CASE REPORT

A hospital-acquired outbreak of catheter-related nontuberculous mycobacterial infection in children on peritoneal dialysis

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Abstract Catheter-related nontuberculous mycobacterial infection in children with chronic renal failure on peritoneal dialysis (PD) is rare. However, there have been five such infections in infants among PD patients at our center. Although the patients were treated with antibiotics to which the organisms showed in vitro sensitivity, they were clinically drug resistant. Hence, all PD catheters needed to be removed. Thereafter, following hemodialysis treatment for approximately 1 month, the PD catheters were replaced, with no recurrence of infection. On investigation of the infection route, it was found that these bacteria had colonized around a shower head in one of the bathrooms. These findings suggest that, in cases where hot water systems at hospitals are considered at a high risk, frequent sterilization is needed, especially around the shower heads. It is also necessary to reconsider current standard practices in the management of catheter exit sites, especially if the national incidence of infection increases.

Keywords Peritoneal dialysis · Peritonitis · Exit-site care · Gram-positive rods · Nontuberculous mycobacteria

Introduction

Catheter-related nontuberculous (NTB) mycobacterial infection in children with chronic renal failure on peritoneal dialysis (PD) is rare. However, the incidence of such infections in infants hospitalized for PD at our

comprehensive pediatric center was found to have increased. These cases and their causes and countermeasures are presented, and the literature was reviewed for reports of similar cases.

Case reports

Case 1

A 25-month-old female with end-stage renal disease secondary to complicated urinary tract malformations had been on continuous ambulatory peritoneal dialysis (CAPD) for 12 months. At that time, she was admitted to the hospital with granulation tissue and purulent discharge at the catheter exit site. Methicillin-sensitive *Staphylococcus aureus* (MSSA) was isolated, and treatment with intravenous vancomycin (VCM) was administered for 1 week. The infection was cured, and the peritoneal catheter remained. One week later, granulation tissue and purulent discharge again developed at the exit site. The peripheral white blood cell (WBC) count was $8,190/\text{mm}^3$, with 59.5 % neutrophils and a C-reactive protein (CRP) level of 1.3 mg/dL. The peritoneal fluid WBC count contained $3.9/\text{mm}^3$. Gram staining demonstrated no organisms, and cultures showed no growth. The patient was treated with intravenous VCM and oral minocycline (MINO), but with no clinical response. The Tenckhoff catheter was removed because purulent material was noted along it. Culture of the PD catheter cuff led to isolation of *M. fortuitum*. The infection subsequently showed clinical improvement without any antibiotic therapy. Since her renal function was adequately maintained thereafter, dialysis was not needed. Four months later, she underwent surgery for urinary diversion. At 3 years of age, the patient was transferred to

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hemodialysis (HD), and after 4 months of HD treatment, she underwent successful renal transplantation with no recurrence of the NTB mycobacterial infection.

Case 2

An 11-month-old female with end-stage renal disease secondary to bilateral hypo-dysplastic kidney had been on CAPD for 8 months. At that time, she was admitted for dry-weight control. Two weeks later, development of granulation tissue and purulent discharge at the catheter exit site were noted, for which empiric therapy with VCM was started. Since the organism was subsequently identified as *M. chelonae*, the antibiotics were changed to imipenem/cilastatin (IPM/CS) and MINO, but there was no clinical response. Therefore, 3 months later, the exit site of the PD catheter was surgically changed. At 25 months of age, she was readmitted for strict dry-weight control; 4 weeks later, granulation tissue and purulent discharge at the catheter exit site were again noted and treated with intravenous VCM and piperacillin sodium, but again there was no clinical response. At that time, laboratory examination results were as follows: peripheral WBC count $16,790/\text{mm}^3$ with 32.9 % neutrophils, CRP of 0.08 mg/dL, and PD fluid cell count of $0.2/\text{mm}^3$. No organisms were seen on Gram staining, and culture showed no growth. Due to the suspicion of NTB mycobacterial infection, oral rifampicin (REF) was added. Finally, after isolation of *M. chelonae*, she was switched to clarithromycin (CAM) and levofloxacin (LVFX), but yet again without clinical resolution of the infection. Two months later, the Tenckhoff catheter was removed, and an abscess along the PD catheter tract was incised and drained. Following HD for 2 months, the PD catheter was replaced and CAPD was resumed. Since then, no recurrences have occurred.

