Case Report

Compartment syndrome due to *Capnocytophaga canimorsus* infection: a case report

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Background: Purpura fulminans secondary to *Capnocytophaga canimorsus* (*C. canimorsus*) infection without a wound is rare and often misdiagnosed initially. We report a patient who died due to *C. canimorsus* bacteremia with purpura fulminans and acute compartment syndrome of all extremities.

Care Presentation: A 38-year-old Japanese man with a history of alcoholism presented with a 2-day history of gastroenteritis. The chief complaints were abdominal pain and diarrhea, and he had abdominal tenderness. Laboratory findings showed multiple organ failure. On day 2, pain in the lower extremities associated with motor and sensory dysfunction developed. On day 3, purpura on the whole body spread to all extremities. All four extremities became rigid, and acute compartment syndrome developed. The patient died due to uncontrolled hyperkalemia and lactic acidosis.

Conclusions: *Capnocytophaga canimorsus* transmission can occur through licking or even close contact with animals when a risk factor of *C. canimorsus* infection, such as alcoholism, is present.

Key words: Capillary leak syndrome, *Capnocytophaga canimorsus*, compartment syndrome, purpura fulminans

INTRODUCTION

CAPNOCYTOPHAGA CANIMORSUS infection occurs most often through animal bites. *Capnocytophaga canimorsus* is known to cause fulminant sepsis. The mortality rate of *C. canimorsus* infections is approximately 30% and was reported to be much higher in immunocompromised patients.[1] Of the patients, up to two-thirds were immunocompromised, 10–33% with asplenia, 7–22% had alcoholism, and 5% were receiving steroid treatment.[1] Healthy adults without any medical history accounted for 30% of all patients.[1] *Capnocytophaga canimorsus* infection is rare in Japan, with just 93 patients (19 of whom died) confirmed from 1993 to the end of 2017 by the Ministry of Health, Labor and Welfare. To the best of our knowledge, there are no reports of *C. canimorsus* infection complicated by compartment syndrome, however, there were some patients who underwent limb amputation.[2]

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CASE REPORT

A 38 -year-old Japanese man with a history of alcoholism presented with 2 days of fever and diarrhea, and was treated with oral antibiotics (cefditoren pivoxil) for gastroenteritis. He then presented to the emergency department due to worsening of symptoms.

Vital signs included: body temperature, 36.1°C; pulse rate, 115 b.p.m.; blood pressure, 95/44 mmHg; respiratory rate, 16 breaths/min; SpO_2, 100% on room air; and mental status was clear. There were no signs of sensory or motor dysfunction of the extremities. He had abdominal tenderness without rebound tenderness. Laboratory data revealed markedly elevated leukocyte count (16,700/μL), thrombocytopenia (platelets, 13,000/μL), abnormal liver enzymes, coagulation dysfunction (prothrombin time – international normalized ratio, 2.32; D-dimer, 71.8 μg/mL), acute kidney

injury (creatinine, 2.08 mg/dL). Disseminated intravascular coagulation (DIC) was recognized at 8 points according to DIC criteria established by the Japanese Association for Acute Medicine. Initially, thrombotic microangiopathy such as that due to Shiga-toxin-producing *Escherichia coli* and hemolytic uremic syndrome (STEC-HUS) was suspected.

His vital signs were within normal limits except for tachycardia. A source of infection was not identified; we decided not to administer antibiotics, and instead to continue supportive care. Stool culture or *Clostridium difficile* toxin test had not been submitted.

On the second hospital day, there was pallor and severe pain in both distal lower extremities. No signs of decreased arterial inflow causing ischemia of the lower extremities were seen on contrast computed tomography scan. Laboratory data revealed decreased platelets of 8,000/μL and elevated lactic acid of 5.3 mmol/L. At this point, the patient was diagnosed with septic shock and treated with broad-spectrum antibiotics (meropenem 1,000 mg i.v. every 8 h + vancomycin 1,250 mg i.v. every 12 h + minocycline 100 mg i.v. every 12 h + tobramycin 240 mg i.v. per day), inotropic agents, and mechanical ventilation were started. Peripheral blood smears showed gram negative bacilli. Due to the finding of hemophagocytic syndrome by bone marrow study, steroid pulse therapy was started (methyl prednisolone 1,000 mg/day).

