Case Report

Capnocytophaga canimorsus infection led to progressively fatal septic shock in an immunocompetent patient

Ryuichi Nakayama,[1,2,3] Shuichi Miyamoto,[2] Toshihiro Tawara,[1] Arisa Aoyagi,[1] Takeo Oguro,[1] Nobumichi Kobayashi,[4] Michio Suzuki,[5] and Yoshihiro Takeyama[1]

[1]Department of Emergency Medicine, Hakodate Municipal Hospital, [2]Department of Gastroenterology, Hakodate Municipal Hospital, Hakodate, Japan, [3]Department of Emergency Medicine, Sapporo Medical University School of Medicine, [4]Department of Hygiene, Sapporo Medical University School of Medicine, Sapporo, Japan, and [5]Department of Veterinary Medicine, National Institute of Infectious Diseases, Tokyo, Japan

Background: Capnocytophaga canimorsus infection is rare, with a high fatality rate; however, there are few cases of death with a rapid course. This study reports a progressively fatal case of C. canimorsus.

Case Presentation: A 68-year-old immunocompetent Japanese man was bitten and scratched on his right hand by a dog 6 days before emergency transportation to the emergency room with abdominal pain, back pain, and melena. The patient developed multiple-organ failure. Despite antibiotic therapy, transfusion, vasopressor therapy, and continuous renal replacement therapy, the patient died from uncontrolled metabolic acidosis 4.5 h after admission. Approximately 80 h after admission, blood cultures were positive for C. canimorsus.

Conclusions: Capnocytophaga canimorsus infection can lead to rapid progression even in immunocompetent patients.

Key words: Capnocytophaga canimorsus, disseminated intravascular coagulation, dog bite, metabolic acidosis, septic shock

INTRODUCTION

CAPNOCYTOPHAGA CANIMORSUS is an anaerobic Gram-negative bacterium in the oral commensal flora of dogs and cats that can be transmitted to humans by penetrating bites, causing sepsis and septic shock.[1] In Japan, *C. canimorsus* has been found in 74% of dogs and 57% of cats.[2]

Although the prevalence of infection in Japan is unknown, the incidence rate of infection has been reported to be 0.67 and 0.5 per million population in the Netherlands[3] and Denmark,[4] respectively. Furthermore, a case fatality rate of 24%–30% was reported between 1990 and 2014. The risk factors for *C. canimorsus* infection include splenectomy, hyposplenism, alcoholism, cirrhosis, malignancies, and other immunosuppressive causes, such as glucocorticoid use. Immunodeficient individuals are more vulnerable to *C. canimorsus* infection than immunocompetent ones.[5] A small number of cases have been reported where the infection was progressively fatal in immunocompetent patients.[6–8] Herein, we report a progressively fatal case with some risk factors due to *C. canimorsus*, resulting in death 4.5 h after admission to the hospital.

Corresponding: Ryuichi Nakayama, MD, Department of Emergency Medicine, Sapporo Medical University, 291 Minami 1-jo Nishi 16-chome, Chuo-ku, Sapporo, Hokkaido 060-8556, Japan. E-mail: ryuichin.smu99@gmail.com

Received 7 Sep, 2021; accepted 3 Feb, 2022

CASE REPORT

A 68-year-old Japanese man was brought to the Department of Emergency Medicine, Hakodate Municipal Hospital, due to persistent lower abdominal pain, back pain, and melena. His medical history included benign prostatic hyperplasia and distal gastrectomy without splenectomy for gastric cancer when he was 46 years old; the latter had an uneventful course and required no chemotherapy. He smoked 20 cigarettes per day and consumed alcohol occasionally, although he was not an alcoholic. He was sufficiently active daily. The patient was bitten and scratched on his right hand by his dog 6 days before emergency transportation. He was asymptomatic until 2 days before transport, when the symptoms of general malaise and mild fever began.

On arrival, the patient was conscious and afebrile. His blood pressure was 142/68 mmHg, with a regular heart rate (76 b.p.m.), respiratory rate of 21 breaths/min, and SpO_2 of 99%. He had tenderness in the lower abdomen without peritoneal irritation. Petechiae were observed on his face and peripheral limbs. A scratch wound was evident on his right hand without any local signs of infection, such as swelling or redness. Blood laboratory data indicated high anion gap metabolic acidosis, thrombocytopenia, coagulopathy, liver failure, renal failure, and elevated C-reactive protein (Table 1). Enhanced computed tomography did not reveal the specific cause of the patient's condition. Sepsis and multiorgan failure with disseminated intravascular coagulation (DIC) of unknown etiology were suspected. At this point, we considered *C. canimorsus* and *Pasteurella* to be potential causative agents.

