

Meningitis caused by *Capnocytophaga canimorsus* in a COVID-19 patient: a rare complication of dog bites

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ABSTRACT

Capnocytophaga canimorsus is a gram-negative rod that is part of the commensal microbiota of dogs' and cats' mouths. In this case, we report an 85-year-old man with COVID-19 who had his right arm bitten by a dog. His symptoms were impaired consciousness, agitation and aggressive behavior. Physical examination revealed neck stiffness and Brudzinski's sign. The cerebrospinal fluid culture was compatible with *Capnocytophaga canimorsus*. He required intensive care and received a 14-day prescription of meropenem. After 40 days of hospitalization, the patient was fully recovered and was discharged. This case highlights the importance of physician and microbiologist be awareness of this disease, mainly in patients with neurological symptoms after a dog or cat bite.

KEYWORDS: *Capnocytophaga canimorsus*. Meningitis. Dog. SARS-CoV-2. COVID-19.

INTRODUCTION

Capnocytophaga canimorsus is a fastidious, fermenter, capnophilic, facultative anaerobic, fusiform or filamentous gram-negative rod found in the commensal oral microbiota of dogs and cats¹. It was first reported as a cause of meningitis and septicemia in the 1970s. Transmission to humans may occur after a bite and rarely after dog/cat licking of pre-existing wounds². Infections related to feline exposure are less frequent^{1,3,4}. Most of the infections occur in men over the age of 50 with a history of dog bites and immunocompromise^{2,3}. Although the pathogen has been reported worldwide, to the authors' knowledge, there have been no previously reported cases of meningitis caused by this microorganism in Brazil. Herein, we report a case of meningitis caused by *Capnocytophaga canimorsus* and perform a brief literature review.

Medical records were reviewed during the patient's hospitalization in September 2020 at the Hospital Sao Jose de Doencas Infecciosas (HSJ), an infectious disease center. We reviewed the literature for similar cases. The patient consented to the publication of his case and images. This study was approved by the Research Ethics Committee of the HSJ (Protocol N° 4.963.906).

CASE REPORT

An 85-year-old man who lived in a rural area and had no previous history of comorbidities sought the emergency room with a dog bite on his right arm

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from 15 days prior to his admission. He reported having a 2-day fever (38.2 °C temperature) and a 5-day history of aggressive behavior, mental confusion, psychomotor agitation and impaired consciousness. On the physical examination, a healing wound measuring 3 × 2 cm was noted in the posterior region of his right arm. No signs of cutaneous or soft tissue infection were observed. The neurological examination revealed nuchal rigidity and Brudzinski's sign. Laboratory findings on admission showed leukocytosis (15,000/mm³) and a low platelet cell count (9,000/mm³). The patient also presented an elevated C-reactive protein (187.7 mg/L). Liver and renal function tests were unremarkable. His glycosylated hemoglobin level was normal. Anti-HIV 1/2 Western blot was negative. Blood cultures were negative. Despite the absence of respiratory symptoms, because of the admission protocol of our intensive care unit (ICU), the patient performed a RT-PCR for SARS-CoV-2, which was positive. The diagnosis of COVID-19 was made through the amplification of the betacoronavirus E gene and the specific SARS-CoV-2 RdRp gene by RT-PCR.

Cranial computed tomography was normal. Based on the suspicion of meningitis, a cerebrospinal fluid (CSF) analysis was performed. This revealed glucose levels of 9 mg/dL, a protein concentration of 171.3 mg/dL, a white blood cell count of 727 cells/mm³ with 89% polymorphonucleocytes and a CSF Gram stain with gram-negative bacilli (Figure 1A). During hospitalization, CSF culture samples revealed translucent, spotty and flat colonies on a chocolate agar plate after 48 h of incubation at 35 °C with 5% CO₂ (Figures 1B and 1C), with no

growth on MacConkey agar or without CO₂. At first, Vitek®2 GN ID card (Biomérieux, Marcy-l'Étoile, France) found three potentially identifiable microorganisms with low discrimination: *Sphingomonas paucimobilis* (34%), *Chryseobacterium indologenes* (33%), and *Brevundimonas diminuta/Brevundimonas vesiculares* (33%). Due to the low discrimination, a matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF – VITEK MS®) (Biomérieux, Marcy-l'Étoile, France) was performed and *C. canimorsus* was identified with a 99.9% confidence value. The patient had no clinical improvement during the first 5 days of ceftriaxone treatment. Thus, he received meropenem with a prompt clinical response. He was admitted to an ICU due to loss of consciousness, although he did not require orotracheal intubation and was discharged from the ICU after 5 days. The patient was discharged after a 14-day regimen of meropenem with full clinical resolution of his symptoms. He presented no sequelae at the six-month follow-up.

