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Case report

Weil Disease as a Differential Diagnosis of Febrile Icteric Syndrome: A Case Report

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Abstract

The clinical case of a 56-year-old woman with febrile icteric syndrome is described, whose clinical course led to the diagnosis of severe leptospirosis, known as Weil disease. Leptospirosis is a re-emerging zoonosis primarily transmitted through contact with urine from infected rodents. It presents in two phases: a septicemic phase and an immune phase, which may progress to multiorgan failure. The patient developed jaundice, severe thrombocytopenia, elevated bilirubin levels, and respiratory deterioration. The diagnosis was confirmed by a positive automated immunoassay (AIA) for *Leptospira*. Due to penicillin allergy, treatment with ceftriaxone was initiated. The patient required management in the intensive care unit (ICU) because of pulmonary involvement, evidenced by pneumonitis and acute respiratory distress syndrome (ARDS). Clinical evolution was favorable, with resolution of symptoms and normalization of clinical parameters. This case underscores the importance of early assessment, accurate diagnosis, and multidisciplinary management. It highlights the need to consider this infection in patients exposed to risk factors such as stagnant water or rodents. In addition, it emphasizes the usefulness of the national protocol issued by the National Institute of Health (INS) for diagnosis and treatment. This report provides valuable information for clinical management and epidemiological surveillance.

Keywords

Leptospirosis; icterohemorrhagic leptospirosis; Weil disease; spirochetes; fever; jaundice.

INTRODUCTION

Definition

Leptospirosis is a reemerging zoonotic disease caused by pathogenic spirochetes of the genus *Leptospira*. These are gram-negative, obligate aerobic bacteria that are highly motile, measuring only 0.1 µm in diameter and 6 to 20 µm in length; their posterior end may exhibit a characteristic hook shape. The genus *Leptospira* includes both saprophytic species, which inhabit aquatic environments, and pathogenic species that cause leptospirosis[1,2].

Epidemiology

Leptospirosis has a worldwide distribution, with higher prevalence in tropical regions. Costa colleagues estimated that there are 1,030,000 cases worldwide (95% confidence

interval [95% CI]: 434,000–1,750,000) and 58,900 deaths (95% CI: 23,800–95,900) due to leptospirosis annually; the highest estimates of morbidity and mortality have been observed in South Asia and Southeast Asia, Oceania, the Caribbean, Andean, Central, and Tropical Latin America, and Eastern Sub-Saharan Africa[3].

According to the National Surveillance Information System for epidemiological period VI of 2024, the incidence of confirmed leptospirosis cases in Colombia was approximately 0.06 per 100,000 inhabitants, with a higher number of cases in men (1,999 [57.8%]) than in women (1,459 [42.2%])[4].

Natural History and Transmission

Leptospirosis persists in nature through chronic infection of the renal tubules in carrier animals (wild and domestic mammals), with rodents serving as the principal reservoir. Humans become infected through direct contact with infected animals or indirectly through contact of injured skin or mucous membranes with water and soil contaminated by their urine (the latter being the main mode of transmission). Consequently, the populations most susceptible to infection include individuals who work with animals (veterinarians and butchers), farmers, as well as those engaged in outdoor sports activities and military operations. Transmission increases particularly during periods of heavy rainfall and natural disasters, which may resuspend the bacteria in water and soil, thereby increasing the risk of exposure[5].

OBJECTIVES

The primary objective is to provide relevant public health information regarding the diagnostic and therapeutic approach to an uncommon condition caused by an emerging zoonotic disease involving multisystem involvement. In addition, the study aims to review the existing literature on the severe form caused by the genus *Leptospira*.

PATHOPHYSIOLOGY

After entering the body, hematogenous dissemination occurs, reaching levels of up to 10^6 leptospires per milliliter of blood. The microorganisms rapidly cross tissue membranes, and their transendothelial migration is facilitated by the phenomenon known as systemic vasculitis, which may produce severe injury leading to pulmonary hemorrhage, renal cortical ischemia, and necrosis of tubular epithelial cells, in addition to destruction of hepatic architecture, resulting in jaundice and hepatocellular injury. Possible virulence factors include immune-mediated mechanisms, adhesins, and the production of hemolytic toxins that may act as sphingomyelinases, pore-forming proteins, and collagenases[1].

