# Case in Point

# Leptospirosis in a Patient with Schizophrenia

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This patient exhibited acute manifestations of leptospirosis—but, initially, negative serology. These authors explain how they handled this case, which was made more challenging by the patient's mental state.

Human leptospirosis is caused by pathogenic spirochetes of the genus *Leptospira*.[1] Mortality rates from severe infections can exceed 50%.[2] Unfortunately, the clinical features of leptospirosis are nonspecific, making it difficult (or impossible) to diagnose the condition on clinical grounds alone. Therefore, a high index of clinical suspicion and the use of diagnostic laboratory tests are essential for diagnosis.[3–5]

The disease is endemic in rural areas of the tropics, although it also has been reported in urban settings—both in tropical and in temperate regions of the world.[6–8] Until leptospirosis was removed from the U.S. list of nationally notifiable infectious diseases in 1995,[9,10] the state of Hawaii consistently had the highest reported frequency of the disease.[11]

Here, we report the case of a patient who acquired leptospirosis in Philadelphia, PA and subsequently developed renal failure and required hemodialysis. A noteworthy feature of this case was the fact that *Leptospira* serology, although initially negative, became strongly positive during the patient's clinical illness.

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## INITIAL EXAM

A 51-year-old, black man was transferred to the Philadelphia VA Medical Center (PVAMC) after a 14-day admission to a non-VA, community hospital in the Philadelphia area. The patient had been admitted to the non-VA hospital with atrial fibrillation, acute renal failure, and hyperbilirubinemia. Upon admission to that facility, he had been intubated for respiratory support.

The patient had schizophrenia and a history of hypertension. Due to his schizophrenia, the patient's ability to function in the community was limited. He had a history of homelessness and had lived in wooded, outdoor areas of Philadelphia. The patient reportedly brushed his hair with leaves and kept earth in his pockets. It also was reported that he had constructed an underground tunnel, with the intention of living in it.

Hemodialysis had been started at the non-VA hospital, where antimicrobial medications had been given empirically, before the patient's transfer to the PVAMC. A serum sample collected nine days before transfer to the PVAMC was tested for *Leptospira* antibody, using an indirect hemagglutination assay (IHA), and yielded a negative titer of 1:50 (1:100 or greater indicates a positive result).[12] Abdominal ultrasonography at the non-VA facility reportedly showed gallstones. The patient was extubated six days before transfer to the PVAMC, and his atrial fibrillation resolved, with the restoration of sinus rhythm, before the transfer.

Upon admission to the PVAMC, the patient was oriented to person but, initially, not to place or time. He spoke in a whisper and his speech was difficult to understand. Physical examination revealed icteric sclerae and an unremarkable temperature of 37.2°C. The patient's serum creatinine and total bilirubin levels were elevated to 7.9 mg/dL (reference range, 0.7 to 1.2 mg/dL) and 9.6 mg/dL (reference range, 0.4 to 2 mg/dL), respectively (Figure 1). His serum aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels were moderately raised to 115 IU/L (reference range, 15 to 41 IU/L) and 98 IU/L (reference range, 17 to 63 IU/L), respectively (Figure 2).

According to the patient's VA medical record, the behavioral health service had been treating him on an ongoing basis. His record also indicated past or current infection with hepatitis B virus (HBV) and hepatitis C virus (HCV), as attested by positiv-

