Pacemaker pocket infection due to *Mycobacterium abscessus* subspecies *abscessus* - Case report and literature review

Running title: Pacemaker pocket infection

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Abstract

Background: Mycobacterium abscessus is a rapidly growing non-tuberculous mycobacterium that can cause various infections in humans. The identification of the nontuberculous mycobacteria is a challenge to date due to available of limited resources. There have been reports of device-related infections caused by these bacteria. Proper care of the cardiac implants can give rise to infections which need to be identified promptly. To emphasize the need of early and prompt diagnosis of non-tuberculous mycobacterium infections.

Case Report: Here, we present a case of a 69-year-old man who presented with an atrioventricular block and hence undergoes a pacemaker implant. The implant became infected with Mycobacterium abscessus which resolved after appropriate treatment and pacemaker removal.

Conclusion: Non-tuberculous mycobacteria must be promptly identified and treated for the correct duration to prevent complications associated with them.

Keywords: Nontuberculous Mycobacteria, *Mycobacterium abscessus*, Atrioventricular block, Pacemaker, Artificial

Introduction

Infections associated with pacemakers are uncommon but can occur. Pacemaker infections can manifest either as pocket infections where infections can occur in the pocket created under the skin where the pacemaker generator is placed or can involve the leads (wires) that act as a connection between the pacemaker and the heart (1). These infections can lead to serious complications, and prompt diagnosis and treatment are essential.

Pacemaker infections can be caused by various microorganisms, including bacteria, and they are generally classified as device-related infections. Among the bacterial agents, the common organisms associated with these infections are Coagulase-negative staphylococci and *Staphylococcus aureus* (2). Non-tuberculous mycobacteria (NTM), especially the rapid growers are rarely implicated. Unlike *Mycobacterium tuberculosis*, NTM is ubiquitously present in the environment. The symptoms and severity of NTM infections can vary depending on the species of mycobacteria involved and the individual's immune status. Pacemaker NTM infections can occur due to contamination during the implantation procedure or from subsequent exposure to environmental sources of NTM (3).

Mycobacterium abscessus is a rapidly growing, multidrug-resistant NTM that is known for causing a variety of infections in humans. *M. abscessus* is commonly found in water and soil. One of the significant challenges in treating infections caused by *M. abscessus* is its resistance to many of the commonly used antibiotics for the treatment of NTM infections. This resistance complicates the management of infections and often requires a combination of antimicrobial agents for an extended duration (4).

The management of pacemaker infections caused by NTM often involves a combination of antimicrobial therapy and, in some cases, removal of the infected device. Removal may be necessary if the infection is severe, or persistent, or if there is evidence of device-related complications (2). This case report emphasizes the need and importance of early diagnosis and treatment of nontuberculous mycobacterial infections in artificial implants and devices.

Case Report

A 69 years old man, with a known case of type 2 diabetes mellitus for 6 years and systemic hypertension for 15 years on regular medications for the past 10 years presented with complaints of breathlessness on exertion lasting for 15 days. He was evaluated in a private hospital and was found to have atrioventricular block for which pacemaker was implanted. After 35 days of implant placement, he noticed pus discharge from the surgical site. He presented to the cardiology outpatient department with history of pus discharge from the surgical site of 10 days duration associated with pain at the surgical site. He also reported intermittent, low grade fever for the past 10 days. There was no history of shortness of breath, palpitation or chest pain.

On general physical examination, patient was well built and nourished. He as afebrile and systemic examination was found to be normal. On local examination, surgical wound appears to be healing and an opening measuring 1x 0.5cm was found near the lateral end of the surgical wound with minimal pus discharge present. Ultrasound revealed pocket site collection and a diagnosis of device related infection/pocket site infection was made. Thoracic echocardiogram was negative for any vegetations on the native valve. As there was minimal pus discharge, pus sample was collected using sterile cotton swab and was sent for bacterial culture and sensitivity. Gram staining from the sample revealed plenty of pus cells and no bacteria was seen. Sample was plated onto 5 % sheep blood agar and MacConkey agar. No growth was observed at the end of 48 hours of aerobic incubation. Since there was clinical suspicion of pocket site infection, plates were reincubated for another 5 days. At the end of 4 days of aerobic incubation, 0.5-1mm, circular, dry non-hemolytic colonies with entire margins were observed in blood agar (Figure 1) while MacConkey agar did not show any growth.

