Bat-Associated Leptospirosis

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Leptospirosis is a globally prevalent disease that affects humans, causing systemic illness that may lead to multi-organ involvement. Clinical signs include sudden fever, general malaise, muscular pain, conjunctival suffusion, and jaundice. Disease is caused by pathogenic bacteria including over 200 serologic variants. Most serologic variants have primary reservoirs in wild mammals, which continually infect and colonize domesticated animals. The organism has been recovered from rats, swine, dogs, cattle, and other animals, notably bats. Most studies have focused on domestic animals as reservoir hosts; however, because of their abundance, spatial distribution, and interrelationship with domestic animals, bats are becoming an epidemiologically significant source of leptospires. We present a case of serologically confirmed leptospirosis after bat exposure to add to the growing literature of bats as a possible source of transmission. Recognition of the common presentation of leptospirosis and Weil's disease, and identification of animal vectors, including bats, allows for the selection of appropriate antibiotic management to aid in resolution of symptomotology.

KEY WORDS: bats; leptospirosis; Weil's disease.
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BACKGROUND

Leptospirosis is a globally prevalent zoonotic disease that affects humans and animals.[1] Human infection most often occurs when mucous membranes or abraded skin are exposed to animal urine, contaminated water or soil, or infected animal tissue.[2,3] A 1999 outbreak of leptospirosis in the Yaeyama Islands, Japan, showed that a history of recreational activities involving water sports was more frequent (71%) than occupational risk factors related to agriculture or construction (29%) in disease acquisition.[4] Infection with leptospirosis causes a systemic illness that may lead to multi-organ involvement. Early clinical signs include sudden fever, severe general malaise, muscular pain, and conjunctival suffusion. Weil's disease, the most severe form of leptospirosis, manifests as profound jaundice, renal, hepatic and pulmonary dysfunction, and hemorrhagic diathesis.[5]

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Leptospirosis is caused by pathogenic spiral bacteria that belong to the genus *Leptospira*.[6] The organisms are coiled, motile, obligate anaerobes known as spirochetes. Recent work has identified over 200 serologic variants (also known as serovars). Most serovars have primary reservoirs in wild mammals, which continually infect and colonize the kidneys of domesticated populations. The organism has been recovered from rats, swine, dogs, cattle, and other animals, notably bats.[2]

Most studies have focused on domestic animals as reservoir hosts; however, because of their size, abundance, spatial distribution, and interrelationship with domestic animals, bats are becoming an epidemiologically significant sources of leptospires.[7,8] We present a case of leptospirosis after bat exposure to add to the growing literature of bats as possible sources of transmission.

CASE REPORT

A 49-year-old otherwise healthy male presented on transfer from an outside institution with fevers, myalgias, and jaundice. One week prior to admission, he presented to an emergency room with chills and fever up to 103°F. He underwent an unrevealing workup, was resuscitated with fluids, and was discharged with the clinical diagnosis of a viral syndrome. Over the next 3 days at home, his symptoms progressed to include anorexia, nausea, headaches, myalgias, non-bloody diarrhea, decreased urine output, weakness, and skin yellowing. Due to his progressive symptoms, he was transferred to our institution.

On further history, he reported two episodes of bat exposure 2 weeks prior to admission. During one instance, he was swimming in his above ground pool and saw a bat alongside him. The next day, he removed the presumably same bat, now deceased, with a net and threw it to the side of the pool. He reported no other contact with wild animals and generally kept his pool covered. He reported no spider bites, no tick bites, no sick contacts, and no recent travel. He denied history of alcohol abuse or acetaminophen ingestion.

On admission, he had a temperature of 101.3°F, blood pressure of 119/66 mmHg, heart rate of 88 beats per minute, respiratory rate of 20 breaths per minute, and oxygen saturation of 98% on room air. He appeared ill and fatigued. He had conjunctival suffusion, scleral icterus, and jaundiced skin. Musculoskeletal exam revealed tenderness to palpation of the hip flexors bilaterally. Cranial nerve, motor, and sensory exams were within normal limits except 4/5 hip flexion strength bilaterally, which was limited by pain. Babinski reflex was downgoing bilaterally. He had no lymphadenopathy, and cardiopulmonary exam along with abdominal exam was unrevealing.

