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Pasteurella multocida septic shock in an immunocompromised woman

D. Larnè[1], F. D'Andrea[1], A. Facciolà[1], I. A. Paolucci[1], M. Ceccarelli[1,2], E. Venanzi Rullo[1,2], G. F. Pellicanò[3]

[1]Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy
[2]Department of Pathology and Laboratory Medicine, School of Medicine, University of Pennsylvania, Philadelphia, PA, USA
[3]Department of Human Pathology of the Adult and the Developmental Age "G. Barresi", University of Messina, Messina, Italy

ABSTRACT:

Pasteurella multocida is a Gram-negative coccobacillus that resides in the gastrointestinal tract of many animals as part of the indigenous flora. It is responsible for a zoonotic disease. Transmission of *Pasteurella* spp can happen after contacts with both wild and domestic animals, especially cats and dogs. Usually, human infection is a result of animal bites or scratches. We describe a case of a septic shock in a 75-year-old immunocompromised woman with positive blood culture for *P. multocida*, successfully treated with a combination of meropenem, doxycycline and ceftobiprole.

Keywords: Pasteurella multocida, Septic shock, Zoonosis, Cat bite.

INTRODUCTION

Pasteurella multocida is a frequent commensal of oropharyngeal and gastrointestinal tracts of many vertebrate species, especially cats and dogs. It can cause a wide range of diseases, including haemorrhagic septicaemia (HS) in ungulates, fowl cholera (FC) in avian species, atrophic rhinitis (AR) in pigs, and rhinitis in rabbits[1,2]. These bacteria have several virulence factors, including capsular lipopolysaccharide (LPS), a cytotoxin, a hemagglutinin, adhesins and iron acquisition proteins and they are also a common cause of bite-associated soft-tissue infections in humans, especially after the bite of cats and dogs[2-4]. Cats and dogs are responsible for about 90% of the animal bites requiring medical attention; of these, 3-18% of dog bites and 28-80% of cat bites become infected[5]. *P. multocida* is the most common organism isolated from dog-bite and cat-bite wounds and it is identified in 50% and 75% of bites, respectively. After the bite, patients can develop signs of infection within the first 24 hours of exposure. In immunocompetent subjects, the infection typically results in cellulitis, lymphangitis or abscess[6]. However, it is well known that these pathogens can cause, in immunocompromised subjects and/or in patients with chronic predisposing conditions, more serious infections, such as pneumonia, peritonitis, UTI, prosthetic joint infection, bacteremia, meningitis, septic shock or even death[7-12].

The purpose of this case report is to highlight the role of *P. multocida* as important pathogen in immunocompromised patients and to evaluate the efficacy of a prompt antibiotic treatment in the resolution of the septic shock induced by this microorganism.

CASE REPORT

We present the case of a 75-year-old woman admitted to the Infectious Disease ward of the "G. Martino" Messina University Hospital (Messina, Italy) for fever (37.3°C), hypotension (93/57 mmHg) and drowsiness arisen 12 hours before.

The patient was tyroidectomized for nodular pathology and consequently treated with levothyroxine. Moreover, she had a history of breast cancer, treated with quadrantectomy four years before. At the moment

Corresponding Author: Damiano Larnè, MD; e-mail: damianolarne@yahoo.it

of the admission, the patient was affected by colorectal cancer. She was treated with surgical resection and adjuvant chemotherapy (aCT) with FOLFOX regimen (Folinic acid, Fluorouracil, Oxaliplatin). The last CT cycle occurred about two weeks before the admission to our ward. Moreover, one week before admission, she referred to the emergency room for the bite of a stray cat on her left foot. Treatment of the bite consisted in stitches, periodic dressings and amoxicillin/clavulanic acid 875/125 mg bis in die (bid), for 7 days.

At the ER, the patient underwent a brain CT scan and a chest X-Ray at the Emergency Room (ER), which resulted negative for cerebrovascular injuries and pulmonary opacities, respectively. The laboratory tests highlighted a low White Blood Cell (WBC) count of 3,600/mm^3 (73% of neutrophils), low platelet count (PLTS) 81,000/mm^3, Potassium (K) 2.9 mEq/L, Creatinine 0.8 mg/dl (normal values < 1.2 mg/dL), C Reactive Protein (CRP) 4.6 mg/dL (normal values < 0.5 mg/dL) and Procalcitonin (PCT) 163 ng/mL (normal values < 0.05 ng/mL).

Upon admission, we rapidly performed blood cultures, started fluid therapy with physiological solution, and stopped the previous antibiotic treatment turning it in a broad-spectrum one, including doxycycline (100 mg bid), meropenem and ceftobiprole according the renal function. An intravenous treatment for hypokalemia was also started, until normalization of the values on the 10th day of admission.

After two days, she had a worsening of renal function (creatinine 2.2 mg/dl, eGFR 21 mL/min) with refractory hypotension (78/46 mmHg) for which, following the advice of anesthesiologists, we started the administration of vasoactive amines (dopamine).

Due to anemia and thrombocytopenia (Hb 7.1 g/dL, minimum PLTS 21,000/mm^3) a consultation with the hematologists was required. The patient underwent two blood, platelet and Fresh Frozen Plasma (FFP) transfusions. Moreover, we started steroid therapy (methylprednisolone, 20 mg per day) that was gradually suspended after 7 days.

