appendage Closure Technology study found that LAA closure with the Watchman device can be safely performed without a warfarin transition, and is a reasonable alternative to consider for patients at high risk for stroke but with contraindications to systemic oral anticoagulation.

A variety of Amplatzer septal occluder devices (AGA, St. Jude Medical, St. Paul, MN, USA) have been available for many years and used extensively for closure of atrial and ventricular septal defects and other cardiac shunts. Eventually, a novel device, the ACP, was developed for the purpose of closing the LAA. Similar to prior trans-catheter LAA closure devices, the ACP system is delivered into the left atrium via a trans-septal approach. The relatively short length of the ACP device allows for implantation into shallow LAA variants, which gives it an advantage over the PLAATO and Watchman devices that require a deeper LAA anatomy because of their longer profiles. The incidence of thrombus formation on devices is relatively uncommon with prior studies showing an incidence for the
Watchman device thrombus formation between 2–4%.

In a study by Urena et al., none of the 52 patients developed a device thrombus on the Amplatzer device; however, there have been two case reports from Europe. Prior studies demonstrate high stroke risk score, high pre-procedural platelet count, and low left ventricular ejection fraction as independent risk factors for the formation of thrombus on the ACP device.

Transthoracic echocardiogram has a lower sensitivity to identify LA thrombus. Use of contrast-enhanced echocardiography significantly improves the sensitivity for identifying intracardiac masses when standard imaging does not reveal diagnostic information.

Individuals who will benefit from LAA closure are probably those who are at the highest risk for both stroke and hemorrhagic complications; therefore, patient selection is of paramount importance in order to realize the optimal device and antithrombotic strategy. As in the present case, thrombosis might be a rare, but possible complication of device-based antithrombotic therapy, and additional studies are needed to know if the current practice of treating patients only with double-antiplatelet therapy before endothelization of the device is sufficient, or if one should use oral anticoagulation in the first 3 months as is advised in biological prostheses. In addition, periodic surveillance by echocardiography with contrast should be recommended to monitor the formation of thrombus in all types of devices. The frequency, duration, and type of echocardiogram (transthoracic or transesophageal) for thrombus formation monitoring still needs further research.

Supplementary Movie Legends

Movie 1. Three chamber view movie clip showing a stalk with pedunculated thrombus.

Movie 2. Contrast-enhanced echocardiogram movie clip showing enhanced view of thrombus.

Movie 3. Transesophageal echocardiogram movie clip confirms a large bi-lobed thrombus.

References

1. Roger VL, Go AS, Lloyd-Jones DM, Adams RJ, Berry JD, Brown TM, Carnethon MR, Dai S, de Simone G, Ford ES, Fox CS, Fuller-
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ton HJ, Gillespie C, Greenlund KJ, Hailpern SM, Heit JA, Ho PM, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, McDermott MM, Meigs JB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Rosamond WD, Sorlie PD, Stafford RS, Turan TN, Turner MB, Wong ND, Wylie-Rosett J; American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics—2011 update: a report from the American Heart Association. Circulation 2011;123:e18-209.

2. Blackshear JL, Odell JA. Appendage obliteration to reduce stroke in cardiac surgical patients with atrial fibrillation. Ann Thorac Surg 1996;61:735-9.

3. Lardizabal JA, Sharma S. Mechanical approaches to stroke prevention in atrial arrhythmias. J Innov Cardiac Rhythm Manage 2012;3:809-13.

4. Holmes DR, Reddy VY, Turi ZG, Doshi SK, Sickert H, Buchbinder M, Mullin CM, Sick P, PROTECT AF Investigators. Percutaneous closure of the left atrial appendage versus warfarin therapy for prevention of stroke in patients with atrial fibrillation: a randomised non-inferiority trial. Lancet 2009;374:534-42.

5. Reddy VY, Möbius-Winkler S, Miller MA, Neuzil P, Schuler G, Wiele J, Sick P, Sievert H. Left atrial appendage closure with the Watchman device in patients with a contraindication for oral anticoagulation: the ASAP study (ASA Plaxir Feasibility Study With Watchman Left Atrial Appendage Closure Technology). J Am Coll Cardiol 2013;61:2531-6.

6. De Backer O, Arnous S, Ihlemann N, Veijstrup N, Jürgensen E, Pehrson S, Krieger TD, Meier P, Søndergaard L, Franzen OW. Percutaneous left atrial appendage occlusion for stroke prevention in atrial fibrillation: an update. Open Heart 2014;1:e000020.

7. Plicht B, Konorza TF, Kahler P, Al-Rashid F, Kaelch H, Jánosi RA, Buck T, Bachmann HS, Siffert W, Heuch G, Erbel R. Risk factors for thrombus formation on the Amplatz Cardiac Plug after left atrial appendage occlusion. JACC Cardivaes Interv 2013;6:606-13.

8. Urena M, Rodés-Cabau J, Freixa X, Sow J, Webb JG, Freeman M, Horlick E, Osten M, Chan A, Marquis JE, Champagne J, Ibrahim R. Percutaneous left atrial appendage closure with the AMPLATZER cardiac plug device in patients with nonvalvular atrial fibrillation and contraindications to anticoagulation therapy. J Am Coll Cardiol 2013;62:96-102.

9. Cardona L, Ana G, Luísa B, Leal A, António F, Lídia S, Cruz FR. Thrombus formation on a left atrial appendage closure device. Circulation 2011;124:1593-6.

10. Lammers J, Elenbaas T, Meijer A. Thrombus formation on an Amplatzer closure device after left atrial appendage closure. Eur Heart J 2013;34:741.

11. Mulvagh SL, Rakowski H, Vannan MA, Abdelmoneim SS, Becher H, Bierig SM, Burns PN, Castello R, Coon PD, Hagen ME, Jollis JG, Kimball TR, Kitzman DW, Kronzon I, Labovitz AJ, Lang RM, Mathew J, Moir WS, Naguehe SF, Pearlman AS, Perez JE, Porter TR, Rosenbloom J, Srachan GM, Thangaraj S, Wei K, Woo A, Yu EH, Zoghbi WA; American Society of Echocardiography. American society of echocardiography consensus statement on the clinical applications of ultrasonic contrast agents in echocardiography. J Am Soc Echocardiogr 2008;21:1179-201; quiz 1281.