Yersinia pestis infection in three dogs

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- Infection with the gram-negative bacterium *Yersinia pestis* is a serious disease in cats, rodents, rabbits, and people.
- In dogs, clinical signs of *Y pestis* infection are rare and have not been well documented. When clinical signs occur, they may be nonspecific, such as fever and lethargy, or may include lesions of the oral cavity or lymph nodes. Infection with *Y pestis* may be difficult to distinguish from other infectious diseases.
- In endemic regions, *Y pestis* infection should be considered in the differential diagnosis when examining dogs with nonspecific fever and lethargy.

In February, a 5-year-old spayed female mixed-breed dog (dog 1) was brought to a veterinary clinic in northern New Mexico with a brief history of anorexia, lethargy, drooling, and coughing. On physical examination, the dog was pyrectic (rectal temperature, 41.1 C), and a cough could be elicited during tracheal palpation. Severe ulceration of the left side of the epiglottis, right ventral portion of the tongue, and gingiva was reported. Thoracic and abdominal radiographs were normal. Clinicopathologic abnormalities included mild hypokalemia (potassium concentration, 3.8 mEq/L) and hypocapnia (CO_2 concentration, 13 mEq/L). Degenerative WBC and cellular elements were seen in blood smears; however, the WBC count was within reference limits. The oral lesions were biopsied, and specimens were submitted for histologic examination and bacteriologic culture. Gingivitis was diagnosed histologically; bacteriologic cultures did not yield any growth. Trimethoprim/sulfamethoxazole (17 mg/kg of body weight, PO, q 24 h) was prescribed, and 1 dose of dexamethasone (1 mg/kg, route was not reported) was given. By the evening of admission, the pyrexia had resolved (rectal temperature, 38.7 C); however, by the next morning the dog's temperature was again high (rectal temperature, 39.7 C), and treatment with cefazolin (22 mg/kg, IV, q 8 h) was initiated. Blood samples were tested for antibodies to *Yersinia pestis*, *Francisella tularensis*, and *Ehrlichia canis*. *Yersinia pestis* passive hemagglutination antibody titer with hemagglutination inhibition was 1:256 (titer > 1:10 is considered a positive result); *F tularensis* microagglutination titer was 1:20 (titer ≥ 1:160 is considered indicative of recent infection[1]); and *E canis* immunofluorescent assay titer was 1:20 (titer > 1:60 is considered indicative of recent infection). Administration of cefazolin was discontinued, and tetracycline (25 mg/kg, PO, q 8 h) and dihydrostreptomycin (dosage was not reported) were prescribed.

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The following day, right submandibular lymphadenitis developed, and soft tissues in the shoulder and neck were markedly swollen. The dog's rectal temperature remained normal, and the dog was alert and eating. The submandibular swelling developed into an abscess, which was lanced and drained. A sample of exudate and a biopsy specimen from the right submandibular lymph node were submitted for bacteriologic culture and fluorescent antibody staining for *Y pestis*; results of both tests were negative. The dog continued to improve, and the right submandibular swelling resolved. Two weeks after the onset of illness, serologic tests were repeated. Titers for *Y pestis* and *F tularensis* were 1:512 and 1:40, respectively. The dog was seronegative for *E canis*.

In July, a 7-year-old neutered male Doberman Pinscher (dog 2) was brought to a veterinary clinic with a history of lethargy and a draining, purulent lesion in the ventral intermandibular region. Results of physical examination were unremarkable other than the lesion. Results of serum biochemical analyses and a CBC were within reference limits. The dog was anesthetized, and the draining lesion was explored and found not to communicate with the oral cavity. The lesion was cleaned and flushed; the dog was given a single dose of amoxicillin (500 mg, route was not reported), and cephalexin (16 mg/kg, PO, q 12 h) was prescribed. Titers for *Y pestis* and *F tularensis* were 1:2,048 and 1:40, respectively. The dog's condition improved, but because of the high *Y pestis* titer, the antibiotic treatment was changed to tetracycline (16 mg/kg, PO, q 8 h). Serologic tests for antibodies to *Y pestis* and *F tularensis* were repeated 2 months after the onset of clinical signs. At that time, the *Y pestis* titer was 1:1,024, and the titer was 1:40 for *F tularensis*.

