A patient with thrombotic thrombocytopenic purpura caused by *Capnocytophaga canimorsus* septicemia

Clin Microbiol Infect 1999; 5: 297–298

A 47-year-old man, without medical history or use of medication, was admitted to our hospital because of icterus. The patient was an unemployed, homeless alcoholic and he owned a dog. He had been well until 7 days earlier, when he developed icterus, right upper abdominal pain, dyspnea, melena and hematemesis. Further anamnesis was unreliable because the patient was seriously confused.

At admission the temperature was 38.4°C, the pulse rate was 100/min, and the respiratory rate was 30/min. The blood pressure was 106/60 mmHg. Physical examination revealed a neglected, icteric man with widespread cutaneous petechiae. Auscultation of the chest showed no abnormalities. There was diffuse epigastric tenderness but no guarding or rebound tenderness. Liver and spleen were not palpable. The results of a rectal examination were normal.

Laboratory tests are shown in Table 1. Peripheral blood film showed leukocytosis with a left shift and red cell fragmentation. The prothrombin time, activated partial thromboplastin time and fibrinogen were normal, ruling out diffuse intravascular coagulation (DIC). Results of serologic testing were negative for hepatitis B, human immunodeficiency virus, Coombs test, immune circulating complex and antinuclear antibodies. Arterial blood samples showed metabolic acidosis (pH 7.28) without hypoxemia. Microscopic hematuria was noted with mild proteinuria. Chest radiographs, abdominal echography and a reliable transesophageal echocardiography were normal.

A diagnosis of thrombotic thrombocytopenic purpura (TTP) and/or septicemia was considered. After aerobic and anaerobic blood cultures were performed, the patient received amoxycillin/clavulanic acid and ofloxacin intravenously. Continuous veno-venous hemodiafiltration (CVV-HDF) was started with administration of fresh frozen plasma and with bicarbonate-buffered hemofiltration solution as substitution fluid. Further, intermittent plasmapheresis was undertaken with the exchange of 3 L of plasma per run. Supplementation with vitamin B_1 was given intravenously.

Table 1 Laboratory tests at admission (normal range)

Hemoglobin (8.7–11.1 mmol/L)	6.7
Leukocytes (4.0–10×10^9/L)	17.5
Platelets (150–350×10^9/L)	<10
Potassium (3.5–5.0 mmol/L)	4.9
Urea nitrogen (1.8–6.4 mmol/L)	88.5
Creatinine (75–110 μmol/L)	1123
Lactate dehydrogenase (<320 U/L)	2800
Aspartate aminotransferase (<30 U/L)	83
Alanine aminotransferase (<30 U/L)	82
Alkaline phosphatase (<100 U/L)	135
Total bilirubin (<17 μmol/L)	468

Twelve hours after admission, the hemoglobin level decreased from 6.7 to 4.1 mmol/L. Two units of packed red cells were transfused. Melena and/or hematemesis could not be observed. The patient developed anuria, lasting for 10 days, and skin necrosis of the right upper foot and left ear. Blood cultures (Bactec 9240, Becton Dickinson, Sparks, Maryland, USA) taken at admission showed after 3 days a slow-growing Gram-negative rod, which was susceptible to penicillin, amoxycillin, amoxycillin/clavulanic acid, co-trimoxazole and ofloxacin, and resistant to gentamicin. Later, this Gram-negative rod was identified as *Capnocytophaga canimorsus* (confirmed by the Dutch reference laboratory for bacterial determination, RIVM, Bilthoven, The Netherlands). Stool and urine cultures were negative. The patient became afebrile rapidly, and laboratory tests improved slowly. During recovery, he developed a venous catheter sepsis (*Staphylococcus epidermidis*) with respiratory insufficiency, and mechanical ventilation was started. In this period, the CVV-HDF was changed to intermittent hemodialysis. After 1.5 months, renal function was improved enough to stop hemodialysis. The patient left the hospital in good health after 2 months with a mild critical illness polyneuropathy. Laboratory tests normalized completely. One month after discharge, the patient was without complaints and the laboratory values stayed normal.

Capnocytophaga canimorsus is a slow-growing Gram-negative bacterium found in the oral flora of dogs, cats and rabbits. Infections occur predominantly in men with immunocompromising conditions (e.g. asplenisme, alcoholic abuse, corticosteroid therapy), frequently following a dog bite or scratch [1]. Our patient was an alcoholic living in detrimental circumstances and owned a dog. However, there was no clear story of a dog bite or scratch. In a review of 72 cases of *C. canimorsus* sepsis, 43% reported a history of dog bite, while 12% reported exposure to dogs, without bites or scratches [2]. *C. canimorsus* can cause septicemia with shock, disseminated purpuric lesions, DIC and renal failure. Our patient had convincing clinical and

laboratory features of TTP and *C. canimorsus* septicemia, without the coagulopathy associated with DIC.

TTP is a life-threatening disease, characterized by fever, thrombocytopenia, purpura, microangiopathic hemolysis, and microvascular thrombotic occlusions affecting the brain, kidneys and other organs. In contrast to DIC, coagulation tests are usually normal in TTP. Some patients experience significant, although not severe, bleeding of uterine, gastrointestinal or other origin. Although many cases of TTP are idiopathic, a variety of underlying causes has been identified. Epidemiologic and laboratory data show that bacterial cytotoxins may be causative agents in TTP. The best known is TTP following a verocytotoxin-producing *Escherichia coli* infection. Less commonly, TTP is associated with gastrointestinal and respiratory infections caused by other cytotoxin-producing bacteria, such as *Shigella dysenteriae, Salmonella typhi, Campylobacter jejuni, Streptococcus pneumoniae* and *Yersinia pseudotuberculosis*. A syndrome of TTP has previously been reported in three cases of *C. canimorsus* septicemia [3,4]. TTP accompanying viral infections, such as human immunodeficiency virus infection, has also been described. Other non-infectious causes of TTP include cancer chemotherapy, lupus anticoagulant or systemic lupus erythematosus, pregnancy, bone marrow transplantation and drug therapy (cyclosporin, quinine, ticlopidine). It is generally assumed that endothelial cell injury is the initial event in the pathogenesis of TTP [5,6]. Endothelial damage triggers a cascade of events that includes local intravascular coagulation, fibrin deposition and platelet activation and aggregation. The end result is histopathologic detection of thrombotic microangiopathy. Other hypotheses of the pathogenesis of TTP are the presence of a platelet aggregator and the lack of a platelet inhibitor. However, many mechanisms remain incompletely understood.

This case demonstrates that the diagnosis of *C. canimorsus* septicemia should be considered in patients with TTP, especially when there is a history of contact with dogs or cats and if the patient has immunocompromising conditions. Penicillin is considered to be the drug of first choice when infection with *C. canimorsus* is suspected, in addition to conventional therapy for TTP.

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