Alerts, Notices, and Case Reports

Tularemia From Domestic Cats

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TULAREMIA IS A ZOONOSIS of considerable complexity, with greater than 100 species of wild mammals, several species of birds, fish, and amphibians, and more than 50 species of blood-sucking arthropods (including ticks, fleas, and deerflies) serving as natural hosts.[1-5] Although the west south-central region of the United States—Arkansas, Louisiana, Oklahoma, and Texas—accounts for about a third of the cases reported to the Centers for Disease Control and Prevention, human tularemia has been reported from every state except Hawaii.[6] Humans generally acquire tularemia by direct contact with infected wild mammals or from arthropod bites, and the diagnosis of tularemia is traditionally considered in a hunter or trapper who presents with an acute febrile illness. Domestic animals, including dogs and cats, may also serve as vectors of tularemia.[8-18]

Two cases of septicemic tularemia recently occurred in the Fairbanks, Alaska, region following contact with domestic cats infected with *Francisella tularensis.* Tularemia was not suspected initially in either case because of the absence of either lymphadenopathy or a typical clinical history involving contact with wild mammals. In both cases, awareness of the clinical presentation of typhoidal tularemia and recognition of the potential for transmission of tularemia by domestic pets guided appropriate empiric antibiotic treatment before serologic confirmation.

Report of Cases

Patient 1

The patient, a 44-year-old man, was admitted to Fairbanks Memorial Hospital with a three-week history of a severe febrile illness unresponsive to treatment with oral cefadroxil. Three and a half weeks before admission, he sustained a cat bite to his right index finger while transporting his 14-year-old house cat to a veterinarian for management of a febrile illness diagnosed as an unspecified bacterial infection. The cat was empirically treated with intramuscular kanamycin sulfate and oral amoxicillin with complete resolution of symptoms. Three days after the cat bite, the patient had hectic spiking fevers to 40.5°C (105°F), chills, localized inflammation of the right index finger, headache, progressive weakness and malaise, nausea, abdominal pain, diarrhea, and anorexia associated with a 13.6-kg (30-lb) weight loss over the ensuing three-week period. He did not have a history of lymphadenopathy, respiratory symptoms, illicit drug use, alcohol abuse, recent travel outside the Fairbanks region, hunting, or trapping.

On physical examination on admission, there was a 1-cm nontender, ulcerated, erythematous skin nodule on the right index finger and relative bradycardia (heart rate 80 to 85 beats per minute in the presence of fever to 41°C). Otherwise, the physical findings were essentially normal. Admission laboratory studies revealed a hematocrit of 0.35, a leukocyte count of 10.5×10^9 per liter (10,500 per μl), aspartate aminotransferase 150 U per liter (normal, 0 to 35), alanine aminotransferase 154 U per liter (normal, 0 to 35), γ-glutamyltransferase 142 U per liter (normal, 0 to 30), alkaline phosphatase 190 U per liter (normal, 30 to 120), and total bilirubin 24 μmol per liter (1.4 mg per dl). A Monospot slide test was negative for infectious mononucleosis, and serologic tests were negative for rheumatoid factor and rapid plasma reagin. Cultures of blood and an aspirate of the right index finger yielded no bacterial growth.

The possibility of tularemia was suspected clinically, and empiric therapy with tetracycline, 500 mg orally every six hours, was initiated, leading to prompt defervescence and a resolution of symptoms within 48 hours. Oral tetracycline therapy was continued following hospital discharge to complete a four-week course of treatment. No relapse in symptoms occurred following the completion of therapy. A tularemia agglutination titer obtained on hospital admission was positive at 1:160; a titer done two months later during convalescence was positive at 1:320. A tularemia titer obtained from the cat a month after its febrile illness resolved was positive at 1:80. Serologic tests were negative for brucellosis in both cases.

Patient 2

The patient, a 42-year-old male veterinarian, presented for medical evaluation following the abrupt development of hectic fevers to 40.5°C (105°F) and chills associated with severe headache, photophobia, depression, generalized weakness, malaise, myalgias, arthralgias, abdominal pain, and diarrhea. Before the evaluation, the patient treated himself with oral cephalexin for a week without improvement. Sinusitis was suspected clinically, but prescribed treatment with oral amoxicillin for a week provided no benefit. The patient was admitted to Fairbanks Memorial Hospital two weeks into the course of his illness after a documented 9-kg (20-lb) weight loss. He did not have a recent history of skin lesions, adenopathy, respiratory symptoms, illicit drug use, alcohol abuse, hunting, travel outside the Fairbanks area, animal bites, or exposure to brucellosis, but he had treated several birds with psittacosis and several cats with tularemia during the

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two-month period before his illness began. None of his family members or co-workers at the veterinary practice had experienced a similar illness.

