

CASE REPORT

BACTEREMIC LEPTOSPIROSIS TO SEVERE LEPTOSPIROSIS: A CASE SERIES

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Abstract:

Leptospirosis is a common zoonotic infection in tropical countries due to contact with water contaminated by the spirochaete Leptospira. Here, we present four different and unrelated cases of patients presenting with leptospirosis. A 23-year-old pregnant woman hailing from Savar presented with aseptic meningitis due to leptospirosis after bathing in contaminated water. She did not respond to Ceftriaxone initially and was treated with adjunct Dexamethasone according to the treatment protocol for bacterial meningitis. We also present cases of three middle-aged gentlemen presenting with Weil's disease. Out of these three patients, two of them presented with fever and jaundice, and one presented with fever, jaundice, and acute kidney injury. Clinical vigilance is required to ensure appropriate recognition of patients with leptospirosis, as the presentation is variable.

Keywords: Leptospira, Weil's disease, Aseptic meningitis

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Introduction

Leptospirosis is one of the most common zoonotic diseases in tropical countries, especially during the monsoon season. It is caused by the spirochaete *Leptospira*, which can penetrate intact skin or mucous membranes.¹ It usually occurs when water or soil contaminated with urine from an infected host, such as rodents or dogs, comes into contact with humans.²

According to the Centers for Disease Control and Prevention (CDC), around 1 million cases occur globally, with a mortality rate of 60,000/annum.³ In Bangladesh, there are very limited epidemiological studies on leptospirosis. In a study done in 2010, leptospirosis accounted for 2 – 8% of patients with fever of unknown origin in an urban area of Bangladesh.⁴ Another study done on four tertiary-level hospitals in Bangladesh from May 2019 – March 2020

exhibited leptospirosis in 1.6% of patients with pyrexia of unknown origin.⁵

Before the beginning of an acute leptospiremic phase, there is an incubation period of 2 to 20 days, which is then followed by an immune leptospiruric phase.¹ Bacteremic leptospirosis can produce an influenza-like illness with high-grade fever, weakness, myalgia, intense headache, photophobia, diarrhea, and vomiting. Conjunctival congestion is the only sign during this phase. The patient spontaneously improves after about 1 week or merges into one of the three other forms of infection during the immune phase. These include aseptic meningitis/neuroleptospirosis, Weil's disease, characterized by fever, hemorrhage, jaundice, and acute kidney injury, and pulmonary syndrome, which includes pulmonary hemorrhage and acute respiratory distress syndrome.²

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Leptospirosis is usually confirmed by the microscopic agglutination test (MAT), which can become positive by the end of the first week, with a fourfold rise in its titer. IgM ELISA and immunofluorescent techniques are easier to perform. Blood cultures are usually positive if taken before day 10 of illness. Detection of leptospiral DNA by polymerase chain reaction (PCR) is possible in blood in early symptomatic disease and in urine from day 8 of illness.²

Treatment should be initiated as early as possible. Oral treatment with tetracycline, doxycycline, ampicillin, or amoxicillin is usually given in mild cases. For severe cases of leptospirosis, intravenous administration of penicillin G, amoxicillin, ampicillin, or erythromycin is recommended.¹

Case Report 1

A 23-year-old female with 20 weeks of pregnancy residing in Narayanganj presented to the emergency department with high-grade fever and myalgia for 7 days. On day 2, after admission to the medicine department, she developed a severe headache. Upon questioning, she revealed a history of bathing in freshwater 15 days back, next to a fishing farm owned by her father.

On admission, her physical examination revealed a pulse rate of 104 beats per minute, normal in volume; blood pressure of 120/70 mmHg; temperature of 40°C; and a respiratory rate of 18 breaths/min. Breath sound was vesicular on auscultation. The patient also presented with subconjunctival suffusion but was non-icteric. Neck rigidity, Kernig's, and Brudzinski's signs were absent.

Laboratory investigations demonstrated anemia and neutrophilic leukocytosis with a normal platelet count. Serum creatinine, alanine aminotransferase and aspartate aminotransferase were normal. The chest X-ray was normal. Ultrasonogram revealed a single live pregnancy of 21 weeks' gestation with a fetal heart rate of 160 beats per minute. Dengue NS1 antigen and dengue IgM antibody were negative. On day 3, IgM antibodies to *Leptospira* were positive. Lumbar puncture was then performed, revealing clear CSF with a white blood cell count of 2000/mm³ and a neutrophil predominance of 80%.

