

Peritoneal Dialysis–Associated Peritonitis Caused by *Mycobacterium abscessus* in Children—A Case Report

Omar Imam,¹ Khaled Al-Zubaidi,¹ Mohammad Janahi,^{1,4,5} Abubakr Imam,^{3,4,5} Bassil Leghrouz,³ Simon Dobson,^{4,5} Sathyavathi Sundararaju,² Kin Ming Tsui,² Mohammad Rubayet Hasan,^{2,4,5} and Andres Perez-Lopez^{2,4,5}

¹Division of Pediatric Infectious Diseases, Doha, Qatar, ²Division of Microbiology, Doha, Qatar, ³Division of Pediatric Nephrology, Doha, Qatar, ⁴Department of Infection Prevention and Control, Sidra Medicine, Doha, Qatar, and ⁵Weill Cornell Medical College in Qatar, Doha, Qatar

Peritoneal dialysis (PD)–associated peritonitis constitutes a major complication associated with the procedure. PD-associated peritonitis caused by nontuberculous mycobacteria, usually as a result of an infection related to the PD catheter, has been reported in adults and is associated with significant complications and poor outcome. The management of PD-associated peritonitis caused by *Mycobacterium abscessus* is particularly challenging because this species is resistant to many antimicrobials commonly used to treat mycobacterial species. We present here the second reported case of PD-associated peritonitis caused by *M. abscessus* in children. Our patient was a 9-year-old boy with end-stage renal disease (ESRD) who presented with suspected peritonitis, and his PD fluid cultures eventually grew *M. abscessus*. The patient received a 3-week course of triple therapy with clarithromycin, amikacin, and meropenem in addition to PD catheter removal. The infection completely resolved even though a susceptibility report at the end of treatment revealed that the isolate was resistant to clarithromycin and had decreased susceptibility to carbapenems. Our observations suggest that PD catheter removal is important in PD-associated peritonitis caused by *M. abscessus* in children and that more studies are needed to define the optimal length of treatment.

Keywords. catheter; clarithromycin; *Mycobacterium abscessus*; nontuberculous mycobacteria; peritoneal dialysis–associated peritonitis.

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Correspondence: O. Imam, MBBS, Division of Pediatric Infectious Diseases, Office no: 7th floor, tower C, I Luqta Street, Education City, North Campus, Qatar Foundation, PO Box 26999, Doha, Qatar (oimam@sidra.org).

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CASE REPORT

A 9-year-old boy with end-stage renal disease (ESRD) secondary to bilateral multicystic dysplastic kidneys who was on ambulatory peritoneal dialysis (PD) was admitted with a 3-day history of severe abdominal pain, fever, runny nose, and elevated C-reactive protein (CRP) (Table 1). For 8 months before admission, the patient had been having recurrent episodes of PD catheter exit site infection caused by *Pseudomonas aeruginosa* treated with topical gentamicin and culture-negative PD-associated peritonitis treated with oral ciprofloxacin and intraperitoneal ceftazidime. No further molecular testing was done on the PD fluid. The infection was managed with the catheter in place because the family did not consent to PD catheter removal at that time.

The patient was suspected to have PD-associated peritonitis. PD fluid analysis revealed 168×10^6 WBC/mL with 68% neutrophils. Purulent discharge collected from the exit site again grew *P. aeruginosa*. He was started on intravenous (IV) ceftazidime and gentamicin. However, as fever and severe abdominal pain persisted and CRP continued to rise (peaked 290 mg/dL), he was switched 3 days later to caspofungin, vancomycin, and cefepime (Table 1). Subsequently, gram-negative coverage was changed from cefepime to meropenem. A PD fluid sample submitted for culture did not yield any organism on solid media (Table 1). However, bacterial growth was detected on the enrichment broth inoculated with an aliquot of the PD fluid on hospital day 6. When the broth was subcultured onto agar plates, a rapidly growing *Mycobacterium* grew on chocolate agar medium (BD). The organism was identified as *Mycobacterium abscessus* by matrix-assisted laser-desorption ionization time-of-flight mass spectrometry (MALDI-TOF; Bruker, Germany). The same organism grew on solid chocolate agar medium from a second PD fluid specimen collected 3 days later. The identification of the organism isolated from both specimens was confirmed as *M. abscessus* by the local tuberculosis (TB) reference laboratory. Consequently, therapy was empirically changed to IV amikacin, oral clarithromycin, and IV meropenem, pending antimicrobial susceptibilities. In addition, the PD catheter was removed on hospital day 13, and the patient was switched to hemodialysis. The patient became afebrile on day 15 of hospitalization, abdominal pain gradually resolved, and inflammatory markers declined to normal values. Antimicrobial susceptibility profiles reported by the reference laboratory 3 weeks later revealed that the isolate was only susceptible to amikacin (Table 2). By contrast, the isolate had intermediate susceptibility to cefoxitin and imipenem and was resistant to tobramycin, clarithromycin, ciprofloxacin, moxifloxacin, doxycycline, minocycline, co-trimoxazole, and linezolid.

