Case report

Rare case of pacemaker infection with *Mycobacterium abscessus*

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SUMMARY

Though prevalent in the environment, nontuberculous mycobacteria (NTM) have been increasingly identified as pathogenic. Sporadic reports of NTM infection of cardiac implantable electronic devices (CIEDs) have appeared but remain rare. This case describes a CIED infection with *Mycobacterium abscessus*, the third reported case in the literature. A 63-year-old male presented with a 3-day history of drainage from his pacemaker extraction site. An aspirate grew *Mycobacterium abscessus*. Together with National Jewish Health, a treatment plan was developed, consisting of an induction phase with amikacin, cefoxitin and clarithromycin followed by a maintenance phase with clarithromycin and clofazimine. The clinical course was complicated by cardiac arrhythmia, abscess formation and thoracic osteomyelitis with epidural abscess. This case highlights a rare manifestation of *Mycobacterium abscessus* disease and suggests the need for further study. Treatment is complicated by unpredictable resistance patterns, complex antimicrobial regimens and the use of arrhythmogenic medications in patients with removed CIEDs.

BACKGROUND

Nontuberculous mycobacteria (NTM) first gained widespread attention as a cause of opportunistic infection in patients with immune compromise or chronic lung disease, namely by *Mycobacterium avium* complex. For the last several decades, however, other NTM species have been increasingly identified as important pathogens behind both nosocomial and community-acquired disease.¹

Rapidly growing mycobacteria is a subset of NTM consisting of three predominantly clinical species: *Mycobacterium fortuitum*, *Mycobacterium chelonae* and *Mycobacterium abscessus*. In comparison to other mycobacteria, these species will usually grow in a subculture within 1 week and can be misidentified as corynebacteria on gram stain if acid-fast staining is not performed.² Clinical manifestations of these rapidly growing NTM primarily include pulmonary, skin and soft tissue, and lymph node infections.^{1,3}

Since the 1990s, sporadic case reports of mycobacterial infections of cardiac implantable electronic devices (CIEDs) have also appeared.^{4–6} Despite the low prevalence of these mycobacterial infections, representing only 0.2% of CIED infections within the Cleveland Clinic, they have important clinical consequences.⁷ NTM infections require a high index of suspicion for diagnosis and

complex, arrhythmogenic treatment regimens due to antibiotic resistance. We present a case of CIED infection with *Mycobacterium abscessus*, which, to our knowledge, is only the third reported case in the literature.^{8,9} This case is one of many increasing reports of NTM pathogenicity that suggest a need for further study to improve prevention and detection as well as provide safe and effective treatments.

CASE PRESENTATION

A 63-year-old male presented to the emergency department with a 3-day history of increased drainage at the site of his pacemaker extraction, which was performed secondary to infection at another institution 9 days earlier. Prior to the extraction, he had complained of 5 months of serosanguinous drainage from the pacemaker site. Wound cultures at that institution were positive for *Mycobacterium abscessus* and *Staphylococcus epidermidis*, and a peripherally inserted central catheter (PICC) line culture was positive for *Mycobacterium abscessus*. The PICC was removed, and he was discharged on linezolid and sulfamethoxazole-trimethoprim, with which he reported compliance. His past medical history included sick sinus syndrome for which the pacemaker was placed at a separate institution 2 years earlier, chronic obstructive pulmonary disease, hypertension, chronic hepatitis C, tobacco use and daily intravenous heroin use.

INVESTIGATIONS

On presentation, the patient was afebrile with normal vital signs. Physical exam revealed an incision in the left upper chest closed with interrupted sutures, surrounding induration, and mild erythema (figure 1). Initial labs were significant for pancytopenia attributed to his hepatitis C, acute kidney injury and negative blood cultures. Ultrasound imaging showed a large, multiseptated fluid collection in the location of the extracted pacemaker, and CT confirmed a soft tissue, mass-like structure residing superficial to the left pectoralis major muscle (figure 2). Aspiration of the site revealed 180 mL of thin, serosanguinous fluid that grew *Mycobacterium abscessus*.