Upon admission, the patient was treated with injectable Ceftriaxone 1 gm 12 hourly for 7 days, to which she didn't respond. Then, she was given injectable Amoxicillin 2 gm 4 hourly and Dexamethasone 10 mg 6 hourly for 4 days. The patient became afebrile, and the headache subsided after 1 day. She was afebrile for 5 days before discharge. Upon discharge, injectable Amoxicillin was switched to oral.

Case report 2

A 45-year-old, hypertensive, non-diabetic gentleman with a history of bronchial asthma, hailing from Chadpur, presented with high-grade fever associated with chills and rigor for 15 days. It was followed by jaundice and oliguria for 10 days. 4 days before admission, the patient developed several episodes of vomiting and generalized body swelling, which started in his legs. His occupation revealed that he was a farmer.

On examination, the patient was anemic and icteric. He also had subconjunctival hemorrhage and bipedal oedema. His pulse was 84 beats per minute, normal in volume; blood pressure was 190/110 mmHg; temperature was 40°C; and spO₂ was 94% on room air. Examination of the respiratory system revealed vesicular breath sounds with prolonged expiration, bilateral basal crepitus, and rhonchi. Abdominal examination revealed a distended abdomen with positive fluid-shifted dullness.

Investigation revealed anemia, a raised erythrocyte sedimentation rate, and neutrophilic leukocytosis. Serum creatinine was raised, which decreased after 3 episodes of hemodialysis. Serum electrolytes revealed hyponatremia and hyperkalemia. Liver function tests revealed hyperbilirubinemia with normal alanine aminotransferase, aspartate aminotransferase, and raised alkaline phosphatase. Serum albumin and prothrombin time were normal. HbsAg and Anti-HCV were negative. Routine urine examination revealed 3+ proteinuria with numerous red blood cells and 6–8 pus cells per high-power field. Chest X-ray revealed features of pulmonary oedema, and ECG showed sinus rhythm with a rate of 85 beats per minute with features of hyperkalemia. The rapid test for IgM antibodies to *Leptospira* was positive.

On admission, the patient was started on injectable Meropenem. However, the fever did not subside. Oral doxycycline was added on the third day, and the patient underwent three episodes of hemodialysis. Afterward, the fever subsided, and the patient gradually improved.

Case report 3

A 50-year-old, normotensive, diabetic gentleman, farmer, hailing from Gopalganj, presented with high-grade fever for 8 days, jaundice and vomiting for 7 days, loose motion for 5 days, and an altered state of consciousness 7 hours before admission.

On examination, the patient was anemic, icteric, and had subconjunctival hemorrhage. A flapping tremor was present. His pulse was 76 beats per minute, within normal limits. His blood pressure was 110/70 mmHg, his temperature was 40.0 °C, and his spO₂ was 98% on room air. Abdominal examination revealed tenderness in the right hypochondriac region.

Investigation revealed anemia with raised erythrocyte sedimentation rate, neutrophilic leukocytosis, and thrombocytopenia. Serum creatinine was raised, which decreased after 2 days. Serum electrolytes revealed hyponatremia, but the potassium level was normal. Liver function tests revealed a raised bilirubin with raised aspartate aminotransferase and alkaline phosphatase. However, alanine aminotransferase was normal. The patient had hypoalbuminemia, but prothrombin time was normal. Anti-HAV IgM, anti-HEV IgM, HbsAg, and anti-HCV were negative. The rapid test for IgM antibodies to *Leptospira* was positive; however, the urine dark-ground illumination for *Leptospira* was negative.

On admission, the patient was started on injectable Ceftriaxone 1 g for 14 days. The patient gradually improved and was discharged on the 7th day after admission.

Case Report 4

A 38-year-old, normotensive, non-diabetic gentleman, a business decorator, hailing from Dhaka, presented with high-grade fever for 15 days and jaundice for 7 days.

On examination, the patient was icteric and had a subconjunctival hemorrhage. His pulse was 100 beats per minute, low volume, blood pressure 70/50 mmHg, temperature 37.0 °C, and spO₂ 95% on room air. Examination of other systems revealed no abnormalities.

Investigation revealed normal hemoglobin, neutrophilic leukocytosis, and thrombocytopenia. Serum creatinine and serum electrolytes were normal on admission. Liver function tests revealed a raised bilirubin and alanine aminotransferase. The patient had hypoalbuminemia. Anti-HAV IgM, anti-HEV IgM, and Dengue NS1+ve antigen were negative. The rapid test for IgM antibodies to *Leptospira* was positive. On admission, the patient was started on injectable Ceftriaxone 1 gm for 14 days, and the patient gradually improved.