Case 3

A 3-month-old male with end-stage renal disease secondary to angiotensin receptor blocker fetopathy had been on CAPD for 2 months. At that time, though he was in the hospital for PD training, tenderness was present over the PD catheter exit site and a circumferential mass was noted over the PD catheter. Purulent material was expressed from the PD catheter exit site, culture of which revealed methicillin-resistant *Staphylococcus aureus* (MRSA). The patient was treated with intravenous VCM and teicoplanin (TEIC), without clinical response. The organism was finally identified as *M. chelonae*, which was resistant to most antimycobacterial drugs, including isoniazid and REF, but it was sensitive to amikacin (AMK). Therefore, VCM and TEIC were discontinued, and AMK and REF were started. However, since there was once again no

clinical improvement, the peritoneal catheter was removed and replaced simultaneously in the opposite abdominal region at 4 months of age. Two weeks later, the patient developed symptoms of peritonitis, including fever, abdominal pain, and cloudy peritoneal dialysis fluid. Laboratory data showed a peripheral WBC count of $4,000/\text{mm}^3$, with 80.0 % neutrophils, a CRP of 0.27 mg/dL, and a peritoneal fluid WBC count of $16.4/\text{mm}^3$. Intraperitoneal AMK and IPM/CS were administered after routine culturing of the peritoneal fluid. As before, *M. chelonae* was isolated on culture of the PD effluent. The Tenckhoff catheter was removed, and the patient was converted to HD at 6 months of age. After 2 months, the PD catheter was replaced and the patient was resumed on CAPD with no further recurrence of infection.

Case 4

A 22-month-old male with end-stage renal disease secondary to diffuse mesangial sclerosis had been on CAPD for 21 months. At that time, granulation tissue and purulent discharge were observed at the catheter exit site. The eventual identification of MRSA resulted in treatment with VCM for 2 weeks. The exit site improved, but 3 weeks later, a purulent discharge recurred during hospitalization. The patient had a peripheral WBC count of $24,040/\text{mm}^3$, a CRP of 1.1 mg/dL, and a peritoneal fluid WBC count of $0.5/\text{mm}^3$. Repeated cultures of the exit site showed a rapidly growing mycobacterium that was identified as *M. chelonae*. AMK and IPM/CS therapy was started, but without resolution of the infection. Two months later, the PD catheter was removed, and the patient was continued on HD and antibiotic therapy with CAM and LVFX. After 1 month, the exit site healed completely, with no evidence of infection on repeat culture. The patient is scheduled to have the peritoneal dialysis catheter replaced so that he can resume PD.

Case 5

A 4-month-old female with end-stage renal disease secondary to right multicystic dysplastic kidney disease and left hypo-dysplastic kidney had been on CAPD for 3 months. At that time, though she was in the hospital for PD training, she developed a granuloma and purulent drainage from the catheter sinus. Culture of the drainage revealed MRSA. After 4 weeks of antibiotic therapy with VCM, since the clinical catheter-related infection still persisted, the peritoneal catheter was surgically removed and a new one was re-inserted. Soon thereafter, however, the exit-site infection relapsed. The peripheral WBC count was $7,040/\text{mm}^3$ with 36.2 % neutrophils. The peritoneal fluid WBC count was $1.2/\text{mm}^3$. Cultures of the exit-site drainage demonstrated a rapidly growing mycobacterium

Table 1 Clinical characteristics of the five cases of catheter-related nontuberculous mycobacterial infection

