

## Clinical report

# *Pasteurella multocida* infections in cancer patients

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**Background:** *Pasteurella multocida* is a small, gram-negative coccobacillus, which most commonly causes soft tissue infections due to animal bites or scratches, mainly from cats and dogs. Immunocompromised hosts, such as cancer patients, are more likely to develop systemic complications as a result of *P. multocida* infections.

**Objective:** Retrospectively analyze the medical records of four afflicted patients being managed at Moffitt Cancer Center, Tampa, USA between 1999 and 2009, and careful study for additional 32 cases of *P. multocida* infection among cancer patients with variegated histology found in the current medical literature.

**Methods:** Of 36 subjects, 67% of the patients had been diagnosed with a solid organ cancer, whereas 33% had a hematologic malignancy. Clinical scenarios described fever as the most frequent initial presentation and bacteremia as the most prevalent mode of infection.

**Results:** Forty-seven percent of the patients had experienced some sort of animal contact and 41% showed evidence of skin or soft tissue infection. The status of the white blood cell count, was available in 22 patients (of 36 patients), and 27% demonstrated neutropenia. The survival percentage of the patients with known clinical outcome was 77%.

**Conclusion:** Medical management mostly involved antibiotics with beta-lactams. Atypical scenario of *Pasteurella multocida* infection may involve bites or scratches (specifically from cats or dogs) in a cancer patient presenting with sepsis and accompanied by skin or soft tissue or respiratory tract infection. A high level of suspicion for *P. multocida* as a possible pathogen in cancer patients would facilitate an amelioration in morbidity ameliorating, and timely initiation of specific antibiotics.

**Keywords:** Beta-lactams, infections, malignancy, *Pasteurella multocida*

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*Pasteurella multocida* is a small, non-motile, non-spore forming, gram-negative coccobacillus, which is found in the oral and nasal secretions of a large variety of household pets such as cats and dogs and barnyard animals including cattle, horses, swine and sheep, as well as rabbits and mice. However, since the highest carriage rate occurs in cats (70 to 90%) and dogs (66%), infections in humans generally occur as a result of cat bites or scratches and dog bites [1]. *P. multocida* causes a wide array of presentations, the most common being cutaneous, or soft tissue infections, followed by infections of the lower

respiratory tract, such as pneumonia, empyema and lung abscess. Systemic infections, such as bacteremia, meningitis or peritonitis are also common presentations [2]. Immunocompromised hosts, particularly cancer patients, are more likely to develop the more severe, systemic presentations as a result of *P. multocida* infections [3]. In this report, we described four such cases from the Moffitt Cancer Center in Tampa, USA, and review 32 other previously-reported cases found in the medical literature.

## Methods

An epidemiology report generated at Moffitt Cancer Center between January 1999 and April 2009 identified four cases of *P. multocida* infections. The medical records of the four affected patients were

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retrospectively analyzed for age, sex, underlying malignancy, animal contact, initial presentation, diagnostic culture source, evidence of neutropenia (ANC  $<0.5 \times 10^9/L$ ). Treatment and outcome were also considered. In addition, we undertook a rigorous search of the current medical literature for cases of *P. multocida* infection among cancer patients, focusing on the preceding parameters. We summarize the data in **Table 1**.

## Results

Among the 36 patients with *Pasteurella* infection, 58% were females and 42% were males. The patients varied in age from 18 to 87 years with a median of 64 years. Sixty-seven percent of the patients had a solid-organ malignancy, and 33% had a hematogenous malignancy. Out of the 36 patients, a history of animal contact was verified in only 19 patients and from that subgroup, most patients (89%) were exposed to a cat or dog. Initial clinical presentation was identified in 27 patients and fever was the most common presenting sign (78%) followed by soft tissue involvement (59%), and altered mental status (19%). Diagnosis was made by culture of different specimens, including blood (18 patients or 50%), lower respiratory tract (nine patients or 25%), and skin, soft tissue, and joint fluid (eight patients or 31%). Rare sites of infection included the female genital tract (two patients) and the central nervous system (two patients). Treatment was described in 25 patients and 23 of those received beta-lactam therapy, including penicillins and cephalosporins. Thirteen patients (52%) were treated with penicillins (including natural penicillin, ampicillin, amoxicillin, and piperacillin) and 10 patients (40%) received some type of cephalosporin, cefepime and ceftazidime. The white blood cell count was available in 22 patients out of the 36 patients. In 27% of patients, it was consistent with neutropenia. Although clinical outcome was unknown in ten patients, the survival and mortality rate of the rest of the patients was 77% and 23%, respectively. Out of the six patients that died, five were diagnosed with bacteremia.

