Acute embolic stroke secondary to thrombus formation on atrial surface of a left atrial appendage occlusion device

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Introduction

Atrial fibrillation (AF) is projected to affect 25% of the world's population above 40 years old. As the population of the United States ages, AF is predicted to affect close to 12 million people by 2050.[1] Prevalence of AF increases with the presence of cardiovascular comorbidities, which in turn amplifies the risk of thromboembolic events.[2] Left atrial appendage occlusion devices (LAAODs) have emerged as an alternative to oral anticoagulation for stroke prophylaxis in patients at high risk for bleeding events. It is standard to perform transesophageal echocardiogram (TEE) 6 weeks post device implant to ensure proper seating of the device and assess for thrombus formation. Future follow-up TEEs at 6 months are commonly employed. We report a case of acute embolic stroke secondary to thrombus formation on the atrial surface of a WATCHMAN device months after anticoagulation was discontinued.

KEY TEACHING POINTS

- Patients with atrial fibrillation and high risk of major bleeding can be considered to undergo a left atrial appendage occlusion with deployment of an occlusive device.
- Currently, the accepted monitoring protocol involves a 45-day follow-up transesophageal echocardiogram for all patients and transition to dual antiplatelet therapy from anticoagulation.
- The current monitoring interval might be inadequate for a select number of patients who are considered high risk for device-related thrombus formation.
- High-risk patients are those with reduced left ventricular ejection fraction, prior embolic events, and vascular disease.

Case report

A 73-year-old woman with prior myocardial infarction, 1-vessel coronary artery bypass graft (CABG), heart failure with reduced ejection fraction secondary to ischemic cardiomyopathy, cardiac resynchronization therapy-defibrillator placement, permanent AF (CHA_2DS_2-VASc score 7) with recurrent gastrointestinal bleeds, and severe anemia status post a WATCHMAN device placement 9 months prior presented to the emergency department with focal numbness and aphasia. Review of records showed a well-seated first-generation WATCHMAN device with no peri-device leak at the time of implantation and on 45-day follow-up TEE (Figure 1). In addition, the device was placed by an experienced electrophysiologist without recapture or repositioning attempts. The patient had ongoing gastritis on a regimen of aspirin and clopidogrel. Aspirin was discontinued approximately 4 months after her WATCHMAN device implantation. Two days prior to her presentation, the patient was scheduled to undergo a complex polyp removal procedure at a tertiary center and her clopidogrel was discontinued.

In the emergency department, the patient received intravenous tissue plasminogen activator in the ED with resolution of her focal neurological symptoms. TEE showed a well-seated WATCHMAN device without peri-device leak and a 17 × 10 mm thrombus on the surface of the WATCHMAN device (Figure 2). In addition, mild-to-moderate mitral regurgitation was noted. Twenty-four hours after tissue plasminogen activator administration, the patient was started on rivaroxaban and clopidogrel with a follow-up TEE scheduled in 1 month.

KEYWORDS Atrial fibrillation; Device-related embolic event; Device-related thrombus; Embolic stroke; Transient ischemic attack; WATCHMAN device
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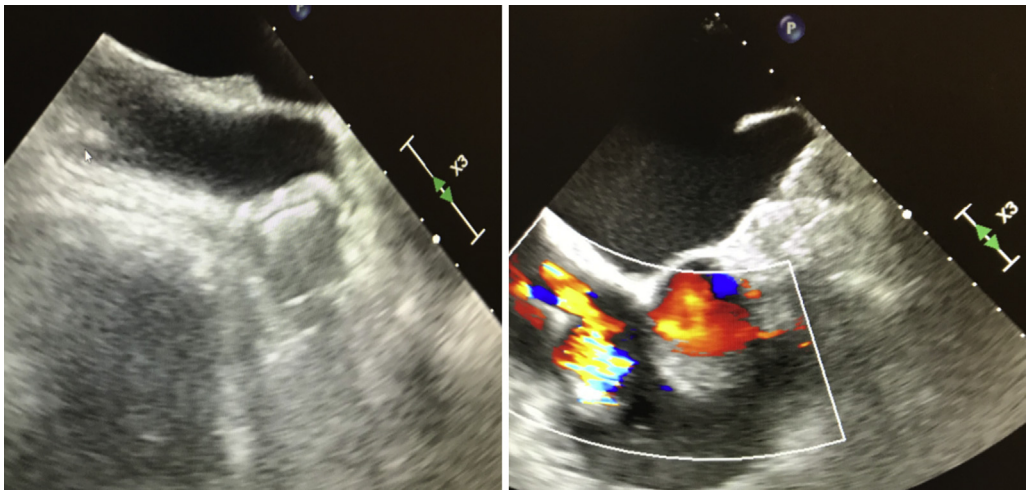

