A Case of Fatal Sepsis from Dog Exposure in a Young Stem-Cell Transplant Patient

Casey Park, MD, Simon Oczkowski, MD, FRCPC, and Anjali Shroff, MD, FRCPC

Abstract

Capnocytophaga canimorsus is a fastidious, slow-growing (up to 10 days), capnophilic gram-negative rod. It is most commonly associated with zoonotic exposure, particularly from dog and cat bites. There is a growing body of literature for the recognition of septic shock caused by Capnocytophaga canimorsus in at-risk populations, including those with asplenia as well as current or previous hematologic malignancy. This is a case of a young man in remission from a hematologic malignancy, complicated by graft versus host disease, presented many years later in fatal septic shock due to Capnocytophaga canimorsus infection.

Résumé

Le Capnocytophaga canimorsus est une gram-négative capnophilique fastidieuse à croissance lente (jusqu’à 10 jours). Il est le plus souvent associée à une exposition zoonotique, en particulier aux morsures de chiens et de chats. Il existe de plus en plus de documentation sur la reconnaissance du choc septique causé par Capnocytophaga canimorsus chez les populations à risque, y compris celles qui souffrent d’asplénie ainsi que de malignité hématologique actuelle ou antérieure. C’est le cas d’un jeune homme en rémission d’une tumeur maligne hématologique, compliquée par la maladie du greffon contre l’hôte, présentée de nombreuses années plus tard dans un choc septique mortel dû à une infection à Capnocytophaga canimorsus.

Case Summary

A 28-year-old male presented initially to a community emergency department (ED) with 24 hours of rigors, nausea, vomiting, and diarrhea. He had also developed a striking, asymptomatic purpuric rash on his face in a malar-like distribution. He was diagnosed with septic shock, having an elevated lactate (>12.2 mmol/L), hypotension, and a triage temperature greater than 39 degrees Celsius. He was resuscitated with 4 litres of intravenous (IV) crystalloid and given empiric IV ceftriaxone and vancomycin. Portable chest and abdominal radiography did not reveal a cause for the patient’s gastrointestinal symptoms or a source of his infection. Initial laboratory results were remarkable for an elevated international normalized ratio (INR) (>10.0), activated partial thromboplastin time (aPTT) (>120 s), and low fibrinogen (0.4 g/L). Leukocyte count was 7.0, hemoglobin 142, and platelets 411. The patients’ initial renal function, electrolytes, and liver enzymes were unremarkable.
The patient was transferred to our institution’s intensive care unit (ICU). His rash rapidly progressed to involve his trunk and limbs. His clinical condition deteriorated, and he was intubated within 12 hours of admission for hypoxemic respiratory failure. His chest x-ray revealed changes consistent with acute respiratory distress syndrome. He developed oliguric renal failure and he was started on continuous renal replacement therapy. Despite maximally aggressive therapy, the patient remained in refractory shock. The patient’s family requested that his goals of care should be focused on comfort instead of curative treatment and he died with his family present at his bedside.

The patient’s past medical history was significant for acute myeloid leukemia (AML) 11 years earlier. He had undergone induction chemotherapy with daunorubicin and cytarabine 3+7 and then three rounds of cytarabine consolidation. Following relapse of AML one-year later, he underwent an unrelated myeloablative stem-cell transplant. He developed chronic graft versus host disease (GVHD) of his lungs, which had been assessed by a respiratory physician for exertional dyspnea in the post-transplant period. Computed tomography of the chest showed findings of bronchiolitis obliterans and a biopsy via bronchoscopy confirmed the diagnosis. His GVHD was treated with sirolimus, which had been discontinued by the patient’s respiratory physician a year before the current presentation, given the patient’s clinical and radiographic improvement.

