Case Report

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Diagnostic Challenges of Weil's Disease with Acute Kidney Injury: A Case Report and Clinical Review

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ABSTRACT

Background: *Severe leptospirosis or Weil's disease can cause multi-organ failure, which is characterized by jaundice and acute kidney injury in approximately 10% of cases. Its nonspecific symptoms often lead to misdiagnosis with other acute febrile illnesses, resulting in delayed diagnosis.*
Case Presentation: *A 48-year-old male construction worker presented with fever, headache, myalgia, epigastric pain, nausea, and vomiting for four days without any signs of bleeding. The patient lived and worked at a project site adjacent to rice fields. Physical examination revealed fever, icteric sclera, conjunctival suffusion, and tenderness of the gastrocnemius muscle. Laboratory tests showed leukocytosis, thrombocytopenia, impaired renal function, elevated liver enzymes, hyponatremia, and hypokalemia. The patient was diagnosed with Weill's disease. He was treated with antibiotics and supportive therapy. Sixteen days after discharge, the patient reported gradual improvement and had resumed normal activities.*
Discussion: *Patients presenting with acute febrile illness should undergo a comprehensive evaluation, and leptospirosis should be considered when leukocytosis, neutrophilia, and thrombocytopenia are observed in a complete blood count. A detailed history focusing on risk factors and associated symptoms, along with additional diagnostic tests based on the criteria, can help guide the diagnosis. Antibiotic therapy should be initiated immediately in patients with suspected or probable leptospirosis without waiting for serological confirmation.*
Conclusion: *This case highlights the diagnostic challenges of leptospirosis, particularly in resource-limited healthcare settings. Enhancing clinical awareness, improving access to rapid diagnostic tools, and optimizing preventive measures are crucial to reducing morbidity and mortality rates.*

INTRODUCTION

Leptospirosis is a zoonotic disease caused by the spirochete bacterium *Leptospira interrogans* [1]. The incidence of this disease is higher in tropical and subtropical regions. In 2021,

28 European Union countries reported 1,246 cases of leptospirosis, of which 836 (67%) were confirmed and 409 (33%) were classified as probable [2]. In contrast, data from Indonesia in 2021 showed 734 reported cases of leptospirosis across eight provinces, with a case fatality rate of 11.4%. The provinces of Central Java and East Java accounted for the highest number of cases nationwide [3]. However, epidemiological data on leptospirosis in Bali remain limited.

Human infection with *Leptospira* typically occurs through direct contact with water or soil contaminated by the urine of infected mammals or rodents, particularly rats, which often serve as chronic carriers [4]. Following an incubation period of 5–14 days, the spirochetes proliferate in the bloodstream and disseminate hematogenously. The clinical manifestations of leptospirosis in humans are highly variable, ranging from subclinical infection to severe disease involving multiple organ dysfunction. Symptoms may resemble influenza-like febrile illness, accompanied by mild renal and hepatic impairment. In severe cases, leptospirosis can progress to hepatorenal failure, encephalopathy, pulmonary haemorrhage, and Weil's disease, characterized by jaundice and acute kidney injury, which occurs in approximately 10% of cases [4,5].

Diagnosing leptospirosis remains a clinical challenge due to its nonspecific presentation, which mimics various other infectious diseases such as dengue, malaria, hepatitis, influenza, and even autoimmune conditions. This often leads to delays in diagnosis and suboptimal clinical management. Although a definitive diagnosis can be established through culture, serological testing, or molecular techniques, each method has its own limitations in sensitivity, specificity, turnaround time, and availability in healthcare settings. Culture methods are time-consuming and have low sensitivity. PCR, while highly sensitive, is not widely accessible in field settings. Serological testing, particularly the Microscopic Agglutination Test (MAT), is considered the gold standard, but it requires reference laboratories and specialized expertise. As an alternative, IgM-ELISA testing has been widely used for its practicality, with several studies demonstrating high sensitivity and specificity. In one analysis, positive detection rates for *Leptospira* were 48% by culture, 62% by PCR, and 97% by serology, highlighting the crucial role of serological methods in facilitating rapid and accurate diagnosis of leptospirosis [6,7].