Results of laboratory tests on admission and over the follow-up period are shown in Table 1. Notably, he had a white blood cell (WBC) count of 19,200/mm^3 and total bilirubin of 19.8 mg/dl. In addition, on admission, he had a myoglobin of 2,033 ng/μl and creatinine kinase of 618 pg/ml, suggesting low level rhabdomyolysis. During the hospital course, two separate blood cultures drawn prior to antibiotic administration were negative, urinalysis revealed large bilirubin, and urine culture was negative. Chest X-ray performed after volume resuscitation revealed slight peripheral opacities consistent with pulmonary edema. These opacities completely resolved by hospital day 2. Lumbar puncture was considered but not pursued given a low suspicion for meningitis as the patient had no nuchal rigidity, resolution of headache within 24 h of admission, and defervescence. Serologies for hepatitis A, B, and C were negative. Cytomegalovirus (CMV) quantitative polymerase chain reaction (PCR) and human immunodeficiency virus-1 antibody were negative. Epstein-Barr virus PCR was positive at 417 copies/ml, which was thought to represent subclinical viremia.

As the patient appeared ill and fulfilled systemic inflammatory response syndrome (SIRS) criteria on admission, he was empirically started on intravenous ceftriaxone pending blood cultures. Intravenous doxycycline was added at 100 mg twice daily for additional coverage of leptospirosis as both of these parenteral agents are effective first-line therapy for severe leptospirosis[9]. With these interventions, he had subjective improvement in his myalgias and malaise, defervesced, and his white blood cell count fell. His acute renal failure and thrombocytopenia resolved. With his clinical improvement and negative cultures at 48 h, all parenteral agents were discontinued, and oral doxycycline at 100 mg twice daily was initiated to complete a 7-day course.

On hospital day 6, the day of discharge, the clinical suspicion of leptospirosis was supported by a Leptospira antibody test at a titer of 1:100. The diagnosis was then confirmed by the microscopic agglutination test (MAT) for leptospirosis, which is the gold standard, having a specificity of 97% and a sensitivity between 30% to 76%.[10] There is cross reactivity between serovars with the MAT test, which can account for multiple positive titers, so the interpretation of the test follows the principle that the highest titers are associated with disease causality.[11] Our patient's MAT had the highest titers of the Bratislava (12,800), Georgia (12,800), and Icterohemorrhagiae (6,400) serovars, which are, therefore, most likely responsible for his illness. Georgia is quite rare, and even rarer in the United States, while Bratislava is often associated with pigs, horses, and sheep.[11–13] As the patient had no travel within the year and no contact with pigs, horses, or sheep, the Icterohemorrhagiae serogroup is the likely causative pathogen.

On follow-up with his primary care physician at 52 days after hospital admission, his hyperbilirubinemia had normalized. He was doing well with complete resolution of his symptoms.

Table 1. Results of Laboratory Tests on Admission and at Different Follow-Up Periods

Laboratory test	Day 1	Day 3	Day 6	Day 10	Day 52
White cell count, k/Ul					
Normal range, 3.5–10.5 k/UL	19.2	17.0	8.0	8.6	6.2
Platelet level, k/Ul†					
Normal range, 140–390 k/Ul	99	106	298	542	274
Creatinine, mg/dl					
Normal range, 0–1.7 mg/dl	2.43	1.40	0.99	1.22	1.14
Total bilirubin level, *mg/dl*					
Normal range, 0–1.3 mg/dl	19.8	23.2	18.9	16.5	2.2
Direct bilirubin level, *mg/dl*					
Normal range, 0–0.2 mg/dl	10.7	10.1	8.8	10.2	No results
Alkaline phosphatase level, *U/l*					
Normal range, 30–115 U/l	97	91	119	No results	No results
Aspartate aminotransferase level, *U/l*					
Normal range, 0–40 U/l	59	40	29	34	44
Alanine aminotransferase level, *U/l*					
Normal range, 0–48 U/l	50	36	36	56	129
Albumin level, *g/l*††					
Normal range, 3.5–5.0 g/l	2.1	2.0	2.0	3.5	4.1

