Mycobacterium chimaera Infection After Aortic Valve Replacement Presenting With Aortic Dissection and Pseudoaneurysm

C. R. O’Neil,1 G. Taylor,1,2 S. Smith,1,2 A. M. Joffe,1 K. Antonation,3 S. Shafran,1 and D. Kunimoto1

1Division of Infectious Diseases, Department of Medicine, Faculty of Medicine & Dentistry, University of Alberta, Edmonton, Alberta, Canada; 2Infection Prevention and Control, Alberta Health Services, Edmonton, Alberta, Canada; 3National Microbiology Laboratory, Winnipeg, Manitoba, Canada

We present a case of Mycobacterium chimaera infection presenting with aortic dissection and pseudoaneurysm in a 22-year-old man with a past history of aortic valve replacement. Clinicians should consider M. chimaera infection in those presenting with aortic dissection as a late complication of cardiovascular surgery.

Keywords. aortic dissection; Canada; heater cooler units; Mycobacterium chimaera.

CASE

A 22-year-old man was referred for infectious diseases consultation in January 2017. He had a past medical history of a bicuspid aortic valve with mechanical aortic valve replacement at our hospital in June 2015. He reported a 1-year history of intermittent drenching night sweats, occurring 1–2 days per week. He denied other constitutional symptoms, fever, weight loss, chest pain, or dyspnea. He reported a small pustule on the superior aspect of his sternotomy incision that had resolved with a seven-day course of cephalexin 2 months prior to presentation. He was taking warfarin and aspirin. On examination, he looked well with normal vital signs. Cardiorespiratory examination was unremarkable. There was no evidence of lymphadenopathy or organomegaly. His sternotomy incision was well healed with no step deformity or instability. Preliminary investigations showed normal complete blood count parameters, electrolytes, creatinine, liver enzymes, and C-reactive protein. Chest x-ray was normal. Transthoracic echocardiogram performed in January 2017 at another center was reported as normal. Investigation for infectious causes including blood cultures, HIV serology, viral hepatitis serology, and syphilis serology were negative. A single mycobacterial blood culture was collected and ultimately reported negative after 7 weeks of incubation.

In March 2017, the patient presented to the hospital with a 1-week history of chest pain. He was hemodynamically stable on presentation. Laboratory investigations showed normal complete blood count parameters and a slightly elevated troponin I of 0.07 ug/L (normal being ≤0.02 ug/L). Electrocardiogram showed normal sinus rhythm. Computed tomography of his chest revealed a dissection of his ascending aorta with a large aortic pseudoaneurysm (Figure 1). He underwent urgent repair of his aortic dissection with placement of a prosthetic graft. His existing mechanical aortic valve was not replaced as transthoracic and transesophageal echocardiograms showed no evidence of endocarditis or paravalvular abscess. Intraoperative specimens were sent for bacterial and mycobacterial culture. An intraoperative specimen was also submitted for pathologic examination; however, only thrombus was identified. He was discharged with infectious diseases follow-up pending intraoperative tissue culture results.

After 21 days of incubation, intraoperative tissue cultures identified a Mycobacterium species ultimately identified as Mycobacterium chimaera. The isolate was sent to the National Microbiology Laboratory (NML; Winnipeg, MB, Canada) for confirmation of identification and whole-genome sequencing. Whole-genome sequencing showed a high degree of relatedness to M. chimaera isolates from LivaNova 3T Heater Cooler Units (HCU) used at the University of Alberta Hospital in Edmonton and to publicly available genomes of isolates associated with the HCU outbreak from the United States and Europe (Supplementary Figure 1). The draft sequence covered >99% of the genome with a depth of coverage ~50× as compared with the reference sequence ZUERICH-1 (Accession No. CP015267). The HCU used at the time of his original aortic valve replacement in 2015 could not be confirmed. The total time from cardiovascular surgery to initial clinical presentation was 18.8 months, and the time from clinical presentation to microbial diagnosis was 82 days. Susceptibility results performed by microbroth dilution are summarized in Supplementary Table 1.

The patient was treated with a combination of azithromycin, rifabutin, ethambutol, and amikacin. When susceptibility results were reported, ethambutol was changed to moxifloxacin. The patient was referred for ophthalmologic assessment and was found to have no ocular abnormalities. Therapeutic drug monitoring performed at the Infectious Disease Pharmacokinetics Laboratory...
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In November 2016, the infection control department conducted a retrospective review of all nontuberculous mycobacteria isolated from patients who underwent open chest cardiovascular surgery in Alberta after January 1, 2011. Of 11500 patients potentially exposed, we identified no other cases of *M. chimaera* infection. As of the date of manuscript acceptance (January 2018), two additional cases of *M. chimaera* infection have been identified in patients who have undergone cardiovascular surgery at our institution.

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**DISCUSSION**
Optimal treatment of *M. chimaera* infections has not been established. *Mycobacterium chimaera* is genetically related to *Mycobacterium avium* complex [11], and therefore, treatment of *M. chimaera* infection might be expected to be similar to treatment of *M. avium* complex infection. The American Thoracic Society/Infectious Diseases Society of America guidelines for disseminated *M. avium* complex infection recommend a macrolide (clarithromycin or azithromycin) and ethambutol with or without rifabutin [12]. Susceptibility testing, other than for clarithromycin, is not recommended for treatment-naive patients as there is a lack of correlation between in vitro susceptibility and clinical outcomes. However, it is unknown whether this is true for *M. chimaera*. Susceptibility results are presented here as it is expected that results will be similar for all strains in this clonal outbreak, barring antibiotic exposure and subsequent development of resistance. For *M. chimaera* infections, the combination of a rifamycin (rifabutin or rifampin), ethambutol, and a macrolide is the most commonly described regimen in the literature [5, 9]. However, it should be noted that the combination of clarithromycin and rifampin may result in subtherapeutic levels of clarithromycin [12]. A combination of antimicrobial therapy and removal of prosthetic material should be considered when feasible. There are no data on reinfection rates for newly placed prosthetic devices. Patients failing initial therapy or those patients in whom surgical source control cannot be achieved may benefit from the addition of moxifloxacin and/or intravenous amikacin [9]. Optimal treatment duration in patients with disseminated disease or those with retained prosthetic devices has not been established. The crude mortality rate of reported cases is approximately 50% [7]. Cure has been achieved for patients with limited disease (e.g., sternal osteomyelitis) treated with surgical debridement and prolonged antimicrobials [5].

**CONCLUSIONS**

We report the first case of *M. chimaera* infection associated with the global HCU outbreak in Western Canada. To our knowledge, this is also the first description of *M. chimaera* infection presenting with aortic dissection. Our case also highlights the challenge in making the diagnosis, especially when patients do not have disseminated disease or clinically apparent localized infection such as sternal osteomyelitis. *M. chimaera* infections will remain difficult to diagnose given the long incubation period and typically nonspecific presentation. Vigilance is necessary to identify patients potentially at risk, and we would advise clinicians to consider *M. chimaera* infection in those patients with previous aortic surgery presenting with aortic dissection or pseudoaneurysm.

**Supplementary Data**

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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**References**