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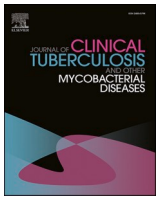

# Management of *M. abscessus subsp. abscessus* early-onset prosthetic joint infection: Case report and literature review

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ABSTRACT

Nontuberculous mycobacteria are a rare but still emerging cause of difficult-to-treat prosthetic joint infection. To our knowledge only 17 cases of *M. abscessus complex* prosthetic joint infection are reported in literature, of which only 1 is by *M. abscessus subps. abscessus*. No guidelines are available for this clinical scenario.

We describe a 68-years-old female patient with an early-onset *M. abscessus subsp. abscessus* prosthetic joint infection, successfully treated with a tailored medical-surgical strategy, and present an overview of cases currently available in the literature to assist physicians in the management of these uncommon infections.

## 1. Introduction

The incidence of prosthetic joint infections (PJI) has raised in recent years as the number of patients undergoing total joint arthroplasty has increased [1]. The cumulative incidence of PJI after total hip arthroplasty (THA) and total knee arthroplasty (TKA) remains unclear; however, it is believed to be approximately 1.5 infections per 1000 person-joint-years [2]. The majority of PJI cases are attributed to gram-positive cocci, especially staphylococci (50–60%), the remaining cases are ascribed to gram-negative bacteria (6%), anaerobes (4%), fungi (1%), polymicrobial (20%) and 7% of cases are culture-negative [3,4]. *Mycobacterium sp* is a rare, but still emerging cause of PJI. The most recent systematic review described 115 mycobacterial PJI in the past 30 years, of which *M. tuberculosis* was detected in 43% of the cases and 16 species of nontuberculous mycobacteria (NTM) were detected in the remaining 57% of the cases [5]. *M. abscessus complex* (MABC) is a member of the rapidly growing mycobacteria (RGM) and actually comprises three subspecies: *M. abscessus subsp. abscessus* (from now *M. abscessus*), *M. abscessus subsp. massiliense* and *M. abscessus subsp. bolletii* [6]. To our knowledge, 17 cases of MABC PJI are reported in the literature, of which only 1 is from *M. abscessus* [7–22] (Table 1). There is no standardized treatment or strength recommendation correlating in vitro RGM susceptibility and clinical response [23]. Even though prosthesis removal has been associated with a favorable outcome at 6 and 12 months after diagnosis, the optimal surgical strategy for the treatment of RGM PJI is still unknown [24].

We present a case of *M. abscessus* early-onset PJI after TKA highlighting therapeutic management and reporting a summary of MABC PJI cases described in the literature.

## 2. Case report

A 68-years-old female patient presented on July 22, 2021 to the ICCS Hospital in Milan lamenting fever, aggravating pain, limited range of motion and swelling of her right knee, with secreting fistula formation. Less than 2 months earlier, she underwent right TKA.

On admission, past medical history included left TKA, hypercholesterolemia, hyperuricemia, arterial hypertension, bilateral glaucoma, seasonal affective disorder and diverticular disease. Drug history included statin, allopurinol, angiotensin receptor blocker, topical beta-blocker and benzodiazepine. She reported a questionable allergy to penicillin. The physical examination evidenced swelling, redness and warmth of her right knee with tenderness and functional restriction; a fistula was present on the surgical wound. Laboratory investigation

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**Table 1**
Cases of PJI due to *M. abscessus* complex (MABC) reported in the literature.

