Renal Replacement Therapy

CASE REPORT

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Repeated streptococcal peritoneal dialysis-related peritonitis following stomatitis and gingival bleeding: a case report

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Abstract

Background: Identification of the pathogenesis of peritoneal dialysis (PD)-related peritonitis is important. However, identification of endogenous peritonitis, especially hematogenous infection, is difficult, and there are few reports of endogenous peritonitis via the bloodstream. We report a case of PD-related peritonitis presumed to be caused by hematogenous infection through the oral mucosa.

Case presentation: A 65-year-old woman commenced PD at the age of 52. Over the next 13 years, she developed two episodes of streptococcal peritonitis caused by *Streptococcus salivarius*, a commensal bacteria of the human oral mucosa, and all episodes occurred following stomatitis and gingival bleeding in the early summer. At the age of 65, she again suffered from stomatitis followed by gingival bleeding in early summer, and 2 weeks later, developed a third case of peritonitis caused by *Streptococcus salivarius*. The streptococcal peritonitis improved immediately following 2 weeks of antibiotic treatment. We surmise that the patient is subject to weakened immunity in the early summer, causing repeated oral problems with gingival bleeding, and subsequently leading to oral streptococcal peritonitis.

Conclusions: Our findings suggest that oral streptococcal peritonitis following oral problems such as stomatitis and gingival bleeding results from a hematogenous infection via the oral mucosa.

Keywords: Oral disease, Oral *Streptococci*, Peritoneal dialysis, Peritonitis

Background

Peritoneal dialysis (PD)-related peritonitis is one of the primary causes of withdrawal from PD, thereby affecting the patient's life prognosis [1]. The pathogenesis of PD-related peritonitis is roughly divided into endogenous and exogenous routes. Exogenous routes include touch contamination and exit-site tunnel infection, whereas endogenous routes include the intra-abdominal cavity and hematogenous infections [2]. A case series of four patients who developed oral streptococcal peritonitis from oral diseases suggests that the mechanism underlying endogenous peritonitis from the oral cavity is mediated via the bloodstream [3]. However, there are few other reports of endogenous peritonitis that were transmitted via the bloodstream. Here, we report an important case of repeated oral streptococcal PD-related peritonitis following stomatitis and gingival bleeding, supporting the existence of an endogenous infectious route of peritonitis that may be frequently overlooked.

Case presentation

A 65-year-old Japanese woman commenced continuous ambulatory PD for end-stage kidney disease because of chronic interstitial nephritis diagnosed at the age of 52.

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She had a past history of left ovarian cystectomy and sudden deafness. She had no particular family history or any history of smoking or drinking. Owing to her good fluid management, adequate dialysis had been achieved by exchanging only 1.5 L of low glucose solution four times a day. She used Y-set disconnect systems for dialysate changes. Because of her long-standing treatment with PD and the loss of residual kidney function, the patient switched to combination therapy with 5-day a week PD and hemodialysis once a week at the age of 63. She had three episodes of PD-related peritonitis between the ages of 56 and 59: one was a culture-negative peritonitis in June; one caused by *Streptococcus mitis* in March; and one caused by group G *Streptococci* in December. She had also developed two episodes of PD-related peritonitis caused by *Streptococcus salivarius* following gingival bleeding and/or stomatitis after falling ill in the early summer for the past 2 years: in June at age 63 and in July at age 64. She had regular dental visits and received dental scaling every 6 months, so she had no problems with her teeth. She was also thorough in hand hygiene and wearing of masks before receiving PD and she performed "flush before fill" at each fluid change; nevertheless, each time she developed peritonitis, she received retraining on the PD exchange technique. In July at age 65, being vulnerable to heat, she became ill and again developed stomatitis. After that, she sometimes experienced gingival bleeding, even though she was diligent in her oral care. Two weeks later, she developed abdominal pain with turbid PD effluent and was urgently admitted to our hospital. Her blood pressure was 113/63 mmHg, pulse rate was 83 beats per minute, and body temperature was 36.7 °C. Her abdomen was soft and undistended, with mild tenderness without rebound or guarding. The results of blood tests and the PD effluent test performed on admission are shown in Table 1. Analysis of the turbid PD effluent revealed an elevated total white blood cell count consisting predominantly of neutrophils. She was diagnosed with PD-related peritonitis, and sulbactam-ampicillin was administered intraperitoneally (Fig. 1). On the second day of hospitalization, *Streptococcus salivarius* was again identified in the culture of the PD effluent and was sensitive to most antibiotics. On the third day

