

[ CASE REPORT ]

## Sepsis Caused by Newly Identified *Capnocytophaga canis* Following Cat Bites: *C. canis* Is the Third Candidate along with *C. canimorsus* and *C. cynodegmi* Causing Zoonotic Infection

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### Abstract:

Sepsis caused by a *Capnocytophaga canis* infection has only been rarely reported. A 67-year-old female with a past medical history of splenectomy was admitted to our hospital with fever and general malaise. She had been bitten by a cat. She showed disseminated intravascular coagulation and multi-organ failure because of severe sepsis. On blood culture, characteristic gram-negative fusiform rods were detected; therefore, a *Capnocytophaga* species infection was suspected. A nucleotide sequence analysis revealed the species to be *C. canis*, which was newly identified in 2016. *C. canis* may have low virulence in humans; however, *C. canis* with oxidase activity may cause severe zoonotic infection.

**Key words:** *Capnocytophaga canis*, *Capnocytophaga canimorsus*, sepsis, oxidase activity

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### Introduction

The genus *Capnocytophaga* consists of gram-negative rod-shaped bacteria that reside in the oral cavities of humans and domestic animals. *Capnocytophaga* formerly comprised eight species (1, 2). Of these, six species (*C. gingivalis*, *C. granulosa*, *C. haemolytica*, *C. leadbetteri*, *C. ochracea*, and *C. sputigena*) inhabit the human oral cavity and commonly cause dental infections. The other two species (*C. canimorsus* and *C. cynodegmi*) inhabit the oral cavities of dogs and cats and sometimes cause local wound infection and systemic infection in humans after a dog or cat bite. Recently, *C. canis* has been added (3). *C. canis* has been isolated from the oral cavity of healthy dogs and is assumed to have low pathogenicity in humans (3).

Sepsis caused by *C. canis* infection has only been rarely reported. We herein report the successful treatment of *C. canis*-related severe sepsis.

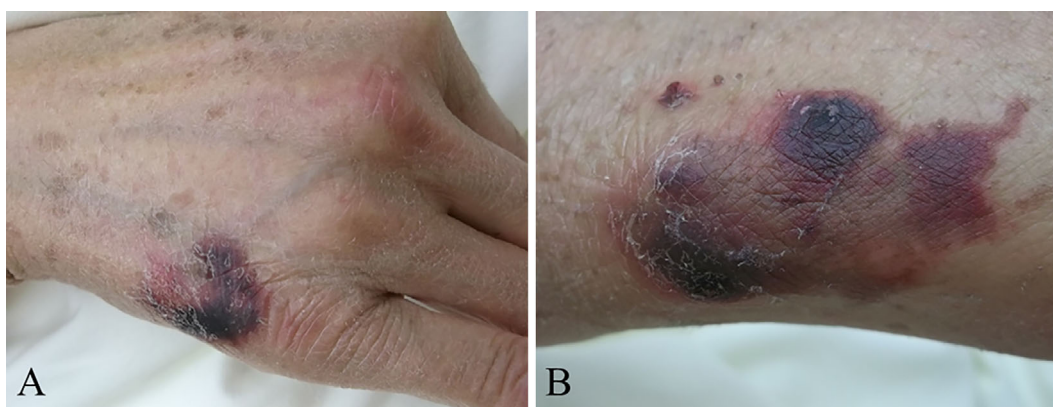
### Case Report

A 67-year-old woman was admitted to our hospital with general malaise and fever for 3 days starting the day after being bitten by a cat on both her hands. She had a medical history of idiopathic portal hypertension and had undergone a splenectomy for esophageal and pharyngeal varices at 44 years of age. She had no pneumococcal and meningococcal vaccination. On admission, she was awake and oriented. Her vital signs were as follows: temperature, 39.8°C; blood pressure, 96/52 mmHg; pulse rate, 99 beats/min; respiratory rate, 20 breaths/min; and percutaneous oxygen saturation (SpO<sub>2</sub>), 96% on room air. The findings of a general examination were unremarkable except for oozing from her lips and cat bite wounds on the back of her right hand and on her left wrist. The cat bite wounds were crusted and dark purple, and had no redness and swelling (Fig. 1). The axillary and cervical lymph nodes were not swollen and there were no signs of lymphadenitis suggesting *Bartonella* infection. The

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**Figure 1.** Small scars with scabs on the back of right hand (A) and left wrist (B).