| Author's reference | Age/ sex | MABC subspecies | Type of prosthesis | Antibiotic regimen (weeks)* | Surgical intervention§ | Follow-up | Outcome |
|---|---|---|---|---|---|---|---|
| **Spanyer JM et al.** [7] | 61/ female | M. abscessus subsp. massiliense | Knee | AMK + CFX + CLR (5)<br>AMK + CFX + TGC (10) | REA. Reimplantation at 6 months | 52 months | No relapse |
| **Goldstein N et al.** [8] | 48/ female | Not specified | Hip | IMP + AMK + AZM + CFZ (60) AZM + CFZ (20) | Debridement and PE insert exchange. Hemipelvectomy | 14 months | Cured |
| **Kim M et al.** [9] | 83/ female | Not specified | Knee | AMK + CFX + MOX + CLR (not reported)<br>AMK (28) + CFX + AZM (40)<br>AZM + RIF + CIP (12)<br>AMK + CFX + AZM (8)<br>RIF + CIP (24) | Multiple debridements. PE insert exchange. REA. Reimplantation at 8 months. Debridement and PE insert exchange 10 months after reimplantation | 51 months | No relapse |
| **Kim M et al.** [9] | 71/ female | Not specified | Knee | CLR + LEV + RIF (1)<br>CFX + AMK + CLR (2)<br>AMK (16) + CLR (24)<br>AMK (2) + TGC + CLR (4)<br>CLR + CIP (40) | Multiple debridements. REA. Reimplantation at 15 months | 24 months | No relapse |
| **Henry MW et al.** [10] | 65/ male | Not specified | Left hip | TGC + CLR (6)<br>CLR (30) | REA. Reimplantation at 3 months | 72 months | No relapse |
| | | Not specified | Right hip | TGC + LNZ (6)<br>AZM (not reported)<br>AMK + IMP + AZM + CFZ (6)<br>CFZ + AZM (not reported)<br>AMK + IMP + AZM (20) | Multiple debridements. PE insert exchange. REA. Reimplantation at 2 ½ after the latest revision surgery | 48 months | No relapse |
| **Wang SX et al.** [11] | 72/ female | Not specified + M. fortuitum | Knee | CFX + AMK + CLR (not reported)<br>DOX + CIP + CLR (12)<br>DOX + CIP + CLR + AMK (8)<br>DOX + CIP + CLR (20) | REA. Reimplantation at 4 months | 10 months | No relapse |
| **Eid AJ et al.** [12] | 71/ female | Not specified | Knee | CFX + CLR (2) | REA. Palliative care | 3 weeks | Death |
| | | Not specified | Elbow | CFX + CLR (2) | REA. Palliative care | 3 weeks | Death |
| **Malhotra R et al.** [13] | 78/ male | Not specified | Right knee | AMK + RFB + CLR (24)<br>LEV + RFB + CLR (32) | REA. Debridements. Arthrodesis | 18 months | No relapse |
| | | Not specified | Left knee | AMK + RFB + CLR (24)<br>LEV + RFB + CLR (32) | REA. Debridement. Reimplantation at 2 ½ months | 18 months | No relapse |
| **Amit P et al.** [14] | 71/ female | Not specified | Knee | CLR + LEV + AMK (3)<br>CLR + LEV + IMP (6)<br>CLR + LEV (13) | REA. Debridement. Reimplantation at 6 ½ months | 24 months | No relapse |
| **Pace V et al.** [15] | 72/ female | M. abscessus subsp. abscessus | Hip | IMP + CLR + AMK + LNZ (2)<br>IMP + CLR + AMK (12)<br>IMP + CLR (1)<br>TGC + AMK (2)<br>IMP + AMK (2)<br>IMP + AMK + CLR (1)<br>IMP + CLR (1)<br>TGC + CLR (1)<br>CLR (2) | REA. Reimplantation at 4 months | 6 months | No relapse |
| **Nengue L et al.** [16] | 82/ male | M. abscessus subsp. massiliense | Knee | AZM + CFX (2)<br>AZM + TGC (12)<br>CIP (4)<br>AZM (8)<br>AZM + AMK + TGC (2)<br>AZM + AMK + CFX (2)<br>AZM + AMK + LNZ (14)<br>AZM + LNZ (8) | Debridement. REA. Reimplantation at 11 months | 6 months | No relapse |
| **Tsuruyama Y et al.** [17] | 74/ male | M. abscessus subsp. massiliense | Knee | IMP + AMK (5)<br>IMP + AMK + AZM (25)<br>IMP + AMK + AZM (not reported)<br>AMK + AZM (not reported) | Multiple arthrocentesis | 6 months | No relapse |

(*continued on next page*)