Leptospirosis is frequently underdiagnosed due to limited access to specific laboratory tests and the relatively high associated costs. Furthermore, its early symptoms closely resemble those of other acute febrile illnesses, such as typhoid fever and dengue, often resulting in diagnostic delays or errors. These challenges hinder effective leptospirosis control, especially considering that it remains one of the leading causes of zoonotic infections globally and is associated with significant morbidity [8]. Therefore, this case report aims to explore the diagnostic process for severe leptospirosis (Weil's disease) to enhance clinical awareness and improve diagnostic accuracy for this potentially life-threatening condition.

CASE PRESENTATION

A 48-year-old male presented to the emergency department with complaints of fever for four days before admission. The fever was described as intermittent, temporarily subsiding with antipyretics, but subsequently recurring. The patient also reported headache, generalized body aches, epigastric pain, nausea, and two episodes of vomiting. He denied experiencing cough, rhinorrhoea, shortness of breath, or diarrhoea. There were no signs of bleeding, such as gum bleeding or epistaxis. Urination was reported to be adequate, occurring 4–5 times daily, but the urine appeared tea-coloured. Bowel movements were within normal limits. The patient reported decreased appetite during the illness. He had recently moved from Java to Bali to work as a construction labourer. He began working on the project site during the rainy season, with frequent exposure to standing water. He lived and slept at the construction site, which was located near rice fields. The patient wore ordinary footwear daily rather than protective boots. He was a smoker (5–10 cigarettes/day), denied alcohol consumption, and had no known history of chronic illnesses.

On physical examination, the patient appeared weak but was fully conscious (GCS E4V5M6). Vital signs were: blood pressure 105/70 mmHg, pulse 87 bpm, temperature 38°C, respiratory rate 18 breaths/min, and oxygen saturation 98% on room air. Ocular examination revealed conjunctival suffusion without jaundice or anemic conjunctiva. Cardiopulmonary examination was within normal limits. An abdominal examination revealed epigastric tenderness without hepatosplenomegaly and normal bowel sounds. There was no pedal edema or calf tenderness.

Initial haematological laboratory tests revealed leucocytosis with WBC 23.47 x 10^3/µL (reference: 3.60–11.00), neutrophils 110.1 x 10^3/µL (reference: 50–70), haemoglobin 14.1 g/dL (reference: 11.7–15.5), haematocrit 38.7% (reference: 40–54), and thrombocytopenia with platelets at 22 x 10^3/µL (reference: 150–450). Follow-up complete blood counts, blood chemistry, electrolytes, and Widal tests were performed every 12 hours. The repeated results showed: WBC 21.87 x 10^3/µL, HGB 13.3 g/dL, HCT 35.9%, PLT 35 x 10^3/µL. Renal function tests showed markedly elevated urea (175 mg/dL; reference: 13.0–43.0) and creatinine (6.1 mg/dL; reference: 0.6–1.1). Liver enzymes were elevated with SGOT 107 U/L (reference: 0–37.0) and SGPT 83 U/L (reference: 0–42.0). Electrolyte analysis revealed hyponatremia (Na^+ 123 mmol/L; reference: 130–145), hypokalaemia (K^+ 3.0 mmol/L; reference: 3.5–5.5), and hypochloraemia (Cl^- 89 mmol/L; reference: 95–108). The Widal test was positive only for *S. paratyphi* BO at 1/80. Additional investigations to exclude differential diagnoses included urinalysis, which revealed dark yellow cloudy urine with leukocyte esterase 75, positive urobilinogen (1+), positive bilirubin (2+), and positive occult blood (1+). IgM anti-Leptospira was reactive. Hepatitis B surface antigen

(HBsAg) and anti-HCV tests were negative. Abdominal ultrasound (both upper and lower) showed normal findings.

The patient was diagnosed with Severe Leptospirosis (Weil's disease) with Acute Kidney Injury (AKI) of renal origin**,** transaminitis**,** hyponatremia, and hypokalaemia. Treatment included IV fluids (NaCl 0.9% at 20 drops/min), paracetamol 750 mg every 8 hours, omeprazole 40 mg IV every 12 hours, ondansetron 4 mg IV every 8 hours as needed for vomiting, ceftriaxone 1 gram IV every 12 hours, potassium supplements (KSR) once daily for 3 days, curcuma tablets three times daily, and folic acid twice daily. The patient was also instructed to maintain fluid balance monitoring.

