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Pasteurella multocida infection in a cirrhotic patient: case report, microbiological aspects and a review of literature

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ABSTRACT

Pasteurellosis is a zoonosis often caused by cat or dog bites or scratches, or by direct exposure to their secretions. *Pasteurella multocida* is the main pathogen involved in infections through domestic animal bites; generally a local infection characterized by its particular virulence with consequent rapid onset. Serious infection has also been reported in persons affected by comobirdity without domestic animal bite injuries. Here we report the case of a woman with lower limb exudating vesicular skin ulcers affected by liver cirrhosis, bilateral knee arthritis, septicemia with positive blood culture and synovial fluid culture for *Pasteurella multocida*. The etiology of *Pasteurella multocida* must be borne in mind in cases of sepsis in immunodeficient individuals, such as the cirrhotic patient, as well as exposure to domestic animals.

Key words: pasteurella multocida, liver cirrhosis, septic arthritis, bacteraemia, skin ulcers

INTRODUCTION

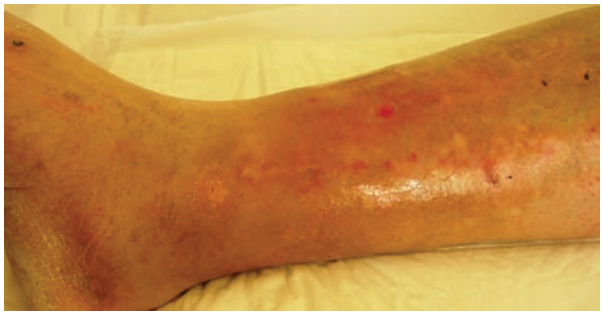
The *Pasteurella* species, above all the *Pasteurella multocida*, is widespread throughout the world, forming a part of the normal gastrointestinal flora and the upper respiratory tract of wild and domestic animals, (especially cats and dogs). It is the main pathogen involved in animal bite or scratch infections [1-3]. Severe systemic and invasive infections with a fatal outcome are rather rare in literature. We report the case of a woman affected by liver cirrhosis with exudating erythematous skin ulcers of the lower limbs, bilateral knee arthritis, septicemia with positive blood culture and synovial liquid culture for *Pasteurella multocida*. Moreover, there is a a brief review of literature and a microbiological approach.

CASE PRESENTATION

We present the case of a 69-year-old woman, who was referred to our department at the end of April 2007 due to a febrile state and bilateral swelling of the knees, accompanied by pain and functional impotence. A medical history showed exotoxic liver cirrhosis (negative viral and immunological serology with an alcohol abuse tendency) diagnosed in October 2005, when the patient had first been admitted to our department for *Methicillin-Sensitive Staphylococcus Aureus* sepsis, cellulitis of the right forearm and lower limb dermatitis.

In February 2006, the patient was once again referred to our department for spondylodiscitis of L3 and a new clinical picture of *Methicillin-Sensitive Staphylococcus Aureus* sepsis, isolated by blood culture. In July 2006, on resolution of the infection, the patient underwent chemoembolization of a hepatocellular carcinoma node with a good outcome. At the beginning of April 2007, the patient noticed a worsening of lower limb dermohypodermitis, characterized by an increase of lymphedema and the appearance of exudating erythematous skin ulcers (*Fig. 1*). Furthermore, an increasingly painful swelling of the knees with functional impotence, predominantly in the left knee, had been evident for 5 days. On admission, the patient was feverish (39°C auricular temperature), in a poor general condition and in distress. Other signs and symptoms included a widespread jaundiced skin colour, enlargement of the liver and spleen, a slight ascitic leak, a systolic murmur at an

Figure 1. **Exudating erythematous skin ulcers.**



aortic focus 3/6 with no clinical portosystemic encephalopathy (Child Pugh class B, score 8).

Laboratory tests evidenced macrocytic anaemia (Hb=10.6 g/dL, MCV=101), a low platelet count (88.000 µL), slight chronic renal failure (creatinine=1.7 mg/dL, clearance calculated according to Cockroft-Gault=40 mL/min), high inflammation indices (ESR=75 mm, C reactive protein=170 mg/L, procalcitonin=3.44 ng/mL), deranged hepatic cytolysis indices (ALT=55 U/L, AST=67 U/L, GGT=84 U/L) an increase in total bilirubin (3.8 mg/dL) and in direct bilirubin (1.3 mg/dL) (probable chronic haemolytic picture linked to enlarged spleen), prolonged prothrombin time (INR 1.67).