**Table 1.** Laboratory Findings on Admission.

		Normal range			Normal range
Albumin	2.3 g/dL	3.8-5.3	WBC	270 ×10 <sup>2</sup> /μL	40-85
ALP	1,086 IU/L	100-350	MYELO	4 %	
AST	47 IU/L	5-40	META	23 %	
ALT	26 IU/L	4-40	BAND	41 %	
T-Bil	4.7 mg/dL	0.3-1.2	SEG	30 %	
			LYMP	2 %	
BUN	45.4 mg/dL	8-22	RBC	370 ×10 <sup>4</sup> /μL	370-510
Cre	0.95 mg/dL	0.4-0.8	Hb	11.7 g/dL	11-15
Na	133 mEq/L	135-148	PLT	0.4 ×10 <sup>4</sup> /μL	13-35
K	2.9 mEq/L	3.5-5.0	FDP	13.4 μg/mL	0-10
CRP	30.65 mg/dL	0.0-0.3	Fibrinogen	378 mg/dL	180-400
PCT	61.85 ng/mL	0.0-0.5	PT-INR	1.28	

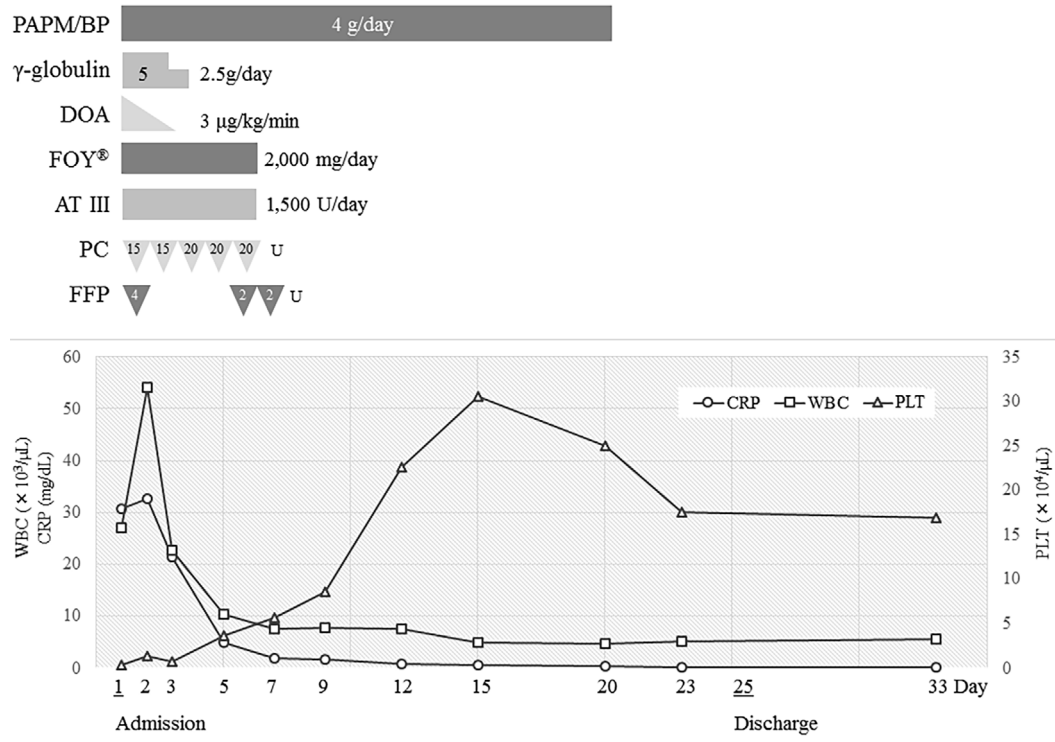
ALP: alkaline phosphatase, AST: aspartate aminotransferase, ALT: alanine aminotransferase, T-bil: total bilirubin, BUN: blood urea nitrogen, Cre: creatinine, CRP: C-reactive protein, PCT: procalcitonin, WBC: white blood cell count, MYELO: myelocyte, META: metamyelocyte, BAND: band neutrophil, SEG: segmented neutrophil, LYMP: lymphocyte, RBC: red blood cell count, Hb: hemoglobin, PLT: platelet count, FDP: fibrin degradation product, PT-INR: prothrombin time-international normalized ratio