Table 1. Laboratory Results Related to Peritonitis

Hospital Day Since Presentation	Peritoneal Dialysis Fluid Cell Count	Peritoneal Dialysis Fluid Culture	CRP, mg/L	Antibiotics
Day 5	150 × 10 ⁶ /L, predominantly monocytes	Negative	197.1	Ceftazidime/gentamycin
Day 6	39 × 10 ⁶ /L, predominantly lymphocytes	Negative	246.2	Ceftazidime
Day 10	168 × 10 ⁶ /L, predominantly neutrophils	<i>M. abscessus</i>	244.9	IP cefepime/casopofungin
Day 11	49 × 10 ⁶ /L, predominantly neutrophils	Not done	296.7	Meropenem/vancomycin
Day 14	109 × 10 ⁶ /L, predominantly neutrophils	<i>M. abscessus</i>	312.3	Meropenem/amikacin/clarithromycin

Abbreviations: CRP, C-reactive protein; IP, intraperitoneal.

The medical team managing the patient decided on 6 months of triple therapy at home. However, during the first follow-up visit 6 weeks later, it was found that all antibiotics had been discontinued after 3 weeks of treatment. This was due to a miscommunication between the teams caring for the patient. As the patient was asymptomatic, it was decided not to pursue further treatment. After a 15-month follow-up, the child remained asymptomatic with normal inflammatory markers and was doing well in hemodialysis. Additionally, a positron emission tomography (PET) scan performed at the end of the follow-up revealed no intra-abdominal enhancement.

In order to characterize the *M. abscessus* strain isolated from PD fluid cultures, whole-genome sequencing (WGS) was performed in our laboratory on an Illumina MiSeq (Illumina, San Diego, CA, USA) platform. DNA extraction and library preparation were prepared as previously described [1]. The raw data were assembled *de novo* using SPAdes, version 3.9.0 [1]. The assembled genome data were analyzed using resource tools such as CARD [2] and Resfinder [3] and the multilocus sequence typing (MLST) provided by the Center for Genomic Epidemiology (<https://cge.cbs.dtu.dk/services/>), as well as

MAB MLST [4]. The species was identified as *Mycobacterium abscessus* subspecies *abscessus*. The draft genome size of the *M. abscessus* isolate was about 5.5 Mb. Using the conventional 7-locus MLST scheme, we determined that the strain belongs to sequence type (ST) 24. Genome analysis indicated the presence of *mtrA* (efflux pump), *erm(41)*, and *rrl* with nucleotide “A” at positions 2269, 2270, and 2271, as well as a mutation at position A2059G, which could be responsible for the observed resistance to clarithromycin [5]. The strain also has prominent mutations at *gyrA* (Ala83) and *gyrB* (Arg447 and Asn464), which can confer resistance to ciprofloxacin (fluoroquinolones) [6].

DISCUSSION

This case, to our knowledge, is the second reported pediatric case of PD-associated peritonitis caused by *M. abscessus* in children. The first case, recently reported from the National University Hospital in Singapore, is similar to our case in that both patients were on PD because of bilateral dysplastic kidneys, and both patients had recurrent PD catheter exit site infection caused by *P. aeruginosa* [7]. Our isolate was only isolated from PD fluid and was only susceptible to amikacin. In contrast, the isolate reported in Singapore was isolated from both PD fluid and PD catheter exit site swab and was susceptible to ceftazidime, amikacin, clarithromycin, and clofazimine. In the first case, the patient became symptom-free after 6 days of treatment with oral clarithromycin and clofazimine and IV amikacin, but treatment with clarithromycin and clofazimine was continued for a further 9 months. On the other hand, our patient received a combination of IV amikacin and meropenem and oral clarithromycin for 3 weeks only. PD catheters were removed in both cases after 8 days and 9 days, respectively.

Peritonitis secondary to peritoneal catheter infection is a common complication of PD and the most common cause of catheter removal in patients with ESRD awaiting kidney transplant [8]. Although improvement in aseptic techniques during insertion and manipulation of PD catheters has led to a decrease in the incidence of PD-associated peritonitis over the last years, its frequency remains higher in the pediatric population compared with adults.

