



Recurrent Septicemia and Osteomyelitis caused by *Pasteurella Multocida* in a Patient with Chronic Lymphatic Leukemia

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Key words: *Pasteurella multocida*, septicemia, osteomyelitis, chronic lymphatic leukemia

IMAJ 2008;10:653–654

For Editorial see page 648

Pasteurella species exist as normal upper respiratory and gastrointestinal flora in dogs, cats, and other domestic and wild animals [1]. *Pasteurella multocida* is a small gram-negative Coccobacillus. Human infections caused by *Pasteurella* species are rare but have been reported with increasing frequency over the last few decades [2]. Life-threatening systemic disease is distinctly uncommon in otherwise healthy persons and usually occurs in patients with chronic predisposing illnesses [1]. Most human *P. multocida* infections are secondary to animal bites and involve soft tissues usually presenting as cellulitis or abscess formation or, less frequently, as bone and joint infections, respiratory tract infections, intraabdominal infections, endocarditis and meningitis [1]. Septicemia is infrequent and is usually responsive to sensitive antibiotic treatment. Recurrence of the disease after completing an appropriate course of antibiotic therapy has not been reported before.

Patient Description

A 64 year old man was admitted to our internal medicine department because of a history of prolonged cough, high fever and confusion. Ten years earlier he was diagnosed with chronic lymphocytic leukemia stage IV according to the Rai staging system. Six years before the present admission he was treated with chlorambucil and prednisone for 3 con-

secutive years. He was then switched to a combination therapy that included rituximab, fludarabine and cyclophosphamide, and remained in remission since then. He required several blood transfusions in the past few years. A year before the present admission he was admitted to a different medical ward because of pneumococcal septicemia with meningitis and bilateral pneumonia. Since then he received regular vaccinations against influenza and streptococcal pneumonia. One month prior to the present admission he developed a productive cough without fever that was treated in an outpatient clinic with amoxicillin/clavulunate and ciprofloxacin without improvement. On the day of admission he developed confusion, shortness of breath and high temperature (39°C).

There was no history of recent travel. He denied having ingested non-pasteurized milk or dairy products, taken illicit drugs or drunk excessive amounts of alcohol. He had no unprotected sexual contact. He kept a vaccinated pet cat that was used to licking and scratching him.

On physical examination, generalized lymphadenopathy was detected. The lungs showed reduced breath sounds bilaterally and inspiratory crackles over the basis of the left lung. A grade 3/6 mid-systolic murmur was heard on heart auscultation. Laboratory tests showed lymphocytosis, thrombocytopenia and hypogammaglobulinemia. A lumbar puncture did not demonstrate signs of infection. A head computed tomography scan revealed polypoid changes in the left nostril and

mucosal thickness of the maxillary and ethmoidal sinuses, known from previous studies. Chest radiograph showed heart enlargement, a left lower lobe infiltrate and a small amount of pleural fluid in the left costophrenic sinus (known from previous films).

Because of fever in an immunocompromised patient and the suspicion of a septic state he was started on intravenous piperacillin/tazobactam. Later, during his hospitalization he complained of a sore throat. Examination revealed lingular tonsillitis and bilateral suppurative otitis media. Several blood cultures drawn on admission yielded *P. multocida*, and antibiotic treatment was changed to intravenous amoxicillin/clavulunate according to antimicrobial susceptibility. His condition improved, the fever declined, and he began eating and drinking normally. He was released from our department with a recommendation for oral treatment with amoxicillin/clavulunate and to remove the cat from his home to prevent further exposure.

One week later he was readmitted with recurrent high fever (40°C), weakness and a productive cough. He had discontinued antibiotic therapy one day before. On physical examination his temperature was 39.4°C. On lung auscultation, few crackles were present over the lower area of the left lung. A chest radiogram performed on admission did not show new findings. Several blood cultures yielded *P. multocida*. Treatment with intravenous trimethoprim-sulfamethoxazole and piperacillin/tazobac-

tam was started according to bacteria sensitivity after infectious disease consultation. A new echocardiography did not display pathological endocardial findings. CT scanning demonstrated retroperitoneal lymphadenopathy and hepatosplenomegaly, probably related to his underlying condition. Later on, during hospitalization, the patient complained of lower left hip pain, for which he underwent a bone and gallium scan, both of which showed findings compatible with osteomyelitis of the left ankle. He received intravenous immunoglobulin G and was given i.v. antibiotic treatment in the hospital for a total of 2 weeks. Fever did not recur and repeated blood cultures were negative. After discharge, antibiotic treatment was continued for another 4 weeks. One month after discharge he remained afebrile and in general good condition.

Comment

Pasteur first isolated the causative agent of fowl cholera, *Pasteurella multocida*, in 1880. *P. multocida*, a small, gram-negative Coccobacillus, is part of the normal oral flora of many animals, including the dog and cat [1]. Animal contact is a significant risk factor for *Pasteurella* infection. In the present case, the patient had close contact with his cat. *Pasteurella* present in animal oral cavities is transmitted to humans by means of secretion droplets requiring close contact such as biting, scratching, licking and kissing [2]. The pathogen might enter the body directly from the cutaneous scratch. Local infections are characterized by the rapid appearance of local inflammatory signs and frequently purulent drainage [1]. It is rare that a patient contracts the disease without clear evidence of previous animal contact [3].

The most common local complications are abscess formation and tenosynovitis.

Serious local complications include septic arthritis [4] proximal to bites or scratches, osteomyelitis [1] resulting from direct inoculation or extension of cellulitis, and the combination of septic arthritis and osteomyelitis, most commonly involving a finger or hand [1].

Osteomyelitis and septic arthritis are the most frequent serious complications caused by *P. multocida* [1]. In their thorough review of the literature, Weber et al. [1] described 36 patients with osteomyelitis caused by *P. multocida*. Osteomyelitis resulted from either local extension of soft tissue infection or direct inoculation of *P. multocida* into the periosteum by the cat or dog bite. Infection may involve any bone but most commonly occurs in the bones of the fingers, hands, wrists, forearms or legs [1]. More recently, some reports have described vertebral osteomyelitis caused by *P. multocida*.

P. multocida can be the cause of other systemic infections, including bacteremia, meningitis, brain abscess, and intra-abdominal abscess [1]. *P. multocida* has a predilection for causing bacteremia in patients with associated diseases, such as diabetes mellitus, chronic liver disease, or in immunocompromised hosts [5].

In older reviews, cats were the source of infection in 60–80% of cases [1], but more recent reports showed injuries caused by dogs accounting for most of the infections [5]. The cause for this difference is not clear.

P. multocida is sensitive to several antibiotics, although first-generation cephalosporins, erythromycin, antistaphylococcal penicillins, aminoglycosides, vancomycin, and clindamycin are not effective against *P. multocida* and have poor activity *in vitro* [2]. The presence of other bacteria, such as staphylococci, streptococci and anaerobes in bite wounds makes amoxicillin/

clavulanate the most appropriate empiric therapy [5]. Treatment is usually effective and recurrences have not been described before.

Animal bites are common injuries that are often not paid appropriate attention by the patients and not always by the attending physician. Besides treatment for the prevention of rabies after animal exposure, there is a greater risk of infection in the injured area and even of more serious infections. As seen in the present case, the infection caused by these bacteria could be serious and life threatening and the disease may recur despite appropriate antibiotic treatment. Physicians have to be aware of the possibility of *P. multocida* infection in case of recent animal exposure and must prescribe prompt and effective treatment to prevent serious complications.

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