UCLA

UCLA Previously Published Works

Title

Capnocytophaga canimorsus sepsis with associated thrombotic thrombocytopenic purpura.

Permalink

<https://escholarship.org/uc/item/3nb4f9xk>

Journal

The American journal of the medical sciences, 345(1)

ISSN

0002-9629

Authors

Ma, Andrew
Goetz, Matthew Bidwell

Publication Date

2013

DOI

10.1097/maj.0b013e318262db1a

Peer reviewed

***Capnocytophaga canimorsus* Sepsis with Associated Thrombotic Thrombocytopenic Purpura**

Andrew Ma, MD^{1,2} and Matthew Bidwell Goetz, M.D.^{2,3}

¹ Department of Medicine, Cedars-Sinai Medical Center, Los Angeles, CA, United States

² Department of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, CA, United States

³ Infectious Diseases Section, Department of Medicine, VA Greater Los Angeles Healthcare System, Los Angeles, CA, United States

Keywords: Zoonoses, thrombotic thrombocytopenic purpura, *Capnocytophaga*, sepsis,

Running title: *C. canimorsus* Sepsis Associated with TTP

Communicating author

Andrew Ma, MD
8700 Beverly Boulevard, Room 5512
Los Angeles, CA 90048
Email: Andrew.Ma@cshs.org
Telephone: 551-404-2986
Fax: 310-423-2574

Alternate author

Matthew Bidwell Goetz, M.D.
Chief, Infectious Diseases Section (111-F)
VA Greater Los Angeles Healthcare System
11301 Wilshire Blvd.
Los Angeles, CA 90073
Tel: 310-268-3015
Fax: 310-268-4928
Email: matthew.goetz@va.gov

Abstract

Capnocytophaga canimorsus, a bacterium commonly transmitted via dog bites, is known to cause sepsis in immunocompromised patients. Thrombotic thrombocytopenic purpura and hemolytic uremic syndrome are rare complications of infection. We present a case of *C. canimorsus* sepsis and thrombotic thrombocytopenic purpura in an asplenic patient and review the relevant literature.

Introduction

Capnocytophaga canimorsus, a pathogen commonly associated with dog bites, is a well-known cause of severe sepsis in asplenic patients. Infections with *C. canimorsus* have also rarely been associated with thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS). Cases of *C. canimorsus* infection are increasing while the organism may still be difficult to identify and may be under identified [1]. At the same time, the diagnostic criteria for TTP are not precise and untreated TTP carries high mortality. Therefore a high level of awareness must be maintained to diagnose and treat both *C. canimorsus* and TTP. Herein, we present a case of *C. canimorsus* infection associated with TTP and review the relevant literature.

Case Report

A 56 year old male presented with progressive fatigue, gait instability, intractable nausea and vomiting five days after sustaining a superficial facial laceration by his dog's teeth. He denied any fevers, chills, headache, diarrhea, abdominal pain, bleeding, or bruising. Past medical history was notable for a motor vehicle accident 22 years ago resulting in a ruptured spleen requiring splenectomy. He denied any active or past alcohol use. Vital signs demonstrated blood pressure of 80/55 and heart rate of 104 beats per minute. The physical exam was significant for 2 small, superficial lacerations on the patient's nose without surrounding signs of infection, a well healed midline abdominal scar, and dry mucous membranes. There were no abnormal pulmonary, cardiovascular, dermatological, or neurological findings. On presentation, platelets were 8 K/ μ L and the serum creatinine was 5.45mg/dL; six months prior, the platelets and creatinine had been 292 K/ μ L and 0.82 mg/dL, respectively. Coagulation parameters were within normal limits,

fibrinogen was elevated, and there was no leukocytosis or anemia on admitting laboratory data (Table 1). Recent HIV testing was negative.

After initial fluid resuscitation, the patient developed fever to 102F, altered mental status and hypoxic respiratory failure requiring intubation. Chest radiograph showed pulmonary vascular congestion. Head CT was normal. The patient was empirically treated with vancomycin and piperacillin-tazobactam. Within 48 hours, two sets of blood cultures grew filamentous gram-negative rods. *Capnocytophaga canimorsus* was suspected and antibiotics were changed to ampicillin-sulbactam. A transthoracic echocardiogram showed no evidence of endocarditis. Further labs showed progressive anemia (hemoglobin 10.4 g/dL), slight hyperbilirubinemia (total bilirubin 1.5 mg/dL), and few schistocytes on peripheral blood smear. A presumptive diagnosis of TTP was made and he was treated with prednisone 1 mg/kg per day plus 3 days of plasma exchange. With these measures, the patient defervesced, blood pressure normalized, renal function improved, and platelet count recovered. Unfortunately the patient's hospital course was complicated by ventilator associated pneumonia, for which he was treated with piperacillin-tazobactam. In total, the patient received 16 days of antibiotics and was discharged in good condition.

