

Fulminant Acute Liver Failure Secondary to Leptospirosis: A Case Report

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ABSTRACT

Background: Leptospirosis is a worldwide zoonosis caused by pathogenic species of the genus *Leptospira*. Although most infections are mild or self-limited, severe forms may progress to multiorgan dysfunction, including acute kidney injury, pulmonary hemorrhage and, less frequently, fulminant acute liver failure. Early diagnosis is often challenging because of the nonspecific clinical presentation, which makes timely antimicrobial therapy crucial to improve outcomes.

Case Presentation: We report the case of a 31-year-old man who presented with fever, progressive jaundice, marked direct hyperbilirubinemia, severe transaminase elevation and rapidly progressive fulminant acute liver failure complicated by hepatic encephalopathy, coagulopathy, septic shock, acute kidney injury requiring renal replacement therapy and lower gastrointestinal bleeding. Initial investigations for viral hepatitis were negative and autoimmune hepatitis was initially considered. The microscopic agglutination test (MAT) subsequently identified *Leptospira interrogans* serovar Mankarso at a titer of 1:800, establishing the diagnosis of severe leptospirosis. Antimicrobial therapy was adjusted to ceftriaxone plus doxycycline, together with intensive supportive care, and the patient was ultimately referred to a tertiary center for liver transplantation evaluation.

Conclusion: This case highlights fulminant acute liver failure as an uncommon but life-threatening manifestation of leptospirosis. Clinicians should maintain a high index of suspicion in patients presenting with acute liver failure and compatible epidemiological risk factors, even when an infectious etiology is not initially apparent. Early recognition and prompt antimicrobial treatment remain essential to improve clinical outcomes.

KEYWORDS: Leptospirosis; Acute liver failure; Weil syndrome; Hyperbilirubinemia; Occupational exposure; Case report.

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I. INTRODUCTION

Leptospirosis is a globally distributed zoonotic disease caused by pathogenic spirochetes of the genus *Leptospira*. Human infection occurs through direct or indirect contact with water or soil contaminated with the urine of infected animals, particularly rodents, and is favored by tropical climates, flooding, poor sanitation, and occupational or

recreational exposure [I, IX, X]. Despite being considered a neglected tropical disease, leptospirosis remains a significant public health problem, with more than one million estimated cases and approximately 60,000 deaths worldwide each year [V, VII], a figure that is probably underestimated because of widespread underreporting [VI, VIII].

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The clinical spectrum ranges from a mild self-limited febrile illness to severe systemic disease involving multiple organs. Classic severe leptospirosis (Weil syndrome) is characterized by jaundice, acute kidney injury and hemorrhagic manifestations, whereas pulmonary hemorrhage syndrome represents one of the leading causes of mortality [I, IV]. In contrast, fulminant acute liver failure is an uncommon presentation, and it often poses a considerable diagnostic challenge because its clinical features overlap with those of viral hepatitis, autoimmune hepatitis, drug-induced liver injury and other causes of acute liver failure [XVI, XVII]. Early diagnosis remains difficult because initial manifestations are nonspecific and laboratory confirmation depends on the stage of infection. Molecular techniques such as polymerase chain reaction (PCR) are more useful during the early bacteremic phase [XI, XII], whereas serological tests, particularly the microscopic agglutination test (MAT), remain the reference standard in many centers [XIII, XIV]. Because microbiological confirmation may be delayed, current guidance recommends initiating empirical antimicrobial therapy when clinical and epidemiological findings strongly suggest leptospirosis, especially in patients with severe disease [II, III, XV].

We report the case of a 31-year-old man who developed fulminant acute liver failure secondary to severe leptospirosis, confirmed by MAT. This case highlights the importance of maintaining a high index of suspicion in patients with acute liver failure of unknown etiology and compatible epidemiological risk factors, and emphasizes the role of early recognition and prompt treatment in improving clinical outcomes.

II. CASE PRESENTATION

This case is reported in accordance with the CARE guidelines [XX].

A 31-year-old man with no significant past medical history was referred to our institution for evaluation of acute liver failure. He presented with a five-day history of high-grade fever (up to 39 °C), nausea, vomiting, generalized myalgia, right upper quadrant abdominal pain, progressive jaundice and dark urine. He denied previous liver disease, blood transfusions, chronic medication use, illicit drug use, recent travel and exposure to known hepatotoxic agents. Alcohol consumption consisted of approximately three to four beers twice weekly during the preceding two months.