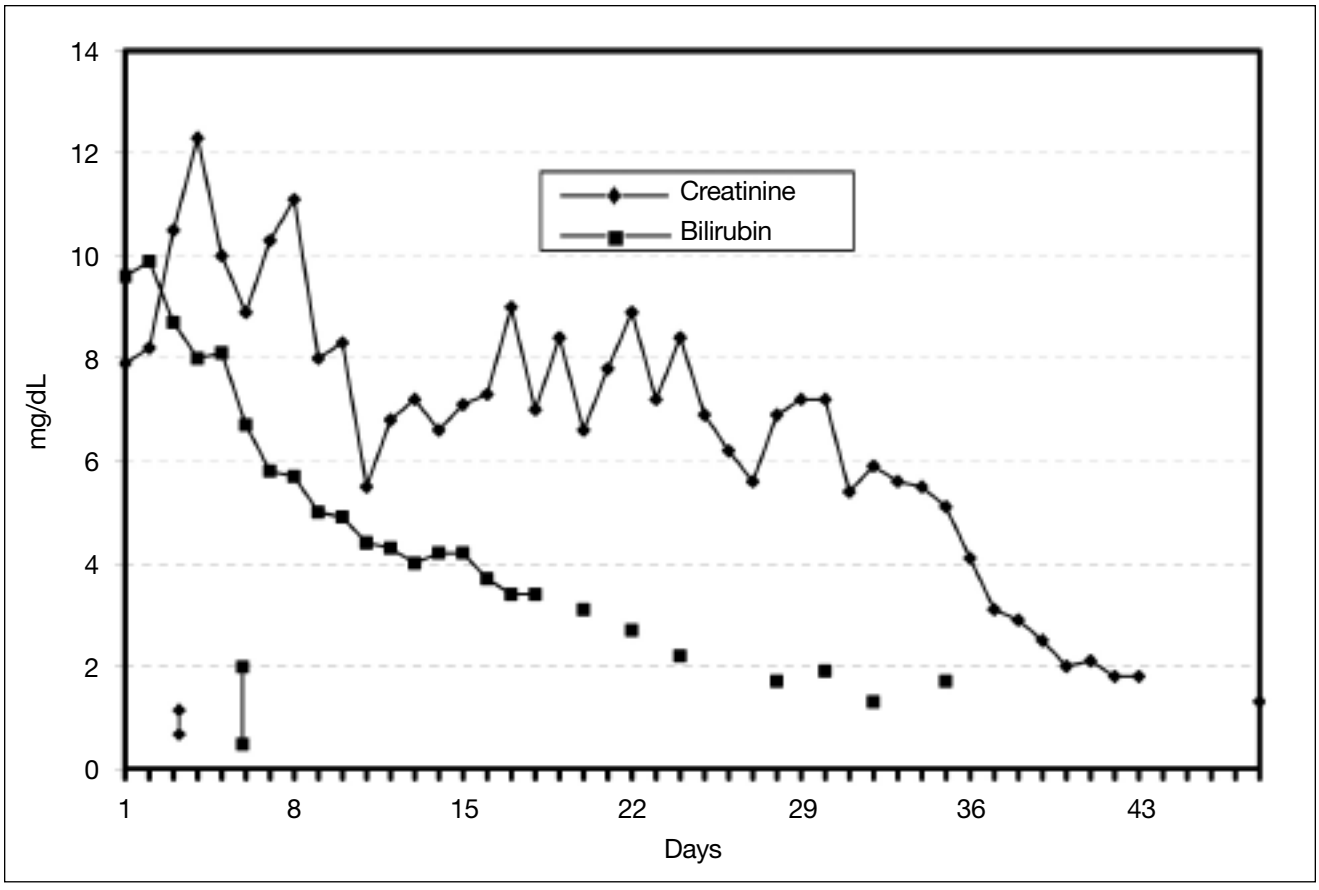


Figure 1. Creatinine and total bilirubin levels in serum samples from the case patient, measured at serial times during his admission to the Philadelphia VA Medical Center. (Reference ranges for creatinine and total bilirubin are shown as vertical bars in the lower left section of the plot graph.)

ity for HBV core antibody and HCV antibody, and documented a previously normal serum creatinine level of 1 mg/dL, which was measured about nine weeks before the start of the acute illness described in this report.

In an attempt to obtain diagnostic information about the patient's uncharacterized acute illness, the treatment team contacted the PVAMC's chief of staff, who had the institutional authority to act as a surrogate for the informed consent process for patients who lack mental competence and have no readily contactable relatives. The chief of staff was asked to endorse the team's plan to pursue magnetic resonance imaging of the patient's brain and computed tomography (CT) scanning of the patient's abdomen and pelvis. Neither imaging test identified the cause of his acute clinical picture; however, the CT scan did reveal a gallstone that measured approximately 1.5 cm at its greatest dimension. In addition, it revealed multiple subcentimeter, low attenuation lesions in the kidneys bilaterally, which were thought most likely to represent renal cysts. The CT scan also showed minimal atelectasis of the lung bases.