Table 1. Laboratory data on admission of a 68-year-old man with Capnocytophaga canimorsus infection

Peripheral blood cell count	
White blood cells	11 500/μL
Red blood cells	519 × 10^4/μL
Hemoglobin	15.5 g/dL
Platelet counts	0.8 × 10^4/μL
Coagulation	
PT-INR	2.83
APTT	78.9 s
Fibrinogen	101 mg/dL
D-Dimer	287.7 μg/mL
Serology, biochemistry	
C-reactive protein	23.03 mg/dL
Total protein	6.5 g/dL
Albumine	3.4 g/dL
Total bilirubin	4.6 mg/dL
Aspartate transaminase	3792 IU/L
Alanine aminotransferase	1357 IU/L
Lactate dehydrogenase	6258 IU/L
Blood urea nitrogen	44.5 mg/dL
Creatinine	4.16 mg/dL
Arterial blood gas (room air)	
pH	6.883
pO_2	145
pCO_2	34.7 mmHg
HCO_3^-	6.2 mmol/L
Base excess	−24 mmol/L
Glucose	60 mg/dL
Lactate	17 mmol/L

APTT, activated partial thromboplastin time; PT-INR, prothrombin time – international normalized ratio.

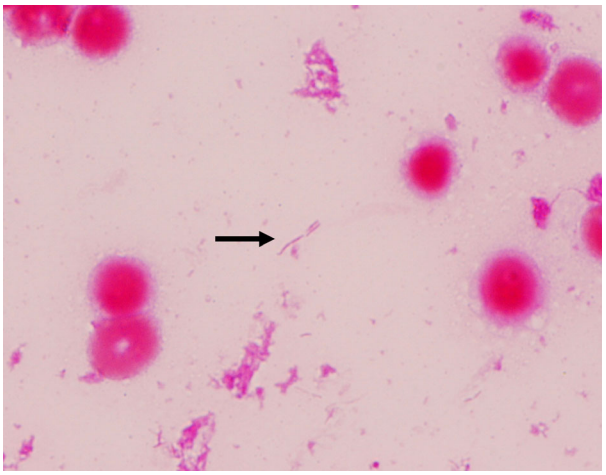

Fig. 1. Gram-negative anaerobic rod-shaped bacteria (arrow) were identified in a 68-year-old man with *Capnocytophaga canimorsus* infection (Gram staining; 400×).

After a computed tomography scan, his condition was seen to progressively worsen, and he was intubated and transferred to the intensive care unit 3 h after his arrival. Three sets of blood cultures were undertaken before initiating empiric antibiotic therapy with intravenous meropenem and vancomycin for septic shock. Despite empiric antibiotic therapy, aggressive fluid resuscitation (30–40 mL/kg crystalloids), transfusion (platelets, fresh-frozen plasma, and red blood cells), vasopressors, steroid application, and continuous renal replacement therapy, the purpura spread throughout his body, and blood was present in his stool and stomach tube. Blood laboratory data at 4 h after admission showed total bilirubin at 2.6 mg/dL, indirect bilirubin at 0.6 mg/dL, and no schistocytes, which did not suggest obvious hemolysis. Approximately 2 days after symptom onset and 4.5 h after admission, the patient died of uncontrolled metabolic acidosis.

Approximately 80 h after admission, one of three blood cultures grew Gram-negative aerobic rod-shaped bacteria (Fig. 1). This strain was identified as *C. canimorsus* by matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) and 16S rRNA polymerase chain reaction results from the National Institute of Infectious Diseases, Tokyo, Japan. ETEST (bioMérieux) showed that this bacterium is susceptible to penicillin, ceftriaxone, and imipenem.

