Infective endocarditis of a left atrial appendage closure device: a case report and literature review

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Background

Due to advances in interventional cardiology in recent years, more and more patients are currently receiving cardiac devices, with a subsequent increase in the number of patients with device-associated endocarditis. Device-associated endocarditis is a life-threatening disease with special diagnostic and therapeutic challenges. Interventional devices for left atrial appendage (LAA) closure have been available for several years. However, there have been very few case reports of LAA closure device–associated endocarditis.

Case summary

An 83-year-old woman presented with fever and fatigue. She had a history of permanent atrial fibrillation and recurrent bleeding on oral anticoagulation. Consequently, the patient underwent interventional LAA closure ~20 months earlier. Blood cultures grew Staphylococcus aureus. Transoesophageal echocardiography revealed an LAA closure device–associated mobile, echo-dense mass that was consistent with infectious vegetation in this clinical context. Intravenous antibiotic therapy was started, and our heart team recommended complete removal of the device, which the patient refused. The patient subsequently died as a result of progressive endocarditis and multiple pre-existing co-morbidities.

Discussion

Left atrial appendage occlusion device–associated endocarditis has rarely been reported. Due to the increase in LAA closure device implantation, device-associated endocarditis is expected to increase in the future. Transoesophageal echocardiography is required for correct diagnosis. Our case report suggests that an infection can occur long after implantation.

Keywords

Endocarditis • Left atrial appendage closure • Case report • Amplatzer

ESC Curriculum

5.3 Atrial fibrillation • 4.11 Endocarditis

Learning points

• Infectious endocarditis of a left atrial appendage (LAA) closure device is very rare. Physicians should be aware of this condition even after the completed endothelialization of the device.
• The physicians should be aware that a late infection as a result of the LAA closure device may occur, even years after device implantation.
• It is difficult to distinguish between thrombus and vegetation. A further diagnostic inclusive positron emission tomography scan may be helpful.

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Introduction

Atrial fibrillation (AF) is one of the most common arrhythmias worldwide. Its prevalence increases with advanced age and higher rates of chronic heart diseases. To reduce stroke in patients with AF, anticoagulation is necessary and is the standard treatment. However, this is contraindicated in patients who are at high risk for bleeding. The primary site of thrombus formation in the vast majority of AF patients is the left atrial appendage (LAA), making occlusion of the LAA a treatment to consider.

The technique of percutaneous closure of LAA with either the Watchman (Boston Scientific, Marlborough, MA, USA) or the Amplatzer device (Abbott, Minneapolis, MN, USA) has been increasingly used over the past several years. In general, intracardiac implantation of a foreign material carries the risk of infection (cardiac device–related infective endocarditis). Olsen et al. reported the lifetime risk of system infection in patients with a pacemaker (1.19%), implantable cardioverter-defibrillator (2.18%), and cardiac resynchronization therapy-defibrillator (3.35%). Little is known about the incidence of infections associated with an LAAO or the subsequent management. To date, five case reports have been communicated in the literature. We report an additional case of an 83-year-old woman with Amplatzer LAA closure device–associated endocarditis.

Timeline

Relevant past medical history

An 83-year-old woman was admitted to the hospital with fever (38.6°C), chills, fatigue, and decreased vigilance. The patient had a history of arterial hypertension, pulmonary hypertension, severe tricuspid regurgitation, and permanent AF and received an LAA occluder (LAAO) (Amplatzer Amulet©) 20 months before admission for recurrent bleedings on anticoagulation.

Diagnostic testing

- Elevated white blood cell count (12110/µL) and C-reactive protein levels (165 mg/L)
- Abdominal sonography showed gallbladder wall thickening (>3 mm) without cholecystolithiasis. Abdominal computer tomography (CT) suggested mild cholecystitis
- Blood cultures grew Staphylococcus aureus
- The transthoracic and transoesophageal echocardiogram (TEE), which revealed a mobile vegetation (0.9×0.8 cm) located on the LAAO

Interventions

- Initially, empirical antibiotic therapy consisting of metronidazole and ceftriaxone for presumptive cholecystitis
- The therapy was narrowed later to flucloxacinil (4×3 g daily) and rifampicin (900 mg i.v.)

