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Case Report

Cat Rearing: A Potential Risk of Fulminant Sepsis Caused by *Capnocytophaga canimorsus* in a Hemodialysis Patient

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Keywords
Chronic renal disease · Dialysis treatment of CKD (peritoneal and hemodialysis) · Infectious diseases · *Capnocytophaga canimorsus*

Abstract
Capnocytophaga canimorsus is a commensal organism colonized in oral flora of dogs and cats and causes severe sepsis through bite wound in immunocompromised patients. To date, hemodialysis has not been reported as a risk of *C. canimorsus* infection. A 75-year-old woman with end-stage renal disease secondary to hypertension suddenly developed septic shock. She reared 6 cats in her home, but no bite or scratch wound was found on her body. She was empirically treated with piperacillin-tazobactam and temporally received continuous hemodiafiltration. On the fifth day after sampling, blood culture revealed *C. canimorsus* as the cause of sepsis. After 4 weeks of antibiotic therapy targeting this organism, she recovered from the sepsis and was discharged on the 109th hospitalization day. Hemodialysis patients may be vulnerable to invasion into the blood stream by *C. canimorsus* due to the presence of punctures in their skin and the impaired immune function associated with uremia. Physicians should consider this organism as a cause of sepsis in hemodialysis patients who rear dogs or cats even in the absence of apparent bite wounds.

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Introduction

Capnocytophaga canimorsus is a commensal organism colonized in oral flora of dogs and cats. When bitten by these animals, it can cause fulminant sepsis in immunocompromised patients [1]. To date, several case reports have described infection by the *Capnocytophaga* species in patients receiving peritoneal dialysis but not in hemodialysis patients [1–3]. We here report a case in which a hemodialysis patient living with cats developed severe sepsis by *C. canimorsus* without any apparent evidence of animal bites.

Case Report

A 75-year-old woman was admitted to our hospital in January 2018 because of persistent fever and appetite loss from the previous day. She had received hemodialysis for 1 year in our hospital due to end-stage renal disease (ESRD) secondary to hypertension. She lived with her husband and 6 cats in her house. On admission, her Glasgow Coma Scale score was 13/15 (E3, V4, M6), her body temperature was 37.1°C, and blood pressure was 93/57 mm Hg. Physical examinations revealed no significant finding, and her skin was intact with no scratch or bites other than puncture holes for hemodialysis. Her white blood cell count was 7,100 per μL, hemoglobin level was 10.4 g/dL, and platelet count was 8,000 per μL. Total bilirubin level was 3.0 mg/dL, and C-reactive protein was elevated to 42.7 mg/dL. The international normalized ratio (INR) and the activated partial thromboplastin time were within normal range; however, fibrinogen-degradation product and D-dimer were 14.4 μg/mL (reference range: <5.0) and 9.10 μg/mL (reference range: <1.0). Computed tomography scans of body trunk and head revealed no abnormality.

From these findings, we suspected severe sepsis caused by an unknown pathogenic organism and secondary disseminated intravascular coagulopathy (DIC). Although bacterial meningitis was suspected, lumbar puncture was avoided because of the low platelet count. We started piperacillin-tazobactam as an empirical therapy immediately after collecting two sets of blood culture samples. Because of low blood pressure, she received continuous hemodiafiltration for 4 days. Fortunately, her consciousness and physiological condition were rapidly recovered, and DIC was gradually resolved after starting therapy.

On the fifth day after blood sampling, *C. canimorsus* was isolated from two bottles of aerobic blood culture. We changed the antibiotics to ampicillin-sulbactam of which spectrum sufficiently covered the bacteria. Although the patient's general condition improved, the back pain, high fever (37–38°C), and high C-reactive protein level (4–8 mg/dL) persisted. The spine magnetic resonance imaging revealed inflammation of the lumbar spine suggesting spondylitis (Fig. 1). Thus, we continued antibiotic therapy for 4 weeks, using piperacillin-tazobactam, ampicillin-sulbactam, ceftriaxone, and clindamycin (Fig. 2). Her symptoms as well as laboratory abnormalities were resolved eventually. After completing a rehabilitation program, she was discharged on the 109th hospitalization day.

