Successful Treatment of *Mycobacterium chelonae* Peritoneal Dialysis-Related Infection by a Combination Regimen Including Local Thermal Therapy

Editor:

Nontuberculous mycobacteria (NTM) are infrequent causes of peritoneal dialysis (PD)-related infection, and treatment protocols for NTM exit-site infection in PD are not well established. *Mycobacterium chelonae* is one species of NTM. Although thermal therapy could possibly be useful for treating cutaneous *M. chelonae* infection, it has not been widely used. We report here a case of *M. chelonae* exit-site infection treated by a combination regimen including thermal therapy. Most cases of exit-site infection caused by NTM need surgical procedures, such as PD catheter removal with partial catheter reimplantation and cuff shaving, even though the infection is restricted to the exit site (1,2). This is the first report of successful treatment of an *M. chelonae* exit-site infection without any surgical procedure.

CASE REPORT

A 59-year-old Japanese male with end-stage kidney disease due to membranous nephropathy, with a 3-year history of automated PD, recognized the presence of mild purulent drainage from the exit site of the PD catheter. He had a history of drug eruption caused by amlodipine, but no history of peritonitis or mycobacterial infection. He had no history of previous immunosuppressive therapy. He was empirically treated with oral levofloxacin (LVFX) and daily dressing with 10% povidone-iodine solution and topical gentamicin ointment. One week later the purulent drainage disappeared, and LVFX was then stopped. Purulent drainage reappeared 2 weeks later, and treatment with LVFX (100 mg/day) was restarted. The drainage from the exit site decreased slightly, but did not disappear. Bacterial cultures of the drainage fluid checking for normal bacterial flora were performed twice and were negative

during this event. *Mycobacterium* species were first isolated by acid-fast staining of the exudate from the exit site 1 month later. Finally, the DNA-DNA hybridization method identified *M. chelonae* infection another 1 month later. Other possible focuses of infection were excluded by chest X-ray and computerized tomography from chest to lower abdomen. According to in vitro susceptibility testing, the isolated *M. chelonae* was resistant to all tested antibiotics, which included isoniazid (INH), rifampicin (RFP), streptomycin (SM), ethambutol (EB), kanamycin (KM), enviomycin (EVM), ethionamide (TH), p-aminosalicylic acid (PAS), cycloserine (CS), pyrazinamide (PZA), and LVFX. Treatment with only these agents was not expected to cure this exit-site infection.

The purulent drainage from the exit site continued, the exit site bled easily, and ultrasonography of the tunnel tract revealed a sonolucent zone around the PD catheter. Treatment with LVFX did not improve the condition. In the treatment of PD-associated NTM infections, the PD catheters are usually removed; such cases are seldom resolved without surgical procedures (3). We explained the necessity of a surgical operation to the patient, but he did not accept either PD catheter removal or any other surgical procedure. Ultrasonography ruled out the possibility of external cuff infection, and there was no evidence of peritonitis. The patient's blood leukocyte count and serum C-reactive protein (CRP) level were both within normal ranges. We judged that the exit-site infection was restricted to a localized area. Localized heating is a possible alternative in treating *M. chelonae* (4,5). After consulting with dermatologists and pulmonologists, we tried a combination regimen of multiple antibiotics (oral clarithromycin (CAM) 400 mg/day, rifampicin (RFP) 450 mg/day, and ethambutol (EB) 500 mg/every other day), intensification of exit-site cleaning with 10% povidone-iodine solution, and direct localized heating by disposable pocket warmers. Local thermal therapy using a disposable pocket body was applied for 2 hours on the undershirt over the gauze of the exit site twice a day. Two weeks after initiation of this combination therapy, the purulent discharge almost disappeared. However, the patient developed fever, liver dysfunction, and drug eruption, and all antibiotics had to be stopped 3 weeks after beginning the combination treatment. Only local thermal therapy and cleaning were continued for 5 additional weeks.

After these treatments, there was no discharge from the exit site, and no sonolucent zone around the PD catheter by ultrasonography was visible. The exit-site infection caused by *M. chelonae* was cured completely. There has been no recurrence for 4 years up to the present day, demonstrating the effectiveness of a combination treatment including thermal therapy.

