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Capnocytophaga gingivalis Bacteremia After Upper Gastrointestinal Bleeding in Immunocompromised Patient

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Abstract

Odontogenic bacteremia, most commonly involving gram-positive oral flora, can result from daily self-care practices or professional dental procedures. Though usually transient and quickly cleared by the immune system, the presence of periodontal disease increases the frequency of exposure and risk of persistence of oral-systemic infections. Comorbidities such as asplenia, alcoholism, and immunocompromise increase the risk of complications of hematogenous spread and severe systemic illness. *Capnocytophaga* is a genus of anaerobic fastidious gram-negative bacilli, which is a common member of human oral flora, and its density is proportional to mass of dental plaques and periodontal diseases. *Capnocytophaga* spp that colonize humans are less virulent and are uncommon causes of bacteremia when compared with the *Capnocytophaga* typical of canines. *C gingivalis* has been rarely reported as a cause of disease in immunocompromised or immunocompetent hosts. In this article, we present a case of an immunocompromised 70-year-old man with poor oral hygiene, on methotrexate and prednisone for rheumatoid arthritis and sarcoidosis, who was admitted for chronic obstructive pulmonary disease exacerbation and developed *C gingivalis* bacteremia and septic shock after an episode of upper gastrointestinal bleeding. Poor oral hygiene in our patient is believed to have increased his risk as an immunocompromised patient to developing *C gingivalis* bacteremia. This case highlights the importance of oral care in immunocompromised patients especially while hospitalized, and those about to receive transplant, chemotherapy, or on immune modulators.

Keywords

sepsis, *Capnocytophaga gingivalis*, immunocompromised, oral flora, gastrointestinal bleeding

Introduction

Bacteria of the genus *Capnocytophaga* are anaerobic or microaerophilic, fastidious, and fusiform gram-negative bacillus that are part of oral flora of humans, dogs, and cats.

Capnocytophaga gingivalis is one of 6 identified human colonist species found in adults and children. So far *C canimorsus* and *C* cynodegmi are the 2 species identified as part of animal oral flora.[1-3]

Capnocytophaga spp have a worldwide distribution across all ages as normal flora of the oral cavity. Pathologically, they can cause nonfulminant diseases such as periodontitis, caries, and plaque across all ages.[4] Comorbidities such as diabetes and malignancies in children increase the oral bacterial burden of *Capnocytophaga* spp isolated.[5,6] The *Capnocytophaga* animal microbiota may be transmitted through bites, scratches, or nontraumatic contact with dog or cat saliva.[2] *C canimorsus* and *C cynodegmi* are more virulent than species found as human flora, and fulminant infections can be seen in immunocompetent patients, though they are more prevalent in immunocompromised patients with comorbidities including alcoholism, asplenia, or malignancies. The infections cause can range from localized cellulitis to fulminant life-threatening illnesses.[7-9] *C canimorsus*, however, is the most frequently isolated species in fulminant life-threatening disease.

In contrast, *C gingivalis* has rarely been reported as an invasive pathogen in humans, which could be a result of only genus-level identification with previous microbiologic technologies. In this case, we present an elderly immunocompromised man with severe *C gingivalis* infection.

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Case Presentation

A 70-year-old man presented with 3 days of loose watery stool, worsening generalized weakness, 1 day of confusion, and inability to walk. He had a history of chronic medical problems including asthma/chronic obstructive pulmonary disease (COPD) requiring 4 L of home oxygen therapy, rheumatoid arthritis, sarcoidosis, and chronic kidney disease. He was on long-term 17.5 mg methotrexate weekly and 10 mg prednisone daily.

Vital signs recorded on admission included normal temperature with normal heart rate and blood pressure. On initial physical examination, he was noted to be awake but lethargic and had poor oral hygiene with multiple dental caries. On auscultation, there was reduced air entry into his lungs, and bilateral wheezing, and his abdomen was tender to palpation. He was noted to have extensive bruising over his left hand and bilateral pitting pedal edema. He was admitted and managed for COPD exacerbation and dehydration due to diarrhea.