In September, a 2-year-old spayed female mixed-breed dog (dog 3) was brought to a veterinary emergency clinic with a history of lethargy and anorexia of short duration. Physical examination revealed pyrexia (rectal temperature, 41.2 C) and abnormal lung sounds. Amoxicillin (22 mg/kg, PO, q 12 h) was prescribed, and the dog was sent home. Three days later, the dog was examined by another veterinarian because of continued lethargy. The dog was still pyrectic (rectal temperature, 39.7 C), but lung sounds were normal. Antibiotic treatment was changed to trimethoprim/sulfamethoxazole (17 mg/kg, PO, q 12 h). The dog's WBC count was 14,800/μl, with 8,900 neutrophils/μl and no band neutrophils. Titers for *Y pestis* and *F tularensis* were 1:32 and 1:80, respectively. The dog improved after receiving trimethoprim/sulfamethoxazole, and treatment was discontinued after 5 days. Serologic titers for *Y pestis* and *F tularensis* were repeated in 3 weeks, and results were 1:4,096 and 1:80, respectively.

Clinical signs in all 3 of these dogs were attributed to infection with *Y pestis*, commonly known as plague. Plague is enzootic and epizootic in the western United States, particularly in New Mexico, Arizona, and Colo-

rado. The principal hosts include wild rodents (especially rock and ground squirrels, *Spermophilus* spp, and prairie dogs, *Cynomys* spp) and rabbits, and the carnivores that feed on them. Plague can be a severe disease in cats, and cats clinically ill with plague are a documented source of direct infection of persons in close contact with them, including veterinarians.[2-7] An average of 10 to 15 human cases occur every year, mostly from the bites of rodent fleas, but also from direct contact with tissues and fluids of infected animals, including domestic cats.[a]

When epizootics of plague occur in wild rodent populations, domestic dogs living in or adjacent to these areas are frequently infected with *Y pestis*. Infection occurs by being bitten by infected fleas or by consuming infected prey, such as rodents or rabbits. Serosurveillance of wild and domestic dogs has been used as an efficient method of monitoring epizootic activity, because dogs develop transient high antibody titers following infection.[8-10] It was believed that dogs did not develop clinical signs of infection when exposed to *Y pestis*, and clinical signs of naturally acquired infection have not, to our knowledge, been previously documented in dogs. Fleas were not observed on any of these dogs in the week prior to development of clinical signs, and none of the owners reported using a flea control product on their dog in that period. However, all 3 dogs were known to hunt rodents and, especially, rabbits.

Although plague was suspected in all 3 of these dogs, the diagnosis was confirmed only in dog 3, which had a fourfold increase in *Y pestis* titer over a period of 3 weeks. The other 2 dogs had high initial *Y pestis* titers. A single titer of 1:32 or greater is considered presumptive evidence of a diagnosis of plague,[5,6] but confirmation that infection was recent as opposed to previous requires documenting a fourfold change in titers or isolation of *Y pestis*. In 10 dogs experimentally infected with *Y pestis*, antibodies were detected by means of passive hemagglutination assay by 8 days after exposure, and titers peaked (1:1,024 to 1:2,048) between day 8 and day 21; antibodies persisted for at least 330 days after exposure, with titers ranging from 1:128 to 1:256.[8] Thus, the high initial titers in dogs 1 and 2 (1:256 and 1:2,048, respectively) and the twofold change in titers (to 1:512 and 1:1,024, respectively) 2 weeks (dog 1) to 2 months (dog 2) later, support, but do not confirm, that the illnesses described were plague.

All 3 of these dogs had a history of lethargy, and 2 of the 3 dogs were pyrectic. In areas of the United States where plague is endemic, it seems prudent, therefore, to consider plague in the differential diagnosis when examining dogs with these signs. *Yersinia pestis* septicemia, without formation of an infected lymph node (bubo) occurs in cats and people[6,11]; therefore, the absence of a bubo should not be used to rule out plague. However, 2 of these dogs had purulent lesions, and in dog 1, the lesion was associated with a lymph node. In cats with plague, lesions are most often found in the neck area,[6] probably because of an oral route of exposure. Thus, finding abscesses on the face or neck of a dog or cat that does not have any history of a recent fight with another animal should increase the index of suspicion for plague.

