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Miyazaki, Dai ; Kunishige, Chika ; Sano, Shigeru ; Urakawa, Kahoru ; Okamoto, Kana ; Morishita, Naomi ; Iwata, Kentaro

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(Citation)

Acute Medicine & Surgery, 11(1):e922

(Issue Date)

2024-01

(Resource Type)

journal article

(Version)

Version of Record

(Rights)

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<https://hdl.handle.net/20.500.14094/0100486173>



## CASE REPORT

A fatal septic shock caused by *Capnocytophaga gingivalis* potentially associated with COVID-19: A case reportDai Miyazaki<sup>1</sup> | Chika Kunishige<sup>1</sup> | Shigeru Sano<sup>1</sup> | Kahoru Urakawa<sup>2</sup> | Kana Okamoto<sup>2</sup> | Naomi Morishita<sup>3</sup> | Kentaro Iwata<sup>4</sup><sup>1</sup>Department of Emergency Medicine, Hyogo Prefectural Kakogawa Medical Center, Kakogawa, Japan<sup>2</sup>Department of Clinical Laboratory, Hyogo Prefectural Kakogawa Medical Center, Kakogawa, Japan<sup>3</sup>Department of Nursing, Hyogo Prefectural Kakogawa Medical Center, Kakogawa, Japan<sup>4</sup>Division of Infectious Diseases, Kobe University Hospital, Kobe, Japan

## Correspondence

Kentaro Iwata, Division of Infectious Diseases Therapeutics, Graduate School of Medicine, Kobe University, Kusunokicho 7-5-2, Chuo-ku, Kobe, Hyogo 650-0017, Japan.  
Email: kentaroiwata1969@gmail.com

## Abstract

**Background:** *Capnocytophaga* spp. is associated with fulminant sepsis, particularly in those with immunosuppression. We here report a rare case of fatal fulminant septic shock caused by *C. gingivalis*, concurrent with COVID-19.**Case Presentation:** A Japanese woman developed septic shock, which led to her death. Polymerase chain reaction (PCR) testing of the respiratory specimen was positive for SARS-CoV-2, and a CT scan of the chests revealed bilateral ground glass opacities. The blood cultures identified *C. gingivalis*. The patient had rheumatoid arthritis and was taking prednisone orally. There were no splenic abnormalities shown on the CT scan.**Conclusion:** A rare case of fulminant septic shock caused by *C. gingivalis*, together with COVID-19 was identified. The precise pathogenesis of this combination, together with the best treatment option should be sought by further studies.

## KEYWORDS

*Capnocytophaga*, COVID-19, sepsis

## INTRODUCTION

*Capnocytophaga* spp. is an encapsulated facultative anaerobic Gram-negative rod. The most well-known pathogenic organism in humans is *C. canimorsus*, which is a commensal organism in the oral cavity of dogs and cats and is associated with fulminant sepsis after dog or cat bite, among those without functioning spleen.<sup>1</sup> On the other hand, *C. gingivalis* is a commensal organism of the human oral cavity. It can be found both in adults and children and has a worldwide distribution, but it is rarely reported as the cause of serious infections in humans, partly because it had been identified to the genus level previously due to the problem with microbiological technologies.<sup>2</sup> Still, it also might be associated with fulminant sepsis, particularly among immunocompromised hosts.<sup>2,3</sup>

There were scarce data on the relationship between coronavirus disease 2019 (COVID-19) and *C. gingivalis*. Here, we

report a case of fatal fulminant sepsis caused by *C. gingivalis*, potentially associated with COVID-19.

## CASE REPORT

A Japanese woman in her 50s developed acute onset nausea and dyspnea on the morning of December 2022. Her symptoms worsened in the afternoon, but she decided to stay home. However, her dyspnea further worsened, and her consciousness level also began to impair. Her husband called the ambulance at about 3 AM on the following day. She was brought to a hospital by ambulance, but her blood pressure was very low. The mechanical ventilation was started after endotracheal intubation. Upon the arrival, polymerase chain reaction (PCR) testing of respiratory specimen was positive for SARS-CoV-2, but negative for influenza virus A and B.