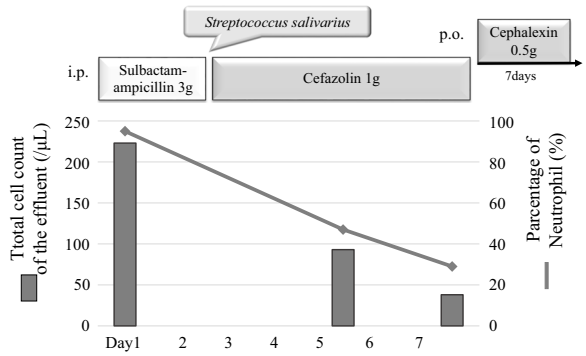

Fig. 1 Clinical course of the most recent episode of peritonitis. The white blood cell count of the peritoneal dialysis effluent and the percentage of neutrophils declined gradually following intraperitoneal administration of antibiotics. Antibiotic treatment was switched to oral administration after discharge. Abbreviations: *i.p.* intraperitoneal administration, *p.o.* per os

Table 1 The results of blood tests and the peritoneal dialysis effluent test

<Complete blood count>			AMY	161	U/L
WBC	12,770	/μL	CK	163	U/L
Neut	78.2	%	BUN	46.3	mg/dL
Eosino	0.9	%	Cr	12.57	mg/dL
Lymph	17.5	%	UA	6.1	mg/dL
RBC	420	$\times 10^4$/μL	Na	139	mEq/L
Hb	13.8	g/dL	K	3.1	mEq/L
Ht	40.6	%	Cl	97	mEq/L
Plt	21.1	$\times 10^4$/μL	Ca	10.3	mg/dL
<Serum chemistry>			Glu	165	mg/dL
TP	6.0	g/dL	<Serum immunology>		
Alb	3.5	g/dL	CRP	0.10	mg/dL
T-Bil	0.5	mg/dL	<Peritoneal dialysis effluent test>		
AST	30	U/L	WBC	223	/μL
ALT	18	U/L	Neut	99	%
LDH	232	U/L	Lymph	0	%
ALP	234	U/L	Eosino	0	%
γ-GTP	11	U/L	Histiocyte	1	%

of hospitalization, the intraperitoneal administration of antibiotics was de-escalated (from sulbactam-ampicillin to cefazolin). The elevated body temperature decreased immediately, and the total white blood cell count in the effluent declined from 223 to 44/μL on the fifth day and to 11/μL on the seventh day. During admission, the patient was seen by a dentist and her oral hygiene condition was evaluated using the decayed, missing, and filled teeth (DMF) score and plaque control record (PCR). Her DMF score was 17 (D: 0, M: 10, F: 7), which was age-appropriate, and no mobile teeth were found. However, her PCR was high at 34.7%, so she was provided with oral hygiene guidance. She was discharged on the seventh day of hospitalization, and oral administration of cephalexin was continued for 7 days after discharge. Her peritonitis was cured and did not relapse. The time course of her 13-year PD treatment and six episodes of PD-related peritonitis is shown in Fig. 2.

Discussion and conclusions

Over the course of 13 years of PD treatment, the patient developed six episodes of PD-related peritonitis, five of which were caused by *Streptococci*. Furthermore, the most recent three of the five peritonitis episodes were caused by *Streptococcus salivarius* and notably occurred following gingival bleeding and/or stomatitis. This bacterium is a commensal bacteria of the human oral mucosa [4, 5] and can be a causative organism of bacteremia via the oral mucosa [6]. These episodes, therefore, suggest the presence of a mechanism by which endogenous peritonitis arises from the oral cavity via the bloodstream.

