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Case report

Capnocytophaga sepsis causing purpura fulminans in a 50-year-old man with chronic opioid use

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ABSTRACT

We present a case of polymicrobial sepsis with *Capnocytophaga* spp. complicated by purpura fulminans following a dog-bite in a 50-year-old-man with an extensive history of opioid use disorder. Generally, severe *Capnocytophaga* cases are thought to occur in patients with underlying immune deficiencies. However, this case highlights the importance of maintaining clinical suspicion for *Capnocytophaga* infection in immunocompetent patients, and we discuss the role of chronic opioid-use in severe infection.

Introduction

Capnocytophaga is a gram-negative rod native to the oral flora of canines [1]. Typically, this bacterium causes subclinical infection in humans. Rarely, it has been associated with severe septic shock, meningitis, endocarditis, and osteomyelitis, with fewer than 500 cases reported in the literature as of 2015. [2]. Risk factors for fulminant infection include asplenia, alcohol abuse, and immunosuppression [2,3]. We present the case of a 50-year-old man with a 25-year history of daily heroin insufflation who presented with polymicrobial septic shock and purpura fulminans of the extremities and genitalia due to *Capnocytophaga* infection complicated by pneumonia and endocarditis. To our knowledge, this is also the first reported case of purpura fulminans involvement of the penis managed non-surgically that spared amputation of the genitals. Furthermore, we examine the potential role of chronic opioid dependence in the development of severe *Capnocytophaga* infection.

Case presentation

A 50-year-old unhoused man with hypertension, recent heroin insufflation and cocaine use presented with a three-day history of progressive bilateral lower-leg pain and weakness. He reported a dog bite on the left hand that occurred three days prior to admission. He admitted to fevers, chills, diffuse abdominal pain and rash on the legs and abdomen. Purpuric mottling of the right lateral abdomen and bilateral legs was present. Lower limbs were cool and exquisitely tender with absent pedal pulses.

The patient presented to the ED tachycardic, tachypneic, and mildly febrile. On admission, he was found to have leukocytosis, rhabdomyolysis, acute renal failure, acute liver failure, profound thrombocytopenia with coagulopathy, and high anion gap metabolic acidosis (Table 1). Initial CT angiogram (CTA) revealed no perfusion below the popliteal arteries, bilateral renal infarcts, splenic infarct, hepatic artery vasospasm, and mesenteric ischemia. Ultrasound revealed bilateral deep vein thrombosis (DVTs) of the femoral veins. Blood cultures collected at admission grew methicillin-resistant *Staphylococcus aureus* (MRSA) and *Proteus* spp. on hospital day two. The same cultures became positive for *Capnocytophaga* spp. on day 10. His clinical status rapidly deteriorated requiring intubation for respiratory failure. Following admission to the MICU, he was started on vasopressors and broad-spectrum antimicrobials with vancomycin, piperacillin-tazobactam and metronidazole for severe septic shock.

Hospital course was complicated by progression of hemorrhagic bullae, purpuric rash, and ischemic necrosis from the lower extremities to involve the upper extremities, nose, sacrum, and genitals, consistent

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Table 1
Laboratory values on admission to the hospital.

Lab Studies	Values on admission
WBC	30,000
Platelet Count	5000
Creatinine Kinase	56,000
Phosphorus	9.3
Potassium	5.4
Calcium	5.5
Creatinine	5.6 (baseline 1.2)
BUN	117
AST	1087
ALT	535
PTT	34.6
D-Dimer	8076
Fibrin Split	> 20
Protein C	39
Protein S	36
Lactate	13.3
Bicarbonate	7
Anion Gap	40
pH	7.05

with purpura fulminans (Fig. 1). ENT examination revealed fungal infiltration of posterior nares, with blood cultures collected four days into hospitalization positive for *Candida albicans*, necessitating treatment with anidulafungin. Urology began treatment of penile ischemia and edema with tadalafil, nitroglycerin paste, and indwelling foley catheter. Amputations of lower legs and fingers were planned for when demarcation had finalized. Steroids and other immunosuppressant agents were not used given ongoing sepsis.

Following extubation on day 6, he had recovery of normal renal function and platelet count. Liver enzymes and creatinine kinase continued to downtrend but remained moderately elevated throughout hospitalization. Peripheral gangrene had stabilized and demarcated by day 10, and by this time, the patient had lost sensation and motor function of his feet, toes, and some fingers, but perfusion and motor function had returned to his forearms and hands.

His hospital course was further complicated by episodic gastrointestinal bleeding requiring temporary cessation of intravenous heparin. Systemic anticoagulation was resumed after duplex ultrasound revealed venous thrombosis of the left basilic and right cephalic veins. Transthoracic echocardiogram revealed thickening of the posterior leaflet of the mitral valve suspicious for endocarditis and subsequent transesophageal echocardiogram performed 2 weeks later confirmed a vegetation on the mitral valve.

The patient developed diarrhea and diffuse abdominal pain on day 14 with negative testing for *Clostridium difficile*, thought to be from diffuse bowel ischemia and bacterial translocation across the compromised gut epithelium. The patient also developed productive cough on day 11, with bilateral pulmonary infiltrates on radiography consistent with multifocal pneumonia. Repeat blood cultures on day 13 grew *Citrobacter* spp., and the patient remained febrile with persistent leukocytosis until day 23.

