Man's best friend? Infective endocarditis due to *Capnocytophaga canimorsus*

Omar Hayani MD¹, Lyall AJ Higginson MD FRCPC¹, Baldwin Toye MD FRCPC^{2,3}, Ian G Burwash MD FRCPC¹

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Infective endocarditis caused by zoonotic microorganisms is an uncommon clinical entity. A 55-year-old man was diagnosed with endocarditis due to *Capnocytophaga canimorsus*, a commensal bacterium contained in the saliva of dogs, that involved the aortic and tricuspid valves and was complicated by a para-aortic valve abscess and aorta-to-right atrial fistula. The patient was successfully treated with antibiotic therapy and surgical intervention. *C canimorsus* endocarditis should be considered in patients with culture-negative endocarditis, particularly in immunosuppressed, asplenic or alcoholic individuals who have recently suffered a dog bite or have had close contact with dogs.

Key Words: Canine; *Capnocytophaga canimorsus*; Endocarditis; Paravalvular abscess

Infective endocarditis caused by zoonotic microorganisms is an uncommon clinical entity. Most reported cases are due to *Brucella* species and *Coxiella burnetii*, both of which are prevalent in cattle-raising communities. *Capnocytophaga canimorsus* is a canine bacterium associated with a variety of human infections including septicemia, meningitis, wound infections, septic arthritis and, rarely, endocarditis (1). These infections can occur in otherwise healthy individuals, although immunocompromised patients, particularly alcoholic or asplenic individuals, are especially predisposed to infections with this organism (1). We report a case of *C canimorsus* endocarditis involving both the tricuspid and aortic valves that was complicated by a para-aortic valve abscess and aorta-to-right atrial fistula.

CASE PRESENTATION

A 55-year-old man presented to the emergency department with a four-week history of intermittent fever, night sweats, mild exertional dyspnea and watery diarrhea with up to 10 bowel movements per day. He also admitted to feeling generally unwell during the previous six months with increasing fatigue, malaise and a 9 kg weight loss. His medical history was remarkable for chronic obstructive pulmonary disease, alcohol abuse and intravenous (IV) drug use, although he denied consuming alcohol during the previous eight months or engaging in IV drug use in the past 10 years. His heart rate was 103 beats/min with a blood pressure of 106/71 mmHg and a body temperature of 37.3°C, which transiently increased to 38.5°C while in the emergency department. His room air oxygen saturation was 96%. No murmurs were detected and his chest was clear. The abdomen was not tender and had no organomegaly. Laboratory investigations revealed a hemoglobin level of 113 g/L and a white blood cell (WBC) count of $20.7 \times 10^9/L$ ($16.9 \times 10^9/L$ neutrophils). Electrolytes, creatinine and liver function

Le meilleur ami de l'homme ? L'endocardite infectieuse imputable au *Capnocytophaga canimorsus*

L'endocardite infectieuse attribuable à des microorganismes zoonotiques est une entité clinique peu courante. Un homme de 55 ans a reçu un diagnostic d'endocardite imputable au *Capnocytophaga canimorsus*, une bactérie commensale contenue dans la salive des chiens, qui a touché les valvules aortique et tricuspide et était compliquée par un abcès de la valvule para-aortique et une fistule entre l'aorte et l'oreillette droite. Le patient a subi une antibiothérapie et une intervention chirurgicale avec succès. L'endocardite à *C canimorsus* devrait être envisagée chez les patients atteints d'une endocardite négative à la culture, notamment chez les personnes immunosupprimées, aspléniques ou alcooliques qui se sont récemment fait mordre par un chien ou qui ont eu des contacts étroits avec des chiens.

tests were normal. A chest radiograph, electrocardiogram, abdominal x-ray and abdominal ultrasound were also normal. Two sets of blood cultures and urine cultures were sent for laboratory examination. He was presumed to have an enteric infection and was discharged with arrangements for stool cultures, ova and parasite examination, and *Clostridium difficile* toxin assay. All culture results were negative, and no parasite or *C difficile* toxin was detected.

During the next two weeks, he continued to have intermittent fevers (as high as 39°C), night sweats and diarrhea, although his diarrhea improved. Abdominal and cardiac examinations remained normal and no murmurs were detected. His hemoglobin level decreased to 101 g/L and his WBC count increased to $25.7 \times 10^9/L$ ($23.2 \times 10^9/L$ neutrophils). Another two blood culture sets were collected and computed tomography of the abdomen was arranged. Three days later, a Gram-negative bacillus grew in the aerobic and anaerobic bottles of both blood culture sets. The patient refused hospital admission and was empirically treated with IV ceftriaxone and ciprofloxacin for a presumed enteric pathogen while awaiting its identification. Transthoracic and transesophageal echocardiography were performed three days later and demonstrated severe (grade 4) tricuspid regurgitation with a large mobile vegetation (1.1 cm × 0.7 cm) on the anterior tricuspid valve leaflet (Figure 1), and multiple vegetations on the aortic valve with severe (grade 4) aortic regurgitation (Figures 2 and 3). A para-aortic valve abscess and small aorta-to-right atrial fistula were also seen.

