A case of bacterial peritonitis caused by *Roseomonas mucosa* in a patient undergoing continuous ambulatory peritoneal dialysis

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Abstract Bacterial peritonitis remains a life-threatening complication of peritoneal dialysis (PD). *Roseomonas* is a bacterial genus of pink-pigmented, oxidized, gram-negative coccobacilli that was first named in 1993. Importantly, *Roseomonas mucosa* exhibits antibiotic resistance, with significant resistance to cephalosporin, which is often selected as an empirical antibiotic regimen for peritonitis in PD patients. We herein report the case of a PD patient with bacterial peritonitis caused by *Roseomonas mucosa* that was fortunately identified using 16S rRNA gene sequencing and successfully treated with ciprofloxacin. Given that *Roseomonas* demonstrates resistance to a variety of antibiotics. The administration of empiric antibiotic therapy based on the recommendation of the International Society of Peritoneal Dialysis guidelines occasionally fails, leading to the aggravation of bacterial peritonitis. Hence, nephrologists should consider *Roseomonas* as one of the potential causative organisms of peritonitis, especially when gram-negative bacilli are resistant to cephalosporin and cannot be identified using standard laboratory methods.

Keywords Antibiotic resistance · Bacterial peritonitis · Peritoneal dialysis · *Roseomonas mucosa* · 16S rRNA gene sequencing

Introduction

Bacterial peritonitis remains a leading cause of lethal complications in patients undergoing peritoneal dialysis (PD) [1]. Because peritonitis is a major cause of PD withdrawal, appropriately selecting antibiotics is mandatory. The International Society of Peritoneal Dialysis (ISPD) recommends that the empiric treatment of bacterial peritonitis should include two types of antibiotics to cover both gram-positive and -negative bacteria [2]. Among the several recommended antibiotics, cephem antibiotics constitute an important option for the treatment of bacterial peritonitis. Because some bacterial genera show resistance to antibiotics, guideline-based empiric therapy occasionally fails, resulting in the aggravation and delayed resolution of bacterial peritonitis [3].

Roseomonas is a bacterial genus of pink-pigmented, oxidized and gram-negative coccobacilli that was first identified in 1993 and has a low pathogenic potential for humans [4, 5]. Of note, the identification of the *Roseomonas* genus infection is accomplished not by the normal bacteriological laboratory techniques, but by 16S rRNA gene sequencing [6]. Regarding the clinical setting, some *Roseomonas* can cause bloodstream infections in immunocompromised patients [5, 6]. However, bacterial peritonitis caused by *Roseomonas mucosa* has rarely been reported in PD patients.

We herein report the case of a PD patient with bacterial peritonitis caused by *Roseomonas mucosa* who was successfully treated with ciprofloxacin. In the present case,

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Roseomonas mucosa was fortunately identified as the causative organism with the use of 16S rRNA gene sequencing.

Case

A 61-year-old male who had received 6 months of PD therapy was admitted to our hospital while demonstrating a cloudy peritoneal dialysate. He had been diagnosed as having type 2 diabetes mellitus at 58 years of age and received conservative management, including treatment with antihypertensive drugs and oral hypoglycemic agents. However, diabetic nephropathy gradually progressed, and he began receiving continuous ambulatory peritoneal dialysis for end-stage kidney disease at 60 years of age. He was dialyzed using a two-bag exchange system four times a day, three times a day at home and once at the fish market. Because the patient was a fisherman and came in contact with water every day, he was relatively susceptible to water-borne infections. Two days prior to admission, he developed general fatigue, followed by a cloudy peritoneal dialysate on the day of admission, thus suggesting the development of peritonitis.

On a physical examination, the patient was alert. His blood pressure was 140/70 mmHg, his heart rate was 88 beats/min, and his body temperature was 36.6 °C. He did not exhibit abdominal tenderness. His exit site and catheter tunnel showed no evidence of infection. His laboratory data on admission revealed a white blood cell (WBC) count of 6,090/ μ l with 72.5 % segmented neutrophils and a C-reactive protein level of 5.4 mg/dl. The serum

procalcitonin level was 0.17 ng/dl. The dialysate fluid cell count was 3,349 WBCs/ μ l with 77 % neutrophils. Gram staining of the dialysis fluid was negative. A tentative diagnosis of bacterial peritonitis was established, and the patient was treated empirically with intraperitoneal administration of cefazolin [loading dose 500 mg/l (750 mg/bag), maintenance dose 125 mg/l (187.5 mg/bag)] and amikacin [loading dose 12 mg/l (18 mg/bag), maintenance dose 12 mg/l (18 mg/bag)] for one 6-h period once every day based on the ISPD guidelines for treating peritoneal dialysis-related infections [2]. We also increased the number of daily bag changes to wash out the bacteria in the abdomen and maintain adequate dialysis; the efficacy of dialysis often decreases when patients develop bacterial peritonitis. On the 3rd hospital day, gram-negative bacteria appeared in the initial PD fluid culture, and we discontinued cefazolin and amikacin and treated the patient with ceftazidime [loading dose 500 mg/l (750 mg/bag), maintenance dose 125 mg/l (187.5 mg/bag)] for one 6-h period once every day (ceftazidime is usually useful for treating gram-negative bacterial infections). At that time, we were unable to identify the genus of the causative gram-negative bacteria using standard laboratory methods. On the 6th hospital day, the results of the susceptibility test showed that the causative bacterium was susceptible to gentamicin, ciprofloxacin and meropenem and resistant to cephalosporins, including ceftazidime. Therefore, we discontinued ceftazidime and started ciprofloxacin [loading dose 50 mg/l (75 mg/bag), maintenance dose 25 mg/l (37.5 mg/bag)] for one 6-h period once every day. The intraperitoneal administration of ciprofloxacin was continued for a total of 21 days, resulting in a normalized dialysate fluid cell count