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Because the hospital was not designated to take care of patients with severe COVID-19, and then the patient was transferred to our hospital.

During the transfer, she developed pulseless electrical activity (PEA) twice inside the ambulance and was resuscitated for both. On arrival, her systolic blood pressure was about 70. No other vital signs were documented. On physical examination, pupils were equally dilated and did not respond to the light. The extremities were cold to the touch. The blood test results on arrival are shown in Table 1. CT scan of the chest without contrast showed bilateral diffuse ground glass opacities with atelectasis (Figure 1). There was a normal-sized spleen.

Despite the mechanical ventilation, massive intravenous hydration, and use of vasopressors, she remained critically ill. The family did not wish the use of ECMO (extracorporeal

membranous oxygenation) or further cardiopulmonary resuscitation. The patient died on the same morning, about 2 h after the arrival. The autopsy was not performed as per the wishes of her family.

The patient had a past medical history of bronchial asthma and rheumatoid arthritis and had received COVID-19 vaccines three times by the time she became ill. She rarely had asthma attacks and was not given specific medication by her primary care physician, but she had been given prednisone 10 mg daily for her arthritis. Her prednisone was increased to 20 mg daily in October 2022, for worsening of her joint pain, and the medication reportedly remained the same until the current case.

The blood cultures taken on admission grew Gram-negative rod (Figure 2), and later, it was identified as *Capnocytophaga gingivalis* by Matrix-assisted laser desorption/ionization-time of flight mass spectrometry (MALDI-TOF MS) with the score of 2.14 (the score >2.0 is considered to have high accuracy to the species level). The antimicrobial susceptibility test was not performed since the patient deceased on the day of specimen submission. The sputum culture taken on the same day grew only oral flora.

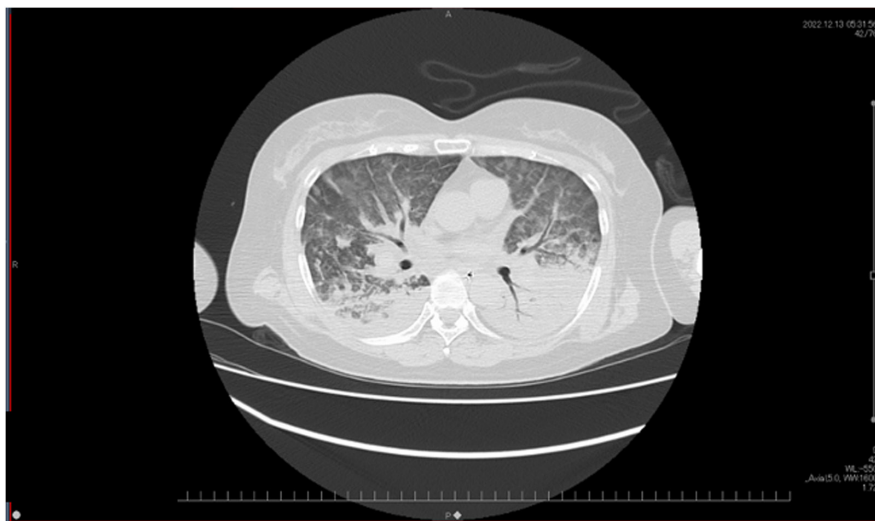
**TABLE 1** Laboratory test results on arrival.