Despite the patient’s presentation of fulminant septic shock, microbiologic diagnosis remained elusive. Blood cultures drawn in the ED revealed a pleomorphic gram-negative bacilli at 32 hours, and the patient’s antibiotics were changed to piperacillin-tazobactam for broader gram-negative coverage. Despite the presence of organisms on gram stain, the subcultures on routine MacConkey plates failed to grow. The incubation was extended and the culture was sent to the regional Public Health Laboratory. After 12 days of incubation, the original blood cultures drawn in the ICU were incubated for 14 days instead of the usual 5 days to help identify slower growing species especially from oral flora of humans and other animals. After 12 days of incubation, the original blood cultures drawn in the ED revealed *Capnocytophaga canimorsus*. Upon discussing the case with his family, they confirmed that they owned two pet dogs. While there were no dog bites, they were unsure of whether there was any canine salivary contact with the patient.

**Discussion**

*Capnocytophaga canimorsus* is a slow-growing, capnophillic, gram-negative rod. It is often associated with zoonotic exposure through contact with dog and cat oral flora mostly via bites and salivary contact (found in up to 74% of dog mouths, and up to 57% of cats). Immunocompetent patients typically present with only a localized skin infection, often 3–5 days after the animal bite, but it can occur anywhere from 1–14 days after exposure.

In the microbiology lab, *Capnocytophaga* is typically a slender, gram-negative rod with tapered ends and can be somewhat fastidious to grow clinically akin to the oral flora implicated in infective endocarditis (i.e., HACEK organisms). As it fails to grow on routine MacConkey plates, it requires prolonged incubation of up to 10 days or longer on enriched blood media with a higher carbon dioxide content. Identification usually occurs after 3–7 days which is longer than the typical gram-negative organism. There is no standardized way to conduct susceptibility testing for this organism, given the difficulties with its growth.

A growing body of literature suggests that *Capnocytophaga* infections can progress rapidly to sepsis, organ failure, meningitis, and disseminated intravascular coagulopathy (DIC). Individuals at high risk of this progression include those listed in Table 1 below.

Humans also do have *Capnocytophaga* species (*C. gingivalis, C. granulosa, C. haemolytica, C. leadbetteri, C. ochracea* and *C. sputigena*) in their gingiva and it has been implicated as the pathogen in many dental diseases. These organisms should be considered as a possible source for sepsis in neutropenic patients with mucositis from chemotherapy.

Asplenic individuals are well known to be at risk of severe sepsis from encapsulated organisms such as *Streptococcus pneumoniae, Neisseria meningitides,* and *Hemophilus influenza* and require vaccination for protection against these organisms. However, severe sepsis from a non-encapsulated pathogen, *Capnocytophaga canimorsus*, has been reported in patients without a spleen, with organ failure and death resulting within 24–72 hours. In fact, asplenics have a 30- to 60-fold increased risk of death from this infection, compared to the general population. This is because, in asplenics, the lipopolysaccharide layer of the cell wall of *Capnocytophaga canimorsus* blocks the complement

Table 1. Conditions at High Risk of Severe Capnocytophaga Infection

<table>
<thead>
<tr>
<th>System/Category</th>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lifestyle/Social</td>
<td>Chronic Alcohol Abuse</td>
</tr>
<tr>
<td>Hematologic</td>
<td>Functional or Anatomic Asplenia, Current or Prior Hematologic Malignancy</td>
</tr>
<tr>
<td>Infectious/Immunity</td>
<td>Human Immunodeficiency Virus, Prolonged Corticosteroid use (&gt;20 mg Prednisone equivalents for &gt;2–4 weeks), Diabetes, Rituximab Use</td>
</tr>
<tr>
<td>Associated</td>
<td></td>
</tr>
</tbody>
</table>
system from acting at the bacterial surface, thus preventing opsonization and perhaps even bacterial lysis.6

Interestingly, up to 40% of life-threatening infections with this organism occur in apparently healthy people and in approximately one-third of individuals, no identifiable risk factor for overwhelming sepsis is found.7

A case series from 2003 made mention of a single patient who died from GVHD with a concomitant Capnocytophaga canimorsus infection; however, there were no further details regarding this individual patient and whether the patient’s infection with this organism complicated their GVHD course.8 This is the only case report in the literature of Capnocytophaga canimorsus infection in patients with a history of GVHD. GVHD does affect endothelial cell activation and inappropriate proinflammatory responses in a similar mechanism to the host response in septic shock.6–8 It can be postulated that the patient in this case report, while not on immunosuppressants, still did have innate and adaptive immune system changes from their GVHD that may have made them more prone to developing septic shock in response to this infection.6,9

