Case report

Native valve endocarditis and pacemaker infection with Mycobacterium fortuitum

Moamen Al Zoubi a,c,*, Joyce Cheng c, Venkate S. Dontaraju c, Colin E. Evans b, Addie B. Spier a,c

a Department of Infectious Disease, Mercyhealth, Rockford, IL, USA  
b Department of Pediatrics, Northwestern University Feinberg School of Medicine, Chicago, IL, USA  
c Department of Internal Medicine, Mercyhealth, Rockford, IL, USA

ARTICLE INFO

Article history:
Received 13 January 2021  
Received in revised form 14 June 2021  
Accepted 14 June 2021

Keywords:
Cardiac pacemaker  
Defibrillator  
Mycobacterium fortuitum  
Nontuberculous mycobacteria

ABSTRACT

Endocarditis and cardiac device infection due to Mycobacterium fortuitum is a rare entity in the hospital settings. We report a case of pacemaker infection and native valve endocarditis due to Mycobacterium fortuitum, which was associated with tricuspid valve vegetation, two days after admission with fever, chills, body aches and swelling around her pacemaker, the patient’s pacing system was surgically removed. The patient was then discharged at day 16 after surgery and treated with a multidrug regimen of azithromycin, levofloxacin, imipenem/cilastatin, and amikacin for six weeks followed by trimethoprim/sulfamethoxazole plus doxycycline for a further three months.

Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Mycobacterium fortuitum, a member of rapidly growing nontuberculous mycobacteria, is a well-known cause of skin and soft tissue infections and postsurgical wound infection. Here, we describe a case of native tricuspid valve endocarditis and pacemaker infection secondary to M. fortuitum. We also review the published literature of cardiac device–associated infections and native valve endocarditis caused by M. fortuitum.

Case report

A 26-year-old female presented to our hospital for evaluation of fever, chills, body aches and swelling around her pacemaker generator of 5 days duration. Four weeks prior, she had implantable cardioverter-defibrillator (ICD) placement for prevention of sudden cardiac death in the setting of ventricular arrhythmias. Vital signs revealed a temperature 38.9 F, pulse 90bpm, and blood pressure 117/76 mmHg. Her physical exam was unremarkable except for tenderness over the pacemaker site. No murmurs were appreciated. Laboratory evaluation showed the following values: white blood cells, 7800 /μL; hemoglobin, 13.4 g/dL; and platelets, 151 × 10⁹/L. Two sets of blood cultures revealed no growth at 5 days. Transthoracic echocardiography (TTE) showed 1.2 cm mobile mass attached to the ICD lead at the base of the posterior leaflet of the tricuspid valve suggestive of vegetation (Fig. 1A). At day 2 after admission, the patient was taken to the operating room where the entire pacing system was removed. The patient was found to have 25 mL of purulent fluid which was. The acid-fast stain was positive (Fig. 1B, left panel), while the gram stain from the intraoperative culture showed beaded gram-positive bacilli (Fig. 1B, right panel). TEE showed hypoechoic mobile vegetation on the tricuspid valve measuring 0.87 cm without evidence of tricuspid regurgitation (Fig. 1C).

At day 5 after admission, the patient was treated empirically with azithromycin (250 mg per mouth daily), imipenem/cilastatin (1 g intravenously every 8 h), amikacin (17 mg/kg intravenously three times per week) and tigecycline (250 g intravenously every 24 h). The surgical specimen was sent to Mayo Clinic (Rochester, Minnesota) for further testing and M. fortuitum was identified by DNA probe analysis. The patient developed significant nausea 5 days after tigecycline was started and this was switched to levofloxacin (750 mg per mouth daily). Drug resistance testing by broth microdilution of the M. fortuitum isolate indicated that this isolate was resistant to macrolides and tobramycin, intermediate to cefoxitin (MIC 32 μg/mL -1), and susceptible to amikacin (MIC <1 μg/mL -1), imipenem (MIC 4 μg/mL -1), tigecycline (MIC 0.12 μg/mL -1), ciprofloxacin (MIC <0.12 μg/mL -1), moxifloxacin (MIC <0.25 μg/mL -1), linezolid (MIC 4 μg/mL -1), doxycycline

