

# Unraveling a Complex Case: A Multidisciplinary Exploration of Alveolar Hemorrhage, Jaundice, and Respiratory Distress in the Context of Leptospirosis

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## Abstract

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This case presentation delves into the compelling narrative of a 45-year-old male patient grappling with fever, jaundice, and an elusive constellation of symptoms. With a backdrop of chronic kidney disease and recent involvement in paddy field activities, the patient's clinical journey unraveled into a complex diagnostic puzzle, necessitating collaboration among nephrology, surgery, and psychiatry specialists. The initial clinical evaluation unearthed alarming findings of severe thrombocytopenia (platelet count: 8,000) and elevated creatinine levels 6. Due to the presentation, a comprehensive treatment approach ensued, incorporating dexamethasone, ceftriaxone, fluid therapy, and dialysis. However, the subsequent emergence of alveolar bleeding on CT scan, respiratory distress, and a decline in mental well-being propelled the patient into the Intensive Care Unit (ICU).

Amidst the evolving clinical scenario, the team sought to untangle the intricate web of symptoms, and the suspicion of leptospirosis emerged. The patient's engagement in paddy field activities and the positive result for leptospirosis IgM antibodies in a urine PCR sample added a new layer to the diagnostic challenge. The interplay of leptospirosis with the existing clinical complexities heightened the need for a nuanced, multidisciplinary approach. Throughout the hospitalization, the patient's condition oscillated, marked by persistent jaundice, anemia, and progressive lung involvement. Despite interventions, including Shaldon catheter placement, dialysis, pleural fluid taps, and drainage, the patient succumbed to pulmonary complications after a series of intricate medical procedures.

This presentation navigates the multifaceted landscape of the case, exploring the challenges posed by the coexistence of leptospirosis with other clinical manifestations. Integrating leptospirosis considerations with imaging, pathology, and laboratory findings contributes to a holistic understanding of the complexities inherent in such a challenging medical scenario. The narrative serves as a poignant reminder of the vital role played by a multidisciplinary approach in unraveling the mysteries surrounding complex medical conditions.

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## INTRODUCTION

Leptospirosis is a zoonotic infection affecting humans and mammals, recognized for several decades and prevalent in nearly all tropical and temperate

regions worldwide (1). It is estimated that 1.03 million cases of leptospirosis and 58,900 deaths related to leptospirosis occur annually (2). The incidence of this infection in tropical low-income countries is ten times

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higher than in other regions. Factors such as high temperature, humidity, rainfall, and socioeconomic challenges like poor hygiene and close contact with domestic animals contribute to the high prevalence of leptospirosis in these areas (3). While rodents are considered the primary reservoir, other mammals can contribute significantly to human infections under specific conditions (4).

This disease is more common among individuals in specific occupations such as rice and sugarcane farming, veterinary practice, laboratory work, slaughterhouse operations, and livestock handling (5). The most characteristic early clinical manifestations include sudden fever, headache, weakness, myalgia, and conjunctival inflammation. Key laboratory indicators for diagnosis include proteinuria, leukocytosis with neutrophilia, and elevated erythrocyte sedimentation rate (6). One of the standard diagnostic methods for leptospirosis is culture and microscopic agglutination testing. Early antibiotic treatment is most effective in managing leptospirosis, highlighting the critical importance of timely diagnosis (7).

Delayed diagnosis can lead to disease progression, marked by hemorrhage, jaundice, and renal failure. Treatment primarily involves a broad spectrum of antibiotics administered orally or intravenously. Common antibiotics include tetracyclines, penicillin, and ceftriaxone. Early administration of these antibiotics significantly reduces the risk of Weil's disease and associated mortality (8). Advanced disease stages may require intensive care measures, including hemodialysis and blood transfusions, while severe pulmonary hemorrhages often necessitate mechanical ventilation (4).

Severe pulmonary involvement is the most common cause of mortality in leptospirosis (9). Therefore, early recognition and treatment initiation are crucial in preventing serious and life-threatening complications. This article reports a case of acute leptospirosis presenting with severe pulmonary symptoms and jaundice. This study aims to review this specific case and emphasize the importance of early diagnosis and treatment of leptospirosis to prevent severe complications and mortality.

