

A diagnosis of leptospirosis: a case report

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Abstract

A male individual, aged 54, exhibited symptoms including fever, rigors, myalgia, dry cough, and dyspnea. Ten days prior, he provided a description of an ailment resembling an upper respiratory infection. The recorded body temperature measured 38.2°C. The physical examination findings included the presence of scleral icterus, jaundice, conjunctival hyperemia, extensive ecchymoses at multiple locations on the body, an antecubital hematoma, bilateral basal rales, hepatomegaly, and splenomegaly. The White Blood Cell Count (WBC) was measured to be 1.100/mm³, Hemoglobin (Hgb) level was found to be 11.8 g/dL, the platelet count was seen

to be 10.000/mm³, the Erythrocyte Sedimentation Rate (ESR) was determined to be 68 mm/h, and C-Reactive Protein (CRP) concentration was measured at 84 U/L. The serum biochemistry analysis revealed elevated levels of liver enzymes and bilirubin. The chest radiograph exhibited bilateral basal interstitial linear opacities and the presence of pleural effusions. The confirmation of leptospirosis diagnosis was achieved through the utilization of both serologic tests and a real-time Polymerase Chain Reaction (PCR) assay. The patient received oral doxycycline at a dosage of 100 mg twice daily and intravenous ceftriaxone at a dosage of 1 gram daily for a duration of one week. After undergoing treatment, the patient experienced a complete remission of symptoms and had a smooth recovery without any complications. The prevalence of pulmonary involvement in individuals diagnosed with leptospirosis has been reported to reach up to 70%. The presence of pulmonary symptoms as the primary manifestation of the atypical clinical spectrum might pose a considerable diagnostic problem for doctors. This is because the illness can appear with a wide range of symptoms affecting many organs throughout the body. The potential consequences of delayed identification and treatment of leptospirosis might be severe. The objective of this review is to elucidate the clinical characteristics of pulmonary leptospirosis. Another objective is to present an analysis of evaluation scores in order to obtain a precise final diagnosis.

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Introduction

Leptospirosis has the potential to give rise to significant global outbreaks. The occurrence of pulmonary complications in cases of leptospirosis has exhibited an upward trend in recent years, with reported prevalence rates reaching as high as 70%.¹⁻⁴ Leptospirosis exhibits a range of clinical manifestations, spanning from mild to severe disease patterns. Severe cases may present with symptoms such as jaundice and renal failure, while lung involvement can vary from a subtle clinical profile to the development of pulmonary bleeding and Acute Respiratory Distress Syndrome (ARDS). The initial documentation of hepato-renal-pulmonary involvement caused by capillary vasculitis leading to acute fever was attributed to Weil in 1886, who identified this condition as leptospirosis. The illness trajectory has the potential to result in mortality for approximately 10-15% of individuals.^{3,5} The immunological phase of the disease typically leads to the development of lung involvement, with pulmonary signs observed in a range of 20-70% of patients. These manifestations generally disappear without any long-term consequences. The development of pulmonary illness can occur as a potentially life-threatening consequence of leptospirosis.^{2,6-9} Due to the sometimes-aberrant presentation of symptoms and laboratory findings associated with leptospirosis, doctors often encounter a diagnostic conundrum that poses a significant difficulty. The pulmonary manifestation of leptospirosis can result in a wide range of symptoms, varying from moderate to severe, ultimately culminating in respiratory failure, lung bleeding, and fatality. This study examines the pulmonary

symptoms of leptospirosis, focusing on recent evidence pertaining to the clinical profile of associated lung injury. Due to the overlapping clinical symptoms of leptospirosis with many infectious, pulmonary, or autoimmune disorders, the process of diagnosing and treating this condition is sometimes subject to delays. Patients frequently exhibit prominent pulmonary signs that mimic those of a primary lung illness. The objective of this review is to present a clinical assessment score that can be used to get a precise diagnosis of leptospirosis, supported by existing literature and our own case observations.