On admission, he was started on intravenous methylprednisolone and bronchodilator treatments; on day 2, his mental status became more altered. He was later intubated urgently after failure of bilevel positive airway pressure (BiPAP) trial for acute on chronic hypercapnic respiratory failure. He was also started on diuretics initially and later hemodialysis for acute kidney injury. After 3 days of intubation, his mental and respiratory status had improved remarkably, and he was successfully extubated on day 5 of admission.

On day 9 of admission, he developed fever of 38.7 °C. Blood and urine cultures were collected, and he was promptly started on empiric vancomycin, cefepime, and metronidazole.

By day 10, his mental status declined, and he was again in hypercapnic respiratory failure. He failed BiPAP trial again and had to be re-intubated. At time of intubation, a pool of blood was noted in mouth and hypopharynx and 2.5 L of bloody fluid suctioned from his stomach. He was placed on pantoprazole infusion for suspected gastrointestinal (GI) bleeding and aspiration was strongly suspected. Broad antibiotics that had been started the prior day were continued. A few hours later, norepinephrine infusion and stress-dose hydrocortisone were started due to persistent hypotension. Esophagogastroduodenoscopy revealed esophageal erosion, gastric, and duodenal ulcers.

On day 11, he still required high doses of norepinephrine despite resolution of fever. Urine culture obtained on day 9 had >100 000 colony forming units/mL of *Escherichia coli.* Vancomycin and metronidazole were stopped to target urinary tract infection with *E coli*. Computed tomography scan of abdomen showed bilateral lower lobe consolidations suspicious for pneumonia.

Blood cultures obtained on day 9 became positive on the fourth day of culture, with Gram-negative bacilli in one anaerobic bottle of 4 culture bottles, his antibiotic was switched to piperacillin-tazobactam and tobramycin. The isolate was identified 2 days later, on hospital day 14, as *Capnocytophaga spp*. The infectious disease (ID) team was consulted, piperacillin-tazobactam and tobramycin was discontinued in favor of renally dosed ampicillin-sulbactam. During a discussion with his wife by the ID team on day 15 of admission, she reported having a dog that was not usually in contact with her husband, and she reported that the patient chews tobacco, stores, and then re-chews tobacco that he stored at room temperature for varying lengths of time. Patient's right upper extremity remained edematous and a venous duplex confirmed suspicion of a deep vein thrombosis in the right internal jugular and right brachiocephalic veins, which was associated with the central venous catheter.

The patient was taken off vasopressors on hospital day 16 and extubated on day 17. The patient was treated for 4 weeks with renally dosed intravenous ampicillin-sulbactam for endovascular infection due to the occlusive thrombosis detected while patient had bacteremia.

Using 16s rRNA gene sequencing, *Capnocytophaga* spp isolated was reported to be *C gingivalis* by Quest Diagnostics, Nichols Institute, Chantilly, Virginia. He was counseled and advised to keep up his dental appointments and stop re-chewing his tobacco.

Discussion

Bacteremia resulting from a break in mucosal barrier is common: from the oral cavity, routine activities such as brushing and flossing regularly cause transient bacteremia with oral flora. Odontogenic diseases pose an increased risk of persistent bacteremia due to undrained foci of infection. Bioburden, such as in extensive dental plaques, or mucosal disruption in gingivitis, oral ulcers, gastritis, colitis, peptic ulcer disease, and inflammatory bowel diseases can also increase the risk of microbial gut translocation.[10-12] Our patient had been on methotrexate and prednisone for rheumatoid arthritis causing him to be immunocompromised. Prolonged use of glucocorticoids and methotrexate have individually been shown to lower the integrity of the gut mucosa leading to ulcerations, perforations, and increased risk of bleeding.[13-15]

