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Single Case

Chryseobacterium indologenes Peritonitis in a Peritoneal Dialysis Patient: A Case Report and Review of Literature

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Keywords
Chryseobacterium indologenes · Peritonitis · Peritoneal dialysis

Abstract
Peritonitis is one of the most important complications in patients with peritoneal dialysis (PD). Appropriate antibiotic treatment against PD-associated peritonitis is necessary to prevent PD catheter removal and withdrawal from PD. *Chryseobacterium indologenes* is a Gram-negative rod that occurs in the natural environment. *C. indologenes* is thought to acquire resistance to β-lactam drugs through the production of metallo-β-lactamase and to become resistant to antibiotic therapy through the formation of biofilms. Only a few cases of PD-associated peritonitis caused by *C. indologenes* have been reported to date, and appropriate treatment strategies have not been clarified. In the past, 5 cases of PD-associated peritonitis caused by *C. indologenes* have been reported and 2 patients required catheter removal because of recurrence or refractoriness. In this case, a 51-year-old man with PD-associated peritonitis caused by *C. indologenes* was treated with 2 susceptible antibiotics, including fluoroquinolones to prevent acquired resistance and biofilm formation. There was no recurrence, and catheter removal was not necessary in this case. Collectively, the present case highlighted that PD-associated peritonitis caused by *C. indologenes* should be treated with 2 susceptible antibiotics including fluoroquinolones for 3 weeks.

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Introduction

Peritonitis is one of the most important complications in patients with peritoneal dialysis (PD). Appropriate antibiotic treatment against PD-associated peritonitis is necessary to prevent PD catheter removal and withdrawal from PD. Morphological alterations and loss of mesothelial cells caused by peritonitis can be risk factors for fluid overload due to a decline in ultrafiltration in PD and the development of encapsulating peritoneal sclerosis [1].

Although Gram-positive bacteria are the most common cause of PD-associated peritonitis, Gram-negative organisms are causative agents in 29.4% of cases [2]. Single-antibiotic use fails to treat 39% of PD-associated peritonitis caused by Gram-negative rods and results in PD withdrawal in 1% of cases [3, 4]. *Chryseobacterium indologenes (C. indologenes)* is a yellow-pigmented, nonmotile, aerobic, glucose-nonfermenting Gram-negative rod widely found in the environment, including soil and water. *C. indologenes* is frequently isolated from ventilators and indwelling devices in hospitalized patients and may result in pneumonia and sepsis. *C. indologenes* often produces metallo-β-lactamases and is resistant to β-lactam drugs, including carbapenems [5]. Principally, *C. indologenes* is also known to form biofilms, which causes antibiotic resistance [6, 7]. So far, only a few cases of PD-associated peritonitis caused by *C. indologenes* are available, and appropriate treatment strategies are missing. Although ISPD guidelines recommend a 3-week course of antibiotics for PD-associated peritonitis caused by Gram-negative rods, an adequate antibiotic regimen (type of antibiotic and duration) for treatment of PD peritonitis caused by *C. indologenes* has not been established [3]. Herein, we present a case of peritonitis caused by *C. indologenes* and suggest a 3-week treatment with a combination of 2 antibiotics with different mechanisms.

Case Report

A 51-year-old Japanese male with hypertension, hyperlipidemia, and diabetes mellitus reached end-stage renal disease, which was deemed to be caused by diabetic nephropathy. Since then, he was treated daily with continuous PD (CAPD), consisting of 3 daily exchanges with 6-h dwell time making up 18 h, not 24 h with 1,500 mL dwell volumes containing 2.5% dextrose. He did not drink and did not smoke. He was an office worker. Laboratory data showed that potassium level was 4.0 mEq/L, phosphate level was 5.7 mg/dL, blood urea nitrogen level was 57 mg/dL, and creatinine level was 8.23 mg/dL the first time during CAPD. Four months after starting CAPD, he presented with abdominal pain and cloudy peritoneal fluid the day after visiting a hot spring. On admission, his blood pressure was 125/97 mm Hg, heart rate was 120 beats/min, respiratory rate was 16 breaths/min, and body temperature was 36.0°C. He had tenderness throughout the abdomen, and the exit site was clear. The peritoneal fluid cell count was increased at 521/μL, of which the percentage of neutrophils was 81%. His peripheral white blood cell count was 7,200/μL (neutrophils: 80.4%, lymphocytes: 10.3%, monocytes: 5.7%, eosinophils: 3.3%, basophils: 0.3%), and his C-reactive protein level was 0.92 mg/dL. Computed tomography showed that peritoneal thickening and increased intra-abdominal fatty tissue concentrations were not evident. Based on these findings, he was diagnosed with PD-associated peritonitis.