**Table 1** (*continued*)

| Author's reference | Age/ sex | MABC subspecies | Type of prosthesis | Antibiotic regimen (weeks)* | Surgical intervention§ | Follow-up | Outcome |
|---|---|---|---|---|---|---|---|
| **Genovese N et al.** [18] | 79/ male | M. abscessus subsp. massiliense<br>S. capitis C. glucuronolyticum<br>A. baumannii<br>C. tropicalis<br>S. epidermidis | Hip | VAN (6)<br>AZM + CFX (not reported)<br>AZM + AMK + TGC (not reported)<br>AZM + AMK + TGC + COL + FCZ (not reported)<br>AZM + TGC + CAZ-AZI + CPT (not reported)<br>AZM + ERV + CAZ-AVI + CPT (not reported)<br>AZM + CFZ (32)<br>AZM + CFZ + TGC (not reported)<br>AZM + CFZ + ERV (12)<br>AZM + CFZ (56)<br>AZM (not reported) | Multiple debridements. REA | 20 months | No relapse |
| **Petrosoniak A et al.** [19] | 70/ female | Not specified | Hip | MEM + CLR (4)<br>CFX + CLR (12) | REA. Reimplantation at 4 months | 18 months | No relapse |
| **Ma Q et al.** [20] | 73/ male | Not specified | Knee | CFX + IMP + AMK (24)<br>CLR + LNZ (56) | Debridement. REA. Reimplantation | Not reported | Cured |
| **Park JW et al.** [21] | 80/ female | Not specified | Knee | AMK + CTX + CLR (16) | REA | 16 weeks | No relapse |
| **Singh D et al.** [22] | 72/ female | Not specified | Hip | CLR + IMP + AMK (8)<br>CLR + TOB (16) | REA. Debridement | | Persistence of infection |

*Abbreviations:* AMK = amikacin, AZM = azithromycin, CPT = ceftaroline, CFX = cefoxitin, CTX = cefotaxime, CAZ-AVI = ceftazidime-avibactam, CIP = ciprofloxacin, CLR = clarithromycin, CFZ = clofazimine, COL = colistine, DOX = doxycicline, EMB = ethambutol, ERV = eravacycline, FCZ = fluconazole, IMP = imipenem, INH = isoniazid, LEV = levofloxacin, LNZ = linezolid, MEM = meropenem, MOX = moxifloxacin, PE = polyethylene, PZA = pyrazinamide, REA = resection arthroplasty, RFB = rifabutin, RIF = rifampicin, TGC = tigecycline, TOB = tobramycin, VAN = vancomycin.

* Not reporting empirical therapy prior to NTM isolation.

§ Not reporting surgical interventions prior to NTM isolation.

demonstrated raised C-reactive protein (CRP) without leukocytosis (Fig. 1) in conjunction with fever. Radiograph evidenced only joint effusion, without signs of periprosthetic bone resorption. Arthrocentesis was performed in the emergency room (ER), with synovial fluid culture testing negative. Therefore, a revision surgery was planned five days after admission, with debridement and polyethylene (PE) insert replacement. Empirical broad-spectrum antibiotic therapy (including levofloxacin, meropenem and daptomycin) was started on the same day. Given the lack of clinical improvement, with persistent signs of local inflammation and no microbiological isolates from routine bacterial culture (synovial fluid and periprosthetic tissue), she underwent resection arthroplasty (REA) on August 13, where the prosthesis was extracted and replaced with gentamicin and vancomycin impregnated cement spacer. Bacterial culture from sonification fluid tested negative and antibiotic therapy was interrupted on September 20, after almost two months, due to ineffectiveness. Periprosthetic fluid aspirate was collected the day after with acid-fast bacilli (AFB) growth on standard bacterial culture, identified as *M. abscessus*. The RGM was isolated from liquid (MGIT) and solid culture (Lowenstein-Jensen), identified using GenoType NTM-DR (Arnika kit). Genotypic drug susceptibility testing (DST) was conducted using the latter method and phenotypic DST using Sensititre™ Myco RAPMYCOI AST Plate. Results were evaluated according to the breakpoints reported in the 2018 CLSI document [25] (Table 2). On October 15 targeted antimycobacterial therapy was started with imipenem/cilastatin 500/500 mg QID plus linezolid 600 mg BID plus amikacin 750 mg QD (10 mg/kg). Six days later another revision procedure was performed, with debridement plus gentamicin loaded spacer renewal, collecting another synovial fluid sample for microbiological examination, which again tested positive for *M. abscessus*. On November 11 the patient was transferred to the Infectious Diseases Clinic of San Raffaele Hospital in Milan. Dosage of linezolid and amikacin was adjusted on therapeutic drug monitoring (TDM) for better tolerance and efficacy. To further implement the bactericidal capacity of the therapeutic regimen in use, cefoxitin 3 g TID was added for 14 days, after assessing the negativity of total IgE and beta-lactam-specific IgE. To optimize therapeutic management, phenotypic DST was extended to other antibiotics, according to the latest evidence [26–30] (Table 2). During hospitalization physical examination of the knee showed no signs of infectious relapse, inflammatory markers and leukocyte count were consistently normal (Fig. 1). The patient became highly intolerant of hospitalization, therefore on December 16 imipenem/cilastatin was discontinued in favor of clofazimine 100 mg QD and the patient was discharged, continuing amikacin 1500 mg (20 mg/kg) 3 times per week and oral linezolid (dosage on TDM) in our Day Hospital (DH) Service and starting physiotherapy at home. On March 30, 2022 after five and a half months of targeted therapy, the patient was readmitted to the ICCS Hospital, where the spacer was removed and arthrodesis was performed. Intraoperative specimen (bone sample) was collected for microbiological examination and tested negative. In the postoperative period, antibiotic therapy was interrupted on May 6 (almost 7 months of antimycobacterial therapy). At 6-months of follow up, no signs or symptoms of relapse were observed. With reference to drug toxicities, transient worsening of renal function, peripheral neuropathy eventually reversed with therapy discontinuation as well as persistent sensorineural hypoacusis and were documented.

