*Case Report*

**SAGE Open Medical Case Reports**

SAGE Open Medical Case Reports
Volume 5: 1–5

DOI: 10.1177/2050313X17748286
journals.sagepub.com/home/sco
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# *Pasteurella* infections in a tertiary centre – from cellulitis to multiple-organ failure: Retrospective case series

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**Abstract**

The purpose of this article is to review the clinical features of pasteurellosis in a tertiary centre over a period of 4½ years. We have identified eight cases of *Pasteurella multocida* and one case of *Pasteurella canis* infection, with a large diversity of clinical pictures and outcomes. All patients were elderly and/or immunocompromised and 55.6% reported animal exposure. Soft tissue infections were the most prevalent (55.6%), followed by pneumonia (22.2%) and sepsis (22.2 %). All isolates were susceptible to beta-lactam antibiotics using in vitro sensitivity testing. The overall mortality was 33.3%, which occurred in patients with no evidence of animal contact.

**Keywords**

Infectious diseases, *Pasteurella* infections, zoonoses, wound infection, sepsis, immunosuppression, aged

Date received 9 August 2017; accepted: 22 November 2017

## Introduction

The majority of emerging and re-emerging infectious diseases are zoonotic in nature.[1,2] Therefore, it is critical that clinicians are aware of the potential for human acquisition of animal diseases. Like other Pasteurellaceae, *Pasteurella* species are ubiquitous among normal microbiota of animal populations.

*Pasteurella* spp are facultative anaerobic Gram-negative coccobacilli, which colonize the oral and nasopharyngeal cavities, as well as the upper respiratory tract of various domestic and wild animal species, particularly cats and dogs. *Pasteurella multocida* (subsp multocida, septica and gallicida), *Pasteurella canis, Pasteurella stomatis* and *Pasteurella dagmatis* are responsible for the majority of human infections.[3]

Pasteurellosis is a zoonosis that typically occurs after animal exposure, through animal scratches or bites, licks on skin abrasions or contact with pets' mucous secretions. It frequently involves the skin and soft tissues, resulting in the rapid appearance of cutaneous swelling and inflammation, ranging from cellulitis and bloody or suppurative exudates with subcutaneous abscesses to septic arthritis and osteomyelitis.[4,5] In the more serious cases, often unrelated to animal exposure, pasteurellosis can promptly progress to life-threatening invasive infections, especially among the elderly and immunocompromised, like fulminant sepsis and other complications such as endocarditis, peritonitis and meningitis.[4,6] The respiratory tract is the second most common site of infection, usually in the setting of chronic pulmonary disease, manifesting in a wide variety of respiratory infections as rhinosinusitis, tracheobronchitis, epiglottitis, consolidating pneumonia, empyema and lung abscesses.[5] The most common risk factors for *Pasteurella* bacteraemia are liver dysfunction and diabetes mellitus.[7–9] The authors report the clinical features, microbiological characteristics and outcomes of *Pasteurella* infections in patients admitted to a tertiary centre between 2011 and 2015.

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## Materials and methods

This retrospective study was conducted at a 1500-bed tertiary teaching hospital centre in Lisbon, Portugal. The microbiology laboratory information system was searched for all patients over 18 years of age with positive *Pasteurella* spp. isolates from 1 January 2011 to 31 May 2015. The demographic and clinical data were reviewed, including age, sex, history of present illness, medical comorbidities, animal exposure history, microbiological results, antimicrobial susceptibility, treatments and outcomes. Identification of *Pasteurella* was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometer (MALDI/TOF). Antibiotic susceptibility was determined according to Clinical and Laboratory Standards Institute (CLSI) guidelines[10] until 2014 and after 2014 following The European Committee for Antimicrobial Susceptibility Testing (EUCAST) recommendations.[11]

### *Case series*

The database search revealed 12 patients with evidence of infection caused by *Pasteurella* spp. during the period from 1 January 2011 to 31 May 2015. Three patients were excluded because of incomplete medical records. The average age of the nine included patients was 71.7 years (extremes 59–87 years, median age 73 years), and seven (77.8%) were women (Table 1). Most of the patients (77.8%) had been hospitalized, and the other two, with mild local disease, received ambulatory care.