The genus *Leptospira* directly activates the conversion of plasminogen into plasmin, the principal enzyme of the fibrinolytic system, thereby promoting hemorrhage[6].

Clinical Diagnosis

The clinical presentation of Leptospirosis includes two phases: a septicemic phase characterized by nonspecific febrile illness followed by an immune phase with generally reversible localized organ dysfunction, in which the kidneys and liver are the most frequent targets.

Weil disease is a severe form of leptospirosis associated with fulminant renal and hepatic dysfunction manifested by a triad of jaundice, acute kidney injury, and hemorrhagic manifestations. In addition, the genus *Leptospira* is an emerging cause of acute respiratory distress syndrome, producing dyspnea and hemoptysis; this form of the disease has increased in frequency in recent years[5].

Laboratory Diagnosis

Leptospirosis can be diagnosed through the isolation of *Leptospira* by culture, detection of antibodies by serologic testing, or identification of DNA by molecular techniques. The National Institute of Health of Colombia (INS) defines laboratory-confirmed leptospirosis as a patient with compatible clinical symptoms and any of the following: seroconversion by microscopic agglutination test (MAT) in paired samples, MAT titers equal to or greater than 1:400 in a single sample for fatal cases, a positive culture, or a positive molecular DNA test such as polymerase chain reaction (PCR)[5,7].

The following case describes a febrile icteric syndrome notable for hepatic and pulmonary organ dysfunction due to marked acute direct hyperbilirubinemia and adult respiratory distress syndrome secondary to leptospiral pneumonitis, with a final diagnosis of Weil disease.

CASE PRESENTATION

This is the case of a 56-year-old female patient with no significant past medical history. She reported a history of penicillin allergy and frequent exposure to rodents, as she lives near a landfill where the presence of these animals and their physiologic waste is evident. She presented to the emergency department with a three-day history of intermittent unquantified fever, malaise, five episodes of watery diarrhea, myalgias, arthralgias, retro-orbital pain, and holocranial headache rated 7/10 on the visual analog pain scale.

Initial physical examination revealed only a facial rash, with no other significant findings.

Initial laboratory testing demonstrated mild thrombocytopenia with normal liver function, renal function, and coagulation studies (**Table 1**). Given her symptom profile and the high prevalence of dengue, serologic tests were requested (nonstructural protein 1 antigen [NS1], immunoglobulin M [IgM], and immunoglobulin G [IgG]), all of which were negative. During her in-hospital course, the patient developed scleral icterus, and follow-up laboratory studies showed progressive elevation of transaminases (aspartate aminotransferase [AST] greater than alanine aminotransferase [ALT], without exceeding three times the upper limit of normal), predominantly direct hyperbilirubinemia, and severe thrombocytopenia, raising suspicion for severe leptospirosis or Weil Disease (**Figures 1–3**).

Given the history of penicillin allergy, antibiotic therapy with a third-generation cephalosporin (ceftriaxone) was initiated, together with intravenous hydration and confirmatory testing. Due to the risk of hemodynamic deterioration, transfer to a higher-complexity center with availability of an intensive care unit (ICU) was indicated. In the ICU, the patient experienced unfavorable clinical progression with persistent elevation of liver function markers and hyperbilirubinemia predominantly involving the direct fraction, in addition to persistent thrombocytopenia with slight improvement. Other infectious causes were ruled out through negative serologic testing for hepatitis A, B, and C, and confirmatory testing for *Leptospira* by automated immunoassay was positive, confirming the diagnosis of severe Leptospirosis. Subsequently, the patient developed progressive respiratory deterioration with clinical findings of bilateral basal crackles and a requirement for supplemental oxygen via a 50% Venturi mask. Chest computed tomography demonstrated bilateral interstitial opacities with multisegmental distribution, involvement of the upper and lower lobes and the right middle lobe, as well as bilateral pleural effusion with left-sided predominance. Given the suspicion of concomitant pneumonia, a respiratory viral panel was requested, and the established management was continued.

