

# Capnocytophaga bacteremia precipitating severe thrombocytopenia and preterm labor in an asplenic host

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## Abstract

*Capnocytophaga* species are gram-negative bacilli that inhabit mammalian oral surfaces and can cause opportunistic infection, especially in asplenic patients. The species *Capnocytophaga canimorsus* is particularly associated with dog bites and is known to cause endocarditis, meningitis, and sepsis in the general population. In pregnant patients, infections tied to *Capnocytophaga* species from human flora have been associated with preterm labor, chorioamnionitis, and neonatal septicemia. There is little known about the effects of zoonotically-acquired *Capnocytophaga* infection in pregnant patients. In this case report, we present a patient with *Capnocytophaga* bacteremia acquired after a dog bite associated with profound thrombocytopenia and preterm labor. Dog bites are common in the United States, and we present basic recommendations for management of dog bites in pregnant patients in order to avoid morbidity associated with delay in time to antibiotic treatment of infection as described in this case.

## Introduction

*Capnocytophaga* spp. are gram-negative bacilli that are colonized in mammalian oral flora but may also cause infection following dog or cat bites.<sup>1</sup> *Capnocytophaga canimorsus*, (*C. canimorsus*), is a component of canine and feline oral flora and infection with *C. canimorsus* is primarily associated with dog bites.<sup>2</sup> *C. canimorsus* is known to cause infections such as endo-

carditis and meningitis and is associated with bacteremia and sepsis.<sup>3</sup> People who are at increased risk of developing infections with *C. canimorsus* are asplenic patients and those who chronically use alcohol and considered functionally immunocompromised.<sup>4,5</sup> Infection in pregnancy is rare however, the few case reports published have described premature labor, chorioamnionitis, and neonatal septicemia associated with *C. ochracea* and other species commonly found in human oral flora.<sup>6-9</sup> However, little is known about the influence of zoonotic-acquired *Capnocytophaga* infection during pregnancy.

## Case Report

A 35-year-old female (gravida 5, para 2022) presented to a tertiary care hospital at 36 weeks and 2 days gestation with new-onset vaginal bleeding and a five-day history of fevers, headache, neck stiffness, and altered mental status three days after being bitten by a neighbor's dog. Her prenatal history was significant for fetal intrauterine growth restriction (IUGR) diagnosed at 32w5d with a fetus weighing 1477g (5<sup>th</sup> percentile). Her past medical history was significant for a motor vehicular accident in a prior pregnancy with multiple traumatic injuries and resultant splenectomy. She also suffered a diffuse axonal brain injury with loss of short-term memory with a secondary seizure disorder. In subsequent pregnancies, she required a cesarean delivery due to an unstable pelvis. Prior to admission, she reported tremulous chills and fevers to 102.7°F (39.3°C). Her husband noted the patient was off-balance and was slurring her words. She also endorsed new-onset significant fatigue, persistent headache, and transient spotting across bilateral visual fields. The patient then began to experience new bright red vaginal bleeding. These symptoms prompted the patient's husband to bring her to the tertiary care hospital system 1.5 hours away from their home. The wound on her index finger from the dog bite appeared to be well-healing with no erythema, swelling, or tenderness to palpation.

Immediately on presentation, she was noted to have a persistently category 2 fetal heart tracing which was initially attributed to a placental abruption given her vaginal bleeding. She underwent an emergent repeat low transverse cesarean section. The neonate was admitted to the neonatal intensive care unit (NICU) and was diagnosed with respiratory failure necessitating intubation, and core temperature lability with stable hemodynamic vitals.

This patient's platelet count on admis-

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sion was  $8 \times 10^9/L$ , which was confirmed with repeat testing. She was transfused prior to surgery with 2 units of platelet and responded appropriately with a count of  $55 \times 10^9/L$ . In the immediate post-operative period, the patient's platelet count decreased to  $16 \times 10^9/L$ , suggesting a thrombophilia. Routine laboratory screening during her pregnancy established a baseline platelet count of  $400 \times 10^9/L$ . Initially, there was a concern for immune thrombocytopenia (ITP) or thrombotic thrombocytopenia (TTP), a hematologic emergency requiring plasmapheresis. However, the clinical history in this patient suggested an infectious etiology and splenic platelet sequestration impossible given the patient's lack of a spleen.