DISCUSSION

WE HAVE DESCRIBED a case of *C. canimorsus* infection with few risk factors that became

Table 2. Review of progressively fatal Capnocytophaga canimorsus cases in immunocompetent patients

Ref.	Age (years)/sex	Exposure	Medical history	Initial symptoms before admission	Interval between admission and death	Antibiotics	Corticosteroid	Other treatment	Bleeding tendency
6	47/F	Dog	Pneumonia	Nausea, vomiting, diarrhea, abdominal pain, back pain	12 h	Ceftriaxione Vancomycin Imipenem	N/A	Transfusion	+
7	53/M	Dog bite	None	Nausea, myalgia, abdominal pain, lethargy	90 min	Ceftriaxione Vancomycin	+	Transfusion	+
8	80/F	Dog bite	Depression	Altered mental status, fever, abdominal pain	12 h	Piperacillin-tazobactam	+	Blood purification	+
Our case	68/M	Dog bite	Cured gastric cancer	Malaise, fever, abdominal pain	4.5 h	Meropenem Vancomycin	+	Transfusion CRRT	+

CRRT, continuous renal replacement therapy; F, female; M, male, N/A, not available; Ref., reference.

progressively severe, resulting in death within a few hours from the onset of septic shock. Fulminant fatal cases of *C. canimorsus* can cause gastrointestinal symptoms, bleeding, coagulopathy, and death even in immunocompetent individuals.

Polymerase chain reaction is necessary to distinguish *C. canimorsus* from other *Capnocytophaga* species.[1] Currently, the community health center hospitals in Japan, such as Hakodate Municipal Hospital, have MALDI-TOF MS, which can identify *C. canimorsus* from positive blood cultures.[9] However, identification takes several days, and the disease may progress in the meantime.

A previous study showed that *C. canimorsus* did not activate signals that lead to the release of pro-inflammatory cytokines, chemokines, and nitric oxide, and mouse and human macrophages were unable to mount a potent inflammatory response when infected with *C. canimorsus*.[10] In addition, the lipopolysaccharides of *C. canimorsus* protect against deposition of complement membrane attack complex and phagocytosis by polymorphonuclear leukocytes.[11] These mechanisms suggest that *C. canimorsus* can evade the immune system, explaining its lethal pathogenesis.[5]

To date, only three immunocompetent cases of progressively fatal *C. canimorsus* infection resulting in death within a day of hospitalization have been reported (Table 2).[6–8] The common features between our case and previously reported cases were that the patients initially had abdominal symptoms, did not respond to antimicrobials, fluid resuscitation, blood transfusion, or vasopressors, and had a tendency to bleed, such as in gastrointestinal hemorrhage or purpura, which were associated with thrombocytopenia and coagulopathy. Two cases involved pathological dissection, and autopsy results revealed bilateral adrenal hemorrhage and necrosis consistent with Waterhouse–Friderichsen syndrome.[6,7] Similarly, systemic bleeding and DIC could be the causes of death in our patient. Some previous reports have indicated that *C. canimorsus* sepsis causes secondary thrombotic microangiopathy, which improves with antimicrobial agents, plasma transfusion, and plasma exchange.[12–14] However, these reports did not include a progressively fatal case

similar to ours. In our case, few findings suggested hemolysis, and fibrinogen levels decreased, which is not typical for thrombotic microangiopathy.[15] This suggests DIC as the main cause of coagulation abnormalities. Type 7 dipeptidyl peptidase of *C. canimorsus* has been reported to inhibit factor X and contribute to bleeding and coagulopathy *in vivo*, which could be one of the factors of DIC.[16] According to a recent systematic review, the case fatality rate of *C. canimorsus* infection in immunocompetent patients was 29.7% between 2002 and 2019.[17] Therefore, physicians should be aware of the risk of rapid progression of *C. canimorsus* infection even in immunocompetent cases and should inform the public and provide early wound cleansing and prophylactic antimicrobial administration to patients bitten or scratched by dogs or cats.[17,18]

CONCLUSION

CAPNOCYTOPHAGA CANIMORSUS infection with abdominal symptoms can lead to rapid progression, even in immunocompetent patients. Physicians should inform the public about this risk and provide early wound cleansing and prophylactic antimicrobial administration to patients bitten or scratched by dogs or cats.

DISCLOSURE

Approval of the research protocol: N/A.

Informed consent: Written informed consent was obtained from the patient for the publication of this case report and any accompanying images.

Registry and registration no. of the study/trial: N/A.

Animal studies: N/A.

Conflicts of interest: None.

ACKNOWLEDGMENTS

WE WOULD LIKE to thank Editage for English language editing.

REFERENCES

1 Brenner DJ, Hollis DG, Fanning GR, Weaver RE. *Capnocytophaga canimorsus* sp. nov. (formerly CDC group DF-2), a cause of septicemia following dog bite, and *C. cynodegmi* sp. nov., a cause of localized wound infection following dog bite. J. Clin. Microbiol. 1989; 27: 231–5.