* Corresponding author at: Mercyhealth Javon Bea Hospital, 8201 E Riverside Blvd, Rockford, IL, USA.  
E-mail address: Malzoubi@mhealth.org (M. Al Zoubi).
(MIC < 0.25 μg/mL⁻¹), and trimethoprim/sulfamethoxazole (MIC 2/38 μg/mL⁻¹). At days 16 after admission, the patient was discharged. The patient completed the multidrug treatment regimen of azithromycin, levofloxacin, imipenem/cilastatin, and amikacin for 6 weeks and was subsequently switched to oral trimethoprim/sulfamethoxazole (800–160 mg twice daily) plus doxycycline (100 mg twice daily) for a further 12 weeks. At weeks 18 after the start of therapy, the patient discovered she was pregnant, and her oral antibiotics were stopped. The patient completed 4.5 months of treatment in total. A follow up transesophageal echocardiography at 20 weeks after discharge showed no vegetation.

Discussion

Cardiovascular infection with M. fortuitum is rarely encountered in clinical practice. However, M. fortuitum infection of a pacemaker system with associated endocarditis has been described previously [1]. We searched the available literature using PubMed with no starting date restrictions through September 31, 2020 and identified only 12 previously reported cases of cardiovascular implantable electronic device (CIED) infections caused by M. fortuitum including our patient species (Table 1). We observed that 4 (33.3 %) of the 12 patients with M. fortuitum infection had associated mycobacteremia [3,9–11].

This finding indicates that the infection had spread beyond the device pocket to the intravascular component of the CIED system, suggesting endovascular infection. In the 4 patients for which positive blood culture results were reported, 3 (31 %) had lead vegetation seen on echocardiographic images [3,9,11]. None of these three patients had evidence of valvular vegetation. The fourth patient had negative echocardiographic images, but she fulfilled pathologic criteria for infective endocarditis based on the isolation of the organism in an operative culture [3,9,11]. This patient was the only one with valvular endocarditis among all the reports in our review. We did not find any cases that described valvular vegetations on transthoracic echocardiogram (TTE) or transesophageal echocardiogram (TEE). We believe that our case is the first case that described pacemaker and valvular and lead vegetations seen on echocardiogram images. The initial transthoracic echocardiogram (TTE) showed lead but no valvular vegetations. The transesophageal echocardiogram (TEE) confirmed a tricuspid valve vegetation. TTE has variable sensitivity for the detection of vegetations (<50 % to >90 % positive), indicating that a negative study does not exclude infective endocarditis (IE). TEE is also more sensitive than conventional TTE. In one report of 96 patients with IE [14], the sensitivity of TEE was 100 %, compared with 63 % for TTE, and the specificity values were identical (98 %).

The first documented case of pacemaker infection associated with M. fortuitum alone was reported in 2005, it was successfully treated with ciprofloxacin/clarithromycin for 6 months and removal of the entire pacing system [3]. This patient had associated mycobacteremia and evidence of lead but not valvular vegetation. All other reported cases were cured with a combination of antimicrobials, except for in the case reported by Giannella et al., in which the patient was treated with quinolone monotherapy because the bacteria was resistant to the remaining agents [4], and in a report by Hu et al., in which the patients course was complicated by a stroke, withdrawal of care, and subsequent death [5]. All reported cases involved the removal of the pacemaker system, except for the case by Pastor et al., in which the patient was treated with ciprofloxacin and clarithromycin for 6 weeks total [9]. Other cases of native valve endocarditis (in patients who did not have any cardiac devices) caused by M. fortuitum have also been reported (Table 2). The first reported case of native valve endocarditis due to M. fortuitum with visible vegetations on echocardiography was reported in 2000 [7]. Spell et al. described a 47-year-old male with newly diagnosed HIV whose blood cultures grew M. fortuitum. Initial transthoracic echocardiography showed no evidence of vegetations, but the repeated transthoracic echocardiography at 3 weeks later displayed peduncular vegetations on the left coronary, noncoronary, and right coronary cusps of the aortic valve. The patient was treated with amikacin, cefoxitin, and ciprofloxacin for a total of 6 weeks then switched to oral ciprofloxacin and trimethoprim-sulfamethoxazole. The patient died 12 weeks after his initial clinical presentation.