On the third hospital day, *Capnocytophaga* spp. was confirmed in the blood culture. Rereview of the history revealed that the patient had close contact, such as kissing, with his tamed dog and even stray dogs. Purpura appeared over his entire body, and all four extremities became rigid (Fig. 1). The serum creatine kinase level was elevated, compartment pressures of the left lower extremity increased to 40–70 mmHg, and extremity compartment syndrome was diagnosed. We performed an exploratory incision to determine the treatment plan. An exploratory incision of both legs revealed intact fascia and no obvious ischemic changes of the muscles. Apparent muscular necrosis, vasculitis, or thrombotic findings which might relate to DIC were not detected in the pathological study. After discussion with his family about further treatment, it was decided not to undertake invasive procedures. Therefore, formal fasciotomy was not carried out. On the same day, the patient died with uncontrollable lactic acidosis and hyperkalemia (Fig. 2).

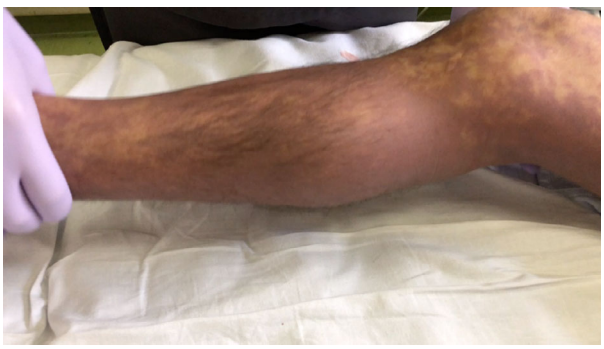

Fig. 1. Rigidity of the extremities of a 38-year-old Japanese man with compartment syndrome due to *Capnocytophaga canimorsus* infection.

DISCUSSION

TO THE BEST of our knowledge, this is the first report of a *C. canimorsus* infection that caused compartment syndrome of all four extremities. This patient had pain and mild pallor on the first day, and other signs of compartment syndrome appeared subsequently. In this patient, according to the findings at exploratory fasciotomy and the pathological report, there was no muscular congestion or signs of hemorrhage. Therefore, compartment syndrome caused by inflammation and capillary leak was suspected.

Systemic capillary leak syndrome is caused by an increase in capillary permeability of proteins and leads to the loss of protein-rich fluid from the intravascular to the interstitial space.[3] Meningococcal sepsis has been reported to cause limb compartment syndrome.[4] The underlying pathophysiology of capillary leak is unclear. Some evidence suggests that meningococci and neutrophils cause the loss of negatively charged glycosaminoglycans that are normally present on the endothelium.[4] It is possible that our case and these cases might be caused by similar pathophysiology, like capillary leakage.

Capnocytophaga canimorsus infection occurs even if a history of animal bites is not evident. Sometimes it can be caused by a lick from an animal, as in the present patient. According to Butler's report, the occurrence of *C. canimorsus* infections without bite accounts for 24% of cases[5]. Nine patients with *C. canimorsus* infection following a lick by an animal have been reported since 1995 (Table 1).

In these nine patients, the mortality rate was approximately 11% (1/9). The mortality rate of systemic *C. canimorsus* infection secondary to an animal bite was about 30%[1]. The mortality rate of lick cases was much lower. This could be due to a smaller inoculum transmitted through the skin defect, not deep into the soft tissue by biting. Unless we meticulously take a patient's history, including their social history, the definitive diagnosis of *C. canimorsus* infection might be delayed.