On day 2 of hospitalization, the patient's symptoms persisted. By day 3, the fever resolved, epigastric pain improved, and no signs of bleeding were noted. However, jaundice developed with yellowing of the eyes and skin, and urine remained tea-coloured. Physical examination revealed icteric sclera, conjunctival suffusion, and gastrocnemius tenderness. Laboratory results showed elevated total bilirubin at 16.95 mg/dL (reference: 0.2–1.0), direct bilirubin 13.5 mg/dL (reference: 0.00–0.02), and indirect bilirubin 3.45 mg/dL (reference: 0.2–0.8).

On day 4, the patient reported significant improvement in epigastric pain, nausea, and leg pain. Appetite also improved. Repeated labs showed WBC 29.75 x 10^3/µL, HGB 13.4 g/dL, HCT 36.1%, PLT 34 x 10^3/µL, BUN 217 mg/dL, and serum creatinine 9.2 mg/dL. Haemodialysis was recommended due to worsening renal function, but the patient and family declined due to financial constraints.

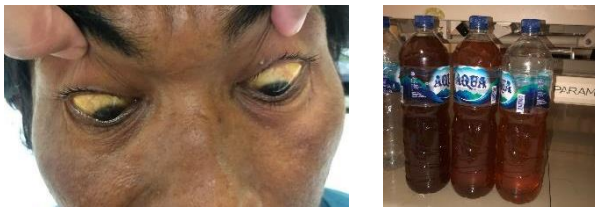

Figure 1. Clinical condition of the patient on day three of hospitalization, showing icteric sclera and tea-coloured urine.

By day 5, the patient remained afebrile, with further improvement in gastrocnemius muscle pain, epigastric pain, and nausea. Vital signs were stable: fully alert (compos mentis), BP 121/88 mmHg, pulse 68 bpm, RR 18 breaths/min, temperature 36.5°C. Icteric sclera persisted, but there was no longer epigastric or calf tenderness. The patient requested discharge due to financial difficulties and planned to return to his hometown. Discharge medications included cefixime 200 mg twice daily, folic acid twice daily, and curcuma three times daily. The patient was educated about his condition and the warning signs of deterioration, and was advised to follow up with local healthcare services.

Sixteen days post-discharge, a follow-up call was made to assess the patient's condition. He reported complete resolution of jaundice, no fever, nausea, vomiting, or muscle pain. Urination was normal, and urine was clear yellow. Appetite had returned to normal, and he had resumed daily activities without limitations.

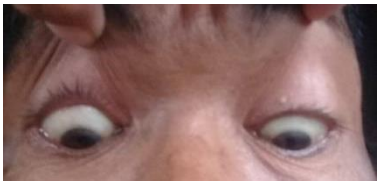

Figure 2. Clinical condition of the patient 16 days after hospital discharge.

DISCUSSION

In this case report, the patient was diagnosed with severe leptospirosis, also known as Weil's disease. The clinical manifestations included acute fever accompanied by generalized myalgia, epigastric pain, nausea, vomiting, and tea-colored urine. Physical examination revealed icteric sclera, conjunctival suffusion, and gastrocnemius tenderness. Laboratory investigations showed leukocytosis, neutrophilia, thrombocytopenia, elevated creatinine with normal renal ultrasonography suggesting acute kidney injury (AKI), electrolyte imbalances (hyponatremia and hypokalemia), elevated liver enzymes, and hyperbilirubinemia. These findings are similar to a case report from India, in which a 33-year-old woman presented with fever, jaundice, conjunctival hemorrhages, and urinary retention. Laboratory findings included elevated urea and serum creatinine, as well as a positive anti-Leptospira IgM result [9]. Another study from Kazakhstan reported a fatal case of Weil's disease characterized by acute fever, myalgia, jaundice, exanthema, hemorrhagic signs, and multi-organ failure involving the liver, heart, and central nervous system [10].