Owing to the rarity of non-tuberculous mycobacteria-related cardiac device-associated infective endocarditis, there are no clear management guidelines for the type and duration of therapy. Based on prior reports, a combination of two or three drugs for 6–12 months appears necessary. The choice of antibiotics depends on the results of susceptibility testing. M. fortuitum isolates are usually susceptible to multiple oral antimicrobial agents, including newer macrolides, quinolones, doxycycline, minocycline, and...
| Year (Ref) | Age/Sex | Time from implant | Presenting signs and symptoms | Bacteremia | Valve or lead vegetation | Time to diagnosis | Method of diagnosis | Pacemaker removal | Antibiotics treatment | Duration of treatment | Outcome |
|-----------|---------|------------------|-------------------------------|------------|--------------------------|------------------|---------------------|-------------------|---------------------|----------------------|---------|
| 1998 [2]  | 74/F    | 13 days          | Fever, pain and purulent discharge | No         | NR                       | 2 days           | Culture of pus      | Yes               | Ofloxacin + gentamycin | 1 month             | Cured   |
| 2005 [3]  | 62/F    | 6 months         | Fever, erythema                | Yes        | Yes (atrial lead)        | 1 month          | Culture of aspirate | Yes               | Ciprofl oxacin/clarithromycin | 6 months             | Cured   |
| 2005 [8]  | 72/F    | 2 weeks          | Subcutaneous nodules and chronic drainage | No         | No                      | 1 week           | Abscess culture     | Yes               | Amikacin/ciprofl oxacin | 6 months             | Cured   |
| 2006 [9]  | 80/M    | 18 days          | NR                             | Yes        | No                       | NR               | NR                  | No                | Ciprofl oxacin/clarithromycin | 6 weeks              | Cured   |
| 2006 [1]  | 78/F    | 6 months         | Swelling and discomfort over the pacemaker pocket, Fever, pain, and erythema | Yes        | Yes (right atrial lead) | 2 weeks          | 16S ribosomal RNA   | Yes               | Linezolid + levofloxacin + clarithromycin | 6 months             | Cured   |
| 2007 [4]  | 84/F    | 2 months         | Fever, pain, and erythema      | No         | No                       | 7 days           | 16S rRNA PCR and culture of aspirate | Yes               | Levofloxacin             | 3 months             | Cured   |
| 2009 [10] | 15/F    | 7 weeks          | Greenish discharge and fever   | Yes        | Yes (endocardial and epicardial leads) | 3 days           | Lead culture        | Yes               | Ciprofl oxacin/clarithromycin | 6 months             | Cured   |
| 2010 [12] | 78/M    | NR               | Not reported                   | NR         | NR                       | NR               | NR                  | NR                | Clarithromycin/Levofloxacin + amikacin | 26 weeks             | Cured   |
| 2011 [8]  | 61/M    | 17 months        | Cutaneous infection overlying the generator | No         | No                       | 1 year           | Lead culture        | Yes               | Clarithromycin/ ciprofl oxacin/amikacin | NR                  | Cured   |
| 2012 [11] | 43/M    | 4 years          | Fever, night sweats, and weight loss | Yes        | Yes (right ventricular lead) | 157 days         | Lead culture        | Yes               | Meropenem + linezolid + doxycycline | 22 weeks             | Died    |