Discussion

In this study, we present four cases of leptospirosis from four districts with exposure to contaminated water. Transmission doesn't occur from human to human. Therefore, contact with water contaminated by infected animals is essential for the transmission of leptospirosis. Occupations at high risk of leptospirosis include farmers, sewage workers, fishermen, veterinarians, and those who work in slaughterhouses.¹

Leptospirosis is caused by the spirochete *Leptospira* in populations, especially in tropical climates, who

come into contact with water and soil contaminated by infected rodents and dogs. Symptoms begin with the phase of bacteraemia leptospirosis in more than 90% of patients who have relatively mild symptoms. In 5 – 10% of patients, it is followed by severe leptospirosis.¹ All four of our patients presented with an initial bacteremic phase, which constituted high-grade fever, nausea, vomiting and conjunctival suffusion. It was then followed by a form of severe leptospirosis.

One form of severe leptospirosis is characterized by neuropsychiatric manifestations, which are seen in 10 – 15% of patients with severe leptospirosis. The most common form is aseptic meningitis, which accounts for 5 – 13% of all cases.⁶

Aseptic meningitis is an immune phase reaction that usually occurs between days 4 and 30.¹ Other neurological manifestations include encephalitis, intracranial hemorrhage, movement disorders, myelitis, flaccid paraplegias, mononeuritis, autonomic lability, polymyositis and acute disseminated encephalomyelitis.⁷

Case definition of meningitis includes fever with severe headache or signs of meningism, non-turbid, non-purulent cerebrospinal fluid (CSF) containing 10–2,000 cells/m³, raised protein and normal glucose.⁸ Although signs of meningism are seen in 80% of patients with neuroleptospirosis, our patient didn't present with these signs.⁷

For countries with limited resources, the World Health Organization (WHO) has developed a modified Faine's criteria in 1982 to make a presumptive diagnosis of leptospirosis. It is based on clinical history (part A), epidemiological history (part B) and laboratory investigations (part C). A diagnosis is made when the total score of parts A, B, and C exceeds 25, or part A and B, or only part A equals 26 or more.⁷ Our patient with aseptic meningitis presented with a total score of 33.

Leptospirosis should be differentiated from other causes of fever with myalgia and headache in Bangladesh, such as dengue, malaria and enteric fever. In our patient, dengue NS1 antigen and dengue IgM antibody were negative. After confirmation of rapid diagnostic test (RDT) for IgM antibodies to *Leptospira*, lumbar puncture for CSF study was done in our patient, which showed CSF pleocytosis with 80% neutrophils. In aseptic meningitis, a polymorphonuclear leukocytosis is followed by an increase in mononuclear cells.¹

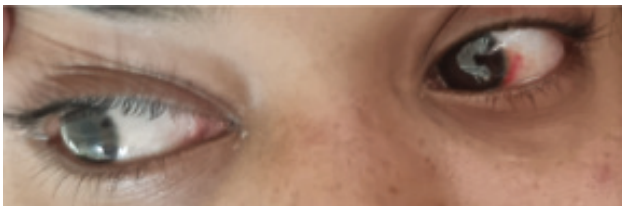
Another severe form of leptospirosis includes Weil's disease, characterized by jaundice and haemorrhage,

Table I
Table of investigations for aseptic meningitis

	Day 1	Day 7
Complete Blood count:		
Hemoglobin	10.4 mg/dl	10.2 mg/dl
Erythrocyte Sedimentation Rate		38mm/1 st hour
Whole Blood count	$7 \times 10^9/L$	$12 \times 10^9/L$
Neutrophil	73%	76%
Lymphocyte	21%	20%
Platelets	$161 \times 10^9/L$	$188 \times 10^9/L$
Dengue NS1 Ag	Negative	-
Dengue IgM Ab	-	Negative
Serum creatinine	0.76 mg/dl	0.7 mg/dl
Alanine aminotransferase	40 U/L	22 U/L
Serum electrolytesNa ⁺	134 mmol/L	
K ⁺	4.30 mmol/L	-
Cl ⁻	99 mmol/L	
HCO ₃ ⁻	25 mmol/L	
Urine R/E:		
Albumin	Nil	Nil
Sugar	Nil	Nil
Pus cell	4-6/HPF	2-3/HPF
RBC	2-4/HPF	Nil/HPF
RDT for IgM Ab to <i>Leptospira</i>		Positive
CSF:		
Colour		
Protein	44.40 mg/dl	
Glucose	52.02 mg/dl	
Cells	$2000/mm^3$	
Neutrophil	80%	
Lymphocytes	20%	
C/S	No growth	
USG of pregnancy profile	About 20 weeks 1 day of single live pregnancy with cephalic presentation	About 21 weeks of single viable pregnancy with unstable presentation
ECG	Sinus rhythm Rate: 100 bpm	
Blood C/S		No growth