On physical examination there was a relative bradycardia: heart rate 75 to 85 beats per minute in the presence of temperatures of 39.5°C to 41.0°C (103°F to 106°F). An initial laboratory evaluation revealed normal electrolyte values, a hematocrit of 0.32, a leukocyte count of 9.6×10^9 per liter (9,600 per μl) with a normal differential cell count, an erythrocyte sedimentation rate of 43 mm per hour, normal liver function test values, and normal urinalysis. A Monospot slide test was negative for mononucleosis, and tests for antinuclear antibody and rheumatoid factor were negative. Three sets of blood specimens for culture yielded no bacterial growth. Chest x-ray and paranasal sinus films were within normal limits. Computed tomography of the abdomen revealed multiple areas of low attenuation in the liver and spleen consistent with multiple small abscesses. A diagnosis of typhoidal tularemia was suspected on the basis of the patient's exposure to documented tularemia in cats. An empiric therapeutic trial with tetracycline, 500 mg orally every six hours, led to a prompt defervescence and marked clinical improvement within 24 hours. The patient was discharged and completed an uneventful four-week course of oral tetracycline.

Serologic studies done at the time of his hospital admission showed normal Weil-Felix agglutinins, titers negative for brucellosis, psittacosis, and typhus, and a tularemia agglutinin titer positive at 1:320. At three months' follow-up, the patient did not have any relapse of his symptoms. Abdominal computed tomography showed resolution of the hepatic and splenic abnormalities. A tularemia titer during convalescence was positive at 1:640. Serologic studies obtained from his family members and veterinary associates were negative for tularemia.

Serology Survey

To determine whether the local veterinarians, who would have exposure to pets afflicted with tularemia, were at increased risk of contracting the disease, we obtained *F tularensis* agglutinin serologic tests (performed by the Northern Regional Laboratory, Fairbanks) of all 14 of the private veterinarians in the Fairbanks region. Elevated titers of 1:80 and 1:160 were present in two veterinarians (14%); brucellosis titers were negative. Neither seropositive person was involved in trapping or hunting.

Tularemia Survey

To assess whether the local medical community recognized the potential for tularemia in the Fairbanks area, we sent a questionnaire to the practicing local primary care physicians (internists, family practitioners, pediatricians, emergency department physicians; 28/33 responding) and veterinarians (12/14 responding). Of the 28 responding physicians, 15 (54%) were aware that tularemia was prevalent in the local wild mammal population and 11 (39%) were aware that local domestic animals were at risk of contracting tularemia and could transmit it to human contacts. Of the 12 responding veterinarians, 11 (92%) were aware that tularemia was prevalent in the local wild mammal population and that local domestic animals were at risk for contracting the disease; 9 (75%) had treated local domestic cats and dogs for tularemia in the past.

Discussion

This report demonstrates that typhoidal tularemia may result from cutaneous exposure to house pets, does occur far outside usually recognized endemic areas, and thus requires a high index of clinical suspicion for prompt diagnosis. Although generally considered to be an infection transmitted by wild mammals or arthropods in the south-central United States, tularemia may be encountered throughout Canada and the United States, except Hawaii. In 1991, 37 cases of tularemia were reported from the Pacific Northwest and Rocky Mountain states.[18] Knowledge of the diverse clinical presentations of tularemia and its routes of transmission is essential to the expedient diagnosis and proper management of an infected patient, as substantial morbidity and possible mortality may be avoided by prompt effective antibiotic treatment.[19]

Human tularemia can be categorized as two distinct clinical syndromes—ulceroglandular (including the glandular designation used in the older literature) and typhoidal, as observed in our first and second patients, respectively.[15] Isolated pharyngeal and pleuropulmonary presentations of tularemia are extremely rare. Pronounced local inflammation at the site of inoculation characterizes the ulceroglandular form, which carries a favorable clinical prognosis. In the typhoidal form of disease, limited local inflammation occurs, and morbidity and the risk of death are much greater.[15] Most cases of human tularemia occurring during summer are acquired from arthropod bites, whereas direct contact with infected mammals during hunting or trapping activities accounts for most human cases in the fall and winter months.[1-5,17]