rabies vaccination history of the cat was unknown, but no abnormal behavior was observed. Laboratory data at admission revealed leukocytosis with a left shift, thrombocytopenia, and liver and renal dysfunction (Table 1), indicating disseminated intravascular coagulation (DIC) and multi-organ failure because of bacterial infection. No source of bacterial infection was identified on whole-body computed tomography scan and echocardiography. After entering the emergency ward, dopamine was administered because she went into septic shock (systolic blood pressure, 60-70 mmHg). Antibiotics were administered after obtaining blood cultures. Since the cat bite wounds were in the healing process, as an empiric therapy for sepsis of unknown origin, we selected broad-spectrum antibiotics (panipenem/betamipron, PAPM/BP, 4 g/day), which are effective in treating pathogens associated with animal bites (including *Pasteurella multocida*, *Streptococcus* species, *Staphylococcus* species and *Capnocytophaga* species). The wounds were small and no sign of infection was noted, so human tetanus immune globulin was not administered.

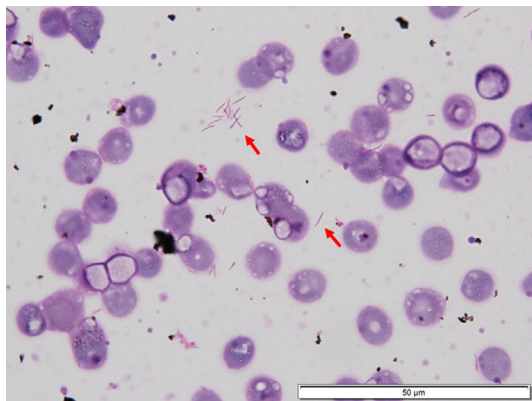
She responded well to the treatment; her fever and hypotension improved quickly, and her C-reactive protein level decreased. Her condition gradually improved, and she was discharged on day 25 after admission. The antibiotics had been administered continuously until her white blood cell count and C-reactive protein level had normalized (for 3 weeks). We did not de-escalate the antibiotics, because it took 21 days to identify the bacteria. Her clinical course is shown in Fig. 2.

### Bacterial identification

On day 2, gram-negative rods were recognized in a smear of an aerobic blood culture fluid (Fig. 3). *Capnocytophaga* species were suspected because of the characteristic morphological features of fusiform appearance of the bacteria and her history of cat bites. The isolates were oxidase activity-positive and catalase activity-positive, suggesting that the bacteria were animal-derived *Capnocytophaga* species, such as *C. canimorsus* and *C. cynodegmi* (4). Based on the results of tests performed using ID Test HN-20 Rapid Kit



**Figure 2.** The clinical course of this case. PAM/BP: panipenem/betamipron, DOA: dopamine, FOY®: gabexate mesilate, AT III: antithrombin III, PC: platelet concentrate, FFP: fresh frozen plasma, WBC: white blood cell count, CRP: C-reactive protein, PLT: platelet count



**Figure 3.** A blood culture smear with gram staining showing gram-negative fusiform-shaped rods (arrow).

(Nissui Pharmaceutical, Tokyo, Japan), the bacteria were presumed to be *C. canimorsus* on day 21. To confirm the bacteria, isolates were sent to the National Institute of Infectious Diseases in Japan. Comparative sequence analyses conducted at this institution revealed that the 16S rRNA and gyrB gene sequence identities were 96.9% and 75.5% for the *C. canimorsus*-type strain (ATCC 35979) and were 96.9% and 77.6% for the *C. cynodegmi*-type strain (ATCC 49044), respectively, on Basic Local Alignment Search Tool (BLAST) search (5). As of 2014, no known bacteria had a 16S rRNA sequence identity exceeding 98.7-99% (6), which is the threshold value above which bacteria are considered to be of the same species. The closest related bacteria were

*C. canimorsus* and *C. cynodegmi* according to the results of the 16S rRNA sequence matching.

In 2015, a novel species *C. canis* was reported (3). Thereafter, we performed the BLAST search again using the database of whole-genome shotgun contigs. The sequence identities between our strain and the *C. canis*-type strain (LMG29146) for 16S rRNA and the gyrB gene were 99.8% and 99.5%, respectively. As the identities were extremely high, our strain was therefore identified as *C. canis*.

