IDCases 25 (2021) e01200

Contents lists available at ScienceDirect

IDCases

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Case report

Native valve endocarditis and pacemaker infection with Mycobacterium fortuitum

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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.

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 × 10^9/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 25mLof 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

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http://dx.doi.org/10.1016/j.idcr.2021.e01200

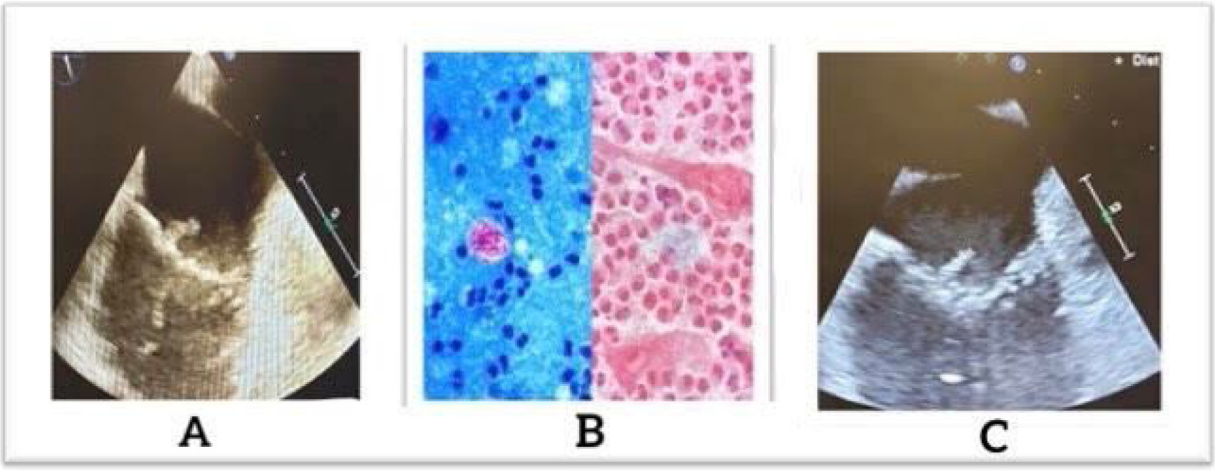

Fig. 1. A case of native valve endocarditis and pacemaker infection with *Mycobacterium fortuitum*.
(A) Two-dimensional transthoracic echocardiography showing 1.2 cm mobile mass attached to the pacemaker lead at the base of the posterior leaflet of the tricuspid valve. (B) Gram stain from OR cultures showing beady gram-positive bacilli (right panel); acid-fast stain showing positive *Mycobacterium* (bright pink, left panel). (C) Two-dimensional transesophageal echocardiography showing 0.872 mm vegetation on the tricuspid valve.

(MIC < 0.25 μg/mL^{-1}), and trimethoprim/sulfamethoxazole (MIC 2/38 μg/mL^{-1}). At days16 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 4.5months of treatment in total. A follow up transeophageal 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 [10,13]. 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) nor 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

Table 1
Pacemaker infections due to *M. fortuitum*.

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	Ciprofloxacin/ clarithromycin	6 months	Cured
2005 [8]	72/F	2 weeks	Subcutaneous nodules and chronic drainage	No	No	1 week	Abscess culture	Yes	Amikacin/ ciprofloxacin	6 months	Cured
2006 [9]	80/ M	18 days	NR	Yes	No	NR	NR	No	Ciprofloxacin/ clarithromycin	6 weeks	Cured
2006 [1]	78/F	6 months	Swelling and discomfort over the pacemaker pocket.	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	Ciprofloxacin/ clarithromycin	6 months	Cured
2010 [12]	78/ M	NR	Not reported	NR	Yes (non-specific pacemaker infection)	NR	NR	NR	Ciprofloxacin/ Clarithromycin	26 weeks	Cured
2011 [8]	61/ M	17 months	Cutaneous infection overlying the generator	No	No	1 year	Lead culture	Yes	Levofloxacin + 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	Clarithromycin/ ciprofloxacin/ amikacin	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	Meropenem + linezolid + doxycycline		Course complicated by right middle cerebral artery (MCA) infarct and withdrawal of care with subsequent death
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

Table 2
Native valve endocarditis due to *M. fortuitum*.

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
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 12months 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 replapse 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.

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