With medical support, the patient showed progressive improvement, and the pulmonary involvement resolved

Table 1. Laboratory Findings During Hospital Stay and Their Clinical Course

Measurement	Platelets (x 10^3/µL)	Total Bilirubin (mg/dL)	Direct Bilirubin (mg/dL)	ALT (U/L)	AST (U/L)
1	152	8.78	6.92	144	69
2	90	10.28	8.58	138	71
3	90	13.43	10.39	136	70
4	50	10.74	8.97	116	71
5	48	9.08	7.10	98	66
6	38	7.50	6.06	87	67
7	51	6.57	5.30	76	62
8	51	5.45	4.66	66	73
9	83	5.13	4.42	69	67
10	93	4.37	3.56	48	90
11	143	4.18	3.39	55	97
12	217	—	—	51	20
13	289	—	—	22	12
14	385	—	—	—	—
15	402	—	—	—	—
16	522	—	—	—	—

Author's own research.

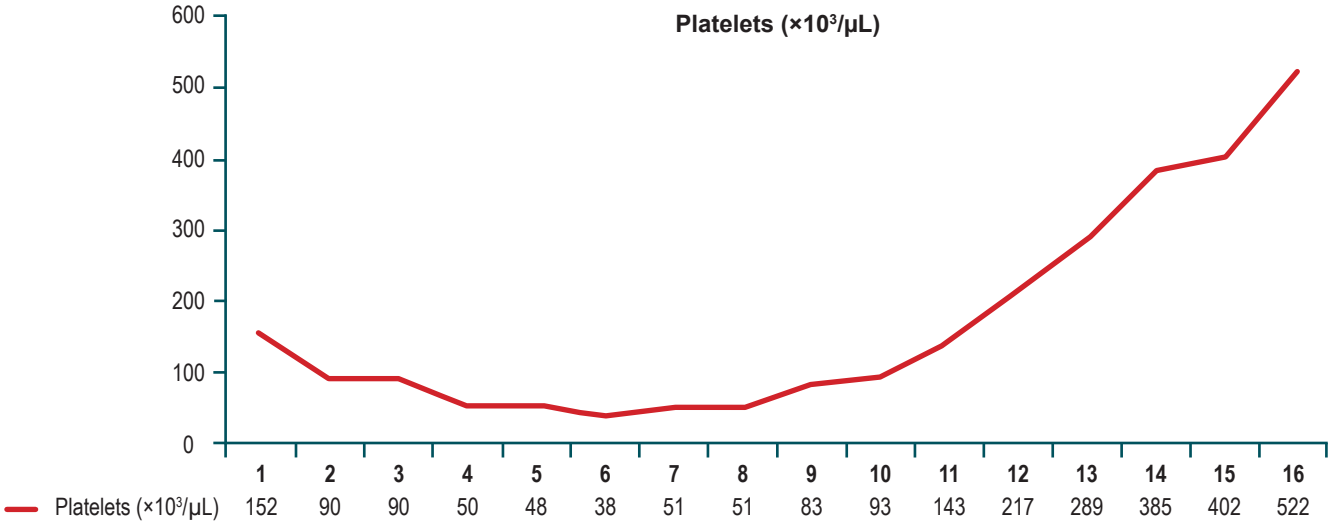


Figure 1. Platelet Trends During Hospital Stay Author's file.