The post-stem-cell transplant population has been known to be prone to Capnocytophaga sepsis. Stem-cell treatment can cause functional asplenia which correlates to the need for immunosuppressive precautions (i.e., positive pressure isolation) in this population due to the derangement of their adaptive immune system.1,9,10 Functional asplenia is hypothesized to occur during the conditioning phase before stem-cell infusion with radiation and systemic chemotherapy having a direct deleterious effect on the spleen and its reservoir of immune cells. Post-transplant asplenia can persist due to the non-native nature of progenitor cells that are introduced to the host. To our knowledge, this patient did not have functional asplenia or a history of recurrent infections.

The patient’s new facial purpuric rash can be described as purpura fulminans given its rapid onset in association with his clinical deterioration. Capnocytophaga canimorsus is associated with purpura fulminans of the limbs and trunk; however, there has been no literature thus far of this form of purpura involving the face. Purpura fulminans is pathophysiologically driven by aberrant coagulation in small vessels leading to necrosis and DIC when faced with organisms or conditions prone to causing this coagulopathy (Table 2).10 Given the association with malignancy and DIC, it can be hypothesized that the patient’s prior malignancy left him with a propensity for an inappropriate response of his coagulation cascade to a septic insult. Purpura fulminans or symmetric gangrene is seen in 20–40% of patients with shock with this organism, which can be a helpful diagnostic clue.11

Table 2. Organisms/Predispositions Commonly Known to Cause a Purpuric Rash

<table>
<thead>
<tr>
<th>Family of Organisms</th>
<th>Species/States Known to Cause Purpura Fulminans</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram Positives</td>
<td>Group A + B Streptococci, Staphylococcus pneumoniae, Staphylococcus aureus</td>
</tr>
<tr>
<td>Gram Negatives</td>
<td>Capnocytophaga canimorsus, Neisseria meningitides, Neisseria gonorrhoeae (only disseminated), Rickettsia rickettsii, Vibrio vulnificus</td>
</tr>
<tr>
<td>Parasitic</td>
<td>Plasmodium Falciparum</td>
</tr>
<tr>
<td>Disease States</td>
<td>More Prone to Purpura</td>
</tr>
<tr>
<td></td>
<td>Asplenia (surgical or functional), Liver failure (due to Protein C+S deficiency), amyloidosis, recent large volume blood transfusion</td>
</tr>
</tbody>
</table>

If suspicion of Capnocytophaga canimorsus exists, antibiotic coverage with a 3rd generation cephalosporin or a penicillin with a beta-lactamase inhibitor should be given as some of the zoonotic strains of Capnocytophaga can produce a beta-lactamase. Human Capnocytophaga strains don’t typically produce this beta-lactamase. Of note, first-generation cephalosporins, which are commonly used to treat skin and soft tissue wounds, are not considered appropriate antibiotic therapy for this organism or any zoonotic associated skin and soft tissue infections.11

Individuals thought to be at high risk of sepsis (see Table 1) from this organism should take measures to prevent dog bites. If a bite occurs, patients should seek medical attention even if they feel well, given that death can occur quickly over 24 to 72 hours with a 30% mortality risk, and a 60–80% mortality risk in the event of multi-organ failure or shock. Often, antibiotic prophylaxis with amoxicillin-clavulanic acid is given for 5 days in these high-risk individuals in the setting of a bite.3

Conclusion

Increased suspicion of Capnocytophaga infection should be triggered in patients who present with rapidly progressive sepsis, DIC, purpura fulminans, bacteremia with a difficult to grow gram-negative organism, exposure to pets or mucosiis, or are a high-risk individual. Empiric antibiotic coverage with at least a third-generation cephalosporin or penicillin with a beta-lactamase inhibitor should be given to include this organism given its slow growth in the microbiology lab. Individuals in these high-risk groups should seek prompt medical attention given their high mortality risk when exposed to this organism.
References
3. Centres for Disease Control. Capnocytophaga. [Internet] Available at: https://www.cdc.gov/capnocytophaga/health-care-professionals/index.html