He received intraperitoneal administration of cefazolin (1.5 g) and ceftazidime (CAZ) (1.5 g) every 24 h for 6 h. Figure 1 shows antibiotic treatment, peritoneal cell counts, peripheral white blood cell counts, and C-reactive protein during treatment. On day 2, abdominal pain dramatically improved. *C. indologenes* was cultured from the peritoneal fluid on day 4. The susceptibility of *C. indologenes* to antibiotics is shown in Table 1. Although *C. indologenes* was susceptible to ceftazidime (minimum inhibitory concentration: 8 μg/mL) in the present case,

Case Reports in Nephrology and Dialysis

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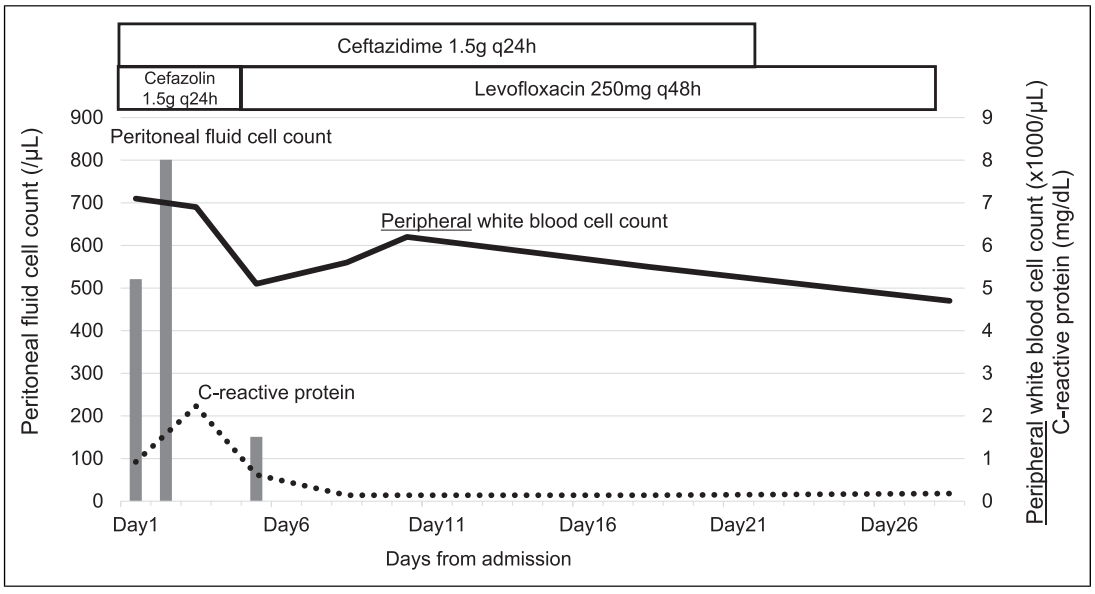

Fig. 1. Clinical course of the present case. Cefazoline 1.5 g and ceftazidime 1.5 g were administered every 24 h for 6 h. LVFX 250 mg was administered every 48 h. Administration of LVFX was switched from intravenous to oral on day 11. Black line indicates the peripheral white blood cell count. The dashed line indicates the C-reactive protein level. The bar graph indicates the peritoneal fluid cell counts.

