Successful Treatment with Clofazimine for Macrolide-Resistant *Mycobacterium abscessus* Infection in a Peritoneal Dialysis Patient: A Case Report and Literature Review

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Abstract

Nontuberculous mycobacteria are rare but serious pathogens in peritoneal dialysis (PD)-associated infections. *Mycobacterium abscessus (M. abscessus*) is usually resistant to standard anti-tuberculosis drugs. Macrolide antibiotics are key drugs for treating *M. abscessus*, but macrolide-resistant strains pose particular challenges, and optimal antimicrobial treatment strategy or duration have not been established for *M. abscessus* PD-associated infections. We report a case of a 63-year-old man on PD who developed persistent purulent discharge from his PD catheter exit site. Skin swab culture identified macrolide-resistant *M. abscessus* with imaging confirming inflammation along the catheter tunnel. These findings led to the diagnosis of *M. abscessus* PD catheter tunnel infection, with peritonitis excluded. Initial management included early catheter removal, extensive surgical debridement and 6 weeks of combination antibiotic therapy including imipenem-cilastatin, amikacin and clarithromycin, achieving clinical cure. However, the infection recurred after 5 months, necessitating retreatment with debridement and an antibiotic regimen including imipenem-cilastatin, amikacin, azithromycin and clofazimine for 4 weeks, followed by a continuation regimen with amikacin, clofazimine and sitafloxacin for 4 months. This approach achieved sustained clinical cure without recurrence at 14 months follow-up. Based on a literature review of 67 cases of *M. abscessus* PD-associated infections, all 6 cases treated with clofazimine achieved clinical cure, but there were no reports on cases of macrolide-resistant *M. abscessus* treated with clofazimine. Our case represents the first successful clofazimine treatment of macrolide-resistant *M. abscessus* PD-associated infection, demonstrating clofazimine as a potentially effective oral antibiotic option in combination therapy, particularly in macrolide-resistant cases with limited therapeutic options.

Keywords:

Clofazimine, Infection, Macrolide resistant species, *Mycobacterium abscessus*, Nontuberculous mycobacteria, Peritoneal dialysis

Background

Nontuberculous mycobacteria (NTM) are rare but important causes of peritoneal dialysis (PD)-associated infections with poor prognosis, leading to PD discontinuation in 92.9% of the affected patients.(1) *Mycobacterium abscessus* (*M. abscessus*), widely found in soil and water, comprises 8.8% of NTM PD-associated infections.(1) While most NTM species are sensitive to standard anti-tuberculosis drugs, *M. abscessus* species are resistant to these drugs,(2) thus antimicrobial treatment strategy or duration for *M. abscessus* in PD-associated infections have not been established.(3) Macrolide antibiotics are key drugs for treating *M. abscessus* due to their antimicrobial activity and immunomodulatory effects. However, treatment becomes difficult with macrolide-resistant strains, which have few available antimicrobial options, especially oral agents for prolonged therapy.

We describe a case of PD-associated infection caused by macrolide-resistant *M. abscessus* that recurred despite multimodal therapy including early catheter removal, extensive surgical debridement and multidrug antimicrobial therapy. The patient finally achieved sustained cure with multidrug antimicrobial regimens including clofazimine. We reviewed *M. abscessus* PD-associated infections in the literature and suggest clofazimine as a potentially effective oral antibiotic in this context, especially for macrolide-resistant cases with limited therapeutic options.

Case Presentation

A 63-year-old man with end-stage kidney disease secondary to autosomal dominant polycystic kidney disease, who had been on PD for one year, presented with persistent purulent discharge from his PD catheter exit site. The patient had used topical gentamicin

cream as prophylaxis for exit-site infection. Despite one week of oral amoxicillin therapy, the purulent discharge continued, prompting hospital admission.