Hematology evaluation was negative for schistocytes on peripheral smear and revealed a normal ADAMST13 level, the latter of which essentially excluded TTP. However atypical, sepsis with or without disseminated intravascular coagulation (DIC) became the most likely underlying etiology. She had no evidence of DIC given

normal coagulation studies including a normal fibrinogen, prothrombin time (PT) and partial prothrombin time (PTT). In sepsis syndromes, platelet counts generally are lower than  $100 \times 10^9/L$  with clinical severity associated with the magnitude of the decrease in platelet count, so this patient's profound thrombocytopenia due to infection was not a classic presentation.<sup>10</sup> On further review, she had a remote history of a platelet count of  $14 \times 10^9/L$  around the time of the patient's traumatic MVA five years prior. ITP was an additional leading diagnosis for her thrombocytopenia that was unresponsive to transfusion, although the plausibility of profound platelet destruction by ITP in an asplenic patient was considered unlikely. Following cesarean delivery for category 2 fetal heart tracing on arrival, she was started on clindamycin, gentamicin, and metronidazole due to concern for an infectious process. The asplenic patient is an effectively immunocompromised patient that lacks cell-mediated immune defenses and are particularly susceptible to encapsulated organisms.<sup>11</sup> In the setting of a dog bite, there is a higher risk of pathologic infection with canine oral flora, particularly *Capnocytophaga*. Bacteremia with *Capnocytophaga* is exceedingly rare but potentially serious, with case reports describing a range of 25% - 60% mortality from sepsis secondary to *C. canimorsus*.<sup>12</sup> Other considerations in this setting included rabies. Per the report of the patient's neighbor, the dog was fully vaccinated. After quarantine, the dog in question showed no evidence of rabies. On immediate evaluation following the dog bite at an urgent care facility, rabies prophylaxis had been deferred due to low suspicion of canine infection. The Infectious Disease specialists were consulted given the high risk for pathologic infection with an atypical organism. As part of a complete workup, she had an x-ray of the finger were unremarkable for acute signs of osteomyelitis. She was started on meropenem for antibiotic therapy, a carbapenem beta-lactam providing broad coverage against both gram positive and negative organisms. On a detailed exposure history, the patient was found to have tick bite in the preceding months as well as contact with goat placenta from goats that had recently given birth on her farm, a known harbinger of *Coxiella burnetii*, the common cause of Q fever.<sup>13</sup> Given the patient's altered state may have been the result of exposure to tick-borne rickettsial diseases, she was also started on doxycycline.

Another difficulty in this thrombocytopenic patient was further evaluation of a meningeal process. She had neck stiffness

and a fluctuating mental status suggesting an intracranial component to her symptoms. With her platelet count of less than  $70 \times 10^9/L$ , a lumbar puncture placed her at high risk for bleeding.<sup>14</sup> In discussion with the Maternal Fetal Medicine, Hematology, and Infectious Disease teams, the benefits and risks of this invasive procedure were discussed. The patient's symptomology was determined to be more suggestive encephalopathy, due to the altered mental status being the predominant neurological finding. Lumbar puncture was deferred. An MRI, in the evaluation of infectious central nervous system disease, is a sensitive form of neuroimaging.<sup>15</sup> She underwent an MRI of the brain with contrast which showed no evidence of encephalitis, no acute intracranial processes but did note some chronic change consistent with her prior brain injury.

Blood cultures obtained at admission were positive for gram negative bacilli and preliminarily grew *Capnocytophaga* species and she was converted to IV ertapenem, a carbapenem beta-lactam antibiotic, for a 10-day course. *Capnocytophaga canimorsus* was eventually isolated from the cultures. Bacterial identification was accomplished via MALDI-TOF mass spectrometry with 16S rRNA sequencing for verification. The neonate was sent to the NICU following delivery and was briefly intubated for respiratory distress, but otherwise had no complications and was discharged to the newborn nursery on the 6<sup>th</sup> day of life. Blood cultures from the neonate were negative. With the administration of IV antibiotics, the patient's platelet count recovered to  $278 \times 10^9/L$  one day after starting the IV ertapenem. Her profound thrombocytopenia, despite not having a spleen, was attributed to platelet consumption and decreased platelet production due to *C. canimorsus* infection. Although the pathogenesis of thrombocytopenia in sepsis is largely unknown, there is some evidence that absolute immature platelet count (AIPC) can decrease past the acute phase of sepsis, suggesting thrombopoietic suppression and a subsequent decrease in platelet production.<sup>16</sup> The patient was discharged on the sixth hospital day and completed IV ertapenem therapy on an outpatient basis at home.

## Discussion

The patient's asplenia presented a clinical challenge. This differential diagnosis for the patient's clinical illness was particularly extensive given her co-morbidities. She had severe thrombocytopenia with an initial

platelet count of  $8 \times 10^9/L$ , suggesting a hematologic pathology. Concurrently, she presented with fevers and altered mental status following multiple zoonotic exposures. The impact of both processes was concerning particularly in the setting of intrauterine growth restriction.

