Case report

*Mycobacterium abscessus* Periprosthetic joint infection following bilateral Total Knee arthroplasty

Rajesh Malhotra, Kiran Bala, Deepak Gautam, Aakashneel Bhattacharya, Ashit Bhusan Xess, Pooja Pandey, Santosh Verma, Urvashi B. Singh

**Department of Orthopedics, All India Institute of Medical Sciences, New Delhi, India**

**Department of Microbiology, All India Institute of Medical Sciences, New Delhi, India**

**A R T I C L E  I N F O**

**Article history:**
Received 13 April 2019
Received in revised form 18 April 2019
Accepted 18 April 2019

**Keywords:**
Periprosthetic joint infection
*Mycobacterium abscessus*
Total knee replacement

**A B S T R A C T**

Periprosthetic joint infection (PJI) can be protracted, incapacitating, needing multiple interventions and could even lead to mortality. Early post-operative PJI has been ascribed to peri-operative introduction of highly virulent bacteria, while delayed post-operative to low-virulence bacteria. Non-tuberculous mycobacteria (NTM) do not figure in the usual list of etiological agents. We report a case of difficult diagnosis of bilateral PJI caused by *Mycobacterium abscessus*, following bilateral total knee arthroplasty in an elderly male, but treated successfully despite prolonged infection. *M. abscessus* complex comprises a group of rapidly growing, multidrug-resistant NTM, capable of forming biofilms on prostheses, responsible for a wide spectrum of hospital-acquired infections. *M. abscessus* as a cause of PJI is not reported widely. There are a few cases described in literature worldwide. There are no policy guidelines available for treating such cases. High clinical suspicion, with a concerted effort to grow and identify the causal pathogen is important. Standard anti-tubercular therapy is not recommended for treatment due to inherent resistance. Complete excision of infected tissues and removal of prosthesis along with prolonged combination antimicrobial regimen is the treatment of choice.

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**Introduction**

Prosthetic joint infections (PJI) are one of the most challenging complications of joint replacement surgery [1]. Most early onset post-operative cases are ascribed to virulent bacteria such as *Staphylococcus aureus*, while late-onset cases are ascribed to low virulence bacteria. Of late, NTM are being reported from several device related infections but PJI due to non-tubercular mycobacteria (NTM) are relatively under-reported [2–7]. NTM, especially *Mycobacterium abscessus*, are capable of forming biofilms on prosthetic material and hence are difficult to treat using antibacterials alone. Removal of prosthetic material with prolonged antimicrobial combination regimen is the treatment of choice. The present case describes delay in diagnosis and arduous but successful management of bilateral PJI after total knee replacement (TKR) caused by *Mycobacterium abscessus*.

**Case report**

A 78-year-old diabetic and hypertensive male patient, presented with pain, swelling and discharging sinuses in both knees, 5 weeks after sequential bilateral TKR at a peripheral hospital, with no response to cefoxacin and ofloxacin. Discharge revealed acid-fast bacilli (AFB), but was negative for cartridge-based-nucleic-acid-amplification test (Xpert MTB/Rif). Empirical anti-tubercular therapy (ATT) was initiated, (rifampin,isoniazid,pyrazinamide and ethambutol) with minimal response, stopped after seven months, followed by bilateral knee debridement and poly-exchange but the discharge continued.

Eleven months after index surgery, he underwent implant removal and articulating antimicrobial cement spacer application in both knees (Fig. 1a) and was referred to our institute. He presented with difficulty in mobilization due to displaced cement spacer in both knees, thick purulent discharge from left knee and copious sero-purulent discharge from right knee. Laboratory investigations revealed Erythrocyte Sedimentation Rate (ESR) of 22 mm and a C-reactive protein (CRP) at 27 mg/L. All antibacterials were stopped, tissue samples excised from sinus edge and discharge from both knees sent for microbiological analysis.

* Corresponding author.
E-mail address: druvrvashi@gmail.com (U.B. Singh).

