The clinical course of peritoneal dialysis-related peritonitis caused by *Corynebacterium* species

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Abstract

**Background.** *Corynebacterium* species are part of the normal skin flora. The incidence of nosocomial infections caused by *Corynebacterium* species has increased substantially over the past two decades. However, the clinical course of *Corynebacterium* peritonitis complicating peritoneal dialysis remains unclear.

**Method.** We reviewed all the *Corynebacterium* peritonitis in our dialysis unit from 1995 to 2002. During this period, there were 1485 episodes of peritonitis recorded; 27 (1.8%) of which were caused by *Corynebacterium* species.

**Results.** The underlying renal diagnosis and prevalence of comorbid conditions of the 27 patients were similar to our whole dialysis population. The bacteria isolated were resistant to penicillin in 8 cases (29.6%). Three cases (11.1%) had concomitant exit-site infection. The overall primary response rate was 74.1%; the complete cure rate was 37.0%. Episodes that received vancomycin as initial antibiotic had a marginally higher primary response rate (9 in 10 vs 11 in 17 episodes, *P* = 0.2) and complete cure rates (7 in 10 vs 3 in 17 episodes, *P* = 0.12) than the episodes that received cephalosporins, although neither of the differences was statistically significant. Thirteen cases (48.1%) had recurrent peritonitis after antibiotic therapy, 8 of which had the recurrent episode at least 30 days after stopping antibiotics (median 54 days, range 43–60 days). Eight recurrent cases (61.5%) were successfully cured by another 3 week course of intra-peritoneal vancomycin.

**Conclusions.** Recurrent *Corynebacterium* peritonitis is common after a 2 week course of antibiotics. Recurrent *Corynebacterium* peritonitis may be delayed up to 2 months after the antibiotic is stopped. Recurrent peritonitis can usually be cured with a 3 week course of intra-peritoneal vancomycin, which is probably the preferred antibiotic regimen for *Corynebacterium* peritonitis.

**Keywords:** peritoneal dialysis; peritonitis; renal failure

Introduction

The skin flora is a mixture of poorly classified micrococcus and coryneform bacteria (formerly called diphtheroids) [1]. In general, *Staphylococcus epidermidis* is found predominantly on the surface and anaerobic coryneform bacteria deep in the hair follicles [1]. In contrast to *S.epidermidis*, which is one of the commonest causes of peritoneal dialysis (PD)-related peritonitis, peritonitis episodes caused by *Corynebacterium* species are unusual in PD, and only isolated case reports and small case series have been published [2–11]. Nevertheless, reported infections caused by *Corynebacterium* species have increased substantially in number over the past two decades. More importantly, isolates of *Corynebacterium* species are often resistant to multiple antibiotics. Here, we report 27 consecutive cases of PD-related peritonitis caused by *Corynebacterium* species.

Patients and methods

All episodes of PD-related peritonitis in our unit from January 1995 to December 2002 were reviewed. The diagnosis of peritonitis was based on standard criteria [12]. In the eight years of the study period, 1485 episodes of peritonitis were recorded; 27 episodes (1.8%) were caused by *Corynebacterium* species. Their case records were reviewed.
Peritonitis episodes were treated with a standard antibiotic protocol of our centre. Initial antibiotics for peritonitis were generally intra-peritoneal (i.p.) administration of a third- or fourth-generation cephalosporin, plus or minus vancomycin, or cefazolin plus netilmicin or ceftazidime. In general, the dosage of antibiotics followed standard guidelines [12,13]. The dosage of vancomycin was 1 g i.p. every 5 days, and that of cefazolin was 1 g i.p. as loading, then 250 mg i.p. every exchange. In case of relapse, the dosage of vancomycin employed during the second course of therapy was the same as that in the first course of therapy. The details of peritonitis management and definitions of response and relapse have been described in our previous reports [12].

Statistical analysis was performed by SPSS for Windows software version 10.0 (SPSS Inc., Chicago). All data were expressed in mean±SD unless otherwise specified. Data were compared by chi-square test or Fisher’s exact test as appropriate. A P-value of less than 0.05 was considered significant. All probabilities were two-tailed.

Results

We reviewed 27 patients (14 men and 13 women) who had peritonitis episodes caused by Corynebacterium species (i.e. 1.8% of all episodes). Their average age was 62.8 ± 10.2 years, and were dialyzed for 34.1 ± 27.7 months. The underlying renal diagnoses were glomerulonephritis (10 cases), diabetes (7 cases), hypertensive nephrosclerosis (5 cases), obstructive uropathy (2 cases) and unknown (3 cases). Sixteen patients were using disconnect PD system. The underlying renal diagnosis and prevalence of comorbid conditions of the 27 patients were similar to our whole dialysis population (details not shown).

