Septic Shock due to *Capnocytophaga*: A Case Report

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Abstract
The genus *Capnocytophaga spp.*, recorded for the first time in 1979, comprises gram-negative bacilli, that colonize the oral mucosa of dogs and, to a lesser extent, cats, so that human transmission can be due to biting, scratching or close contact. Though it is not a common cause of infection in humans, it is a potentially serious one, which can occasionally go unnoticed causing sepsis, bacteremia, meningitis and endocarditis. A high clinical suspicion is essential for its diagnosis, especially in high-risk patients, such as alcoholics or splenectomized patients, as time to positivity of blood cultures may take as long as 6 days. Antibiotic treatment should last several weeks.

Introduction
The genus *Capnocytophaga spp.*, recorded for the first time in 1979, comprises slow-growing gram-negative bacilli, catalase and oxidase negative, which are facultative anaerobics of spindle-shaped characteristics [1]. They are oropharyngeal commensal of dogs, and to a lesser extent, cats [2], so its transmission to humans occurs due to biting, scratching or close contact. *C. canimorsus* is the most frequent pathogen causing serious human infections, usually in immunosuppressed patients, such as alcoholics or splenectomized patients, although
occasionally also in immunocompetent hosts [3, 4]. Though it is not a common cause of infection in humans, it is a potentially serious one, which can occasionally go unnoticed [5] but causing sepsis, bacteremia, meningitis and endocarditis [6, 7].

**Case Presentation**

A 46-year-old man was admitted to hospital with abdominal pain, vomiting and diarrhea, associated with a sudden rise in temperature of up to 38°C over the last 48 h. His only past medical history comprised a splenectomy. Upon initial clinical examination, there were evident signs and symptoms of septic shock and multiorgan failure, such as confusion, profuse sweating, and coldness. He also presented hypotension with a mean BP measurement of 60/40 mm Hg, an elongated capillary refill over 3 s, tachycardia with 120 bpm, a mean oxygen saturation of 99% at the expense of intense tachypnea as well as a decreased urinary output (anuria).

The physical examination revealed no abnormality, except for the presence of a traumatic wound on the left arm, in the form of two 1-cm-long lacerations outlined in black (Fig. 1), which appeared to be the only source of infection.

Blood tests revealed 11,830 leukocytes per microliter (90.6% segmented), a C-reactive protein value of 14.13 mg/L, 14,000 platelets per microliter, as well as coagulopathy (prothrombin time 35 s, INR 2.56) and a low fibrinogen count of 0.8 g/L, both adding up as diagnostic criteria for disseminated intravascular coagulation (DIC). The patient also presented with an altered liver profile with a total bilirubin count of 1.53 mg/dL, ASAT (GOT) 157 IU/L and ALAT (GPT) 125 IU/L. Kidney failure was also present with a serum creatinine of 2.35 mg/dL, with a normal electrolyte balance but lactic metabolic acidosis (pH 7.24, paCO2 23 mm Hg, pO2 226 mm Hg, bicarbonate 8.6 mEq/L, base excess –18 mEq/L and lactate 12 mmol/L). Pancreatic enzymes were in the normal range.

An urgent CT scan with intravenous contrast was performed, showing periportal edema and a small amount of intraperitoneal fluid, all of them nonspecific findings of a possible hepatitis, cholangitis or pancreatitis but inconclusive as to determining the origin of infection.

Upon admission to the Intensive Care Unit (ICU), he presented a septic shock and multiorgan failure with a calculated SOFA score of 15. He was promptly sedated and intubated at the ICU, and aggressive fluid replacement, noradrenaline infusion (mean doses 4 mcg/kg/min) and renal replacement therapy were initiated. The suspected infection site was either abdominal or the left-arm wound. Given the discrepancy of the findings from the laboratory and imaging studies, the family was reinterviewed, revealing that the patient had been bitten by a dog 24 h prior to the initiation of symptoms. The species was a Dogo Argentino who had his vaccination schedule up to date.

On this basis, treatment with clindamycin, linezolid, and meropenem was initiated, with the later addition of penicillin. Microbiological confirmation of a bacteremia caused by C. canimorsus was obtained in blood cultures, although no evidence of infection in the wound exudate was found, and targeted antibiotic therapy was switched to amoxicillin-clavulanate plus adjuvant levofloxacin.

