Aspergillus infection of pacemaker in an immunocompetent host: a case report

Yuan GAO, Rong-Fang LAN, Ning ZHANG, Shao-Xian WANG, Zhong-Lin HAN, Wei XU#
Nanjing Drum Tower Hospital, Clinical College of Nanjing Medical University, Nanjing, China

J Geriatr Cardiol 2020; 17: 58–60. doi:10.11909/j.issn.1671-5411.2020.01.007

Keywords: Aspergillus flavus; Device explantation; Pacemaker infection

The incidence of CIED (Cardiac Implantable Electronic Devices) infections is 0.13%–8.0%.[1,2] Fungal organisms account for up to 10% and Aspergillus infections are extremely rare. Here, we present a case of CIED-related Aspergillus infection in an immunocompetent patient.

A 53-year-old man with past medical history notable for poorly controlled type 2 diabetes mellitus, persistent left superior vena cava, status post permanent pace maker placement for sick sinus syndrome came to our hospital for routine evaluation of his device. Interrogation of his device revealed a recent increase in his atrial pacing threshold (3.5 v/0.4 ms) and several episodes of non-capture. During the initial attempt to replace his generator, he was found to have a large amount of cheese-like necrotic material in his generator pocket.

On physical examination, he was afebrile. There is no swelling or tenderness around the pocket area. Cardiac examination revealed no abnormal murmurs. The ventricular pacing threshold was normal and pacemaker was programmed to VVI mode. The patient denied intravenous drug use, blood transfusion, malignancy or any use of immunosuppressive agents. The laboratory data were remarkable for Serum Beta-D-glucan Assay of 385.5 pg/mL, CRP of 23.9 mg/L, hemoglobin of 124 g/L (Normal range 130–175 g/L). HIV test was negative. His chest X-ray and transthoracic echocardiogram failed to show any abnormalities. Transesophageal echocardiography revealed a 30 × 28 mm vegetation adherent to one of the pacing leads (Figure 1A). Contrast-enhanced CT of the chest revealed large filling defect from the level of aortic arch to right atrium. We assumed the filling defect is due to the necrotic substance (Figure 1C). Swabs of the electrodes and generator were sent for culture and each sample yielded Aspergillus flavus on blood agar (Figure 1D & E). Treatment was transitioned to intravenous voriconazole 200 mg b.i.d. for the following six weeks. We were going to surgical implant another device but decided to do a less invasive procedure due to the patients concerns. Finally, we implanted a permanent pacemaker percutaneously. After one-year follow-up, the patient presented no systemic signs of infection relapse.

With the increasing use of intracardiac devices, clinicians are prone to encounter more patients with CIED-related complications. Infection related to devices causes significant mortality. Aspergillus species account for 20% to 30% of fungal endocarditis and are less common than Candida species as causative pathogens.[3] CIED-related Aspergillus infection should be suspected in persons with underlying hematological malignancies, recent cardiothoracic surgery, intravenous drug use, and immunosuppression with culture-negative endocarditis and/or systemic or pulmonary emboli.[4] Our patient is immunocompetent without any other known risk factors except uncontrolled diabetes. He may have had some occupational exposure to Aspergillus due to work as a sanitary worker.