## Discussion

*Capnocytophaga* species are facultative anaerobic, fusiform, fastidious gram-negative rods. They grow slowly (2-7 days) on blood or chocolate agar in 10% CO<sub>2</sub>. *C. canimorsus* and *C. cynodegmi* can cause zoonotic infection ranging from local infection to severe sepsis, and fatal cases are mainly associated with *C. canimorsus* (1). The mortality rate of *C. canimorsus* infection has been estimated at 26% (7). As *C. canis* can also cause severe sepsis, it may have the mortality rate comparable to that of *C. canimorsus*.

*C. canis* is a novel species of the genus *Capnocytophaga*, and it was identified in the oral cavity of healthy dogs. Although the clinical features of *C. canis* infection have not yet been reported, experimental results suggest that *C. canis* is less virulent than *C. canimorsus* in humans (3). Most strains of *C. canimorsus* have a cytochrome-oxidase activity and the ability to deglycosylate human IgM, and these characteristics are related to its pathogenicity in humans. The

**Table 2. Drug Susceptibility.**

Classification	generic name	Abbreviation	Sensitivity
Penicillin	ampicillin	ABPC	S
	amoxicillin / clavulanate	AMPC/CVA	S
Cephem	ceftriaxone	CTRX	S
	cefotaxime	CTX	S
Carbapenem	imipenem / cilastatin	IPM/CS	S
	meropenem	MEPM	S
Macrolide	azithromycin	AZM	S
Tetracycline	tetracycline	TC	S
Fluoroquinolone	ofloxacin	OFLX	S
	ciprofloxacin	CPFX	S
Chloramphenicol	chloramphenicol	CP	S
Antitubercular	rifampicin	RFP	S
ST	sulfamethoxazole / trimethoprim	ST	R

Defined as "susceptible : S", "intermediate : I" or "resistance : R" based on the Clinical and Laboratory Standards Institute M100-S23 (criteria for *Haemophilus influenzae*).

detailed mechanism of oxidase activity is still unknown, but the fact that *C. canimorsus* strains without oxidase activity could not grow in human serum suggests that oxidase activity is responsible for pathogenicity of *C. canimorsus* (3). On the other hand, almost all strains of *C. canis* are oxidase-negative (97.1%) and cannot deglycosylate human IgM (97.1%) (3). An isolate from a patient reportedly suspected of having sepsis caused by *C. canimorsus* because of cat scratches in 2013 (8) was also identified as *C. canis* through the same analysis as that in our report (Suzuki et al., manuscript in preparation). Both this strain and our strain were oxidase positive. In addition, a strain of *C. canis* with oxidase activity isolated from cat bite wounds was reported (9). The rare *C. canis* strain with oxidase activity is a dangerous pathogen for humans and can cause severe sepsis similar to that caused by *C. canimorsus*.

On the host side, the risk factors for severe infection of *C. canimorsus* are splenectomy, alcoholic addiction (liver disease caused by alcohol abuse), and immunosuppression (1, 7). Our case had undergone a splenectomy and the past case of *C. canis* infection (8) was a heavy drinker, so the risk factor of *C. canis* infection may be similar to that of *C. canimorsus*.

Our case is the first clinical report of severe sepsis caused by *C. canis*. However, *C. canis* can be mistakenly identified as *C. canimorsus* with catalase and oxidase activity tests and simple bacterial identification kits that are based on biochemical characteristics, and therefore, some cases of *C. canis* infection may have been reported as *C. canimorsus* infection previously (8). We recommend identifying bacteria by genetic procedures, if *Capnocytophaga* species infection is suspected. The clinical features of *C. canis* infection will be revealed by collecting a large number of *C. canis* infection cases.

In drug susceptibility tests, the *C. canis* strain in this case was broadly susceptible to many antibiotics, including  $\beta$ -

lactam antibiotics, except trimethoprim-sulfamethoxazole (Table 2), and the drug susceptibility was similar to that of previously reported *C. canimorsus* strains (7). Amoxicillin-clavulanic acid (Augmentin) recommended for *C. canimorsus* (10) is also effective for *C. canis* as prophylactic administration and treatment following dog and cat bites.

In conclusion, we herein reported a rare case of *C. canis*-related severe sepsis. The possible presence of *C. canis* should therefore be considered along with *C. canimorsus* and *C. cynodegmi* in patients presenting with infection after cat and dog bites or cat scratches.

**The authors state that they have no Conflict of Interest (COI).**

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