Although reported to be present in only 26 of 62 patients (42%) reviewed recently,[15] the presence of a pulse-temperature dissociation, a characteristic of certain bacterial infections caused by intracellular pathogens, increased the clinical suspicion of tularemia in the cases reported here. Severe constitutional symptoms of high fever, chills, malaise, and headache were present in both of our patients. Lymphadenopathy and the complications of pneumonia, pericarditis, and pharyngitis previously reported in typhoidal tularemia were not observed. Gastrointestinal symptoms, including abdominal pain, anorexia, nausea, and diarrhea, were pronounced during the course of illness in both patients. Hepatic involvement was also present as demonstrated by the abnormalities on abdominal computed tomography—which resolved with appropriate antibiotic treatment—in patient 2 and elevated hepatic enzyme levels in patient 1. Elevated serum levels of at least one hepatic enzyme—lactate dehydrogenase, alanine and aspartate aminotransferases, and alkaline phosphatase—were reported in 58% of patients in a large series of tularemia.[15]

The laboratory diagnosis of tularemia is largely by serologic studies. Other laboratory tests for this disorder, including the leukocyte count and erythrocyte sedimentation rate, are extremely variable. Serum agglutinins are usually detectable by days 10 to 14 of infection; a fourfold rise in antibody titer is diagnostic. A single titer of 1:160 or higher in a patient suspected of having tularemia on clinical grounds is also considered diagnostic.[1-5,19] Titers may remain elevated for years after the acute episode. The formalin-fixed *F tularensis* used in agglutination reactions may cross-react with *Brucella* or *Proteus* O-19 antibodies, but the elevation in *F tularensis* titer is far greater than the titers to cross-reacting antigens.[1-5] Although immunity following tularemia is usually permanent, studies in animals suggest that cell-mediated immunity, rather than serum antibodies, confers protection.[20,21]

Before the introduction of antibiotics, the case-fatality ratio for tularemia was 5% to 15%. In recent years, reported mortality has declined to less than 1%, with typhoidal tularemia carrying the greatest risk.[1-5] Streptomycin is considered the drug of choice for tularemia, but gentamicin sulfate, chloramphenicol, and tetracycline are recognized as acceptable therapeutic alternatives.[1-5] An aminoglycoside should be used in the initial antibiotic regimen for the treatment of suspected tularemia in a patient with serious underlying disease.[19,22] In certain clinical situations, however, tetracycline is particularly attractive given its relative low toxicity and convenient administration compared with the other agents. When treating a seriously ill patient with tularemia, tetracycline may be used to complete a course of therapy following clinical stabilization with streptomycin or gentamicin. If used for this purpose, tetracycline therapy (2.0 grams per day orally) should be continued for three to four weeks to prevent relapses that may occur if therapy is limited to less than two weeks. Chloramphenicol can be substituted for tetracycline for the treatment of tularemia in children younger than 9 years. Response to appropriate antibiotic therapy is usually rapid, as seen in the two patients reported here, in whom notable clinical improvement was observed within 48 hours.[1-5,19] The importance of the early diagnosis and prompt initiation of appropriate antibiotic therapy against tularemia was emphasized in a recent report, where a delay in diagnosis and treatment correlated with a poor clinical outcome.[19]

In the Fairbanks, Alaska, region, the snowshoe hare (*Lepus americanus*), the local common native wild rabbit, is considered to be the predominant wild mammal host of *F tularensis;* hare ticks serve as the major pathogen reservoir.[23] Whereas about 1% of the American population is estimated to have an elevated titer for tularemia,[24] previous studies have documented that 3% to 7% of native Eskimos and Indians in central and western Alaska demonstrate serologic evidence of past exposure to *F tularensis.*[23,25] Although clinical tularemia is virtually nonexistent among native populations for unclear reasons, four cases of tularemia in white residents of the Fairbanks region were reported to the Alaska State Office of Epidemiology from 1982 to 1985. The two cases presented here represent the first reported instances of the transmission of tularemia by domestic animals in Alaska. Given the large reservoir of *F tularensis* in the snowshoe hare-tick population and the tendency of domestic dogs and cats to hunt and feed on sick prey, domestic pets in interior Alaska represent a potential vector for the transmission of *F tularensis* to human contacts. Furthermore, the finding that 14% of the veterinarians in the Fairbanks region had elevated tularemia titers (see Serology Survey) suggests that persons involved with domestic animal care should be regarded as a population at risk for tularemia in regions where *F tularensis* is enzootic.

Previous reports of cat-transmitted tularemia have described isolated cases of classic ulceroglandular tularemia.[7-9,11-13] The first case reported here is unique in that typhoidal tularemia developed following apparent exposure to an infected cat. Although veterinarians in the Fairbanks region were aware that local domestic animals were at risk for contracting tularemia, the potential for the transmission of tularemia from infected pets to human contacts was not generally recognized by the medical community (see Tularemia Survey), raising the possibility that additional cases of tularemia may have been misdiagnosed, possibly as unspecified viral syndromes.

