Successful Treatment of Vancomycin-Resistant *Enterococcus* Peritonitis Using Linezolid Without Catheter Removal in a Peritoneal Dialysis Patient

Peritoneal dialysis (PD) is an established treatment modality in patients with end-stage renal disease, and approximately 150 000 patients worldwide, including more than 7500 in Korea, are being maintained on PD (1). Although the incidence of peritonitis has declined significantly since the introduction of the Y-set, PD peritonitis is the most frequent and serious complication of treatment, causing technique failure and death in the population using the PD modality (2).

Many organisms have been implicated in PD peritonitis. Vancomycin-resistant *Enterococcus* (VRE) has been reported, but remains an uncommon causative organism of peritonitis in PD patients (3–13). The available data about the appropriate treatment for VRE peritonitis are limited. Whether the catheter must be removed as part of treatment for this infection is also unclear.

Here, we describe a case of VRE PD-related peritonitis treated with linezolid that achieved eradication of the infection without catheter removal.

CASE DESCRIPTION

A 77-year-old woman was admitted for surgery to repair a ventral hernia. This patient had been on continuous ambulatory PD for almost 2 years with no episodes of peritonitis. Her history was unremarkable, except for

well-controlled hypertension. She underwent a successful ventral hernioplasty, with removal and re-insertion of the PD catheter after the procedure. Seven days after the operation, the patient developed abdominal pain and cloudy effluent. On presentation, she was afebrile, with a blood pressure of 130/80 mmHg. Abdominal examination showed diffuse generalized tenderness, associated with rebound and normal bowel sounds. No expressible pus, drainage, or erythema was observed surrounding the surgical site or the catheter exit site. The initial effluent cell count was 14 900/mm³, with 80% polymorphonuclear neutrophils).

After the initial investigation, empiric antibiotic therapy for PD-associated peritonitis was initiated with intraperitoneal (IP) cefazolin (150 mg/L) and ceftazidime (150 mg/L). Three days later, cultures from the initial effluent sample grew vancomycin-resistant *E. faecium* sensitive to daptomycin (minimal inhibitory concentration: 4 µg/mL) and linezolid (minimal inhibitory concentration: ≤2 µg/mL). Because the patient showed considerable clinical improvement (decreased leukocyte count of 250/mm³ with 0% polymorphonuclear neutrophils, clear dialysate, and normalized abdominal tenderness), the initial antibiotic regimen was continued beyond day 7. However, on day 8 of treatment, the effluent became cloudy again, and the leukocyte count in effluent increased to 3385/mm³, with 86% polymorphonuclear neutrophils.

Given the initial results of the effluent culture, the antibiotic regimen was changed to linezolid 600 mg intravenously at 12-hour intervals, replacing the IP cefazolin and ceftazidime. On day 11 of treatment, effluent cloudiness had improved, and the leukocyte count in effluent had declined below 100/mm³.

Culture of effluent samples obtained on day 8 of treatment yielded vancomycin-resistant *E. faecium* sensitive to linezolid (minimal inhibitory concentration: ≤2 µg/mL). On day 14 of treatment, all leukocytes in the dialysate had disappeared, and the patient was discharged with oral linezolid (600 mg twice daily for 14 days) to complete a 3-week course of therapy as recommended by the International Society for Peritoneal Dialysis guidelines (14).

Serious side effects—such as bone marrow suppression, especially thrombocytopenia—were not observed during treatment. Follow-up cultures of effluent performed on days 11 and 14 of treatment were negative. During outpatient follow-up, the woman remained on PD without recurrence for 5 months.

DISCUSSION

The prevalence of VRE, which first reported in the late 1980s, has risen rapidly in many countries (15).

Among all clinical isolates, VRE has been estimated to have a prevalence in the range 12%–21% in Korea (16), and the organism has become a significant problem in terms of nosocomial infection, spreading from patient to patient in health care settings and producing infections, including PD-related peritonitis, in patients with various comorbid conditions (17). In addition, there is major concern about the fact that up to 14.4% of patients treated with dialysis have been colonized by VRE (18) and that the bacterium is contributing significantly to increased morbidity and mortality in that population (19).

The widespread use of vancomycin has become another matter of great concern because of the increase in VRE in dialysis patients. Reports of VRE are most often seen in conjunction with various host factors, including recent hospitalization. Our patient also had multiple factors predisposing her to the development VRE infection, including prolonged hospitalization (8 days before her peritonitis), abdominal surgery, and the presence of an indwelling central venous catheter (she was maintained temporarily on hemodialysis, performed using a jugular double-lumen catheter, before and after her ventral hernioplasty for a total of 2 weeks) (20).

Because of limited availability of effective antimicrobial agents, there is no established therapy for VRE peritonitis in PD patients. New agents with activity against VRE—such as linezolid, quinupristin–dalfopristin, and daptomycin—have recently been introduced, but data about their efficacy, dosing regimens, duration of activity, and means of administration for patients with VRE peritonitis are limited. Few reports of treatment using those drugs for PD-associated VRE peritonitis have been published (Table 1).