## 3. Discussion

*M. abscessus*, as the others RGM, is a ubiquitous environmental organism, quite resistant to disinfectants and potentially able to cause post-surgical and post-procedural infections [6,23,24]. RGM are increasingly being recognized as a possible cause of early-onset PJI, with a clinical presentation that does not differ significantly from non-mycobacterial PJI [5,24]. Their growth requires specific media, yet

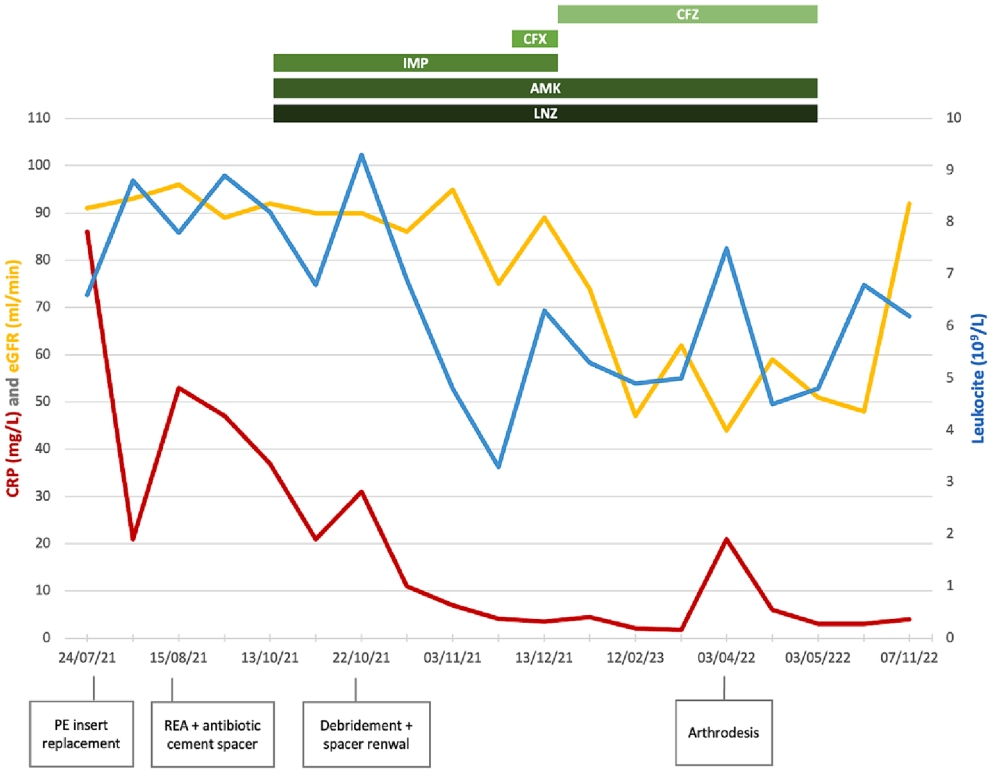


**Fig. 1.** Laboratory investigations, medical and surgical interventions. Abbreviations: AMK = amikacin, CFX = cefoxitine, CFZ = clofazimine, CRP = C-reactive protein, eGFR = estimated glomerular filtration rate, IMP = imipenem, LNZ = linezolid, PE = polyethylene, REA = resection arthroplasty.