Genital ischemia was stabilized, and gangrene progression was halted by use of sildenafil, nitroglycerin paste, and indwelling foley, sparing the genitalia from surgical intervention through preservation of blood flow. The patient underwent bilateral above the knee, and multiple digital amputations on day 21. Necrotic lesions of the nose were surgically debrided with plans for nose reconstruction by plastic surgery. The patient was discharged to subacute rehabilitation on hospital day 51.

Discussion

Although extremely rare, *Capnocytophaga* infection has been documented to cause life-threatening sepsis with an initial presentation of purpura fulminans, especially in individuals with asplenia [3]. The clinical picture seen in our patient of septic shock with multiorgan failure, suspected DIC, purpuric rash, and peripheral gangrene of limbs, digits, and the nose leading to amputation has been described in prior reports and is classic for purpura fulminans [4]. In infectious purpura fulminans, endotoxins trigger consumption of antithrombin III, protein C and protein S, resulting in a hypercoagulable state that causes thrombosis and thus ischemia to extremities [5]. Diffuse ischemia of limbs and bowel can serve as a nidus for further infectious complications. However, the concomitant, multiple infectious sequelae presented in this case (pneumonia, persistent diarrhea, fungal infiltration of the nasal cavity, candidemia and endocarditis) warrant exploration of potential factors that led to such extensive complications. Certain virulence factors of the bacteria allow for development of high-grade bacteremia. In human blood, *Capnocytophaga* has been shown to elicit lower quantities of cytokines, suggesting a potential mechanism of initial immune-surveillance escape [1]. However, even accounting for the known immunogenicity of this bacteria, the number of infectious sequelae seen in this case has sparsely been reported.

Chronic opioid dependence has long been implicated in diminished immune response through a variety of mechanisms. Demonstrated effects include decreases in populations of NK cells [6]. Long term opioid use has also been demonstrated in mouse models to increase progression to LPS-induced sepsis [7], potentially due to translocation of bacteria through the gut epithelium and subsequent inflammation [8]. The increase in translocation of bacteria through the gut epithelium is of interest in this case, as the mesenteric ischemia seen on initial imaging suggests a link to the dysregulation of gut epithelial homeostasis.

Clinicians should maintain high suspicion for *Capnocytophaga* infection in the appropriate clinical setting despite initial culture results. *Capnocytophaga* is slow-growing and difficult to grow on traditional agars [9]. It also is difficult to identify with commercially available diagnostic tools which can contribute to under-diagnosis [10]. Beta lactamase producing *Capnocytophaga* species have been increasingly identified [11]. Due to the absence of randomized controlled studies and guidelines, there is some uncertainty about the most appropriate antibiotic regimen. However, broad spectrum agents including imipenem, clindamycin, and B-lactamase inhibitor combinations have shown to be appropriate for all types of *Capnocytophaga* infections [12]. This case serves to bolster the clinical recognition of *Capnocytophaga* and purpura fulminans. Further research should be done on the possible association with chronic opioid use and severe sepsis from *Capnocytophagia*.

CRediT authorship contribution statement

Christopher Hogge: Writing – original draft. **Miriam Holzman**: Writing – original draft. **Sahiba Khurana**: Data curation. **Diana Finkel**: Writing– original draft. **Milos Brankovic**: Data curation. **Chrystal Chang**: Data curation. **Gabriel Fernandez**: Data curation.

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Consent

Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Declaration of interest

None.