During the first week at the ICU, the patient continued to present multiorgan dysfunction, evidenced by neurological impairment, hemodynamic failure, cardiogenic shock, anuric renal failure, liver failure, hematological failure and persistence of DIC. Septic myocardial depression was diagnosed by transthoracic ultrasound evidencing a depressed LVEF (left ventricle...
ejection fraction) of 15% without associated pericardial effusion, and non-dilated right ventricle which required dobutamine perfusion at 4 mcg/kg/min for the first 10 days, until full recovery of LVEF, assessed by daily ultrasound. He also presented an acute respiratory distress syndrome on the 10th day after admission, with a PaO2/FIO2 ratio of 150–200, and the need of long-term ventilation requiring a tracheostomy and drainage of bilateral pleural effusion (initially a hemothorax which evolved to transudate). Digital ischemia was also present in both hands, as another sign of DIC and hypoperfusion.

During hospitalization, the patient underwent a progressive clinical improvement both of the multiorgan failure as well as blood test values, until weaning from mechanical ventilation and decannulation was achieved on the 30th day. The patient had been on inotropic vasopressor drugs for the first 10 days so that kidney function progressively improved until discontinuation of renal replacement therapy was possible on the 20th day after admission.

The dog bite injuries initially worsened after admission becoming swollen and erythematous with signs of cellulitis and necrotic areas but evolving favorably after debridement (Fig. 2). A total of 35 days after ICU admission, the patient was discharged.

Discussion

Most C. canimorsus infections in humans are caused by wounds inflicted by domestic animals, although cases in which no traumatic injuries are evidenced have also been documented [5]. Its virulence relies on its ability to evade the immune system in the early stages of infection, triggering a much less powerful immune response [1]. The incubation period is on average 5–7 days, and most cases take place in males aged 50–70 years [8]. Clinical suspicion is essential for its diagnosis, especially in high-risk patients, such as our splenectomized patient [3–7]. As we have described, microbiological isolation in wound cultures is very rare due to a decreased sensitivity, and the bacteria is usually isolated in blood cultures instead [9].

The most common clinical presentation includes cold-like symptoms, such as fever, intense myalgias, general malaise, gastrointestinal manifestations such as abdominal pain, vomiting and diarrhea, dyspnea or headache [5]. Severe cases occasionally present with sepsis, meningitis, osteomyelitis, endocarditis, pneumonia, ocular infection, purulent arthritis, disseminated intravascular coagulation or fulminant purpura [5–9]. Mortality and morbidity rates are higher in the setting of sepsis, increasing up to 30% [4, 9].

A long-course antibiotic regime with either imipenem, clindamycin, linezolid, tetracycline, or chloramphenicol is recommended, and should be administered for several weeks [8, 10, 11]. Extended-spectrum beta lactamases are increasingly frequent amongst this group of bacteria, so that a broad-spectrum antibiotic should be the initial choice, de-escalating after obtaining microbiological results and after reassessing clinical response. Blood cultures may however take an average of 6 days to become positive, Capnocytophaga being a slow-growing bacteria.

In summary, clinical suspicion of a Capnocytophaga spp. infection is mandatory when establishing the differential diagnosis of a septic shock of unknown origin, especially in cases of a previous contact history with a dog and/or cat, and even more so in high-risk patients.
Statement of Ethics

Written informed consent was obtained from the patient so as to publish this case report and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Guillermo Jiménez-Álvarez: collecting clinical case data, writing text, reviewing bibliography. Sonia López-Cuenca: reviewing bibliography, reviewing text. Belén Quesada-Bellver: obtaining informed consent, obtaining images.

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Fig. 1. a, b Physical examination revealed no abnormality, except for the presence of a traumatic wound on the left arm, in the form of two 1-cm-long lacerations outlined in black, which appeared to be the only source of infection.

Fig. 2. a, b The dog bite injuries initially worsened after admission becoming swollen and erythematous with signs of cellulitis and necrotic areas but evolving favorably after debridement.