Discussion

C. canimorsus is known as one of the causes of zoonotic infection in patients bitten by dogs or cats. Although this bacterium is considered to be low virulent in healthy people, it can develop fulminant sepsis in patients carrying risk factors such as asplenia, alcohol abuse,

cirrhosis, and receipt of immune-suppressive therapy [4]. Previously, hemodialysis has not been recognized as a risk factor of *C. canimorsus* infection; there have been only a few case reports of peritoneal dialysis patients who developed peritonitis caused by the *Capnocytophaga* species [1–3].

However, our case suggests that hemodialysis patients might have an increased risk of infection by this organism for several reasons. First, hemodialysis patients have some skin defects through which the bacteria could enter the blood stream, including puncture holes on their skin that result from regular hemodialysis procedures, or scarring of the foot caused by circulatory insufficiency [5, 6]. Although our patient had no past and present history of cat bites or scratch wound, it should be noted that a bite-related injury and even an unnoticed scratch or licking by dogs or cats may cause septicemia presumably through skin defects unique to hemodialysis patients [7]. Second, uremia in hemodialysis patients impairs macrophage phagocytosis, leading to vulnerability to invasion by pathogens. Thus, the immunological function in hemodialysis patients is reduced. Patients who have undergone a splenectomy are at the greatest risk for a *Capnocytophaga* infection because of the absence of splenic macrophages in the red pulp which diminishes the innate immunity [8]. A similar mechanism might occur in uremic hemodialysis patients, leading to vulnerability to the pathogen.

In our case, *C. canimorsus* was isolated in blood cultures 5 days after sampling. This bacterium is generally slow growing and requires an average of 4–14 days to grow [9]. However, rapid diagnosis is warranted in case of critical condition. Therefore, preferred ways are to directly detect the bacterial bodies by Gram staining in centrifuged fluid samples (e.g., blood or cerebrospinal fluid) or Giemsa staining of blood smear [10]. 16S rRNA gene sequencing is a widely used method for fast diagnosis [11]. Moreover, recent advancements in detection technology such as exhaustive genome sequencing and mass spectrometry may improve the accuracy and promptness in diagnosis [12, 13]. Still, even with these various techniques, it is necessary for physicians to include this organism in the list of differential diagnoses as a cause of sepsis by taking a thorough history to find out whether a patient lives with animals and having physical findings such as animal bites, skin defects, or risk factors.

In the present case, piperacillin-tazobactam, one of the broadest-spectrum antibiotics, was used as an empirical therapy because she was in a life-threatening condition and the causative pathogen of sepsis had not been identified at the time of initial treatment. Hemodialysis patients are mostly at risk of infection by Gram-positive cocci, including *Staphylococcus aureus*, coagulase-negative cocci, and, in a few cases, Gram-negative rods [14]. Therefore, initial therapy should include third- or fourth-generation cephalosporins with or without vancomycin that target methicillin-resistant *S. aureus*. Notably, recent studies show that some strains of *C. canimorsus* produce beta-lactamase that degrades antibiotics with beta-lactam including penicillin and cephalosporin. As such, drugs containing a beta-lactamase inhibitor may be required for initial therapy when *C. canimorsus* infection is suspected. As with the present case, when patients with chronic kidney disease have septic shock, continuous renal replacement therapy (CRRT) is frequently required. However, many patients receiving CRRT do not reach target antibiotic concentrations in plasma. In these cases, extended infusion (e.g., 4-h infusion) of piperacillin-tazobactam may be beneficial for achieving the optimal plasma concentration [15].

In conclusion, physicians should be aware that hemodialysis patients are potentially vulnerable to infection by *C. canimorsus*. When these patients rear dogs or cats and develop severe sepsis, this organism should be considered as a causal pathogen even when a wound is apparently absent. When *C. canimorsus* is suspected, targeted examination to establish

accurate diagnosis is warranted with prompt initiation of appropriate antibiotics that cover the pathogen.