Case report

An 83-year-old woman was admitted to the hospital with fever (38.6°C), lasting for 2 days, accompanied by chills, fatigue, and decreased alertness. The patient did not take any medication or antibiotics before admission or undergo any invasive procedure with the potential for bacteremia during the previous year. The patient had a history of arterial hypertension, pulmonary hypertension, severe tricuspid regurgitation, and permanent AF and had received an LAAO (Amplatzer amulet©) 20 months before admission for recurrent bleedings on different oral anticoagulants (vitamin K antagonists and apixaban). The LAAO implantation had been uneventful. The patient had been treated for three months with aspirin and clopidogrel. A routine TEE examination revealed mild cholecystitis. An additional abdominal CT suggested mild cholecystitis.

Blood cultures were drawn, and an intravenous empirical antibiotic therapy consisting of metronidazole and ceftriaxone for presumptive cholecystitis was initiated.

On Day 2, blood cultures grew Staphylococcus aureus, and the antibiotics were narrowed to flucloxacinil (4×3 g i.v. daily) in combination with rifampicin (900 mg i.v.) based on susceptibility results. The patient underwent a TEE, which demonstrated a mobile and echo-dense mass (~0.9×0.8 cm) located on the LAAO (Figure 2, Supplementary material online, Videos S4 and S3). An additional abdominal CT suggested mild cholecystitis.

The clinical condition of the patient improved. Her fever and white blood cell count normalized within 3 days, and the CRP and procalcitonin level of 14.74 ng/mL (reference range <0.5 ng/mL). Even though the patient did not have abdominal complaints, abdominal sonography was performed to exclude any intraabdominal focus. This revealed gall bladder wall thickening (>3 mm) without cholecystolithiasis. Blood cultures grew Staphylococcus aureus, and the antibiotics were narrowed to flucloxacinil (4×3 g i.v. daily) in combination with rifampicin (900 mg i.v.) based on susceptibility results. The patient underwent a TEE, which demonstrated a mobile and echo-dense mass (~0.9×0.8 cm) located on the LAAO (Figure 2, Supplementary material online, Videos S4 and S3), which was consistent with vegetation in this clinical context. According to the modified Duke’s criteria, the LAAO endocarditis was diagnosed.

The subsequent clinical course was dominated by her congestive heart failure and other pre-existing co-morbidities, without fever or sepsis under antibiotic therapy. The patient was referred to a palliative unit and died within 2 weeks with end-stage heart failure after diuretics were discontinued at the patient’s request. An autopsy was not performed.

Discussion

Cardiac device–related infectious endocarditis (IE) is a rare but serious complication. Despite the increased use of LAAOs, data about the incidence of LAAO-associated endocarditis are lacking.

We present a rare case of an infected Amplatzer LAAO 20 months after implantation despite complete endothelialization and adequate postprocedural antiplatelet therapy. The development of IE probably
Infective endocarditis of an LAA closure device requires several independent events. An initial event is the adherence of microorganisms to pre-existing non-bacterial thrombotic material attached to the indwelling prosthetic devices/electrodes. Thus, any thrombotic material attached to (native valves or) intracardiac prosthetic material may be colonized by microorganisms at any time during transient bacteraemia. The incidence of device-related (non-infectious) thrombosis after LAAO implantation with Amplatzer Amulet varies in the literature between 4.4 and 16.7%. It has been suggested that thrombus formation after implantation of an LAAO is dependent on an incomplete sealing of the LAA ostium, as the thrombus is detected in the majority of cases between the Amulet disk and the uncovered portion of the limbus (secondary to suboptimal device sizing).

Taken together, the presence of mobile masses attached to intracardiac prosthetic material is a prerequisite for the development of IE. The diagnosis of IE is usually based on clinical and laboratory signs for infection, positive blood cultures and echocardiographic imaging, and in selected cases, may require additional multimodality imaging such as soft tissue ultrasound, magnetic resonance imaging and PET scan. Particularly in case of cardiovascular implantable electronic device (CIED) infection, an F-FDG PET scan could provide helpful information. A meta-analysis by Juneau et al. showed high accuracy in the diagnosis of CIED infection with a sensitivity of 87% and a specificity of 95%. However, it remains uncertain whether this latter imaging modality could have demonstrated the small vegetation close to a metal-containing occluder in our case.

The diagnosis of IE in our case is also based on positive blood cultures with the detection of a typical germ, laboratory findings, and the echocardiographic detection of a mobile mass related to the LAAO, suggestive of vegetation within this context.