DISCUSSION

Many species of microorganisms with varying degrees of human pathogenicity have been identified in the oral flora of canids and felines. *C. canimorsus* is not a unique organism that causes infection in humans through dog bites. *Capnocytophaga cynodeginia* and *Capnocytophaga canis* are also part of the gingival flora of dogs and cats, although they usually present themselves as mild and localized cutaneous and soft tissue infections⁴. Infection due to *C. canimorsus* may present itself as a fever, skin

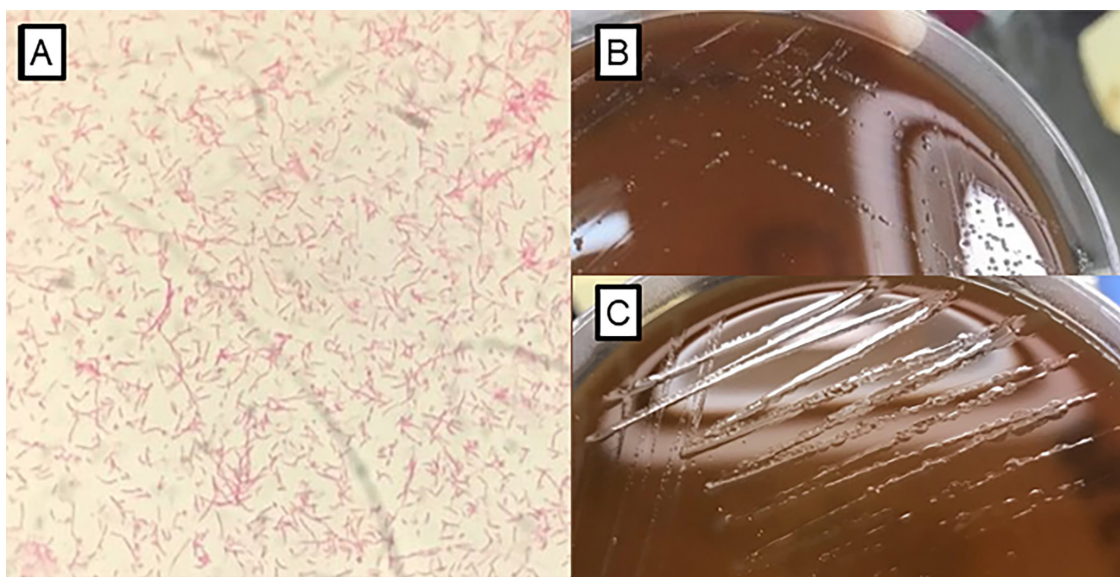


Figure 1 - A) Gram stain of *C. canimorsus* culture showing fusiform gram-negative rod. The same microscopic appearance that have been found on the CSF Gram stain; B-C) CSF culture with translucent, stained, and flat colonies on a chocolate agar plate after 48h of incubation at 35 °C with 5% CO₂.

wounds with infection, fatigue, gastrointestinal symptoms, and purpura^{4,5}. This case did not show any skin rash or purpura but was considered a severe disease based on sepsis criteria and central nervous system involvement upon presentation. The prognosis of meningitis caused by this microorganism is usually better than acute sepsis^{2,5}. It is hypothesized that the incubation period after dog bites is longer for meningitis, giving more time for an immune response to develop^{3,5}. Few cases of *Capnocytophaga canimorsus*-meningitis in immunocompetent patients have been described (Table 1).

This patient arrived with a clinical syndrome of meningitis. The symptoms, however, were unspecific and could be compatible with infection due to several agents. Thus, the differential diagnosis is important. The pathogens that usually cause meningitis in the elderly are *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Neisseria meningitidis* and *Listeria monocytogenes*. Patients who undergo neurosurgery are more likely to present *S. aureus* or *Pseudomonas aeruginosa*. Rare causes of meningoencephalitis related to dog bites are *Pasteurella multocida* and rabies⁶.

Brazil uses a national health information system on diseases of compulsory notification (SINAN) to record

all patients seeking medical care in public health facilities following direct contact with an animal suspected of rabid⁷. In Ceara State, Northeastern Brazil, where the dog bite occurred, SINAN recorded 219,504 attacks on humans by potentially rabid mammals, with dogs being the main aggressors⁸. There is no data available in the country regarding other bite-related complications. Due to the absence of additional data from these reported bites, we do not know the complete extent of non-rabies complications in Brazil. To date, no other similar cases of *C. canimorsus*-meningitis have been reported in Brazil. The diagnosis of *C. canimorsus* infection is challenging. To reach the diagnosis, high clinical suspicion associated with assertive microbiological methods is necessary. Microbiological diagnosis may be delayed as the blood culture results usually take up to 14 days. In our case, MALDI-TOF-MS was performed to reach the diagnosis since the Vitek[®]2 GN card (Biomérieux, Marcy- l'Étoile, France) was unable to differentiate the poorly discriminated microorganisms, since it did not contain the biochemicals needed for identifying *Capnocytophaga* species. Furthermore, the three suggested bacteria had no metabolic correspondence with the isolated bacteria, as they were non-fermenting and aerobic. MALDI-TOF-MS is a new and powerful

Table 1 - Description of reported cases of meningitis caused by *Capnocytophaga canimorsus* in immunocompetent hosts from 1994 to 2021.