catheter removal was required in two previous reports of PD-associated peritonitis caused by *C. indologenes*, despite its susceptibility to ceftazidime. Thus, we were concerned about acquisition of resistance and biofilm formation by *C. indologenes* in our patient. Intraperitoneal administration of cefazolin was discontinued, and intravenous administration of levofloxacin (LVFX) 250 mg every 48 h was initiated on day 4. The peritoneal fluid cell count decreased to 151/μL on day 5. His peripheral white blood cell count was 5,500/μL (neutrophils: 71.9%, lymphocytes: 16.4%, monocytes: 6.7%, eosinophils: 4.2%, basophils: 0.8%), and his C-reactive protein level was 0.14 mg/dL on day 8. He was discharged on day 11, and the administration of LVFX was switched from intravenous to oral. He was treated with intraperitoneal administration of ceftazidime until day 21 and oral administration of LVFX until day 27. There has been no recurrence, and catheter removal has not been necessary 1 year after PD-associated peritonitis. The CARE Checklist has been completed by the authors for this case report and is attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531154).

Discussion

In the past, 5 cases of PD-associated peritonitis caused by *C. indologenes* have been reported (Table 2) [8–12]. Two patients required catheter removal because of recurrence or refractoriness. Although the ISPD guidelines recommend 3 weeks of antibiotic therapy for PD-associated peritonitis caused by Gram-negative rods, both successful and unsuccessful cases of PD-associated peritonitis caused by *C. indologenes* have been treated with antibiotics for 16–21 days. Three patients were treated with intraperitoneal administration of ceftazidime only, one of them relapsed after 26 days of treatment, and catheter removal was required.

The previously reported susceptibility of PD-associated peritonitis caused by *C. indologenes* to antibiotics is shown in Table 1 [8–11]. *C. indologenes* detected in the drainage fluid

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Table 1. Susceptibility of antibiotics to *C. indologenes* peritonitis in PD in previous reports including current case

Antibiotics	This case	Kitagata et al. [8]	Minami et al. [9]	Myung et al. [10]	Afshar et al. [11]
Ampicillin/sulbactam	S				R
Piperacillin/tazobactam	S	S	S		S
Cefazoline					R
Ceftazidime	S	S	S	R	S
Ceftriaxone	R		I		R
Cefepime	S	S	S	S	S
Cefmetazole					
Meropenem	S	S	S		
Imipenem/cilastatin					R
Aztreonam	R	R	R	S	
GM	I	I			R
LVFX	S	S	S	S	
Sulfamethoxazole/ trimethoprim	S	S	S		S
Amikacin	S	S			
CPFX	S	S	S	S	S

S, susceptible; I, intermediate; R, resistant; GM, gentamicin; CPFX, ciprofloxacin.

culture of patients with PD-associated peritonitis seem to be relatively susceptible to most antibiotics. In the present case, *C. indologenes* was not susceptible to ceftriaxone, aztreonam, and gentamicin, but was susceptible to other antimicrobial agents, such as carbapenem. However, *C. indologenes* isolated from hospitalized patients with ventilator-associated pneumonia and sepsis was only 7.7% susceptible to ceftazidime and carbapenems and is often difficult to treat clinically [5]. PD-associated peritonitis cases caused by *C. indologenes*, including the present case, are community-required infections, and *C. indologenes* is thought to be environmental bacteria, from either the water or soil, which may have resulted in a low resistance. Also in the present case, PD-associated peritonitis occurred after bathing in a hot spring and thus thought to be caused by touch contamination with environmental *C. indologenes*. However, there is a concern that *C. indologenes*, which was susceptible to ceftazidime upon admission, may have acquired resistance against ceftazidime due to the production of metallo-β-lactamase during insufficient treatment with monotherapy [13]. Indeed, treatment with 2 antibiotics for PD-associated peritonitis caused by Serratia, Pseudomonas, and indole-positive organisms, such as Proteus and Providencia, Citrobacter, and Enterobacter (SPICE) organisms with amp-C β-lactamases that inactivate cephalosporin has been reported to prevent relapse. Thus, it has been reported that relapse and recurrence rates were lower when patients with PD-associated peritonitis caused by Gram-negative rods were treated with 2 antibiotics rather than with a single drug [3]. Treatment by 2 susceptible antibiotics was recommended for *C. indologenes* infection in pediatric cases because *C. indologenes* often produces metallo-β-lactamases [14]. Myung et al. [10] reported a case of PD-associated peritonitis caused by *C. indologenes* in which the patient was treated with 2 susceptible antibiotics, and catheter removal was not required.