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	Female	Female	Male	Male	Female
Primary disease	Complicated urinary tract malformations	Hypo-dysplastic kidney	Drug-induced	Diffuse mesangial sclerosis	Left hypo-dysplastic kidney and right MCDK
Date of diagnosis	June 2005	Jan 2006	Apr 2007	March 2007	May 2007
Age (months)	25	11	26	3	5
Interval between catheter insertion and infection (months)	12	8	23	2	4
Causative organism	<i>M. fortuitum</i>	<i>M. chelonae</i>	<i>M. chelonae</i>	<i>M. chelonae</i>	<i>M. chelonae</i>
Presentation	Catheter-related infection	Catheter-related infection	Catheter-related infection	Peritonitis	Catheter-related infection
Antibiotic treatment	VCM, MINO	VCM, IPM/CS, MINO	VCM, PIPC, REF, CAM, LVFX	VCM, TEIC, AMK, REF	AMK, IPM/CS
Catheter removal	Yes	Yes	Yes	Yes	Yes
HD	No	No	Yes	No	Yes
The interval between removal and reinsertion of PD catheter (weeks)			7	7	5
Follow-up periods (months)	69		62	48	46

AMK amikacin, CAM clarithromycin, HD hemodialysis, IPM/CS imipenem/cilastatin, LVFX levofloxacin, MCDK multicystic dysplastic kidney, MINO minocycline, PD peritoneal dialysis, PIPC piperacillin sodium, REF rifampicin, TEIC teicoplanin, VCM vancomycin

that was identified as *M. chelonae*, for which treatment with IPM/CS, CAM, LVFX, and AMK produced no clinical response. Two months later, the Tenckhoff catheter was removed and the patient was switched to HD. After 1 month, the PD catheter was replaced and the patient was resumed on CAPD with no further recurrences of infection.

The clinical characteristics of these cases are summarized in Table 1. The age at onset of the five cases reported was 3–26 months. The period from PD catheter insertion to the occurrence of infection was 2–23 months. As for the causative bacteria, one case was *M. fortuitum* and four were *M. chelonae*. All cases were living in the hospital at the time of infection for PD training, dry-weight control, or treatment of catheter-related other bacterial infection. Although antibiotics were selected after evaluating antibiotic sensitivity, catheter removal was required in all cases. All cases with localized catheter-related infection showed the presence of pus and granulomas. Following HD treatment for approximately 1 month, the PD catheters were replaced with no recurrence of infection in any of the cases during follow-up. The infections of case 2 (second episode), 3, 4, and 5 occurred in the short period from March to May 2007, though case 1 and 2 (first episode) occurred sporadically. During the outbreak periods, no other PD

patients were in the hospital, and non-PD patients in the hospital did not develop the same infections.

Discussion

So far, at least 65 different kinds of mycobacteria species have been identified, and the fundamental taxonomic division of mycobacteria has been based on growth rate and pigmentation. By these criteria, the genus *Mycobacterium* has been divided into four Runyon groups: group I, the photochromogenic species of slow growers; group II, the scotochromogenic species of slow growers; group III, the nonphotochromogenic species of slow growers; and group IV, the rapid growers [1]. *M. fortuitum* and *M. chelonae* are rapid growers that are often associated with infections of the skin and soft tissue. NTB mycobacteria are acid-fast Gram-positive bacteria that look similar to *C. diphtheriae* on Gram staining, which sometimes leads to misdiagnosis.

The best treatments for the different NTB mycobacterial infections have still to be established. Combined therapy with various antituberculous medicines has sometimes been administered empirically. However, bacterial species other than *M. kansasii* show resistance to most of the drugs

Table 2 Clinical characteristics of the previously reported cases ($N = 29$) [3–16]

Characteristics	<i>N</i>	%
Primary disease		
DM	7	24.1
HTN	4	13.8
SLE	3	10.3
CGN	2	6.9
PKD	2	6.9
FSGS	1	3.4
Others	5	17.2
Not reported	5	17.2
Causative organism (Runyon group [1])		
Group IV		
<i>M. fortuitum</i>	20	69.0
<i>M. chelonae</i>	3	10.3
<i>M. abscessus</i>	1	3.4
<i>M. chelonae-abscessus complex</i>	1	3.4
Group I		
<i>M. kansasii</i>	1	3.4
Group II		
<i>M. gordonae</i>	1	3.4
Not available	1	3.4
Group III		
<i>M. xenopi</i>	1	3.4
Peritonitis	20	69.0
Required peritoneal catheter removal	25	86.2
Death	1	3.4