The patient had a history of subarachnoid hemorrhage but no history of peritoneal dialysis-related infections or immunocompromising conditions such as cancers, diabetes mellitus or use of immunosuppressants. Physical examination revealed localized erythema and purulent discharge at the catheter exit site, without fever, abdominal tenderness, or abnormal vital signs. Laboratory findings showed slight elevation in C-reactive protein (0.17 mg/dL), while peritoneal dialysis effluent remained clear with normal white blood cell count (18 cells/μL) and negative bacterial culture, ruling out peritonitis. Ultrasound, computed tomography and magnetic resonance imaging demonstrated a fluid collection with subcutaneous inflammation along the catheter tunnel tract, without extension into deeper fascial layers or the peritoneal cavity.

Skin swab culture from the catheter exit site revealed NTM, subsequently identified as *M. abscessus.* Antimicrobial susceptibility testing based on Clinical and Laboratory Standards Institute standards (document M24, 3rd edition) revealed clarithromycin susceptibility at day 3 (minimum inhibitory concentration (MIC) 1 μg/mL) but resistance at day 14 (MIC >128 μg/mL), indicating inducible macrolide resistance. Susceptibility to amikacin (MIC 8 μg/mL) and intermediate susceptibility to imipenem/cilastatin (MIC 8 μg/mL) were confirmed. Blood culture was negative.

The patient was diagnosed with *M. abscessus* PD catheter tunnel infection. Under consultation with an infectious disease specialist, management included PD catheter removal on day 4 of hospitalization without second catheter replacement, transition to hemodialysis, extensive surgical debridement, and antimicrobial therapy including imipenem-cilastatin, amikacin and clarithromycin. Inflammatory markers normalized and

purulent drainage resolved, thus antibiotic therapy was completed after 6 weeks with apparent clinical cure (Figure 1).

However, 5 months later, purulent discharge recurred at the same site. Extensive debridement was performed, and therapy consisting of imipenem-cilastatin, amikacin, azithromycin and clofazimine (MIC 1 μg/mL) was administered for four weeks during hospitalization. Following treatment initiation, the purulent drainage ceased and inflammatory markers improved. Subsequently, a continuation regimen of amikacin, clofazimine, and sitafloxacin was administered for 4 months. The post-surgical wound achieved complete epithelialization without inflammatory recurrence, and antimicrobial therapy was completed (Figure 1). Safety monitoring including assessment for skin discoloration, liver function, and electrocardiography showed no adverse effects. At the 14-month follow-up, the patient remained recurrence-free while continuing hemodialysis.

Discussion

We report the first case of macrolide-resistant *M. abscessus* PD catheter tunnel infection successfully treated with clofazimine-containing therapy combined with PD catheter removal, extensive surgical debridement and prolonged antimicrobial treatment. Our case demonstrates the challenges of this disease, which initially responded to therapy but recurred 5 months later. The use of topical gentamicin prophylaxis may have contributed to this infection through selection pressure of resistant organisms.(4)(5) Given the limited evidence for antimicrobial therapeutic strategies, particularly for macrolide-resistant strains, our case suggests the potential effectiveness of clofazimine as a viable oral antibiotic option for prolonged therapy.

Literature search on PubMed identified 67 cases of *M. abscessus* PD-associated infections reported between 1998 and 2024 (Supplementary Table 1). While 56 cases achieved cure, 10 cases (15.2%) died due to progression to peritonitis, concurrent secondary infections, or sepsis, highlighting the life-threatening nature of these infections. Our analysis of these reported cases showed macrolide-sensitive *M. abscessus* achieved clinical cure in 94% of cases compared to 80% for macrolide-resistant strains. Importantly, catheter management appeared critical for outcomes. PD catheters were removed in 60 of 67 cases (89.6%), while 3 of the 7 non-removal cases (42.9%) resulted in death. Among the 39 cases with documented catheter removal timing, all 25 cases (64.1%) with removal within 22 days achieved cure, whereas 3 of the 14 cases (21.4%) with delayed removal (>22 days) died. These findings support early catheter removal as crucial for successful treatment. In our case, catheter removal 11 days after symptom onset likely contributed to the favorable initial response.