In this patient, the symptoms were easily misdiagnosed as infectious gastroenteritis because the initial presentation

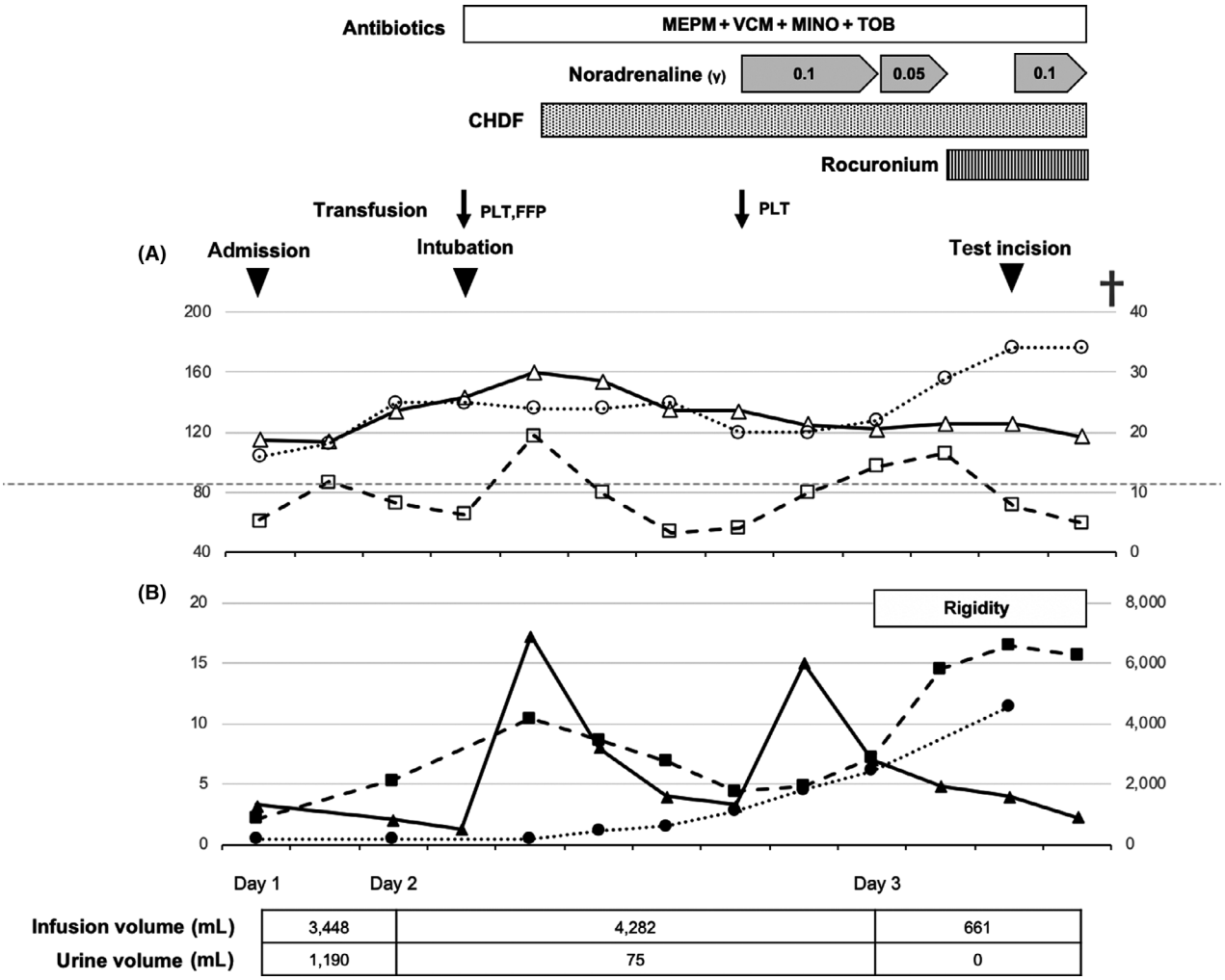

Fig. 2. Clinical course, vital signs, and laboratory data trends of a 38-year-old Japanese man with compartment syndrome due to *Capnocytophaga canimorsus* infection. (A) Vital signs. Vertical axis (left): □ mean arterial pressure (mmHg); △heart rate (b.p.m.). Vertical axis (right): ○ respiratory rate (breaths/min). (B) Laboratory data. Vertical axis (left): ■ lactate (mmol/L). Vertical axis (right): ▲ platelets (×10/μL); ● creatine phosphokinase (U/L). Horizontal axis: time from admission (days). CHDF, continuous hemodiafiltration; FFP, fresh frozen plasma; MEPM, meropenem; MINO, minocycline; PLT, platelet; TOB, tobramycin; VCM, vancomycin †Deceased.

included diarrhea and pain in the epigastric region. We suspected STEC-HUS because of thrombocytopenia, elevated lactate dehydrogenase, and elevated creatinine. All of the above manifestations might delay the diagnosis and treatment with antibiotics at the time of admission. Twenty-six percent of *C. canimorsus* infections present with abdominal pain and diarrhea as the initial symptoms.[1]

In this patient, a disintegrin-like and metalloproteinase with thrombospondin type 1 motifs 13 (ADAMTS13) and Shiga toxin were negative. However, as ADAMTS13 and Shiga toxin are outsourced laboratory tests, early diagnosis to rule in or rule out these possibilities was difficult.

CONCLUSION

WE PRESENT A patient with a rare *C. canimorsus* infection complicated by acute compartment syndrome due to suspected capillary leak syndrome. *Capnocytophaga canimorsus* transmission can occur not only through animal bites, but also through licks, or even close contact with animals when a risk factor for *C. canimorsus* infection such as alcoholism exists. As the diagnosis might be confounded because of mimicking STEC-HUS, a detailed history, physical examination, and suspicion of this disease are necessary for appropriate intervention.

