Drug Fever in an Elderly Patient After Pacemaker Implantation

Dong Wook Lee, Ju Hee Ha, Jun Ho Kim, Ki Beom Park, Jae Joon Lee, Han Il Choi, Jin Hee Kim

Department of Internal Medicine, Busan Medical Center, Busan, Korea

Corresponding Author: Jin Hee Kim, MD
Division of Cardiology, Department of Internal Medicine, Busan Medical Center, 359 Wordcup-daero, Yeonje-gu, Busan 47527, Korea
Tel: +82-51-507-3000, Fax: +82-51-507-3001
E-mail: yoplait83@hanmail.net

Received: July 26, 2016
Revised: October 11, 2016
Accepted: October 17, 2016

Key Words: Pacemaker implantation, Drug fever, Infective endocarditis

INTRODUCTION

Pacemaker implantation is a relatively safe procedure with few complications, which is commonly performed to treat patients with cardiac arrhythmia. Infective endocarditis involved in an implanted intracardiac electrode is reported to occur, on average, in 0.5% of patients with a pacemaker, although different studies have reported different occurrence rates. Although infective endocarditis rarely occurs in patients with a pacemaker, when it occurs, it is a very serious complication that can be fatal and is difficult to diagnose. A diagnosis of infective endocarditis is typically made by observing clinical patterns, blood culture results, and echocardiograms of cardiac vegetation; however, transthoracic echocardiography findings are unclear in the case of endocarditis involved in an electrode. In most cases, treatment requires surgical removal of the electrode causing the infection; thus, accurately making a diagnosis is especially important. In this case study, we report a case in which drug fever following pacemaker implantation could have been misdiagnosed as infective endocarditis; we additionally reviewed the relevant literatures.

CASE REPORT

An 80-year-old female patient visited the cardiology department of Busan Medical Center as an outpatient with primary complaints of breathing difficulty and dizziness during physical exercise, which had started a month previously and were gradually worsening. She had a history of hypertension and asthma and was taking drugs to treat them. She had no history of smoking or drinking and no family history of heart disease. Regarding her vital signs, blood pressure was 100/60 mmHg, pulse was 34 beats/min, respiration was 20 breaths/min, and body temperature was 36.0°C. Thus, bradycardia was observed, and complete atrioventricular block was found on electrocardiogram (Fig. 1A). After it was confirmed that none of the drugs she was taking caused the condition, a pacemaker was implanted (Fig. 2). Following the implant and confirmation that her systemic condition and the condition of the surgical area were good and her heart rate was well controlled, she was transferred to the general ward for observation (Fig. 1B). Prophylactic antibiotic therapy, ceftriaxone (2 g daily) was administered for 8 days starting a day before the procedure, after which fever, chills, and weakness were observed. There was no jugular vein distention, her breathing sounds were normal, and her heart sounds were regular without cardiac noise. The abdomen was soft and smooth without tenderness, and there was no palpable mass. There was no abnormality in limb mobility or pitting edema. An electrocardiogram showed that the heart pulsed by the pacemaker, and simple chest radiographs did not show any abnormalities such as car-
Fig. 1. (A) Initial electrocardiogram on admission showed complete absence of atrioventricular conduction. (B) The electrocardiogram after pacemaker implantation showed a paced rhythm with a small spike.

Fig. 2. Chest radiograph after pacemaker implantation.

Fig. 3. Transthoracic echocardiography shows no definite vegetation attached to the pacemaker leads in the right atrium and right ventricle. (A) Apical 4-chamber view. (B) Subcostal view.

Fig. 4. Skin lesion of chest and neck.

Diomedegy or pulmonary congestion,

On peripheral blood testing, the patient’s white blood cell count was 11,800/mm³ (polymorphonuclear leukocytes 78%), her hemoglobin level was 11.5 g/dL, and her platelet count was 154,000/mm³. She had an elevated C-reactive protein (CRP) level (35.62 mg/L) but normal creatine kinase-MB (2.8 ng/mL) and troponin I (0.005 ng/mL) levels. Additionally, liver and kidney function and urine tests revealed no notable findings.

On transthoracic echocardiography, a pacemaker electrode, but no vegetation, was seen in the right atrium and the right ventricle (Fig. 3). Pathogens were not detected on the wound swab or on blood cultures repeated 3 times. Fever and chills were observed, and skin flare-ups and pruritus were spread over the upper body, including the face and neck, in addition to local flare-ups around the area of the pacemaker implant (Fig. 4). In the beginning, infective endocarditis was suspected based on the clinical observations. However, a bacterial culture test and echocardiography, i.e., the primary diagnostic standards for infective endocarditis, returned negative results and there was no other severe or systemic symptoms. Thus, we considered the possibility of drug fever because of the accompanying flare-ups and hypereosinophilia, and switched the prophylactic antibiotic therapy. Subsequently, the patient’s condition improved regarding the skin lesions, fever, and chills, and she was discharged. Currently, she has shown no notable findings and is being followed up as an outpatient.

