

Case Report: Two Cases of Mycobacterium Abscessus Peritonitis in Patients on Continuous Ambulatory Peritoneal Dialysis (CAPD)

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ABSTRACT

CAPD is an important mode of dialysis for end stage renal failure patients. However, CAPD associated peritonitis remains a challenge with increasing number of cases reported leading to significant morbidity and mortality. CAPD peritonitis caused by Nontuberculous Mycobacteria (NTM) is often under-recognized and associated with poor outcome. We report two cases of Mycobacterium abscessus CAPD peritonitis at our centre with different clinical outcomes. The first patient responded well to the antimicrobial therapy while the

second patient succumbed to the infection.

Keywords: NTM; Nontuberculous mycobacterium; Peritonitis; CAPD; Continuous ambulatory peritoneal dialysis; *Mycobacterium abscessus*

Key Messages: NTM peritonitis in CAPD patients can lead to significant morbidity and mortality. It is thus vital to have high index of suspicion if CAPD peritonitis patients do not respond to conventional antimicrobial therapy. Accurate early diagnosis and prompt treatment with appropriate antimicrobials may improve patients' outcomes.

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INTRODUCTION

Peritoneal dialysis (PD); with regards to Continuous Ambulatory Peritoneal Dialysis (CAPD), represents an important modality for the management of patients with end stage renal failure (ESRF). It is shown that patients on CAPD have similar survival rates and quality of life with patients on hemodialysis^[1,2,3]. Nonetheless, CAPD peritonitis remains a major challenge amongst nephrologists with overall reported rates of 0.24-1.66 episodes per patient-year. CAPD peritonitis often results in catheter removal and discontinuation of CAPD. It may also cause patient's death. It is projected that for every 0.5 episode per year increase, the rate of mortality increases from 4% to 18%^[4]. At our centre, the reported rate of peritonitis is 0.40 episode per patient-year^[5]. The commonest microorganisms implicated for CAPD peritonitis at our centre are gram positive organisms (33.9%). This is followed by gram negative organisms (29.0%), fungi (3.2%) and Mycobacterium tuberculosis (1.6%)^[5].

Nontuberculous Mycobacteria (NTM) have been infrequently im-

plicated as the cause of CAPD peritonitis^[6,7,8]. Due to under recognition of the importance of these bacteria in CAPD peritonitis, proper diagnosis was frequently missed or delayed and resulted in significant morbidity and mortality^[9].

Here, we would like to report two cases of CAPD peritonitis caused by *Mycobacterium abscessus*.

CASE HISTORY

A 53-year-old lady (Madam BSL) with background of diabetes mellitus and hypertension with ESRF on CAPD for the past 18 months was admitted into our hospital with complains of severe generalized abdominal pain, fever and diarrhea for one week. She was diagnosed with CAPD peritonitis as she exhibited signs of peritonism on clinical examinations and her return PD fluid was turbid in appearance. Her first PD fluid cell count was 677 cells/mm³. She was treated with intraperitoneal antibiotics (Ceftazidime and Cloxacillin). Her treatment was then switched to intraperitoneal Vancomycin, Meropenem and Fluconazole after five days as her PD effluents remained turbid and cell counts remained high (Table 1).

The Ziehl-Neelsen (ZN) staining for PD fluid samples obtained on day one and day five of admission were both positive. PD fluid cultures were positive for *Mycobacterium abscessus*. This was confirmed via Matrix Assisted Laser Desorption/Ionization-Time of Flight Mass Spectrometry (MALDI-TOF MS). Samples were then sent to our national public health laboratory for antibiotics sensitivity testing (Table 2).

Tenckhoff catheter was removed on day nine of admission as she failed to respond to intraperitoneal antibiotics with persistent turbid PD fluid appearance and raised PD cell counts. Based on the preliminary results, her treatment was subsequently switched to intravenous Meropenem, Amikacin and oral Clarithromycin after catheter removal. Her condition improved with resolved signs of peritonism so after two weeks of intravenous antibiotics, she was discharged and given oral Clarithromycin and Ciprofloxacin. She was switched to hemodialysis post catheter removal. Upon follow-ups, she remained well, did not exhibit any signs of recurrent infection and hence oral antibiotics were discontinued after three months.

The second patient was a 55-year-old lady, Madam JS, with background of diabetes mellitus, hypertension, ischaemic heart disease with congestive cardiac failure (ejection fraction 25 to 35%), cerebrovascular accident and end stage renal failure. She was on CAPD for the past 15 months prior to admission. She had multiple admissions for the past 15 months for complications related to CAPD. During the first admission which occurred two weeks after Tenckhoff catheter insertion for CAPD training, she was given oral Unasyn (Ampicillin and Sulbactam) for two weeks as there was pus noted at the exit site. She presented again four months after Tenckhoff catheter insertion with purulent discharge, pain and redness over exit site. Abdominal ultrasound showed small focal collection at the superficial subcutaneous layer with no extension into deep subcutaneous layer and peritoneal cavity. She was given oral Unasyn for one month. She had her 3rd recurrence of exit site infection in about three months after the previous episode and received another course of oral Unasyn.