| Tests                                                  | Results          |
|--------------------------------------------------------|------------------|
| White blood cells                                      | 42,060/ $\mu$ L  |
| Blast                                                  | 0%               |
| Stab leukocytes                                        | 8.7%             |
| Segmented leukocytes                                   | 60.6%            |
| Eosinophils                                            | 0.3%             |
| Basophils                                              | 0%               |
| Lymphocytes                                            | 15.7%            |
| Atypical lymphocytes                                   | 0%               |
| Hemoglobin                                             | 14.6 g/ $\mu$ L  |
| Platelet counts                                        | 187,000/ $\mu$ L |
| PT-INR                                                 | 2.98             |
| APTT                                                   | >180.0 s         |
| Fibrinogen                                             | 116 mg/dL        |
| D-dimer                                                | 16.7 $\mu$ g/mL  |
| Sodium                                                 | 141 mmol/L       |
| Potassium                                              | 6.4 mmol/L       |
| Chloride                                               | 110 mmol/L       |
| Aspartate aminotransferase                             | 302 U/L          |
| Alanine aminotransferase                               | 376 U/L          |
| Total bilirubin                                        | 0.1 mg/dL        |
| Lactate dehydrogenase                                  | 1143 U/L         |
| Blood urea nitrogen                                    | 16 mg/dL         |
| Creatinine                                             | 0.61 mg/dL       |
| C reactive protein                                     | 0.79 mg/dL       |
| Procalcitonin                                          | 0.07 ng/mL       |
| HIV screening test                                     | Negative         |
| Arterial blood gas (F <sub>i</sub> O <sub>2</sub> 1.0) |                  |
| pH                                                     | 6.76             |
| pO <sub>2</sub>                                        | 73.0             |
| pCO <sub>2</sub>                                       | 74.1             |
| HCO <sub>3</sub> <sup>-</sup>                          | 10.8             |
| Lactate                                                | 18.0 mmol/L      |

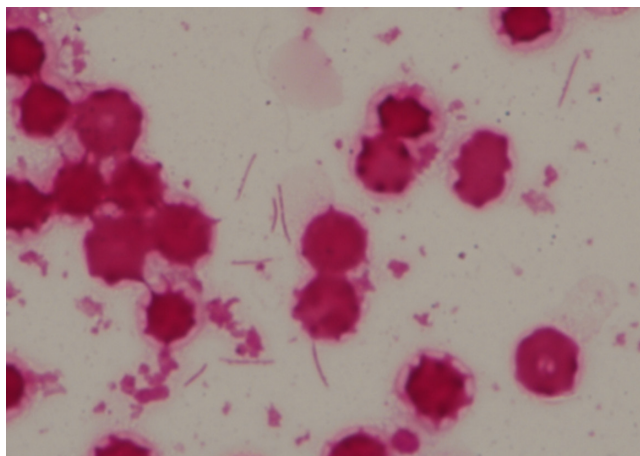
## DISCUSSION

This is a case of *C. gingivalis* bacteremia and sepsis, accompanied by COVID-19. The source of the organism is likely to be from the patient's oral cavity. The routine sputum culture does not go through the sub-culture of oral flora; therefore, we were not able to detect *C. gingivalis* from the patient's sputum. Multiorgan failure the patient suffered is likely due to septic shock.

Unlike *C. canimorsus* bacteremia, which is known to be associated with humoral immunity deficiency including asplenia,<sup>4</sup> there were scarce reports of *C. gingivalis* bacteremia associated with this type of immunodeficiency. Mantadakis et al. reported a case of *C. gingivalis* bacteremia in a 6-year-old girl with B-cell precursor acute lymphoblastic leukemia.<sup>5</sup> On the other hand, Lawal et al. reported a case of *C. gingivalis* bacteremia in a 70-year-old man with rheumatoid arthritis and sarcoidosis, who had received 10 mg prednisone daily and 17.5 mg methotrexate weekly.<sup>2</sup> In fact, many *C. canimorsus* bacteremia could occur without humoral immune dysfunction and can occur in patients who had received immunosuppressants such as prednisone.<sup>3</sup> The comparison between *C. canimorsus* and human oral-associated *Capnocytophaga* spp. such as *C. gingivalis* bacteremia revealed that the latter tended to have hematopoietic stem cell transplantation or receive immunosuppressive medications.<sup>3</sup> The same reported the higher mortality of human oral-associated *Capnocytophaga* bacteremia than *C. canimorsus* bacteremia (6-month all-cause mortality 36.4% vs. 6.2%,  $p = 0.03$ ).<sup>3</sup> The precise mechanism of *C. gingivalis* to cause fulminant sepsis is unclear but may be associated with its surface lipopolysaccharides, as in many Gram-negative organisms.