Table II
Table of investigations for Weil's disease

Investigations	Case 1	Case 2	Case 3
Complete Blood Count:			
Hemoglobin	10.7 g/dl	9.8 g/dl	13.5 g/dl
Erythrocyte Sedimentation Rate	100mm/1 st hour	85mm/1 st hour	25mm/1 st hour
White Blood Cell Count	14.5 × 10 ⁹ /L	12.5 × 10 ⁹ /L	10.9 × 10 ⁹ /L
Neutrophil	83%	82%	84%
Platelets	66 × 10 ⁹ /L	100 × 10 ⁹ /L	97 × 10 ⁹ /L
Serum Creatinine (mg/dl)	11.72 (8/12/23) 14.54 (10/12/33) 8.38 (17/12/23)	5.06 (11/12/23) 2.65 (13/12/23)	0.80
Alanine aminotransferase (U/L)	15	55	130
Aspartate aminotransferase (U/L)	34	201	-
Serum electrolytes (mmol/L)Na+K+	1226.80	1313.50	1353.80
Ultrasonogram of whole abdomen	Bilateral renal parenchymal disease;	Coarse hepatic parenchyma with mild	-
	Features suggestive of hepatocellular diseasehepatomegaly		
Routine Urine Examination			
Albumin	3+	-	Trace
Sugar	Nil		Nil
Pus cells	6-8/HPF		2-4/HPF
Red blood cells	Plenty/HPF		Nil/HPF
Serum bilirubin (mg/dl)	4.7	19.3	2.85
Serum albumin (g/dl)	3.7	1.9	2.13
Prothrombin time	18 seconds	13 seconds	-
Immunochromatographic test for malaria	Negative	-	-
D – dimer	5.1ugm/ml	-	-
IgM antibodies to <i>Leptospira</i>	Positive	Positive	Positive



Picture I: Picture showing subconjunctival hemorrhage in the patient with aseptic meningitis (Case – 1).

which includes purpura, epistaxis, haematemesis and acute kidney injury.² Two out of three of our patients presented with jaundice and acute kidney injury following high-grade fever. However, one of them presented with jaundice only. Hepatic

encephalopathy or acute liver failure is uncommon in leptospirosis.¹ However, 30.3% of patients have been reported to have hepatic failure in patients with leptospirosis.⁹

Complete blood counts include neutrophilic leucocytosis, mild thrombocytopenia and elevated erythrocyte sedimentation rate. Liver function tests show elevated bilirubin, elevated alkaline phosphatase, and mildly elevated aminotransferases. This is because leptospirosis is not associated with severe hepatocellular necrosis.¹

Blood cultures are positive if obtained within 10 days of illness onset, and leptospire are shed in urine during thesecond week of illness. IgM antibodies to

Leptospira were positive in all three patients who presented with features of leptospirosis. IgM antibodies are specific but have moderate sensitivity.² However, the confirmatory investigation is a microscopic agglutination test (MAT) or isolation of the organism from the patient.¹

In severe cases of leptospirosis, intravenous administration of penicillin G, amoxicillin, ampicillin, or erythromycin is recommended. Studies demonstrated equal efficacy between intravenous ceftriaxone and intravenous penicillin G for the treatment of severe leptospirosis.¹⁰ Initially, our patient with leptospiral meningitis was started on Ceftriaxone for 7 days. However, she didn't respond to it. Then, treatment with Amoxicillin and Dexamethasone was initiated according to the protocol for bacterial meningitis, after which the patient remained afebrile for 5 days before discharge. Two of three patients presenting with leptospirosis responded well to injectable Ceftriaxone, and one responded to oral Doxycycline.

Conclusion

This case series highlights the need for a high index of clinical suspicion, given the wide range of presentations, and early recognition and timely treatment are critical to reducing morbidity and preventing complications. Strengthening diagnostic capacity, improving clinician awareness, and integrating leptospirosis into routine differential diagnoses are essential.

Consent for Publication

Written informed consents were obtained from the patient and his/her legal guardian for the publication of this case report and the accompanying images. All identifying information has been removed to ensure patient confidentiality.

Availability of Data and Materials

All data generated or analysed during this study are included in this published article.

Competing Interests

The author declares that they have no competing interests.

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Authors' Contributions

The authors were responsible for study conception, data interpretation, manuscript preparation, and final approval of the version to be published.

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Use of Artificial Intelligence

Artificial intelligence tools (Grammarly and Open AI) were used for language editing and structuring of the manuscript under the author's supervision. All scientific content, interpretations, and conclusions are the responsibility of the author.

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