The initial symptoms of CIED-related Aspergillus infection may be minimal and insidious making the diagnosis difficult. Diagnosis ultimately requires confirmation of histology and culture.[5] Here we demonstrate the importance of transesophageal echocardiography (TEE) to such patients suspected of CIED-related infections. A study conducted in 2003 reveals TEE has superior sensitivity (> 90%) over TTE (< 30.5%) and shows significant advantages on visualizing vegetations.[6] Noninvasive marker, such as galactomannan, may be positive but are not specific for the site of disease. False-positive results can occur with fungal infections (i.e., histoplasmosis, blastomycosis, cryptococcosis, and penicilliosis), as well as concomitant antibiotic therapy with piperacillin–tazobactam and amoxicillin-clavulanate.[4]
Infections related to intracardiac devices should be treated with removal of the infected hardware and appropriate antimicrobial therapy.[7,8] Voriconazole or liposomal AmB (3–5 mg/kg per day) are recommended as first-line agents. However, the duration of antifungal therapy is still controversial. Guidelines recommend long duration of anti-fungal therapy (> 2 years) with consideration of lifelong therapy concomitant with frequent clinical and echocardiographic assessment for possible recurrence.[8] In our patient, we used vancomycin and cefuroxime empirically before the final diagnosis. The patient responded well with his C-reactive protein (CRP) dropping from 23.9 to 4.6 mg/L. Treatment was transitioned to intravenous voriconazole 200 mg b.i.d. for the following six weeks after the positive culture of *Aspergillus flavus*. For the next one year follow up, there is no recurrence of infection and both TEE and chest CT showed a marked decrease in size of the vegetation. We conducted a MEDLINE search for CIED-related aspergillus infection, the duration of antibiotics varies, ranging from three weeks to lifelong time. Whether CIED-related *Aspergillus* infection patients without immunocompromising status need the lifelong antifungal medications still need to be proved.

Finally, we want to share our single case experience on the choice of re-implantation strategy. Considering the patient had left persistent superior vena cava and refused the insertion of an epicardial pacemaker, we decided to implant a permanent pacemaker percutaneously through the infectious side. His pacemaker worked well during the one-year follow-up. Although it is recommended the re-implantation should be on the contralateral side of the infection, we present our single case experience of reimplanting on the side of the infection.

In conclusion, the CIED infections due to fungal organisms are rare but fetal. The initial symptoms may be minimal and insidious. When CIED infections are suspected, TEE should be performed. The guidelines recommend combining surgical and medical treatments but more specific management consensus is still required, these should address the choice of antifungal agents and their duration, the timing of surgery, and follow-up.

**Statement of Ethics**

In this case report, all the treatment comply with the guidelines for human studies and research was conducted.
ethically in accordance with the World Medical Association Declaration of Helsinki. In the manuscript, we had the written informed consent to publish their case (including publication of images) from our patient. Also, the study protocol was approved by the institute’s committee on human research. Information revealing the subject’s identity is to be avoided. All patients should be identified by numbers or aliases and not by their real names.

Disclosure Statement

The authors have no conflicts of interest to declare.

Funding Sources

This work was supported by National Natural Science Foundation of China (No. 81600267) to HAN ZL. The funder had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

References

1 Klug DD, Lacroix C, Savoye, et al. Systemic infection related to endocarditis on pacemaker leads: clinical presentation and management. Circulation 1997; 95: 2098–2107.
2 Young JB, Abraham WT, Smith AL, et al. Combined cardiac resynchronization and implantable cardioversion defibrillation in advanced chronic heart failure: the MIRACLE ICD trial. JAMA 2003; 289: 2685–2694.
3 Rubinstein E, Lang R. Fungal endocarditis. Eur Heart J 1995; 16 (Suppl B): 84–89.
4 Kalokhe AS, Rouphael N, Chami El MF, et al. Aspergillus endocarditis: a review of the literature. Int J Infect Dis 2010; 14: e1040–e1047.
5 McCormack J, Pollard J. Aspergillus endocarditis 2003–2009. Med Mycol 2011; 49 (Suppl 1): S30–S34.
6 Rallidis LS, Komninos KA, Papasteriadis EG. Pacemaker-related endocarditis: the value of transoesophageal echocardiography in diagnosis and treatment. Acta Cardiol 2003; 58: 31–34.
7 Pasha AK, Lee JZ, Low SW, et al. Fungal endocarditis: update on diagnosis and management. Am J Med 2016; 129: 1037–1043.
8 Patterson TF, Thompson GR, 3rd, Denning DW, et al. Practice guidelines for the diagnosis and management of aspergillosis: 2016 update by the infectious diseases society of America. Clin Infect Dis 2016; 63: e1–e60.