<i>Mycobacterium abscessus</i>: A Rare Cause of Periprosthetic Knee Joint Infection

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Authors:
Jonathon M. Spanyer, MD Scott Foster, MD Jasmine A. Thum-DiCesare, MD Young-Min M. Kwon, MD, PhD Dennis W. Burke, MD Sandra B. Nelson, MD

Author Affiliation | Disclosures

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Dr. Spanyer is an Orthopaedic Surgeon, OrthoCincy Orthopaedics and Sports Medicine, Cincinnati, Ohio. Dr. Kwon is an Orthopaedic Surgeon, Department of Orthopaedic Surgery; and Dr. Nelson is an Infectious Disease Specialist, Division of Infectious Diseases, Department of Medicine, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts. Dr. Foster is an Orthopaedic Surgeon, Avita Orthopaedics, Ontario, Ohio. Dr. Thum-DiCesare is a Neurosurgery Resident, Department of Neurosurgery, University of California Los Angeles (UCLA), Los Angeles, California. Dr. Burke is an Orthopaedic Surgeon, Department of Orthopaedics, Beth Israel Deaconess Hospital, Milton, Massachusetts.

Address correspondence to: Jonathon Spanyer, MD, OrthoCincy Orthopaedics and Sports Medicine, 560 South Loop Road, Edgewood, KY 45017 (tel, 859-301-2663; email,jspanyer@orthocincy.com).

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Take-Home Points:

- Periprosthetic joint infections due to <i>Mycobacterium abscess</i> have been rarely reported, and no specific guidelines exist to inform treatment.
- Medical management alone was not successful in our clinical case and cannot be recommended.
- Combination medical and surgical management may provide the best opportunity for clinical cure of periprosthetic infections.
- In complicated periprosthetic joint infections involving rare and intrinsically resistant organisms, a collaborative multidisciplinary approach likely represents the preferred path to clinical cure.
- Successful eradication of periprosthetic infection with <i>M. abscessus</i> may not preclude acceptable outcomes after revision TKA.

Total knee arthroplasty (TKA) procedures are projected to increase by more than 6-fold by 2030, with concurrent increases in revision TKA for infection projected. Infection after TKA remains one of the most serious complications of the procedure, occurring in <2% of primary TKAs. The majority of prosthetic joint infections (PJIs) are caused by staphylococci and streptococci. Although infection and treatment of PJIs by mycobacterial species have been described, there are presently no established treatment guidelines for mycobacterial PJIs.
Given the scarcity of clinical experience in dealing with these organisms, and the predicted increasing incidence of revision knee arthroplasty due to infection, we describe an unusual case of a PJI caused by *Mycobacterium abscessus* (*M. abscessus*), which was successfully treated using a combination of antimicrobial therapy and staged reconstruction. The patient provided written informed consent for print and electronic publication of this case report.

**Background**

Mycobacteria are common environmental organisms that can survive harsh conditions, including low pH and extreme temperatures. They form biofilms and may be difficult to eradicate in cases of infection. *M. abscessus* has proven to be difficult to eradicate due to limited antimicrobial susceptibility, lack of bactericidal options, and the variable presence of the *erm* gene, which yields inducible resistance to macrolides. Post-procedural outbreaks due to mycobacteria have been reported, often attributed to contaminated multiuse instruments, inadequate sterilization of tap water, multiuse vials, or improper skin preparation.

**Case Report**

A 61-year-old woman was referred with a 3-year history of progressive left knee pain and swelling. Before 8 months, she had undergone knee arthroscopy and had been treated with multiple steroid and hyaluronic acid injections, as well as ultrasound-guided aspiration of a Baker’s cyst (Figures 1A, 1B). She elected to proceed with TKA 1 month after her last steroid injection. There was no preoperative concern for native joint infection. At the time of arthroplasty, clear joint fluid was encountered, and a deep tissue culture was taken (Figures 2A-2C). Routine screening cultures for acid-fast bacilli (AFB) returned positive 9 days after the index arthroplasty, with subsequent identification of a nontuberculous mycobacterium (NTM), *M. abscessus*, subspecies *massiliense*. Sensitivity tests revealed susceptibility to amikacin, cefoxitin, and tigecycline (Table 1). The isolate was found to have inducible macrolide resistance by *erm* gene testing.