Figure 1 Transesophageal echocardiogram showing a well-seated WATCHMAN device without a device thrombus.

Discussion

Multiple clinical trials have validated percutaneous LAAOD implantation with low rate of significant complications. The WATCHMAN device has been most extensively studied and is the only occlusion device currently approved for use in the United States. Routine postprocedural transesophageal echocardiogram is essential for detection of peri-device leak, thrombus formation, or late dislodgement, as these can be clinically silent. However, TEE lacks sensitivity for detecting device endothelialization.

Thrombus formation on the atrial surface of the WATCHMAN device was assessed by combining the device arm of 4 studies, PROTECT AF, PREVAIL, CAP, and CAP2. These studies included 1739 patients who underwent WATCHMAN device implantation. Sixty-five patients were found to have device thrombus (DT). The 5-year follow-up rate of embolic events was reported to be 25% in patients with DT and 6.8% in patients without DT.[3,4] It is worth noting that in the PREVAIL and PROTECT AF studies in addition to the 45-day TEE, patients underwent a 6-month TEE evaluation as well. In addition, a strong correlation between detection of DT and embolic events was found, with 46% of events after 30 days and 63% after 6 months of DT detection.[3,4]

Similar findings were reported in a study conducted in France. A 5-fold increase in ischemic stroke was reported in patients with DT.[4] Given independent risk factors for embolic events in addition to DT, such as AF, vascular disease, prior embolic events, and reduced ejection fraction of left ventricle, it is not surprising that approximately 86%

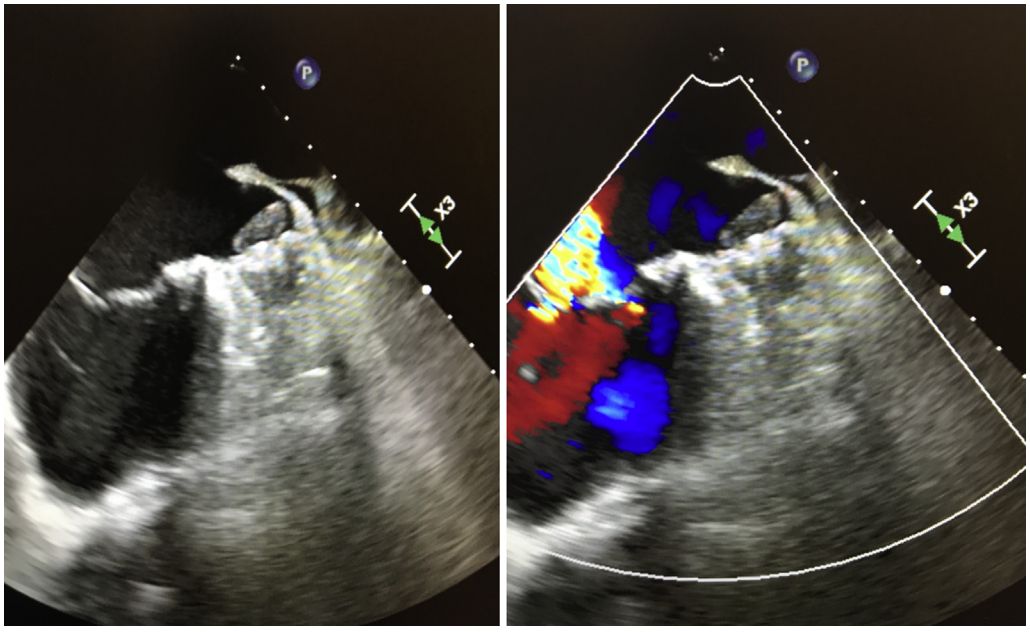

Figure 2 Transesophageal echocardiogram showing a thrombus on the atrial surface of WATCHMAN device.