| 2012 [5]  | 56/M    | 4 months         | Pain and swelling at the BiV ICD pocket site | No         | Yes (right atrial and ventricular leads) | 10 days          | OR culture          | Yes               | Azithromycin + Levofloxacin + imipenem then TMX/SMX + doxycycline | 4.5 months            | Cured   |
| 2020      | 27/F    | 1 month          | Fever, purulent discharge      | No         | Yes (tricuspid valve and ICD lead) | 1 month          | OR culture          | Yes               | Azithromycin + Levofloxacin + imipenem then TMX/SMX + doxycycline | 4.5 months            | Cured   |
| Year (Ref) | Age/sex | Presenting signs and symptoms | Bacteremia | Valve affected | Time to diagnosis | Method of diagnosis | Surgical therapy | Antibiotics therapy | Duration of treatment | Outcome |
|-----------|---------|--------------------------------|------------|----------------|-------------------|-------------------|-----------------|-------------------|---------------------|---------|
| 1992 [6]  | 54/F    | Fever, headache, productive cough, shortness of breath, fever | Yes        | Mitral + aortic | 2 weeks          | Blood cultures    | No              | Amoxycillin, TMP/SMX, ciprofloxacin, clofazimine, cefoxitin, amikacin | 6 weeks | Died               |
| 1999 [15] | 20/F    | NR                             | NR         | Mitral         | NR               | NR               | No              | Amikacin, azithromycin, rifampin | NR            | Died               |
| 2000 [7]  | 47/M    | Dysphagia, odynophagia, fever, and chills | Yes        | Aortic         | 8 days           | Blood cultures    | No, patient preferred medical management | Amikacin, cefoxitin, ciprofloxacin, | 6 weeks | Patient died 12 weeks after his initial clinical presentation |
| 2015 [17] | 64/F    | Pulmonary edema and multifocal pneumonia | Yes        | Pulmonic       | NR               | PCR of a tracheal aspirate | No              | Amikacin, imipenem, and clarithromycin | 16 days | Patient decided to stop antibiotic therapy and entered hospice Died |
| 2006 [16] | 50/M    | NR                             | NR         | Mitral + aortic | NR               | NR               | AVR + MVR        | Clarithromycin, imipenem, moxiﬂoxacin, amikacin | NR            | Died               |
| 2012 [18] | 49/F    | Fever, malaise nausea          | Yes        | Aortic + tricuspid | 15 days          | Blood cultures    | No              | Linezolid and ciprofloxacin, and oral TMP/SMX | 6–12 months | Not reported       |
| 2013 [19] | 12/F    | Fever, fatigue                | Yes        | Tricuspid      | NR               | GenoType Mycobacterium CM assay | No              | Amikacin, ciprofloxacin, and imipenem | 6 weeks | Alive at 12 months after diagnosis |
| 2/F       | Fever, fatigue                | Yes        | Tricuspid      | NR               | GenoType Mycobacterium CM assay | No              | Amikacin, ciprofloxacin, and imipenem | 6 weeks |                   |
| 0.5/F     | Fever, fatigue                | Yes        | Tricuspid      | NR               | GenoType Mycobacterium CM assay | VSD patch removal | Amikacin, ciprofloxacin, and imipenem | 6 weeks |                   |
| Current   | 27/F    | Fever                          | No         | Tricuspid      | 1 month          | OR culture, DNA Gene probe | No              | Azithromycin + Levofloxacin + imipenem then TMX/SMX + doxycycline | 4.5 months | Cured             |
sulfonamides. Removal of the infected pacemaker device is of paramount importance given the high relapse rate despite prolonged antimicrobial therapy. In summary, we describe a rare case of pacemaker infection and native valve endocarditis with M. fortuitum, which highlights this mycobacterium as an important possible cause of cardiovascular infections.