Given no prior surgical suspicion for infection and the uncertain significance of the culture result, treatment options were debated. Medical management was selected based on the presumption that if infection was present, it was a native joint infection in which surgical débridement had already been undertaken at the time of primary arthroplasty. Similar reports for the treatment of *M. tuberculosis* infection in the knee have been reported with some success. Short-interval reassessment was planned. Antimicrobial therapy was selected based on susceptibility data and clinical experience and consisted of intravenous (IV) cefoxitin, oral clarithromycin, and thrice-weekly intravenous amikacin. Over the ensuing weeks, she developed fevers, knee swelling, and persistent elevation of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). With known potential of this organism for biofilm formation in other areas of the body and positive repeat cultures of the knee joint fluid, confirming the offending organism, a deep and resistant infection of the implant could not be excluded. Therefore, in an attempt to give the patient the best opportunity for clinical cure, the patient subsequently underwent a 2-stage antibiotic spacer explantation and exchange (Figures 3A, 3B). Moderate caseous material was present throughout the knee joint and the subcutaneous tissues. All bone was débrided, and complete synovectomy was undertaken, along with the removal of all implants. The antibiotic concentrations within the spacer were selected by guidance from the Infectious Disease and Pharmacy based on minimal inhibitory concentrations, with 3 packages of cement (40 g each) utilized and a total of 10 g of amikacin and 24 g of cefoxitin contained within the spacer. The patient continued systemic administration of amikacin, cefoxitin, and clarithromycin.

One month postoperatively, her constitutional symptoms, including fevers and night sweats, abated and
inflammatory markers (ESR and CRP) had normalized. There were no clinical signs of infection. Amikacin was discontinued due to a 10-dB change on audiologic screening (4-6 kHz range), and tigecycline was substituted. Ultimately, she underwent 15 weeks of antimycobacterial therapy, 10 of which were after the explantation.

Eight weeks after cessation of her antibiotics, she underwent open biopsy. Multiple operative tissue samples showed negative results in pathology and culture tests.

Replantation was performed 14 weeks after stopping antimicrobials and 24 weeks after her explantation. The bone appeared healthy without evidence of osteomyelitis. A constrained reconstruction was secured with tobramycin-impregnated cement. One small island of necrotizing granuloma was observed within the bony cortex on histologic review; the granulomata appeared active with scattered neutrophils along with histiocytes and lymphocytes. AFB stains were negative. Intraoperative cultures, including mycobacterial cultures, were negative.

Based on the histologic evidence that infection may have persisted, and given the high stakes, antimicrobial treatment was reinitiated. Amikacin was again stopped after 3 weeks due to the development of tinnitus; tigecycline was substituted to complete the fourth and final week, at which point all antibiotics were discontinued. The patient was followed up uneventfully for 4 years (Figures 4A-4D and 5A-5C) with normal ESR and CRP. She continues to be ambulatory without assistive devices and walks an average of 30 miles per week without pain or constitutional symptoms.

**Discussion**

Diagnosis of acute infection after TKA remains challenging, as some degree of pain, swelling, and even postoperative fevers may be common in noninfected TKA patients. Synovial white blood cell count and differential as well as alpha-defensin levels have been cited as predictive factors of infection.\(^{16,17}\) Deep tissue and synovial fluid cultures offer the advantage of both identification and antimicrobial sensitivity testing of the offending organism. In this case, culture of the knee joint fluid at the time of TKA led to the unexpected finding of *M. abscessus* infection.

Preventable outbreaks due to *M. abscessus* have been reported and attributed to contaminated multiuse instruments, inadequate sterilization of tap water, multiuse vials, and improper skin preparation.\(^{11-13}\) Rarely, *M. abscessus* has been reported as the cause of PJI. When an unusual organism is encountered after native joint instrumentation, an investigation should be undertaken to identify the source of contamination, with the assistance of infection control practitioners and/or the US Food and Drug Administration reporting. Reporting and investigation was undertaken in this case, though no suspect source could be identified.