**Table 2**
*M. abscessus*: phenotypic DST and genetic sequencing. Clinical breakpoints according to 2018 CLSI.

| Antibiotics | MIC (μg/ml) | Antibiotics | MIC (μg/ml) |
|---|---|---|---|
| Amikacin | 16 (S) | Linezolid | 8 (S) |
| Imipenem | 8 (I) | Cefoxitin | 32 (I) |
| Ciprofloxacin | 4 (R) | Moxifloxacin | 8 (R) |
| TMP-SMX | 8/132 (R) | Doxicycline | > 16 (R) |
| Rifampicin | 8 | Rifabutin | 8 |
| Clarithromycin | 8 (R) | | |
| Clofazimine | 0.5 | | |
| *erm*(41)wild-type: detected | | | |

*Abbreviations:* MIC = minimum inhibitor concentration, TMP-SMX = trimethoprim-sulphametoxazole.

they can develop also into routine bacterial plates or broth culture media in about one week. Indeed, in our case no AFB culture was submitted for examination. However, their isolation can be missed when cultures are incubated for only 48 h, so it is necessary to advise microbiologist in case of a high degree of suspicion [23]. Definitive identification to the subspecies level is no longer possible without molecular techniques, since the recent changes in the RGM's taxonomy [6]. Consequently, identification of RGM in most laboratories is either incomplete or imprecise (Table 1). In vitro antimicrobial susceptibility testing should be performed on all clinically significant isolates of RGM [23,25]. Regimen selection depends upon the presence and activity of the *erm*(41) gene, which confers inducible macrolide resistance despite in vitro susceptibility at three to five days. The majority of *M. abscessus* and some *M. abscessus subsp. bolletii* contain an *erm*(41) gene. However, some isolates have a T-to-C polymorphism at nucleotide 28 of the *erm*(41) gene, which inactivates it [31]. In our case mycobacterial isolate was identified and *erm*(41) gene was detected by GenoType NTM-DR. Phenotypic DST showed favorable MIC for amikacin and linezolid and intermediate for imipenem and cefoxitin, while clinical breakpoints were not available for clofazimine and rifampicin/rifabutin. Extended incubation with clarithromycin was performed to assess the functionality of the gene (Table 2). Regarding antimycobacterial therapy, there are no randomized controlled trials or comparative observational studies examining the treatment of MABC PJI nor NTM PJI. Thus, treatment guidance is primarily based on DST data, as well as case reports of NTM PJI and small retrospective reviews on MABC pulmonary infections, which have contributed to the recent guidelines on NTM pulmonary infections [23,25,32]. For most NTM soft tissue and skeletal disease, medical therapy should be continued for a minimum of six months and is sometimes given for 12 months or longer [23]. There is a high grade of variability in the number of molecules and duration of therapy used to treat MABC PJI. As reported in Table 1 [7–22] in all but two [10,19] cases of successfully treated MABC PJI, a multidrug regimen containing at least 3 molecules was used, at least for the intensive phase. The mean duration of antimycobacterial therapy of successfully treated MABC PJI was 39 ± 23 weeks. In our case, antimycobacterial therapy was administered for 7 months with a regimen containing at least 3 drugs for the entire duration of treatment (Fig. 1). For a brief period, we combined cefoxitin with imipenem/cilastatin to increase the efficacy of the multidrug regimen in use, considering the in vitro synergism of dual β-lactams against *M. abscessus* proved by recent studies [28,29]. Based on the results of the initial phenotypic DST, the range of drugs tested was broadened to maintain 3 active molecules in the simplified regimen (Table 2). Subsequently, imipenem/cilastatin was replaced with clofazimine in outpatient treatment, considering multiple evidence, despite the absence of established MIC breakpoints [26,27]. Actually, MICs suggested for susceptibility were higher than our [26]. TDM was performed in order to minimize toxicities, nevertheless the patient still developed side effects attributable to the long treatment with the multidrug regimen, in particular aminoglycoside-induced hearing loss [33] and reversible linezolid-related polyneuropathy [34]. Although linezolid is typically used once-daily for mycobacterial infections, PK-PD data do not exist for RGM infections, as they do for TB [35–37]. In addition, linezolid MICs are typically much lower for *Mycobacterium*