The patient worked in warehouses and storage facilities operating heavy machinery, an occupational setting associated with potential exposure to rodents and to environments contaminated with animal urine, which represents an epidemiological risk factor for leptospirosis. At the time of presentation, however, leptospirosis was not initially suspected because the clinical picture predominantly suggested acute severe hepatitis.

On admission the patient was hemodynamically stable but febrile. Physical examination revealed marked scleral and

generalized jaundice (Figure 1), palpable hepatomegaly and tenderness in the right upper quadrant without signs of peritoneal irritation. No stigmata of chronic liver disease were identified. The remainder of the physical examination was unremarkable.



Figure 1. Clinical photograph demonstrating marked generalized jaundice and scleral icterus, consistent with severe conjugated hyperbilirubinemia in a patient with fulminant acute liver failure secondary to leptospirosis.

Initial laboratory evaluation demonstrated severe hepatocellular injury, marked conjugated hyperbilirubinemia, coagulopathy and a pronounced inflammatory response, while renal function was initially preserved. The main laboratory findings are summarized in Table 1.

Table 1. Laboratory findings on admission.

Parameter	Result	Reference range
Hemoglobin (g/dL)	15.1	13.5-17.5
Leukocytes (×10 ³ /μL)	13.44	4.0-10.0
Platelets (×10 ³ /μL)	217	150-450
AST (U/L)	750	<40
ALT (U/L)	2250	<41
Alkaline phosphatase (U/L)	154	40-129
Gamma-glutamyl transferase (U/L)	244	8-61
Total bilirubin (mg/dL)	15.4	0.2-1.2
Direct bilirubin (mg/dL)	9.0	<0.3
Albumin (g/dL)	3.0	3.5-5.2
Lactate dehydrogenase (U/L)	3300	125-220
INR	2.83	0.8-1.2
Creatinine (mg/dL)	0.8	0.7-1.2
Blood urea nitrogen (mg/dL)	5.61	7-20

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Parameter	Result	Reference range
C-reactive protein (mg/dL)	54	<0.5
Procalcitonin (ng/mL)	25.08	<0.05

AST: aspartate aminotransferase; ALT: alanine aminotransferase; INR: international normalized ratio.

Abdominal ultrasonography demonstrated hepatomegaly without focal hepatic lesions or evidence of biliary obstruction (Figure 2). Contrast-enhanced abdominal computed tomography confirmed hepatomegaly with diffuse hepatic edema and showed no biliary obstruction, focal hepatic lesions, vascular thrombosis or other structural abnormality that could account for the acute liver failure (Figure 3). Serological testing for hepatitis B and C viruses was negative.



Figure 2. Abdominal ultrasonography demonstrating hepatomegaly without focal hepatic lesions or evidence of biliary obstruction, findings that excluded obstructive hepatobiliary disease as the cause of acute liver failure.



Figure 3. Contrast-enhanced abdominal computed tomography showing hepatomegaly with diffuse hepatic edema and no evidence of biliary obstruction, focal hepatic lesions, vascular thrombosis or other structural abnormality explaining the acute liver failure.

Given the marked elevation of aminotransferases and the absence of an immediately identifiable infectious etiology, autoimmune hepatitis was initially considered and empirical corticosteroid therapy was started. Although mild biochemical improvement was observed, the clinical

condition progressively deteriorated, prompting referral to our tertiary-care center for further evaluation.

During hospitalization the patient developed rapidly progressive acute liver failure complicated by grade IV hepatic encephalopathy according to the West Haven classification, requiring endotracheal intubation for airway protection and admission to the intensive care unit. His clinical course was further complicated by septic shock, acute kidney injury requiring renal replacement therapy and lower gastrointestinal bleeding. Despite aggressive supportive management, liver function continued to deteriorate, with progressive coagulopathy and worsening hyperbilirubinemia. Considering the occupational exposure, the multisystem involvement and the absence of an alternative diagnosis, leptospirosis was included in the differential diagnosis. Serological confirmation was obtained by the microscopic agglutination test (MAT), which identified *Leptospira interrogans* serovar Mankarso at a titer of 1:800, confirming severe leptospirosis. Antimicrobial therapy was adjusted to intravenous ceftriaxone combined with doxycycline, and intensive supportive care was continued.