Case Report

A 60-year-old male presented with a 10-days history of fever, rigors, fatigue, lassitude, myalgia, dry cough, dyspnea, and five kilograms of weight loss in three weeks. Personal or family history did not reveal any disease. Occupational exposure, encounters with rats, or travel to endemic areas were not present. The patient described an upper respiratory tract infection-like illness that started approximately twenty days ago. Fever was 38.2°C, he had a regular sinus rhythm heart rate of 96/minute, and a blood pressure of 120/70 mmHg. Inspection revealed scleral icterus, jaundice, conjunctival hyperemia, large ecchymoses at various sites of the body, and an antecubital hematoma. Physical examination showed bilateral basal fine rales, hepatomegaly, and splenomegaly of 3 cm below the costal line. White Blood Cell Count (WBC) was 1.100/mm³ with 20% segmented neutrophils, 8% band forms, 4% eosinophils, 28% atypical mononuclear cells, 36% lymphocytes, and platelets 10.000/mm³. Hemoglobin (Hgb), Erythrocyte Sedimentation Rate (ESR), and C-Reactive Protein (CRP) were 11.8 g/dL, 68 mm/h, and 38.6 U/L. Serum biochemistry revealed SGOT 1.025 IU/L, SGPT 6.835 IU/L, LDH 13.135 IU/L, ALP 1.330 IU/L, CPK 2.025 IU/L, and creatinine 1.8 mg/dL.



Figure 1. Chest x-ray revealing bilateral linear interstitial opacities and bilateral pleural effusions due to Leptospirosis pneumonia.

Coagulation parameters were as follows: prothrombin time 13.60 s, aPTT 94.20s, INR 1.22, D-dimer 1.666 g/L, and FDP >20 g/ml. Renal function tests were within normal limits. Total and conjugated bilirubin were 3.75 mg/dL and 2.90 mg/dL. Electrocardiogram (ECG) showed a sinus rhythm of 96/min. Chest X-ray revealed bilateral basal linear interstitial, small ground-glass opacities up to 2 cm in diameter, and pleural effusions (Figure 1). High-Resolution Computed Tomography (HRCT) displayed similar findings. The effusion was an exudate with a 74% lymphocyte ratio. Analysis of BAL fluid and transbronchial biopsy specimens were not diagnostic. The culture of BAL and pleural effusion did not grow any organisms. Serologic testing and real-time (Polymerase Chain Reaction) PCR assay were positive for leptospirosis infection. Oral doxycycline 100 mg twice daily and IV ceftriaxone 1 gr daily for one were given for 10 days. The patient had a full convalescence of symptoms, amelioration of physical findings, normalization of laboratory results, and complete resolution of radiological manifestations (Figure 2) with an uneventful recovery. The final diagnosis was leptospirosis infection with pulmonary, hepatic, and splenic involvement.

Discussion

Leptospirosis is a zoonotic disease characterized by a wide range of clinical symptoms, which is caused by pathogenic spirochetes belonging to the genus *Leptospira*. The doctor faces significant challenges in making a diagnosis due to the ambiguous clinical picture that often shares similarities with other disorders.¹⁰ The presentation and clinical profile of leptospirosis exhibit significant variability, often manifesting in the involvement of many organs, hence posing challenges in diagnosis. The majority of instances exhibit moderate symptoms and resolve on their own or show no symptoms at all, whereas a minority of cases are severe and have



Figure 2. Chest x-ray following treatment showing complete resolution of pulmonary interstitial opacities and pleural effusion.

the potential to result in death.^{5,11} The diagnosis of leptospirosis in an individual patient is contingent only upon the clinical presentation. Regrettably, the presence of ambiguous symptoms, the involvement of several organs, and particularly the ambiguity of laboratory and imaging manifestations sometimes result in a diagnostic stalemate when dealing with instances of leptospirosis that mostly affect a single organ, such as the lung. In this paper, we provide a comprehensive analysis of leptospirosis with the aim of guiding doctors in their diagnostic approach. We propose the development of a diagnostic assessment score based on a thorough examination of existing literature and our own case studies.

The critical stage in achieving an accurate diagnosis of leptospirosis involves a thorough evaluation of the patient's medical history. Risk factors encompass several animals or activities that may result in skin abrasions due to contact with water or soil. The factors contributing to exposure can be categorized into various

domains, including occupational exposure, recreational activities, household exposure (such as pet dogs and domesticated livestock), utilization of rainwater catchment systems, infestation by infected rodents, low socioeconomic status (such as residing in overcrowded urban areas with inadequate sanitation), travel to endemic areas, and additional factors like walking barefoot through surface water, contact with wild rodents, or accidental laboratory exposure.^{11,12} The identification of such elements in the historical context holds significant importance in the study of leptospirosis. The diagnostic assessment score analysis involved the evaluation of the presence of any of these factors using a scoring system of one and two points (Table 1, Table 2).