DISCUSSION

Leptospirosis is a globally distributed disease with the majority of clinical cases occurring in the tropics. In the industrialized world, leptospirosis is rare, and even in the US, most reported cases occur in tropical regions, especially Hawaii.[14,15] We report a unique case presenting within the city of Chicago in Midwest America. Infection is quite infrequent in this region, with only six reported cases in Illinois since 2005.[11]

Clinical presentation of leptospirosis is variable, ranging from subclinical to potentially fatal illness. The disease course often follows a biphasic pattern, first presenting with nonspecific constitutional symptoms, including fever, malaise, conjunctival suffusion, and muscular pain, followed by an immune-mediated symptomatic phase after an intervening several day period of improvement. Jaundice is only seen in Weil's syndrome, the most severe icteric-hemorrhagic form of disease. It is potentially fatal, manifesting with disproportionately elevated serum bilirubin concentrations, renal failure, and pulmonary hemorrhage. Outpatients with mild disease can be treated with 5–7 days of oral doxycycline to reduce the duration of illness and prevent shedding of organisms through the urinary tract.[16] Prompt initiation of intravenous penicillin G and supportive care are the treatment of choice for hospitalized patients with severe disease; however, open-label randomized trials of intravenous ceftriaxone, cefotaxime, and doxycycline have demonstrated equal efficacy to penicillin G.[9,17,18]

The role of bats as reservoir animals and sources of transmission to humans is incompletely understood. Current literature focuses on domestic animals because of their close association with humans. Bats, however, may be potential sources of leptospirosis infection because of their abundance, spatial distribution, and close contact with both domestic animals and humans.[7,8] Studies in Peru have elucidated that bats harbor leptospires in their kidneys similar to other domestic animals.[19,20] In addition, circulating antibodies specific for *Leptospira* have been identified in Australian fruit

bats, and serological investigation of 195 domestic and 766 wild animals in Sudan isolated leptospirosis in 2 shortheaded fruit bats.[21,22] A recent study quantifying the prevalence of leptospiral colonization in bats in the Peruvian Amazon found that of 589 bats analyzed, the kidneys of 23 had culture and molecular evidence of leptospiral colonization, yielding a 3.4% colonization rate.[7] This finding of chronic renal colonization of bats with a variety of pathogenic and intermediate *Leptospira*, including two new species, further supports the potential transmission of leptospirosis through contact with bats.

More than 200 antigenic variants of leptospirosis are described worldwide, making *Leptospira* quite diverse.[6] When specific serovars colonizing bats match those causing human infection, transmission through contact with bats is supported. Icterohemorrhagiae, the implicated serovar in our patient, is often associated with pigs, horses, and sheep; however, it is also commonly found in dogs, rats, mice, and other domesticated animals.[8,11,12] Unpublished data[8] have shown that 40–50% of peridomestic rats carry this serovar. Matthias et al.'s analysis of leptospiral colonization of bats in a highly endemic region isolated the serovar Icterohemorrhagiae from one bat and from this proposed a rodent-bat cycle for infection.[8] Given the patient's lack of exposure to other carriers of leptospirosis, this case adds support to the growing awareness that bats may be an important link in the transmission cycle of leptospirosis and are potential sources of transmission to humans.

This case illustrates the classic biphasic presentation of leptospirosis complicated by Weil's disease that resolved with prompt initiation of antibiotics along with supportive care. The patient's history of bat exposure provides further support to growing literature that bats may harbor pathogenic leptospira and serve as vectors in disease transmission to human hosts.

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