The antimicrobial treatment strategy has not been established for *M. abscessus* PD-associated infections, particularly for macrolide-resistant species, as evidenced by varied antibiotic selections and treatment durations in the literature (Supplementary Table 1). For skin NTM infections, the ATS/IDSA statement recommends combination therapy with intravenous antibiotics (amikacin, imipenem-cilastatin, or cefoxitin) and oral antibiotics (clarithromycin or azithromycin) but provides no specific guidance for macrolide-resistant species.(6) For pulmonary NTM infections, guidelines recommend initial treatment with three or more antibiotics for macrolide-resistant *M. abscessus*, including parenteral agents (amikacin, imipenem-cilastatin, or tigecycline) and oral agents (clarithromycin, azithromycin, clofazimine, or linezolid), followed by continuation

regimen with two or more antibiotics.(2) Despite macrolide resistance, macrolide antibiotics remain treatment options due to potential immunomodulatory effects. These guidelines do not specify treatment recommendation durations due to insufficient evidence. Our literature analysis of 57 patients with PD catheter removal showed clinical cure rates increased with antimicrobial combination therapy: 2 drugs (81.8%), 3 drugs (89.5%), 4 drugs (100%), supporting use of three or more antimicrobial agents.

Our initial treatment strategy closely followed these guidelines, combining imipenem-cilastatin, amikacin and azithromycin for 6 weeks. Given localized subcutaneous tissue involvement on imaging, we performed early catheter removal and extensive surgical debridement. Despite this comprehensive approach, the infection recurred after 5 months. For the recurrence, we maintained the same initial regimen but added clofazimine, followed by a continuation regimen with amikacin, clofazimine and sitafloxacin for 4 months. This approach resulted in clinical cure without recurrence at 14 months follow-up. The addition of clofazimine appears crucial in achieving sustained cure in this challenging case.

Among the 67 reported cases of *M. abscessus* PD-associated infections, 6 cases with macrolide-sensitive species were treated with clofazimine (Table 1). Importantly, all these 6 cases achieved clinical cure. Clofazimine was originally developed as an oral antituberculosis drug and is currently used primarily for the treatment of leprosy. The drug accumulates in tissues rich in fat and macrophages such as skin tissue,(7) supporting efficacy for *M. abscessus* PD-associated infections involving skin tissue. In our patient, the MIC for clofazimine was 1 μg/mL, which we considered as susceptible based on reported breakpoints (≦2 μg/mL) (8)(9) and wild-type *M. abscessus* ATCC 19977 MIC of 2 μg/mL.(10) Notably, clofazimine undergoes hepatic metabolism with

negligible renal clearance,(7) requiring no dose adjustment for patients with kidney dysfunction at the standard dose of 100 mg once daily for NTM infections.(11) Furthermore, clofazimine and amikacin demonstrate significant synergistic activity *in vitro*, with a 4- to 8-fold MIC reduction for both drugs in 56 of 68 strains of *M. abscessus*.(12) Additionally, omadacycline, a novel tetracycline active against *M. abscessus,* shows synergistic effects with clofazimine, further supporting clofazimine as a valuable treatment option for combination therapy.(13) However, macrolide-resistant *M. abscessus* PD-associated infections treated with clofazimine have not been reported. Given its oral availability and the limited therapeutic options, clofazimine would represent a valuable option for such challenging cases.

One potential limitation of our case report is the relatively short initial treatment duration. As adequate debridement was achieved and clinical improvement was observed, our patient received 6 weeks of antimicrobial therapy, which falls at the lower limit of IDSA-recommended duration (6-12 weeks) for NTM skin and soft tissue infections.(14) Our review of 55 reported cases with PD catheter removal and documented outcomes showed that clinical cure was achieved with mean treatment duration of 4.6 ±3.3 months, compared to 0.75 ±0.5 months in poor-outcome cases. These findings suggest that macrolide-resistant *M. abscessus* appears to require more prolonged antimicrobial therapy despite adequate source control and absence of peritonitis. Collectively, these observations indicate that optimal treatment duration for *M. abscessus* infections remains difficult to define due to substantial heterogeneity among reported cases, and that macrolide resistance and the intensity of combination antimicrobial therapy are important determinants of treatment response.

