Positive Culture of Atypical *Mycobacterium Avium* Following Revision Total Knee Arthroplasty

JONATHAN LIU, MD; JACOB LAPERCHE, BS, MD'24; MARGUERITE NEILL, MD; DEREK JENKINS, MD

ABSTRACT

CASE: We report a rare case of mycobacterial periprosthetic joint infection (PJI) after primary total knee arthroplasty 14 years earlier. Progressive knee pain over three years with a negative PJI infectious workup led to revision total knee arthroplasty. A surprising result was isolation of *Mycobacterium avium* from tissue cultures taken at time of revision surgery. After six months of antibiotic treatment, the patient is alive with well-functioning pain-free TKA at over one-year follow-up.

CONCLUSION: Periprosthetic joint infection can present acutely or chronically years following total knee arthroplasty. Depending on the infecting organism, patients can present with sepsis, or a more indolent slower course that mimics aseptic loosening. In the absence of positive pre-operative labs and cultures, and based on the Musculoskeletal Infection Society (MSIS) criteria, aseptic loosening is a diagnosis of exclusion. An atypical infectious organism should be considered a possible cause and may require specialized cultures of operative specimens.

KEYWORDS: *Mycobacterium avium*, revision total knee arthroplasty, prosthetic joint infection

INTRODUCTION

In the last 20 years, the number of total knee arthroplasties (TKA) performed worldwide has steadily increased, and with that there have been increasing numbers of periprosthetic joint infections (PJI).[1,2] PJI is among the most common reasons for revision TKA.[2,3] Common bacterial causes of PJI include staphylococcus aureus, staphylococcus epidermidis and enterococcus faecalis.[4] Mycobacteria as a cause of PJI is quite unusual, accounting for only 0.5%.[5]

Gold-standard treatment for patients with PJI is generally considered two-stage revision with removal of hardware, antibiotic spacer placement, and IV and oral antibiotic treatment, followed by a second surgery to reimplant knee hardware. Single-stage revision has been reported to have acceptable outcomes in some clinical scenarios.[3,6] The decision to revise a TKA is often preceded by advanced imaging to evaluate for evidence of osteolysis, labs including ESR and CRP, synovial fluid aspirate, microscopic analysis, and culture in accordance with MSIS criteria.[7] Patients with evidence of component loosening and clinical symptoms limiting their function can be indicated for revision arthroplasty aimed at attaining a well-fixed stable joint replacement. Even with a preoperative work-up of low suspicion for infection, patients may later be diagnosed with infection based on results of intra-operative cultures at the time of revision surgery.[8,9] Pragmatism dictates obtaining an odd number of cultures at revision so there is a tiebreaker sample if needed. If cultures return with unexpected growth after revision surgery, treatment algorithms have been suggested with retention of implants and targeted antibiotic therapy.[10] When an unexpected organism is isolated, the question arises whether the result is a true infection or a contaminant.

We report a patient with non-insulin dependent diabetes mellitus (NIDDM) who was 14 years status post-primary TKA and presented with over one year of knee pain. After low-suspicion infectious work-up, with a mildly elevated CRP 11.8 mg/ml (reference <5 mg/ml) and otherwise normal laboratory and synovial aspirate values, the TKA was revised. However, a non-tuberculous mycobacterium (NTM) was isolated from two of three intra-operative smears and subsequent tissue culture. The patient was treated with a three-drug regimen for six months and is pain free at 1.5 years follow-up.

Consent: Verbal consent was obtained from the patient for this case report.

CASE REPORT

A 78-year-old woman with NIDDM had an uncomplicated right TKA in 2008. In 2022, she presented with slowly progressive knee pain affecting her mobility. On exam, the right knee range of motion was 0 to 120 degrees, stable to varus and valgus stress throughout flexion extension arc. Plain radiographs showed lucency suggesting polyethylene wear and osteolysis (**Figure 1).** CT scan confirmed lucencies anterior to tibial keel and medial aspect of tibial tray (**Figure 2A, 2B)** and about the femoral component**.** Pre-operative knee aspirate yielded 975 nucleated cells, 1% polymorphonuclear leukocytes, and no aerobic or anaerobic growth of aspirate cultures at 14 days. She failed a trial of conservative therapy over several months and was scheduled for revision TKA for presumed aseptic loosening due to polyethylene bearing

Figure 1. Anteroposterior X-ray of patients' right knee at the time of presentation.

