**clinical investigations**

**Pasteurella multocida Pneumonia in a Man With AIDS and Nontraumatic Feline Exposure**

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A case of acute pneumonia due to *Pasteurella multocida* ssp *multocida* occurred in a young man with AIDS and chronic sinusitis. The pneumonia was diagnosed by bronchoscopy and responded to treatment with aztreonam. Epidemiologic investigation revealed the case was temporally related to nontraumatic exposure to cat secretions that the patient presumably had acquired via an aerosol. The cat's oral cavity was cultured and an isolate of *P. multocida* ssp *multocida* with identical biochemical reactions, DNA restriction patterns, and nearly identical fatty acid profile to that of the patient's isolate was obtained suggesting they were identical strains and therefore epidemiologically linked. A control strain with identical biochemical reactions and antibiotic sensitivities exhibited different patterns. To our knowledge, this is the first such reported infection in a patient infected with human immunodeficiency virus.

(Chest 1993; 103:7-11)

AZT = zidovudine; HIV = human immunodeficiency virus

**Pasteurella multocida** is a small Gram-negative cocacobacillus that comprises part of the normal oral flora of many types of animals, including domestic dogs and cats. Human infection with this organism usually follows cat bites, cat scratches, and dog bites. These infections usually involve soft tissues and/or bone as a sequela of the mechanical inoculation. Respiratory tract involvement with this organism, however, is second only to animal bites as a source. Cases of bronchitis, sinusitis, empyema, and pneumonia have been described in the literature. The majority of the individuals with *Pasteurella* pneumonia possessed some underlying pulmonary disease, most commonly bronchiectasis or COPD, suggesting a predilection of the organism to infect hosts with impaired local defenses.

We report a young man with longstanding AIDS and chronic sinusitis but no underlying chronic pulmonary abnormality who developed a well-documented acute pneumonia due to *P. multocida*. Epidemiologic investigation revealed that this pneumonia was temporally related to a nontraumatic feline exposure, suggesting an aerosol mode of infection. Detailed biochemical typing, DNA restriction site, and fatty acid analysis of the patient's isolate and that from the implicated cat's saliva revealed that they were identical.

**CASE REPORT**

A 27-year-old man presented to the Walter Reed Emergency Department in August 1991 with two-day history of dry cough, shortness of breath, and fevers to 39°C. The patient had a complex history of human immunodeficiency virus (HIV) infection dating to October 1987 when he was found to be HIV-positive on the military force screen. At that time, he was determined to be Walter Reed stage 4 as evidenced by partial anergy on delayed hypersensitivity skin testing and a CD4- cell count of less than 400 cells per cubic millimeter. He was medically retired at that time and continued to reside in suburban Washington, DC. Despite zidovudine (AZT) therapy he exhibited continued loss of CD4+ cells and therefore was initiated on prophylaxis to prevent *Pneumocystis carinii* pneumonia with inhaled pentamidine in March 1988. By March 1989, he was completely anergic and his CD4+ cells numbered 10 cells per cubic millimeter. He had suffered recalcitrant chronic sinusitis, thrush, recurrent furunculosis, and seborrheic dermatitis over the course of his illness. He also exhibited numerous true allergic reactions to many drugs, among them many antibiotics, including sulfa drugs, erythromycin, clindamycin, rifampin, and many β-lactam agents such as penicillin. He had acute pneumonia due to *Haemophilus influenzae* in March 1990. In October 1990, he developed fevers and night sweats that were determined to be due to disseminated *Mycobacterium avium-intracellulare* documented by culture of blood and bone marrow. Ciprofloxacin and ethambutol therapy resulted in resolution of his symptoms. In February 1991, he developed a complicated illness that was determined to be due to extrapulmonary pneumocystosis involving the pleural space. His
condition improved with parenteral pentamidine and was switched to oral dapsone Pneumocystis prophylaxis to prevent a systemic recurrence. He had been doing reasonably well until his current illness that occurred while visiting a relative in San Francisco, Calif. Prior to hospital admission, his long-term medications included the following: dapsone, 200 mg every Monday, Wednesday, and Friday; ciprofloxacin, 500 mg twice daily; ethambutol, 600 mg every day; metronidazole, 250 mg three times a day; fluconazole, 200 mg every day; Megace 160 mg twice daily; Entex LA twice daily; and beclomethasone dipropionate (Vancenase) nasal inhaler bid.