Although there were no signs of infection prior to the TKA, there is an ongoing debate as to whether intra-articular corticosteroid injections increase the risk of PJI, and if so, what the optimal amount of time to wait between procedures is. Although several earlier studies have been underpowered to answer these questions,\(^{18}\) this patient underwent TKA 1 month following the corticosteroid injection. Recent meta-analyses have shown no definitive evidence to indicate that this increased her risk of PJI.\(^{19,20}\)

Treatments for mycobacterial infections have been described with variable efficacy,\(^{21,22}\) and only 2 cases of successfully treated PJs have been reported after infection with *M. abscessus*. Both these cases were described in total hip arthroplasties,\(^{23,24}\) and to the authors’ knowledge, this report represents the first described successfully treated case after TKA. Staged reconstruction remains a standard treatment for invasive organisms chronically infecting prosthetic joint implants, with reimplantation pending joint sterility and improvement in inflammatory
markers.\textsuperscript{3} Previous successful reports of treating \textit{M. abscessus} describe either resection arthroplasty\textsuperscript{21} or staged reconstruction.\textsuperscript{23,24} The authors reported variable multidrug antimicrobial regimens, as summarized in \textbf{Table 2}, as guidelines for the treatment of mycobacterial PJI are currently not available.\textsuperscript{4,5,25,26}

\section*{Conclusion}

This case report represents an episode of iatrogenic septic arthritis caused by \textit{Mycobacteria} of the native knee after previous history of instrumentation, corticosteroid, and hyaluronic acid injections, with an overall indolent clinical course until subsequent arthroplasty. There were several important lessons learned, which are as follows: 1) Multidrug combination with antimicrobial therapy combined with aggressive surgical débridement and staged reimplantation permitted successful eradication of TKA PJI caused by \textit{M. abscessus} in this patient. 2) Initial medical management alone was not successful and cannot be recommended for the treatment of \textit{M. abscessus} in the setting of PJI. 3) Delaying the surgical débridement and the reconstructive course for a trial of medical management contributed to the ultimate requirement of a tibial tubercle osteotomy for an ankylosed knee at replantation. In this case, we initially had a low index of suspicion for deep infection, contributing to delayed surgical débridement. Ideally, a high degree of clinical suspicion should be maintained for joint infection in the presence of positive culture isolates of \textit{M. abscessus}, as it may have a delayed clinical presentation of the typical features of PJI (fevers, swelling, erythema, etc). In such cases, the authors recommend consideration of early surgical débridement. 4) Medical management of TKA PJI is not without risks. Careful monitoring of patient side effects during antimicrobial administration remains paramount, as this patient did sustain a degree of hearing loss associated with prolonged medical therapy. 5) In complicated PJIs involving rare and intrinsically resistant organisms, a collaborative multidisciplinary approach, including specialists in orthopedic surgery, infectious disease, microbiology, pharmacy, and pathology, may be the preferred path to clinical cure.

\section*{Key Info}

\section*{Figures/Tables}

Figures / Tables:

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Figure 1. Preoperative radiographs of the left knee in (A) anterior-posterior view and (B) lateral view.
Figure 2. Left knee 6-week postoperative radiographs in (A) sunrise patellar, (B) anterior-posterior, and (C) lateral views.
Figure 3. Left knee after explant and antimicrobial spacer placement in (A) anterior-posterior and (B) lateral views.
Figure 4. Radiographs of the left knee, standing at 1 year post-reconstruction in (A) lateral view, (B) anterior-posterior views of both knees, (C) posterior-anterior view of the left knee, and (D) sunrise view.
**Table 1.** Initial *Mycobacterium abscessus massiliense* Susceptibilities

<table>
<thead>
<tr>
<th>Medication</th>
<th>Minimum Inhibitory Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amikacin</td>
<td>16 (S)</td>
</tr>
<tr>
<td>Cefoxitin</td>
<td>16 (S)</td>
</tr>
<tr>
<td>Imipenem</td>
<td>8 (I)</td>
</tr>
<tr>
<td>Linezolid</td>
<td>16 (I)</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>2 (S)*</td>
</tr>
<tr>
<td>Tigecycline</td>
<td>1 (S)</td>
</tr>
</tbody>
</table>

*At 3 days; *erm* gene detected at 7 days.*
Table 2. Cases of Mycobacterium abscessus Orthopedic Infections and Treatment Regimens

