Left atrial appendage occlusion device infection: Take it or leave it?

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Introduction

Atrial fibrillation (AF) is the most common sustained arrhythmia worldwide, and its prevalence is expanding owing to advanced age and higher rates of chronic heart disease.[1] The standard treatment for stroke reduction in patients with nonvalvular AF is anticoagulation. However, alternative therapy may be advisable in a certain subset of patients, owing to either previous failure of oral anticoagulation or presence of contraindications to anticoagulation.[1]

The left atrial appendage has been identified as the primary site of thrombus formation in more than 90% of patients with AF.[2] The PLAATO[3] study in 2002 was the first to demonstrate the use of a device to occlude the left atrial appendage for stroke reduction in patients with AF and provided the fundamental ground for future development in that field. Since its publication several percutaneous left atrial appendage occlusion (LAAO) devices have been developed and tested, including the Watchman, Amulet, and LARIAT, among others.[4] The Watchman (Boston Scientific, Marlborough, MA) is the most extensively studied and is the only FDA-approved percutaneous LAAO device currently available in the United States.[5] More than 100,000 devices have been implanted since it gained its approval in 2015.[6]

LAAO devices are approved for use in patients with nonvalvular AF who are not candidates for long-term coagulation with comparable outcomes in terms of risk of stroke, bleeding, and cardiovascular complications.[7,8] Percutaneous LAAO has also been used in patients with recurrent cardioembolic stroke while on oral anticoagulation.[9]

Implantation of any intracardiac device carries the risk of device thrombosis and infection. However, risk of LAAO device infection is low owing to complete endothelialization. Currently, there are no guidelines regarding prophylaxis of bacterial endocarditis with Watchman device placement. Similarly, management of LAAO device infections remains uncertain, with no clear guidelines. We report a case of a 74-year-old man with Watchman device infection that was managed conservatively with a long course of antibiotics without the need for surgical extraction.

KEY TEACHING POINTS

- Left atrial appendage occlusion devices, despite endothelialization, can carry a late risk of device-related infective endocarditis.
- Review of literature suggests role of transesophageal echocardiogram in the diagnosis of left atrial appendage occlusion device infections.
- While surgical extraction has been previously described, we report a case of successful antibiotic suppression at 6-month follow-up.

Case report

A 74-year-old man with a past medical history significant for persistent AF with history of LAAO device implantation 12 months prior owing to stroke while on apixaban (CHA_2DS_2-VASc score of 4, HAS-BLED score of 3), prostate cancer status post radiation therapy, and metastatic melanoma on intravenous pembrolizumab via a right subclavian central intravenous catheter presented to the emergency center with symptoms of fatigue, myalgias, fever, and cough. He was febrile (101°F), hypotensive (81/53 mm Hg), and in AF

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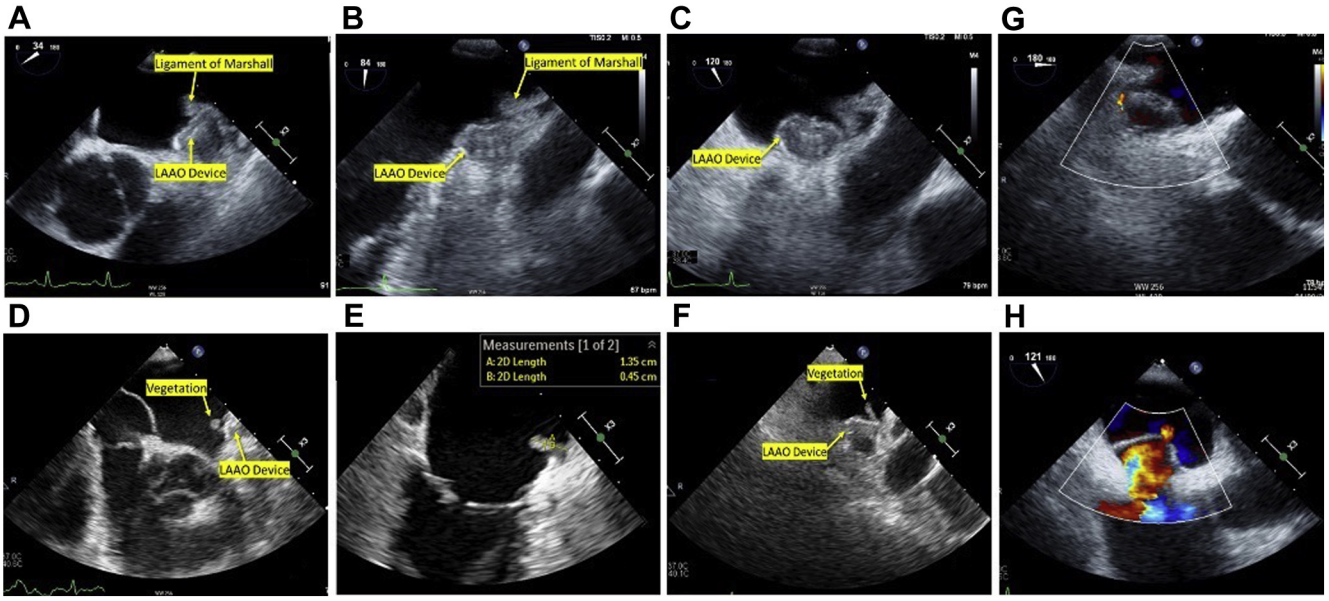