After blood culture and bilateral knee arthrocentesis, empiric antibiotic therapy was established with 3 doses of 12 mg/Kg intravenous teicoplanin, each dose taken at 12 hour intervals (load dose), then every 24 hours with further halved doses based on renal function from the fourth day. After 3 days, 2 blood cultures and 2 cultures of purulent synovial fluid were positive for *Pasteurella multocida.* Data from literature and an antibiogram were used to begin antibiotic IV therapy with amoxicillin clavulanate (2.2 g every 12 hours) and ciprofloxacin (200 mg every 12 hours), with the dose adapted to creatinine clearance values.

For the next few days, a repeated bilateral arthrocentesis was performed to reduce knee arthritis symptoms owing to the effectiveness of the procedure described in literature [4]. After initial clinical improvement, renal function progressively worsened (creatinine=2.8 mg/dL, clearance=25 mL/min), accompanied by anaemization (Hb=7.6 g/dL, Ht=23%) with no signs of gastro-enteric bleeding with consequent repeated blood transfusions. Cardiac function also worsened as episodes of paroxysmal atrial fibrillation occurred with a high degree of penetrance and progressive congestive cardiac failure.

On detection of a recent aortic systolic murmur, a transthoracic electrocardiogram was performed, excluding endocarditic vegetation, since the trans-oesophageal approach was unsuitable due to the presence of gastro-oesophageal varices. The patient's renal function worsened, therefore, she was transferred to the Nephrology Unit to initiate haemodialysis therapy. Over the course of the next few days, the patient presented a clinical picture of disseminated intravascular coagulation (DIC), confirmed by increased D-Dimer values, fibrinogen consumption and antithrombin III, as well as further prolonged clotting time. Moreover, the patient showed initial signs of portosystemic encephalopathy, and she died of multi – organ failure (MOF) one month after admission.

DISCUSSION

Pasteurella multocida is a small gram-negative non–spore-forming facultative anaerobe coccobacillus, widespread throughout the world, commonly colonizing the oropharynx and the gastro-intestinal tract of healthy domestic animals, above all cats (50-90%), dogs (50-70%), and pigs (50%) [1-3]. The bacterium was first discovered by Loius Pasteur in 1881 as an etiological agent of fowl cholera [5]. The *pasteurella multocida* species is further subdivided into four subspecies (*multocida, gallicida, septica, tigris*) in 5 distinct serogroups *(A, B, D, E, F)* based on their capsular antigens, and 16 serotypes on the basis of their polysaccharide antigens.

Blood specimens and arthocentesis fluid were sent to the Microbiology and Bacteriology Service in the Analysis Laboratory in our hospital, where they were inoculated into aerobic and anaerobic culture media (Bactec 9240, Necton Dickinson). Enrichment cultures FOS containing NAD and hemine were added. Culture bottles (BD Bactec plus + Anaerobic/F) used by our laboratory contain Soy Resin Casein Digest Broth which allows neutralization of possible antibioticotherapy in use at the time of blood taking. Detection of bacterial growth during the liquid phase occurs by a fluorimetric method. TTD (time to detection) was 4.5 hours for all the samples. Positive culture bottles thus underwent:

- gram staining and slide viewing (Gram negative coccobacillus with characteristic bipolar staining, whereby they resembled a closed safety pin);
- culture on Columbia agar added to 5% sheep blood, MacConkey agar and chocolate blood agar. Growth of mucoid colonies are obtained only on Columbia agar with a typical smell of mould since *Pasteurella multocida* only grows in media containing blood or hemine;
- incubation at 35°C for 18 hours;

Definitive identification of the bacterium was made by the Phoenix automated identification system. A mobility test showed the micro-organism to be immobile with positive oxydase and catalase enzymes. The MIC (minimum inhibitory concentrations) of the various antibiotics were calculated using the E-test in accordance with the Clinical and Laboratory Standards Institute (CLSI) criteria (*Tab. 1*) [6]. Pasteurellosis is a zoonosis caused by dog or cat bites or scratches or by direct exposure to their secretions. It manifests mainly with purulent wound exudate, cellulitis and/or subcutaneous abscesses [7,8]. More serious clinical manifestations are rare and include sepsis, mono or polyarticular arthritis, osteomyelitis, endocarditis, pneumonia, meningitis and peritonitis [8]. The micro-organism is the main pathogen responsible for domestic animal bite infections and is characterized by its particular

Table 1. **Antibiogram with sensibility spectrum and MIC (μg/mL).**

ANTIBIOGRAM	RSI	MIC
Penicillin	S	0.38
Amikacin	S	0.38
Cefepime	S	0.38
Ceftazidime	S	0.38
Ciprofloxacin	S	0.016
Levofloxacin	S	0.012
Gentamicin	I	6

virulence with consequent rapid onset of infection. However, at times, the infection may occur without any apparent animal exposure [8,9]. Although the incidence of bacteremia in patients with skin infections is underestimated, it still remains not well known, whereas the infection site is detected in over 80% of cases of confirmed bacteremia [4].

