Urticarial exanthem associated with *Capnocytophaga canimorsus* bacteremia after a dog bite

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INTRODUCTION

Capnocytophaga canimorsus (Latin, *canis*, dog; *morsus*, bite) is a commensal gram-negative rod present in the oral flora of dogs; there are almost 500 reported infections, 60% of which have occurred after a dog bite, more than 80% after dog exposure, and more than 35% in the setting of alcoholism or splenectomy.[1] Half of infections present with cutaneous manifestations[2] including petechiae, purpura, cellulitis, gangrene, and eschars[2]; there is one report of urticarial lesions.[3] This is an important disease to recognize given the 25% mortality rate associated with *C canimorsus* bacteremia.[4] Here we report the second case of an urticarial exanthem after *C canimorsus* bacteremia.

CASE REPORT

A 59-year-old man with a history of homelessness, alcoholism, right total knee arthroplasty, and type 2 diabetes presented to the emergency department with a 1-day history of worsening right knee pain, 2-day history of spreading rash, subjective fever, and generalized pain. He also had a 2-week history of cough, sore throat, headaches, congestion, rhinorrhea, and sneezing.

On examination, the patient was alert; oriented to person, time, and place; and in no acute distress. His vital signs were stable and within the normal range. On the right buccal mucosa there were few pinpoint vesicles. On the trunk and extremities there were multiple 5- to 10-cm erythematous, targetoid plaques, which lacked scale, crust, exudate, or bullae (Fig 1). Only 1 lesion, located over his ankle, was tender to palpation or painful. Over the thighs and calves were multiple, diffuse, nonblanching pink patches with scattered petechiae. On the inferior and anterolateral aspect of the right thigh there was an 8-cm well-healed linear scar (Fig 2). On the dorsal aspect of the right hand, there were several dark red-to-black, sharply demarcated, 2- to 5-mm oval eschars and crusted linear erosions. Upon further questioning, the patient recalled that 3 weeks before presentation, he had been bitten on his right hand while playing with his vaccinated dog; later that day, he washed the wounds with soap and water but did not seek medical attention or receive additional treatment. The right knee was warm, and there was mild-to-moderate swelling and diffuse tenderness to palpation. The rest of the examination findings were normal.

Laboratory tests found a neutrophilic leukocytosis of 24.2 × 10^3/mm^3 (90.2% neutrophils), an elevated erythrocyte sedimentation rate of 49 mm/h, and a C-reactive protein level of 187 mg/L. Additional laboratory tests and results are shown in Table I. Blood samples were sent for culture. Erythrocyte morphology findings were normal. Chest radiographs and echocardiogram findings were noncontributory, and the right knee radiograph showed a suprapatellar joint effusion. Right knee joint aspirate analysis found 49,000/mm^3

Abbreviation used:

H&E: hematoxylin-eosin

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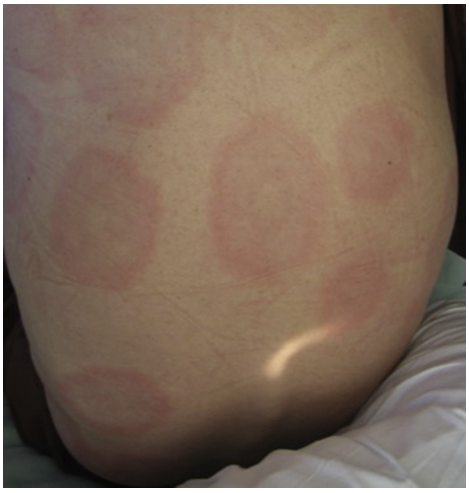

Fig 1. Generalized urticated exanthem. The upper and lower extremities, back, and abdomen show multiple, sharply demarcated, annular, targetoid, blanching, edematous, and erythematous plaques, some of which had scattered petechiae in areas where erythematous dermal edema was receding.

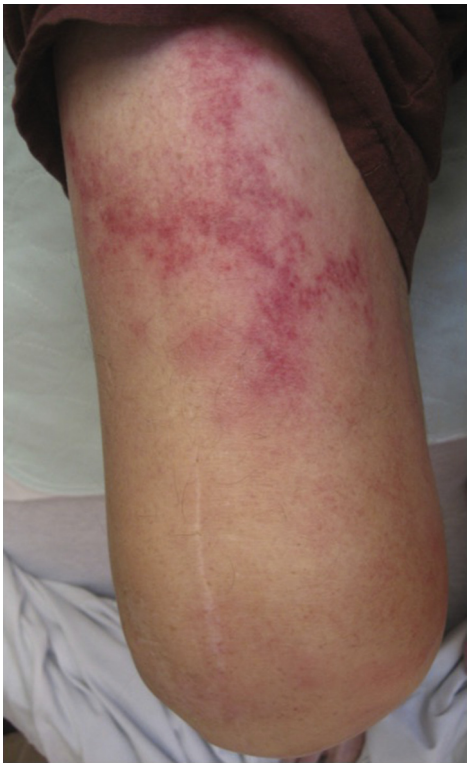

Fig 2. Lower extremity nonpalpable purpura. The thighs bilaterally show diffuse, irregularly shaped, nonpalpable petechiae and purpura; the right inferior and anterolateral aspect of the thigh showed a well-healed 8-cm scar from a total knee arthroplasty that had been performed more than a decade before presentation.

leukocytes with 79% neutrophils; the aspirate was submitted for culture.