Case Reports in Nephrology and Dialysis

Case Rep Nephrol Dial 2023;13:90–96
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Table 2. Previous reports including current case of *C. indologenes* peritonitis in PD

Authors	This case	Kitagata et al. [8]	Minami et al. [9]	Myung et al. [10]	Afshar et al. [11]	Carvalho et al. [12]
Country	Japan	Japan	Japan	Korea	USA	Portugal
Age	51	12	60	24	51	76
Sex	Male	Female	Male	Female	Male	Male
Cause of renal insufficiency	Diabetes mellitus	Unknown	Diabetes mellitus	Diabetes mellitus	HIV	Hypertension
PD duration, months	4	4	12	18	N/A	60
PD fluid cell count on day 1, μL	521	19,035	6,143	1,050	13,440	1,033
Initial treatment	CAZ+CEZ	CAZ+CEZ	CEZ+GM	CAZ+CEZ	Ertapenem+VCM	CAZ+CPFX
Treatment after detection of *C. indologenes*	CAZ+LVFX for 21 days	CAZ for 21 days	CAZ for 26 days Relapse on day 66 CAZ was restarted	CFPM+LVFX for 16 days	CAZ+FLCZ for 21 days	CAZ+CPFX+FLCZ for 42 days Relapse after the initial 3-week treatment
Catheter removal	No	No	Yes	No	No	Yes

CAZ, ceftazidime; CEZ, cefmetazole; LVFX, levofloxacin; GM, gentamicin; VCM, vancomycin; CPFX, ciprofloxacin; FLCZ, fluconazole; PD, peritoneal dialysis.

In addition, *C. indologenes* often forms biofilms, which protect bacteria from antibiotics [6, 7]. PD-associated peritonitis caused by *Pseudomonas aeruginosa*, which often forms biofilms, should be treated for 3 weeks using 2 antibiotics with different mechanisms of action [4]. Biofilm formation is regulated by bacteria through a microbial communication system, quorum sensing, which is a mechanism that senses the density of bacteria and controls the production of substances accordingly. Fluoroquinolones have been shown to be effective in inhibiting biofilm formation by downregulation of the quorum sensing system-regulated genes involved in biofilm formation [15]. Some cases reported relapse of PD-associated peritonitis caused by *C. indologenes* within a few weeks, indicating biofilm formation [9, 12]. In the present case, empiric therapy was initiated by administration of cefazolin and ceftazidime. After *C. indologenes* was detected from the peritoneal fluid culture, we decided to administer 2 susceptible antibiotics listed in Table 2 from concern of acquisition of resistance and biofilm formation in *C. indologenes*. LVFX was initiated in addition to ceftazidime in the present case to prevent acquisition of resistance and biofilm formation. However, we should also pay attention to resistance profiles of *C. indologenes* because it often develops resistance to fluoroquinolone in hospitalized patients. Collectively, the present case highlights the fact that PD-associated peritonitis caused by *C. indologenes*, even when showing minor resistance, should be treated with 2 susceptible antibiotics including fluoroquinolones for 3 weeks.

Statement of Ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval is not required for this case report in accordance with the Ethics Review Board of Tokyo Saiseikai Central Hospital.

Conflict of Interest Statement

The authors declare no conflict of interest.

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Author Contributions

Akira Miyakawa and Kentaro Fujii drafted the manuscript. Ai Kato, Wataru Sugi, Ayumi Yoshifuji, and Motoaki Komatsu contributed to reviewing, editing, and revisions of the manuscript. Munekazu Ryuzaki was the senior supervising author to the case report including writing the report and revisions.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its online supplementary material files. Further inquiries can be directed to the corresponding author.

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Case Reports in Nephrology and Dialysis

Case Rep Nephrol Dial 2023;13:90–96
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