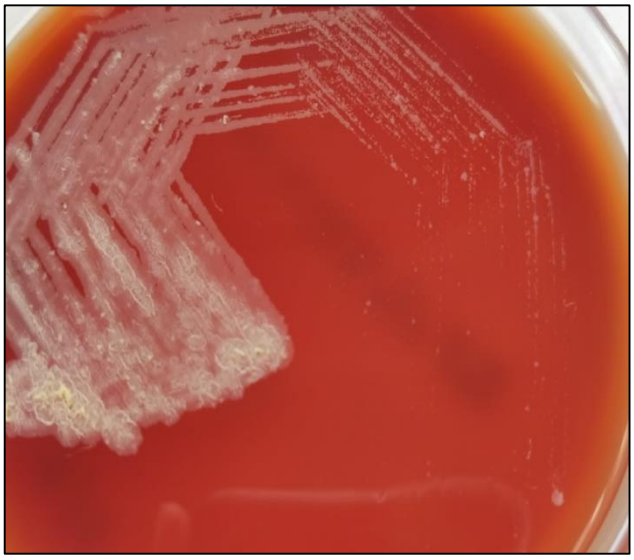

Figure 1. Shows a blood agar plate with colonies of *Mycobacterium abscessus* after 7 days of incubation

The Gram stain from the minute colonies showed short, thin Gram-positive bacilli. Acid-fast staining with 25% sulfuric acid revealed acid-fast bacilli (Figure 2).

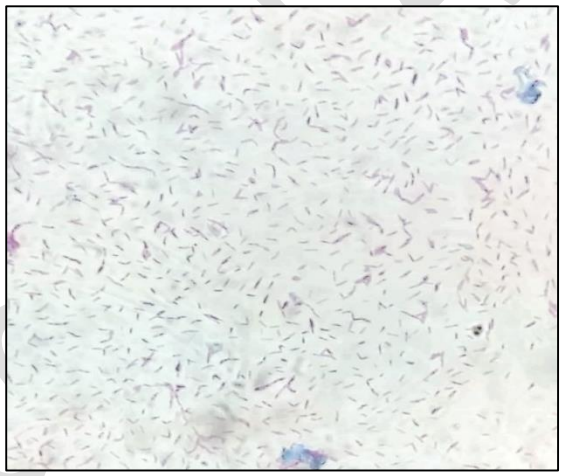

Figure 2. Acid-fast staining from the minute colonies grown on Blood agar showing Acid-fast bacilli

The colony was simultaneously given for identification using MALDI-TOF MS. The organism was identified as *Mycobacterium abscessus* with 99.9% confidence. Gram stain from the sample was de-stained completely and acid-fast staining was performed which revealed short thin acid-fast bacilli. From the blood agar, colonies were subcultured onto the Lowenstein-Jensen medium. Dry, non-pigmented colonies were observed after 3 days of incubation (Figure 3).

Figure 3: Dry, non-pigmented colonies were observed on Lowenstein Jensen medium after 3 days of incubation

Line probe hybridization using GenoType NTM- DR (Hain Lifesciences, Germany) was performed for further characterization and drug susceptibility testing. The organism was identified to be *Mycobacterium abscessus* subspecies *abscessus* which was sensitive to amikacin and resistant to macrolides. The treating clinical team was informed regarding the isolation of *Mycobacterium abscessus* and the drug resistance pattern, resistance to the commonly used disinfectants as well as chances of recurrence if left untreated.
Surgical debridement was done. The infected pacemaker and leads were removed and a temporary pacemaker was implanted. After two weeks of antibiotic treatment on a temporary pacemaker, a new pacemaker was implanted from the other side. Intraoperatively pus sample -from the pocket site was sent for culture and *Mycobacterium abscessus* was isolated from the second sample too. The patient was followed up after 4-5 months after the new implant and the wound was healthy.

Discussion

With the increase in the global burden of cardiovascular diseases, the demand for cardiovascular implantable devices is also on the rise (CIED). The incidence of pocket infections without bloodstream infections was noted to be 1.37 per 1000 devices and defibrillators were associated with an increased risk when compared to pacemakers. Risk factors associated with CIED infections can be either patient-related, procedure-related, or device-related. Patient-related risk factors include the presence of co-morbidities like obesity, diabetes mellitus, systemic hypertension, renal disease, or any other conditions that may impair wound healing. Procedure and device-related risk factors include the duration of the procedure, pre and post-antimicrobial prophylaxis and antisepsis during the procedure, intra-operative complications, duration of the stay in the hospital, and post-operative wound care.
Common organisms associated with these infections are mainly Coagulase-negative staphylococci and *Staphylococcus aureus* and rarely Gram-negative pathogens. Infections caused by NTM are on the rise mainly due to the ubiquitous nature of these pathogens.
Mycobacteria are categorized into two major groups for diagnosis and treatment: *Mycobacterium tuberculosis* complex, which includes *M. tuberculosis,* and nontuberculous mycobacteria (NTM), which comprise all of the other mycobacteria species that do not cause tuberculosis.
M.abscessus is one of the multi-drug resistant NTM species that are ubiquitously present in the soil and water. *M. abscessus* was first reported as a pathogen in 1953, when it was cultured from synovial fluid in a case of post-traumatic arthritis and gluteal abscesses in the same patient

(5). However, it was only in 1992, after its separation from the *M.chelone* group, it gained importance that it can cause a range of infections in humans, including skin and soft tissue infections, post-injection abscesses (6), along with *M.avium* complex involved in broncho-pulmonary infection in patients with cystic fibrosis or chronic pulmonary disease (7-10), central nervous system involvement in the form of meningitis and cerebral abscess especially in HIV negative individuals, patients who have undergone neurosurgical procedures, who had intracranial catheters (11), ocular infections in the form of keratitis, scleral buckle infections (12) and disseminated infections in immunocompromised individuals. Infections caused by this pathogen are often underreported mainly due to the lack of facilities required for the speciation of non-tuberculous mycobacteria in resource-poor settings.

