Case Report

A Case of Pacemaker Associated *Aspergillus fumigatus* Endocarditis

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Abstract

The use of cardiovascular implantable electronic devices (CIED) is associated with improved quality of life and decreased fatal outcomes in patients with cardiac dysfunctions. As with all foreign devices that are inserted or implanted in the body, CIED also carries the risk of device-related infections. Infections account for <2% of the complications associated with CIED, and only about 2% of these are secondary to a fungal pathogen. The first case of *Aspergillus* endocarditis secondary to a transvenous pacing lead was reported in the 1980s, and a limited number of cases have been documented in the literature since then. *Aspergillus* endocarditis is a highly fatal disease and establishing the diagnosis sufficiently early is challenging. We here report a case of *Aspergillus* endocarditis secondary to permanent pacemaker insertion which was successfully treated following the establishment of the diagnosis using imaging studies and galactomannan assay.

Keywords: *Aspergillus fumigatus*, cardiovascular implantable electronic device infection, endocarditis, galactomannan assay

Introduction

The advances in cardiovascular sciences have led to the increased use of cardiovascular implantable electronic devices (CIED) which now include permanent pacemakers (PPMs), implantable cardioverter defibrillators, and cardiac resynchronizing therapy devices. The increasing use of CIED is also associated with increasing risk of cardiac infections with the potential to cause metastatic infections. Timely diagnosis of CIED infection (CIEDI) allows for early management with antibiotics and device removal, which is usually needed for the resolution of the infection. Endocarditis including CIED-related endocarditis are most often caused by bacterial pathogens and less commonly by fungal agents, the latter being the most serious. The index of suspicion for fungal endocarditis (FE) is low and in many instances, the diagnosis is not made till at the time of post mortem.[1] We here describe a case of *Aspergillus* endocarditis following PPM insertion.

Case Report

A 65-year-old diabetic, the hypertensive gentleman was admitted with low-grade fever, cough, joint pain, swelling of lower limbs, and worsening dyspnea of 3 months duration. Important clinical findings included pallor, engorged jugular veins, decreased breath sounds, S3 gallop, systolic murmur in tricuspid area, ascites, and pedal edema. History was significant for dual-chamber permanent pacemaker insertion intended for complete heart block 5 years ago. The pacemaker lead was replaced 3 years later due to pacing failure. Investigations during the present illness revealed low hemoglobin (7.8 mg/dl), total count (2700/mm), and high erythrocyte sedimentation rate (123 mm/1st h). Chest X-ray showed moderate pleural effusion with pleural thickening. Transesophageal echocardiographyshowed a mobile mass 11 mm × 11 mm attached to the pacemaker lead at tricuspid valve level on right atrial side, moderate tricuspid regurgitation, and mild pericardial effusion [Figure 1]. A diagnosis of cardiac device related tricuspid valve infective endocarditis (IE) with pneumonia was made. All six sets of blood cultures were sterile. The initial empiric antibiotic regimen included intravenous ciprofloxacin and vancomycin. The patient failed

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Access this article online

Quick Response Code:

Website: www.jgid.org

DOI: 10.4103/jgid.jgid_67_21

How to cite this article: Ray U, Dutta S, Khan A. A case of pacemaker associated *Aspergillus fumigatus* endocarditis. J Global Infect Dis 2022;14:38-40.

Received: 16 March 2021 **Revised:** 26 April 2021
Accepted: 27 May 2021 **Published:** 09 November 2021

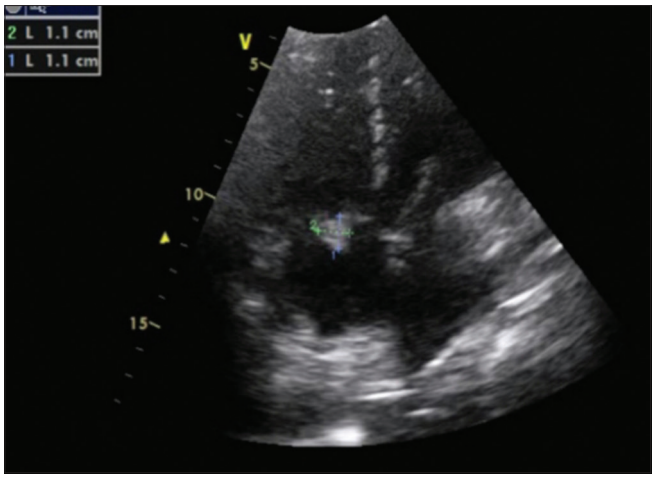

Figure 1: Two-dimensional echo showing 1.1 cm × 1.1 cm mobile vegetation in subtricuspid region of pacemaker lead