At the time of hospital admission, the patient was acutely ill with moderate distress secondary to shortness of breath. He was lethargic but his mental status was otherwise intact. His temperature was 38°C, pulse was 200, BP was 61/36, and respirations were 35 and labored without accessory muscle usage. Oral hairy leukoplakia was present but there was no evidence of thrush. Auscultation of the lungs revealed scattered rales and rhonchi. An ECG at the time of hospital admission revealed supraventricular tachycardia that resolved with parenteral adenosine and did not recur. The white blood cell count on hospital admission was 6.7 with a hematocrit of 30. A differential cell count was not performed. The serum urea nitrogen and creatinine levels were elevated at 53 and 2.5 mg/dl, respectively, suggesting prerenal azotemia. A blood gas determination on room air demonstrated a pH of 7.42, Pco₂ of 20, and Po₂ of 64. Lactate dehydrogenase (LDH) was elevated at 355 U/dl. A chest roentgenogram revealed multiple fluffy infiltrates in the peripheral right lung fields. The patient was administered intravenous fluid for intravascular volume expansion as well as other supportive measures and started empirically on a regimen of the following: aztreonam, 1 g every 8 h; tetracycline, 1 g every 12 h; and vancomycin, 1 g every 12 h. Treatment with ciprofloxacin, ethambutol, and metronidazole was discontinued during this illness. Blood cultures were negative. The patient underwent bronchoscopy with bronchoalveolar lavage (BAL) and biopsy the next day. The BAL fluid revealed 2+ Gram-negative rods and many polymorphonuclear white blood cells on Gram stain (Fig 1) and subsequently grew out P multocida in pure culture. The isolate was further subspeciated as ssp multocida. The protected biopsy specimen grew out the same organism. No other pathogens were isolated.

The patient's condition improved gradually and by five days he had defervesced. He completed a 14-day course of aztreonam for the pneumonia and was discharged from the hospital at his baseline health with radiologic and clinical clearing of the pneumonia.

**RESULTS**

**Epidemiology**

On learning that the patient was infected with a zoonotic organism, we questioned him with this in mind and he related that he had been in the same apartment with a cat while visiting his relative for two weeks. He denied other recent feline or other animal exposures and had no personal pets. This cat had never bitten or scratched him. Indeed, since the patient was not fond of cats, he had avoided it altogether, an attitude mutually exhibited by the cat as well. The cat was a 14-year-old female tabby whom the patient perceived to have problems with hairballs. It would regurgitate the hairballs throughout the house which gave the apartment a sour smell as perceived by the patient. The cat had a favorite rug which, according to the patient, was completely matted with secretions. The patient did not handle this rug. The cat was otherwise healthy and has remained so. No

**Figure 1.** Gram stain of bronchoalveolar lavage (×100). Gram-negative coccobacilliary organisms are apparent (arrowheads). Sheets of polymorphonuclear white cells are in the background. One else in the domicile had been ill. We arranged to have this cat taken to a veterinarian who cultured the oral cavity. This specimen also grew out P multocida and the isolate was mailed to our laboratory for further study.

The patient had undergone previous bronchoscopies for previous acute pulmonary processes most recently in February 1991. *Pasteurella multocida* had never been isolated from the specimens obtained by these procedures nor from routine sputum samplings suggesting he had not been colonized. Two months after the presentation under discussion, the patient had another bronchoscopy for a new process that revealed no evidence of persistent *P multocida*.

**Bacteriology**

The patient's isolate, that of the cat, and an unrelated *P multocida ssp multocida* from our strain library at Walter Reed exhibited identical biochemical reactions and antibiograms. These reactions are part of the standard evaluation of a *Pasteurella* species. The organisms were not mucoid unlike most strains isolated from the respiratory tract of patients with chronic pulmonary disease.