Leptospirosis exhibits a diverse range of clinical presentations among individuals. While the majority of cases exhibit a moderate, self-limiting, or even asymptomatic course, there is a possibility of a potentially deadly outcome in certain instances. The prevailing

Table 1. Clinical manifestations of leptospirosis.

Clinical manifestations of leptospirosis	Index score
Absence of granulomatous infection, drug, or occupational exposure	1
Occupational history	1
Low socioeconomic status	1
Travel to endemic areas	2
Exposure to rats	2
Systemic febrile illness	1
Multiple organ involvement	2
Pulmonary involvement	1
Lassitude, fatigue	1
Weight loss	1
Fever, myalgia, headache, vomiting	1
Jaundice	2
Pulmonary hemorrhage	1
Oliguric or nonoliguric renal failure	1
Dyspnea, dry cough	1
Absence of finger clubbing	2
Skin rash	1
Pretibial petechiae	2
Conjunctival hyperemia or subconjunctival hemorrhage	3
Hepatomegaly, splenomegaly	1
Aseptic meningitis	2
Myocarditis	1
Rhabdomyolysis	1
Vasculitis and/or extremity necrosis	1
Thrombocytopenia, anemia, or pancytopenia	1
High conjugated serum bilirubin and liver enzymes	1
Elevated serum creatinine, potassium abnormalities, and hyponatremia	1
Proteinuria, pyuria, granular casts, and microscopic hematuria	1
Abnormal clotting tests	1
EKG abnormalities	1
Hypoxemia and high alveolo-arterial gradient	1
Chest x-ray findings*	1
HRCT manifestations**	1
Serology	4
PCR	4

*Chest-x ray findings: interstitial involvement, alveolar infiltrations, and ground-glass opacities. **Thorax CT manifestations: interstitial involvement, alveolar infiltrations, and ground-glass opacities. Positive findings of our patient were written in bold character.

kind of anicteric form is commonly observed, but the icteric form, characterized by jaundice, is known to be the most severe, fulminant, and potentially fatal presentation.^{9,13} A considerable number of individuals exhibit the anicteric manifestation of the disease, characterized by a two-phase course with an initial acute phase followed by an immunological phase. The acute phase is distinguished by the presence of acute febrile bacteremia.^{3,5,6,8} The occurrence of extrapulmonary signs in instances of leptospirosis is characterized by the sudden onset of fever, rigors, and myalgias, primarily affecting the calves and lower back, as well as headache, which is observed in a significant proportion ranging from 75-100% of cases. Nausea, vomiting, and diarrhea are reported in around 50% of the patient population.^{3,4} A dry cough may manifest in approximately 25-35% of the patient population. Less often observed symptoms include arthralgia, bone discomfort, sore throat, and abdominal pain.^{5,6} Conjunctival hyperemia, which has been documented in a significant proportion of individuals diagnosed with leptospirosis in certain case series, may manifest as a distinctive characteristic resulting from the expansion of blood vessels, leading to conjunctival erythema in the absence of purulent discharge. The occurrence of subconjunctival bleeding might manifest either with or without conjunctival suffusion.¹⁴ Recurrent uveitis is an additional characteristic observed throughout the immunological phase, with the anterior uvea being the most often affected site, presenting as iritis or iridocyclitis. Posterior uveitis may infrequently manifest as painless visual alterations.¹⁵ In a subset of patients, ranging from 7-40%, various clinical manifestations may be observed, including muscle pain, splenomegaly, lymphadenopathy, pharyngitis, hepatomegaly, muscle rigidity, and skin rash. The rash may exhibit maculopapular, urticarial, petechial, or purpuric characteristics, and is often of short duration, lasting between one to two days. In certain instances, the occurrence of pretibial petechiae has been seen.^{9,10,16,17} The presence of these symptoms was assigned a score of one point in the analysis conducted for the assessment. Pretibial petechiae has been identified as a distinctive manifestation, indicated by the presence of two specific spots. Aseptic meningitis can manifest as a characteristic feature of the immunological or delayed phase, presenting symptoms such as headache and neck discomfort or stiffness in around 50% of patients. Physical examination commonly indicates nuchal rigidity. Papilledema is a condition that occurs seldom. The symptoms of meningitis often subside after a span of one to two days, however in certain cases, they may endure for a period of two to three weeks.¹⁸ Within this set of indications, conjunctival hyperemia, uveitis, and aseptic meningitis were assigned a score of two points due to their heightened specificity in relation to leptospirosis. Icteric leptospirosis manifests in an estimated 5 to 10% of individuals exhibiting symptoms. The condition is distinguished by a swiftly advancing multisystemic ailment presenting symptoms such as fever, jaundice, renal failure, and a mortality rate ranging from 5 to 15%.^{1,5,9} In addition, it has been observed that pulmonary bleeding, Acute Respiratory Distress Syndrome (ARDS), myocarditis, and rhabdomyolysis can manifest as well.^{19,20} The presence of scleral icterus and jaundice is accompanied by elevat-