We considered the possibility that streptococcal peritonitis is derived from the oral cavity via the bloodstream. In Japan, although streptococcal peritonitis is the second most common form of peritonitis after culture-negative peritonitis [7], the origin of streptococcal peritonitis is usually considered to be unknown or to occur via touch contamination. However, according to the guidelines of the International Society for Peritoneal Dialysis [1], streptococcal peritonitis frequently originates from the mouth [8]. A retrospective examination at our facility revealed that the incidence of total peritonitis and peritonitis caused by oral *Streptococci* was significantly lower in groups with superior oral hygiene compared with those with inferior oral hygiene [9]. Furthermore, the fact that *Streptococci* are relatively major causative organisms of spontaneous bacterial peritonitis in cirrhotic patients [10] supports the observation that oral *Streptococci* cause PD-related peritonitis from the oral cavity via the bloodstream. This is because spontaneous bacterial peritonitis is never caused by exogenous pathogens in cirrhotic patients. There have also been reports of infective endocarditis [11], pancreatic abscess [12], and meningitis [13] caused by *S. salivarius*, and these cases were associated with intraoral insufficiency. Furthermore, a case series of four patients who developed oral streptococcal peritonitis from oral diseases, such as gingival bleeding, swelling of the gingiva, trauma to the lips, and dental treatment, suggests that the transmission of endogenous peritonitis from the oral cavity is mediated via the bloodstream [3]. However, it is unknown whether the mechanism responsible for oral streptococcal peritonitis functions only via the blood flow, as is the case with secondary peritonitis associated with infective endocarditis [14, 15]. Although merely hypothetical at this stage, oral splash contamination is postulated as a cause of PD-related peritonitis. This hypothesis is supported by a study that demonstrated the most common bacteria cultured from splash

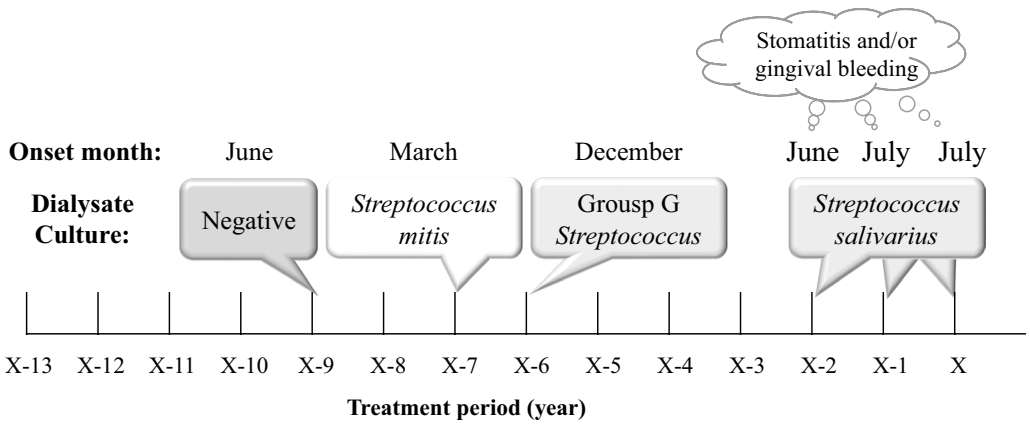

Fig. 2 Time course of the 13-year peritoneal dialysis (PD) treatment period and six episodes of PD-related peritonitis. Five of six episodes of PD-related peritonitis were caused by oral *Streptococci*, and the last three episodes developed following gingival bleeding and/or stomatitis in early summer