### **Presenting clinical case**

In this case study, we present a 45-year-old male patient who initially presented to Razi Hospital in Qaemshahr with symptoms of fever and jaundice. The patient had a history of chronic kidney disease and had recently been working in rice paddies. Upon examination, he had been suffering from dyspnea, and fine crackles were heard on lung auscultation. Initial lab work was done. The patient's platelet count was markedly low at 8,000, and his creatinine level was

elevated to 6 mg/dL. The initial therapeutic approach was developed in consultation with nephrology and surgery specialists: IV dexamethasone, ceftriaxone, fluid therapy, and dialysis. Dialysis was performed using a Shaldon catheter.

Following dialysis, the patient developed respiratory distress, prompting further investigations. A chest X-ray revealed patchy pulmonary involvement, which became more pronounced in subsequent imaging and demonstrated alveolar hemorrhage on a CT scan. The patient's oxygen saturation declined, necessitating transfer to the intensive care unit (ICU). Subsequently, he exhibited agitation and delirium, which interfered with medication administration. Under nephrologist supervision, the patient underwent dialysis and received daily intravenous methylprednisolone pulse therapy (1 gram) for three days, leading to a gradual increase in platelet count and improvement in respiratory distress. Concurrently, a psychiatric consultation was conducted, and antipsychotic medications alleviated the patient's delirium.

Throughout the hospitalization, the patient persistently exhibited jaundice and anemia. Despite blood transfusions, hemoglobin levels remained low due to evident hemolysis and a reduced reticulocyte count. Platelet counts increased to 100,000; however, jaundice persisted, accompanied by elevated liver enzymes and bilirubin levels. The patient complained of back, chest, and flank pain. Subsequent imaging revealed pleural effusion, proper lung involvement, and a mass-like lesion in the lung. A biopsy was performed under imaging guidance due to the observed mass-like lesion near the lung hilum and extensive pleural effusion. The biopsy results indicated a necrotic hemorrhagic lesion. Thoracentesis confirmed the transudative nature of the pleural fluid, but the patient's respiratory distress worsened, necessitating readmission to the ICU. Ultrasound-guided placement of a pleural catheter temporarily alleviated respiratory discomfort. However, the patient developed hypotension and sepsis, requiring norepinephrine therapy. Unfortunately, the patient expired due to pulmonary complications on the same day the drainage procedure was performed.

Early in the course of treatment, elevated procalcitonin levels and leukocytosis led specialists to suspect a potential infection, prompting the initiation of antibiotic therapy. However, an indeterminate tumor-like lesion in the lung was observed, with pathological examination revealing hemorrhagic necrosis resulting from resorption of alveolar hemorrhage. Despite medical efforts, the patient's condition remained ambiguous, ultimately culminating in a fatal outcome. Notably, the patient's bilirubin levels decreased by half during the treatment, while creatinine levels remained dialysis-dependent. Differential diagnoses considered

for the patient included hepatitis, viral hemorrhagic fevers, cholangitis, and leptospirosis. Subsequently, a PCR urine sample for leptospirosis was obtained, and the patient's blood tested positive for leptospirosis IgM antibodies (IgM leptospirosis: 20). Thus, a definitive diagnosis of leptospirosis was established.

### Paraclinical findings

#### Ultrasound findings:

Initial ultrasonography findings on the first day revealed a standard liver size of 150 mm, with no masses or abnormalities observed in the liver, portal vein, or gallbladder. The spleen measured 64×140 mm and appeared normal. By the seventeenth day, renal echogenicity had mildly increased; however, no stones, masses, or hydronephrosis were detected. The prostate volume was measured at 21 cc, with no abdominal or pelvic abnormalities identified, except for 250 cc of fluid in the right paracolic space.

Right-sided pleural fluid was aspirated on the nineteenth day and sent for cytological analysis. A subsequent repeat chest CT scan on the twenty-second hospitalization day revealed a large solid mass (92×111 mm) with vascular involvement located in the mid-lower zone of the right lung near the mediastinum. Additionally, ultrasonography detected over 1500 cc of fluid in the right pleural space, and approximately 750 cc of fluid was drained via pleural catheter placement. On the same day, a color Doppler ultrasound of the lower limbs and lungs showed intact arterial and venous dimensions without evidence of deep vein thrombosis. The arterial waveform was triphasic and normal.

#### Pleural Fluid Analysis:

- Acid-fast bacillus (AFB): Negative
- Cell counts:
- White blood cells (WBC): 1,000
- Neutrophils (PMN): 95%
- Lymphocytes: 5%
- Red blood cells (RBC): 24,000
- Biochemical findings:
- LDH: 1,147 U/L
- Total protein: 2.8 g/dL
- Albumin: 2.6 g/dL
- Glucose: 45 mg/dL
- BS (Blood Sugar): 70 mg/dL

Given less than 50% protein content, the pleural fluid was classified as transudative.