ed levels of conjugated bilirubin and aminotransferases. Liver failure is an infrequent occurrence, but laboratory indicators of liver involvement typically exhibit a tendency to revert to normal levels without consistent evidence of liver damage. Oliguric or non-oliguric renal failure may manifest. The serum creatinine levels exhibit a significant increase in conjunction with prevalent serum potassium irregularities and hyponatremia.²¹ Myocarditis can manifest as a characteristic symptom of leptospirosis, with severe instances potentially leading to the development of heart failure or cardiogenic shock.^{17,22} The most often observed results in electrocardiograms are nonspecific abnormalities.^{1,5} The occurrence of vasculitis resulting in necrosis of the extremities is infrequent.^{1,5} Renal failure, myocarditis, rhabdomyolysis, vasculitis, and extremities necrosis were assigned a score of one, as these manifestations have been observed in various pathological conditions.

Lung involvement has been observed in a significant proportion, around 70%, of individuals diagnosed with leptospirosis.^{1,2} Symptoms manifest in a range of 20-70% of individuals, typically presenting as mild and without any further complications. Patients may exhibit symptoms such as a dry cough, chest discomfort, dyspnea, and varying degrees of hemoptysis when presenting with acute respiratory distress syndrome.^{4,6,7} The most frequently observed pulmonary manifestation is a non-productive cough that arises during the phase of leptospirosis. Severe pulmonary leptospirosis is characterized by the presentation of pulmonary bleeding, typically of a significant magnitude, resulting in respiratory failure and ultimately leading to mortality due to asphyxiation.²³⁻²⁷ The occurrence of pulmonary bleeding may precede the appearance of other symptoms associated with leptospirosis, including jaundice and acute renal failure. The occurrence of hemoptysis, which is a symptom of pulmonary bleeding, has been documented in a range of 17-50% among patients.^{28,29} The clinical presentation may exhibit an accelerated and severe trajectory, characterized by elevated rates of mortality ranging from 30% to 60%. In certain instances, individuals may exhibit the occurrence of ARDS, necessitating the utilization of mechanical ventilation. It is noteworthy that this condition carries a significant mortality risk, with reported rates reaching as high as 51%. ARDS frequently exhibits a correlation with pulmonary bleeding due to the presence of endothelial injury. The occurrence of pulmonary edema may arise due to myocarditis, renal failure, and/or excessive fluid intake in the context of oliguria. Typically, these symptoms manifest within a timeframe ranging from the fourth to the sixth day of the disease. According to the cited sources,²⁹⁻³² it has been observed that lung disease has the potential to result in mortality within a timeframe of fewer than three days. The occurrence of vascular damage, primarily affecting the capillaries, is a result of a toxin-mediated process leading to small vessel vasculitis. Potential poisons include outer membrane proteins, membrane glycolipoproteins, hemolysins, and lipopolysaccharides. Tumor Necrosis Factor α (TNF- α) has been implicated in the pathogenesis of renal failure, lung damage, and hemorrhagic symptoms.³³

In nearly all cases, the admission profile is characterized by the presence of a systemic febrile illness for which no obvious alterna-

Table 2. Diagnostic assessment score analysis for leptospirosis.