Despite appropriate antimicrobial treatment and multidisciplinary intensive care, the patient continued to fulfill criteria for fulminant acute liver failure and was therefore referred to a tertiary referral center for liver transplantation evaluation.

III. DISCUSSION

Leptospirosis is a globally important zoonosis with a highly variable clinical spectrum, ranging from a mild self-limited febrile illness to severe multiorgan dysfunction [I, IV]. Although hepatic involvement is common, it is usually characterized by disproportionate hyperbilirubinemia with only mild to moderate elevations of aminotransferases. In contrast, fulminant acute liver failure remains an uncommon manifestation and is rarely the predominant clinical presentation [XVI, XVII].

Our patient presented with rapidly progressive acute liver failure accompanied by marked hepatocellular injury, severe direct hyperbilirubinemia, grade IV hepatic encephalopathy, septic shock, acute kidney injury requiring renal replacement therapy and lower gastrointestinal bleeding. This constellation of findings initially suggested alternative diagnoses, including viral hepatitis, autoimmune hepatitis and other causes of fulminant hepatic failure, which delayed consideration of leptospirosis despite the presence of epidemiological risk factors.

The diagnostic difficulty in this case illustrates one of the principal limitations in the management of leptospirosis: its nonspecific clinical presentation during the early stages of disease. Initial manifestations frequently overlap with viral hepatitis, autoimmune hepatitis and other infectious or inflammatory disorders [XVII]. Consequently, definitive microbiological confirmation is often delayed, particularly in centers where the microscopic agglutination test is not

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immediately available [XIII, XIV]. This case underlines the importance of integrating epidemiological exposure with the clinical presentation in order to avoid delays in diagnosis and treatment.

Several published reports describe jaundice and acute kidney injury as the most frequent manifestations of severe leptospirosis [V, VI]. Progression to fulminant acute liver failure requiring consideration for liver transplantation, however, has been reported only rarely [XVI, XVII]. Our patient developed progressive hepatic dysfunction despite appropriate supportive care, which emphasizes that severe hepatic injury, although uncommon, may represent the predominant clinical manifestation of leptospirosis. Experimental models suggest that an early, intense cytokine-mediated inflammatory response contributes to the organ injury observed in severe disease [XVIII].

Another relevant aspect of this case was the patient's occupational exposure. Although he denied direct contact with floodwater or recreational freshwater activities, his work in warehouses and storage facilities operating heavy machinery represented a plausible source of exposure to environments contaminated by rodent urine [IX]. Pathogenic *Leptospira* can persist in moist environments and surface water for prolonged periods, which facilitates indirect transmission [XIX]. This observation reinforces that leptospirosis should not be restricted to traditionally recognized risk groups, particularly in endemic regions.

Current evidence supports the early administration of antimicrobial therapy in patients with suspected severe leptospirosis, even before microbiological confirmation [II, III, XV]. In our patient, treatment with ceftriaxone and doxycycline, together with comprehensive intensive care support, was instituted only after diagnostic confirmation. The patient nevertheless continued to deteriorate and ultimately required referral for liver transplantation evaluation, an unfavorable evolution that underscores the aggressive nature of fulminant hepatic involvement once advanced organ dysfunction has developed.

The main limitation of this report is that PCR testing was not available at our center, so the diagnosis relied on a single MAT titer, and the final outcome after referral for transplantation evaluation could not be documented.

IV. CONCLUSIONS

Fulminant acute liver failure represents an uncommon but potentially life-threatening manifestation of severe leptospirosis and may closely mimic other causes of acute hepatitis, including viral and autoimmune liver disease, creating a significant diagnostic challenge. This case underscores the importance of obtaining a thorough epidemiological and occupational history, since exposure to environments with potential rodent contamination may provide a critical clue to the diagnosis even in the absence of classic risk factors. Clinicians should maintain a high index of suspicion for leptospirosis in patients presenting with acute

liver failure of unknown etiology, particularly in endemic areas or in individuals with compatible occupational exposure. Early recognition, prompt initiation of appropriate antimicrobial therapy and multidisciplinary supportive care remain essential to improve clinical outcomes and may reduce progression to irreversible multiorgan dysfunction.

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ETHICAL STATEMENTS

Informed consent. Written informed consent was obtained from the patient for publication of this case report and the accompanying images.

Conflict of interest. The authors declare that they have no conflicts of interest.

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