Figure 1 Pre and post implant images with similar views showing complete endothelialization at 30 days (**A, B, C**) and mobile vegetation at index presentation (**D, E, F**). Thirty-day postimplant transesophageal echocardiogram demonstrating 1.5 mm leak (**G**) and aneurysmal interatrial septum with right-to-left shunting (**H**). LAAO = left atrial appendage occlusion.

with rapid ventricular response and heart rate of 120 beats per minute. Work-up revealed mild anemia with hemoglobin of 9.6 g/dL and thrombocytopenia with platelet count of $1.47 \times 10^{9/L}$. Cardiac-sensitive troponin was mildly elevated at 0.11 ng/mL, but then normalized following intravenous fluid resuscitation. Procalcitonin was elevated at 3.20 ng/mL. COVID swab was negative. Extensive work-up including pan computed tomography scan failed to reveal an infectious source. Blood cultures were obtained and he was started on broad-spectrum intravenous (IV) antibiotics for presumptive pneumonia given his elevated procalcitonin.

Blood cultures grew methicillin-sensitive *Staphylococcus aureus* and antibiotics were narrowed from vancomycin and piperacillin-tazobactam to cefazolin based on susceptibility results. The central venous catheter was removed. A transthoracic echocardiogram was obtained and no valvular or device vegetations were identified. Repeat sets of blood cultures obtained on days 3 and 5 were persistently positive for *Staphylococcus aureus* despite targeted antibiotic therapy and removal of the indwelling venous catheter. The following day the patient underwent transesophageal echocardiogram (TEE), which demonstrated an appropriately seated LAAO device with a mobile echodensity measuring 1.35×0.45 cm attached to the device, which was consistent with a vegetation in this clinical context (Figures 1 and 2). The antibiotic regimen was modified to nafcillin and rifampin combination therapy for device-related endocarditis. Given the patient's comorbidities and high procedural risk, a multidisciplinary team including cardiothoracic surgery, cardiology, infectious disease, oncology, and the patient decided to continue with nonoperative therapy. Consecutive repeat blood cultures on days 7 and 9 were sterile. Over the course of his stay, the patient clinically improved without fever or hemodynamic instability. He developed acute kidney injury owing to nafcillin-related acute interstitial nephritis. His antibiotic therapy was changed to cefazolin and subsequently to vancomycin after renal function improved. The patient was discharged from the hospital on IV vancomycin and oral rifampin for 6 weeks. At the time of follow-up 6 weeks later, intravenous antibiotics were stopped and he was treated with oral cefalexin for lifelong suppressive therapy. On clinical follow-up at 6 months, he continues to fare well, with no recurrent hospitalizations for infection.

In our case, the patient presented well outside the window of endothelialization and 30-day postimplant TEE confirmed that the device was well seated and healed in the left atrial appendage with minimal residual leak (1.5 mm) and iatrogenic aneurysmal interatrial septum with right-to-left shunting (Figure 1).

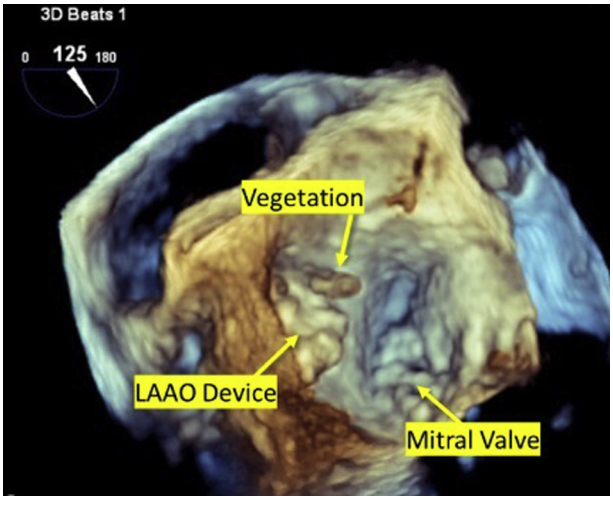

Figure 2 Three-dimensional view of the vegetation, which measured 1.35×0.45 cm. LAAO = left atrial appendage occlusion.