**https://doi.org/10.1016/j.idcr.2019.e00542**

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Bacteriology and mycology laboratory reports were inconclusive. In the mycobacteriology laboratory, the Ziehl Neelsen stain and Gene-Xpert MTB/RIF from the material was negative. Some growth was observed on MacConkey agar on day 3. Colonies were confirmed as AFB and grew on Lowenstein Jensen’s media with 5% NaCl. Nitrate reduction test was negative. MGIT automated liquid culture system (Becton Dickinson, NJ, USA) revealed the growth of the same phenotype. As per the growth pattern and biochemical properties the isolate was identified as *Mycobacterium abscessus*. The isolate was sequenced for 16S ribosomal gene and confirmed as *M. abscessus*. The sequence was submitted to Genbank and granted Accession No. MH720215. Drug susceptibility test was done by broth micro-dilution assay as per CLSI guidelines [8]. The isolate was sensitive to amikacin, clarithromycin, linezolid and rifampin but resistant to imipenem.

The patient was started on rifabutin 300 mg, clarithromycin 1000 mg and injection amikacin 500 mg daily. Baseline audometry, renal function tests, ECG and liver function tests were within normal limits. Serial QT, monitoring, renal function, electrolytes and liver enzymes were closely monitored. After 3 weeks of antibacterial, thorough debridement of right knee with sinus excision, and distal femoral canal curettage followed by arthrodesis using Lizarov ring fixator was done. After two weeks, the left knee was debrided and left with antimicrobial impregnated cement spacer in-situ. After another 8 weeks of antibacterials, the left knee was re-implanted with revision knee prosthesis and the patient was mobilized with full weight bearing on both knees. The intraoperative tissue samples on both knees revealed negative culture for mycobacteria.

Post-intervention, there was no fresh discharge from both knee joints (Fig. 1b). PET scan at end of four months revealed no metabolic uptake. Amikacin was replaced with oral levofloxacin due to bilateral sensory-neural hearing loss for higher frequencies after 6 months. By end of 7 months, his wounds were clean and dry, ESR, CRP were within normal limits. Lizarov ring fixator was removed and knee brace used as the X-ray showed signs of trabeculae across the distal femur and proximal tibia. Currently the patient is on one-and-half year follow-up and is antimicrobial free for last four months. He is mobile without braces, is able to bear weight on both his legs for last two months, and a normal for age renal and liver functions. His latest X-rays showed bony ankylosis of right knee with stable revision knee arthroplasty implants in situ in his left knee (Fig. 1c).

Discussion

Rapidly growing mycobacteria (RGM) are ubiquitous in environment and reported worldwide. They are implicated in nosocomial infections following medical or surgical interventions leading to wound infections and sepsis. *M. fortuitum*, *M. chelonae* and *M. abscessus* are potentially pathogenic RGM responsible for 90% of the clinical cases [2,9]. *M. abscessus* complex demonstrates inducible macrolide resistance due to a novel erm gene (erm41) [10]. *Mycobacterium abscessus* is resistant to disinfectants and therefore can cause post-surgical and post-procedural infections. It is associated with a wide range of skin and subcutaneous tissue, respiratory tract, central nervous system, pulmonary and ocular infections, bacteremia and disseminated infections [11–16]. Possible sources for nosocomial outbreaks include contaminated saline, disinfectants or surgical equipments and contact transmission between patients [14].

Incidence of PJJ ranges from 2.05% to 2.18% after total knee replacement (TKR) with primary arthroplasties [17]. There are 43 cases of PJJ reported by RGM, including 17 cases of knee–PJJ caused by RGM, including *Mycobacterium chelonae*, *M. smegmatis*, *M. fortuitum*, *M. wolinskyi* and *M. abscessus* [12,10]. *M. abscessus* is reported in eight cases, one from India [2,3,5–7,9]. (Table 1). Diagnosis is frequently delayed due to lack of clinical suspicion or lack of appropriate laboratory support.

This case reported discharge from surgical wounds, without fever since the TKR. Mycobacterial infection was suspected considering his prolonged illness and repeated negative bacterial cultures. Clear temporal association of symptoms with surgery and involvement of both knees, with a typical presentation suggestive of RGM, suggests that infection was likely acquired from the hospital setting during or after initial intervention.

RGM infections are resistant to several groups of antibacterials and combination therapy of oral macrolides with parenteral medications (amikacin, cefoxitin or imipenem) is advocated for serious bone and soft tissue infections by *M. abscessus*. Isolate in this case was resistant to imipenem and there is limited availability of cefoxitin in India. Rifabutin is active against *M. abscessus* and inhibits clarithromycin resistant strains [18], hence regimen was designed with rifabutin, clarithromycin and intravenous amikacin. There are no guidelines for the optimal empiric therapy or duration for PJJ caused by RGMs.