Article	Case	Month/Year ^a	Country	Age	Sex	Circumstance	Diagnostic Method	Outcome
Blanche <i>et al.</i> ¹³	<i>C. canimorsus</i> Lymphocytic Meningitis in a 57-year-old Man	April/1994	France	57y	M	Dog Bite	N/A	N/A
Beltramone <i>et al.</i> ¹⁴	<i>C. canimorsus</i> Meningitis in a 49-year-old Man	January/2017	France	49y	M	Dog Bite	Blood culture ^b	Discharge
Delman <i>et al.</i> ¹⁵	<i>C. canimorsus</i> Meningitis in a 70-year-old Woman	March/2017	United States	70y	F	Dog Bite	Blood culture ^b	Discharge
Bertin <i>et al.</i> ¹⁶	Two cases of <i>C. canimorsus</i> meningitis in a 69-year-old woman and a 65-year-old man	June/2018	Italy	69/65y	F/M	Dog Bite	16S ribosomal RNA gene sequence analysis	Discharge ^c
Malik <i>et al.</i> ¹⁷	Rare case of <i>C. canimorsus</i> meningitis in a man without risk factors	May/2021	United Kingdom	N/A	M	Dog Bite	N/A	N/A
Asif <i>et al.</i> ¹⁸	<i>C. canimorsus</i> meningitis diagnosed using next-generation sequencing of microbial cell-free DNA in a 55-year-old woman	April/2021	United States	55y	F	Dog Bite	Next-generation sequencing of microbial cell-free DNA (NGS cfDNA)	Discharge
O'Riordan <i>et al.</i> ¹⁹	<i>C. canimorsus</i> meningitis and bacteraemia without a dog bite in a 75-year-old male	July/2021	Ireland	75y	M	None	N/A	Discharge

M = Male; F = Female; N/A = Not Available; m = months; y = years; ^aPublication date; ^bCSF cultures were negative; ^cBoth patients were discharged despite life-threatening complications.

technique for detecting a large array of proteins rather than just small molecules. In many studies, this technique outperformed conventional methods. MALDI-TOF-MS is a rapid diagnostic method that is less affected by culture media, cultivation conditions or incubation time⁹.

Chesdachai *et al.*¹ found that meningitis associated with *Capnocytophaga* bacteremia primarily occurs in immunocompromised patients. *Capnocytophaga* infection may cause a life-threatening condition. The main risk factors are immunosuppressive medications, hematologic malignancies, diabetes, hematopoietic stem cell transplantation, renal disease, alcohol use disorder, solid organ transplantation and splenectomy^{10,11-19}. Although the patient did not have these aforementioned risk factors, his age may have played a significant role in the severity of the infection. Data from literature suggest that the stimulation of the immune system throughout our lives may induce immune changes, probably due to unbalanced inflammatory profiles, which can lead to a weaker immune system. The extent of this immunodepression can vary according to the individual²⁰.

We cannot confirm the role of SARS-CoV-2 infection in the patient's immunity. He did not present with any respiratory symptoms, and steroid administration was not necessary in his case. A positive test for SARS-CoV-2 in this patient was an incidental finding since it is less likely that these two infections are related. During the pandemic, COVID-19 infections were much more common than *C. canimorsus* infections. Therefore, it is possible to diagnose a wide variety of patients with asymptomatic COVID-19 infections, even in those with rare conditions. The case occurred during the second COVID-19 wave in Brazil, when most cases were caused by the Gamma (P.1) variant. At the time of diagnosis, reverse transcription-polymerase chain reaction (RT-PCR) for SARS-CoV-2 in CSF was not available at our center.

Treatment is usually based on the susceptibility tests of blood or CSF cultures. In general, β -lactam antibiotics, third-generation cephalosporins, doxycycline, clindamycin and chloramphenicol or carbapenems are effective against *C. canimorsus*. Some guidelines suggest that the preferred intravenous agents should include clindamycin, doxycycline, cefuroxime and meropenem¹². The patient was treated with meropenem for 14 days and had a good clinical response. Although he was treated for a prolonged period, mainly due to the severity of the case, more studies are necessary to better understand the duration of antibiotic therapy. Infection prophylaxis after a dog/cat bite with amoxicillin/clavulanic acid is possible. Doxycycline or clindamycin can be considered in case of penicillin allergy^{1,10,12}.

CONCLUSION

Herein, we present a rare case of meningitis caused by *C. canimorsus* in a patient coinfecting with SARS-CoV-2. This report is special because it describes a rare case of a SARS-CoV-2 infected immunocompetent patient with a severe neurological disease due to *C. canimorsus*, and the diagnosis was possible only due to the high discrimination achieved by MALDI-TOF. This case highlights the importance of awareness about this disease and maintaining a high index of suspicion when a patient presents neurological symptoms compatible with meningitis and a history of dog or cat bite and/or licking. Molecular methods are usually necessary for the prompt diagnosis and may not be available in every center, worldwide.

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CONFLICT OF INTERESTS

The authors report no conflict of interests.

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