CGN chronic glomerulonephrosis, DM diabetes mellitus, FSGS focal segmental glomerulosclerosis, HTN hypertension, PKD polycystic kidney disease, SLE systemic lupus erythematosus

presently available. Furthermore, although it has been recognized that some new quinolones and macrolides have proven efficacy as bacteriostatic agents, NTB mycobacteria have shown fundamental resistance to many different kinds of drugs. It has been reported that NTB mycobacteria may form biofilms, resulting in some protection from conventional disinfectants [2]. The sensitivity of NTB mycobacteria to disinfectants is similar to that of tuberculous species, with few sensitivity differences between the species and strains. NTB mycobacteria are susceptible to heat, sunshine, and ultraviolet light. However, the cell wall of the bacteria contains many lipids. As a result, it shows strong resistance to disinfectants and is not affected by gluconic acid cleansing, chlorhexidine gluconate, and benzalkonium chloride.

It is extremely rare to find PD catheter-related NTB mycobacterial infections. Previous articles dealing with PD catheter-related infection were reviewed, and their main features are shown in Table 2 [3–16]. Summarizing the

previous reports, adults (17 men, 12 women) had an average age of 47.7 ± 18.1 years at the time of diagnosis with PD catheter-related infection. As for the causative bacteria, *M. fortuitum* was responsible for an overwhelming majority, at 69.0 % of the cases. Of all species found in the cases reported, rapid growers comprised 79.3 %. Twenty of the 29 cases suffered from peritonitis, this being fatal in one of the cases, and all except one case had their catheters removed.

The courses of the five cases presented suggest that, if PD catheter infection leads to granulation and pus formation, but general culture is negative, NTB mycobacterial infection should be suspected, and repeat cultures of smear samples for NTB mycobacteria, using media that are fast and appropriate, should be considered. However, most NTB mycobacteria show resistance to many treatments.

At our department, we had maintained cleanliness of the PD catheter exit sites by open bathing, shower washing, and physiological saline washing. The 2010 International Society for Peritoneal Dialysis (ISPD) guidelines note that extensive use of topical gentamicin ointment for exit-site infection might predispose patients to NTB infections [17]. On investigation of the infection route, it was found that these bacteria had colonized around a shower head in one of the bathrooms. A culture of these bacteria grew *M. chelonae*, and its susceptibility showed a pattern identical to the present cases. All cases were living in the hospital at the time of infection for PD training, dry-weight control, or treatment of catheter-related other infection. Although the infection route of case 1 was unknown, in the other four cases, it seemed to be from colonization of the bacteria around a shower head in the bathroom. As a consequence, the practice of cleansing the exit site of PD catheters under the shower following a bath was ended, and soap and physiological saline washing was used. It has been reported that NTB mycobacteria can colonize very quickly in the water distribution systems of hospital departments, including hemodialysis and dental units [18–20]. In addition, the species prefers warm water to cold water and can even proliferate in shower heads. The probable reasons underlying the increased incidence of PD catheter-related infections in the infants at our center during this period are as follows. The temperature that the heated bathing water could reach was restricted to prevent scalding. As a result, it was not possible to prevent NTB mycobacteria from thriving. The present cases suggest that, in cases where hot water systems at hospitals are considered at a high risk, it is necessary to perform frequent sterilization, especially around the shower heads. It is also necessary to reconsider current standard practices in the management of catheter exit sites, especially if the national incidence of infection increases.

Conflict of interest All the authors have declared no competing interest.