Two major mechanisms for acquiring an *M. abscessus* complex–associated skin and soft tissue infections are either by direct contact with contaminated material or water through traumatic injury, surgical wound, or environmental exposure and secondary involvement of skin and soft tissue in case of disseminated disease. Though rarely implicated, *M.abscessus* is one of the common species isolated from device-related infections next to *M.fortuitum*. Nosocomial outbreaks due to *M. abscessus* in cardiac patients have been reported (13,14). The most common cause of infections is either contamination of the leads or the pulse generator during implantation or subsequent exposure of the wound to the environmental sources of these pathogens. In the community setting, water supply systems have been postulated as the source of these pathogens (15, 16). In the hospital setting, its usually contaminated disinfectants and solutions used during the surgery.

Mycobacterium abscessus has been classified into three subspecies based on the rpoB and other housekeeping gene sequences-*Mycobacterium abscessus* subsp. *abscessus, Mycobacterium abscessus* subsp. *bolletii,* and *Mycobacterium abscessus* subsp. *massiliense* (17). They constitute what is known as the *M. abscessus* group, or *M. abscessus sensu lato* (18). *Mycobacterium abscessus* subspecies *abscessus* is the major subspecies among the three and is usually refractory to standard antibiotic therapy. The 2 major subspecies, *M. abscessus* subsp. *abscessus* and *M. abscessus* subsp. *massiliense*, have different *erm* (41) gene patterns that confer resistance to macrolides through methylation of the 23S ribosomal RNA (19). This leads to the intrinsic resistance to macrolides.

The intrinsic and acquired resistance of *M. abscessus* complex limits the therapeutic options for the treatment of infections caused by this pathogen. In addition to this, there is a lack of consensus on the optimum antimicrobial agents used for therapy and the optimum duration of treatment. Natural resistance of *M. abscessus* and other mycobacterial species to drugs could be due to slow growth, the presence of a waxy impermeable cell wall, which acts as a physical and a hydrophobic barrier, drug export systems, and genetic polymorphism of targeted genes (20). The recommended drug regimen for the treatment of skin and soft tissue infections due to *M. abscessus* consists of macrolide in combination with amikacin plus cefoxitin/imipenem with a minimum of 2 weeks of intravenous agents plus surgical debridement for a minimum of 4 months (21).

Search Strategy and Selection Criteria

A review of the English literature search was conducted using Pubmed with the search terms “pacemaker infection and mycobacterium abscessus”. A total of 4 cases of device-related infections were found. Key points are summarised in Table 1.

Table 1. Summarises the key points

S.No	Age/Sex	Treatment	Complications	Outcome	Reference
1	63/M	Surgical debridement + Induction phase with amikacin, cefoxitin and clarithromycin and Maintenance therapy with clarithromycin and clofazimine	Cardiac arrhythmia, abscess formation and thoracic osteomyelitis with epidural abscess due to *M. abscessus* complex.	Survived	4
2	53/F	Removal of the pacemaker + 6 months course of Clarithromycin	N/A	Survived	22
3	68 /M	Surgical debridement with removal of the leads	N/A	Survived	23
4	72/F	Surgical debridement and removal of the leads	N/A	Survived	24

Conclusion

Prevention of pacemaker-related infections includes adherence to sterile techniques during implantation, careful wound care, and monitoring for signs of infection in individuals with implanted devices. Antibiotic treatment for NTM infections can be challenging, as these bacteria are often resistant to multiple antibiotics. Therefore, selecting an appropriate antibiotic regimen requires consideration of the specific NTM species involved and their susceptibility to various drugs.

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Conflicts of interest

None.

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None.

Ethic statement

Informed consent was taken from the patient. The patient and the patient party was explained that the names and initials would not be published and due efforts would be made to conceal the identity.

Author contribution

Maanasa Bhaskar M: Writing – Original draft, Ankita Mohanty: Data collection and analysis, Noyal Maria Joseph: Data collection and analysis, Methodology, Raja Jaisundar Selvaraj: Writing- Review and editing, Sujatha Sistla*: Writing- Review and editing
All authors have read and approved the final manuscript.

Data availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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