## Discussion

*P. multocida* is a small, non-motile, non-spore forming, aerobic and facultative anaerobic gram-negative coccobacillus. This bacteria grows on blood, chocolate, and Mueller-Hinton agar at 37 degrees, but it will not grow on MacConkey's medium [1, 3].

Seventy to ninety percent of cats and 50 to 60% of dogs carry *P. multocida* in their oral or nasal secretions. This organism is also found in the respiratory and digestive tract of horses, cattle, sheep, rabbits and swine as well as wild animals such as rats, mice, reindeer, and monkeys, and in large mammals like buffaloes, lions, and panthers [1, 4]. Kimura et al. [5] proposed that transmission of *Pasteurella* to humans involves close contact with the animal's oral cavity. Therefore, the most common portal of entry of *P. multocida* in humans is through local wound infection after direct animal bites or a scratch, which can deposit the bacteria directly on damaged skin, or after a pet lick on an exposed human mucosal surface [6].

Infections due to *P. multocida* in a normal population have been categorized as: 1) a local infection following an animal bite or scratch that can progress to variegated presentations such as abscess formation, tenosynovitis, septic arthritis and osteomyelitis, 2) an infection of the respiratory tract (pneumonia, empyema and lung abscess), and 3) a systemic infection, for instance, intra-abdominal infections, peritonitis, meningitis and brain abscess [2, 7, 8].

Specific settings such as in elderly patients, and especially those with associated immunosuppressed states from chronic disease or cancer, are at higher risk of more complicated severe infections. The most common chronic medical condition predisposing to *P. multocida* infections is liver cirrhosis [3, 4]. As a corollary *P. multocida* bacteremia is uncommon in the general population, it is diagnosed mostly in immunocompromised populations, mainly in cirrhotics and cancer patients [6]. Similarly, this review, encompassed a substantial number of immunodeficient patients, and unsurprisingly, demonstrated that half of the patients had been diagnosed with bacteremia.

Weber et al. [1] analyzed various *P. multocida* isolates for *in vitro* antibiotic susceptibility and noted that, in general, the antibiotics with the best activity were penicillin G, penicillin V, ampicillin, carbenicillin, ticarcillin, piperacillin and mezlocillin. In addition, second and third generation cephalosporins, tetracyclines and chloramphenicol were also effective. It is worth noting that fluoroquinolones (ciprofloxacin and levofloxacin) are endowed with *in vitro* activity.

Nevertheless, penicillin is the drug of choice to treat *P. multocida* infections in the non-allergic population. However, Jordan et al. [9] reported a case

**Table 1.** Case reports of *Pasteurella multocida* infections in cancer patients from medical literature and from Moffitt Cancer Center and Research Institute (Tampa, USA).

Patient [Reference]	Age/Sex	Type of malignancy	Animal contact	Initial presentation	Culture source for the diagnosis of <i>P. multocida</i>	Treatment	Neutropenia (WBC<0.5 x 10 <sup>9</sup> /L)	Outcome
1 [11]	79/F	Diffuse large B-cell lymphoma	Cat scratch	Fever, altered mental status, hypotension, pain in right upper extremity	Blood Subcutaneous abscess of the right hand	Cefepime	yes	Survived
2 [13]	51/M	Hairy-cell Leukemia	none	Fever, erythematous lesions in Right upper extremity, left leg lesions	Blood	unknown	yes	Died
3 [2]	67/F	Breast cancer	Cat scratch	Fever, erythematous rash with central necrotic ulcer on left forearm	Blood	Imipenem, Ciprofloxacin	yes	Survived
4 [3]	78/F	Multiple myeloma	Cat bite	Fever, altered mental status, erythema and abrasion on the right lower leg	Blood Cerebrospinal fluid Right knee effusion Right leg wound	Penicillin G	no	Survived
5 [4]	54/F	Carcinoma of the ovary	Cat scratch, pet cats and dogs	Fever, malaise, tender cervical lymphadenopathy, multiple scratches	Blood	Penicillin G	no	Survived
6 [14]	62/F	Breast cancer	Cat at home without scratch	Fever, malaise, left knee and right shoulder pain, warmth, and erythema Left knee effusion	Blood Synovial fluid from left knee and right shoulder	Cefazolin and gentamicin	no	Died
7 [8]	64/M	Chronic lymphocytic leukemia	Cat scratch	Fever, altered mental status, shortness of breath  Readmission with fever, weakness, productive cough	Blood  Blood	Piperacillin/Tazobactam, Amoxicillin/clavulanic acid Trimethoprim-sulfamethoxazole	unknown	Survived
8 [15]	80/F	Cervical adenocarcinoma	Unknown	Fever and mucopurulent vaginal discharge	Aspirate from uterus	Clamoxil-clavulanic acid	Unknown	Unknown