DISCUSSION

The classification of NTM is dependent on the growth rate, rapid or slow. Both cutaneous NTM infections and PD-related NTM peritonitis are often caused by rapid growers, especially *M. fortuitum*, *M. chelonae* and *M. abscessus*, rather than slow

growers such as *M. avium*, *M. kansasii*, and *M. goodii* (3). This may indicate that PD-related peritonitis is mainly induced through a transcutaneous infection route such as the PD exit site. The treatment protocol for NTM peritonitis is not well established and requires individualized protocols based on susceptibility testing (6).

Mycobacterium chelonae causes the second-highest number of PD-associated NTM infections, after *M. fortuitum* (3). Usually, both *M. chelonae* and *M. abscessus* do not grow at 43°C, while *M. fortuitum* does grow at that temperature. Many strains of *M. chelonae* either do not grow or grow poorly and slowly at 35°C (7). The temperature sensitivity of *M. chelonae* indicates possible applicability of thermal therapy for the treatment of cutaneous *M. chelonae* infection. Indeed, Levine and Rothschild reported that a localized cutaneous infection caused by *M. chelonae* was successfully treated by controlled local heating with a hand-held radiofrequency heat generator (4).

To the best of our knowledge, 16 cases of *M. chelonae* infection in PD patients have been reported. Most patients (12/17), including the present patient, had an exit-site infection, and 5 cases had both an exit-site infection and peritonitis. Regarding surgical treatment, all patients except the present patient needed surgical procedures such as catheter removal and reimplantation. Besides the present case report, only one study (5) has examined the effectiveness of thermal therapy in *M. chelonae* PD infection. In that case, an *M. chelonae* PD exit-site infection was successfully treated by local heat therapy together with a combination of prolonged antibiotics, derroofing and shaving of the outer cuff of the Tenckhoff catheter (5). The present case is the first instance of successful treatment of an *M. chelonae* PD-related infection with a combination treatment including thermal therapy and without any surgical procedure.

We applied local thermal therapy using disposable pocket warmers that reached a maximum temperature of 63°C and maintained a temperature of more than 40°C over a 12-hour period. In addition we simultaneously started both multiple antibiotics including CAM and intensification of exit-site cleaning with 10% povidone-iodine solution. Local treatment with thermal therapy and exit-site cleaning was performed over 8 weeks. Although the period of antibiotic administration lasted only 3 weeks, 2 weeks after initiation of this combination therapy, the exit-site infection showed marked improvement. Therefore this combination therapy significantly accelerated the cure in the present case.

In choosing therapy for PD-related infection, it is important to consider the characteristics of the causative bacteria. If caution is exercised to prevent low temperature burns, direct local heating is a simple, easy, and inexpensive therapy. Thermal therapy can be tried as part of an early combination regimen against cutaneous *M. chelonae*-related PD infection.

DISCLOSURES

The authors have no conflicts of interest to declare.

T. Okado*
S. Iimori
H. Nishida
N. Yui
E. Sohara
T. Rai
S. Uchida
S. Sasaki

Department of Nephrology
Tokyo Medical and Dental University
Tokyo, Japan

*email: tokado.kid@tmd.ac.jp

REFERENCES

1. Jo A, Ishibashi Y, Hirohama D, Takara Y, Kume H, Fujita T. Early surgical intervention may prevent peritonitis in cases with Tenckhoff catheter infection by nontuberculous mycobacterium. *Perit Dial Int* 2012; 32:227–9.
2. Gehr TW, Walters BA. Catheter-related *Mycobacterium chelonae* infection in a CAPD patient. *Perit Dial Int* 2012; 14:278–9.
3. Song Y, Wu J, Yan H, Chen J. Peritoneal dialysis-associated nontuberculous mycobacterium peritonitis: a systematic review of reported cases. *Nephrol Dial Transplant* 2012; 27:1639–44.
4. Levine N, Rothschild JG. Treatment of *Mycobacterium chelonae* infection with controlled localized heating. *J Am Acad Dermatol* 1991; 24:867–70.
5. Siu YP, Leung KT, Tong MK, Lee MK. *Mycobacterium chelonae* exit site infection in a patient on peritoneal dialysis. *Clin Nephrol* 2005; 63:321–4.
6. Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, et al. Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30:393–423.
7. Ota R, Iwasawa M, Ohkusu K, Kambe N, Matsue H. Maximum growth temperature test for cutaneous *Mycobacterium chelonae* predicts the efficacy of thermal therapy. *J Dermatol* 2012; 39:205–6.

doi: 10.3747/pdi.2013.00161