Infect Dis Trop Med 2023;9: e1099

Capnocytophaga canimorsus septic shock complicated by multiorgan failure: an unexpected case with a favourable outcome

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ABSTRACT:

— ***Background:*** The aim of our report was to describe an unusual and exemplary case of *Capnocytophaga canimorsus* septic shock in a patient who has not been exposed to dogs or cats.

— ***Case report:*** A splenectomized 60-year-old male without a known at-risk bite wound was diagnosed with *C. canimorsus* septic shock, complicated by multiorgan failure and disseminated intravascular coagulation. The patient was empirically treated and recovered without sequelae. The favorable outcome was related to a prompt diagnosis and a timely treatment, despite the absence of epidemiological and suspicion clues. A narrative review and case series demonstrates that only one previous article has reported a case of bacteremia and meningitis without a dog bite in an immunocompetent individual.

— ***Conclusions:*** It is important to recognize any case of *C. canimorsus* sepsis in splenectomized patients, particularly those presenting with fulminant sepsis, even without a history of dog bites, scratches and licks.

— ***Keywords:*** Capnocytophaga canimorsus*, Septic shock, Multiorgan failure, Asplenic patients.*

INTRODUCTION

Capnocytophaga canimorsus is an encapsulated, microaerophilic gram-negative rod belonging to the *Flavobacterium* family and newly named since 1989[1,2]. It often colonizes the mouth of pets like dogs and cats and can be transmitted even in the absence of an animal bite[1-2]. Recently recognized as a true agent of zoonosis, it may cause significantly severe infections in humans, described in both immunocompromised and immunocompetent subjects, respectively[1,2]. Butler et al[1] estimated 484 *C. canimorsus* laboratory-confirmed cases reported in the literature, between 1961 and 2014. Most patients were males over 50 years of age, bitten by dogs a few days before their illnesses, and underlying diseases included prior splenectomy, alcoholism or other immunocompromising conditions, and the case-fatality rate was about 27%[2].

CASE PRESENTATION

A 60-year-old male was directly admitted to our Intensive Care Unit after abdominal trauma. He presented with a severe clinical picture of shock with fever, hypotension, peripheral cyanosis, hypoglycemia and metabolic acidosis. Contact with dogs/cats or other pets was not reported. He was splenectomized at the age of 25 and suffered from arterial hypertension. No further comorbidities were reported. A chest CT scan excluded pulmonary embolism. Upon admission, the physician ordered routine blood tests and two peripheral blood cultures and diagnosed the patient with a septic shock. Laboratory examination showed leukocytosis (16,610 cells/mL, normal range 4-9,000 cells/mL), extremely elevated serum C-reactive protein levels (313.4 mg/L, normal range 0-3 mg/L), and severe thrombocytopenia (12,000 cells/mL,

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normal range 50-90,000 cells/mL). Moreover, high alanine aminotransferase (ALT) levels (1,071 U/L, normal range 10-50 U/L), and disruption of coagulative profile [prothrombin time 2.19 (normal range, 0.8-1.2), activated partial thromboplastin 87 (normal range, 30-40 seconds)] were reported. Severe concomitant kidney damage was also present (glomerular filtration rate 11 mL/min, normal range >90 mL/min). An extensive supportive treatment with volume repletion, non-invasive ventilation (NIV), and continuous renal replacement therapy (CVVT) was required. Also, an immediate broad-spectrum antimicrobial treatment with meropenem, teicoplanin, and ciprofloxacin was started, while waiting for blood cultures results and antibiotic susceptibility testing. Five days later, the growth of *C. canimorsus* from both first drawn sets of blood cultures was notified by the laboratory. Definitive identification of *C. canimorsus* was attempted using matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF). *C. canimorsus* was susceptible to all tested molecules.

An antibiotic de-escalation was not considered because of the development of hospital-acquired *Enterococcus faecalis* pneumonia and *Klebsiella pneumoniae* urinary tract infection. The etiologic diagnosis of septic shock caused by *C. canimorsus* met the following criteria: (i) *C. canimorsus* growth from multiple blood cultures performed upon admission, before starting antibiotic therapy, unrelated to another site of infection; (ii) the patient had fever (>38.5°C), hypotension, and positive laboratory results unrelated to other sites of infection and common skin contaminating organisms. The detection of other microorganisms responsible for pneumoniae and urinary infections occurred more than 72 hours after admission to the Intensive Care Unit; thus, they were ruled out as possible primary causes of septic shock.