PJJ due to *Mycobacterium abscessus* have been infrequently reported and no specific guidelines exist to inform treatment. *M. abscessus* is resistant to disinfectants, intrinsically resistant to first line ATT and increasingly reported resistant to macrolides; are known to form biofilms on prosthetic material and hence difficult to eradicate. High clinical suspicion, accurate laboratory diagnosis, combination of surgical and carefully designed medical regimen can eradicate non-responding PJJ even after delayed diagnosis and a long course of infection.
Table 1
Summary of all the cases of prosthetic knee joint infections due to Mycobacterium abscessus reported in the literature.

| S. no | Author’s Reference | Age/sex | Underlying Disease | Region | Arthroplasty & period of prosthetic joint infection | Organism Cultured | Antibiotic Regimen | Surgical Intervention | Final Outcome |
|-------|--------------------|---------|---------------------|--------|--------------------------------------------------|------------------|-------------------|----------------------|--------------|
| 1     | Eid Aj et al.      | 71/F    | Rheumatoid arthritis | Not known | Knee (652 days) | M. abscessus | CFX & CLR (2 weeks) | Resection arthroplasty | Palliative care (3 weeks) |
| 2     | Ryu SW et al.      | 58/F    | Degenerative joint disease | 2001, Korea | Left Knee arthroplasty (21 days) | M. abscessus | Kanamycin + Clarithromycin + Pyrazinamide (9 months) Amik (2 mts Perioperatively) | Debridement | Palliative care (not known) |
| 3     | Wang SX et al      | 72/F    | Intra articular steroid injection & osteoarthritis | 2011, Taiwan | Right Knee arthroplasty (5 months) | M. abscessus & M. fortuitum | Doxycycline + Ciprofloxacin + Clarithromycin (5 months) Amik (2 mts Perioperatively) | Reimplantation at 4 months | No relapse (43 weeks) |
| 4     | Amit P et al       | 71/F    | Degenerative joint disease | 2010, New Delhi, India | Right Knee arthroplasty (2 years) | M. abscessus | CLR+LEV+AMK(3 WEEKS) | Resection arthroplasty | No Relapse Follow up 104 weeks |
| 5     | Kim et al          | 83/F    | Degenerative joint disease | 2017, South Korea | Right Knee arthroplasty (18 Days) | M. abscessus | CLR+LEV (13 WEEKS) Cefoxitin (IV) Clarithromycin+ Amikacin (IV)Moxifloxacin (6 months) | Reimplantation at 6.5 months | No Relapse Follow up 4 years and 3 months |
| 6     | Spanyer et al      | 71/F    | Degenerative joint disease | 2017, South Korea | Right Knee arthroplasty (13 month) | M. abscessus | ATT (6 weeks)Cefoxitin (IV) Clarithromycin+ Amikacin (IV) (Cefoxitin replaced by tigecycline) (6 mnts+10 months) (IV) cefoxitin, oral clarithromycin, and thrice-weekly intravenous amikacin. (15 weeks) | Reimplantation after 10 months of surgery(Open debridement and polyethylene insert exchange) | No relapse Follow up 2 years |
| 7     | Present Case       | 78/ M   | Degenerative joint disease | 2018, New Delhi, India | Bilateral Total Knee arthroplasty | M. abscessus | Rifabutin + Clarithromycin + Amikacin (IV) | Reimplantation after 2 years | No relapse Follow up 4 years |

Conflict of interest

None.

Research funding

None.

Consent

Written informed consent has been taken from the patient regarding publication of the case report and is available for review as per the request of Editor-in-chief.

CRediT authorship contribution statement

Rajesh Malhotra: Conceptualization, Methodology. Kiran Bala: Conceptualization, Writing - review & editing. Deepak Gautam: Methodology. Aakashneel Bhattacharya: Formal analysis, Writing - original draft, Writing - review & editing. Ashit Bhusan Xess: Formal analysis, Writing - review & editing. Pooja Pandey: Investigation. Santosh Verma: Investigation. Urvashi B. Singh: Conceptualization, Methodology, Writing - review & editing.

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