The majority of the infections was caused by *P. multocida* (eight patients), while *P. canis* was isolated in only one case. Polymicrobial infection was verified in two cases. Besides *P. canis, Klebsiella pneumoniae* was isolated from a sample of exudate from a diabetic foot, and along with *P. multocida*, methicillin-sensitive *Staphylococcus aureus* (MSSA) was identified from the sputum sample in a patient with healthcare-associated pneumonia.

All of the isolated *Pasteurella* species were susceptible to the tested beta-lactam antibiotics (Table 1), in most of the cases penicillin or ampicillin. Most of the isolates were also susceptible to quinolones, tetracycline and trimethoprim-sulfamethoxazole.

Five patients reported animal contact (55.6%), four of them with a cat scratch or bite, and one referred frequent exposure to both cats and dogs, without known trauma.

In this cohort, the most common comorbidity was diabetes mellitus, in four patients (44.4%). Two patients had alcoholic liver disease and one of them with documented cirrhosis. Heart failure was present in two cases. Two patients suffered from haematologic disorders, one from pancytopenia and the other from thrombocytopenia and macrocytic anaemia, devoid of documented cause or origin. Three of the patients in the cohort did not present with any identified conditions causing immunosuppression, other than their advanced age (i.e. over 70 years old).

Five patients presented with soft tissue infections, four of which had a history of a cat bite or scratch. In three cases of local disease, *Pasteurella* was isolated from local wound cultures, and surgical intervention (drainage or debridement) was necessary. Among them, the one patient without any known animal contact developed a serious soft tissue infection with abscess formation and osteomyelitis on a background of a diabetic foot. One case of necrotizing fasciitis was also observed. The two other patients with soft tissue infection, in the absence of abscess development, did not require surgical treatment. One of them presented with leg ulcer, and *P. multocida* infection was proven by skin biopsy. In the other case, the patient presented with cellulitis, and *P. multocida* was isolated from blood cultures. All the patients with local infection recovered and none of them required intensive care unit admission.

Two patients included in this study were diagnosed with pneumonia. One of them was a 60-year-old woman with a history of diabetes mellitus, heart failure and exposure to cats and dogs, with no evidence of recent wounds. *P. multocida* was isolated from blood cultures. She presented parapneumonic pleural effusion and underwent thoracocentesis, but the pleural fluid was a transudate with no isolation of pathogens. She recovered and was discharged after 2 weeks of treatment with intravenous ceftriaxone. The other patient was a 78-year-old woman. Her comorbidities included macrocytic anaemia and thrombocytopenia of unknown origin, atrial fibrillation, and severe chronic venous disease, with no known animal contact. She was admitted to a surgical ward with infected venous ulcers of both lower extremities with no specific pathogen identified in wound cultures. After empiric treatment with ertapenem and during preparation for discharge, her clinical condition deteriorated, with refractory septic shock and respiratory failure that led to the patient's death. The blood cultures yielded methicillin-resistant *Staphylococcus aureus* (MRSA), and from the sputum cultures, *P. multocida* and MSSA were isolated.

We identified two other cases of septic shock caused by *P. multocida*, which ensued in the two younger patients of this cohort, both 59 years old, but with multiple and severe comorbidities. Neither had known animal contact. One of them, a woman, was diagnosed with alcoholic liver disease, ischaemic heart disease, chronic kidney disease (mesangial proliferative glomerulonephritis), myelodysplastic syndrome, chronic venous disease, neurofibromatosis type 1 and scleromyxedema. She presented to the emergency department with vomiting, diarrhoea and epigastric pain. Purpuric rash was noted on her left thigh, which promptly spread to the abdominal wall and to the flank area with no signs of circulatory compromise (no skin samples were obtained for bacteriological analysis). Blood cultures collected on admission evidenced *P. multocida* bacteraemia. The patient rapidly developed septic shock and multiple-organ dysfunction and, despite ventilator and circulatory support and broad-spectrum empirical antibiotic therapy, died 3 days after the first symptoms appeared.