produced in dental practices are *Streptococci*, followed by *Staphylococcus* species [16, 17]. To support the theory that oral splash contamination leads to PD-related peritonitis, it must be proven that the incidence of streptococcal peritonitis decreases when a face mask is fitted or when a connection device is used. However, because it was reported that the proportion of streptococcal peritonitis increased and decline of the staphylococcal infections following the introduction of the Y-set system [8], it is still believed that the main infection pathway of streptococcal peritonitis is endogenous rather than contamination. Additionally, Y-set system and twin-bag systems have been reported to be associated with significantly decreased peritonitis rates compared with the conventional spike systems [18]. The most significant factor in the reduction of peritonitis with this system has been consider to be the reduction of touch contamination during fluid changes due to "flush before fill". In several observational study, "flush before fill" technique has been reported to reduce peritonitis in continuous ambulatory peritoneal dialysis (CAPD) [19], and similarly in automated peritoneal dialysis (APD) patients [20, 21]. Consequently, we believe it is likely that streptococcal peritonitis originates from the oral cavity via the bloodstream. In the present case, blood culture was not performed. In general, bacteremia after dental procedures is difficult to detect. Furthermore, the number of bacteria entering the bloodstream after a dental procedure decreases over time, reducing the number of microorganisms in the blood sample [22]. Furthermore, bacteremia after tooth extraction or oral care is temporary and is only proven by blood culture for a few minutes to 10 min after a dental procedure [23]. Therefore, it may be difficult to prove the presence of bacteremia after oral procedures by blood culture. However, bacteremia was found in 11% of patients with PD peritonitis, and blood culture collection is recommended, especially in immunocompromised patients [24]. In this case, the possibility of hand contamination cannot be completely ruled out. However, she had thoroughly washed her hands and wearing of mask, and had also thoroughly performed a "flush before fill" at each fluid change, and she received retraining each time she was hospitalized for peritonitis. There were no obvious episodes of poor technique and no episodes of peritonitis caused by *Staphylococci*. In addition, she had three repeated episodes of peritonitis caused by the same organism. These fact makes it unlikely that the peritonitis was caused by contact contamination.

The three most recent peritonitis episodes caused by *Streptococcus salivarius* following gingival bleeding and/or stomatitis in the present case occurred in early summer. Factors explaining repeated peritonitis in summer include seasonality and immunity. A descriptive study of all presenting cases of acute necrotizing ulcerative gingivitis over 6 years at a single health center suggested that most of these patients presented during summer [25]. Mouth breathing for thermoregulation and dehydration leading to dry mouth were believed to be the major causes of the increased prevalence of gingivitis in summer. Other reports indicate that immune function may be suppressed in early summer with long daylight hours and high ultraviolet exposure [26, 27]. These findings suggest that stomatitis and bacteremia via the oral cavity are likely to occur in summer [28] and may explain the occurrence of repeated peritonitis in summer in the present case.

In this report, we have discussed the following facts: that *Streptococci*, including *Streptococcus salivarius*, detected in the last three peritonitis episodes of this case, can be resident in the oral cavity; that *Streptococci* in the oral cavity can cause hematogenous peritonitis via the oral mucosa; and that dry mouth and weakened immunity due to ultraviolet rays are more likely to cause stomatitis and/or gingivitis in summer. We hope that it is widely recognized that oral diseases, including minor oral problems such as stomatitis and/or gingival bleeding, can cause PD-related peritonitis from the oral cavity via the bloodstream, as in this case.

Only one other report has described the clinical course of oral streptococcal PD-related peritonitis associated with oral problems [3]. However, the infection route of oral streptococcal PD-related peritonitis is still a source of contention, and in fact, it is assumed that more cases of hematogenous peritonitis than expected are due to oral problems.

Abbreviations

PD: Peritoneal dialysis; DMF: Decayed, missing, and filled teeth; PCR: Plaque control record.

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Author contributions

KF participated in the conception and drafted and wrote the paper. HO contributed to the writing and revising of the paper. TI, MK, YH, TK, TN and TK contributed to final approval of the paper. All authors read and approved the final manuscript.

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Availability of data and materials

All data in this case are available from the corresponding author on reasonable request.

Declarations

Ethical approval and consent to participate

This article does not contain any studies with human participants or animals performed by any of the authors.

Consent for publication

Informed consent was obtained from the patient included in this case report.

Competing interests

The authors declare that they have no conflicts of interest.

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