PD-associated peritonitis is commonly caused by coagulase-negative staphylococci, *Staphylococcus aureus*, and *P. aeruginosa*,

Table 2. Antibiotic Susceptibility Profile of the *Mycobacterium abscessus* Isolate

Antibiotic	MIC, µg/mL	Interpretation
Cefoxitin	64	I
Imipenem	16	I
Ciprofloxacin	>4	R
Moxifloxacin	>8	R
Clarithromycin ^a	8	R
Amikacin	16	S
Tobramycin	16	R
Doxycycline	>16	R
Minocycline	>8	R
Tigecycline	0.5	^b
TMP/SMX	>8/152	R
Linezolid	>32	R

Abbreviations: I, intermediate; MIC, minimum inhibitory concentration; R, resistant; S, sensitive; TMP/SMX, trimethoprim-sulfamethoxazole.

^a*M. abscessus* isolate was incubated for 14 days with clarithromycin for inducible resistance (*erm* gene), and inducible clarithromycin resistance was detected.

^bNo established interpretive guideline available.

with nontuberculous mycobacteria (NTM) only rarely involved [8–10]. *M. abscessus* has been sporadically reported in PD-associated peritonitis in adults, for whom the treatment is particularly challenging because of the presence of multiple intrinsic and acquired resistance mechanisms that frequently render antimicrobials, employed to treat other species, ineffective [11]. It is also worth noting that topical application of gentamicin cream for exit site infection has been notoriously associated with *M. abscessus* peritonitis, albeit anecdotally, and our patient had been using it for a prolonged period. A study showed 9 cases of adult NTM peritonitis with patients using gentamicin cream, with no cases in patients not using gentamicin cream [12].

M. abscessus is a rapidly growing NTM found ubiquitously in soil and water. It has been recognized as an emerging pathogen responsible for a broad range of infections, especially in immunocompromised patients. For instance, *M. abscessus* is currently the main NTM isolated from broncho-pulmonary infections in children with chronic lung diseases, particularly cystic fibrosis [13]. It has also been reported to cause a broad spectrum of infections in the immunocompromised host such as skin and soft tissue infections, lymphadenitis, bacteremia, central nervous system infection, and ocular and dental infections [6, 14]. Furthermore, *M. abscessus* has also been associated with surgical site infections after cosmetic surgery in immunocompetent patients [15].

The isolate recovered from the PD fluid of our patient was phenotypically resistant to most antibiotics tested except amikacin. WGS analysis of the isolate revealed potential mutations that could be responsible for the resistance to clarithromycin and fluoroquinolone antibiotics. *M. abscessus* is intrinsically a multidrug-resistant organism. The thick lipophilic cell wall of the organism makes it resistant to most beta-lactam antibiotics. Furthermore, the mycobacteria possess antibiotic-modifying enzymes that confer resistance to rifampin and sometimes aminoglycosides. They also have polymorphisms in the genes that encode DNA gyrase enzymes, which confer resistance to fluoroquinolones. As a result, only a limited number of the antibiotics can be used to treat infections with *M. abscessus*. These include amikacin, carbapenems, ceftazidime, and clarithromycin. However, resistance to these antibiotics is not uncommon as well. Amikacin susceptibility remains high (90%). However, a study showed only 55% pooled susceptibility to imipenem. Furthermore, target-modifying enzymes, such as those encoded by the *erm(41)*, result in inducible resistance to macrolides [4, 16].

Peritonitis caused by *M. abscessus* is usually managed in adults with catheter removal and a combination of 2 to 3 agents for 3 to 6 months [11]. Notably, our patient improved clinically despite that the organism had decreased susceptibility to carbapenems and was resistant to macrolides, 2 antibiotic classes used for his treatment, suggesting that catheter removal is the cornerstone for the treatment of such infections. Moreover, the fact that our

patient improved with a short course of antibiotic treatment highlights the need for more data to define the optimal length of treatment for *M. abscessus* and other rapidly growing mycobacteria in PD-associated peritonitis.

In summary, PD-associated peritonitis caused by *M. abscessus* is a very uncommon entity. Although antibiotic treatment is challenging due to the common resistance of this microorganism to antimycobacterial drugs, our report suggests that if the PD catheter is promptly removed, prolonged antibiotic courses may not be necessary.

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Patient consent. The patient's guardian and the patient provided written informed consents to publish their child's personal or clinical details along with any identifying images. This conforms with the criteria placed by Sidra Institutional Review Board for the publication of case reports.

Availability of data. The sequence data has been deposited at DDBJ/ENA/GenBank under the BioProject PNJNA577539 and BioSample SAMN13885210.

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