**Funding**

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

**Declaration of Competing Interest**

None.

**Acknowledgements**

None.

**References**

[1] Siu Cw, Cheng Lc, Woo Pc, Lau Cp, Tse Hf. A patient with relapsing pacemaker infection due to “Gram-positive bacilli”. Int J Cardiol 2007;114(2):E40–1. doi: http://dx.doi.org/10.1016/j.ijcard.2006.07.211.

[2] Verghese S, Mullaseri A, Padmaja P, Subhadra AC, Cherian KM. Pacemaker implant site infection caused by atypical mycobacteria. Indian Heart J 1998;50(2):201–2.

[3] Sharma S, Telyjeh IM, Espinosa RE, Costello BA, Baddour LM. Pacemaker infection due to Mycobacterium fortuitum. Scand J Infect Dis 2005;37(1):66–7.

[4] Giannella M, Valerio M, Franco JA, Marin M, Bouza E, Muñoz P. Pacemaker infection due to Mycobacterium fortuitum: the role of universal 16S rRNA gene PCR and sequencing. Diagn Microbiol Infect Dis 2007;57(3):337–9. doi: http://dx.doi.org/10.1016/j.diagmicrobio.2006.08.010.

[5] Hu VL, Bridge B, Wang J, Jovin IS. Mycobacterium fortuitum causing infection of a biventricular pacemaker/implantable cardioverter defibrillator. Int J Mycobacteriol 2012;1(4):221–3. doi: http://dx.doi.org/10.1016/j.ijmyco.2012.10.001.

[6] Singh M, Bofinger A, Cave G, Boyle P. Mycobacterium fortuitum endocarditis in a patient with chronic renal failure on hemodialysis. Pathology 1992;24(3):197–200. doi: http://dx.doi.org/10.1111/1440-1614.e01200.

[7] Spell DW, Szurgot JG, Greer RW, Brown 3rd JW. Native valve endocarditis due to Mycobacterium fortuitum: two case reports. J Clin Microbiol 2000;38(3):1022–3. doi: http://dx.doi.org/10.1128/JCM.38.3.1022-1023.2000.

[8] Hemmersbach-Miller M, Cardenes-Santana MA, Conde-Martel A, Balonas-Guerra JA, Campos-Herrero MI. Cardiac device infections due to Mycobacterium fortuitum. Can J Infect Dis Med Microbiol 2005;16(3):183–5. doi: http://dx.doi.org/10.1016/j.2005.07.205.

[9] Pastor E, Luz Andreu A, Llosar M, Chiner E. Mycobacterium fortuitum: a rare cause of pacemaker infection [in Spanish]. Enferm Infecct Microbiol Clin 2006;24(2):136–7. doi: http://dx.doi.org/10.1016/j.2006.07.205.

[10] Al Soub H, Al Maslamani M, Al Khawaiter J, El Deeb Y, Abu Khattab M. Myocardial abscess and bactereemia complicating Mycobacterium fortuitum pacemaker infection: case report and review of the literature. Pediatr Infect Dis J 2009;28(11):1032–4. doi: http://dx.doi.org/10.1097/INF.0b013e3181aa6592.

[11] Sharma H, Keshavan A, Little MA, Cross J, Lipman MC, Talukdar S, et al. Fortuitous vasculitis. Ren Fail 2012;34(3):378–82. doi: http://dx.doi.org/10.3109/0886022X.2011.647337.

[12] van Duin D, Goldfarb J, Schmitt SK, Tomford JW, Tuohy MJ, Hall GS. Nontuberculous mycobacterial blood stream and cardiac infections in patients without HIV infection. Diagn Microbiol Infect Dis 2010;67(3):286–90. doi: http://dx.doi.org/10.1016/j.diagmicrobio.2010.02.006.

[13] Li JS, Sexton DJ, Mick N, Nettles R, Fowler VG, Ryan T, et al. Proposed modifications to the Duke criteria for the diagnosis of infective endocarditis. Clin Infect Dis 2000;30(4):633–8. doi: http://dx.doi.org/10.1086/313753.

[14] Erbel R, Rohmann S, Dreixel M, Mohr-Kahaly S, Gerharz CD, Iversen S, et al. Improved diagnostic value of echocardiography in patients with infective endocarditis by transesophageal approach: a prospective study. Eur Heart J 1999;20(9):1–13.

[15] Kuruvila MT, Mathews P, Jesudason M, Ganesh A. Mycobacterium fortuitum endocarditis and meningitis after balloon mitral valvotomy. J Assoc Physicians India 1999;47(10):1022–3.

[16] Collisson SP, Trehan N. Native double-valve endocarditis by Mycobacterium fortuitum following percutaneous coronary intervention. J Heart Valve Dis 2006;15(4):836–8.

[17] Mulhall AM, Hebbeler-Clark RS. Native pulmonic valve endocarditis due to Mycobacterium fortuitum: a case report and literature review. Case Rep Infect Dis 2015;274819. doi: http://dx.doi.org/10.1155/2015/274819.

[18] Natsag J, Min Z, Hamad Y, Alkhalil B, Rahman A, Williams R. A mysterious gram-positive rods. Case Rep Infect Dis 2012;841834. doi: http://dx.doi.org/10.1155/2012/841834.

[19] Vuković D, Pareznavović V, Savić B, Đakić I, Laham-Nestorović Š, Ilić S, et al. Mycobacterium fortuitum endocarditis associated with cardiac surgery. Serbia. Emerg Infect Dis 2013;19(3):517–9. doi: http://dx.doi.org/10.3201/ eid1903.120763.