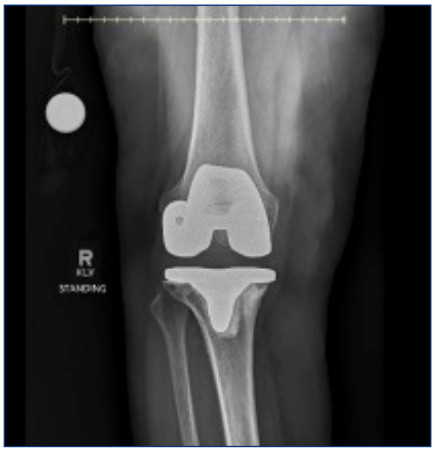


Figure 2A. Coronal CT images of patients' right knee taken pre-operatively.

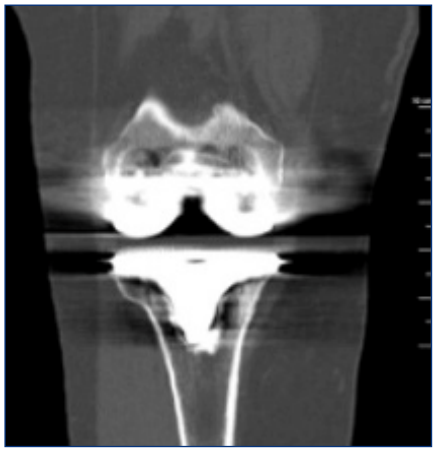
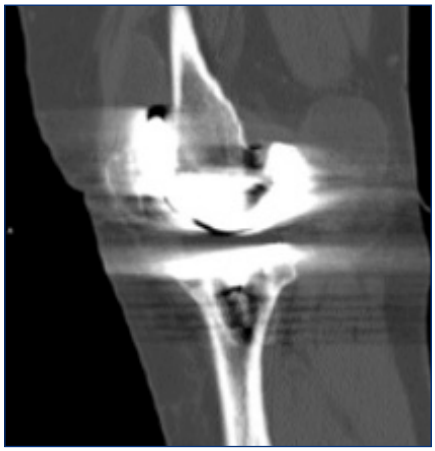


Figure 2B. Sagittal CT images of patients' right knee taken pre-operatively.



wear and osteolysis. Intra-operatively, a standard midline incision was made through patient's previous scar. The patella component was found to be well-fixed. Three specimens were sent for bacterial, fungal and AFB cultures. Bacterial and fungal cultures were negative at 14 days. Two of three specimens had a positive AFB smear and AFB culture was positive at day 13 in culture. The isolate was identified as *Mycobacterium avium intracellulare* (MAI) by mass spectrometry. The result was surprising given the patient's lack of immunosuppression. Lab contamination was ruled out by whole genome sequencing of the two isolates from two other culture-positive mycobacterial specimens obtained from different patients processed the same day. These isolates were determined to be non-MAI mycobacterial species.

The patient denied fevers, chills or night sweats, and had not been on systemic steroids or immunomodulator medications. The patient was treated with ethambutol, azithromycin and rifampin daily for six months with monitoring of labs, EKG, and visual acuity and color discrimination. Post-operative imaging showed well-aligned and fixed implants which remained true at two weeks and one year post-operatively **(Figures 3, 4A, 4B)**. The patient was without pain or signs of infection at one year with excellent knee stability and knee range of motion 0–120 degrees.

Figure 3. Two-week post-operative X-ray of patients' right knee.

Figure 4A. One-year post-operative anteroposterior X-ray of patients' right knee.

Figure 4B. One-year post-operative lateral X-ray of patients' right knee.

DISCUSSION

This case reports a rare occurrence of *M. avium* positive intra-operative culture during revision TKA for chronic knee pain 14 years after primary TKA in an otherwise healthy patient with well-controlled DM. Non-tuberculous mycobacteria (NTM) infections of prosthetic joints have been reported previously but are rare. Ingraham et al report a case of a 74-year-old with *Mycobacterium avium-intracellulare* PJI of the hip 15 years after primary total hip arthroplasty with previous revisions five and 10

years ago. This patient had multiple comorbidities including rheumatoid arthritis (RA) on prednisone, leflunomide and infliximab, Alzheimer's dementia, and coronary artery disease. Due to comorbidities the patient was treated with antibiotics, and incision and drainage of the hip. Four months of therapy did not resolve the infection and the patient expired six months after presentation.[11] Maimaiti et al reported six cases of NTM PJI following total joint arthroplasty with a mean onset of four months post-surgery. There was only one case of *M. avium*, which was the slowest growing of the NTM infections.[12]

