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Report of case: leptospirosis after exposure to alligator carcass

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In the past decade, leptospirosis has emerged as a globally important infectious disease. Mortality remains significant; this may be related to delays in diagnosis because of lack of infrastructure and adequate clinical suspicion, and to other poorly understood reasons that may include inherent pathogenicity of some leptospiral strains or genetically determined host immunopathological responses. Leptospirosis is a spirochete parasitic bacterium most commonly reported from rodents and contracted through contact with rodent urine, but also reported from cows and other domestic animals and contracted through contact with contaminated water. Humans are infected by direct contact with animals or through exposure to fresh water or soil contaminated by infected animal urine. Leptospires enter the body through cuts and abrasions, mucous membranes or conjunctivae, or aerosol inhalation of microscopic droplets. From 1995-1998, approximately nine people working with alligators in south Florida have apparently contracted leptospirosis. All of the victims were working with wild alligators; most had contact with alligator nests and nearly half required hospitalization. Although it has been postulated that leptospires may be transmitted directly from infected, large reptiles to the hands of handlers, it has been felt that it was probably more likely that handlers were indirectly exposed by water contaminated with the urine of leptospiruric reptiles or that the swamps and waterways from which eggs are harvested are contaminated by the infected urine of rodents or other animals. This report describes a case in which a Florida State Trooper became symptomatic after removal of an alligator carcass from a south Florida roadway.

In the past decade, leptospirosis has emerged as a globally important infectious disease. Mortality remains significant, related both to delays in diagnosis because of lack of infrastructure and adequate clinical suspicion, and to other poorly understood reasons that may include inherent pathogenicity of some leptospiral strains or genetically determined host immunopathological responses.[1] *Leptospirosis is* a spirochete parasitic bacterium, most commonly reported from rodents and contracted through contact with rodent urine, but also reported from cows and other domestic animals and contracted through contact with contaminated water. Humans are infected by direct contact with animals or through exposure to fresh water or soil contaminated by infected animal urine. Leptospires enter the body through cuts and abrasions, mucous membranes or conjunctivae, or aerosol inhalation of microscopic droplets.[2] From 1995-1998, approximately nine people working with alligators in south Florida have apparently contracted leptospirosis. All of the victims were working with wild alligators; most had contact with alligator nests and nearly half required hospitalization.[3] Although it has been postulated that leptospires may be transmitted directly from infected, large reptiles to

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the hands of handlers, it has been felt that it was probably more likely that handlers were indirectly exposed by water contaminated with the urine of leptospiruric reptiles or that the swamps and waterways from which eggs are harvested were contaminated by the infected urine of rodents or other animals.[4] This report describes a case in which a Florida State Trooper became symptomatic after removal of an alligator carcass from a south Florida roadway.

Outbreaks of leptospirosis are usually caused by exposure to water contaminated with the urine of infected animals. Many different kinds of animals carry the bacterium; they may become sick but can also remain asymptomatic. Leptospira organisms have been found in cattle, pigs, horses, dogs, rodents, and wild animals. Humans become infected through contact with water, food, or soil containing urine from these infected animals. This may happen by swallowing contaminated food or water, or through skin contact, especially with mucosal surfaces, such as the eyes or nose, or through broken skin.[5] We encountered a case in which the disease may have been spread through contact with the carcass of an alligator.

Report of case

A 43-year-old male with no significant past medical history presented to a walk-in clinic with generalized malaise, upper respiratory infection symptoms, weakness, and neck pain. The patient was prescribed amoxicillin 500 mg three times per day (tid), clemastine fumarate/phenylpropanolamine hydrochloride, prochlorperazine 5 mg as needed (prn), acetaminophen #3 prn, and acyclovir tid. The patient's symptoms progressed over the next several days when he presented to his personal physician with hallucinations, disorientation, fevers of 104 to 105 °F, severe headaches, a bright red rash on his chest, bloodshot eyes, and a bright cherry red tongue. He was admitted to the hospital for further evaluation.

Upon admission, physical examination revealed an ill-appearing man with a flat affect and swollen red eyes. Temperature was 100.9 °F, pulse 132 beats per minute, respirations 24 respirations per minute, and blood pressure 110/70 mm Hg. The sclera were injected, the oral pharynx was red, and the tongue was glossy red. The patient's neck was tender with resistance to flexion and extension. Heart was regular, lungs were clear, abdomen was soft. There were no other significant physical findings.