**Table 1.** Patient characteristics, clinical features and microbiological data.

| Patient | Age (years), sex | Species | Specimen source | Comorbidities | Animal exposure | Hospital setting | Clinical presentation | Required ICU | Antibiotic susceptibility | Surgical intervention | Outcome | Polymicrobial infection |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | 59, F | *Pasteurella multocida* | Blood | Alcoholic liver disease, heart failure, chronic kidney disease, myelodysplastic syndrome, venous insufficiency, neurofibromatosis type 1 | Unknown | Inpatient | Septic shock | Yes | Amoxicillin/clavulanic acid, piperacillin/tazobactam, cefotaxime, levofloxacin, ciprofloxacin, trimethoprim/sulfamethoxazole | No | Died | No |
| 2 | 59, M | *P. multocida* | Blood | Alcoholism, heart failure (Class III NYHA), mechanical aortic valve, COPD | Unknown | Inpatient | Septic shock | Yes | Penicillin, ampicillin, amoxicillin/clavulanic acid, ceftriaxone, tetracycline, trimethoprim/sulfamethoxazole | No | Died | No |
| 3 | 60, F | *P. multocida* | Blood | Diabetes mellitus, heart failure, hypertension | Contact with cats and dogs | Inpatient | Pneumonia with parapneumonic pleural effusion | No | Penicillin, ampicillin, ceftriaxone, tetracycline, trimethoprim/sulfamethoxazole | Thoracocentesis | Recovered | No |
| 4 | 72, M | *Pasteurella canis* | Exudate | Diabetes mellitus, venous insufficiency | Unknown | Inpatient | Diabetic foot with ulcer, abscess and osteomyelitis | No | Ampicillin, amoxicillin/clavulanic acid, ceftriaxone, levofloxacin, trimethoprim/sulfamethoxazole | Surgical debridement | Recovered | *Klebsiella pneumoniae* |
| 5 | 73, F | *P. multocida* | Exudate | Hypertension | Cat scratch | Inpatient | Necrotizing fasciitis of hand and forearm | No | Penicillin, ampicillin, tetracycline, trimethoprim/sulfamethoxazole | Surgical drainage | Recovered | No |
| 6 | 78, F | *P. multocida* | Exudate | Diabetes mellitus, hypertension | Cat bite | Outpatient | Abscess of forearm | No | penicillin, ceftriaxone, levofloxacin, trimethoprim/sulfamethoxazole | Surgical drainage | Recovered | No |
| 7 | 78, F | *P. multocida* | Sputum | Venous insufficiency, atrial fibrillation, thrombocytopenia of unknown origin | Unknown | Inpatient | Pneumonia, infected leg ulcer, septic shock | Yes | Oxacillin, gentamicin, erythromycin, clindamycin, tetracycline, trimethoprim/sulfamethoxazole | No | Died | MSSA in sputum, MRSA in blood |
| 8 | 79, F | *P. multocida* | Skin biopsy | Diabetes mellitus | Cat bite | Outpatient | Leg ulcer | No | Ampicillin, ciprofloxacin, tetracycline, trimethoprim/sulfamethoxazole | No | Recovered | No |
| 9 | 87, F | *P. multocida* | Blood | Hypertension, atrial fibrillation | Cat bite | Inpatient | Leg cellulitis | No | Ampicillin, levofloxacin, trimethoprim/sulfamethoxazole | No | Recovered | No |

MRSA: methicillin-resistant *Staphylococcus aureus*; MSSA: methicillin-sensitive *Staphylococcus aureus*.