A transesophageal echocardiogram (TEE) showed a thin, serpentine echo density at the base of the pulmonic valve as well as a mobile echo density at the origin of the inferior vena cava (IVC) that extended into the right atrium. Cardiac MRI performed 2 days later showed no vegetation

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Figure 1 Examination of the patient's left chest wall on presentation showing his previous surgical incision closed with interrupted sutures, surrounding induration, and mild erythema.

or thrombus at the IVC or pulmonic valve, and a second TEE performed 12 days later showed a residual thrombus cast in the superior vena cava but no valvular abnormalities. The original findings were most likely thrombi or residual fibrous structures related to pacemaker removal and less likely vegetations secondary to endocarditis.

TREATMENT

Antibiotic resistance testing for the *Mycobacterium abscessus* cultures showed sensitivity to tigecycline, clarithromycin, azithromycin and clofazimine. In conjunction with National Jewish Health Division of Mycobacterial and Respiratory Infections, a treatment plan was developed: a 2-month induction phase with amikacin, cefoxitin and clarithromycin followed by a 12-month maintenance phase with clarithromycin and clofazimine. Debridement of the pacemaker pocket was determined

unnecessary due to the unremarkable course of healing without further purulent drainage, abscess or erythema. The patient's hospital stay was complicated by a patient-administered heroin overdose requiring naloxone as well as a brief interruption of care when he left against medical advice for several hours. He was offered cardiac ablation or replacement of the pacemaker, but he declined. The patient was discharged to a long-term care facility with a PICC in place to complete the induction phase and then discharged on oral clofazimine and clarithromycin with a plan to total 1 year of therapy.

OUTCOME AND FOLLOW-UP

The patient's outpatient course was complicated by progressive corrected QT interval prolongation on EKG necessitating a change from clofazimine to minocycline as well as nonadherence with medication. The pacemaker pocket was surgically debrided twice in the outpatient setting due to persistent wound drainage and erythema with the formation of an abscess 2 months after discharge. Unfortunately, the patient was readmitted 6 months later with a positive acid-fast bacilli vertebral osteomyelitis with thoracic epidural abscess. A T4-T5 vertebral laminectomy as well as further debridement and split-thickness skin graft was performed with subsequent T2-T8 laminectomy and T2-T7 fusion performed 2 months later. He remains homeless but reports early remission from heroin use. The clinical course remains uncertain, although he will likely require lifetime antibiotics due to the implanted hardware.

DISCUSSION

NTM are prevalent in the soil and water worldwide. Exposure is common, but disease is rare, especially in immunocompetent persons. Of all clinically significant NTM species within the United States, *Mycobacterium avium* complex and *Mycobacterium kansasii* are the most frequently detected; within the rapidly growing subset, *Mycobacterium fortuitum* predominates non-pulmonary disease, while *Mycobacterium abscessus* is the most common pulmonary pathogen.¹ While *Mycobacterium abscessus* is best known for its role in pulmonary infections, particularly in patients with underlying pulmonary disease, there are increasing reports of skin and soft tissue infections, central nervous system infections, lymphadenitis and disseminated disease.^{1,3,10} Extrapulmonary disease is commonly due to direct inoculation through trauma, injection or surgery.³

The source of exposure is likely linked to NTM's natural presence in the environment. Multiple studies have shown the prevalence of NTM species in water supplies.¹¹⁻¹⁴ In a 1999 study of water samples from 21 states, the greatest percentage of NTM-positive samples (61%) were from hospitals, followed by public buildings including hotels, office buildings and state laboratories (43%).¹¹ Another study of municipal water supplies or treated water supplies used in dialysis centres in the United States showed 95 of 115 (83%) were contaminated.¹² Attempts to eliminate mycobacteria from water supplies are fraught with challenges. Large plumbing systems with dead ends contain biofilms that can harbour these organisms, and zinc present in galvanised pipes is thought to facilitate growth. Mycobacteria are highly adaptable and can even survive in chlorine and other industrial solvents.^{1,13-15}

Despite this high prevalence, NTM infections remain uncommon. In the case of our patient, who was homeless and injecting drugs intravenously daily, infection could have occurred through a number of mechanisms, including environmental exposure, injection, or surgery. He also had multiple

Figure 2 CT of the chest obtained on presentation demonstrating a soft tissue, mass-like structure residing superficial to the left pectoralis major muscle measuring 2.6x8.2 cm.

comorbidities that put him at risk for diminished immune function, further increasing his chance of developing disease.

