Naturally occurring tularemia in a dog

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Tularemia is a zoonotic disease caused by Francisella tularensis, a gram-negative, facultative intracellular bacterium.

Tularemia has been documented in more than 100 species of wild and domestic mammals and humans.

Dogs and cats can acquire the infection, although clinical illness is more common in cats.

Infection is initially local with inflammation at the site of exposure, followed by dissemination via regional lymphatics or blood.

A 4-year-old spayed female Irish Setter was examined because of acute onset of lethargy, anorexia, and weakness. Thirty-six hours previously, the dog had eaten an adult rabbit.

Examination revealed that the dog had moderate signs of depression, fever (rectal temperature, 40.5°C [104.9°F]), and slightly enlarged mandibular lymph nodes. Bilateral mucoid ocular discharge and mild conjunctival hyperemia were noted. Small vessels in the mucous membranes were slightly swollen; no icterus was observed. Slight salivation was also noticed, although oral ulcers were not found. Hydration status appeared normal. Results of abdominal palpation and thoracic auscultation were unremarkable.

Tularemia was suspected because of the rabbit exposure; however, other common diseases characterized by fever, malaise, and lymphadenopathy of acute onset were also considered (ie, ehrlichiosis and Rocky Mountain spotted fever). The dog was treated with doxycycline (5 mg/kg [2.3 mg/lb], PO, q 24 h) for 14 days, as well as supportive treatment with a balanced electrolyte solution (lactated Ringer’s solution [200 mL, SC]).

The following morning, the dog remained anorectic but appeared more responsive. Rectal temperature was 39.6°C (103.3°F). Mandibular lymph nodes were substantially enlarged and firm. Slight mucoid ocular discharge was noticed. Blood was collected for CBC, serum biochemical profile, and serologic testing for Francisella tularensis, Ehrlichia canis, and Rickettsia rickettsii. Lymph node aspirates were collected from mandibular, prescapular, and popliteal lymph nodes for cytologic evaluation and immunofluorescent antibody testing for F tularensis antigen. Additionally, lymph node tissue was collected in an attempt to culture F tularensis. Fine-needle aspirates were collected from lymph nodes via a 22-gauge needle attached to a 3-mL syringe prefilled with approximately 2 mL of blood culture medium. Following aspiration, which yielded scant bloody fluid, the culture medium and aspirated lymph tissue were expelled from the syringe into a sterile culture tube and submitted for culture.

Results of the CBC indicated mature neutrophilia with lymphopenia suggestive of a stress response. All RBC parameters were within reference limits. Platelet concentration was slightly low, although platelet clumping was detected on the smears. Results of the serum biochemical analyses revealed mild hypocalemia (9.1 mg/dL [reference range, 9.7 to 12.2 mg/dL]), unremarkable albumin concentration, and moderately high alkaline phosphatase activity (365 U/L [reference range, 20 to 155 U/L]). All other parameters were within reference ranges. Cytologic examination of the lymph node aspirates revealed reactive hyperplasia with moderate numbers of neutrophils. A lengthy search for bacteria revealed a few partially degraded bacterial rods within the neutrophils. Results of the indirect fluorescent antibody test for F tularensis were nondiagnostic because of high background fluorescence.

On the third day after exposure, the dog was bright and alert with a normal appetite. Mandibular lymph nodes were still enlarged. The dog’s rectal temperature was 38.6°C (102.2°F). There was continued improvement during the next 3 days, at which time the dog was clinically normal.

Francisella tularensis was isolated from the lymph node aspirates on cystine heart agar supplemented with 1% hemoglobin. Genus and species identification of the isolate was confirmed serologically by use of slide agglutination and indirect fluorescent antibody testing. The isolate was further characterized as F tularensis subsp tularensis via metabolic fingerprinting and polymerase chain reaction (PCR) assay by the use of primers specific for F tularensis subsp tularensis and subsp holarctica.

Serology results for serum collected 48 hours after exposure were negative for antibodies against F tularensis by use of the microagglutination test (titers < 20 are considered negative) and negative for canine ehrlichiosis and Rocky Mountain spotted fever by use of ELISA. Subsequent serum samples revealed an increasing titer to F tularensis, which peaked to a titer of 320 at approximately 4 weeks and declined to a moderate but stable titer of 160 that persisted for at least 6 months after exposure (Figure 1). Results of ELISA for canine ehrlichiosis and Rocky Mountain spotted fever remained negative for serum samples collected 14 days and 6 months after exposure.

Tularemia is a zoonotic disease caused by F tularensis, a gram-negative, facultative intracellular bacterium. It has been documented in more than 100 species of wild and domestic mammals and humans. In the United States, rabbits are commonly infected.
and are important in the transmission of *F. tularensis* to humans. Cats and dogs can acquire the infection, although clinical illness is more common in cats. Cats infected with *F. tularensis* have severe acute disease. Reports of tularemia in dogs are rare. In the naturally occurring canine cases that have been reported, clinical signs in affected dogs were mild and included fever, anorexia, and mild lymphadenopathy. Antemortem definitive diagnosis is difficult and requires detection of an increasing antibody titer or detection of the organism in biopsied tissue via culture, immunofluorescent staining, or PCR analysis.