to show any signs of improvement despite persistently negative blood cultures. At this point, BAL and serum galactomannan levels were done and they were markedly raised (BAL galactomannan Index was 4.1 and serum galactomannan index was 2.3, Kit cut off was 0.5). Antifungal in the form of liposomal amphotericin B (3 mg/kg body weight/day) was initiated and the patient was taken up for surgery. The surgical approach involved the opening of the right atrium and removal of vegetation along with the pacing lead. As the vegetation involved the septal cusp, all cusps were excised and a 27 mm bioprosthetic valve was implanted by continuous technique. The pacemaker was resited (epicardial lead was placed in the inferolateral wall and new pulse generator placed in the right hypochondrium pocket). The vegetation subsequently grew *Aspergillus fumigatus*. Intravenous liposomal amphotericin was administered from 48 h before to 1 week after system removal, followed by oral voriconazole (400 mg BD loading dose followed by 200 mg BD). Therapeutic drug monitoring of voriconazole could not be done but the subsequent course was favorable. The patient continues to be under regular (6 monthly) follow-up. Although serum galactomanan assay was not repeated following the surgical removal of the vegetation and device, transesophageal ECHO was done before discharge and transthoracic echocardiogram is done at each follow-up visit. ECHO findings are essentially within normal limits without any evidence of vegetation. The patient took voriconazole (200 mg BD) for close to 5 years. At the time of writing of this report, he is off voriconazole for the last 1 year and is doing well both clinically and radiologically.

Discussion

CIEDI is defined as an infection extending to the device leads, cardiac valve leaflets, or endocardial surface. It is a severe disease associated with high mortality. Most of these infections (>50%) are caused by staphylococcal species, and many are becoming resistant to methicillin.[2] Other species include gram-negative organisms (9%), enterococci (4.2%), streptococci (2.5%), and fungi (1%). In general, *Aspergillus* accounts for 24%–28% of all FE cases and between 0.25%–2.5% of all IE cases including CIED associated infection. The risk of infection for CIED is 0.5%–1%, for first-time implantation which increases to 1%–5% for a device replacement or upgrades.[3] These infections can involve the generator pocket, bloodstream, or cardiac structures, leading to IE.[4] Risk factors associated with CIED infection included renal failure, heart failure, diabetes, and fever within the last 24 h before CIED implantation, anticoagulation, and steroid use.[3] A CIED can become infected at the time of implantation or during device revision. The majority (60%) of CIED infections is pocket infections, characterized by erythema, tenderness, warmth and erosion.[5] The infection can also track along the endovascular portion of the leads resulting in endovascular infection and possibly endocarditis.[2] A CIED can also become infected as a consequence of the hematogenous seeding of the leads or pocket during an episode of bloodstream infection. In the present case presence of a cardiac device and revision of the pacemaker device in the background of diabetes were the risk factors identified for the development of endocarditis.

Endocarditis in general and FE, in particular, are associated with high mortality. The survival rate following FE appears to be <20%.[6] *Aspergillus* endocarditis is associated with even higher mortality and morbidity. The diagnosis of endocarditis is based on a combination of history, clinical findings, laboratory and microbiological parameters, and imaging studies. The Duke criteria which to a large extent on the microbiological recovery of a typical pathogen of endocarditis from blood cultures is less efficient in diagnosing *Aspergillus* endocarditis as blood cultures are almost always negative (unlike Candida endocarditis). Also important is the fact that blood cultures are negative in 2%–40% of cases of endocarditis, with some studies reporting blood culture-negative rates up to 71%.[7] The reasons for the apparent blood culture-negative results are twofold: Presence of an organism such as Bartonella, Coxiella which do not grow in routine culture and initiation of antibacterials before collection of blood culture, the later being more common. The diagnosis of IE on the basis of imaging and laboratory parameters results in the initiation of antibacterials. In absence of any specific pointers towards FE, antifungals are not considered till late in the course of disease progression. Candida is likely to be recovered in blood cultures but the timely diagnosis of *Aspergillus* endocarditis still remains elusive. A search of the available literature reveals *Aspergillus* endocarditis was diagnosed post-mortem in approximately one-third of cases and was diagnosed preoperatively in less than half of patients.[5]