Other infectious diseases that may resemble plague and are endemic to parts of the western United States include tularemia, ehrlichiosis, and coccidiomycosis; tularemia, in particular, can be differentiated from plague only on the basis of results of paired serologic or other confirmatory tests. For instance, during the same period that the 3 dogs of this report were examined and treated, 2 other dogs, also from northern New Mexico, were initially thought to have clinical signs resulting from *Y pestis* infection. One of these was an 8-month-old neutered male pit bull examined because of vomiting, diarrhea, and lethargy of several days' duration. The dog was dehydrated and pyrectic, and treatment consisted of IV administration of fluids and SC administration of procaine penicillin G. The dog eventually improved and was sent home. Serum titers for *Y pestis* and *F tularensis* were 1:128 and 1:80, respectively. Three weeks later, however, the dog was seronegative for *Y pestis*, and the *F tularensis* titer had increased to 1:320. The other dog was a 2-year-old spayed female German Shepherd Dog that was examined because of weight loss, listlessness, anorexia, and coughing. The dog was treated with a penicillin/dihydrostreptomycin combination (dosage was not reported), enrofloxacin (3 mg/kg, IM, q 12 h), dipyrone (dosage was not reported), and metronidazole (16 mg/kg, PO, q 12 h) and gradually improved. The initial *Y pestis* and *F tularensis* titers were 1:256 and less than 1:20, respectively, and plague was diagnosed. Antibiotic treatment was changed to tetracycline (25 mg/kg, PO, q 8 h); however, 2 weeks later, the *Y pestis* titer was still 1:256, but the *F tularensis* titer increased to 1:320. The *Y pestis* titers indicate that these 2 dogs had been exposed to *Y pestis*, probably within the past several months. However, infection with *F tularensis*, and not *Y pestis*, appears to have been the cause of their clinical signs.

The current drug of choice for treatment of plague in people is streptomycin.[12] Because streptomycin is not available for veterinary use, other aminoglycosides such as gentamicin, as well as the tetracyclines and chloramphenicol have been recommended for use in cats.[13] In a retrospective study of 119 cats with plague,[6] 70 of 77 (91%) cats treated with antibiotics survived, whereas only 10 of 42 (24%) cats not treated with antibiotics survived. Forty-three percent of the cats treated with antibiotics received either tetracycline or doxycycline. The efficacy of various antibiotics in dogs with plague has not been studied; however, in 1 study, all 10 dogs that were experimentally infected with *Y pestis* recovered within 7 days without treatment. It is not known whether the 3 dogs described in this report would have recovered without antibiotic treatment; however, antibiotic treatment is recommended for dogs suspected of having plague, because of the potential for transmission to people. Animals infected with *Y pestis* are considered noninfectious after 48 hours of appropriate antibiotic treatment.

The likelihood that human disease would result from exposure to a dog infected with *Y pestis* is unknown. Between 1970 and 1993, 4 cases of human plague were attributed to contact with an infected coyote or gray fox.[9] In all 4 cases, the affected person had skinned an infected animal. In 1975, primary plague septicemia was diagnosed in a woman whose pet dog had

died the same weekend that the woman had first developed clinical signs. The dog had been examined at a veterinary clinic several days before it died, and the diagnosis was acute purulent cervical lymphadenitis. A bone marrow specimen obtained from the dog after it died was tested by means of fluorescent antibody staining and was positive for *Y pestis*.[a] In 1 study,[8] *Y pestis* was isolated from skin lesions and oral secretions of experimentally infected dogs. Additionally, dogs can serve as vehicles, carrying wild rodent fleas from rodent burrows to their homes.[9,10] To minimize human exposure to *Y pestis*, flea repellent powders or sprays should be applied regularly to dogs during the transmission season (April through October) in affected areas. In addition, premise treatments may be used to kill any fleas that are brought into the home from outdoors. Preventing dogs from hunting and eating rodents and rabbits is probably the most critical factor in preventing *Y pestis* infections in dogs.

In none of these dogs was the diagnosis confirmed by means of bacteriologic culture. In cats with plague, bacteriologic culture is frequently not performed or results are negative because of improper collection techniques.[6] If infection with *Y pestis* is suspected in an animal, a rapid presumptive diagnosis can be made by performing fluorescent antibody staining on a bubo aspirate, lesion exudate, pharyngeal swab specimen, or tissue sample (this test is available at some state public health laboratories and the Centers for Disease Control and Prevention). Confirmation may be achieved by either serologic or bacteriologic methods. Preferred antemortem samples include whole blood, lymph node aspirates, lesion exudates, or pharyngeal swabs for bacteriologic culture. It is preferable to obtain specimens prior to the administration of antibiotics. Serologic confirmation is obtained by demonstrating a fourfold or greater change in serum antibody titers to *Y pestis*. Preferred postmortem samples include tissue from lymph nodes, liver, spleen, or lung (if there is evidence of respiratory involvement). Tissue samples should be placed in a clean container without formalin or alcohol and shipped overnight with a cold pack or frozen. In addition, local or state public health officials should be contacted promptly.

[a]Division of Vector-Borne Infectious Diseases, Centers for Disease Control and Prevention, Fort Collins, Colo, unpublished data, 1970–1993.

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