Leptospirosis is a zoonotic disease commonly found in areas with standing water and poor sanitation. *Leptospira* organisms excreted in the urine of infected animals (such as rats, dogs, and livestock) can survive in water and soil for weeks to months. Transmission to humans occurs through direct contact or ingestion of contaminated water, soil, or food [1]. In this case, risk factors included exposure to stagnant water during the rainy season and residence near rice paddies.

Weil's disease is a severe form of leptospirosis characterized by jaundice, renal failure, and haemorrhagic manifestations. The diagnosis of AKI in this patient was based on the Kidney Disease: Improving Global Outcomes (KDIGO) criteria, which define AKI as an increase in serum creatinine ≥26.4 μmol/L (0.3 mg/dL) or a 1.5-fold rise from baseline within one week.¹¹ Renal involvement in Weil's disease may occur through two primary

mechanisms: (1) direct nephrotoxic effects of the bacteria and toxin-induced immune responses, and (2) indirect effects of infection, such as dehydration, rhabdomyolysis, and hypoxia due to hemodynamic changes. The hallmark renal lesion is tubulointerstitial nephritis, characterized by interstitial edema and mononuclear cell infiltration. The proximal tubules are a favoured site for *Leptospira spp.* Due to their affinity for Na^+/K^+-ATPase pumps, whose inhibition reduces sodium/hydrogen ion exchanger activity and aquaporin-1 (AQP-1) expression on both apical and basolateral membranes. This leads to urinary loss of sodium and potassium, and the accumulation of free water in the tubular lumen, causing polyuria, hypovolemia, and secondary hypotension. In addition, leptospiral toxins can injure tubular cells, triggering nitric oxide release that lowers systemic vascular resistance, reducing renal blood flow and glomerular filtration rate. This also leads to decreased expression of the $Na^+/K^+/2Cl^-$ co-transporter (NKCC2). Disruption of these ion transport systems results in hyponatremia, hypokalaemia, hypomagnesemia, and non-oliguric AKI, which are characteristic of leptospiral nephropathy [12-14].

Another notable finding in this case was conjunctival suffusion, characterized by conjunctival injection involving the bulbar conjunctiva, typically appearing 2–3 days after fever onset. Unlike conjunctivitis, this finding lacks purulent or serous discharge, eyelid adhesion, or foreign-body sensation in the eye [15]. Jaundice is seen in nearly all cases of Weil's disease and serves as a key diagnostic clue. While the exact mechanism remains unclear, animal studies suggest that spirochaetal infiltration of the space of Disse, followed by intercellular migration between hepatocytes, damages the bile canaliculi. This destruction results in elevated levels of conjugated bilirubin, aspartate aminotransferase (AST), and alkaline phosphatase (ALP) in the blood. Meanwhile, alanine aminotransferase (ALT)and gamma-glutamyl transferase (GGT) levels are only mildly elevated. Moreover, high bilirubin levels have been associated with oliguria and cholestatic changes , which are linked to AKI development [16]. Thrombocytopenia in this patient may be associated with haemorrhagic pneumopathy and is a significant predictor of respiratory failure. Possible mechanisms include disseminated intravascular coagulation (DIC), cytotoxic effects, and direct vascular injury from vasculitis [17].

A definitive diagnosis of leptospirosis is established by culture, but this requires specialized media and prolonged incubation periods, making it impractical in acute clinical settings. Polymerase Chain Reaction (PCR) testing is currently under development for rapid and accurate detection, though it is not yet widely available for routine use. Serological tests can detect IgM or IgG antibodies to *Leptospira*, using techniques such as the Microscopic Agglutination Test (MAT), Enzyme-Linked Immunosorbent Assay (ELISA), Immunofluorescence Assay (IFA), and Lateral Flow Assay. Ideally, two samples should be taken during different phases, acute and convalescent (7–14 days apart), with a fourfold increase in IgG titers confirming

diagnosis. Although MAT is considered the gold standard, it is not widely accessible. A single titer ≥1:320 or serial titer ≥1:100 may raise suspicion, but is not definitive for diagnosis [1].