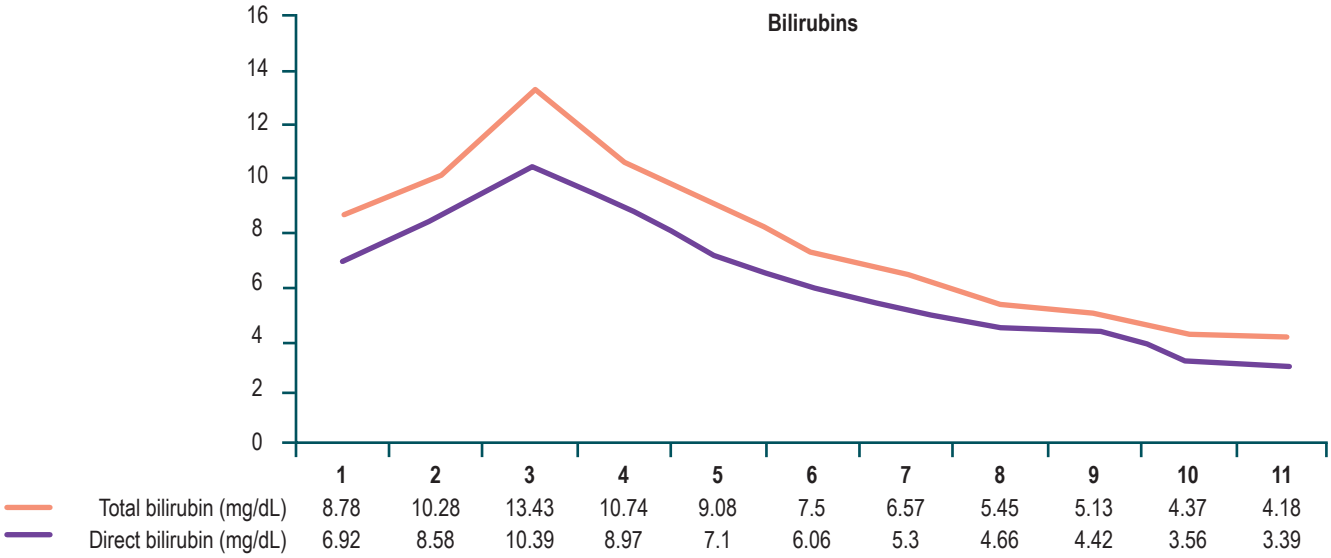


Figure 2. Bilirubin Level Trends During Hospital Stay Author's file.

following oxygen therapy, with gradual reduction in bilirubin levels and persistence of mild transaminase elevation during the first days. Renal function remained preserved, and the complete blood count demonstrated grade II normocytic normochromic anemia according to the World Health Organization (WHO) classification, without transfusion criteria. The antibiotic regimen with a third-generation cephalosporin was completed as a therapeutic alternative, and follow-up laboratory tests demonstrated normalization of the liver profile, resolution of thrombocytopenia, and complete clinical recovery. Finally, the patient was discharged on day 16 after symptom onset, completely asymptomatic and without associated complications.

The final diagnosis was severe Leptospirosis (Weil disease) with hepatic and pulmonary involvement.

DISCUSSION

Leptospirosis, although mild in most cases, may progress to severe forms with multiorgan involvement. Weil Disease and severe pulmonary hemorrhagic syndrome (SPHS) are the most lethal presentations, with mortality rates that may