<table>
<thead>
<tr>
<th>Author Name</th>
<th>Case Type</th>
<th>No. of Cases</th>
<th>Organisms Cultured</th>
<th>Antibiotic Regimen Used</th>
<th>Regimen Duration</th>
<th>Surgical Procedure Required</th>
<th>Final Result</th>
<th>Author Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eid et al. 2007</td>
<td>Concomitant total elbow arthroplasty and total knee arthroplasty (single patient)</td>
<td>1</td>
<td>Mycobacterium abscessus</td>
<td>Cefoxitin plus clindamycin</td>
<td>2.5 weeks before patient opera for palliative care</td>
<td>Resection arthroplasty for both the elbow and knee</td>
<td>Palliative care</td>
<td>The preferred treatment of PJ due to RGM is resection arthroplasty and antimicrobial therapy guided by sensitivity testing</td>
</tr>
<tr>
<td>Petropaniotis et al. 2009</td>
<td>Right total hip arthroplasty</td>
<td>1</td>
<td>Mycobacterium abscessus in right hip joint fluid, right ilopsoas abscess fluid and in an intraoperative periarticular tissue specimen</td>
<td>Imipenem, clindamycin, gentamicin, and amikacin. Empirical antibiotic therapy: parenteral meropenem 500 mg QID + oral clarithromycin 500 mg twice daily, Susceptibility-based therapy: IV cefoxitin 2 g QID + clarithromycin 500 mg.</td>
<td>Empirical therapy: 4 weeks. Susceptibility-based therapy: 3 months until 7 days post second-stage revision.</td>
<td>Two-stage revision arthroplasty</td>
<td>Cure</td>
<td>Factors contributing to cure likely include 1) removal of the infected orthopedic implant 2) extended exchange interval between the first and second-stage surgical revision allowing for 2) protracted antibiotics course that implemented 4) in vitro susceptibility pattern</td>
</tr>
<tr>
<td>Yinkey et al. 2010</td>
<td>Left total hip arthroplasty</td>
<td>1</td>
<td>Mycobacterium abscessus</td>
<td>Tobramycin-impregnated cement spacer. Tigecycline in combination with azithromycin and cefoxitin after initially failing to eradicate the infection with standard first-line therapy (aminoglycosides, azithromycin, and cefoxitin).</td>
<td>Initial antibiotic regimen: 1 month. Total antibiotic therapy 5 months.</td>
<td>Implant of spacer followed by repeat total hip arthroplasty 10 months after infection</td>
<td>Cure</td>
<td>Tigecycline may be an effective alternative to a typical antibiotic combination of amikacin, and either cefoxitin or imipenem if the combination is ineffective or if a single drug is intolerable for treating PJ due to RGM.</td>
</tr>
<tr>
<td>Mustatt and Witzig* 1995</td>
<td>Three years post right total hip arthroplasty, right total knee arthroplasty (single patient)</td>
<td>1</td>
<td>Mycobacterium abscessus from the hip and knee and coagulase-negative Staphylococcus species in the hip</td>
<td>Tobramycin-impregnated beads. Amikacin, erythromycin, and ciprofloxacin. After signs of knee infection and knee prosthesis removal, therapy was changed to cefoxitin and oral clarithromycin.</td>
<td>Initial antibiotic regimen: 5 months. Altered therapy after knee infection: 5 additional months (4 months clarithromycin concurrent with 5 months cefoxitin).</td>
<td>Removal of the hip prosthesis and eventually the knee prosthesis</td>
<td>Palliative care</td>
<td>High dose clarithromycin appears to be effective for M. abscessus treatment but an initial “induction phase” with combinations of parenteral agents may decrease resistance to clarithromycin in monotherapy treatment. Surgical débridement is also an important adjunct to medical management.</td>
</tr>
</tbody>
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Abbreviations: IV, intravenous; PJ, prosthetic joint infection; RGM, rapidly growing Mycobacterium.

References

References

References


Multimedia

Product Guide

Product Guide

- BioComposite SwiveLock Anchor
- BioComposite SwiveLock C, with White/Black TigerTape™ Loop
- BioComposite SwiveLock Anchor, With Blue FiberTape Loop
- Knotless SutureTak® Anchor

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