**Table 1.** Case reports of *Pasteurella multocida* infections in cancer patients from medical literature and from Moffitt Cancer Center and Research Institute (Tampa, USA). (Continued)

Patient [Reference]	Age/Sex	Type of malignancy	Animal contact	Initial presentation	Culture source for the diagnosis of <i>P. multocida</i>	Treatment	Neutropenia (WBC<0.5 x 10 <sup>9</sup> /L)	Outcome
9 [16]	73/M	Non-Hodgkin's Lymphoma	Unknown	Fever, cough, pleuritic chest pain	Pleural effusion	Cephalosporins Aminoglycosides	no	Unknown
10 [17]	50/F	Squamous cell carcinoma of the left auditory canal	Dog licked patient's face	Facial cellulitis and complete sensorineural hearing loss	Blood	Ciprofloxacin Ceftazidime	no	Survived
11 [18]	48/F	Endometrial adenocarcinoma	Cats licked abdominal incision	Fever, malaise, pain at abdominal incision site	Subcutaneous fluid collection at abdominal incision site	Piperacillin and Gentamicin Penicillin	Unknown	Survived
12 [1]	69/F	Squamous cell lung carcinoma, oral carcinoma and cervical carcinoma	Unknown	Fever, shortness of breath, fatigue, cough	Sputum, bronchial washings	Cefazolin/ tobramycin/ cephalexin	no	Survived
13 [19]	56/F	Rectosigmoid adenocarcinoma	Had a pet dog but no animal bites	Fever and rigors Perirectal abscess Readmitted twice with fever and recurrent bacteremia	Blood	Cephalothin/ Gentamicin	no	Died
14 [19]	72/F	Biliary adenocarcinoma	unknown	Fever	Blood	Unknown	Unknown	Died
15 [19]	41/M	Acute monoclastic leukemia	unknown	unknown	Thigh abscess	Unknown	yes	Unknown
16 [19]	60/F	Breast Adenocarcinoma	unknown	Unknown	Arm ulcers	Unknown	Unknown	Unknown
17 [19]	60/F	Lung adenocarcinoma	unknown	Unknown	Sputum	Unknown	Unknown	Unknown
18 [19]	57/M	Acute myelogenous leukemia	unknown	Unknown	Sputum	Unknown	yes	Unknown
19 [19]	75/M	Ameloblastoma	unknown	Unknown	Bronchial washings	Unknown	Unknown	Unknown
20 [19]	64/F	Cervical cancer	unknown	Unknown	Vaginal drainage	Unknown	Unknown	Unknown
21 [19]	65/F	Squamous gingival carcinoma	unknown	Unknown	Sputum	Unknown	Unknown	Unknown
22 [19]	55/F	Soft palate and epidermoid carcinoma	unknown	Unknown	Sputum	Unknown	Unknown	Unknown
23 [20]	53/F	Breast cancer	Unknown	Fever	Blood	Ceftazidime, Amikacin	no	Survived
24 [21]	87/M	Squamous cell Lung cancer	none	Weight loss	Lung abscess	Amoxicillin/ Clavulanic acid	no	Died

**Table 1.** Case reports of *Pasteurella multocida* infections in cancer patients from medical literature and from Moffitt Cancer Center and Research Institute (Tampa, USA). (Continued)