As a result of the recurrent infection, her catheter was removed and reinserted at a new site. Her CAPD was suboptimal as she only performed two exchanges per day at home instead of the recommended four times. As a result, she had to come on a weekly basis to the hospital for cyclical inpatient PD to prevent fluid overload. In this studied admission, she presented with one day history of fever, abdominal pain and diarrhoea. She also noticed that her PD fluid was turbid.

Table 1 Summary of PD cell counts, PD cultures and antibiotics prior removal of PD catheter for first patient; Madam BSL.

Date	PD Cell Count (cells/mm ³)	PD Culture	Antibiotics
Day 1	677; predominantly lymphocytes	<i>M. abscessus</i> isolated; AFB 3+	IP Cloxacillin; IP Ceftazidime
Day 2	341; predominantly lymphocytes		
Day 3	1936; predominantly lymphocytes		
Day 4	737; predominantly lymphocytes	<i>M. abscessus</i> isolated	IP Meropenem; IP Amikacin; IP Fluconazole
Day 5	1584; predominantly lymphocytes		
Day 6	1232; predominantly lymphocytes		
Day 7	935; predominantly lymphocytes		
Day 8	1628; predominantly lymphocytes		

*At Day 9, intravenous Meropenem, Amikacin and oral Clarithromycin were commenced; IP: intraperitoneal

Table 2 Sensitivity of *Mycobacterium abscessus* for Madam BSL.

Antibiotics	MIC(ug/ml)	Result
Trimethoprim/ Sulfamethoxazole	>8/152	Resistant
Ciprofloxacin	4	Resistant
Moxifloxacin	4	Resistant
Cefoxitin	64	Intermediate
Amikacin	8	Sensitive
Doxycycline	2	Intermediate
Tigecycline	1	NA
Clarithromycin	<0.06	Sensitive
Linezolid	8	Sensitive
Imipenem	16	Intermediate
Cefepime	>32	NA
Amoxicillin/Clavulanic acid	>64/32	NA
Ceftriaxone	>64	NA
Minocycline	2	NA
Tobramycin	8	Resistant

NA: Not available, ranges for result's interpretation not available.

Table 3 Summary of PD cell counts, PD cultures and antibiotics prior removal of PD catheter for Madam JS.

Date	PD Cell Count (cells/mm ³)	PD Culture	Antibiotics
Day 1	594; predominantly lymphocytes		IP Cefazolin; IP Amikacin
Day 2	825; predominantly lymphocytes	<i>M. abscessus</i> isolated; AFB 3+	
Day 3	1056; predominantly lymphocytes	<i>M. abscessus</i> isolated	
Day 4	858; predominantly lymphocytes		IP Meropenem*; IP Vancomycin*; IP Fluconazole*
Day 5	1089; predominantly lymphocytes		
Day 6	1452; predominantly lymphocytes		
Day 9 onwards			IV Amikacin; IV Cefepime

IP: intraperitoneal IV: intravenous.

Testing performed on the PD fluid showed cell count of 594 cells/mm³. First and second line of intraperitoneal antibiotics were administered as per local antibiotic guidelines with no clinical improvement and rising PD fluid cell counts (Table 3). The PD fluid Ziehl-Neelsen (ZN) staining was positive and culture grew *M. abscessus* (Table 4). Patient underwent Tenckhoff catheter removal procedure on day five of admission due to poor response to antibiotics. Based on the pre-

liminary identification of *M. abscessus*, her antibiotics were switched to empirical intravenous Amikacin and Cefepime pending full antimicrobial sensitivity results. However, she deteriorated rapidly due to overwhelming sepsis and succumbed to her illness on day 12 of admission.

DISCUSSION

Nontuberculous Mycobacteria (NTM) are commonly derived from the environment including soil and water; thus, they are labelled as environmental mycobacteria^[10]. The identification of NTM at species level is vital because different mycobacteria species have different predicted antimicrobial susceptibility. NTM infection is usually resistant to conventional therapy^[11]. Conventionally, NTM are subdivided into four main groups based on the Runyon classification^[11,16]. The rapid growers include *M. fortuitum*, *M. chelonae*, and *M. abscessus* as they can form colonies in culture media within one week. On the other hand, slow growing NTM includes *M. avium*, *M. intracellulæ* and *M. kansasii*, *M. marinum* and *M. ulcerans*. The majority of the reported NTM peritonitis in PD patients are due to rapid growing NTM whereas only a small number of cases are caused by slow growing NTM (predominantly causing pulmonary and cutaneous disease)^[17,18].