Diagnostic assessment score	Probability of leptospirosis infection
DAS \leq 6	Inconsistent
6<DAS \leq 12	Low
12<DAS \leq 18	Intermediate
DAS>18	Definitive

DAS, Diagnostic Assessment Score.

tive explanation can be identified. The presence of specific geographic patterns and the identification of persistent risk variables are crucial elements in raising suspicion for the occurrence of leptospirosis infection. Additional compatible features include non-specific febrile illness, particularly when accompanied by conjunctival hyperemia, aseptic meningitis, or uveitis, followed by a febrile illness, unexplained jaundice, and acute kidney injury with fever, or an unexplained pulmonary hemorrhage.^{1,5,7-10} Clinicians commonly include leptospirosis in the differential diagnosis of acute undifferentiated febrile disease when patients exhibit the classic triad of fever, jaundice, and renal failure.^{3,5,8} Pulmonary hemorrhage can also be linked to thrombocytopenia, consumption coagulopathy, and vasculitis. Severe illness is characterized by mostly extensive hemorrhaging, resulting in respiratory insufficiency and ultimately leading to death by asphyxiation.

Patients frequently develop ARDS, a condition that commonly necessitates the use of mechanical ventilation. This intervention is typically accompanied by pulmonary bleeding, which can be attributed to endothelial damage. The mortality rate associated with severe pulmonary leptospirosis has been reported to reach up to 60% among affected patients.^{23,34,36}

In addition to fever, an often disregarded manifestation that exhibits discriminant features is conjunctival hyperemia. This condition is defined by the bilateral dilatation of blood vessels in the conjunctiva, resulting in conjunctival erythema, without the presence of purulent discharge. Subconjunctival bleeding may also manifest in certain cases. Uveitis has been observed to manifest as a characteristic of ocular involvement.^{14,15} The ophthalmologic abnormalities were classified using a three-point system owing to their elevated sensitivity. Up to 40% of patients exhibit manifestations such as muscle pain, splenomegaly, lymphadenopathy, pharyngitis, hepatomegaly, muscle rigidity, and/or skin rash.^{1,5,10,16} The lack of specificity in these observations resulted in a single-point score, reflecting their limited diagnostic relevance. Approximately one-third of patients exhibit the presence of jaundice or icterus. The evaluation of leptospirosis focused on two specific aspects: its high occurrence and its distinctive characteristics. Individuals who have significant pulmonary involvement may manifest symptoms such as rapid breathing (tachypnea) and bluish discoloration of the skin and mucous membranes (cyanosis). The respiratory system might exhibit either normal characteristics or demonstrate the presence of rales at the bases of the lungs.

The laboratory results have the potential to indicate the presence of thrombocytopenia, anemia, and findings that are in line with disseminated intravascular coagulation. These findings may include higher coagulation tests and D-dimer levels, as well as decreased levels of fibrinogen. Pancytopenia may manifest in certain instances. ESR and CRP levels typically exhibit an increase. Elevated liver enzymes and conjugated bilirubin levels are commonly observed without causing irreversible liver damage. In individuals experiencing oliguric or non-oliguric renal failure, there is a notable increase in serum creatinine levels, along with frequent occurrences of serum potassium anomalies and hyponatremia. The conclusive diagnosis is characterized by the isolation of the organism and the occurrence of seroconversion or an increase in antibody titer as determined through the Microscopic Agglutination Test (MAT). A clinical profile that is consistent with leptospirosis is characterized by a MAT antibody titer ranging from 1:200 to 1:800. This titer range provides substantial evidence to support the diagnosis. However, significant levels of antibodies are not observed until the second week of infection. The organism can be isolated from serum and/or cerebrospinal fluid within the initial ten days of infection, and from urine for an extended period of several weeks.³⁷⁻⁴² The results of this study were evaluated using a four-