Patient [Reference]	Age/Sex	Type of malignancy	Animal contact	Initial presentation	Culture source for the diagnosis of <i>P. multocida</i>	Treatment	Neutropenia (WBC < 0.5 x 10 <sup>9</sup> /L)	Outcome
25 [6]	70/M	Waldenstrom macroglobulinemia	Dog lick	Unknown	Blood	Amoxicillin, amikacin	Unknown	Survived
26 [6]	81/M	Chronic Lymphocytic leukemia	Cat bite	Cellulitis	Blood	Penicillin Cephalothin Gentamicin Unknown	Unknown	Survived
27 [22]	37/M	Hairy Cell Leukemia	Unknown	Pneumonia	Respiratory secretions	Unknown	no	Survived
28 [23]	62/M	Epidermoid carcinoma of the tongue	Patient owned a dog; no history of bites or scratches	Fever, altered mental status, headache, meningeal signs	Oropharynx Blood	Ampicillin	No	Survived
29 [24]	18/M	Hepatocellular carcinoma	Dog at home, no history of dog bite	Fever, abdominal pain, jaundice, vomiting and hypotension	Subdural empyema Blood	Ampicillin	unknown	Died
30 [25]	74/M	Chronic lymphocytic leukemia	Cat bite	Painful and swollen left ankle	Liver abscess Synovial fluid	Ampicillin/ Sulbactam; Amoxicillin Penicillin	No	Survived
31 [26]	65/F	Breast cancer	Patient had pet cat	Fever, chills	Blood	Penicillin	No	Survived
32 [7]	74/M	Transitional cell carcinoma of the bladder	Multiple cat bites and scratches	Purulent ulcerations in breast Fever, altered mental status, hypotension, multiple tender lacerations	Breast ulcerations Blood	Ampicillin, Gentamicin, Penicillin	No	Survived
33*	74/F	Malignant melanoma	Unknown	Fever, chills Right groin erythema	Right groin wound	Levofloxacin	No	Survived
34*	60/M	Acute Myelocytic Leukemia	Had a dog, Denied cuts, bites or scratches from dog	Right groin erythema Fever	Blood	Cefepime, Levofloxacin	Yes	Survived
35*	45/F	Breast Cancer	Unknown	Left breast pain, redness and drainage	Left breast wound	Ciprofloxacin	Unknown	Survived
36*	60/F	Breast Cancer	Unknown	Fever, chills, drainage from abdominal wound	Abdominal wound	Cefepime	No	Survived

\* Patients from Moffitt Cancer Center and Research Institute.

of *P. multocida* meningitis treated effectively with aztreonam. It is worth emphasizing however, that aminoglycosides, vancomycin, erythromycin, and clindamycin should be avoided in the penicillin-allergic patient since drug resistance may result [3]. In addition, when considering empiric antibiotic therapy for an animal bite wound, dicloxacillin, erythromycin, and clindamycin should be avoided as well as cephalosporins such as cephalexin, cefaclor and cefadroxil, since *P. multocida* isolates have been shown to be resistant to all of these antibiotics [10]. Finally, Yokose et al. [11] described a severely neutropenic cancer patient with *P. multocida* bacteremia and sepsis who was successfully treated with cefepime monotherapy.

In summary, *P. multocida* should be considered as a possible etiologic agent in any patient with a local wound infection secondary to an animal bite or scratch. This pathogen is recognized as opportunistic, and it should always be included in the differential diagnosis of any immunocompromised patient with bacteremia and a history of an animal bite wound and/or close animal contact [6]. Post-chemotherapy neutropenic patients or anyone afflicted with severe immunosuppression should avoid close or accidental contact with pet or barnyard animals [11].

Among our study patients, vital epidemiological information, such as animal contact, either may have been either absent or was inadequately documented in some of the cases, which may represent a methodological flaw. Nevertheless, cases of *P. multocida* bacteremia lacking history of animal exposure have been repeatedly described; perhaps simply representing previous asymptomatic colonization of the respiratory or gastrointestinal tract in those afflicted [12]. Furthermore, patients presenting with *Pasteurella* sepsis without a documented animal exposure should undergo extensive evaluation in order to exclude the presence of an underlying immunodeficiency [13].

The authors have no conflict of interest to report.

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