Repeated plasma-platelet transfusions were also needed. Abdominal ultrasonography, total body positron emission scan (PET CT) and a bone marrow biopsy with cytological examination were also performed, but no specific results were obtained. *C. canimorsus* was isolated from blood cultures taken upon hospitalization, in absence of relevant *in vitro* antibiotic resistances. Broad spectrum antibiotic treatment was maintained until discharge due to the extremely severe patient's conditions. After 35 days, the patient was weaned from ventilation, ultrafiltration, and enteral nutritional supported and moved to our Infectious Diseases ward, reaching final discharge after further 16 days. No sequelae were recognized in careful and prolonged outpatient follow-up including clinical and laboratory check for the next four weeks.

DISCUSSION

C. canimorsus is a gram-negative, capnophilic, fastidious, slow-growing rod-shaped bacterium, formerly called CDC group DF-2. It is part of the normal bacterial flora of dogs and cats' oral cavity. It is transmitted to humans principally by bites (54% of described cases), scratches (8.5%), or mere contact with animals (27%)[3]. In addition, some cases of human infections result from pets that lick skin wounds/ulcers. However, in 10.5% of cases, the source of infection remains unknown[3], as occurred in our patient.

C. canimorsus has emerged as a causative agent for serious human infections that may lead to multiple complications, including septicemic infection with disseminated intravascular consumption coagulopathy or purpura, high-grade bacteremia, endocarditis, eye infections, gangrene of the digits or extremities, meningitis and fulminant septic shock, more commonly reported in literature in patients with prior splenectomy, alcoholism or with immunodeficiency. Other risk factors include smoking and diabetes mellitus.

C. canimorsus infection can lead to severe rapid progression and death even in immunocompetent patients[1-3]. For example, a review made by Nakayama et al[4] reported four cases of fatal *C. canimorsus* cases in immunocompetent patients published in the current literature.

Our patient did not show any dog bite or other contact with dogs or cats, so the source of contamination remained unexplained. However, we hypothesized a presumably pre-existing skin contamination of the abdominal surface, favoring the subsequent bacterial penetration into the deep tissues.

A comprehensive literature search to identify other reported cases of *C. canimorsus* in patients without a history of bites or scratches revealed the case[5] of an immunocompetent 75-year-old man with *C. canimorsus* bacteremia and meningitis. Despite being a dog owner, the patient had no history of bites or scratch marks. Immediate antibiotic treatment may influence the course of *C. canimorsus* infection. However, despite appropriate therapy, the prognosis of *C. canimorsus* sistemic disease may remain very poor. *C. canimorsus* infections can induce a systemic illness, complicated by fulminant septic shock, Waterhouse-Friderichsen Syndrome[6], hemolytic uremic syndrome[7], and a mycotic aortic aneurysm[8]. Regarding local epidemiology, *C. canimorsus* remains a rare infection in Italy. We conducted research on PubMed, where we found a total of nine original articles from Italian authors[9-17], that described 18 cases reported from 2003 until 2022 (Table 1). Most of the cases reported a wound infection and septic shock. Bertin et al[13] published a case of a 69-year-old woman who was diagnosed with *C. canimorsus* septic gangrene of both forefeet and hands, infective aortic endocarditis, and large ischemic septical lesions. Marmo et al[12] presented a case series of *C. canimorsus* infections treated with HBO_2 in adjunction to antibiotic therapy. Mantovani et al[15] reported a fatal septic shock with fulminant purpura in an elderly patient without specific risk factors, which occurred two days after an irrelevant dog bite. The case described by Sabbatani et al[10] reported efficacy of linezolid in contrast with the poor effectiveness of the initial combination of imipenem, amikacin and clindamycin. The efficacy of linezolid in the treatment of *C. canimorsus* was also reported[10] for a cerebral abscess due to *Capnocytophaga spp.* Moreover, Geisler et al[18] reported a case of pneumonia and sepsis due to fluoroquinolone-resistant *C. gingivalis* following autologous stem cells transplantation; the patient responded to treatment with linezolid and metronidazole.

Table 1. A summary of articles pertinent to culture-documented cases of *C.canimorsus* infections published from Italian authors, from 2003 to 2022.