*tuberculosis* (usually <1 μg/ml, even in cases of XDR-TB) than for RGMs. Considering the exposure-dependent antibacterial activity of linezolid and T > MIC at least > 85% as a PK-PD index that can predict clinical efficacy [38], it is reasonable to assume that linezolid dosing used for TB is inadequate for RGM infections and dosage should be individualized based on the MIC of the isolate (Table 2). Given the above and despite the concentration-related toxicity reported by various studies [39], but not others [40,41], we tried to maintain $C_{min}$ around 8 mg/L through a twice-daily dosing. PK-PD studies in RGM infections are warranted to determine the most appropriate linezolid dosing. We did not ask the reference laboratory to test synthetic tetracyclines (tigecycline and eravacycline) as the intravenous regimen was already adequate and we needed instead effective oral drugs in order to manage the patient with triweekly DH admissions. Note that omadacyclin is not available in Europe yet. Still, this class of antibiotics has proven to be a viable option in the treatment of M. abscessus infections [42]. As for surgical interventions, aggressive ones in the early stages of the disease may shorten the course of antimycobacterial therapy and improve infection control rate. Prosthesis removal has been associated with a favorable outcome at 6–12 months, and in NTM PJI is required in almost 90% of cases, but the optimal surgical strategy for the treatment of RGM PJI has yet to be defined [5,24]. As reported in Table 1 [7–22] 14 of 17 (82 %) successfully treated MABC PJI cases required a 2-stage revision arthroplasty, one patient [8] underwent hemipelvectomy and one [13] underwent arthrodesis. Only one patient [17] was successfully treated with debridement, antibiotics and implant retention (DAIR). Our patient underwent a revision surgery, with debridement and spacer renewal, approximately one week after the start of targeted therapy. Arthrodesis was performed after five and a half months of antimycobacterial treatment, due to significant bone loss and soft tissue compromise, collecting a sample for microbiological examination, which resulted negative. The multidrug regimen was then continued for another 5 weeks (Fig. 1).

In summary, *M. abscessus* is a rare but emerging cause of PJI and should be suspected particularly when dealing with early-onset, culture negative and/or refractory PJI. In the management of MABC PJI, the critical points are the combination of antimycobacterial drugs, the correlation between DST and clinical outcomes, the optimal type and timing of surgery, and the duration of antimycobacterial therapy. Based on the reported case, the proposal for the management of this uncommon infection is to tailor medical and surgical therapy according to the DST data and the clinical course.

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## Authors' contribution

GM and MG conceived the report. GM performed the literature review, wrote the draft and edited the manuscript for content and wording. All co-authors were responsible for critically reviewing the draft. All authors read and approved the final manuscript.

## Patient consent

The patient described in this report has signed informed consent to the use of her clinical data. No formal approval by an ethics committee is required for this type of paper.

## Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jctube.2024.100440.