of embolic events occurred in patients without a device thrombus. However, there have been no data suggestive of increased cardiac or all-cause mortality associated with DT.

The process of occlusive device endothelialization is not completely understood. However, a small study at the University of Minnesota, including dog and human hearts, was done to assess the healing process and stages leading to endothelialization of atrial surfaces of LAAODs.

Interval sampling was done and the healing was studied by histopathologic findings. The healing process began with deposition of fibrin-thrombus complex. Initially disorganized thrombus changed to a denser formation, followed by resolution of thrombus by macrophages. Endothelial coverage of the device was achieved by smooth muscle growth and fibrous tissue formation. The left atrial surface of the device eventually resembled the endocardium.[5] It is worth noting that at 45 days post device implantation endocardial growth, a layer of granulation tissue composed of endothelial-like cells, completely covered the atrial surface of the device in a continuous fashion.[5] Interval changes consistent with thrombus resorption, followed by collagen and pannus formation and continued healing, were seen in the 90-day animal group. It is not known what parameters are protective against device-related thrombus formation. However, there has been a lower rate of DTs in patients with severe mitral regurgitation.[5] Perhaps the direction of the regurgitant jet plays a role in this phenomenon. It is unclear what is the best surveillance period after device implantation for detection of DT formation. Given the mentioned independent parameters in formation of DT, it may be prudent to tailor the screening time to each patient's case. Currently, the 45-day postimplantation TEE is the widely accepted approach with 6 weeks of oral anticoagulation post implantation followed by dual antiplatelet therapy. However, the number of detected DTs at the 6- and 12-month period was reported to be double the number of DTs detected within the first 45 days.[3]

Different postimplantation strategies have been proposed in order to allow adequate time for device endothelialization and to minimize the risk of bleeding. The PREVAIL and PROTECT AF trials suggested warfarin for a duration of 45 days, followed by dual antiplatelet therapy (DAPT) with clopidogrel and aspirin followed by lifelong aspirin therapy. Later, the EWOLUTION trial suggested novel oral anticoagulants can be a substitute for warfarin with similar rates of DTs, stroke, and bleeding events.[6] The European Society of Cardiology, however, deemed DAPT with aspirin and clopidogrel acceptable after device implantation in patients with contraindications to oral anticoagulants, based on ASAP study.[6]. Both the United States Food and Drug Administration and Centers for Medicare and Medicaid Services restricted the approval for WATCHMAN device implantation in the United States to those patients who are a candidate for at least periprocedural anticoagulation.[7] However, intolerance to aspirin has not been taken into account. In addition, a report of 323 patients who underwent a WATCHMAN device implantation showed clopidogrel resistance based on its reduced metabolism secondary to a CYP2C19 polymorphism, adding to the complexity for selecting the appropriate patient population for LAAOD placement.[8]

Conclusion

As LAAODs have emerged as an alternative to anticoagulation in preventive measures of embolic stroke in patients with AF, it is important to monitor patients for complications of device placement and formation of device-related thrombus. In addition, postprocedural factors such as anticoagulation and DAPT tolerance must be considered when selecting patients for LAAOD implantation. It may be prudent to have a patient-tailored follow-up plan after device implantation, especially in high-risk patients such as those with AF, reduced LVEF, prior embolic events, and vascular disease, to detect device-related thrombi. Prompt treatment with anticoagulation in patients with DT is warranted to reduce the number of systemic embolic events.

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