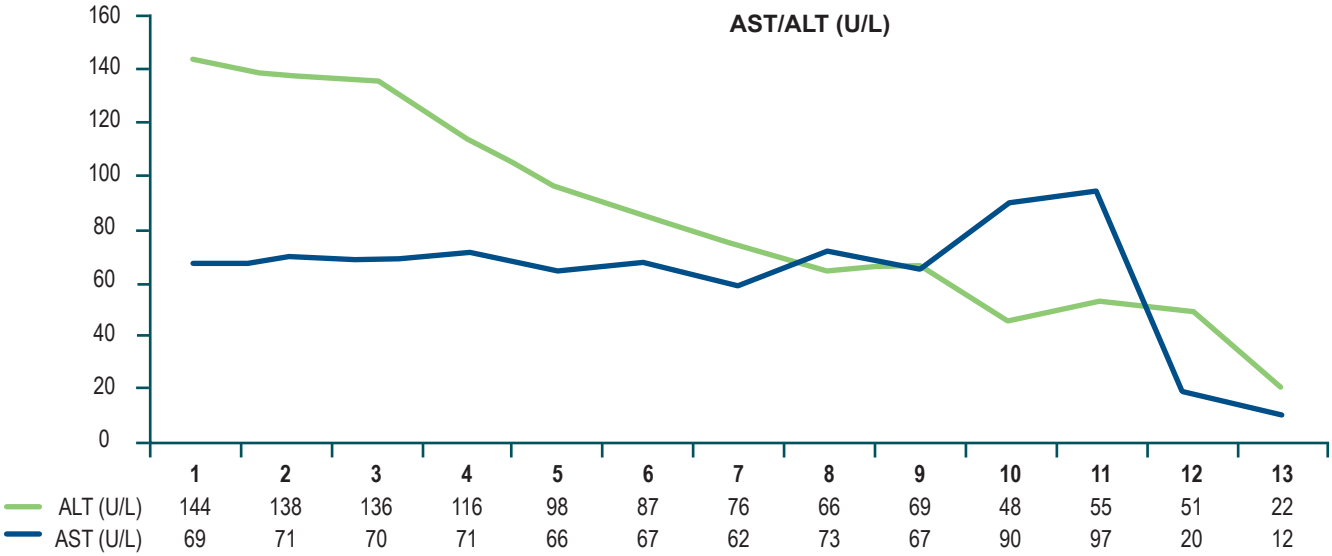


Figure 3. AST/ALT Level Trends During Hospital Stay Author's file.

exceed 50%[8,9]. In these severe forms, phenomena such as the "cytokine storm" and immune dysregulation play a key role in pathogenesis and explain the rapid clinical progression observed in some patients[8,10]. From an immunopathological perspective, the genus *Leptospira* has developed sophisticated immune evasion mechanisms, including the ability to avoid efficient activation of human TLR4 due to structural particularities of its lipopolysaccharide (LPS), thereby promoting a weak initial inflammatory response and systemic dissemination[8,10,11]. In addition, the action of outer membrane proteins, hemolysins, and phospholipases facilitates tissue invasion and hepatocellular injury, which constitutes a central mechanism underlying the jaundice observed in Weil disease[10,11].

In this context, the differential diagnosis of febrile icteric syndrome is essential. Conditions such as severe dengue, viral hepatitis, Malaria caused by *Plasmodium falciparum*, and Yellow Fever must be considered in endemic regions because they share similar initial clinical manifestations. The integration of epidemiological history, such as exposure to stagnant water or contact with animals, is decisive in directing clinical suspicion toward leptospirosis and guiding timely decision-making[12,13]. The recommended diagnostic approach is stepwise. During the leptospiremic phase (the first seven days), polymerase chain reaction (PCR) testing in whole blood with ethylenediaminetetraacetic acid (EDTA) is prioritized, whereas in later phases, serologic tests (enzyme-linked immunosorbent assay for immunoglobulin M detection [IgM ELISA] and microscopic agglutination test [MAT]) are the most useful methods for confirming the diagnosis[7].

Early initiation of antibiotic therapy is critical and should not be delayed while awaiting confirmatory results. In mild cases, doxycycline or amoxicillin are the treatments of choice, whereas in severe cases, sodium penicillin G or ceftriaxone are recommended, the latter as second-line therapy in penicillin-allergic patients[7]. In the present case, the early initiation of ceftriaxone as empirical treatment was consistent with national recommendations and allowed control of infection progression, although the patient developed severe pulmonary and hepatic complications before recovery.

This report emphasizes that unfavorable progression with hepatic and respiratory involvement highlights the value of comprehensive multidisciplinary management combining epidemiological surveillance, stepwise microbiological diagnosis, and immediate antibiotic treatment. Such an approach, in accordance with the provisions established in the Public Health Surveillance Protocol for Leptospirosis, version 6 of the National Institute of Health of Colombia (2024), constitutes a determining factor in the survival of patients with severe leptospirosis.

CONCLUSION

The presented case corresponds to a patient with febrile icteric syndrome and a history of rodent exposure, an epidemiologically relevant sociodemographic factor. The clinical course included acute hepatic dysfunction, evidenced by marked direct hyperbilirubinemia, and severe pulmonary involvement in the form of acute respiratory distress syndrome secondary to leptospiral pneumonitis. The final confirmed diagnosis was Weil disease. This report unders-

cores the importance of considering this etiology in the diagnostic approach to febrile icteric syndromes, particularly in high-risk situations such as slaughterhouse workers, farmers, freshwater swimming, flooding, residence in areas with open sewage systems or inadequate waste management, among others, in order to facilitate timely and appropriate intervention.

Ethical Considerations

This case report was conducted in accordance with the principles of the World Medical Association Declaration of Helsinki and the guidelines of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use Good Clinical Practice standards for research.

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