## References

[1] Tande AJ, Patel R. Prosthetic joint infection. Clin Microbiol Rev 2014;27(2):302–45.
[2] Beam E, Osmon D. Prosthetic joint infection update. Infect Dis Clin North Am 2018;32(4):843–59.
[3] Del Pozo JL, Patel R. Clinical practice. Infection associated with prosthetic joints. N Engl J Med 2009;361(8):787–94.
[4] Azzam K, Parvizi J, Jungkind D, Hanssen A, Fehring T, Springer B, et al. Microbiological, clinical, and surgical features of fungal prosthetic joint infections: a multi-institutional experience. J Bone Joint Surg Am 2009;91(Supplement_6):142–9.
[5] Santoso A, Phatama KY, Rhatomy S, Budhiparama NC. Prosthetic joint infection of the hip and knee due to *Mycobacterium species*: a systematic review. World J Orthop 2022;13(5):503–14.
[6] Brown-Elliott BA, Philley JV, Schlossberg D. Rapidly growing mycobacteria. Microbiol Spectr 2017;5(1).
[7] Spanyer JM, Foster S, Thum-DiCesare JA, Kwon YM, Burke DW, Nelson SB. Mycobacterium abscessus: a rare cause of periprosthetic knee joint infection. Am J Orthop (Belle Mead NJ) 2018;47(9).
[8] Goldstein N, St Clair JB, Kasperbauer SH, Daley CL, Lindeque B. Nontuberculous mycobacterial musculoskeletal infection cases from a tertiary referral center, Colorado, USA. Emerg Infect Dis 2019;25(6):1075–83.
[9] Kim M, Ha CW, Jang JW, Park YB. Rapidly growing non-tuberculous mycobacteria infection of prosthetic knee joints: a report of two cases. Knee 2017;24(4):869–75.
[10] Henry MW, Miller AO, Kahn B, Windsor RE, Brause BD. Prosthetic joint infections secondary to rapidly growing mycobacteria: two case reports and a review of the literature. Infect Dis (Lond) 2016;48(6):453–60.
[11] Wang SX, Yang CJ, Chen YC, Lay CJ, Tsai CC. Septic arthritis caused by Mycobacterium fortuitum and Mycobacterium abscessus in a prosthetic knee joint: case report and review of literature. Intern Med 2011;50(19):2227–32.
[12] Eid AJ, Berbari EF, Sia IG, Wengenack NL, Osmon DR, Razonable RR. Prosthetic joint infection due to rapidly growing mycobacteria: report of 8 cases and review of the literature. Clin Infect Dis 2007;45(6):687–94.
[13] Malhotra R, Bala K, Gautam D, Bhattacharya A, Xess AB, Pandey P, et al. Mycobacterium abscessus Periprosthetic joint infection following bilateral Total Knee arthroplasty. IDCases 2019;17:e00542.
[14] Amit P, Rastogi S, Marya S. Prosthetic knee joint infection due to Mycobacterium abscessus. Indian J Orthop 2017;51(3):337–42.
[15] Pace V, Antinolfi P, Borroni E, Cirillo DM, Cenci E, Piersimoni C, et al. Treating primary arthroprosthesis infection caused by Mycobacterium abscessus subsp. abscessus. Case Rep. Infect Dis 2019;2019:5892913.
[16] Nengue L, Diaz MAA, Sherman CE, Bhasin A, Libertin CR. Mycobacterium abscessus Prosthetic Joint Infections of the Knee. J Bone Jt Infect 2019;4(5):223–6.
[17] Tsuruyama Y, Mori N, Fujisawa T, Katayama M. Disseminated Mycobacterium abscessus subspecies massiliense infection and subsequent prosthetic joint infection in a hemodialysis patient: a case report. J Infect Chemother 2021;27(10):1504–7.
[18] Genovese N, Auld T, Dever LL, Rossman SR. Mycobacterium abscessus periprosthetic hip infection complicated by superimposed polymicrobial infection: a case report. JBJS Case Connect. 2021;11(4).
[19] Petrosoniak A, Kim P, Desjardins M, Lee BC. Successful treatment of a prosthetic joint infection due to Mycobacterium abscessus. Can J Infect Dis Med Microbiol 2009;20(3):e94–6.
[20] Ma Q, Chen R, Yang E, Yuan Y, Tian Y, Han Y, et al. Non-tuberculous Mycobacterial Infection of the Musculoskeletal System Detected at Two Tertiary Medical Centres in Henan, China, 2016–2020. Front Microbiol 2021;12:791918.
[21] Park JW, Kim YS, Yoon JO, Kim JS, Chang JS, Kim JM, et al. Non-tuberculous mycobacterial infection of the musculoskeletal system: pattern of infection and efficacy of combined surgical/antimicrobial treatment. Bone Joint J 2014;96-B(11):1561–5.
[22] Singh D, Johnson M, Kitchens CS, Boone A. Challenges in treating *Mycobacterium chelonae/abscessus* prosthetic joint infection. J Pharm Pract 2022;35(3):492–4.
[23] Griffith DE, Aksamit T, Brown-Elliott BA, Catanzaro A, Daley C, Gordin F, et al. An official ATS/IDSA statement: diagnosis, treatment, and prevention of nontuberculous mycobacterial diseases. Am J Respir Crit Care Med 2007;175(4):367–416.
[24] Jitmuang A, Yuenyongviwat V, Charoencholvanich K, Chayakulkeeree M. Rapidly-growing mycobacterial infection: a recognized cause of early-onset prosthetic joint infection. BMC Infect Dis 2017;17(1):802.
[25] Clinical and Laboratory Standards Institute. Susceptibility testing of mycobacteria, nocardia spp, and other aerobic actinomyces. 3rd ed. M24. Clinical and Laboratory Standards Institute. Wayne, PA 2018.