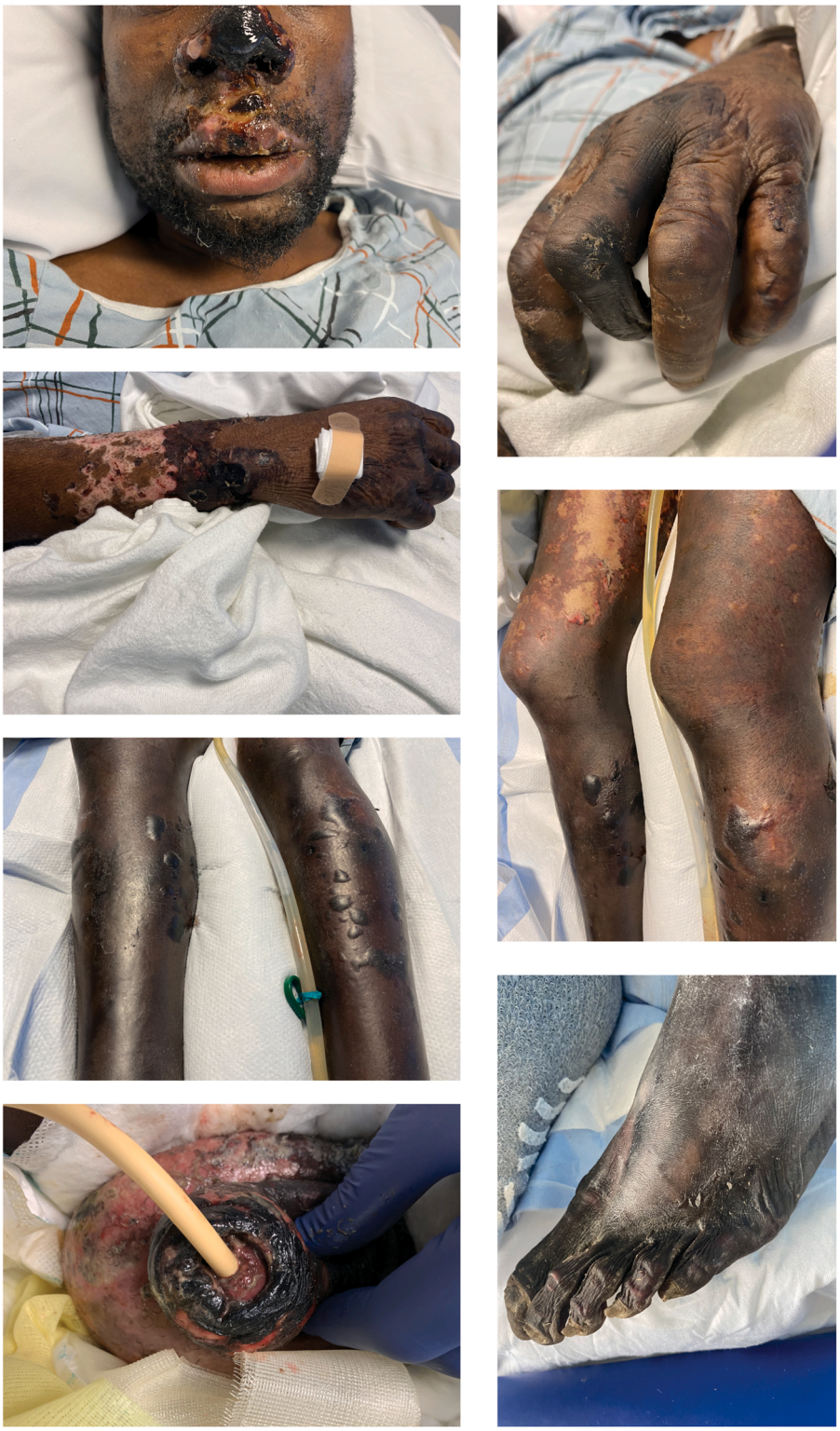

Fig. 1. Peripheral gangrene and purpura fulminans lesions of nose, fingers, hands, arms, legs, feet, and genitalia.

References

[1] Chesdachai S, Tai DBG, Yetmar ZA, Misra A, Ough N, Abu. The characteristics of capnocytophaga infection: 10 years of experience. Open Forum Infect Dis 2021;8 (7):ofab175.

[2] Butler T. Capnocytophaga canimorsus: an emerging cause of sepsis, meningitis, and postsplenectomy infection after dog bites. Eur J Clin Microbiol Infect Dis 2015;34 (7):1271–80.

[3] Mader N, Lührs F, Herget-Rosenthal S, Langenbeck M. Being licked by a dog can be fatal: capnocytophaga canimorsus sepsis with purpura fulminans in an Immunocompetent man. Eur J Case Rep Intern Med 2019;6(10):001268.

[4] Mellor DJ, Bhandari S, Kerr K, Bodenham AR. Man's best friend: life threatening sepsis after minor dog bite. BMJ 1997;314(7074). 129-30.

[5] Bendapudi PK, Whalen MJ, Lahoud-Rahme M, Villalba JA. Case 7-2021: a 19-Year old man with shock, multiple organ failure, and rash. N Engl J Med 2021;384(10): 953–63.

[6] Diasso PDK, et al. The effects of long-term opioid treatment on the immune system in chronic non-cancer pain patients: a systematic review. Eur J Pain 2020;24(3):481–96.
[7] Ocasio FM, Jiang Y, House SD, Chang SL. Chronic morphine accelerates the progression of lipopolysaccharide-induced sepsis to septic shock. J Neuroimmunol 2004;149(1–2):90–100.
[8] Meng J, et al. Morphine induces bacterial translocation in mice by compromising intestinal barrier function in a TLR-dependent manner. PLoS One 2013;8(1):e54040.
[9] Gaastra W, Lipman LJ. Capnocytophaga canimorsus. Vet Microbiol 2010;140(3–4):339–46.
[10] Janda JM, Graves MH, Lindquist D, Probert WS. Diagnosing Capnocytophaga canimorsus infections. Emerg Infect Dis 2006;12(2):340–2.
[11] Ehrmann E, Handal T, Tamanai-Shacoori Z, Bonnaure-Mallet M, Fosse T. High prevalence of beta-lactam and macrolide resistance genes in human oral Capnocytophaga species. J Antimicrob Chemother 2014;69(2):381–4.
[12] Jolivet-Gougeon A, Sixou JL, Tamanai-Shacoori Z, Bonnaure-Mallet M. Antimicrobial treatment of Capnocytophaga infections. Int J Antimicrob Agents 2007;29(4):367–73.