The patient was admitted to the hospital for further treatment. On admission, he was febrile (39.2°C) with a blood pressure of 115/55 mmHg. His jugular venous pressure was elevated at 8 cm with a prominent CV wave. A grade 2/6 holosystolic murmur was detected at the left lower sternal border as well as a grade 2/6 blowing decrescendo diastolic murmur at the left upper sternal border. Breath sounds

¹Division of Cardiology, Department of Medicine, University of Ottawa Heart Institute; ²Division of Microbiology, Department of Pathology and Laboratory Medicine, The Ottawa Hospital, University of Ottawa; ³Ontario Public Health Laboratories, Ottawa, Ontario

Correspondence: Dr Ian G Burwash, University of Ottawa Heart Institute, 40 Ruskin Street, Ottawa, Ontario K1Y 4W7. Telephone 613-761-5490, fax 613-761-5081, e-mail iburwash@ottawaheart.ca

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Figure 1) Transthoracic echocardiogram. Apical four-chamber view demonstrating a vegetation (arrow) on the anterior tricuspid valve leaflet. RA Right atrium; RV Right ventricle

were normal. There were no peripheral stigmata of infective endocarditis. An electrocardiogram demonstrated sinus rhythm with a PR interval of 170 ms and chest radiography identified a new soft tissue density nodule in the left lower lung zone suggestive of pulmonary infarction or abscess formation. The antibiotics were changed to IV meropenem and ciprofloxacin because of the unknown etiology of the Gram-negative bacilli and the severity of the disease.

The Gram-negative bacillus isolated from blood cultures was subsequently identified as a *Capnocytophaga* species. Further biochemical testing and 16S ribosomal RNA sequencing analysis of the organism by the Ontario Public Health Laboratories (Toronto, Canada) were consistent with *C. canimorsus*. The isolate was beta-lactamase-positive (Cephinase [Becton Dickinson and Company, USA] method) and susceptibility testing by the Etest (AB Biodisk, Sweden) method indicated a minimum inhibitory concentration to penicillin, meropenem and ciprofloxacin of higher than 32 mg/L, 0.032 mg/L and 0.016 mg/L, respectively. The patient initially improved on IV meropenem and ciprofloxacin with resolution of his fever and a decrease in WBCs. However, he subsequently developed pulmonary edema and surgery was required after 18 days of antibiotic therapy. The patient underwent tricuspid valve repair, mechanical aortic valve replacement and an aortoplasty with pericardial closure to repair the aortic root abscess and aorta-to-right atrial fistula. Surgical pathology of the aortic and tricuspid valve demonstrated microscopic changes consistent with healing endocarditis (ie, cusp/leaflet destruction, necrosis, acute and chronic inflammation, and macrophage infiltration). Tissue sections were stained for bacteria, but none were identified by Gram staining. Periodic acid-Schiff and Giemsa stains were negative, and the Grocott methenamine silver stain showed no fungi.

The patient's postoperative course was unremarkable. He was treated with IV meropenem and ciprofloxacin for four weeks following surgery and was free of recurrent infection at a four-month follow-up examination. On further questioning, the patient disclosed that he had two to three dogs in his household at any given time before his illness, and that he was frequently scratched when he came into close facial contact with them.

DISCUSSION

C. canimorsus was first described by Bobo and Newton in a 1976 case report of Gram-negative septicemia with meningitis. Formerly designated as Dysgonic fermenter 2, it is a facultatively anaerobic, fastidious Gram-negative bacillus considered to be a commensal oral flora of dogs (1). As implied by the name (*canimorsus* means 'dog bite'), humans with *C. canimorsus* infections have a history of being bitten by a dog in as many as 54% to 63% of cases (1,2). However, infections

Figure 2) Transesophageal echocardiogram. Short-axis view of the aortic valve during diastole (top) and systole (bottom) demonstrating vegetations on the aortic valve (arrows) and a large para-aortic valve abscess (asterisks). LA Left atrium; RA Right atrium; RV Right ventricle

can also be acquired by lesser injuries such as a scratch or exposure to a dog (1,2), which we believe occurred in our patient. While *C. canimorsus* infections can occur in otherwise healthy adults, immunocompromised individuals, particularly asplenic patients or alcoholics, are especially predisposed to severe infections such as fulminant sepsis (1). Two separate reviews by Lion et al (1) and Janda et al (2), consisting of 103 and 56 patients, respectively, identified septicemia as the most common manifestation. However, *C. canimorsus* has also been implicated less frequently in a variety of other infections including meningitis, cellulitis, septic arthritis, endocarditis, pleuritis, phlebitis, mycotic aortic aneurysm and, rarely, localized ocular infections (1,2).