References, Age/Sex	Diagnosis	Underlying condition	History of dog or cat contact	Time between pet contact and symptoms	Symptoms at hospital admission	Treatment	Outcome
Frigiola et al[9], 41 y/F	Blood cultures	Mitral infective endocarditis, previous rheumatic mitral endocarditis	Dog bite by her dog	About 2 weeks	Fever of unknown origin	CEF; a mechanical prosthesis implantation	Cured
Sabbatani et al[10], 47 y/M	Cerebral tissue biopsy and purulent material	An extensive right frontal brain abscess. Immunocompetent	Cat bite and /or a missed mandibulary granuloma	NR	Fever and neuro-psychological symptoms	Neurosurgery, LIN	Cured
Ulivieri et al[11], 28 y/M	Cerebral purulent aspirated fluid	Temporal brain abscess Immunocompetent	Dog bite	NR	Fever, headache and left size seizure	Surgical resection; PEN, CFT, MTZ	Cured
Marmo et al[12], 6M, 3F mean age 38 y	Bood cultures (3), wound (6).	A case series of complicated wounds in 9 patients Immunocompetent (6), diabetes (2) and one was asplenic	Dog bites	24 hours	Signs and symptoms of sepsis and meningitis	HBO_2, different antibiotic therapy	Cured
Bertin et al[13], 69 y/F	Blood cultures	Septic shock, gangrene of both forefeet and hands, aortic endocarditis, and cerebral ischemic lesions. Immunocompetent	Dog bite by her dog	3 days before admission	Shortness of breath, profound fatigue, hyperpyrexia, and a small wound on right hand	PIP/TAZ and VAN	Gradually recovered
Bertin et al[13], 65 y/M	CSF culture	Meningitis, cerebritis Immunocompetent	Dog bite by his dog	Three days	Signs of meningitis	AMPS, MOX	Cured
Piccinelli et al[14], 22/M	PCR and sequencing on post mortem samples	Fulminant septic shock spherocytosis and splenectomy	The patient owned a dog but he did not have dog bite	Unknown	Headache, vomiting, muscle pain, high fever and diffuse petechiae	CEF	Died
Mantovani et al[15], 80 y/F	Blood culture	Purpura fulminans and septic shock. DP	Dog bite	3 days before admission	Altered mental status and high fever	Empiric PIP/TAZ	Died
Sabia et al[16], 78 y/M	Blood culture	Septic shock. DM and HP	Dog bite	Dog bite 6 day before admission	Fever of unknown origin	Cured	VAN and CLI
Nisi et al[17], 63 y/M	Blood cultures	Septic shock. Asplenic, and chronic myelomonocytic leukemia	The patient lived with his two dogs, however no skin wound or scar was found.	Unknown	Fever, cough, and asthenia	PIP/TAZ	Cured

CEF=ceftriaxone; PEN=penicillin G; CFT=cefotaxime; MTZ=metronidazole; CSF=cerebrospinal fluid; AMPS=ampicillin-sulbactam; MOX=moxifloxacin; ICU=Intensive Care Unit; LIN=linezolid; NR=not reported; PIP/TAZ=piperacillin/tazobactam; VAN=vancomycin; CLI=clindamycin; DM=diabetes mellitus; HP=arterial hypertension; DP=depression.

There is very little information in the current literature regarding the activity of linezolid toward *C. canimorsus*; however, it may be an effective alternative against multidrug-resistant *Capnocytophaga* isolates or in patients with multiple drug allergies. Penicillin is considered the first choice in *C. canimorsus* infections. However, third-generation cephalosporins or beta-lactamase inhibitor may be used.

CONCLUSIONS

In summary, enhanced surveillance is vital for the early detection of human cases of *C. canimorsus* infection and the prompt implementation of response measures. The prognosis of septic shock induced by *C. canimorsus* is often unfavorable, especially in splenectomized or immunocompromised patients that are at higher risk of life-threatening course of the infection. Clinicians must maintain a very high level of suspicion for this infection and promptly implement empirical antibiotic therapy with penicillin in combination with beta-lactamase inhibitors.

Funding:
None.

Conflicts of Interest:
The authors declare no conflict of interest.

Informed Consent:
A signed informed consent for publication was obtained.

Authors' Contributions:
RM wrote the initial manuscript. AM, MV M and SG guided, corrected and revised the paper. All authors read and approved the final manuscript.

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