Only one case of bacteremia due to *Capnocytophaga* has been previously reported in a patient with rheumatoid arthritis on methotrexate. This individual subsequently died of disseminated intravascular coagulation, and acute respiratory distress syndrome from *C canimorsus* infection following dog bite.[16] Our patient notably had poor dentition with dense plaques, multiple dental caries, and a habit of re-chewing saved tobacco, stored at room temperature, which may have contributed to increased oral bacterial colonization. The mechanism of his bacteremia in this patient was thought to be translocation of oral flora colonized with *C gingivalis* through compromised gastric mucosa due to the upper GI

Table 1. Microbiology Susceptibility Report for Isolated *Capnocytophaga gingivalis*.

Organism isolated: *Capnocytophaga gingivalis* (sequence ID)		
MIC report	MIC	
Antibiotic	(μg/mL)	Interpretation
Ampicillin/sulbactam	0.094	Susceptible
Clindamycin	>256	Resistant
Meropenem	0.032	Susceptible
Metronidazole	8.0	Susceptible
Penicillin	2.0	Resistant

bleeding. The *Capnocytophaga* isolated was finally reported to be *C gingivalis* using 16s rRNA sequencing sensitive to ampicillin-sulbactam, meropenem, and metronidazole, resistant to clindamycin and penicillin (Table 1).

A detailed literature search was conducted using the search words "*Capnocytophaga gingivalis"* in PubMed. Ninety-three abstracts were found for *Capnocytophaga gingivalis* as shown in flow diagram in Figure 1. *Capnocytophaga gingivalis* + Filters: Humans yielded 71 abstracts. Addition of filter case reports yielded 7 abstracts. This contained 4 human case reports of *C gingivalis* systemic infections, 1 Japanese abstract, 2 periodontal diseases abstracts, and 1 molecular immunology abstract. This initial search erroneously eliminated a previously found case report, prompting a manual review after alternate search parameters were used. Finally, search using *Capnocytophaga gingivalis* [Title] Filters: Abstract yielded 14 abstracts that included all 5 case reports for *C gingivalis* systemic infection in humans, which is reflected in Figure 1.

Polymicrobial and primary oral/periodontal abstracts were excluded from this review. Five case reports of human non-oral *C gingivalis* infections were found and included in this case review. Three of the cases were related to lung infections, 2 cases were in immunocompromised hosts, 1 joint infection, and 1 related to oral infection. The cases included bacteremia in a 6-year-old with acute lymphocytic leukemia and gingivitis,[8] pneumonia, and bacteremia in 30-year-old man post autologous stem cell transplant,[17] lung abscess in a normal host,[18] insidious joint infection in a normal 3-year-old,[19] and an acute COPD exacerbation[20] (Table 2).

Antimicrobial susceptibilities in the identified cases followed no specific pattern as 4 of the 5 cases had class resistance reported, with only one multi-drug resistant case resistant to 4 classes of antibiotics. As in our case, many of the *C gingivalis* strains appear to remain susceptible to cephalosporins and β-lactam/β-lactamase inhibitor combinations.

In conclusion, in this case, poor dental hygiene with periodontitis posed an increased risk of infection with human oral strains of genus *Capnocytophaga* in immunocompromised patients. Optimal oral care while inpatient can reduce the oral bacterial burden in the event of aspiration and is an