In conclusion, our case represents the first successful treatment of macrolide-resistant *M. abscessus* PD-associated infection using clofazimine-containing combination therapy, demonstrating clofazimine as a potential therapeutic option in combination therapy. Multimodal therapy including early catheter removal, extensive surgical debridement, and prolonged multidrug antimicrobial regimens containing clofazimine may represent a viable treatment strategy for sustained cure in this challenging clinical context.

Declarations

Acknowledgements

The Institutional Research Ethics Board does not require board review for a single case report when the patient's privacy is protected.

Ethics statement

The patients provided informed consent for publication of their case details and images.

Authors' Contributions

MK and KW-K conceptualized the case report and drafted the manuscript. MK collected and analyzed case data, performed the literature search. ME, FH, DN, SN, TH, KK, TA critically reviewed and revised the manuscript. All the authors approved the final manuscript.

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Conflict of interest

The authors declare no competing financial interests.

Table 1. **Reported cases of *M. abscessus* PD-associated infections treated with clofazimine**

Age /Sex	Infection type	Surgical intervention	Days until removal	Macrolide resistance	Antibiotics	Combined antibiotics no.	Duration (month)	Outcome	Ref
63M	TI	Debridement, Catheter removal	11	resistance	AMK, AZM, Clofazimine, IPM/CS→AMK, Clofazimine, STFX	4	5	cure/HD	This case
6F	peritonitis	Catheter removal	8	sensitive	AMK, CAM, Clofazimine→ CAM, Clofazimine	3	9.7	cure/HD	(15)
53M	N/A	Catheter removal and reinsertion at a later date	16	sensitive	AMK→CAM, Clofazimine	2	7.5	cure/PD	(16)
58M	N/A	Catheter removal	1	sensitive	AMK→CAM, Clofazimine	2	7	cure/HD	(16)
68M	N/A	Catheter removal	2	sensitive	AMK, CAM, Clofazimine	3	1	cure/HD	(16)
64F	N/A	Catheter removal and reinsertion at a later date	730	sensitive	AMK, CAM, Clofazimine→AMK→CAM, Clofazimine	3	9	cure/PD	(16)
63F	N/A	Catheter removal	730	sensitive	AMK, CAM→ CAM, Clofazimine	2	6	cure/HD	(16)

AMK, amikacin; AZM, azithromycin; CAM, clarithromycin; ESI, exit-site infection; HD, hemodialysis; IPM/CS, imipenem and cilastatin; PD, peritoneal dialysis; STFX, sitafloxacin; TI, tunnel infection.

Figure Legends

Figure 1. The patient's clinical course

Antibiotic dosing regimens: AMK 260-320 mg after HD (dose adjusted based on drug monitoring); AZM 250 mg q24h; CAM 200 mg q12h; clofazimine 100 mg q24h; IPM/CS 0.5g q12h; MEPM 0.5g q24h; STFX 50 mg q24h.

AMK, amikacin; AZM, azithromycin; CAM, clarithromycin; CRP, C-reactive protein; HD, Hemodialysis; IPM/CS, imipenem and cilastatin; MEPM, meropenem; PD, peritoneal dialysis; STFX, sitafloxacin.

