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

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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[12-23]. Nonetheless, CAPD peritonitis remains a major challenge amongst nephrologists with overall reported rates of 0.24-1.66 episodes per patient-year[10]. The commonest microorganisms implicated for CAPD peritonitis at our centre are gram positive organisms (33.9%), gram negative organisms (29.0%), fungi (3.2%) and Mycobacterium tuberculosis (1.6%)[11].

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 complaints of severe generalized abdominal pain, fever and diarrhoea for one week. She was diagnosed with CAPD peritonitis as she exhibited signs of peritonitis on clinical examinations and her return PD fluid was turbid in appearance. Her first PD fluid cell count was 677 cells/mm\(^3\). She was treated with intraperitoneal antibiotics (Cefazidime 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 peritonitis so two weeks of intravenous antibiotics, she was discharged and given oral Clarithromycin and Ciprofloxacinx. She was switched to hemo dialysis 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 (Amoxicillin 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 3\textsuperscript{rd} 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 reinseted 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 cycler 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.

| Date   | PD Cell Count (cells/mm\(^3\)) | PD Culture | Antibiotics                  |
|--------|-------------------------------|------------|------------------------------|
| Day 1  | 677; predominantly lymphocytes | M. abscessus isolated; AFB 3+ | IP Cloxacillin; IP Cefazidime |
| Day 2  | 341; predominantly lymphocytes |            |                              |
| Day 3  | 1936; predominantly lymphocytes|            |                              |
| Day 4  | 737; predominantly lymphocytes | M. abscessus 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

| Antibiotics     | MIC(\text{ug/ml}) | Result |
|-----------------|-------------------|--------|
| Trimetoprim      | >8/152            | Resistant |
| Sulfamethoxazole |                   |        |
| Ciprofloxacins   | 4                 | Resistant |
| Moxifloxacins    | 4                 | Resistant |
| Cefoxitin        | 64                | Intermediate |
| Amikacin         | 8                 | Sensitive |
| Tobramycin       | 8                 | NA |
| Cefpime          | >32               | NA |
| Amoxicillin/Clavulanic acid | >64/32 | NA |
| Ceftriazone      | >64               | NA |
| Minocycline      | 2                 | NA |
| Tobramycin       | 8                 | Resistant |

| Date   | PD Cell Count (cells/mm\(^3\)) | PD Culture | Antibiotics                  |
|--------|-------------------------------|------------|------------------------------|
| Day 1  | 594; predominantly lymphocytes |            | IP Cefazolin; IP Amikacin    |
| Day 2  | 825; predominantly lymphocytes | M. abscessus isolated; AFB 3+ | IP Cefazolin; IP Amikacin    |
| Day 3  | 1056; predominantly lymphocytes| M. abscessus isolated | IP Cefazolin; IP Amikacin    |
| Day 4  | 858; predominantly lymphocytes |            | IP Cefazolin; IP Amikacin    |
| Day 5  | 1089; predominantly lymphocytes|            | IP Meropenem; IP Vancomycin; IP Fluconazole* |
| Day 6  | 1452; predominantly lymphocytes|            | IP Meropenem; IP Vancomycin; IP Fluconazole* |

| Date   | PD Cell Count (cells/mm\(^3\)) | PD Culture | Antibiotics                  |
|--------|-------------------------------|------------|------------------------------|
| Day 9  | onwards                       |            | IV Amikacin; IV Cefpime      |

\*IP: intraperitoneal IV: intravenous.

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

Testing performed on the PD fluid showed cell count of 594 cells/mm\(^3\). 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-
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\[20\]. 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\[29\]. 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%\[29\]. 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 peritonitidis\[21,22\]. 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 growing NTM. We were then able to identify the species of bacteria using MALDI-TOF MS. This method is shown to be equal or better than conventional diagnostic methods in bacteria identification\[23\]. However, 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 growing NTM. We were then able to identify the species of bacteria using MALDI-TOF MS. This method is shown to be equal or better than conventional diagnostic methods in bacteria identification\[23\].

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.

### DISCUSSION

Nontuberculous Mycobacteria (NTM) are commonly derived from the environment including soil and water; thus, they are labelled as environmental mycobacteria\[19\]. 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\[10,19\]. 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. intracellulare and M. kansasi, 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)\[12,18\].

**Table 4** Sensitivity of Mycobacterium Abscessus for Madam JS.

| Antibiotics                  | MIC (ug/ml) | Result   |
|-----------------------------|-------------|----------|
| Trimethoprim/ Sulphamethoxazole | >8/152     | Resistant |
| Ciprofloxacin               | >4          | Resistant |
| Meropenem                   | >8          | Resistant |
| Cefoxitin                   | 64          | Intermediate |
| Amikacin                    | 16          | Sensitive |
| Doxycycline                 | >16         | Resistant |
| Tigecycline                 | 4           | NA       |
| Clarithromycin              | 0.5         | Sensitive |
| Linezolid                   | 32          | Resistant |
| Imipenem                    | 64          | Resistant |
| Ceftazidime                 | >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.