Prior to the development of Corynebacterium peritonitis, 11 patients (40.7%) had no history of peritonitis, 7 patients (25.9%) had one episode, and 9 patients (33.3%) had two or more episodes of peritonitis in the past. However, there was a history of peritonitis due to another organism within 30 days of the onset of Corynebacterium peritonitis in two cases (7.4%).

The bacteria isolated were resistant to penicillin in eight cases (29.6%); five patients received penicillin or cephalosporin group of antibiotics within 30 days prior to the onset of the peritonitis. All bacterial strains isolated were sensitive to vancomycin. In three cases (11.1%), there was concomitant exit-site infection. However, according to phenotypic characteristics, the same Corynebacterium species was isolated in only one case.

Clinical outcome

The overall primary response rate was 74.1%; the complete cure rate was 37.0%. Episodes that received vancomycin as part of the initial antibiotic regimen had a marginally higher primary response rate (9 in 10 vs 11 in 17 episodes, P = 0.2) and complete cure rates (7 in 10
Corynebacterium peritonitis in PD

Five cases developed relapse within 30 days (median 16 days, range 7–20 days) after initial antibiotics were stopped. Five cases had late relapse at least 30 days after stopping antibiotics (median 54 days, range 43 to 60 days). Only one case of late relapse had co-existing exit-site infection of the same Corynebacterium species. Notably, six of the eight episodes (75.0%) that showed primary response to cephalosporin had recurrent peritonitis with phenotypically the same organism after 30 days of stopping antibiotics.

All relapse episodes were treated with i.p. vancomycin for 3 weeks; 8 cases (61.5%) responded. The response rate was marginally lower than that of fresh cases treated with vancomycin (P = 0.064). Five cases required catheter removal; three of them (60.0%) could successfully return to PD after around 4 weeks of temporary haemodialysis.

Discussion

Contrary to the decreasing incidence of peritonitis caused by S. epidermidis (another normal skin flora), the incidence of Corynebacterium peritonitis remained static after the widespread use of disconnect PD-system of our centre since late 1990s. It is probably because S. epidermidis predominates on the skin surface and peritonitis is caused by touch contamination, which is prevented by the flush-before-fill mechanism of disconnecting PD systems. On the other hand, Corynebacterium species are generally present deep in hair follicles [1]; touch contamination is unlikely to be the major route of infection. It has been suggested that Corynebacterium species colonize skin only after broad spectrum antibiotic therapy [14]. However, only a small proportion of our patients had a history of antibiotic exposure prior to the onset of Corynebacterium peritonitis.

Because of the retrospective nature of our study, the exact grouping and species of the Corynebacterium isolated from our patients could not be ascertained. For example, C. jeikeium, the more resistant species, is mixed with other mostly susceptible species. Similarly, we have no data on the minimal inhibitory concentrations (MICs) of the organisms, or the serum or dialysate antibiotic concentrations in relation to the MICs.

We observed a high incidence of relapse Corynebacterium peritonitis following the treatment with 2-week course of i.p. antibiotics. Repeated episodes were particularly common after cephalosporin therapy in spite of the in vitro sensitivity, and could be delayed up to 2 months after the initial course of antibiotic was completed. Our result is consistent with other reports (Table 1). Notably, a substantial number of recurrent episodes were successfully treated with prolonged course (3 weeks or more) of i.p. vancomycin without further relapse, suggesting inadequate initial therapy rather than the presence of biofilm on the dialysis catheter. Based on our limited data, we believe a 3-week course of i.p. vancomycin is the treatment of choice for Corynebacterium peritonitis, irrespective of sensitivity to the antibiotics. Given the low incidence of Corynebacterium peritonitis, the problem of excessive vancomycin usage and inadvertent resistance would be bearable. Although many of the Corynebacterium species are sensitive to erythromycin, resistance strain is emerging [15], and patient compliance is foreseeably suboptimal with erythromycin therapy because gastrointestinal upset is common.

For recurrent peritonitis, catheter exchange after dialysis effluent cleared up, without temporary haemodialysis support, has been advocated for other organisms [12], especially when there is persistent catheter exit-site or tunnel infection. However, there is virtually no data in Corynebacterium peritonitis. Previous reports did not find Corynebacterium biofilm on the dialysis catheters removed from patients with recurrent Corynebacterium peritonitis [5,7]. Our data showed that a repeated course of vancomycin without immediate catheter removal can be tried for recurrent episode of Corynebacterium peritonitis.

In conclusion, recurrent Corynebacterium peritonitis is common after a 2 week course of antibiotics. Recurrent Corynebacterium peritonitis may be delayed up to 2 months after antibiotic is stopped. Recurrent peritonitis can usually be cured with a 3 week course of i.p. vancomycin, which is probably the preferred antibiotic regimen for Corynebacterium peritonitis.

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References


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