References

- Runyon EH. Anonymous mycobacteria in pulmonary disease. *Med Clin N Am*. 1959;43:273–90.
- Schulze-Robbecke R, Fischeder R. Mycobacteria in biofilms. *Zentralbl Hyg Umweltmed*. 1989;188:385–90.
- London RD, Damsker B, Neibart EP, Knorr B, Bottone EJ. *Mycobacterium gordonae*: an unusual peritoneal pathogen in a patient undergoing continuous ambulatory peritoneal dialysis. *Am J Med*. 1988;85:703–4.
- Merlin TL, Tzamaloukas AH. *Mycobacterium chelonae* peritonitis associated with continuous ambulatory peritoneal dialysis. *Am J Clin Pathol*. 1989;91:717–20.
- Soriano F, Rodriguez-Tudela JL, Gómez-Garcés JL, Velo M. Two possibly related cases of *Mycobacterium fortuitum* peritonitis associated with continuous ambulatory peritoneal dialysis. *Eur J Clin Microbiol Infect Dis*. 1989;8:895–7.
- Sennesael JJ, Maes VA, Pierard D, Debeukelaer SH, Verbeelen DL. Streptomycin pharmacokinetics in relapsing *Mycobacterium xenopi* peritonitis. *Am J Nephrol*. 1990;10:422–5.
- Dunmire RB 3rd, Breyer JA. Nontuberculous mycobacterial peritonitis during continuous ambulatory peritoneal dialysis: case report and review of diagnostic and therapeutic strategies. *Am J Kidney Dis*. 1991;18:126–30.
- Hakim A, Hisam N, Reuman PD. Environmental mycobacterial peritonitis complicating peritoneal dialysis: three cases and review. *Clin Infect Dis*. 1993;3:426–31.
- White R, Abreo K, Flanagan R, Gadallah M, Krane K, el-Shahawy M, Shakamuri S, McCoy R. Nontuberculous mycobacterial infections in continuous ambulatory peritoneal dialysis patients. *Am J Kidney Dis*. 1993;22:581–7.
- Gehr TW, Walters BA. Catheter-related *Mycobacterium chelonae* infection in a CAPD patient. *Perit Dial Int*. 1994;14:278–9.
- Vera G, Lew SQ. *Mycobacterium fortuitum* peritonitis in two patients receiving continuous ambulatory peritoneal dialysis. *Am J Nephrol*. 1999;19:586–9.
- Hevia C, Bajo MA, Sánchez-Tomero JA, del Peso G, Fernández-Perpén A, Millán I, Aguilera A, Selgas R. Peritoneal catheter exit-site infections caused by rapidly-growing atypical mycobacteria. *Nephrol Dial Transplant*. 2000;9:1458–60.
- Kleinpeter MA, Krane NK. Treatment of mycobacterial exit-site infections in patients on continuous ambulatory peritoneal dialysis. *Adv Perit Dial*. 2001;17:172–5.
- Youmbissi JT, Malik QT, Ajit SK, al Khursany IA, Rafi A, Karkar A. Non tuberculous mycobacterium peritonitis in continuous ambulatory peritoneal dialysis. *J Nephrol*. 2001;14:132–5.
- Tang S, Tang AW, Lam WO, Cheng YY, Ho YW. Successful treatment of *Mycobacterium fortuitum* peritonitis without Tenckhoff catheter removal in CAPD. *Perit Dial Int*. 2003;23:304–5.
- Ellis EN, Schutze GE, Wheeler JG. Nontuberculous mycobacterial exit-site infection and abscess in a peritoneal dialysis patient. A case report and review of the literature. *Pediatr Nephrol*. 2005;20:1016–8.
- Tse KC, Lui SL, Cheng VC, Yip TP, Lo WK. A cluster of rapidly growing mycobacterial peritoneal dialysis catheter exit-site infections. *Am J Kidney Dis*. 2007;50:e1–5.
- Covert TC, Rodgers MR, Reyes AL, Stelma GN Jr. Occurrence of nontuberculous mycobacteria in environmental samples. *Appl Environ Microbiol*. 1999;65:2492–6.
- Carson LA, Bland LA, Cusik LB, Favero MS, Bolan GA, Reingold AL, Good RC. Prevalence of nontuberculous mycobacteria in water supplies of hemodialysis centers. *Appl Environ Microbiol*. 1988;54:3122–5.
- Schulze-Robbecke R, Feldmann C, Fischeder R, Janning B, Exner M, Wahl G. Dental units: an environmental study of sources of potentially pathogenic mycobacteria. *Tuber Lung Dis*. 1995;76:318–23.