Two punch biopsy specimens of the patient's left thigh were obtained. Hematoxylin-eosin (H&E) staining found a mild, superficial and deep, perivascular and interstitial, mixed inflammatory cell infiltrate with lymphocytes, neutrophils, and eosinophils, with extravasated erythrocytes and no evidence of vasculitis (Fig 3). Direct immunofluorescence studies were unrevealing.

The patient was admitted to the medicine service in stable condition. On the first day of hospitalization, incision and drainage of the right knee found turbid yellow synovial fluid without necrotic or infected tissue; the fluid was sent for culture and intravenous vancomycin was initiated. On the second day of the hospitalization, the targetoid lesions were less erythematous and not as raised. By the third day of hospitalization, all cutaneous lesions had resolved.

On the third day of hospitalization, blood cultures grew aerobic gram-negative rods; findings from cultures of the right knee aspiration and the right knee incision and drainage remained negative. Vancomycin was discontinued and piperacillin/tazobactam was initiated. *Pasturella* and *C canimorsus* infections were suspected; on the 13th day of hospitalization, the organism was definitively identified as *C canimorsus* on blood culture. The patient was treated with ceftriaxone for 6 weeks via a peripherally inserted central catheter followed by oral doxycycline for 6 months; basic metabolic panel and liver function tests were monitored weekly. The patient recovered without any resultant disability and remained well 7 months after he was discharged from the hospital.

DISCUSSION

This report describes a case of *C canimorsus* bacteremia presenting with a diffuse urticarial exanthem, with lesions having targetoid morphology and diffuse purpura and a right knee monoarthritis. One case of an urticarial exanthem caused by *C canimorsus* infection is described in the literature[3] in a pet dog owner with moderate alcohol abuse who had no history of a dog bite. His bacteremia was symptomatic but self-limited and resolved without antibiotics. The authors suggest the patient either had superior host defenses or was infected with a less virulent strain.

Previously known as dysgonic fermenter type 2,[5] *C canimorsus* is a commensal capnophilic, fastidious, oxidase, and catalase-positive gram-negative rod with a fusiform shape present in the oral flora of between 25.5%[6] and 74%[7] of dogs and 17% of cats. The strain was first received by the Centers for Disease Control and Prevention in 1961,[5] and the

Table I. Laboratory values at presentation to the emergency department

	Laboratory test	Value	Reference range	Unit
(H)	**Leukocytes**	**24.2**	**4.4–10.8**	**× 10^3/mm^3**
(H)	**Neutrophils**	**90.2**	**44–78**	**%**
(H)	**Neutrophils**	**21.8**	**2.5–7**	**× 10^3/mm^3**
	Lymphocytes	3.7	15–42	%
	Lymphocytes	0.9	1–4	× 10^3/mm^3
	Monocytes	5.8	0–14	%
	Monocytes	1.4	0.2–1.0	× 10^3/mm^3
	Eosinophils	0.1	0–6	%
	Eosinophils	0	0–0.5	× 10^3/mm^3
	Basophils	0.2	0–2	%
	Basophils	0.1	0–0.2	× 10^3/mm^3
(H)	**Erythrocyte sedimentation rate**	**49**	**0–15**	**mm/h**
(H)	**C-reactive protein**	**187**	**≤3.0**	**mg/L**
(H)	**Sodium**	**123**	**131–142**	**mmol/L**
(L)	**Potassium**	**3.2**	**3.5–5**	**mmol/L**
(L)	**Chlorine**	**86**	**95–108**	**mmol/L**
(H)	**Glucose**	**451**	**71–109**	**mg/dL**
(H)	**Blood urea nitrogen**	**35**	**7–23**	**mg/dL**
	Bicarbonate	23	21–32	mmol/L
	Anion gap	17	10–22	mmol/L
	Creatinine	1.3	0.8–1.5	mg/dL
	Serum osmolality	290	285–295	mOsm/kg

Values outside of the reference range are bolded. Neutrophils, lymphocytes, monocytes, eosinophils, and basophils are quantified in absolute number and as a percentage of total leukocytes in separate rows.
H, Patient's value above upper limit of reference range; *L*, patient's value below lower limit of reference range.