Recognition of the possible vectors and diverse clinical presentations of tularemia can expedite the appropriate diagnostic studies and the initiation of appropriate empiric antibiotic therapy, thereby reducing potential morbidity and mortality. In regions where *F tularensis* is endemic in the wild mammal population, common domestic pets can acquire and transmit tularemia to human contacts. The finding that 48% to 62% of domestic dogs surveyed in two outbreaks of human tularemia had antibody titers to *F tularensis* of 1:40 or higher provides further evidence that common house pets may serve as hosts and vectors of the disease.[26,27] The high degree of virulence of *F tularensis* may allow for the transmission of tularemia to human contacts by bites or licks from apparently well domestic pets that harbor viable *F tularensis* organisms, acquired while preying on diseased wild mammals, in their mouths. Because *F tularensis* may survive in mud, water, or decaying carcasses for three to four months,[16] the carcasses of wild prey transported by pets to residential locations should be regarded as possible sources of *F tularensis.* Therefore, special care to avoid direct physical contact with mammal carcasses should be exercised in regions where tularemia is prevalent. Given the high virulence and substantial morbidity associated with *F tularensis,* physicians should consider the possibility of tularemia in a patient who presents with an acute febrile illness and a history of exposure to carnivorous domestic animals, including house cats, with access to the outdoors.

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Babesiosis in California

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BABESIOSIS IS A TICK-BORNE ZOONOSIS caused by an intraerythrocytic parasite. The cycle of transmission of the protozoan *Babesia* species between the tick vector and vertebrate host is occasionally interrupted by humans, resulting in human infection. Babesiosis is most common in otherwise healthy persons, many of whom remain asymptomatic. Although patients who have had a splenectomy are not more susceptible to infection with a *Babesia* species, they are more likely to become symptomatic, probably due to suppressed immune function. Symptomatic babesiosis is characterized by persistent fever and chills, hemolytic anemia, myalgias, fatigue, and hepatosplenomegaly. *Babesia divergens* causes severe and often fatal disease and is found throughout Europe. *Babesia microti,* found most often in the northeastern United States, typically causes a mild flulike illness, but a broad range of severity exists, and *B microti* babesiosis can be severe and occasionally fatal. Sporadic cases in other parts of America, often caused by non-*B microti* species, have been reported over the past 25 years, including two cases in California.[1,2] We report the third case of babesiosis contracted in California.

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Report of a Case

The patient, a 22-year-old male soldier, presented to Hays Army Community Hospital at Ford Ord, California, with fever and chills, headaches, nasal congestion, and vomiting of five days' duration. He had been on field exercises at Fort Hunter Liggett in central California when his symptoms first began. There he was prescribed penicillin V (previously called penicillin phenoxymethyl) at a battalion aid station when he reported a history of splenectomy in 1986 for idiopathic thrombocytopenic purpura. Symptoms persisted after several days of penicillin treatment, and when he began to complain of neck pain radiating down his back, he was admitted to the hospital. On admission he also noted generalized weakness, myalgias, and anorexia. He did not have sore throat, diarrhea, or productive cough.

He had spent most of the preceding year on field exercises in central California. He had not had recent mosquito or rodent bites but did recall a tick bite at Fort Ord, in the coastal region of central California, about five months previously without subsequent illness. He had no travel to the American Northeast, Wisconsin, or Minnesota within the previous year and had never traveled to Eastern or Western Europe, Africa, Asia, or South America. He had no pets and had not had close contact with any domestic animals including dogs, cattle, or horses. There was no history of blood transfusion or intravenous drug use. He had received a pneumococcal vaccine shortly before his splenectomy.

On physical examination the patient appeared lethargic but oriented. His temperature was 39.4°C (103°F), his blood pressure was 136/70 mm of mercury, and pulse 98 beats per minute. The skin was without rashes or bite marks. There was neck pain that radiated down his back on neck flexion. The physical examination was otherwise unrevealing.

The initial laboratory blood findings are summarized in Table 1. A urinalysis was remarkable for 2+ protein and 10 to 15 red blood cells per high-power field. A lumbar puncture yielded clear, colorless fluid; the Gram's stain showed no organisms or cells; latex agglutination tests for *Streptococcus pneumoniae, Neisseria meningitidis,* and *Haemophilus influenzae* were negative; and