Fig. 1 Clinical course after hospitalization. AMK amikacin, CAZ ceftazidime, CEZ cefazolin, CPFX ciprofloxacin

Fig. 2 Gross appearance of the colonies in the cultured medium. The colonies derived from the peritoneal dialysate were pale pink in color, compatible with the characteristic features of *Roseomonas*

and negative culture at the end of the therapy (Fig. 1). Following the resolution of the peritonitis, the patient decided to discontinue PD therapy and began hemodialysis as renal replacement therapy of his own will.

In order to identify the causative gram-negative bacteria, we sent the colonies of the causative gram-negative bacteria to another microbiology reference laboratory. The gross appearance of the colonies on the culture medium obtained from the dialysate fluid was mucoid and pale pink (Fig. 2). To obtain a definitive identification of the organism, 16S rRNA gene sequencing was performed. The detailed mechanisms and methods of 16S RNA gene sequencing have been previously described [7]. The 16S rRNA gene fragments were amplified using standard methods. The sequencing data were analyzed by comparing the consensus sequences [8]. The percentage of similarity to other sequences was determined, and *Roseomonas mucosa* (GenBank accession no. AF538712) was finally identified at 99.9 % reliability based on the presence of pairwise similarities; only one base difference between the isolate and *Roseomonas mucosa* was detected, while 13 base differences between the isolate and *Roseomonas gilardii* were detected.

Discussion

We herein presented the case of a patient with bacterial peritonitis caused by *Roseomonas mucosa*, which was identified as the causative organism on 16S rRNA gene sequencing and successfully treated with ciprofloxacin. The clinical implications of the present case include several points. First, *Roseomonas mucosa* can induce bacterial peritonitis in PD patients. Second, *Roseomonas mucosa*

exhibits resistance to several types of antibiotics, which can lead to treatment failure if third-generation cephem antibiotics are selected to cover gram-negative bacilli. Third, *Roseomonas* cannot be identified using routine laboratory techniques and requires 16S rRNA gene sequencing, which thus makes it difficult to diagnose bacterial peritonitis caused by this organism.

Roseomonas is a bacterial genus of pink-pigmented gram-negative coccobacilli that have been cultured from blood and other clinical specimens for the last several decades. The genus and its species were first named in 1993 to include three named species (*Roseomonas gilardii*, *Roseomonas cervicalis* and *Roseomonas fauriae*) and three unnamed species (genomospecies 4, 5 and 6), and *Roseomonas mucosa* and *Roseomonas gilardii* were first proposed in 2003 [8]. Because the *Roseomonas* genus cannot be identified using the standard biological method, 16S rRNA gene sequencing is an important and reliable method for identifying this genus.

There are four previous reports of PD peritonitis caused by *Roseomonas*; our case is the fifth report and the second report caused by *R. mucosa* (Table 1) [9, 10–12]. Possibly due to the low virulence of *Roseomonas*, four of the five reported patients exhibited mild symptoms, including no or mild abdominal pain and no fever, etc. Although the pathogenesis of *Roseomonas* infection is currently poorly understood, a possible association between water contamination and *Roseomonas* infection has been clinically reported. Indeed, the three previous reports of peritonitis in PD patients also suggested that the infection was water related. In our case, interestingly, the patient was a fisherman, an occupation with much greater opportunities to come in contact with watery substances. Although it is difficult to prove that the source of *Roseomonas* was the fish market, given that the patient exchanged his PD bag once at his fish market, there may be an association between the patient's *Roseomonas* infection and his daily job.