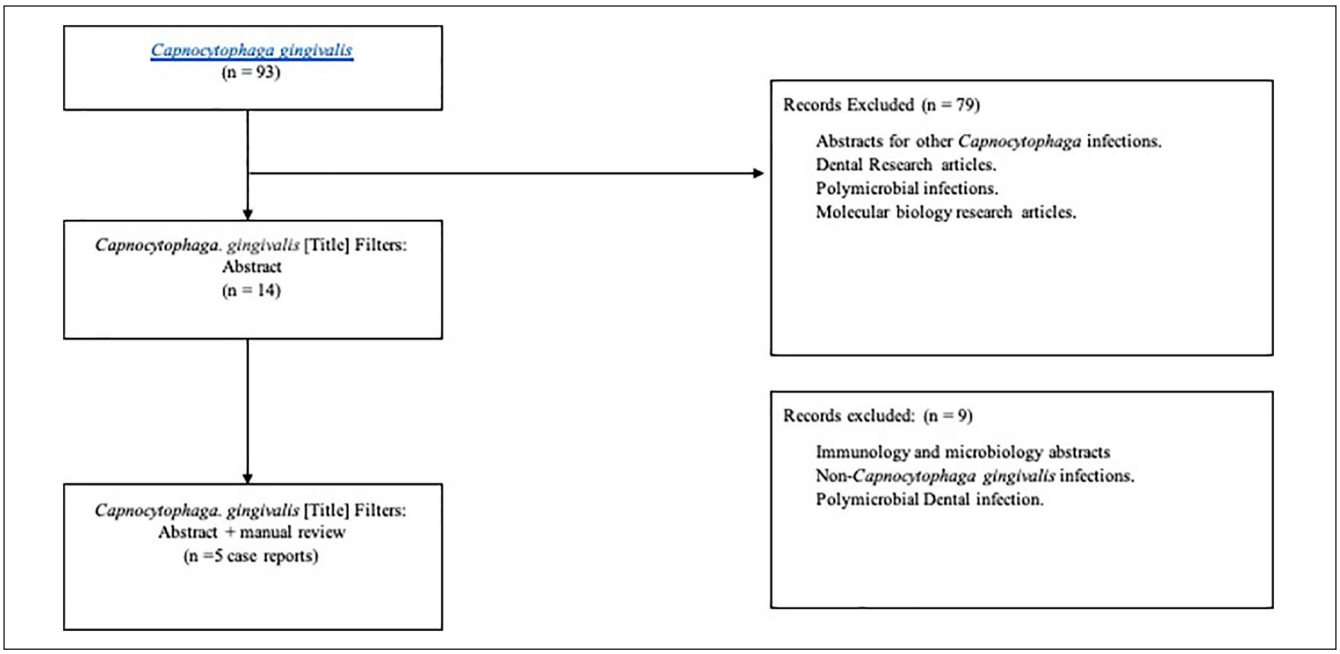

Figure 1. Case reports search flow diagram.

Table 2. *Capnocytophaga gingivalis* Case Report Summary.

Case	Patient demography	Comorbidity	Immune status	Manifestation	Management	Drug resistance	Outcome
Elodie, 2006	78 years, male	Chronic respiratory failure	Abnormal	COPD exacerbation/ respiratory infection	Amoxicillin-clavulanate 14 days	Fluoroquinolone, macrolide, lincosamide and streptogramin, and β-lactamase	Resolution
Fukuoka, 2000	48 years, male	None	Normal	Lung abscess	Ceftizoxime and clindamycin 28 days (4 weeks)	Tobramycin, fosfomycin	Resolution
Geisler, 2001	30 years, male	Autologous stem cell transplant	Abnormal	Pneumonia, bacteremia	Linezolid and metronidazole	Gentamicin, fluoroquinolones	Resolution
Mantadakis, 2003	6 years, female	B cell ALL, and gingivitis	Abnormal	Bacteremia	Ceftazidime and amikacin 10 days	Bactrim	Resolution
Rodgers, 2001	3 years, male	None	Normal	Septic arthritis	Ampicillin-sulbactam 21 days (3 weeks)	None	Resolution

Abbreviation: COPD, chronic obstructive pulmonary device.

important part of the ventilator acquired pneumonia bundle. This case highlights the importance of oral care in immunocompromised patients and the risk of bacterial translocation with GI bleeding or aspiration.

Authors' Note

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient for their anonymized information to be published article.

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