The general conditions of the patient were progressively worsening. The onset of respiratory failure, made necessary the administration of high flow oxygen with Non-Invasive Ventilation (NIV) (7 liters/min). On the fifth day of hospitalization, positive blood culture for *P. multocida* was obtained. The isolated organism was sensitive to all the tested antibiotics (Table 1), but we decided to continue the initial antibiotic therapy until discharge. Progressively, her general conditions improved, and multi-organ failure gradually resolved. We discharged the patient after 21 day in good clinical conditions, vigilant, collaborative, oriented in time and space, afebrile, without the need of oxygen therapy, with a normal white blood cells count (WBC 5,000 mm^3 with 54% of neutrophils), PLTs 100,000/mm^3, a normal kidney function (creatinine 0.5 mg/dl) and negative infection indexes (CRP 0.50 mg/dl and PCT 0.25 ng/ml).

Table 1. Blood culture susceptibility testing results for *Pasteurella multocida*.

ANTIBIOTIC	MIC	RSI
Cefepime	<= 0.12	S
Cefotaxime	<=0.25	S
Ceftazidime	0.25	S
Ciprofloxacin	<=0.06	S
Meropenem	<=0.25	S
Piperacillin/tazobactam	<=4	S

DISCUSSION

P. multocida infection could be an important complication especially if it is a consequence of a cat bite, due to the depth of wound caused by cats' teeth. Infection can result in a number of local complications such as necrotizing fasciitis, septic arthritis, osteomyelitis or, less commonly, in systemic diseases characterized by septic shock, endocarditis and meningitis.

Complications have been reported in "at-risk" categories such as infants, pregnant women, and immunocompromised patients (people living with HIV, patients in treatment with steroids or chemotherapy, transplanted patients)[13].

In general, the microorganism is very sensitive to β-lactam antibiotics, but some β-lactamase-producing isolates have been reported and this is the reason why empiric treatment is recommended with β-lactam/β-lactamase combinations, such as ampicillin/sulbactam or amoxicillin/clavulanic acid[14]. The second and third generation cephalosporins, tetracyclines, co-trimoxazole and fluoroquinolones represent an alternative treatment showing good activity against *P. multocida*.

Concerning the management of bites, there is a consensus for dividing the patients into low- and high-risk groups depending on the cause and location of the injury and the patient characteristics, but no evidence-based guidelines are currently available. However, it is well known that the quality of the primary medical care has a better result on the long-term functional and aesthetic outcome. Both patients and physicians often undervalue the gravity of smaller bites, especially the cat bites, because punctate skin lesions may cover the real depth of the injury.

The treatment includes local therapy, surgery and infection prophylaxis. The local therapy consists of cleansing of the wound (e.g., with 1% organic iodine solution), irrigation with saline solution, debridement of necrotic tissue, primary wound suture or its healing by second intention and limb immobilization. Infection prophylaxis includes the immunization (tetanus and rabies) and antibiotic therapy[15]. The suture of facial wounds is recommended while, with regard to wounds in the limbs, the existing recommendations are not concordant yet[16,17]. Moreover, the authors agree that the 6- to 8-hour time limit for primary suturing can be prolonged to 12 hours or longer. Several studies have shown that infection does not occur most frequently in sutured wound than in the one that heals by second intention[18,19]. Conversely, primary closure is not indicated for the wounds with deep inoculation of pathogens (typically cat bites), bite wounds

of the hands and human bites (except for facial ones)[15]. Universal prophylaxis with antibiotics is not recommended. However, despite the lack of the evidence, most experts recommend starting the antibiotic therapy for 3 to 5 days if the wounds are deep, especially for those occurred in certain critical body areas (hands, feet, areas near the joints, face, genitals). Moreover, it is recommended for people having a high risk of infection or having implants, e.g., or artificial heart valves[20-22]. There is no need of antibiotic treatment if the bite occurred more than 24 hours and there are no clinical signs of infection[22]. The antibiotic treatment includes aminopenicillin + a beta-lactamase inhibitor (oral, intravenous), piperacillin/tazobactam (intravenous), carbapenem (intravenous), cefotaxime + metronidazole. Clindamycin, macrolides, isoxazyl penicillins, first generation-cephalosporins, and aminoglycosides are ineffective for the treatment of *P. multocida* and should not be used[15]. The duration of antibiotic treatment depends on the severity of the clinical condition, the spread of the infection, the isolated pathogen and the treatment response. Along with the clinical findings, the CRP value is a useful marker of treatment efficacy. In our paper, we report a *P. multocida* infection in an immunocompromised woman bitten by a cat. At the admission, the conditions of the patient were critical and she had all the symptoms of a septic shock (hypotension, drowsiness, fever and a rapid deterioration in renal function). The antibiotic therapy started for prophylaxis at the ER did not have any effect, leading to a rapid worsening of her clinical condition. However, the broad-spectrum antibiotic therapy resulted in a regression of the septic shock and in a complete restoration of clinical conditions. Probably, the amoxicillin/clavulanic acid alone has failed because of the critical conditions of the patient, immunocompromised and suffering from many co-morbidities, which led to a rapid proliferation and general spread of bacteria. Moreover, it is possible that infection had polymicrobial etiology even if in blood culture only *P. multocida* was isolated. For these reasons, we decided not to carry out the de-escalation of the antibiotic therapy continuing with three drugs until discharge.

CONCLUSIONS

Cat bites and scratches can transmit many pathogenic bacteria and cause deep wounds. Usually, these lesions are treated with a local approach. Only in few cases, patients require an appropriate systemic antibiotic therapy.

However, in elderly patients, especially when immunocompromised and affected by co-morbidities, cat bites can lead to local complications or even to sepsis. A higher awareness of this issue may be important in order to prevent life-threatening conditions after pet bites[23], especially in the above-mentioned "at-risk" people. If fever occurs after cat bite or scratch, it is important considering this possible complication and hospitalization of the victim may be required.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

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