Statement of Ethics

A written consent for publication has been obtained from the patient, and all research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

All authors contributed to writing the manuscript. J.M. was responsible for the original diagnosis and treatment.

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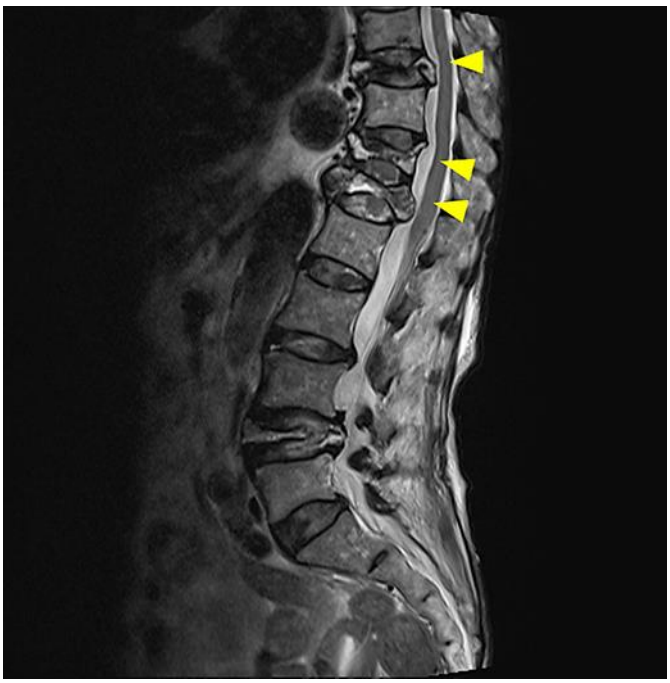

Fig. 1. Magnetic resonance imaging of the spine. Arrowheads denote high-intensity lesions by the short-tau inversion recovery method, suggesting inflammation of the spine.

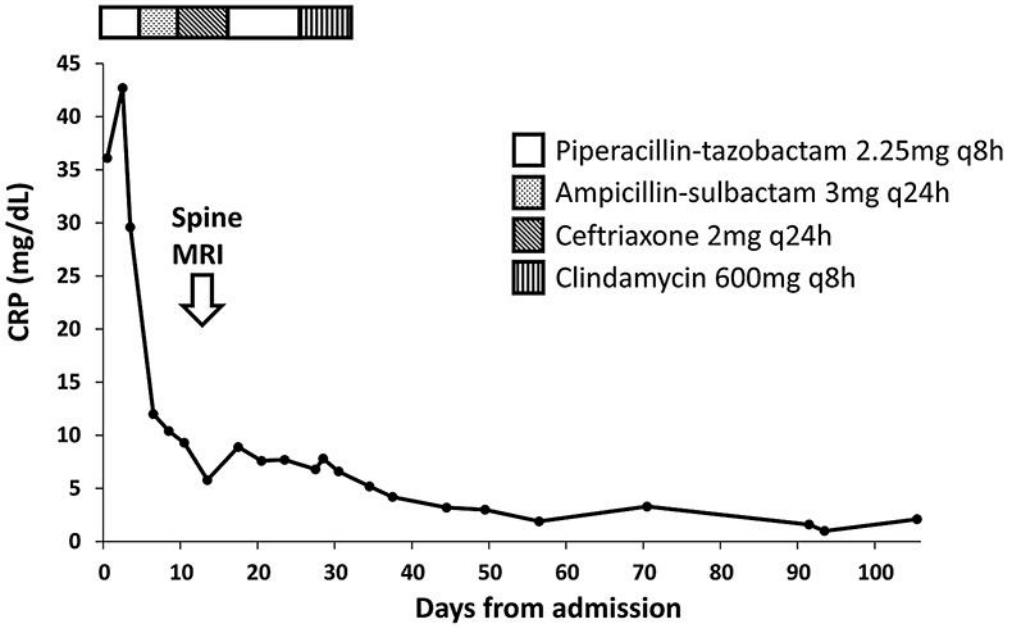

Fig. 2. Antibiotic therapies and clinical response. Line plots show the values of C-reactive protein (CRP) and boxes indicate antibiotics.