Non-tuberculous mycobacteria infections in peritoneal dialysis: Lessons from a 16-year single-centre experience

Dear Editor,

Non-tuberculous mycobacteria (NTM) infections in peritoneal dialysis (PD) patients are uncommon, but they have been increasingly recognised as causes of morbidity. NTM are generally non-pathogenic, but given their abundance in the environment, they pose a threat to PD patients who have broken integument, indwelling devices and relative defects in cell-mediated immunity.¹

The growth of NTM is enhanced in warmer climates, which is common in tropical Asian countries. NTM are classified as rapid or slow growing, defined by their capacity to form visible colonies before or after 7 days of subculture. Most NTM infections reported in the literature were of rapidly growing species.² Despite the rapid growth of NTM, it still takes 3–7 days to culture them. This delays diagnosis, which is often further delayed due to a low index of suspicion, with misdiagnosis as culture-negative PD infections. The treatment of NTM infections is challenging; PD patients with NTM infections have been reported to do poorly.^{2–5} Rates of PD catheter loss and change of dialysis modality are high. Encapsulating peritoneal sclerosis (EPS) is a late complication from NTM with significant mortality.^{3,4,6} In this study, we describe the clinical outcomes of PD-associated NTM infections in National University Hospital PD Unit and propose treatment strategies.

As a follow-up to an earlier series from our centre,³ a retrospective study of all NTM infections in our PD programme from January 2011 to May 2020 was conducted. Data collected included demographics, diagnosis method, treatment regimen, and patient outcomes including catheter loss, switch of dialysis modality and mortality. Ethics approval was obtained from our institutional review board (reference number 2020/00662).

There were 18 patients with NTM infections during our study period: 4 peritonitis cases, 10 exit site infections (ESI), and 4 concomitant ESI with peritonitis. *Mycobacterium abscessus* accounted for 89% of infections. The patient population was multiethnic, with a median age of 53 years and a median dialysis vintage of 2 years. Diabetes mellitus was the commonest cause of end-stage kidney disease. The median time from presentation to diagnosis of NTM infection was 6 days (range 2–35 days). All patients were treated with combination antibiotics

in consultation with an infectious disease specialist. Eighty-nine percent of patients received amikacin and 78% received clarithromycin, with a median treatment duration of 5 months. PD catheter was removed in 17 of 18 patients and all 4 patients who did not undergo early catheter removal eventually developed recurrence, requiring removal 1.5–2 years after the first diagnosis of NTM infection. Three of 18 patients had a new PD catheter reinserted at a different site shortly after removal of the infected catheter (Table 1).

To the best of our knowledge, this is the largest single-centre case series of PD-associated NTM infection reported for Asia and internationally. PD-associated NTM peritonitis was first described in 1983 by Pulliam et al. with 100% mortality.⁷ More reports of PD-associated NTM infections have since emerged.^{3,4} Early diagnosis at the ESI stage instead of the peritonitis stage may improve outcomes. However, this is challenging, as initial presentation and PD effluent findings are often indistinguishable from bacterial infections. Furthermore, acid-fast bacillus (AFB) smear-negative disease is common.⁵ Only 2 of the 10 patients with ESI in our study had positive AFB smears of the exit site discharge. A high index of suspicion and early testing for AFB is required to avoid the sequelae of late diagnosis. If initial gram stain and bacteria culture are negative, or response to first-line antibiotics is poor, mycobacterial and fungal investigation should be conducted.² We recommend repeat AFB smears especially if the exit site discharge is mucoid, sticky or greyish. *M. abscessus* accounted for the majority of cases in our series, similar to previous Singapore data collected.^{3,8} In contrast, *M. fortuitum* and *M. chelonae* are more prevalent in other countries.⁵ It is important to identify the causative NTM species because susceptibility to antimicrobials is often highly species-specific.⁵ For *M. abscessus*, subspecies identification, if available, may be additionally helpful.⁹

PD-associated NTM infections are difficult to eradicate and invariably lead to high rates of catheter loss.^{3–5} Prolonged antimicrobial use exposes patients to risks of complications such as ototoxicity and hepatitis.³ Treatment failure is also an issue—in a series of 12 patients, 11 required prescription change to second-line antibiotics, while a further 5 patients needed third-line antibiotics due to poor response.⁴ Our experience