Table 1. Patients reported with *Capnocytophaga* septicemia caused by an animal lick

Author	Year	Age, years	Gender	Risk	Wound	Animal	DIC/ purpura	Clinical features	Outcome
Pers *et al.*[1]	1995	81	Female	None	Toe ulcer	Cat	Negative	CellulitisRenal insufficiency	Survived
	1995	60	Male	Alcoholism	Chronic ulcerous eczema	Dog	Positive	Septic shock, AKI	Died
Uldbjerg[6]	1996	54	Male	None	Leg ulcer	Dog	Positive	Ischemia of both feet	Survived
Ehrbar *et al.*[7]	1996	53	Male	Asplenia	Leg wound	Dog	Positive	Acute myocardial infarction	Survived
Tierney *et al.*[8]	2006	65	Male	None	Forearm wound	Dog	Positive	Mycotic AAA	Survived
Low *et al.*[9]	2008	48	Female	None	Burn wound	Dog	Positive	Loss of limb	Survived
Wilson *et al.*[10]	2016	70	Male	None	None	Dog	Negative	SeizureSepsisMultiorgan dysfunction	Survived
Morandi *et al.*[2]	2017	41	Male	Asplenia	Leg wound	Dog	Positive	Septic shockLost both legs, nose, and all fingers	Survived
Present patient	2018	38	Male	Alcoholism	None	Dog	Positive	Septic shockExtremity compartment syndrome	Died

AAA, abdominal aortic aneurysm; AKI, acute kidney injury; DIC, disseminated intravascular coagulation; STEC-HUS, Shiga-toxin-producing *Escherichia coli* and hemolytic uremic syndrome.

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DISCLOSURE

Approval of the research protocol: N/A.
Informed consent: Written informed consent was obtained from the patient for publication of this case report and any accompanying images.
Registry and registration no. of the study/trial: N/A.
Animal studies: N/A.
Conflict of interest: None.

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