Discussion

Capnocytophaga canimorsus are fastidious, capnophilic, facultative anaerobic, gram-negative fusiform bacteria closely related to *Fusobacterium* and *Bacteroides* species. *C. canimorsus* is found as part of the oral flora of dogs and, less commonly, cats. The bacterium is of low virulence. Risk factors for infection are classically asplenia, alcoholism, and

immunosuppression. Infection commonly takes the form of sepsis, although localized infections such as meningitis and endocarditis also occur. Onset of symptoms can range from 1-8 days and include fever, chills, myalgia, malaise, vomiting, diarrhea, abdominal pain, and headache [1, 2, 3]. Overall mortality is about 30%.

There are numerous antibiotic options for treatment. While other *Capnocytophaga* species have been reported to produce beta-lactamase, this has not been found in *C. canimorsus* [4]. Active antibiotics for *C. canimorsus* include penicillin, ampicillin, beta-lactam/beta-lactamase combinations, third-generation cephalosporins, imipenem, clindamycin, linezolid, tetracyclines, chloramphenicol, and fluoroquinolones [5].

Our patient was asplenic and exhibited features of TTP without the dysregulation of coagulation characteristic of disseminated intravascular coagulation (DIC). This is unusual since *C. canimorsus* infections are more commonly associated with DIC, with TTP being rarely seen. In three reviews of *C. canimorsus* infections, no instances of TTP were reported [1, 2, 3]. In total, we found 4 cases of TTP and 2 cases of HUS associated with *C. canimorsus* infection in the English language literature (Table 2) [6, 7, 8, 9, 10].

HUS and TTP are overlapping syndromes that can be difficult to distinguish because they share the same diagnostic criteria of microangiopathic hemolytic anemia and thrombocytopenia. Though renal failure, fever, and neurological abnormalities may or may not be seen with either syndrome, the presence of these features is traditionally characteristic of TTP [11]. The pathophysiology of TTP is not completely understood, but studies highlight a deficiency in the

von Willebrand Factor (VWF) cleaving protease, ADAMTS13. A deficiency of ADAMTS13 activity leads to the accumulation of large VWF multimers that activate platelet aggregation causing microvascular thrombi [11, 12]. Treatment with plasma exchange has decreased the mortality due to TTP from 90% to 22% [13].

It is unclear if TTP in *C. canimorus* infections is attributable to a characteristic of the organism or more generally to the resulting sepsis. It has been shown that sepsis itself can cause a decrease in ADAMTS13 activity and an increased release of large VWF multimers [12, 14]. Sepsis caused by various organisms can also be associated with a clinical diagnosis of HUS/TTP [13, 15].

Regardless of the underlying cause, it is apparent that TTP is associated with *C. canimorsus* infections. When the diagnosis of one is present, it is important to consider a diagnosis of the other in the proper clinical setting. *C. canimorsus* and TTP are each associated with significant mortality; therefore timely recognition and treatment can be critical to successful outcomes.

Conflict of Interest

None

Acknowledgments

We thank Oliver Caniga, MD for his assistance in gathering the data for this report

References

1. Janda JM, Graves MH, Lindquist D, Probert WS. Diagnosing *Capnocytophaga canimorsus* infections. *Emerg Infect Dis.* **2006**; 12:340-2.
2. Pers C, Gahrn-Hansen B, Frederiksen W. *Capnocytophaga canimorsus* septicemia in Denmark, 1982-1995: Review of 39 Cases. *Clin Infect Dis.* **1996**; 23:71-5.
3. Lion C, Escande F, Burdin JC. *Capnocytophaga canimorsus* infections in human: review of the literature and cases report. *Eur J Epidemiol.* **1996**; 12:521-33.
4. Gastra W, Lipman LJ. *Capnocytophaga canimorsus*. *Vet Microbiol.* **2010**; 140:339-46.
5. Jolivet-Gougeon A, Sixou J, Tamanai-Shacoori Z, Bonnaure-Mallet M. Antimicrobial treatment of *Capnocytophaga* infections. *Int J Antimicrob Agents.* **2007**; 29:367-73.
6. Finn M, Dale B, Isles C. Beware of the dog! A syndrome resembling thrombotic thrombocytopenic purpura associated with *Capnocytophaga canimorsus* septicaemia. *Nephrol Dial Transplant* **1996**; 11:1839-40.
7. Scarlett JD, Williamson HG, Dadson PJ, Fasset R, Peel MM. A syndrome resembling thrombotic thrombocytopenic purpura associated with *Capnocytophaga canimorsus* septicemia. *Am J Med.* **1991**; 90:127-8.