**FIGURE 1** The CT scan of the chest of the patient on the initial visit.



**FIGURE 2** Blood culture showing Gram-negative rods.

Although the precise reasons for the mortality difference are not known, *C. gingivalis* bacteremia can have more significant morbidity and mortality than *C. canimorsus* bacteremia. Since there was no association between *C. gingivalis* bacteremia and animal bites, detailed history taking may not raise the possibility of this particular infection.

There was a case of concurrent *C. canimorsus* bacteremia and severe COVID-19. A 68-year-old man with dog exposure developed both severe COVID-19 and fulminant septic shock, which led to his death.<sup>6</sup> Also, there was a case of *C. canimorsus* meningitis and COVID-19 in an 85-year-old man with dog exposure, and he survived after a lengthy hospitalization.<sup>7</sup> This is the first to report, as far as our literature search could find, to describe *C. gingivalis* bacteremia concurrent with COVID-19.

Severe COVID-19 with massive lung destruction can cause many oral microbiomes such as *C. gingivalis* to colonize in the lung and subsequent infections there.<sup>8</sup> This, in turn, could lead to fulminant sepsis, particularly among those with immunosuppression, such as the current patient.

This assumption could have significant clinical implications since many patients with severe COVID-19 would receive immunosuppressants as a treatment modality such as dexamethasone, tocilizumab, or baricitinib.<sup>9</sup> Therefore, the presence of acute onset fulminant septic shock among those with severe COVID-19 on immunosuppressants should raise the possibility of bacteremia caused by human oral-associated *Capnocytophaga*, such as *C. gingivalis*, with prompt administration of antimicrobials to save the patients' life.

Currently, there is no standard antimicrobial susceptibility guide for *Capnocytophaga* species, although its breakpoint is often based on the one for anaerobes.<sup>3</sup> The antibiotics of choice for *C. gingivalis* bacteremia remains undetermined, but it is likely that antibiotics such as ampicillin-sulbactam, fluoroquinolones, or carbapenems such as meropenem could be chosen,<sup>2,5</sup> although fulminant septic shock might not be cured even with the use of these antibiotics with susceptibility. A clinical case of multidrug-resistant *C. gingivalis* infection has been identified in France, where the patient with chronic obstructive lung disease exacerbation with *C. gingivalis* respiratory infection was treated with a combination of levofloxacin and amoxicillin-clavulanate.<sup>10</sup> Again, the routine use of broad-spectrum antibiotics for severe COVID-19 patients might make the treatment of subsequent *C. gingivalis* infection difficult.

## CONCLUSION

A rare case of fulminant septic shock caused by *C. gingivalis*, together with COVID-19 was identified. The precise pathogenesis of this combination, together with the best treatment option should be sought by further studies.

## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

## DATA AVAILABILITY STATEMENT

Data sharing does not apply to this article as no datasets were generated or analyzed during the current study.

## ETHICS STATEMENT

This case report is exempted from the ethics committee approval of Kakogawa Medical Center.

Approval of the research protocol: N/A.

Informed consent: Verbal informed consent over the phone was obtained from the patient's family 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.

## ORCID

Dai Miyazaki  <https://orcid.org/0000-0002-4830-0542>

Shigeru Sano  <https://orcid.org/0000-0002-8186-151X>

Kentaro Iwata  <https://orcid.org/0000-0003-2148-3016>

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**How to cite this article:** Miyazaki D, Kunishige C, Sano S, Urakawa K, Okamoto K, Morishita N, et al. A fatal septic shock caused by *Capnocytophaga gingivalis* potentially associated with COVID-19: A case report. *Acute Med Surg*. 2024;11:e922. <https://doi.org/10.1002/ams2.922>