CIED infections are an unfortunate but not unexpected risk, estimated to be approximately 0.5% to 1% for first-time implantation and 1%–5% for replacement or upgrade.⁷ The most common causative organisms of CIED infection are consistently identified as *Staphylococcus aureus* and coagulase-negative staphylococci.^{7–16} A 2017 Cleveland Clinic Journal of Medicine report indicated that mycobacterial infections represented just 0.2% of their pacemaker infections in contrast to 68.4% caused by *Staphylococcus* and 8.9% caused by gram-negative organisms.⁷ Multiple reviews published in 2016 documenting NTM CIED infections discussed 14–23 cases, two of which were caused by *Mycobacterium abscessus*, and over half of which were secondary to *Mycobacterium fortuitum*.^{4–6} The majority of the reports occurred within the last 15 years; whether this is secondary to increasing detection or truly increasing infection rates is unclear.

As noted above, only two reports exist in the literature that document CIED infection with *Mycobacterium abscessus*. The first reported case occurred in 1998 in a 68-year-old male who presented with 4 months of serosanguinous drainage from the site of his epicardial pacing leads placed 20 years earlier during coronary artery bypass grafting. He was treated with cefoxitin, amikacin and clarithromycin but died secondary to renal failure 1 month later.⁸ A second case was reported in 2004 in a 53-year-old female who developed infection of an ICD placed 2 weeks earlier during coronary artery bypass grafting. She was treated with a 6-month course of clarithromycin and removal of the pacemaker wire and remained well several months after completion of treatment.⁹

Treatment for mycobacterial infections is extremely challenging due to the length of treatment required and the frequent resistance of mycobacteria to antibiotics. In contrast to *Mycobacterium tuberculosis*, NTM infections are not effectively treated by agents such as isoniazide, rifampin and pyrazinamide. Resistance patterns are unpredictable, making culture susceptibilities crucial for proper treatment.^{1–10} Some *Mycobacterium abscessus* species have acquired resistance to clarithromycin and amikacin, two mainstays of treatment. Currently, most treatment regimens involve both an induction phase as well as a prolonged maintenance phase, often lasting 6–12 months.^{1,3} This presents multiple challenges, including compliance and access due to cost or availability.

These challenges are highlighted in our patient's case, in which clofazimine was chosen as a long-term maintenance therapy. Clofazimine is considered by the WHO to be an 'essential medicine' and is available in many parts of the world for the treatment of leprosy and multidrug-resistant tuberculosis.¹⁷ In the United States, this medication is not available commercially but can be obtained through a joint programme between its manufacturer and the Food and Drug Administration (FDA). After institutional review board approval at our institution, the FDA approved a 12-month supply of clofazimine that was distributed to the patient by our infectious disease clinic.

Lastly, treatment of NTM infection of CIEDs poses a problematic clinical dilemma. Current regimens utilise multiple arrhythmogenic medications, and, as in the case of our patient, most patients who required a CIED have long-term cardiac conduction defects. Close examination and discussion of risks and benefits are needed to determine the safest and most effective therapy.

In summary, we present the third reported case of CIED infection with *Mycobacterium abscessus*. NTM infection is

uncommon, and NTM CIED infection is rarer yet, but increasing reports suggest both may be more common than previously believed. This case illustrates the value of clinical suspicion when dealing with an indolent infection in an immunocompromised patient with multiple environmental exposures, the need for easily obtainable and safe medications, and the importance of further study to improve prevention and treatment.

Learning points

- ▶ While rare, nontuberculous mycobacteria (NTM) infections are increasing in prevalence, and clinicians should retain a high index of suspicion for NTM infections in order to arrive at the correct diagnosis.
- ▶ Antibiotic sensitivity testing is imperative as NTM infections have a high rate of antimicrobial resistance.
- ▶ Direct observational therapy can be considered in patients who struggle with compliance and barriers to successful treatment.
- ▶ Careful consideration must be given to administering potentially arrhythmogenic antimicrobial regimens to patients with a history of removed cardiac implantable electronic devices.
- ▶ Effective multidisciplinary teamwork is crucial for treating such rare and complicated infections.

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