In this regard detection of galactomannan antigen in the serum may prove to be a useful adjunct in the diagnosis of AE. Galactomannan, a component of the cell wall of *Aspergillus* is released during fungal growth and is a useful biomarker for detecting invasive aspergillosis. The galactomannan antigen is phagocytosed by neutrophils and this limits its diagnostic usefulness in nonneutropenic patients and may result in

false negatives. Despite the limitations, several studies have shown the usefulness of galactomannan antigen in diagnosing *Aspergillus* endocarditis. Meshaal *et al*. in their retrospective cohort study on *Aspergillus* endocarditis showed that of the 26 patients with histologically proven *Aspergillus* endocarditis, galactomannan antigen results were available for 18 patients and the antigen was raised significantly in all the eighteen patients.[8] In another study, serum *Aspergillus* Galactomannan antigen detection was useful for the diagnosis of cardiac aspergillosis in two non-neutropenic patients. In the study, the galactomannan index initially was more than two-fold greater than the cut-off index of the kit, which decreased in response to surgical and antifungal therapies.[9] Badiee *et al*. also reported the usefulness of galactomannan antigen detection in diagnosing patients with *Aspergillus* endocarditis. In their study, the galactomannan antigen tested positive in 5 of 6 patients with documented aspergillosis.[10] In the present case, the galactomannan was raised more than fourfold of the kit cut off which led to the provisional diagnosis of *Aspergillus* endocarditis and initiation of antifungal therapy. This finding was confirmed later when *A. fumigatus* grew in culture from the excised vegetation. Therefore, the detection of galactomannan antigen looks promising in the diagnosis and follow-up of patients with aspergillus endocarditis. The Infectious Disease Society of America also endorses the use of galactomannan as an aid for the early detection of invasive aspergillosis.

The treatment of pacemaker infection consists of complete removal of the infected hardware followed by appropriate antimicrobial therapy. The successful management of *Aspergillus* endocarditis as documented in the literature consists of through surgical debridement of the vegetation along with explantation of the device. Voriconazole seems to be the most effective antifungal for the treatment of *Aspergillus* endocarditis with better tolerability and less side effects for the patients as compared to amphotericin B deoxycholate.[8] However Liposomal amphotericin B provides an alternative to voriconazole for the treatment of invasive aspergillosis. The duration of antifungal therapy is not clear and probably needs to be life-long. Early diagnosis and combination of medical and surgical approach are essential for successful outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given his consent for his images and other clinical information to be reported in the journal. The patient understands that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

Research quality and ethics statement

The authors followed applicable EQUATOR Network ("http://www.equator-network.org/) guidelines, notably the CARE guideline, during the conduct of this report.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. McCormack J, Pollard J. *Aspergillus* endocarditis 2003-2009. Med Mycol 2011;49 Suppl 1:S30-4.
2. Tarakji KG, Ellis CR, Defaye P, Kennergren C. Cardiac implantable electronic device infection in patients at risk. Arrhythm Electrophysiol Rev 2016;5:65-71.
3. Lambert CT, Tarakji KG. Cardiac implantable electronic device infection. Cleve Clin J Med 2017;84:47-53.
4. Deharo JC, Quatre A, Mancini J, Khairy P, Le Dolley Y, Casalta JP, *et al.* Long-term outcomes following infection of cardiac implantable electronic devices: A prospective matched cohort study. Heart 2012;98:724-31.
5. Baddour LM, Epstein AE, Erickson CC, Knight BP, Levison ME, Lockhart PB, *et al.* Update on cardiovascular implantable electronic device infections and their management: A scientific statement from the American Heart Association. Circulation 2010;121:458-77.
6. Badiee P, Amirghofran AA, Ghazi Nour M, Shafa M, Nemati MH. Incidence and outcome of documented fungal endocarditis. Int Cardiovasc Res J 2014;8:152-5.
7. Brouqui P, Raoult D. Endocarditis due to rare and fastidious bacteria. Clin Microbiol Rev 2001;14:177-207.
8. Meshaal MS, Labib D, Said K, Hosny M, Hassan M, Abd Al Aziz S, *et al. Aspergillus* endocarditis: Diagnostic criteria and predictors of outcome, A retrospective cohort study. PLoS One 2018;13:e0201459.
9. García-Rodríguez J, García-Guereta L, De Pablos M, Burgueros M, Borches D. Galactomannan detection as a tool for the diagnosis and management of cardiac aspergillosis in 2 immunocompetent patients. Clin Infect Dis 2008;47:e90-2.
10. Badiee P, Amirghofran AA, Ghazi Nour M. Evaluation of noninvasive methods for the diagnosis of fungal endocarditis. Med Mycol 2014;52:530-6.