2 Suzuki M, Kimura M, Imaoka K, Yamada A. Prevalence of *Capnocytophaga canimorsus* and *Capnocytophaga cynodegmi* in dogs and cats determined by using a newly established species-specific PCR. Vet. Microbiol. 2010; 144: 172–6.

3 van Dam AP, Jansz A. *Capnocytophaga canimorsus* infections in The Netherlands: a nationwide survey. Clin. Microbiol. Infect. 2011; 17: 312–5.

4 Pers C, Gahrn-Hansen B, Frederiksen W. *Capnocytophaga canimorsus* septicemia in Denmark, 1982–1995: review of 39 cases. Clin. Infect. Dis. 1996; 23: 71–5.

5 Butler T. *Capnocytophaga canimorsus*: an emerging cause of sepsis, meningitis, and post-splenectomy infection after dog bites. Eur. J. Clin. Microbiol. Infect. Dis. 2015; 34: 1271–80.

6 Mirza I, Wolk J, Toth L, Rostenberg P, Kranwinkel R, Sieber SC. Waterhouse-Friderichsen syndrome secondary to *Capnocytophaga canimorsus* septicemia and demonstration of bacteremia by peripheral blood smear: a case report and review of the literature. Arch. Pathol. Lab. Med. 2000; 124: 859–63.

7 Cooper JD, Dorion RP, Smith JL. A rare case of Waterhouse-Friderichsen syndrome caused by *Capnocytophaga canimorsus* in an immunocompetent patient. Infection 2015; 43: 599–602.

8 Mantovani E, Busani S, Biagioni E, Venturelli C, Serio L, Girardis M. Purpura fulminans and septic shock due to *Capnocytophaga canimorsus* after dog bite: a case report and review of the literature. Case report. Crit. Care 2018; 2018: 7090268.

9 Tanabe K, Okamoto S, Hiramatsu Asano S, Wada J. *Capnocytophaga canimorsus* peritonitis diagnosed by mass spectrometry in a diabetic patient undergoing peritoneal dialysis: a case report. BMC Nephrol. 2019; 20: 219.

10 Shin H, Mally M, Kuhn M, Paroz C, Cornelis GR. Escape from immune surveillance by *Capnocytophaga canimorsus*. J. Infect. Dis. 2007; 195: 375–86.

11 Shin H, Mally M, Meyer S *et al*. Resistance of *Capnocytophaga canimorsus* to killing by human complement and polymorphonuclear leukocytes. Infect. Immun. 2009; 77: 2262–71.

12 Maezawa S, Kudo D, Asanuma K, Takekoshi D, Egashira R, Kushimoto S. Severe sepsis caused by *Capnocytophaga canimorsus* complicated by thrombotic microangiopathy in an immunocompetent patient. Acute Med. Surg. 2017; 4: 97–100.

13 Smeets NJL, Fijnheer R, Sebastian S, De Mast Q. Secondary thrombotic microangiopathy with severely reduced ADAMTS13 activity in a patient with *Capnocytophaga canimorsus* sepsis: a case report. Transfusion 2018; 58: 2426–9.

14 Tani N, Nakamura K, Sumida K, Suzuki M, Imaoka K, Shimono N. An immunocompetent case of *Capnocytophaga canimorsus* infection complicated by secondary thrombotic microangiopathy and disseminated intravascular coagulation. Intern. Med. 2019; 58: 3479–82.

15 Wada H, Matsumoto T, Suzuki K *et al*. Differences and similarities between disseminated intravascular coagulation and thrombotic microangiopathy. Thromb. J. 2018; 16: 14.

16 Hack K, Renzi F, Hess E *et al*. Inactivation of human coagulation factor X by a protease of the pathogen *Capnocytophaga canimorsus*. J. Thromb. Haemost. 2017; 15: 487–99.
17 Mader N, Luhrs F, Langenbeck M, Herget-Rosenthal S. *Capnocytophaga canimorsus* - a potent pathogen in immunocompetent humans - systematic review and retrospective observational study of case reports. Infect. Dis. 2020; 52: 65–74.
18 Stevens DL, Bisno AL, Chambers HF *et al*. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the infectious diseases society of America. Clin. Infect. Dis. 2014; 59: 147–59.