#### Biopsy and pathologist report:

On the nineteenth day, the biopsy sample was sent to pathology, and the pathological report described coagulative necrosis due to hemorrhagic infarction.

### Discussion

The presented case intricately combined a range of symptoms and diagnostic challenges, highlighting the need for a comprehensive and collaborative medical approach. The simultaneous presence of alveolar hemorrhage, jaundice, and respiratory distress, along with leptospirosis, created a complex clinical condition that required thorough investigation.

The presentation of fever and jaundice in a patient with a history of chronic kidney disease were the initial symptoms that made this complex diagnosis challenging. Severe thrombocytopenia, elevated creatinine levels in subsequent tests, and alveolar hemorrhage on imaging further complicated the diagnostic process. Due to the patient's recent activity in the rice paddies and the positive IgM antibody result, leptospirosis was confirmed with both lab work and history. This report emphasizes the importance of considering environmental exposures in clinical evaluations.

A similar case was reported in Japan in 2017 in a 50-year-old male chef. The patient presented to healthcare facilities with symptoms including fever, myalgia, thrombocytopenia, jaundice, and renal failure. His condition worsened due to a decrease in platelet count, increased bilirubin levels, and respiratory distress. The patient's leptospirosis test results were positive. On the fifth day, the patient was intubated. Due to the deterioration of his respiratory status, venovenous extracorporeal membrane oxygenation (V-V ECMO) was performed. Additionally, treatment with inotropes and broad-spectrum antibiotics, such as benzylpenicillin, was initiated, along with renal replacement therapy.

Leptospirosis is a disease that responds very well to antibiotic treatment. In the case we presented, antibiotic therapy was initiated from the outset, and the patient also had renal involvement, requiring dialysis. However, the medications used in our case, dexamethasone and ceftriaxone, differed from those used in the Japanese case. The patient was discharged on the 19th day. This case report demonstrates that venovenous ECMO (V-V ECMO) may prevent mortality in patients with severe pulmonary hemorrhagic syndrome (SPHS) due to leptospirosis who do not respond to conventional treatment. In the case we presented, the multidisciplinary collaboration of pulmonology and infectious disease specialists played a more significant role in the patient's treatment compared to other cases. Although the patient faced respiratory issues, venovenous ECMO (V-V ECMO) was not used, and unfortunately, the patient passed away. Therefore, V-V ECMO is likely an effective method for managing pulmonary complications associated with leptospirosis.

In a 2006 case report, a 68-year-old Greek male with leptospirosis and diffuse alveolar hemorrhage was admitted to healthcare facilities due to progressive CNS dysfunction and later transferred to the intensive care unit (ICU) through hospitalization. Laboratory test results revealed severe liver and kidney dysfunction, leading to the initiation of hemodialysis. IV methylprednisolone with a dose of 1 gram per day for three days, followed by prednisone 20 mg every 6 hours, was administered. The patient responded to treatment with cessation of bleeding. Hemorrhagic alveolitis may

occur in leptospirosis, and it responds well to high-dose steroid treatment. In our case, intravenous corticosteroids, including dexamethasone and methylprednisolone, were used, but unfortunately, the patient's respiratory symptoms were not controlled. Therefore, it seems that methylprednisolone and prednisone are effective in managing symptoms in some patients. Additionally, the life-saving effects of pulse corticosteroid therapy in treating some cases should also be noted.

Reference range	Last day	20th day	15th day	10th day	5th day	On	Lab date
13.5-17.5	7.9	8.3	7.3	7.2	8.2	8.4	hemoglobin (g/dl)
4,500-13,000	16,20	11,200	16,200	34,00	19,20	8,200	WBC (در هر $\mu$ l)
150,000-	315,0	184,00	96,000	136,0	40,00	8,000	Platelet count (در)
6-24	293	205	146	204	179	154	Blood urea
0.60-1.50	5.7	4.6	4.6	3.8	3.4	4.9	blood creatinine
135-145	137	129	128	131	134	131	sodium (mEq/L)
3.5-5.5	6.2	5	4.4	4.3	3.7	3.9	potasium(mEq/L)
7.35-7.45	-	-	7.39	7.42	-	7.38	pH
22-28	-	-	17.4	20.2	-	21.9	(mEq/L)HCO3
35-45	-	-	29.2	31.6	-	37	PCO2 (mmHg)
0-22	93	-	-	-	-	111	ESR
0-10	45	-	-	-	-	3	CRP (mg/liter)
10-40	106	75	77	67	95	292	ALT (U/liter)
10-40	83	72	70	50	82	421	AST
44-196	822	886	639	590	430	258	ALP (U/liter)
0.1-1.2	11	30	27.5	54	65.5	33.9	Total bilirubin
<0.3	6.7	28	24.3	43	57.9	29.3	Direct bilirubin
3.4-5.4	2.5	2.6	2.8	-	2.9	3.2	Serum albomin