Risk factors that have been identified for NTM infection include increasing age, BMI, lung disease, immunosuppressive therapies, and immunocompromised state.[13] The possibility of a false-positive culture from lab contamination was considered in our patient. This was ruled out by whole genome sequencing of the patient's isolate and two other mycobacterial isolates processed the same day which demonstrated different mycobacterial strains. The false-positive rate of *Mycobacterium avium-intracellulare* in prosthetic joint cultures has not been reported; however, the false positive rate of *Mycobacterium tuberculosis* (TB) has been reported to be around 2% secondary to lab cross-contamination and around 15% with a single-positive as well as a negative culture.[14] The decision to treat, despite the presence of significant risk factors for this infection, was ultimately based on the risk of significant morbidity if this was a true infection that, in the absence of treatment, would become a more advanced infection in the future.

The incidence of extrapulmonary *M. tuberculosis* has been more widely reported in the literature. Of the total extrapulmonary cases in the US from 2010 to 2019, approximately 9–11% of a total 1,800 to 2,400 cases per year involve bones or joints.[15] Though rare, there have been a few case reports of TB PJI reporting various outcomes and risk factors that may have been associated with this rare occurrence.[16,17] Risk factors for TB PJI, and likely *Mycobacterium avium-intracellulare* PJI, include immunocompromised state, travel to endemic regions, and prior or latent infections. Treatment options are typically antibiotic therapy combined with surgical management, including debridement, wash-outs, and revisions in cases of PJI.[17]

This case highlights the rarity and challenges associated with diagnosis and treatment of an *M. avium* PJI. Our patient was not immunosuppressed, and had well-controlled diabetes, which initially decreased our pre-diagnostic suspicion of atypical mycobacterium infection. The AFB smears of two specimens were positive, making accidental contamination unlikely. To enhance the likelihood of culture growth, the three specimens were pooled for culture, and it was positive after 13 days. The necessity of advanced testing and longer culture incubation time presented an initial barrier to rapidly starting treatment. In the present case, with 2/3 positive AFB smear and a positive culture for *M. avium*, and once contamination was ruled out, discussions were held with the patient, the orthopaedic and infectious disease care team members, and the final decision was made to treat as an atypical PJI.

CONCLUSION

This case reports an unsuspected positive culture for *M. avium* from the knee following revision TKA for presumed aseptic loosening of knee implants despite the patient's lack of risk factors, and negative preoperative PJI screening per MSIS criteria. While this case presents an uncommon finding, the authors recommend a multidisciplinary discussion including the patient and infectious disease specialists to determine if positive cultures should be treated. In the absence of definitive clinical guidelines in such cases, the authors recommend multidisciplinary team discussions with expert consultants, use of best clinical judgment and appropriate antibiotic treatment to prevent untoward consequences of infection, further revisions, and other complications for the patient, while balancing the potential side effects and cost of treatment.

References

1. Delanois RE, Mistry JB, Gwam CU, Mohamed NS, Choksi US, Mont MA. Current Epidemiology of Revision Total Knee Arthroplasty in the United States. J Arthroplasty. 2017 Sep;32(9):2663-2668. PMID: 28456561.
2. Duncan ST, Schwarzkopf R, Seyler TM, Landy DC. The Practice Patterns of American Association of Hip and Knee Surgeons for the Management of Chronic Periprosthetic Joint Infection After Total Knee Arthroplasty. J Arthroplasty. 2023 Nov;38(11):2441-2446. PMID: 37142069.
3. Liukkonen R, Honkanen M, Skyttä E, Eskelinen A, Karppelin M, Reito A. Trends in Revision Knee Arthroplasty for Prosthetic Joint Infection: A Single-Center Study of 384 Knees at a High-Volume Center Between 2008 and 2021. J Arthroplasty. 2023 Nov;38(11):2447-2454. PMID: 37236284.
4. Migliorini F, Eschweiler J, Tingart M, Rath B. Posterior-stabilized versus cruciate-retained implants for total knee arthroplasty: a meta-analysis of clinical trials. Eur J Orthop Surg Traumatol. 2019 May;29(4):937-946. PMID: 30649620.
5. Patel R. Periprosthetic Joint Infection. N Engl J Med. 2023 Jan 19;388(3):251-262. PMID: 36652356.
6. Shichman I, Ward SA, Lu L, Garceau S, Piuzzi NS, Seyler TM, Schwarzkopf R. Failed 2-Stage Revision Knee Arthroplasty for Periprosthetic Joint Infection-Patient Characteristics and Outcomes. J Arthroplasty. 2023 Oct;38(10):2177-2182. PMID: 37179023.
7. Parvizi J, Tan TL, Goswami K, Higuera C, Della Valle C, Chen AF, Shohat N. The 2018 Definition of Periprosthetic Hip and Knee Infection: An Evidence-Based and Validated Criteria. J Arthroplasty. 2018 May;33(5):1309-1314.e2. PMID: 29551303.
8. Eriksson H, Lazarinis S. Low accuracy in preoperative tissue biopsies for diagnosing chronic periprosthetic joint infection: an observational retrospective single-centre study. J Int Med Res. 2023 Jun;51(6):3000605231158972. PMID: 37389568.
9. Schwarze J, Moellenbeck B, Gosheger G, Puetzler J, Deventer N, Kalisch T, Schneider KN, Klingebiel S, Theil C. The Role of Single Positive Cultures in Presumed Aseptic Total Hip and Knee Revision Surgery-A Systematic Review of the Literature. Diagnostics (Basel). 2023 May 8;13(9):1655. PMID: 37175046.