**DNA Restriction Analysis**

Genomic DNA of *P multocida* was prepared as described previously. Briefly, an overnight culture was lysed in Tris EDTA buffer (0.5 percent SDS and 100 μg/ml proteinase K) at 37°C for 1 h. Cell debris was removed by addition of 10 percent CTAB/0.7 M NaCl (hexadecyltrimethyl ammonium bromide) solution with further incubation at 65°C for 10 min. Following organic extraction and ethanol precipitation, the DNA was briefly dried and resuspended in Tris EDTA buffer to which 10 μg/ml boiled RNase had been added. DNA concentration was determined spectrophotometrically at 260 nm.
Approximately 3 μg of the extracted DNA was incubated in the presence of 20 U of restriction endonuclease Clal (New England Biolabs, Beverly, Mass), 30 U EcoRI, or 30 U HindIII (Bethesda Research Labs, Gaithersburg, Md) for 1 h at 37°C in the recommended buffer. A horizontal gel was prepared with Tris-Borate-EDTA buffer, 1 percent agarose, and 0.5 μg/ml ethidium bromide. Each complete digest was loaded into a well and electrophoresis was performed at 1.5 V/cm for 20 h. Fragment size markers included were a HindIII digest of Lambda DNA and a HaeIII digest of φX 174 RF DNA. The gel was photographed under UV light using specific film (Polaroid type 55 film, Polaroid Co, Cambridge, Mass).

Figure 2 illustrates HindIII digestion of P. multocida ssp multocida genomic DNA from the patient, the cat, and the library strain. The fragment pattern for the cat and patient isolates appear identical while the DNA of the library strain differs in several size fragments. Similar results were obtained with Clal and EcoRI digests (data not shown).

**Fatty Acid Analysis**

Organisms were grown in trypticase soy agar enriched with 5 percent sheep blood. Approximately 50 mg of wet weight of bacterial cells were harvested. Extraction of the cell wall and plasma membrane fatty acids was performed as previously described. Briefly, the organisms were saponified in the presence of sodium hydroxide and methanol in a boiling water bath for 30 min. The fatty acids were methyl esterified in the presence of methanol and hydrochloric acid. The fatty acid methyl esters were extracted with N,N-dimethyl-tert-butyl ether. The organic phase containing the fatty acid methyl esters was analyzed using a gas chromatography system utilizing methylphenyl silicone as the stationary phase (HP5898A Microbial Identification System, Hewlett-Packard Inc, Avondale, Pa).

Cluster analysis to produce unweighted pair matchings based on fatty acid compositions was done and is displayed graphically as a dendrogram with units in Euclidian values. Use of dendrogram analysis to determine relative relatedness of organisms has shown Euclidian values of 6 or less to represent the same subspecies and 10 or less to represent the same species.

Dendrogram analysis revealed that the isolates from the cat and the patient are more closely related to each other than to the library strain. All the isolates are related at the subspecies level as expected (Fig 3).

**DISCUSSION**

In a recent exhaustive review of human P. multocida infections by Weber et al., 25 cases of well-documented pneumonia are mentioned. The median age of patients with this infection was 69 years and the majority possessed some form of chronic lung disease. Pasteurella multocida colonized the respiratory tract of these individuals. Occasionally, the organism can colonize the respiratory tracts of apparently healthy people as well. In one study, 2 of 100 animal handlers were colonized compared with none of 75 unselected individuals. However, 42 of 75 of the unselected group had some degree of animal exposure as well.

Carriage of the organism by a variety of healthy animals occurs and these rates can be quite high. In cats, for example, the rates are 70 to 90 percent. Pasteurella multocida can be pathogenic in many species of animals as well. It is the agent of hemorrhagic septicemia of cattle and causes pneumonia in sheep and goats as well as upper respiratory infections in rabbits. In the environment the organism can...
remain viable in water for 7 to 25 days and in soil for up to 21 days. It is rapidly killed by direct exposure to sunlight in 10 min.\textsuperscript{19} Human infections following animal exposure without bites probably are due to some exposure with the secretions in which the case of respiratory tract infections or colonizations probably arises from aerosolized secretions. Neither human-to-human spread nor food or water-borne routes of infection have been described. A hospital outbreak of \textit{P. multocida} infections has been reported but the mode of transmission was not defined.\textsuperscript{80}