DISCUSSION

Since approximately 30 years ago, when a pacemaker was implemented for the first time, the use of permanent pacemakers and defibrillators has increased with the aging of the population and the expanded clinical indications. Accordingly, complications related to the procedure are often encountered in practice. Infection due to an intracardiac electrode rarely occurs after pacemaker implantation, but if it does, the complication can have fatal consequences. The occurrence rate is reported between 0.5% and 7% depending on the study, and the mortality rate of infective endocar-
ditis due to pacemaker implantation is approximately 30%–50%\(^{10}\).

Most infections that occur immediately following pacemaker implantation are known to be caused primarily by local contamination of the electrode catheter due to the lack of aseptic processing control at the time of implantation, with the common pathogen being *Staphylococcus aureus*\(^{1}\). Therefore, it is crucial to minimize local contamination factors while performing the procedure.

The main difficulty in diagnosing infective endocarditis related to an intracardiac electrode is the lack of clearly established diagnostic standards. Typically, a diagnosis of infective endocarditis is made if pathogens are detected on a blood culture or vegetation is confirmed on an echocardiogram\(^{6}\). In addition, when a blood test shows an elevation in inflammatory indices such as the complete blood count (CBC), erythrocyte sedimentation rate, or CRP level in conjunction with such symptoms as flare-ups and pain in the area of pacemaker implant, fever, chills, and systemic weakness, a link with infective endocarditis should be considered.

If a diagnosis of infective endocarditis is confirmed or infective endocarditis due to pacemaker implantation is strongly suspected based on several clinical signs and symptoms, all involved parts should be removed at an early stage. A new pacemaker should be implanted in another area after a certain amount of time has passed only in cases where a pacemaker is inevitable. Recently, it has been reported that the condition improved with single-antibiotic therapy, but most studies recommend early removal of the pacemaker as the standard treatment in all cases. Practically, there are marked differences, by severalfold, between conservative and surgical treatments in treatment success rates and in-hospital and overall mortality rates\(^{9}\).

When an artificial object such as a pacemaker, catheter, artificial heart valve, or artificial joint is implanted in the human body, biofilms are formed composed of substances such as fibrin and collagen from the object’s surface or the surrounding area of the body and glycocalyx from the pathogens. Once the pathogens form colonies on the biofilm around the artificial part, it functions as a protective membrane against the neutrophils, macrophages, and antibodies of the host. So, if treated only with antibiotics, the strength of the antibiotics needs to be 100 times higher than standard antibiotic therapy, and ultimately, the removal of the artificial part is essential to overcome it\(^{11}\).

The patient reported in this case study showed clinical symptoms of fever accompanied by local flare-ups around the surgical area, chills, and other symptoms after pacemaker implantation; an elevation in inflammatory indices such as CBC and blood CRP level was also found. As in the current case, being an older female and the use of steroids to treat asthma can be crucial risk factors for infection related to pacemaker implantation. The possibility of pacemaker-related infective endocarditis could have been considered in this situation; however, pathogens were not detected on bacterial cultures and no vegetation was observed on an echocardiogram, which are the major diagnostic standards for infective endocarditis. In the current case, the primary diagnostic standards according to the Duke criteria (widely used to make a diagnosis of infective endocarditis) were not met; among the secondary diagnostic standards, only one criterion of fever above 38°C was met. Although the clinical evaluation of fever was unclear, the patient’s recovery course was not serious and overall stable: she had fever accompanied by flare-ups, hypereosinophilia detected through a blood test, and skin lesions accompanied by pruritus spreading to the overall upper body including the face and neck. Thus, we determined that drug fever was a possibility and switched the prophylactic antibiotic that she had been on, after which her systemic symptoms such as periodically occurring fever and chills and skin flare-ups improved.

As reported above, it is difficult to diagnose infective disease involved in an intracardiac electrode, and a misdiagnosis can even lead to an unnecessary surgery. Therefore, if a patient with a pacemaker shows an ambiguous clinical pattern and the findings of blood cultures and echocardiography are unclear, the physician should consider various causes including drug fever to increase diagnostic accuracy and prevent unnecessary surgery.

Drug-related allergy occurs due to immunological mechanisms and is characterized by a history of exposure to a suspected drug and hypersensitivity even to a small amount after sensitization and reproducibility. Elderly patients are more likely than younger patients to have already been exposed to multiple medications; therefore, the possibility of drug allergy should be considered in diverse treatment situations in which fever or skin lesions occur.

**Conflicts of Interest Disclosures:** The researchers claim no conflicts of interest.

**REFERENCES**