We chose intravenous (IV) linezolid for this case of VRE peritonitis because linezolid has not previously been administered in dialysate, and determining the dose that would be adequate for such use is thus difficult. Use of linezolid also gave us the flexibility to switch the patient to oral from IV administration after 7 days of treatment, given that previous reports indicated that the drug has excellent penetration into PD fluid after both IV and oral dosing (8).

We also had to decide whether to remove the PD catheter. Because our patient wanted to remain on PD and because she showed clinical improvement after linezolid treatment, we decided to continue the antibiotic therapy without catheter removal. Only two previous reports have described cases of VRE peritonitis treated with IP daptomycin (10) or IV linezolid (13) without removal of the PD catheter. It therefore remains unclear whether the catheter must be removed in case of VRE peritonitis.

TABLE 1
Summary of Reported Cases of Vancomycin-Resistant *Enterococcus* Peritonitis In Patients on
Peritoneal Dialysis (PD), 1994–2011

Reference	Pts (n)	Route and regimen of antibiotics	Duration of therapy	Clinical course
Lynn <i>et al.</i> , 1994 (3)	3	Quinupristin/dalfopristin IV 250 mg twice daily alternating with IP 25 mg/L IV 500 mg twice daily IV 250 mg twice daily alternating with IP 25 mg/L	14 Days 14 Days 16 Days	PD catheter was changed at the end of therapy. PD catheter was removed before treatment. PD catheter was removed at the time of relapsed peritonitis (72 hours after therapy ended)
Troidle <i>et al.</i> , 1996 (4)	9	No treatment (<i>n</i> =1) IV chloramphenicol (<i>n</i> =1) IV chloramphenicol plus IV tetracycline (<i>n</i> =1) IV chloramphenicol plus IV gentamycin (<i>n</i> =2) IV ampicillin plus IV gentamycin (<i>n</i> =1) IV ampicillin-sulbactam (<i>n</i> =1) IP cefazolin (<i>n</i> =1) IP vancomycin and ceftazidime (<i>n</i> =1)	Not described (dosage and duration)	The PD catheter was removed in 6 patients: • In 3 within 24 hours of the peritonitis diagnosis • In 3 patients at 5, 8, and 11 days after the peritonitis diagnosis The PD catheter was not removed in the remaining 3 patients. 2 Patients died: • 1 Before treatment • 1 During IP cefazolin treatment 1 Patient improved with IP vancomycin and ceftazidime without PD catheter removal.
Carey <i>et al.</i> , 1999 (5)	1	IV chloramphenicol (500 mg every 6 hours)	14 Days	PD catheter was removed on day 3 of therapy; 14 days of treatment was then completed.
Bailey <i>et al.</i> , 2001 (6)	1	IV linezolid 600 mg twice daily	3 Weeks	PD catheter was removed on day 2 of therapy; 3-week course of linezolid therapy was then completed.
O’Riordan <i>et al.</i> , 2002 (7)	1	PO linezolid 600 mg twice daily	More than 10 days	PD catheter was removed during the period of linezolid therapy. Linezolid was prescribed for 10 more days after catheter removal.
Allcock <i>et al.</i> , 2004 (8)	1	IV linezolid 600 mg twice daily	More than 14 days	PD catheter was removed and antifungal therapy was initiated on day 7 of linezolid therapy because of combined fungal peritonitis.
Tedla <i>et al.</i> , 2004 (9)	1	IV linezolid 600 mg twice daily	14 Days	PD catheter was removed on day 5 after the onset of peritonitis (with initiation of IV linezolid).
Huen <i>et al.</i> , 2009 (10)	2	IP daptomycin (20 mg/L)	10–14 Days	PD catheter was not removed.
Chang <i>et al.</i> , 2010 (11)	1	IV daptomycin (6 mg/kg), every other day	6 Days	PD catheter was removed on day 3 of therapy, but the patient died from septic shock on day 6 of therapy.

TABLE 1 (cont'd)

Reference	Pts (n)	Route and regimen of antibiotics	Duration of therapy	Clinical course
Unal <i>et al.</i> , 2011 (12)	1	IV linezolid 600 mg twice daily	15 Days	PD catheter was removed on day 9 of therapy because of persistent abdominal pain; 15 days of IV linezolid was then completed.
Yang <i>et al.</i> , 2011 (13)	1	IV linezolid 600 mg twice daily	14 Days	PD catheter was not removed.

Pts = patients; IV = intravenous; IP = intraperitoneal; PO = oral.

We suggest that catheter removal should be considered if peritonitis does not readily resolve, as indicated by the recommendations in the International Society for Peritoneal Dialysis guideline (14).

CONCLUSIONS

Linezolid, intravenous and oral, was effective in treating VRE peritonitis in this case, and the PD catheter was not removed. Those observations support a relatively good distribution of linezolid in dialysate with either route of administration. Further studies are warranted to determine the best linezolid dosing regimen and duration of administration for VRE peritonitis in PD patients. In addition, future studies should determine whether the PD catheter must be removed in cases of VRE peritonitis.

DISCLOSURES

The authors have no business relationships or financial conflicts of interest to declare.

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