The patient described herein had a well-documented pyogenic pneumonia diagnosed by bronchoscopy that was temporally related to exposure to a relative's cat. On biochemical analysis, the isolates proved to be within the same subspecies, multocida. Identity was further suggested by restriction endonuclease site analysis, a technique currently useful in epidemiologic investigations.\textsuperscript{43} Fatty acid analysis revealed that the isolates were closely related. Fatty acid analysis is another analytic method that may prove useful for epidemiologic investigations.\textsuperscript{26} The slight differences between the isolates on fatty acid analysis could be accounted for as adaptations to different environments, that is, the cat's mouth vs the patient's lower respiratory tract. The value of both of these analytical methods would be enhanced if the restriction patterns and fatty acid profiles of many geographically diverse isolates were studied and correlated with epidemiologic information.

In the context of the current case, the fact that the cat and patient isolates were highly related by these tests compared with a biochemically indistinguishable control strain, however, suggests these techniques would be useful in similar situations. Recently it has been shown for veterinary purposes that phage typing can be another useful technique in the epidemiologic classification of \textit{P. multocida} strains, but this was unavailable to us.\textsuperscript{43} Conceivably, the patient could have been colonized prior to the feline exposure with a remarkably similar strain, but the patient denied any other significant animal exposures and his baseline respiratory secretions did not contain this organism on previous or subsequent samplings. The description of the environment that the patient and cat shared for two weeks certainly seemed one in which aerosols of secretions could have occurred. Pneumonic disease due to nontraumatic exposure to cats is not a novel observation. An outbreak of Q fever occurred in a group of card players sharing quarters with a parturient cat. The outbreak was mediated by inhalation exposure to aerosolized birth products.\textsuperscript{44}

We postulate that this patient became colonized by \textit{P. multocida} after high-density exposure to aerosolized secretions of this cat. The patient may have been at increased risk for colonization and infection secondary to alterations in mucosal immunity by virtue of his chronic sinusitis with the attendant postnasal drip. Soon after exposure, this patient went on to develop lower respiratory tract infection that presented fairly abruptly like other bacterial pneumonias. The patient became volume depleted, hypoxic, and developed a paroxysmal supraventricular tachycardia as a result of the infection. His condition improved with effective antibiotic and supportive therapy and on a later sampling demonstrated no evidence of persistent colonization. The patient's isolate, like those of most cases, was sensitive to most of the antibiotics tested.\textsuperscript{9} Of note, the patient developed pneumonia with this organism, while he was receiving ciprofloxacin to which the organism was susceptible. The reason for this is not clear since adequate levels of the drug should have occurred to inhibit growth of the organism in the bronchopulmonary tree.

To our knowledge, \textit{P. multocida} pneumonia has not been previously described in an HIV-infected patient. In addition to the chronic sinusitis, this patient had bacterial pneumonia (\textit{Haemophilus influenzae}) in the past and problems with recurrent furunculosis (\textit{Staphylococcus aureus}) suggesting problems handling bacterial pathogens. Problems with pyogenic immunity have been reported as a result of HIV infection and this presumably made our patient more susceptible to lower respiratory infection.\textsuperscript{28} Similar cases have probably not been observed in HIV-infected individuals because a unique amalgam of high-density aerosol exposure and chronic sinusitis or a chronic pulmonary condition may be required for infection to occur in addition to the baseline HIV-induced immunosuppression. Nevertheless, this case demonstrates that nontraumatic pet exposure can lead to disease in selected HIV-infected patients and decisions regarding the keeping of pets should be thoughtfully considered by patients who may be more at risk for this infection.

ACKNOWLEDGMENTS: We acknowledge Cynthia B. Easton, D.V.M., of Pets Unlimited, San Francisco, Calif, and Rachel A. Geddit, M.T.(A.S.C.P), of Consolidated Veterinary Diagnostics, West Sacramento, Calif, for their invaluable assistance with this case.

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