In our literature review, we searched the PubMed, Medline, Google Scholar, SCOPUS, and EMBASE databases up to January 2022 using the keywords infective endocarditis, left atrial appendage occluder, closure, Watchman occlusion device, and Amplatzer Amulet occluder to find published case reports with similar conditions. We were aware of only five cases of endocarditis related to LAA closure occlusion devices (Table 1).

In general, the antimicrobial treatment of CIED infection should be individualized and based on the results of blood cultures. Because most CIED infections are due to staphylococcal species and, of those, up to 50% are methicillin-resistant, an empirical therapy of vancomycin should be initiated and continued until the results of cultures are known. In the case of definite CIED-related IE, medical therapy alone is frequently not sufficient and may be combined with complete removal of the device.

It is interesting to note that the infectious process has been detected within the range of 6 days up to 36 months after LAAO implantation. Since we routinely check our patients for residual leakage 3 months after LAAO implantation, we could confirm, at least in our case, that there was no leakage, and the endothelialization process was presumably complete. We assume that, in our case, advanced heart failure with reduced cardiac output in combination with long-standing AF may have prompted the formation of LAAO thrombi and eventually endocarditis.
|                  | Khurmi et al.⁵ | Boukobza et al.⁶ | Jensen et al.⁷ | Madanat et al.⁸ | von Roeder et al.⁹ | This case |
|------------------|----------------|------------------|----------------|------------------|-------------------|-----------|
| **Age (years)**  | 75             | 83               | 74             | 74               | 54                | 83        |
| **Sex**          | Female         | Male             | Male           | Male             | Female            | Female    |
| **Blood culture**| Staphylococcus aureus | Pseudomonas aeruginosa | Enterobacter | Staphylococcus aureus | Staphylococcus aureus | Staphylococcus aureus |
| **LAA device**   | Watchman       | Amplatz Amulet   | Watchman       | Watchman         | Amplatz Amulet    | Amplatz Amulet |
| **Time since implantation** | 6 days | 30 months | 13 weeks | 12 months | 3 years | 20 months |
| **Medication**   | Initially vancomycin and then switched to nafcillin | Cefotaxime + ciprofloxacin + amikacin | Not known | Initially vancomycin, then piperacillin-tazobactam, and then switched to cefazolin | Vancomycin | Initially metronidazole and ceftriaxone and then switched to flucloxacillin |
| **Surgical removal** | Yes | Yes | Yes | No | Yes | No |
| **Vegetation size** | 5 mm | 'Huge' | 1.38 x 1.58 cm | 1.35 x 0.45 cm | Not known | 0.9 x 0.8 cm |
| **Outcome**      | Discharged home | Died from refractory cardiogenic shock | Discharged home after a long postprocedural course | Discharged home | Discharged home | Died in the palliative unit |
| **Embolization** | No | Yes | No | No | Yes | No |
| **Follow-up**    | Alive 6 months after discharge | — | Alive 10 months after discharge | Alive 6 months after discharge | No | — |
The entry of *S. aureus* into the bloodstream remains obscure. In our case, we do not think that the mild cholecystitis was the entry since this process is usually associated with enteric pathogens other than *S. aureus*.

The management of LAAO endocarditis has not yet been defined. In four out of six cases, patients were referred to cardiac surgery for removal of the infected LAAO. However, a single case was presented, in which medical therapy alone was successful.\(^5\) Our patient responded initially to antibiotic therapy, too, and the infectious process appeared to be under control before the patient refused further treatment.

Physicians should be aware that a late infection of the LAAO may occur, even years after device implantation.\(^6\)

### Lead author biography

Hani Al-Terki is a consultant in ICU and cardiology in Bochum, Germany.

### Supplementary material

**Supplementary material** is available at *European Heart Journal – Case Reports*.

**Slide sets:** A fully edited slide set detailing this case and suitable for local presentation is available online as **Supplementary data**.

**Consent:** The patient reported in this case is deceased. Despite the best efforts of the authors, they have been unable to contact the patient’s next-of-kin to obtain consent for publication. Every effort has been made to anonymize the case. This situation has been discussed with the editors.

**Conflict of interest:** A.M. was a speaker for Bristol-Myers Squibb, Novartis, and Pfizer. M.G. was a speaker for Abbott, Bristol-Myers Squibb, Novartis, and Pfizer. H.A.-T. wrote the initial version of the manuscript and edited it later after the initial review. M.G. wrote the abstract and inserted the figures and the videos. A.M. optimized the manuscript and edited it later after the initial review. M.G. wrote the **References**.

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