Endocarditis as a result of *C. canimorsus* infection is extremely rare, with only 14 cases reported in the literature since 1977 (3-5). Including the current case, there is a male predominance (male to female ratio of 3:1) with an average age of 51 years (range 24 to 69 years) (3-5). Cardiac disease was documented before the episode of endocarditis in five patients (33%). In addition, five patients (33%) had an underlying condition that predisposed them to infection; four patients had a history of alcohol abuse and one patient had chronic lymphocytic leukemia requiring steroid therapy. Six of the 15 patients (40%) had been bitten by a dog and another five patients (33%) had contact with a dog. Our patient had a history of both alcohol abuse and exposure to dogs with frequent scratch injuries.

C. canimorsus endocarditis most commonly affects the aortic valve; seven of the 15 patients (47%) had aortic valve involvement (3-5). One additional patient had involvement of an aortic prosthesis (4). The tricuspid valve was involved in 40% of patients, whereas the

Figure 3) Transesophageal echocardiogram. Long-axis view of the aortic valve during diastole demonstrating vegetations on the aortic valve (arrows) and the para-aortic valve abscess (asterisk). Ao Aorta; LA Left atrium; LV Left ventricle; RV Right ventricle

mitral valve was affected in only 20%. Two cases (including the current case) had both aortic and tricuspid valve involvement. Para-aortic valve abscess formation has been described previously (5), although our case is the first to report the complication of an aorta-to-right atrial fistula.

The diagnosis of *C. canimorsus* endocarditis typically requires a high clinical suspicion because symptoms are often nonspecific and routine blood cultures are frequently negative (3-5). The organism grows slowly in culture and prolonged incubation of blood cultures for longer than five days may be required before growth is detected. If the suspicion of infective endocarditis is high despite initially negative cultures, consultation with the microbiology laboratory is recommended for consideration of a longer incubation or terminal subculture of the blood culture bottles. In our patient, *C. canimorsus* infective endocarditis was diagnosed based on positive blood cultures and the diagnostic

echocardiographic findings. While our patient's blood cultures were positive for this fastidious Gram-negative bacillus, molecular techniques have also been used to establish a diagnosis of *C. canimorsus* endocarditis using amplification of bacterial nucleic acid from infected valve tissue by the polymerase chain reaction (5).

C. canimorsus is often susceptible in vitro to a variety of antibiotics including penicillin, cephalosporins, carbapenems, macrolides, quinolones and rifampin, with several different antibiotic regimens having been used to successfully treat endocarditis due to this pathogen (4). Most reported patients received prolonged IV penicillin or cephalosporin therapy. However, there has been an increased prevalence of beta-lactamase-producing strains of *Capnocytophaga* species (as found in the present case), and choosing an antibiotic that is stable against beta-lactamases is required in this situation. In our patient, meropenem and ciprofloxacin were instituted after endocarditis was diagnosed by echocardiography because the etiology of the Gram-negative bacilli was initially unknown, and because of the severity of the cardiac disease (abscess formation, etc). Minimum inhibitory concentrations were subsequently determined for our isolate of *C. canimorsus* but there are no interpretive criteria for susceptibility testing of this organism and obtaining accurate results is complicated by its slow growth and fastidious growth requirements. It was decided to maintain our patient on both meropenem and ciprofloxacin after identification of the organism because of the apparent clinical response. It is unknown whether combination therapy rather than monotherapy is required for treatment of endocarditis due to *C. canimorsus*.

Surgical intervention has been required in a significant proportion of reported cases (47% of patients). Surgery was the inevitable outcome in our patient because of the para-aortic valve abscess and refractory congestive heart failure (3-5). Three of the 15 previously reported patients with *C. canimorsus* endocarditis died, translating into an overall survival rate of 80%.

The current case highlights the capacity of *C. canimorsus* infection to manifest as infective endocarditis with multiple complications including a para-aortic valve abscess and aorta-to-right atrial fistula. The potential for this fastidious organism to cause infective endocarditis should be considered, especially in immunocompromised, asplenic or alcoholic patients with culture-negative endocarditis who have had exposure to dogs.

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