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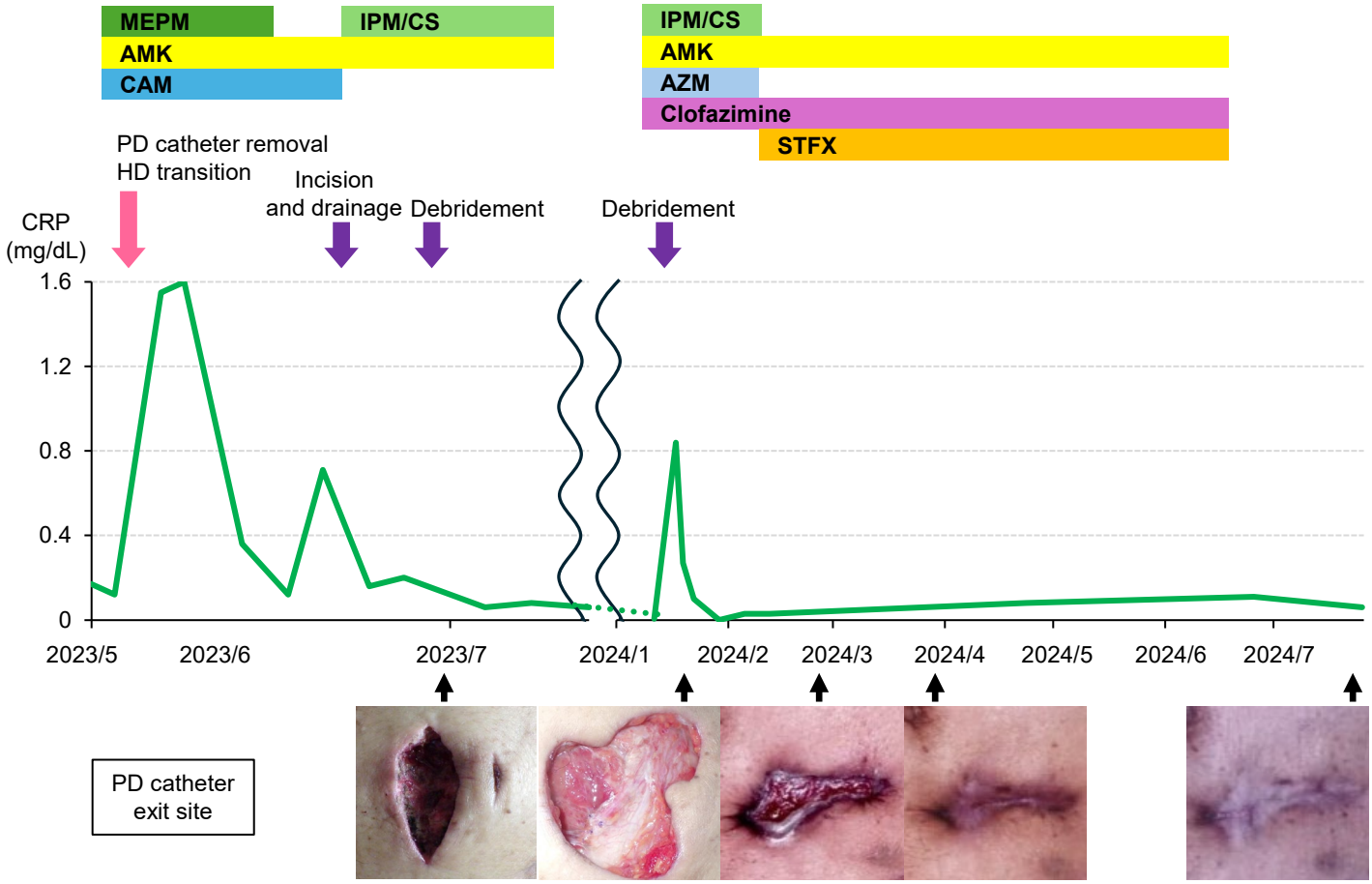
MEPM
IPM/CS
AMK
CAM
IPM/CS
AMK
AZM
Clofazimine
STFX
PD catheter removal
HD transition
Incision
and drainage
Debridement
Debridement
CRP
(mg/dL)
1.6
1.2
0.8
0.4
0
2023/5
2023/6
2023/7
2024/1
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2024/4
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2024/6
2024/7
PD catheter
exit site

Figure 1