Table 1. Comparison of treatments and outcomes in peritoneal dialysis patients with non-tuberculous mycobacteria infections from 2 case series

No.	Age, years/ Sex	Catheter removal	Time from diagnosis to catheter removal	NTM infection recurrence	Mycobacterium species and antibiotic susceptibility Sensitive [S] Resistant [R]	Antibiotic therapy and duration	Technique failure (conversion to permanent HD)	3-month mortality	Adverse drug reaction
1	68/M	Yes	2 days	No	<i>M. abscessus</i> [S] A, K, Cef, Clo, Cip	A, K, Clo 1 month	Yes	No	
2	44/M	Yes	2 days	No	<i>M. fortuitum</i> [S] A, Cef, Cip [R] K	A, Cip 3 months	Yes	No	
3	66/M	Yes	3 months	No	<i>M. abscessus</i> [S] A, K, Cef, Clo, Cip	A, Cef 1 month K 1 year	Yes	No	
4	56/M	Yes	1.5 years	Yes	<i>M. fortuitum</i> [S] A, Cef, Clo, Cip [R] K	A, K 9 months Peritonitis relapse; K, Clo 9 months	Yes	No	Ototoxicity
5	63/F	Yes	2 years	Yes	<i>M. abscessus</i> [S] A, K, Cef, Clo, Cip	A, K 5 months Peritonitis relapse; K, Clo 6 months	Yes	No	
6	63/M	Yes	1 day	No	<i>M. neoaurum</i> [S] A, K, Cef, Cip, Dox, Lev	A, Lev, Dox 1.5 months	Yes	No	
7	43/F	Yes	3 days	No	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A 1 month K 9 months	No (HD 1 year then PD)	No	
8	64/M	Yes	4 days	No	<i>M. abscessus</i> [S] A, K, Cef	A, Cef 3 months	Yes	No	
9	63/M	No	NA	No	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	K, Cip, Met 2 weeks	No	No	
10	58/M	Yes	4 days	No	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A 2 months K 6 months	Yes	No	

Current case series

Table 1. Comparison of treatments and outcomes in peritoneal dialysis patients with non-tuberculous mycobacteria infections from 2 case series (Cont'd)

No.	Age, years/ Sex	Catheter removal	Time from diagnosis to catheter removal	NTM infection recurrence	<i>Mycobacterium</i> species and antibiotic susceptibility Sensitive [S] Resistant [R]	Antibiotic therapy and duration	Technique failure (conversion to permanent HD)	3-month mortality	Adverse drug reaction
11	29/M	Yes	2 years	Yes	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A, K 2 months Peritonitis relapse; A 2 months K 6 months	Yes	No	
12	64/F	Yes	2 years	Yes	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A, K, Clo 2 months ESI relapse; A 2 months K, Clo 7 months	No	No	
13	67/F	Yes	8 days	No	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A, K, Cef 4 months	No (simultaneous PD catheter removal and insertion)	No	
14	58/M	Yes	1 day	No	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A 1 month K, Clo 6 months	Yes	No	
15	53/M	Yes	16 days	No	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A 1.5 months K, Clo 6 months	No (HD 3 weeks then PD)	No	
16	54/M	Yes	4 months	No	<i>M. abscessus</i> [S] A, Lin [R] K, Cef	A, K, Cip, Lin 4 months	No (HD 6 months then PD)	No	Ototoxicity
17	75/F	Yes	8 days	No	<i>M. abscessus</i> [S] A, K, Cef [R] Cip	A, K, Cef 5 months	Yes	No	Ototoxicity
18	31/F	Yes	10 days	No	<i>M. abscessus</i> [S] A, K, Cef	A, K 6 months	Yes	No	

Current case series

Table 1. Comparison of treatments and outcomes in peritoneal dialysis patients with non-tuberculous mycobacteria infections from 2 case series (Cont'd)