In reviewing the patient's medical record, the chief of staff noted the combination of renal failure and liver disease and asked the team to consider the possibility that the patient might have leptospirosis. Accordingly, serologic testing for this infection (using IHA) was repeated. Testing of serum collected from the patient on the fifth day of admission to the PVAMC yielded a strongly positive IHA titer of 1:6,400. Another serum sample, collected on the 10th day of admission, was tested for *Leptospira* antibodies by a rapid immunoglobulin M dipstick assay, as well as by a microagglutination test (MAT).[13,14] Both of these tests were positive. The highest titers for the MAT were greater than 1:12,800 (with a positive result indicated in endemic areas by a titer of 1:800 or greater or at least a

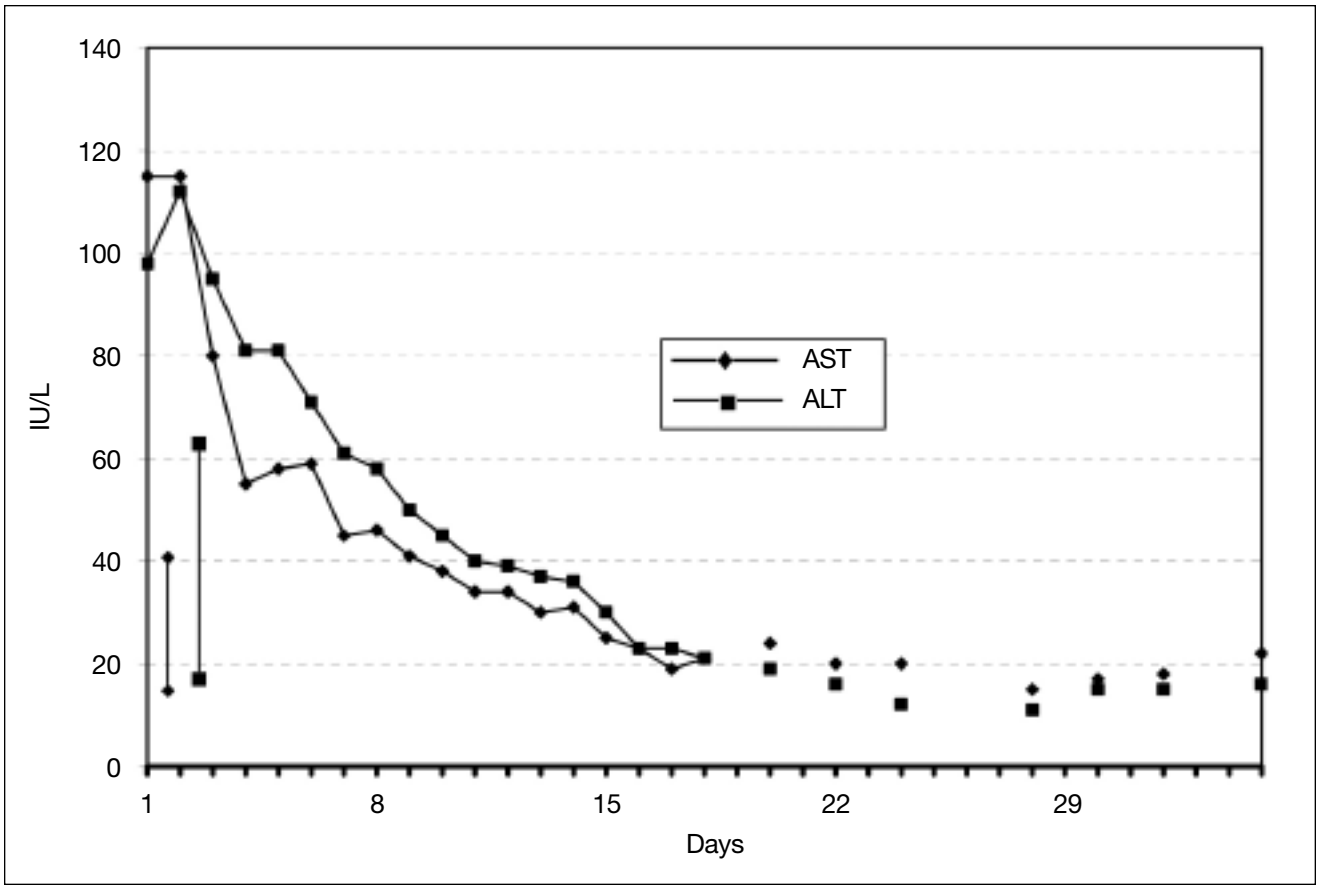


Figure 2. Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels in serum samples from the case patient, measured at serial times during the first five weeks of his admission to the Philadelphia VA Medical Center. (Reference ranges for AST and ALT are shown as vertical bars in the lower left section of the plot graph.)

fourfold increase in titer[15]) and were directed against *Leptospira interrogans* serogroups Icterohaemorrhagiae, Mini, and Australis.