The other, a male patient, had a history of alcohol abuse with no categorized liver disease, Class III heart failure (New York Heart Association (NYHA)), mechanical aortic valve and smoking-related chronic obstructive pulmonary disease (COPD). He presented with fatigue and fever and met sepsis criteria upon assessment at the emergency department. Consequently, empirical antibiotic, vasopressor therapy and fluid resuscitation were promptly initiated. No skin lesions or other potential access pathways on examination were noted. *P. multocida* was isolated from the blood cultures drawn in the emergency department. The source of infection was not possible to determine as the patient rapidly developed refractory shock with multiple-organ failure and died the day after admission.

The mortality was 33.3% in this cohort, corresponding to the three patients requiring intensive care. All deaths occurred in patients without any known animal bite/scratch.

## Discussion

This retrospective study analyzed the clinical characteristics and outcomes of patients with local or systemic pasteurellosis. All the patients in this cohort were elderly, and/or immunocompromised, with diabetes mellitus being the most prevalent comorbidity. A wide range of clinical pictures were observed, from uncomplicated cellulitis to osteomyelitis, pneumonia and septic shock. Both cases of septic shock that were caused by *P. multocida* had a rapid fatal onset in patients with alcoholic liver disease.

Most of the infections were community-acquired. Only one was nosocomial, in the patient with concomitant MRSA bacteraemia after antibiotic treatment with ertapenem. This study supports the existing literature by indicating that invasive *Pasteurella* infections are severe with high mortality.[12]

Most of the invasive infections occurred in the absence of recognized animal bites or scratches and in patients with severe comorbidities and impaired host defences. None of the deceased patients had any known animal contact. Three of the four cases of bacteraemia occurred in patients with conditions associated with secondary immunodeficiency, such as chronic liver disease or diabetes mellitus. This is consistent with other studies, suggesting that these are the most prevalent comorbidities in patients who develop invasive pasteurellosis and bacteraemia.[4,6,8,9]

In this cohort, there were two patients with respiratory tract infections. In one of the cases, *P. multocida* was the only confirmed pathogen, isolated from blood cultures. The other patient had a polymicrobial infection, as *P. multocida* and MSSA were identified in sputum cultures, MRSA was isolated from blood cultures. It is important to emphasize that this patient had no known history of chronic lung disease, as *P. multocida* might be a commensal organism of the respiratory tract in patients with underlying pleuropulmonary illnesses, yet it should be recognized and treated as a serious pathogen.[13]

In conclusion, clinicians should consider *Pasteurella* species in any patient presenting with soft tissue infection following domestic animal bites or scratches and remember the possibility of this pathogen in cases of sepsis in immunodeficient individuals, even without animal exposure. Our contacts with pets and other domestic and wild animals are unlikely to reduce in the future. Evidence suggests that contacts that result in *Pasteurella* infection can lead to consequences ranging from benign to disastrous. Since the prevalence of *Pasteurella species* is high in the microbiota of domestic and wild animals, it seems prudent to always admit zoonotic transmission as a serious risk for infection.

Broad-spectrum antibiotics that target *Pasteurella*, as well as other Gram-negative and Gram-positive bacteria, are the preferred prophylaxis for animal bites. While *Pasteurella spp* are generally susceptible to several antibiotics, in the case of an animal bite, a polymicrobial infection should be considered, being a combination of amoxicillin and a beta-lactamase inhibitor, clavulanic acid, the empiric therapy of choice in these situations. Alternatively, doxycycline plus metronidazole for patients with penicillin allergies, or clindamycin plus a fluoroquinolone (ciprofloxacin), or trimethoprim-sulfamethoxazole combination for children or ceftriaxone for pregnant women are also suitable.[12,14,15] To prevent severe invasive infections, chronically ill individuals should maintain appropriate hand hygiene after handling pets, aim for appropriate initial treatment of skin lesions and avoid direct pet contact with uncovered or open wounds.

### Acknowledgements

All authors contributed equally.

### Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

### Ethical approval

Our institution does not require ethical approval for reporting individual cases or case series.

### Funding

The author(s) received no financial support for the research, authorship and/or publication of this article.

### Informed consent

Informed consent for patient information to be published in this article was not obtained because it is based on anonymous archival data.

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