The diagnostic challenge in this case stemmed from the initial presentation mimicking other acute febrile illnesses such as dengue fever, malaria, typhoid, or hepatitis. Epidemiologically, in our region, Weil's disease and leptospirosis are relatively rare compared to dengue and typhoid fever. Furthermore, culture and serological tests, such as Leptospira IgM, are not available at our facility and must be outsourced to private laboratories, leading to diagnostic delays. To facilitate early diagnosis, clinical diagnostic criteria , such as those issued by the Indonesian Ministry of Health (Table 1) and the Modified Faine Criteria (Figure 3), can be used [14]. Although serological results took time to obtain, the clinical and laboratory features in this case met the probable case criteria 1 and 3 as defined by the Ministry of Health. They scored >26 on the Modified Faine Criteria (Score A + Score B), supporting the diagnosis of leptospirosis.

Table 1. Diagnostic Criteria for Leptospirosis according to the Ministry of Health of the Republic of Indonesia [1]

Suspected Case	Probable Case	Confirmed Case
Acute fever with or without headache, accompanied by: 1. Myalgia 2. Malaise, with or without; 3. Conjunctival suffusion (red eyes without exudate); AND 4. A history of exposure to contaminated environments or activities representing risk factors for leptospirosis within the previous two weeks, such as: a. Contact with water contaminated by *Leptospira* or rat urine during flooding; b. Contact with rivers or lakes during activities such as washing, bathing, or occupation-related exposure (e.g., boatmen, bamboo raft workers); c. Exposure in rice fields or plantations associated with agricultural or plantation work without the use of footwear; d. Close contact with animals	1. A suspected case with at least two of the following clinical signs/symptoms: calf muscle pain, jaundice, oliguria/anuria, hemorrhagic manifestations, dyspnea, cardiac arrhythmia, cough with or without hemoptysis, and skin rash; OR 2. A suspected case with a positive rapid diagnostic test (RDT) for anti-*Leptospira* IgM; OR 3. A suspected case presenting with at least three of the following laboratory findings: a. Thrombocytopenia <100,000 cells/mm^3; b. Leukocytosis with neutrophilia >80%; c. Elevated total bilirubin >2 g/dL,	A suspected or probable case accompanied by at least one of the following: 1. Isolation of *Leptospira* spp. from a clinical specimen; 2. Positive polymerase chain reaction (PCR); 3. Seroconversion in the microscopic agglutination test (MAT) from negative to positive, or a fourfold rise in antibody titer between paired sera obtained 1–2 weeks apart; 4. A single MAT titer ≥1:320.

such as cattle, goats, or dogs confirmed by laboratory testing to be infected with *Leptospira*; e. Exposure through handling dead animals, contact with infectious fluids during urination, or handling materials such as placenta, amniotic fluid, or livestock during milking, assisting animal delivery, etc.; f. Handling animal or human specimens suspected of leptospirosis infection in a laboratory or other settings; g. Occupational exposure involving contact with potential sources of infection, such as veterinarians, physicians, nurses, slaughterhouse workers, farmers, plantation workers, hospital sanitation staff, sewer cleaners, miners, freshwater aquaculture workers (shrimp/fish), military personnel, hunters; h. Contact with potential sources of infection related to hobbies or sports, such as mountain climbing, fishing, swimming, rafting, or triathlon competitions.	or increased amylase, or creatine phosphokinase (CPK); d. Urinalysis showing proteinuria and/or hematuria.

Part A: Clinical Data	Score
Headache	2
Fever	2
If fever, temperature 39°C or more	2
Conjunctival suffusion (bilateral)	4
Meningism	4
Muscle pain (especially calf muscle)	4
Conjunctival suffusion+Meningism+Muscle pain	10
Jaundice	1
Albuminuria or nitrogen retention	2
Part B: Epidemiological Factors	**Score**
Rainfall	5
Contact with contaminated environment	4
Animal contact	1
Part C: Bacteriological and Laboratory Findings	
Isolation of *Leptospira* on culture	Diagnosis certain
Positive serology	
ELISA IgM positive*; SAT positive*; MAT single high titre* (Any one of the three tests should be scored)	15
MAT rising titre (paired sera)	25