The empirical antibiotic regimen for peritonitis in patients on PD usually includes a cephalosporin to cover gram-negative bacilli; however, the *Roseomonas* genus is estimated to have antibiotic resistance, with significant resistance to cephalosporin. In contrast, *Roseomonas* is generally susceptible to aminoglycosides, fluoroquinolones and carbapenems. However, it remains undetermined as to why and how *Roseomonas* species acquire antibiotic resistance to multiple antibiotics. Dé et al. [6] reported 36 cases of bacteremia or catheter-related infection caused by *Roseomonas*. The causative species included *Roseomonas mucosa* (22 cases, 61 %). The antibiotic susceptibility pattern shows that *Roseomonas* is consistently susceptible to amikacin and imipenem and frequently susceptible to ciprofloxacin and ticarcillin, but essentially not susceptible to ceftazidime or cefepime [3, 5]. The authors reviewed the

Table 1 Summary of the clinical characteristics of the four reported cases of PD-related peritonitis due to the *Roseomonas* genus

Case	Age	Sex	Publication	Kidney disease	Symptom	Mode	Antibiotics	Outcome	Bacteria
1	62	Female	1997, [10]	Unknown	Vague abdominal pain	CAPD	VCM + NTL	Recovery	<i>R. gilardii</i>
2	65	Female	2000, [11]	Unknown	Mild abdominal pain	CAPD	VCM + NTL → CPFX	Recovery	<i>R. fauriae</i>
3	48	Male	2012, [12]	CGN	Cloudy dialysate	APD	CAE + CAZ → CPFX → CEZ + GM	Recovery	<i>R. genus</i>
4	19	Male	2012, [9]	CGN	Abdominal pain, fever	CCPD	CAZ + VCM → CPFX + GM + VCM	PD withdrawal	<i>R. mucosa</i>
Ours	61	Male	–	DM	Cloudy dialysate	CAPD	CEZ + AMK → CAZ → CPFX	Recovery	<i>R. mucosa</i>

AMK amikacin, APD automated peritoneal dialysis, CAPD continuous ambulatory peritoneal dialysis, CAZ ceftazidime, CCPD continuous cycling peritoneal dialysis, CEZ cefazolin, CGN chronic glomerulonephritis, CPFX ciprofloxacin, DM diabetes mellitus, GM gentamicin, NTL netilmicin, PD peritoneal dialysis, *R. Roseomonas*, VCM vancomycin

antibiotic susceptibility of *Roseomonas*, using 80 strains, in three published series [6]. The previously examined 80 strains of the *Roseomonas* genus are all susceptible to amikacin (100 % of the strains) and are frequently susceptible to imipenem (99 %), ciprofloxacin (90 %) and ticarcillin (83 %). However, they are far less susceptible to ceftriaxone (38 %), trimethoprim-sulfamethoxazole (30 %) and ampicillin (13 %) and are essentially not susceptible to ceftazidime (5 %) or cefepime (0 %). Therefore, a third- or fourth-generation cephalosporin (such as ceftazidime, ceftriaxone or cefepime) would be a poor choice for treatment [6].

In the present case, the results of the antibiotic sensitivity test were similar to those of previous reports. We treated the patient empirically with the intraperitoneal administration of cefazolin and amikacin, and after the gram-negative bacillus appeared in the initial PD fluid culture, we changed cefazolin and amikacin to ceftazidime. However, the susceptibility pattern showed that the bacterium was resistant to cephalosporins, including ceftazidime and cefepime. Hence, we started ciprofloxacin and fortunately avoided treatment failure.

Infectious complications of PD can result in significant morbidity, hospitalization and death. Therapy is usually initiated prior to identifying the causative organism and should be administered as soon as possible after appropriate microbiological specimens are obtained. According to the guidelines proposed by the ISPD in 2010, empiric antibiotic therapy must cover both gram-positive and -negative organisms [2]. Gram-positive organisms may be covered by vancomycin or a cephalosporin, while gram-negative organisms can be treated with a third-generation cephalosporin or aminoglycoside [2]. In the clinical setting, physicians often avoid using aminoglycoside to maintain the residual kidney function, as aminoglycosides are potentially nephrotoxic. Consequently, a cephalosporin

(ceftazidime or cefepime) may be more easily selected. However, as in the present case, when the causative bacillus is of the *Roseomonas* genus, treatment with a cephalosporin can possibly lead to the aggravation of bacterial peritonitis. Accordingly, when treating peritonitis, special attention should be paid to selecting the most effective antibiotics, once the sensitivity pattern of the offending bacillus is obtained.

Several limitations to this study should be described. We could have provided APD for the patient at the time of initiation of renal replacement therapy in order to prevent the development of bacterial peritonitis by *Roseomonas mucosa*; the fish market may not have been a suitable location for bag exchange, and the use of APD could have prevented exposure to *Roseomonas mucosa* in the present case. Furthermore, we could have continued the treatment with cefazolin and amikacin until the bacterial susceptibility test results returned, as both drugs appeared to be effective based on the changes in the WBC count in the peritoneal fluid and the serum CRP level observed in the first 3 hospital days. However, we discontinued amikacin in order to prevent renal function decline caused by the drug.

In conclusion, the occurrence of bacterial peritonitis caused by *Roseomonas* in a patient undergoing PD is very rare. When treating single-organism gram-negative peritonitis, a *Roseomonas* should be considered if there is high resistance to cephem antibiotics. In addition, the antibiotic treatment should be adjusted to the sensitivity pattern of the antibiotics, and 16S rRNA gene sequencing can be an important method for identifying the causative organism with a high probability.

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