No.	Age, years/ Sex	Catheter removal	Time from diagnosis to catheter removal	NTM infection recurrence	Mycobacterium species and antibiotic susceptibility Sensitive [S] Resistant [R]	Antibiotic therapy and duration	Technique failure (conversion to permanent HD)	3-month mortality	Adverse drug reaction
1	58/M	Yes	5 days		<i>M. chelonae</i> Pansensitive	K, Cip 6 weeks	No (HD 6 months then PD)	No	
2	63/M	Yes	9 days		<i>M. abscessus</i> [S] A, K	K 6 weeks	Yes	No	
3	81/M	No	NA		<i>M. abscessus</i> Pansensitive	No	NA (death)	Yes (sepsis)	
4	78/F	No	NA		<i>M. fortuitum</i> Pansensitive	A, Cip 3 months	NA (death)	Yes (cancer)	
5	56/F	No	NA		<i>M. fortuitum</i> [S] A, K	No	NA (death)	Yes (sepsis)	
6	70/M	Yes	NA		<i>M. abscessus</i> [S] A, K, Lin	A, K, Mero 1 month	Yes	Yes (AMI)	
7	50/M	Yes	5 days		<i>M. abscessus</i> Pansensitive	K, Cip 3 months	Yes	No	
8	56/M	Yes	1 month		<i>M. abscessus</i> [S] A, K	A, K 1 month	Yes	Yes (sepsis)	Hepatitis
9	69/F	Yes	1 month		<i>M. abscessus</i> [S] A, K	K 6 weeks	No (HD 6 weeks then PD)	No	Psychosis
10	60/M	Yes	6 days		<i>M. abscessus</i> [S] A, K	A, K 3 months	No (HD 3 months then PD)	No	Deafness

Case series by Renaud et al., 2011

A: amikacin; AMI: acute myocardial infarction; Cef: cefoxitin; Cip: ciprofloxacin; Clo: clofazimine; Dox, doxycycline; F: female; HD: haemodialysis; K: clarithromycin; Lev: levofloxacin; Lin: linezolid; M: male; Mero: meropenem; Met: metronidazole; NA: not available; NTM: non-tuberculous mycobacteria; PD: peritoneal dialysis; [R]: resistant; [S]: sensitive

showed that conservative management, even with prolonged antimicrobials, resulted in poor outcomes and adverse effects. Three cases (Cases 4, 16 and 17) suffered permanent hearing loss from prolonged aminoglycoside use despite therapeutic drug monitoring. In contrast, Cases 13 and 15 were eradicated of NTM and remained on PD without recurrence after early removal of the catheter with reinsertion at a different site. Our centre has previously published a case series of 10 patients with PD-associated NTM infections from 2004–2009;³ all patients suffered technique failure with none returning to PD. The 3-month mortality was higher in that series.

Table 1 outlines the treatments and outcomes in our case series in comparison with that of Renaud et al.³ Both series proved the high rates of catheter loss and technique failure. Importantly, our series demonstrated 3 key points, the first being the futility of conservative management with catheter preservation and prolonged antimicrobials. Secondly, recurrence-free return to PD was achieved in 28% of patients with isolated ESI through diagnosis, catheter removal, appropriate antibiotics use and PD catheter reinsertion, either early on (Case 13), or at an appropriate time later (Cases 7, 9, 15, 16). No patient with NTM peritonitis returned to PD. NTM peritonitis did not recur in patients after conversion to haemodialysis, suggesting that effective antibiotics may prevent dissemination of NTM peritonitis. Thirdly, recurrence-free continuation of PD without conversion to haemodialysis is possible for patients with isolated ESI, with removal of the infected catheter and simultaneous reinsertion at a different site (Case 13); however, we caution that further study is required to define the patient selection criteria for this option.

Adjunct surgical techniques such as local thermal therapy and catheter deroofing have been found to be successful to prevent NTM peritonitis in Japan.¹⁰ However, these techniques are operator dependent, and the species involved were mainly *M. chelonae* and *M. fortuitum*. It is unclear how effective these techniques would be for *M. abscessus*.

In conclusion, PD-associated NTM infections are associated with high morbidity, are very difficult to eradicate, and prolonged antimicrobials alone without catheter removal are associated with high recurrence, catheter loss and a significant risk of adverse effects. NTM infections require a high index of suspicion for diagnosis, and outcomes may be better with early recognition and prompt catheter removal. Early staged, or simultaneous catheter reinsertion is possible, and may allow patients to remain on PD if residual kidney

function is adequate. There is a pressing need for better diagnostics and therapeutics to improve outcomes in infections.

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