Laboratory findings

A screening hepatitis panel was normal. Typhoid H, O; paratyphi A, B; *Brucella* serologies; and *Proteus* Ox 19 agglutination were all negative. Serum *Mycoplasma* IgM titer was negative [0.22 ISR (immune status ratio)]; cytomegalovirus IgM titer was negative (<1:10 OD ratio); *Legionella pneumophila* IgM titer was positive (1:10 U); Leptospira agglutinin was negative; antinuclear antibody was negative; C3 complement was 120 (within normal limits); and anti-streptolysin O titer was normal. Urine and blood cultures were negative for aerobes and anaerobes. See Table 1 for a complete admissions profile.

Table 1 Admission profile

Laboratory test	Admission	Normal
Blood		
White blood cell count	24.9 mm^3	3.5-9.6 mm^3
Hemoglobin	13.7%	34.7-45.2%
Hematocrit	38.3 g/dL	11.8-15.4 g/dL
Platelets	333 K/μL	147-354 K/μL
Sodium	132 mmol/L	135-150 mmol/L
Potassium	4.3 mmol/L	3.5-5.2 mmol/L
Chloride	91 mmol/L	95-110 mmol/L
Glucose	125 mg/dL	70-110 mg/dL
Carbon dioxide	17 mmol/L	19-34 mmol/L
Blood urea nitrogen	85 mg/dL	6-25 mg/dL
Creatinine	8.8 mg/dL	0.6-1.3 mg/dL
Total bilirubin	4.8 mg/dL	0.1-1.1 mg/dL
Aspartate aminotransferase	33 IU/L	10-40 IU/L
Alanine aminotransferase	53 IU/L	7-55 IU/L
Urine		
Protein	≥500 mg/dL (5+)	Negative
White blood cells	25-30/HPF	0-5/HPF
Red blood cells	5-8/HPF	0-3/HPF
Cast, granular	>15/LPF	0-2/LPF

HPF, high power field; LPF, low power field.

Cerebrospinal fluid was clear (12 mL), with no red blood cells or white blood cells (WBCs), and normal protein levels at 22 mg/dL (15-45 mg/dL); Gram stain was negative, with no organisms seen; India ink preparation was negative with no growth; and no acid-fast bacilli were seen.

Serum markers for viruses were negative, VDRL (Venereal Disease Research Laboratory) was in normal range, acid-fast bacilli was negative, Gram stain was negative, India ink preparation was negative, and *Meningococcus* A, B, and C were all negative. The *Haemophilus influenzae* antigen was negative, and the group B *Streptococcus* antigen and *Streptococcus pneumoniae* antigen were negative. Purified protein derivative standard test was positive at 25 mL.

Bronchoscopy washings were negative for viruses, with light growth of *Candida albicans*. The washing and biopsy revealed mild chronic inflammation, hyperplasia of the alveolar lining cells, and no evidence of granuloma or neoplasm. Sputum revealed fungal hyphae and necrotic debris.

Electrocardiogram demonstrated normal sinus rhythm with nonspecific ST-T wave changes. Electroencephalogram was diffusely abnormal, indicative of diffuse enceph-

alopathy of moderate degree because of the generalized slowing of background activity.

Radiology studies

Chest x-ray revealed increased interstitial markings seen throughout both lung fields, with development of patchy infiltrates at the left lung base. Later, on the same day as admission, chest x-ray revealed cardiac decompensation with fluid overload.

Computerized tomography of the brain was normal. Computerized tomography of the abdomen and chest demonstrated bilateral pleural effusions and possible basal infiltrate of the left lung base, otherwise normal.

Sinus x-ray revealed bilateral mucosal thickening involving both maxillary sinuses.

Clinical course

The patient was admitted for fever of unknown origin, disorientation, and stupor. During his stay, the patient's stupor and disorientation progressively worsened, being complete at times. After the patient's blood urea nitrogen increased to 106 mg/dL and his creatinine increased to 10.6 mg/dL, a dialysis catheter was placed for renal dialysis.

Blood and urine cultures were obtained. A lumbar puncture was done to rule out meningitis.

A Swan-Ganz catheter was placed in the patient's right subclavian vein, with the following pressures obtained: right ventricle 36/00 mm Hg, pulmonary artery 34/18 mm Hg, and pulmonary wedge pressure of 17 mm Hg.

With a leading diagnosis at the time of encephalitis or meningitis, the patient was given 500 mg of ampicillin intravenously (IV) every six hours initially on hospital day one, and then the dose was increased to 2 g of ampicillin IV every six hours on hospital day two. He was also placed on tobramycin 80 mg IV every eight hours, and then 500 mg of erythromycin IV every six hours was added to his medications on hospital day three.

The patient developed intrapulmonary bleeding with respiratory failure. A bronchoscopy with biopsy was done, followed by intubation as a result of intrapulmonary bleeding with respiratory failure. The patient remained febrile during his course at the hospital.