## Fetal considerations

Perinatal infection with *Capnocytophaga* species is rare with only scattered cases across medical literature with a predominance of focus on species found in human flora. Infection with these species are a demonstrated potential risk factor for preterm birth and an infrequent cause of chorioamnionitis and neonatal infection.<sup>17</sup> Several reported cases involved afebrile women who presented in preterm labor with intact membranes and mild leukocytosis.<sup>18-21</sup> Three cases described neonatal morbidity as a result of maternal infection.<sup>8,22,23</sup> These reports are based on relatively healthy mothers and could suggest that overall, infections from human flora *Capnocytophaga* species are relatively benign with low risk of long-term morbidity.

## Immunocompromised host

Our case uniquely illustrates the potential gravity of zoonotic *Capnocytophaga* infection in an immunocompromised pregnant woman, especially in the setting of asplenia. *C. canimorsus* was isolated in this case and is the most common *Capnocytophaga* species associated with dog bites.<sup>2</sup> *C. canimorsus* has a polysaccharide capsule that is implicated in resistance to the innate immunity of the host.<sup>22</sup> One study showed that infection with *C. canimorsus* does not elicit an inflammatory response, and this is potentially due to the protective nature of a polysaccharide structure from deposition of the complement membrane attack complex and from efficient phagocytosis by polymorphonuclear leukocytes (PMNs).<sup>25,26</sup> This may suggest that although the clinical presentation in a relatively healthy patient may be unremarkable, the underlying infection could still be severe, and the risk of infection on both maternal and neonatal morbidity during pregnancy could be increased with maternal immunocompromise. Our case illustrates an acutely ill patient who is immunocompromised at baseline. Although she was hemodynamically stable, our patient may have been in subclinical or atypical sepsis from *C. canimorsus* infection, as seen by fetal distress, dramatic maternal thrombocytopenia, labile fevers, central nervous system symptoms, and altered mental status.

## Severe thrombocytopenia

The profound thrombocytopenia in this case is of particular interest. Given the magnitude of the depression in platelet counts, thrombocytopenia in this case was almost certainly not attributable to gestational thrombocytopenia alone.<sup>14</sup> Also, gestational thrombocytopenia is not associated with symptomatic patients and other findings such as this patient's altered mental status. Thrombotic microangiopathy was unlikely due to two peripheral smears negative for schistocytes.<sup>27</sup> The patient's relatively unremarkable ADAMTS13 result essentially excluded TTP, and ITP is not consistent with sudden rebound of platelet levels after antibiotic administration. DIC is unlikely as the patient's fibrinogen levels remained elevated throughout her course. A possible explanation is direct bone marrow suppression in the setting of fulminant infection or sepsis, although it is intriguing that the patient was never classically septic and that only the platelet cell line was remarkably depressed, as the patient's red blood cell counts were only slightly below normal range and her white blood cell counts were normal to elevated.

## Dog bite

Animal bites account for 1% of all injury-related emergency department visits and incur more than \$50 million in inpatient care costs annually.<sup>28,29</sup> Most animal bites are from dogs, with most animals being familiar to the victim. Antibiotic prophylaxis is recommended for patients suffering a dog bite, especially if the patient is immunosuppressed. Amoxicillin-clavulanate is the first-line antibiotic for treatment of dog bites, and is safe in pregnancy.<sup>30,31</sup> *Capnocytophaga* infections are covered by amoxicillin-clavulanate, and early treatment of infection in our patient may have prevented the ensuing morbidity, including preterm labor and preterm delivery.<sup>32</sup> Our patient reported being prescribed antibiotics to treat her dog bite but was instructed not to start her regimen until she was able to be seen by her regular Ob/Gyn. The delay in time to antibiotic treatment may have been the precipitous factor in her preterm labor and delivery.

## Conclusions

*Capnocytophaga canimorsus* was identified in blood cultures after a dog bite in a pregnant patient with baseline immunocompromise due to asplenia. In this case, infection was associated with fetal distress, preterm labor, vaginal bleeding, severe

maternal thrombocytopenia, and a brief period of neonatal respiratory distress requiring intubation, although the latter finding may be more specifically related to prematurity rather than a direct consequence of specific maternal infection. This case report suggests that both maternal and neonatal effects of *C. canimorsus* infection can be serious, especially with zoonotic-acquired infections and with a delay in time to treatment. As effective and safe treatment exists, we recommend that all pregnant patients who present to any medical provider with dog bite be treated prophylactically with antibiotics, especially in patients with any form of immunocompromise. For symptomatic pregnant patients, evaluation in a labor and delivery triage unit for fetal monitoring may be necessary. The outcomes in this case were favorable, and this may be partly due to the arrival of the patient to a tertiary care hospital system, where infectious disease, hematological, and neonatal intensive care resources were plentiful and readily accessible. Further research is needed to better understand the mechanism of the profound, isolated depression of platelet counts during this patient's illness.

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