A presumptive diagnosis of leptospirosis may be made if: (i) Score of Part A+Part B = 26 or more (Part C laboratory report is usually not available before fifth day of illness; thus it is mainly a clinical and epidemiologic diagnosis during early part of disease) or Part A+Part B+Part C≥25.
A score between 20 and 25: Suggests a possible but unconfirmed diagnosis of leptospirosis.
doi:10.1371/journal.pntd.0000579.t001

Figure 3. Diagnostic Criteria for Leptospirosis Based on the Modified Faine's Criteria [18]

Antibiotic therapy should be initiated promptly in patients suspected of having leptospirosis without waiting for serological or culture results. For mild leptospirosis, doxycycline is the first-line treatment, with amoxicillin as an alternative. In cases of severe leptospirosis, ceftriaxone or penicillin is recommended [1]. The recommended antibiotic dosages are listed in Table 3. Corticosteroids may be considered in patients with pulmonary complications. Indications for haemodialysis include deteriorating general condition (e.g., uremic encephalopathy, uremic pericarditis, refractory pulmonary edema, fluid overload, anuria >5 days), and laboratory findings such as metabolic acidosis (pH < 7.1), blood urea > 200 mg/dL, and hyperkalaemia > 7 mEq/L [19]. In this case, the patient received ceftriaxone in accordance with current treatment guidelines. The patient met the indication for haemodialysis based on a blood urea level of 217 mg/dL, but refused the procedure. Given the patient's clinically stable condition with no shortness of breath, edema, or altered consciousness, treatment was focused on intravenous hydration, antibiotic therapy, symptomatic management, and close monitoring of fluid balance, clinical status, and laboratory parameters. Following discharge, the patient was routinely followed up and showed progressive clinical improvement. A case report from Jakarta also documented a patient with Weil's disease and multiple organ failure, including AKI, who improved clinically and biochemically with antibiotic therapy and hydration alone, without

haemodialysis [20]. However, regular monitoring of renal function is essential to detect any potential progression to chronic kidney disease.

Table 2. Antibiotic Dosages in the Management of Leptospirosis [1]

Mild Leptospirosis	Severe Leptospirosis	Chemoprophylaxis
Doxycycline 100 mg twice daily for 7 days (contraindicated in children and pregnant women)	Penicillin 1.5 million units intramuscularly every 6 hours for 7 days	Doxycycline 200 mg once weekly
Amoxicillin 500 mg three times daily for 7 days	Ceftriaxone 2 g intravenously once daily for 7 days	Azithromycin 250 mg once to twice weekly
Azithromycin 500 mg once daily for 3 days	Cefotaxime 1 g intravenously every 6 hours for 7 days	
	Doxycycline 200 mg intravenous loading dose, followed by 100 mg intravenously twice daily for 7 days	

The strength of this study lies in its detailed documentation of a rare case of Weil's disease in Bali, including comprehensive clinical presentation, diagnostic work-up, treatment, and follow-up until discharge. However, a limitation of this case report is the absence of haemodialysis as supportive therapy for acute kidney injury (AKI), which was tailored to the patient's specific condition. Although several previous case reports have noted that haemodialysis is not routinely required in patients with Weil's disease and AKI since renal function may improve alongside resolution of the infection, this approach cannot be generalized to all cases and should always be based on the patient's clinical signs and symptoms [20, 21]. Additionally, a further limitation is the lack of follow-up laboratory data, particularly renal function tests after antibiotic therapy, which makes it difficult to objectively assess laboratory improvement, even though clinical recovery was observed.

CONCLUSION

The diagnosis of Weil's disease in this case was based on the presence of acute fever accompanied by myalgia, jaundice, conjunctival suffusion, leukocytosis, thrombocytopenia, acute kidney injury, elevated liver enzymes, and electrolyte disturbances. In cases of acute febrile illness, leptospirosis or Weil's disease should be considered using the diagnostic criteria established by the Indonesian Ministry of Health or the Modified Faine Criteria, allowing for the early initiation of antibiotic therapy without waiting for culture or serological confirmation.

Meanwhile, supportive therapies, such as hemodialysis, should be considered based on the patient's clinical condition.

DECLARATIONS

Ethics approval

None

Conflict of interest

The authors declare no conflict of interest.

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