A Spanish retrospective study encompassing the period of 1994-2001, revealed a low incidence of bacteremia from *Pasteurella multocida*. Out of 31 samples, which were positive for the micro-organism, only 5 (16%) consisted of a blood culture, performed in immunodeficient patients over 50 years of age, with important co-morbidity and a confirmed exposure to domestic animals. The Authors, therefore, suggested greater hygienic care for these patients [10].

Invasive forms of Pasteurella infection usually occur more frequently in patients with a compromised immune system, such as chronic renal failure, cancer, or liver cirrhosis. In particular, a greater susceptibility to this type of infection by cirrhotic patients is attributed to a compromised reticuloendothelial system and a portosystemic shunt [4].

In literature, about 100 cases of major infection, mostly individual cases, by *Pasteurella multocida* are reported. A high proportion of the latter refer to septicemia in patients with multiple comobirdity whether or not linked to spontaneous bacterial peritonitis with a clinical picture of liver cirrhosis, above all exotoxic. Moreover, some cases of pulmonary infection, meningoencephalitis, septic arthritis and aortic valve endocarditis are reported [11-17]. Most of the patients described were exposed to domestic animals (cats or dogs), and not all of them had been scratched or bitten. In 3 cases of septic shock in subjects with liver cirrhosis, due to alcohol abuse there was a likelihood of contamination with cat saliva through lower limb skin ulcers [18].

To the best of our knowledge, our case is the first, besides the other 3 reported in literature, to be characterized by esotoxic hepatic cirrhosis, vesicular dermatitis with skin lesions of the lower limbs (probably transmitted by dog saliva), septicemia (2 positive blood cultures), and polyarticular arthritis (positive culture). Analysis of the salivary secretion of the dog, which the patient had been exposed to for about six months, allowed the isolation of the micro-organism in question. The patient's general immunodeficient state of health was confirmed by her specific susceptibility to infectious events during the previous two years (two hospitalizations for S*taphylococcus aureus* and the presence of spondylodiscitis). The patient's general immuno-compromised state and terminal renal failure, as well as the ensuing antibiotic therapy adjustment, further contributed to the unfavourable outcome. As far as antibiotic therapy is concerned, sensitivity tests for the *Pasteurella* species have recently been standardized by the National Committee for Clinical Laboratory Standards [19]. For isolates from bites wounds, routine testing is usually not necessary. Multiple organisms are often present in these specimens; therefore, empiric therapy directed towards these organisms is generally effective for *Pasteurella multocida*, as well. Testing of isolates from normally sterile sources (blood cultures, deep tissue, implanted prosthetic devices) and also respiratory specimens may be warranted, especially in immunodeficient patients [20].

Pasteurella multocida and the other species are typically penicillin sensitive yielding a zone inhibition of ≥ 25 mm when tested with a McFarland 0.5 inoculum suspension on a Mueller-Hinton agar plate. However, micro-organisms producing lactamase of the Pasteurella species are rarely reported [20]. Besides penicillin, other antimicrobial agents to be tested are amoxicillin clavulanate, second and third generation cephalosporins, fluorochinolones, tetracyclines, macrolides, and trimethoprim-sulfamethoxazole [4, 20, 21]. Moreover, there are recent reports on the same effectiveness of aztreonam in patients who are particularly allergic to various antimicrobial drugs [13, 22].

CONCLUSIONS

This case study draws attention to the need for cirrhotic patients to adopt greater hygienic measures in order to avoid the least possible exposure to domestic animals, above all cats and dogs which represent the principal reservoir for *Pasteurella multocida* infections. From a clinical point of view, although the likelihood of *Pasteurella multocida* transmission through cat or dog exposure is infrequent, it is to be borne in mind as a cause of infection in patients affected by liver cirrhosis, immunodeficiency and with recent-onset arthritis.

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