In 2015, a case of leptospirosis with alveolar hemorrhage was successfully treated. The patient presented with acute fever and respiratory symptoms. Following the necessary tests and confirmation of leptospirosis, the patient was managed with high-flow oxygen, non-invasive ventilation, antibiotics, and steroids. Early diagnosis and management with oxygenation, antibiotics, and immunosuppressive drugs can prevent complications and reduce mortality (12). However, in our study, treatment for leptospirosis was initiated upon hospital admission based on clinical suspicion. Prior to the onset of severe symptoms, the patient's condition was not diagnosed during outpatient visits. As a result, the delayed diagnosis of leptospirosis contributed to the patient's demise. Therefore, early diagnosis in such cases is critical, as failure to identify the disease in time may result in fatal outcomes.

In another case reported in 2015 in Thailand, a 31-year-old man with leptospirosis, diffuse alveolar hemorrhage, and acute renal failure was treated with initial plasma exchange and a 7-day course of moxifloxacin. Both pulmonary hemorrhage and hypoxemia significantly improved by the fourth day of

hospitalization. The patient fully recovered from the disease after a 6-week hospital stay (13). Ceftriaxone is the treatment of choice for treating alveolar hemorrhage caused by leptospirosis, and plasma exchange may also be effective in some cases.

In another case report from 2020, a 20-year-old laborer presented with a 3-day history of malaise, fever, diarrhea, vomiting, and jaundice. On the day of emergency admission, he developed hemoptysis, severe headache, neck stiffness, and photophobia. In our patient, jaundice and fever were observed, but photophobia and headache were not the reasons for hospital admission. Similar to our study, the patient experienced anemia and thrombocytopenia. Acute anuric kidney injury required urgent hemofiltration. Due to progressive respiratory failure, broad-spectrum antibiotics and methylprednisolone were administered. As in the study by Katsanoulas C. et al, methylprednisolone was used, showing positive outcomes in both cases. Laboratory results confirmed leptospirosis. The patient was intubated 48 hours after admission. Despite efforts, hypoxia persisted, and the patient underwent venovenous extracorporeal

membrane oxygenation (VV-ECMO) in the intensive care unit. After 8 days, the patient recovered. Therefore, respiratory support with ECMO can aid in clearing bronchial clots, improving parenchymal recovery, and preventing ventilator-induced lung injury (14). In our study, VV-ECMO was not utilized, and the patient expired due to pulmonary complications.

A review of similar cases highlights the critical importance of early diagnosis in managing leptospirosis with alveolar hemorrhage. Renal involvement often necessitates urgent dialysis in such cases. The prompt administration of broad-spectrum antibiotics is vital to halt disease progression. Furthermore, clinical practice should carefully consider the therapeutic potential of VV-ECMO and plasma exchange as pivotal interventions in improving patient outcomes.

### Conclusion:

Although leptospirosis is often a mild and self-limiting disease, pulmonary involvement significantly increases its mortality rate. As such, follow-up care for patients with leptospirosis, even after initial clinical

improvement, is critical. In hospitalized patients with severe forms of the disease, especially those presenting with alveolar hemorrhage, close monitoring becomes even more essential.

Education plays a vital role in controlling the spread and mortality associated with leptospirosis. Raising awareness among at-risk individuals, such as farmers, about preventive measures and training general practitioners and medical students for early diagnosis can significantly contribute to reducing the disease burden.

Given the high mortality associated with leptospirosis, persistent jaundice and pulmonary hemorrhage must be monitored closely. Further studies are needed to optimize antibiotic regimens and explore advanced treatment modalities like plasmapheresis. Additionally, secondary infections may cause or exacerbate leptospirosis complications. Therefore, more attention is needed to the prevalence and impact of secondary infections in these patients to improve outcomes.

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