The family of the patient requested transfer to a tertiary care facility, university teaching hospital. Four days after admission, the patient was transferred via helicopter to the intensive care unit of a university hospital in acute renal failure, respiratory failure and fever of unknown origin.

The patient was admitted to the medical intensive care unit at the university hospital with a blood pressure of 100/50 mm Hg, pulse of 95 beats per minute, and temperature of 101 °F. At examination, he was noted to have injected sclera, his neck was stiff, and his lungs revealed rales greater on the left than right. There was a pericardial friction rub on heart examination and there were decreased bowel sounds.

In the medical intensive care unit the patient was treated with 1 g of ampicillin IV every six hours and erythromycin 1 g IV every six hours. The patient's respiratory status began to improve and he was extubated and transferred to the medical floor for further workup. After transfer, the patient was very lethargic, with no acute distress.

During the hospital stay, the patient's symptoms slowly improved. He continued hemodialysis with gradual improvement of his renal function.

Although leptospira agglutination titers drawn at the community hospital were negative, the infectious disease team at the university hospital believed that the patient had leptospirosis and repeated titers were drawn and found to be positive. The patient's hematocrit decreased to 20 g/dL and he was transfused. Hemodialysis was stopped as the patient's renal function increased. He maintained good urine output and his blood urea nitrogen dropped to 51 mg/dL with a creatinine of 4.1 mg/dL. His liver function tests returned to normal and he was discharged with a hematocrit of 23 g/dL, a platelet count of 150,000 K/μL, blood urea nitrogen of 49 mg/dL, and creatinine of 3.5 mg/dL.

Case discussion

This patient's presentation was consistent with leptospirosis. The patient was a Florida State Trooper, and after discharge it was discovered that initial symptoms appeared approximately 10-14 days after removing an alligator carcass from a roadway without using gloves.

Leptospirosis is a zoonosis of global distribution, caused by infection with pathogenic spirochetes of the genus *Leptospira.* Although underreported, it has been suggested that it may be the most common zoonosis. The disease is maintained in nature by chronic renal infection of carrier animals, which excrete the organism in their urine, contaminating the environment. Human infection occurs by direct contact with infected urine or tissues or, more commonly, by indirect exposure to the organisms in damp soil or water. The mean onset of symptoms of the primary illness is 10 days (range 5-14). With a broad spectrum of severity, leptospiral infection ranges from subclinical illness followed by seroconversion to two clinically recognizable syndromes—a self-limited systemic illness seen in approximately 90% of infections, and a severe, potentially fatal illness accompanied by any combination of renal failure, liver failure, and pneumonitis with hemorrhagic diathesis. The disease can have two distinct phases, an initial septicemic stage followed by a temporary decline in fever followed by an immune phase in which the severe symptoms occur. There may be no apparent distinction between these two phases, or patients may present only with the onset of the second phase of the illness. Weil disease, characterized

by impaired hepatic and renal function, is the most distinctive form of severe illness that occurs after the acute phase of the illness. Mortality with severe disease ranges from 5% to 40%.[6]

Case classification as *probable* is described as a clinically compatible case with supportive serologic findings. Case classification as c*onfirmed* is defined as a clinically compatible case that is laboratory confirmed.[7] WBC counts are generally less than 10,000, urinalysis frequently is abnormal, and elevated creatine kinase is found in approximately 50% of patients. About 40% of patients have minimal to moderate elevations of liver enzymes. Unlike *Treponema pallidum*, leptospira can be grown from blood, urine, and cerebrospinal fluid. It is slow growing and the laboratory needs to be notified. Isolation of the organism from the blood is successful in 50% of cases.[6]

Patients with mild or anicteric disease usually get better without treatment. Although doxycycline 100 mg daily has been shown to shorten the duration of the illness,[8] patients may be treated with intravenous penicillin G (benzylpenicillin) or cefotaxime.[9] In severe cases, hospitalization with excellent supportive care with particular attention to fluid and electrolyte balance and pulmonary and cardiac function is critical. Renal failure should be treated by peritoneal or hemodialysis.[9]

Conclusion

Although anecdotal evidence suggests that alligator handling may be a risk factor for leptospirosis, and the findings of this case support this, there is still no conclusive evidence. Nonetheless, this case is sufficient to support the promotion of self-protective measures for law enforcement officers and others removing alligator (and other animal) carcasses from roadways, as well as others who may handle alligators. Clinicians in areas indigenous to alligators or crocodiles should be aware of the types of occupational and recreational activities that predispose to this condition, and they should have a low threshold for testing for leptospirosis in those with consistent symptoms.

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