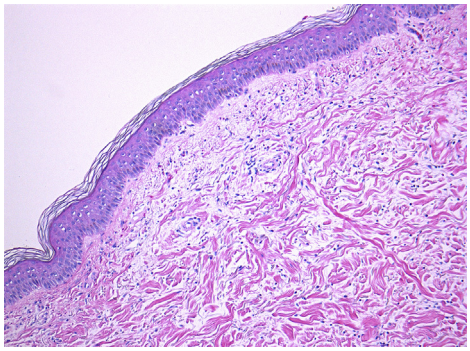

Fig 3. Microscopic examination of H&E-stained sections of right thigh punch biopsy find a mild, superficial and deep, perivascular and interstitial, mixed inflammatory cell infiltrate characterized by some lymphocytes, neutrophils and eosinophils, with extravasated erythrocytes. Vasculitis was not identified on H&E or direct immunofluorescence. (H&E stain; original magnification, ×100.)

first recorded human infection was reported in 1976.[8,9] Nearly 500 laboratory-confirmed cases have been reported, two-thirds of which have been in male patients; the median patient age is 55 years.[1]

The most important risk factor for infection is exposure to dogs (>80% of cases); a history of dog bites is present in 60% of cases, and a history of dog scratches, licking, or other contact is present in 24% of patients (cat exposures are reported in fewer than 5% of cases).[1] Although immunosuppression and a history of alcohol abuse are strong predisposing factors.[5] healthy individuals without obvious risk factors comprise nearly 40% of confirmed infections.[1]

Dermatologic findings are common; 50% of patients with *C canimorsus* infection have cutaneous lesions.[2] The most common lesions are petechiae or purpura (46%), cellulitis (35%), gangrene (12%), and eschars (8%).[2] There is 1 case report of wheals,[3] 1 report of Sweet's syndrome (acute febrile neutrophilic dermatosis),[10] and several reports of morbilliform eruptions.[2]

The clinical course of *C canimorsus* infection ranges from self-limited disease to fulminant sepsis, multiorgan failure, and death. Reported extracutaneous clinical features include ocular infections, peripheral gangrene, pneumonia, hepatitis, bacterial endocarditis, meningitis, disseminated intravascular coagulation, cardiopulmonary arrest, septic shock, renal failure, and bilateral adrenal hemorrhage (Waterhouse-Friderichsen syndrome).[11-13] The portal of entry is often through the skin,[11,13] and *C canimorsus* can spread hematogenously to the meninges, endocardium, and synovium.[13] The reported overall mortality rate is between 26%[1] and

36%, but is about 60% in patients who present with septic shock.[14] In addition to splenectomy and alcoholism, known risk factors include lung disease and immunosuppression.[13]

The diagnosis is usually made by blood culture; however, 16S rRNA gene sequencing is an increasingly common, specific, and reliable diagnostic tool that significantly reduces the time to a definitive diagnosis.[12] *C. canimorsus* is susceptible to penicillins, imipenem, erythromycin, vancomycin, clindamycin, third-generation cephalosporins, chloramphenicol, rifampicin, doxycycline, and fluoroquinolones; it is resistant to aztreonam, trimethoprin-sulfamethoxazole, and aminoglycosides.[13] Penicillin is an appropriate therapy,[1] but third-generation cephalosporins or combination β-lactam antibiotic/β-lactamase inhibitor may be used in cases of β-lactamase–resistant strains, which have been reported.[13]

The differential diagnosis of the cutaneous lesions in this case included erythema multiforme, urticaria multiforme, annular erythema, urticarial vasculitis, neutrophilic urticarial dermatosis, urticaria with capillaritis, urticaria with a prominent neutrophilic infiltrate (eg, Schnitzler syndrome), acute febrile neutrophilic dermatosis (Sweet's syndrome), neutrophilic urticaria with systemic inflammation,[15] and neutrophilic urticarial dermatosis.[16]

Research efforts focused on the molecular biology of *C canimorsus* have resulted in the complete sequencing of its genome[17] and led to the discovery that *C canimorsus* has the capacity to deglycosylate human IgG,[18] perhaps representing an interesting in vivo mechanism for delaying, curtailing, or circumventing an effective host immune response.

C canimorsus rarely results in documented clinical infections, and this may be in part because of the use of post–dog bite prophylaxis. However, a thorough clinical history allows providers to recognize the potential for *C canimorsus* infection and treat empirically before culture results become positive or serious sequelae develop. Even though further reports need to be accumulated to determine whether *C canimorsus* is significantly associated with an urticarial exanthem, when faced with a patient with an urticarial rash with no signs of vasculitis in the setting of a systemic infection, providers should be aware that *C canimorsus* can cause urticarial and targetoid lesions, particularly in cases in which there is *C canimorsus* bacteremia.

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