Historically, serologic testing has been the major means of diagnosis. Infection with *F. tularensis* results in local infection and inflammation at the site of exposure, followed by dissemination via regional lymphatics or blood. In humans, the clinical signs and severity vary with route of infection. Most human cases are ulceroglandular, although cases of the more severe pneumonic disease have been reported recently in association with lawn mowing and brush cutting.

In cats, naturally occurring disease resulting from ingestion of infected tissue causes a severe acute disease characterized by marked signs of depression, fever, oral or lingual ulceration, regional or generalized lymphadenopathy, splenomegaly, and hepatomegaly, with a high mortality rate. Dissemination of bacteria and cell debris can lead to thrombosis of many organs. On postmortem examination, cats commonly have icterus, ulceration of oral and pharyngeal mucosa, enlarged lymph nodes with necrotic foci, and splenomegaly and hepatomegaly with multiple discrete foci of necrosis. A detailed review of tularemia in cats is available.

In contrast, dogs appear to be relatively resistant to tularemia, and clinical reports of naturally occurring tularemia in this species are rare. In those reports, the incubation period was 36 hours and 24 hours, respectively; this short incubation is consistent with the findings reported here. Clinical signs included pyrexia, anorexia, and mild lymphadenopathy, and all dogs recovered. Results of a CBC and chemistry profile were unremarkable in the only dog in which they were performed and diagnosis was made by use of serologic testing performed because of clinical suspicion of tularemia (known exposure to a wild rabbit). Experimentally induced tularemia has also been reported in dogs. As in other species, severity and localization of lesions were dependent on the route of inoculation. In most instances, the disease was self-limiting with spontaneous recovery.

The severity of tularemia is also dependent on the subspecies of *F. tularensis*. Two subspecies of *F. tularensis* are recognized in North America. The most commonly reported is subspecies *tularensis* (often referred to as type A), which is highly virulent for rabbits, humans, and cats and is associated naturally with a rabbit-tick cycle. *Francisella tularensis subsp holarctica* (type B) is less virulent for rabbits and humans and is associated with water and aquatic mammals. Because the 2 subspecies are quite similar antigenically and phenotypically, characterization has been based mainly on differences in virulence and on a small number of nonroutine biochemical characteristics. Thus, isolates often have not been identified to the subspecies level because of the expense and difficulty in subspecies identification. However, such information is important in characterizing clinical signs, transmission, and animal susceptibility, relative to the respective subspecies. Fortunately, metabolic fingerprinting and PCR methods have resulted in more reliable subspecies identification. The isolate from the dog reported here was *F. tularensis subsp tularensis*, which supports the impression that dogs are somewhat resistant to the infection, even with the more virulent subspecies.

A diagnosis of suspected tularemia is confirmed by culture of the organism or detection of an increasing titer. Serologic diagnosis is most common because of the fastidious growth requirements of *F. tularensis* and the potential for exposure of laboratory personnel. Timely diagnosis of acute tularemia by use of serologic testing is limited by the fact that antibodies may not be detectable until 2 to 3 weeks after exposure. In the dog reported here, serum obtained from blood collected at 48 hours yielded negative results for antibodies against *F. tularensis*. A low titer was detectable at 1 week and peaked at 4 weeks after exposure. Similarly, caution must be used in interpreting a single titer because many dogs without clinical signs may be seropositive as a result of previous exposure and may maintain titers for months to years. The dog in this report maintained a substantial titer for at least 6 months.

Successful antemortem culture of *F. tularensis* from clinical specimens is difficult. The organism may be cultured from the blood of septicemic animals, although this technique has low sensitivity. The diagnosis in the dog reported here was first confirmed by results of cultures made from fine-needle aspirate samples taken from lymph nodes, as has been reported in a cat and a human. Fine-needle aspiration is a relatively noninvasive technique to collect samples of deep tissues for culture and could be applied to tissues other than lymph nodes. The technique of prefilling a syringe with blood culture medium and expelling this material through the needle used for the aspiration procedure made it easy to inoculate culture medium, despite the minute amount of material retrieved by
fine-needle aspiration. Amplification of bacterial DNA in the PCR assay by the use of primers specific for F. tularensis was used in this case as an additional method to confirm the identity of the organism cultured from the lymph nodes and to identify the isolate to the subspecies level. In humans, PCR amplification of F. tularensis DNA from tissue specimens has been used in place of attempts to culture the organism and has had greater sensitivity than culture in some studies. This method of diagnosis also reduces the risk of laboratory-acquired disease.

It is likely that tularemia is underreported in dogs because of the self-limiting nature of the disease and difficulty in confirming the diagnosis. Results of numerous studies indicate high seroprevalence in dogs from areas in which tularemia is endemic. Although there are no recorded transmissions of tularemia directly from dogs to humans, the potential exists, as documented experimentally by the recovery of F. tularensis from oropharyngeal swab specimens from a dog after clinical recovery. Dogs may also play a role in dissemination of and increased exposure of humans to Dermacentor variabilis, one of the vectors of F. tularensis, as well as increased exposure to infected rabbits. Although clinical signs of tularemia in dogs can be subtle, accurate diagnosis may help decrease human exposure. Successful and timely ante-mortem diagnosis of tularemia in dogs can be accomplished through lymph node aspiration and bacteriologic culture.

References