Predisposing factors for NTM peritonitis include history of recurrent peritonitis, local trauma, catheter exit site leakage, breach in sterile technique, immunocompromised state, inadequate dialysis, poor residual renal function, exposure to contaminated soil or water sources and history of prolonged broad-spectrum antibiotics use for peritonitis^[15]. Both of our patients were immunocompromised as they suffered from ESRF and diabetes mellitus. Madam BSL could have been exposed to the organism when water supply to her house was disrupted due to some dredging work in her neighbourhood. She described the water as brownish in colour, suggestive of contamination with soil. As for Madam JS, her risk factors for NTM peritonitis were likely due to multiple courses of broad spectrum antibiotics which she received and suboptimal dialysis as she only performed two CAPD exchanges per day. Her death could partly be attributed to her poor premorbid status as she had poor heart function. A comparison between both patients were made in terms of social background, place of stay and surrounding community, types of PD fluid used, CAPD training duration and time of hospitalization. We were not able to identify any common links between these two patients.

NTM infection in PD patients, although rare, had been reported since 1982^[19]. To our knowledge, there is no reported case of peritonitis caused by *M. abscessus* thus far in Malaysia. Among all the NTM, *M. abscessus* is the commonest pathogen causing PD infections. The PD catheter loss rate is 80% and three months' mortality rate is 40%^[20]. This highlights the significant morbidity and mortality of NTM PD infections. The diagnosis of NTM peritonitis remains challenging as the signs and symptoms are often indistinguishable from other bacterial or tuberculous peritonitis^[21,22]. There should be high level of suspicion when the peritonitis is refractory to conventional antimicrobial therapy. The cell counts are not helpful in differentiating between NTM, tuberculous or other bacterial infections^[21,22]. Therefore, it is important to perform ZN staining to enable clinicians to identify the possibility of tuberculous or NTM peritonitis. In our case, we were able to pick up the diagnosis as the ZN staining for PD fluid was positive and the culture was positive for mycobacterium species. The bacteria, which grew rapidly in Ogawa media approximately three days after incubation, demonstrated that they were rapid grower NTM. We were then able to identify the species of bacteria

Table 4 Sensitivity of Mycobacterium Abscessus for Madam JS.

Antibiotics	MIC (ug/ml)	Result
Trimethoprim/ Sulfamethoxazole	>8/152	Resistant
Ciprofloxacin	>4	Resistant
Moxifloxacin	>8	Resistant
Cefoxitin	64	Intermediate
Amikacin	16	Sensitive
Doxycycline	>16	Resistant
Tigecycline	4	NA
Clarithromycin	0.5	Sensitive
Linezolid	32	Resistant
Imipenem	64	Resistant
Cefepime	>32	NA
Amoxicillin/Clavulanic acid	>64/32	NA
Ceftriaxone	>64	NA
Minocycline	>8	NA
Tobramycin	>16	Resistant

NA: Not available, ranges for result's interpretation not available.

using MALDI-TOF MS. This method is shown to be equal or better than conventional diagnostic methods in bacteria identification^[23]. The drawback, however, is that this method does not provide information regarding antimicrobial susceptibility.

Mycobacterium abscessus is uniformly resistant to standard anti-tuberculous drugs^[28]. As it has variable in vitro susceptibility to antimicrobial therapy, antibiotic susceptibility testing on all clinically significant isolates is recommended^[11]. Treatment usually consists of combination therapy, usually with Cefoxitin, Imipenem, Amikacin or Clarithromycin. For both our patients, Cefoxitin was not used as it was not available in our setting. The *M. abscessus* isolated was sensitive to Amikacin and Clarithromycin. This is consistent with published reports that *M. abscessus* is usually susceptible to these two drugs. Susceptibility to other antibiotics varies. These include drugs such as Imipenem and Ciprofloxacin^[12]. For Madam JS, the *M. abscessus* isolated was resistant to Cefepime and Imipenem. Meropenem has poorer potency against NTM compared to Imipenem but it was successfully in some case series^[13,14]. The result of antimicrobial susceptibility usually takes time. We only obtained the result of antimicrobial susceptibility pattern after two months. In both our cases, we started empirical treatment based on recommendations from clinical guideline^[11] after the species of NTM was identified rapidly through MALDI-TOF MS. Prolonged treatment is usually recommended but there is no clear recommendation on duration of treatment as well as role of PD catheter removal following the diagnosis of NTM peritonitis. However, we believe prompt removal of PD catheter helped in the management of Madam BSL's case.

CONCLUSION

Although rare, NTM infections pose severe medical problems for patients on PD. Nonresponsiveness to first line conventional antibiotics should prompt further testing for mycobacterium infection. The failure in doing this may lead to delay in diagnosis and treatment. Early identification for the presence of NTM using ZN staining and Ogawa culture in PD fluid samples as well as isolation up to species level is important to ensure correct empirical antimicrobial drugs are administered. It is equally important to know the drug susceptibility pattern to facilitate future treatment as the result is not readily available. Prompt removal of PD catheter should be considered as part of NTM peritonitis management.

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