[26] Hajikhani B, Nasiri MJ, Hosseini SS, Khalili F, Karimi-Yazdi M, Hematian A, et al. Clofazimine susceptibility testing of Mycobacterium avium complex and Mycobacterium abscessus: a meta-analysis study. J Glob Antimicrob Resist 2021; 26:188–93.
[27] Van Ingen J, Totten SE, Helstrom NK, Heifets LB, Boeree MJ, Daley CL. In vitro synergy between clofazimine and amikacin in treatment of nontuberculous mycobacterial disease. Antimicrob Agents Chemother 2012;56(12):6324–7.
[28] Kumar P, Chauhan V, Silva JRA, et al. Mycobacterium abscessus l, d-transpeptidases are susceptible to inactivation by carbapenems and cephalosporins but not penicillins. Antimicrob Agents Chemother 2017;61(10):e00866–917.
[29] Story-Roller E, Maggioncalda EC, Lamichhane G. Select β-lactam combinations exhibit synergy against Mycobacterium abscessus in vitro. Antimicrob Agents Chemother 2019;63(4). e02613–18.
[30] Aziz DB, Low JL, Wu M-L, Gengenbacher M, Teo JWP, Dartois V, et al. Rifabutin is active against Mycobacterium abscessus complex. Antimicrob Agents Chemother 2017;61(6). e00155–17.
[31] Nash KA, Brown-Elliott BA, Wallace Jr RJ. A novel gene, erm(41), confers inducible macrolide resistance to clinical isolates of Mycobacterium abscessus but is absent from Mycobacterium chelonae. Antimicrob Agents Chemother 2009;53 (4):1367–76.
[32] Daley CL, Iaccarino JM, Lange C, Cambau E, Wallace RJ, Andrejak C, et al. Treatment of nontuberculous mycobacterial pulmonary disease: an official ATS/ERS/ESCMID/IDSA clinical practice guideline. Clin Infect Dis 2020;71(4):905–13.
[33] Steyger PS. Mechanisms of aminoglycoside- and cisplatin-induced ototoxicity. Am J Audiol 2021;30(3S):887–900.
[34] Migliori GB, Eker B, Richardson MD, Sotgiu G, Zellweger J-P, Skrahina A, et al. A retrospective TBNET assessment of linezolid safety, tolerability and efficacy in multidrug-resistant tuberculosis. Eur Respir J 2009;34(2):387–93.
[35] Abdelwahab MT, Wasserman S, Brust JCM, Dheda K, Wiesner L, Gandhi NR, et al. Linezolid population pharmacokinetics in south african adults with drug-resistant tuberculosis. Antimicrob Agents Chemother 2021;65(12):e0138121.
[36] Alghamdi WA, Al-Shaer MH, An G, Alsultan A, Kipiani M, Barbakadze K, et al. Population pharmacokinetics of linezolid in tuberculosis patients: dosing regimen simulation and target attainment analysis. Antimicrob Agents Chemother 2020;64 (10). e01174–20.
[37] Tietjen AK, Kroemer N, Cattaneo D, Baldelli S, Wicha SG. Population pharmacokinetics and target attainment analysis of linezolid in multidrug-resistant tuberculosis patients. Br J Clin Pharmacol 2022;88(4):1835–44.
[38] Bandín-Vilar E, García-Quintanilla L, Castro-Balado A, Zarra-Ferro I, González-Barcia M, Campos-Toimil M, et al. A review of population pharmacokinetic analyses of linezolid. Clin Pharmacokinet 2022;61(6):789–817.
[39] Song T, Lee M, Jeon H-S, Park Y, Dodd LE, Dartois V, et al. Linezolid trough concentrations correlate with mitochondrial toxicity-related adverse events in the treatment of chronic extensively drug-resistant tuberculosis. EBioMedicine 2015;2 (11):1627–33.
[40] Imperial MZ, Nedelman JR, Conradie F, Savic RM. Proposed linezolid dosing strategies to minimize adverse events for treatment of extensively drug-resistant tuberculosis. Clin Infect Dis 2022;74(10):1736–47.
[41] Jaspard M, Butel N, El Helali N, Marigot-Outtandy D, Guillot H, Peytavin G, et al. Linezolid-associated neurologic adverse events in patients with multidrug-resistant tuberculosis, France. Emerg Infect Dis 2020;26(8):1792–800.
[42] Li A, He S, Li J, Zhang Z, Li B, Chu H, et al. Omadacycline, eravacycline, and tigecycline express anti-Mycobacterium abscessus activity *in vitro*. Microbiol Spectr 2023;11(3):e0071823.