## TREATMENT COURSE

Given the patient's renal impairment, hemodialysis was begun on admission, with an approximate schedule of three times per week.

By the time the diagnosis of leptospirosis was confirmed, so much time had elapsed since the onset of the patient's acute illness (three to four weeks) that antibiotic therapy directed at the *Leptospira* organisms was not deemed necessary. By this point, his condition also had begun to exhibit clinical and biochemical improvements. He did receive antibiotic therapy, from day 18 to day 35 of his hospital stay, for a urinary tract infection and bacteremia (with *Escherichia coli*) that developed more than two weeks after his admission to the PVAMC.

At three weeks into his PVAMC admission, the patient's serum total bilirubin, AST, and ALT levels all showed improvement. His mental status also improved, as judged by an increase in coherence of his speech and reduction in his confusion. According to the patient's serum creatinine levels, his renal function remained impaired after three weeks of hemodialysis, and this treatment was performed for another week. Chest radiographs obtained approximately three and five weeks after admission to the PVAMC showed "well aerated lungs with no acute infiltration or congestion."

At the end of an inpatient stay of approximately seven weeks, the patient was discharged from the PVAMC to a personal care facility. By that time, his serum creatinine level had fallen to approximately 1.3 mg/dL. Thereafter, follow-up was provided by the PVAMC on an outpatient basis, and when the patient was retested for *Leptospira* antibodies nine months later, his serum IHA titer had reverted to negative (less than 1:50).

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## ABOUT THE CONDITION

The typical clinical presentation of leptospirosis involves fever, headache, photophobia, myalgia, and acute renal failure, with or without jaundice.[1,16,17] Additional clinical features include thrombocytopenia, lung involvement (pulmonary radiodensities seen on chest radiographs and, in some cases, massive and fatal pulmonary hemorrhage), and cardiac involvement manifested by atrial fibrillation and other electrocardiographic abnormalities.[18–24]

In the case patient, the acute presentation of atrial fibrillation and the combination of acute renal failure, hyperbilirubinemia, and modestly elevated serum AST and ALT levels were all characteristic of leptospirosis.[16] The nature of the presumed respiratory problem that led to his intubation at the non-VA hospital (before transfer to the PVAMC) is unknown. During his PVAMC stay, he had no documented respiratory symptoms.

The diagnosis of leptospirosis in this patient might not have been recognized if clinical suspicion had not prompted a second IHA test for *Leptospira* antibody. Although the time of exposure for this patient could not be determined, the initial negative serologic test was early in the acute phase, and the second IHA test, approximately two weeks later, was strongly positive. These findings reflect the recommendation to collect both acute and convalescent sera for serologic diagnosis of leptospirosis.[1]

The decision was made not to treat the patient's leptospirosis with antibiotics, in view of the relatively late stage at which the infection was confirmed. Although some medical literature suggests that antibiotics are therapeutically effective at this stage of the infection, other publications cast doubt on the efficacy of such treatment at that time.[25–27]

Risk factors for acquiring leptospirosis include exposure to contaminated environmental or animal sources of leptospires.[28–34] Contaminated lake and river water can put swimmers and boaters at risk, and contact with rodent urine or such infected animals as dogs or pigs can put livestock handlers and abattoir workers at risk.[28–34] Leptospirosis also is an occupational hazard for sewer workers and public cleansing workers—at least as judged by prevalence of *Leptospira* antibodies in individuals from these professions.[35]

Skin cuts can act as a portal of entry for the causative organism: A laboratory worker reportedly developed leptospirosis as a result of the inadvertent irrigation of leptospires into a skin cut that occurred when the glass container that held cultures collected from a patient broke.[36] Walking barefoot on the ground outdoors is an additional risk factor for acquiring leptospirosis, at least in tropical areas, as determined by presence of *Leptospira* antibodies.[37]

Although it is unclear how the case patient acquired leptospirosis, his tendency to live outdoors in semirural areas, to dig in the ground, and (according to some descriptions) to eat earth and grass, may have exposed him to rat urine containing leptospires.[8,33] The behaviors described were at least partly ascribable to the patient's schizophrenia—which, accordingly, can be regarded as a risk factor for this patient's leptospirosis.

The fact that leptospirosis is no longer a nationally notifiable disease in the United States may be a disincentive to clinical and laboratory efforts to diagnose the infection in this country.[9,10] Therefore, we support the view, which has been expressed by other authors,[11] that leptospirosis be reinstated to the list of nationally notifiable infections in the United States. ●

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