8. Kok RH, Wolfhagen MJ, Mooi BM, Offerman JJ. A patient with thrombotic thrombocytopenic purpura caused by *Capnocytophaga canimorsus* septicemia. *Clin Microbiol Infect.* **1999**; 5:297-8.
9. Mulder AH, Gerlag PG, Verhoef LH, van den Wall Bake AW. Hemolytic uremic syndrome after *capnocytophaga canimorsus* (DF-2) septicemia. *Clin Nephrol.* **2001**; 55:167-70.
10. Tobe TJ, Franssen CF, Zijlstra JG, de Jong PE, Stegeman CA. Hemolytic uremic syndrome due to *Capnocytophaga canimorsus* bacteremia after a dog bite. *Am J Kidney Dis.* **1999**; 33:E5.
11. George JN. Thrombotic thrombocytopenic purpura. *N Engl J Med.* **2006**; 354:1927-35.
12. Claus RA, Bockmeyer CL, Sossdorf M, Losche W. The balance between von-Willebrand factor and its cleaving protease ADAMTS13: biomarker in systemic inflammation and development of organ failure? *Curr Mol Med.* **2010**; 10:236-48.
13. George JN, Vesely SK, Terrell DR. The Oklahoma thrombotic thrombocytopenic purpura-hemolytic uremic syndrome (TTP-HUS) registry: a community perspective of patients with clinically diagnosed TTP-HUS. *Semin Hematol.* **2004**; 41:60-7.
14. Kremer Hovinga JA, Zeerleder S, Kessler P, et al. ADAMTS-13, von Willebrand factor and related parameters in severe sepsis and septic shock. *J Thromb Haemost.* **2007**; 5:2284-90.

15. Wang Z, Yu Z, Su J, Cao L, Zhao X, Ruan C. Sepsis-induced disseminated intravascular coagulation with features of thrombotic thrombocytopenic purpura: a fatal fulminant syndrome. *Clin Appl Thromb Hemost*. **2011**; 17:251-53.

Table 1: Admission Laboratory Data

Laboratory Data	Reference Ranges
Hgb 15.1 g/dL	13.3-17.7 g/dL
Wbc 8.9 K/ μ L	4.5-11 K/ μ L
Plt 8 K/ μ L	150-440 K/ μ L
Bun 82 mg/dL	5-25 mg/dL
Cr 5.78 mg/dL	0.66-1.28 mg/dL
PT 12.5 sec	9.2-12.4 sec
PTT 22.2 sec	24.8-38.8 sec
INR 1.2	
Fibrinogen 651 mg/dL	185-458 mg/dL
LDH 203 U/L	87-165 U/L

Table 2: Review of case reports of *Capnocytophaga canimorsus* associated with thrombotic thrombocytopenic purpura (TTP) and hemolytic uremic syndrome (HUS)

	Finn et al	Scarlett et al	Scarlett et al	Kok et al	Tobe et al	Mulder et al
Age/Sex	53 year old female	72 year old male	49 year old male	47 year old male	50 year old male	66 year old male
Exposure	Owned dog	Owned cat Received cat scratches	None	Owned dog	Bitten by dog 1 day prior to admission	Bitten by dog a few days prior to admission
Risk factors/ Comorbidities	Tobacco use	None reported	Splenectomy 15 years ago	Alcoholism	None reported	Diabetes mellitus Hypertension Hypercholesterolemia Transient ischemic attack
Symptoms/Signs	Fever Headache Neck stiffness Arthralgia Purpura Confusion Hypotension Oliguria	Fever Malaise Rigors Dyspnea Tachycardia Retinal artery occlusion Splinter hemorrhage Petechiae Purpura Melena Hematuria	Fever Vomiting Diarrhea Sweating Rigors Arthralgia Productive cough Tachycardia Petechiae Vasculitic lesions	Fever Icterus Abdominal pain Dyspnea Melena Hematemesis Confusion Petechiae Tachycardia Tachypnea Anuria	Fever Arthralgia Oliguria	Fever Malaise Chills Vomiting Diarrhea Hematemesis Melena Purpura Hematomas Anuria
Diagnostic Data	Hemoglobin (g/dL)	14.5	10.4	14.5	6.6	Hematocrit 30%
	WBC (K/ μ L)	11.3	2.8	10.7	17.5	15.9
	Platelets (K/ μ L)	27	8	26	<10	9
	BUN (mg/dL)	32	106	37	248	143
	Creatinine (mg/dL)	0.86	0.27	1.16	1.27	10.9
	Coagulation parameters	INR 1.9	PT & PTT normal	PT & PTT normal	PT & PTT normal	PT 12.4 sec PTT 19.3 sec
	Fibrinogen (mg/dL)	470	600	>500	Normal	468
	Total Bilirubin (mg/dL)	1.4	No information	No information	27	3.2
	Lactate Dehydrogenase (U/L)	No information	960	No information	2800	3102
Anatomic Pathology	+ schistocytes	+ schistocytes	TTP diagnosed with skin biopsy	+ schistocytes	+ schistocytes	+ schistocytes
Diagnosis	TTP	TTP	TTP	TTP	HUS	HUS
Treatment	Benzylpenicillin Netilmicin High dose steroids Plasma exchange Hemofiltration	Gentamicin Flucloxacillin Penicillin Prednisolone Plasma exchange	Imipenem	Amoxicillin/clavulanate Ofloxacin Plasma exchange Hemodiafiltration	Amoxicillin/clavulanate Plasma exchange	Cefuroxime Metronidazole Amoxicillin/clavulanate Plasmapheresis Hemodialysis
Outcome	Survived to discharge	Improved	Improved	Survived to discharge	Survived to discharge	Improved