10. Leone JM, Hanssen AD. Management of infection at the site of a total knee arthroplasty. J Bone Joint Surg Am. 2005 Oct;87(10):2335-48. PMID: 16224857.
11. Ingraham NE, Schneider B, Alpern JD. Prosthetic Joint Infection due to *Mycobacterium avium-intracellulare* in a Patient with Rheumatoid Arthritis: A Case Report and Review of the Literature. Case Rep Infect Dis. 2017;2017:8682354. PMID: 28280641.
12. Maimaiti Z, Li Z, Xu C, Fu J, Hao L, Chen J, Li X, Chai W. Non-Tuberculosis Mycobacterium Periprosthetic Joint Infections Following Total Hip and Knee Arthroplasty: Case Series and Review of the Literature. Orthop Surg. 2023 Jun;15(6):1488-1497. PMID: 37154097.
13. Liu Q, Du J, An H, Li X, Guo D, Li J, Gong W, Liang J. Clinical characteristics of patients with non-tuberculous mycobacterial pulmonary disease: a seven-year follow-up study conducted in a certain tertiary hospital in Beijing. Front Cell Infect Microbiol. 2023 Jun 22;13:1205225. PMID: 37424783.
14. Barac A, Karimzadeh-Esfahani H, Pourostadi M, Rahimi MT, Ahmadpour E, Rashedi J, Mahdavipoor B, Kafil HS, Spotin A, Abate KH, Mathioudakis AG, Asgharzadeh M. Laboratory Cross-Contamination of Mycobacterium tuberculosis: A Systematic Review and Meta-analysis. Lung. 2019 Oct;197(5):651-661. PMID: 31203380.
15. Table 15 | Reported TB in the US 2019 | Data & Statistics | TB | CDC. https://www.cdc.gov/tb/statistics/reports/2019/table15.htm (2023).
16. Elzein FE, Haris M, Alolayan SS, Al Sherbini N. Total knee prosthesis infected with *Mycobacterium tuberculosis*. BMJ Case Rep. 2017 Sep 7;2017:bcr2017220596. PMID: 28883009.
17. Lo CKL, Chen L, Varma S, Wood GCA, Grant J, Wilson EW. Management of *Mycobacterium tuberculosis* Prosthetic Joint Infection: 2 Cases and Literature Review. Open Forum Infect Dis. 2021 Aug 31;8(10):ofab451. PMID: 34631919.

Authors

Jonathan Liu, MD, Brown University, Department of Orthopedics, Providence, RI.

Jacob Laperche, BS, MD'24, University Orthopedics, Inc., East Providence, RI; Frank H. Netter School of Medicine, Quinnipiac University, North Haven, CT.

Marguerite Neill, MD, Brown University, Department of Infectious Diseases, Providence, RI.

Derek Jenkins, MD, Brown University, Department of Orthopedics, Providence, RI; University Orthopedics Inc, East Providence, RI.

Correspondence

Jacob Laperche, BS, MD'24
University Orthopedics Total Joints Research Fellow
1 Kettle Point Ave
East Providence, RI 02914
401-862-0438
jacoblaperche@gmail.com