Table 1 Review of current literature of left atrial appendage occlusion device infections

	Study/publication			
	Jensen et al[6]	Khumri et al[13]	Boukobza et al[14]	Madanat et al (current study)
Age	74	75	83	74
Sex	Male	Female	Male	Male
Presentation at index hospitalization	Fever/sepsis	Sepsis/persistent bacteremia	Sepsis/subarachnoid hemorrhage	Sepsis/persistent bacteremia
Likely source of infection	Diverticulitis	Peri-implantation bacteremia	Recent blood transfusion vs endophthalmia	Central venous catheter, immunosuppression
Detection of device infection by TTE	No	N/A	Yes	No
Utilization of TEE	Yes	Yes	Yes	Yes
Time since Watchman implantation	5 months	Within 1 week	30 months	12 months
Anticoagulation/ antiplatelets at time of presentation	Aspirin, prasugrel	Warfarin	Aspirin	None
Causative microorganism	*Enterobacter/ Enterococcus*	*Staphylococcus aureus*	*Pseudomonas aeruginosa*	Methicillin-sensitive *Staphylococcus aureus*
Management of device infection	Surgical extraction	Surgical extraction and 6 weeks of IV antibiotics	Surgical extraction	6 weeks of IV antibiotics + Rifampin followed by lifelong oral suppressive therapy
Follow-up	10 months	6 months	Death 3 days post-op from cardiogenic shock	6 months

IV = intravenous; TEE = transesophageal echocardiogram; TTE = transthoracic echocardiogram; N/A = not available.

Discussion

We present a rare and unique case of an LAAO device–related infection 12 months following implantation in a patient with sepsis and persistent bacteremia despite appropriate IV antibiotics. No alternative source for sepsis was identified and removal of his central venous catheter did not result in clearing of the bacteremia. As demonstrated in our case, initial testing with transthoracic echocardiogram may be insensitive for detection of device-related vegetations. Therefore, a high degree of clinical suspicion should be maintained by physicians when a patient with a cardiac device presents with an infection, regardless of the timeline. Risk of LAAO device infections is presumed to be highest during the first 45 days following implantation, after which complete endothelialization has likely occurred.[6]

According to most recent guidelines, TEE is recommended in patients with clinical suspicion of infective endocarditis when a prosthetic heart valve or intracardiac device is present (class 1 recommendation).[10] Although the ability to differentiate thrombus and vegetations may prove difficult with echocardiography alone, the patient's clinical presentation must also be considered. Guidelines for treating LAAO device infections are lacking; in our patient, we adopted the standard treatment for prosthetic valve endocarditis.[11] The patient was successfully treated with a 6-week course of IV vancomycin in addition to oral rifampin. Ideally, he should have received IV gentamicin for the first 2 weeks, but given his age and comorbidities, risk of renal toxicity was a limiting factor.

Cardiac implantable electronic devices have been increasingly utilized for a variety of medical conditions owing to technological advances and acceptable or superior outcomes to alternative management strategies. However, increased number of device implantations necessarily results in increased prevalence of complications including device-related infections. Mortality from cardiac implantable electronic device infections is reported to occur in 16%–23% of patients at 12 and 24 months, respectively.[12] While data are lacking for LAAO devices, we speculate similar mortality rates. Despite increased use of LAAO devices, cases of device infections are rarely reported in literature. The first case of a Watchman device infection was reported within 1 week of implantation in a patient who, similar to our case, failed to clear his bacteremia despite continuous IV antibiotics.[13] Another report demonstrated a patient to have developed a Watchman device infection more than 2 years after implantation. Despite surgical extraction of the device, he died 3 days later from cardiogenic shock.[14] Recently, Jensen and colleagues[6] demonstrated a case of an infected Watchman treated with surgical extraction. None of these cases mentioned periprocedural antibiotic administration. In all previous cases of LAAO device infections, patients were managed with surgical extraction of the device. One of 3 patients died and the other 2 were doing well at 6-month[13]and 10-month[6] follow-up (Table 1). Our case is unique in that it is the only reported case demonstrating success of chronic antibiotic suppressive therapy at 6-month follow-up.

There are no clear guidelines regarding infection prophylaxis in patients undergoing placement of LAAO devices, given the rarity of this complication. Antibiotic prophylaxis during the period of device endothelialization[13] and for 6 months following implantation[6] have been expert opinion based, without clear consensus. Management of device infection also poses an area of uncertainty owing to lack of high-quality evidence and anecdotal reports. With expanding indications for LAAO device implantation, it is anticipated that device infection will become more prevalent.

Conclusion

LAAO device–related infections remain a rarely reported complication despite increased device implantations. Currently, there are no clear guidelines on the need for or duration of antibiotic prophylaxis following device placement nor the treatment options in case of device infection. At this time, management of patients should be individualized and tailored according to each patient. The treatment plan should be taken after a multidisciplinary discussion with the patient and essential personnel, including cardiothoracic surgery and infectious disease consultants.

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