point scoring system. Approximately 50% of individuals may have elevated levels of creatine kinase as a result of rhabdomyolysis.⁴³ The occurrence of abnormalities in arterial blood gases and spirometry may manifest. The occurrence of alveolar hyperventilation with hypocapnia is possible. Hypoxemia is a prevalent condition affecting 75% of patients, mostly attributed to the presence of pulmonary veno-arterial shunts in compromised pulmonary regions. This is seen by elevated values of $Q_s/Q_t\%$ and $p(A-a)O_2$. Notably, DLCO levels typically remain within the normal range. Individuals suffering from oliguric renal failure, exhibiting pulmonary abnormalities and radiologic pulmonary involvement, demonstrated decreased levels of pO_2 . Patients without any additional clinical indications of pulmonary involvement may still exhibit a high rate of Arterial Blood Gas (ABG) abnormalities.⁴⁴ In their study, Fontes *et al.*⁴⁵ found that a significant proportion of patients exhibited different spirometric patterns. Specifically, 38.1% of the patients demonstrated normal spirometric values, whereas 33.3% and 19% of the patients exhibited restrictive and obstructive pulmonary function patterns, respectively. The presence of abnormal spirometric results was found to be correlated with more severe APACHE II scores and observable abnormalities on chest X-ray images.⁴⁵

The prevalence of pulmonary radiologic abnormalities ranges from 11% to 67% and can manifest as early as 24 hours following the onset of respiratory symptoms, but they often appear within a timeframe of 3 to 9 days. Leptospirosis is associated with the presence of peripheral diffuse or confluent lung infiltrations. Chest imaging commonly exhibits bilateral patchy peripheral infiltrates that have the potential to evolve into confluent consolidation or a ground-glass look, indicative of alveolar hemorrhage, ARDS, or pulmonary edema. Alveolar infiltrates were observed in 74.3% of the patient population, with bilateral involvement noted in 54.3% of cases and lower lobe involvement observed in 45.5% of patients. Occasionally, the manifestation of confluent consolidation and/or ground glass opacities may occur. Pleural effusions have been shown to occur in 8.6% of cases, although the occurrence of basal linear opacities associated with interstitial inflammation is exceedingly uncommon. Radiographic abnormalities typically exhibit resolution within a two-week timeframe, without the presence of any lasting lesions. However, it is important to note that the severity of pulmonary symptoms is often associated with these abnormalities.⁴⁶⁻⁴⁸ Marchiori⁴⁹ observed that the radiographic findings mostly consisted of diffuse ground glass opacities, which were predominately seen in the peripheral and dorsal regions of all lung lobes. These opacities were more commonly observed in the lower lung zones as visualized using thoracic computed tomography. HRCT reveals ground glass opacities in the upper lobes, which are not clearly visible on chest radiographs, and are attributed to airspace bleeding. The histological examination indicated that the observed HRCT abnormalities, including ground glass opacities, airspace consolidation, and airspace nodules, were attributed to airspace hemorrhage.⁴⁹ The patient exhibited bilateral basal linear interstitial opacities and bilateral significant pleural effusions. The existence of such a shared radiological appearance has not been previously documented in the academic literature.

Bronchoscopy and bronchoalveolar lavage have the potential to detect lung bleeding that could otherwise go unnoticed. Hemorrhage is observed in all patients presenting with respiratory symptoms, as evidenced by bronchoalveolar lavage. According to the findings of a study, it was observed that a mere 70% of individuals who did not exhibit any chest symptoms displayed indications of hemorrhage while undergoing bronchoscopy.² An increased level of serum Platelet-Activating Factor Acetylhydrolase (PAF-AH) has been suggested to potentially correlate with the occur-

rence of pulmonary hemorrhage in individuals with severe conditions. The aforementioned reagent exhibits potential as a candidate tool for disease monitoring.⁵⁰ Due to the absence of precise diagnostic evidence from laboratory and radiographic findings, a single point was assigned to their contribution to the diagnostic assessment analysis for leptospirosis. Regarding the pulmonary signs observed in our patient, it is noteworthy that this particular case represents a unique occurrence in the existing body of literature. Specifically, the patient had interstitial linear opacities and bilateral pleural effusions, a combination that has not been previously documented. The radiological presentation poses a diagnostic challenge, necessitating clinicians to be cognizant of the possibility of seeing a picture that has not been previously observed, but may be indicative of leptospirosis.

The prognosis of leptospirosis can have a very equivocal profile, characterized by the presentation and clinical signs. The prevalence of mortality in extreme situations might reach up to 15%. The criteria linked to severe and catastrophic outcomes encompass hemodynamic disruptions, thrombocytopenia, elevated blood creatinine accompanied by high serum potassium levels, and pulmonary involvement. Pulmonary bleeding is observed to be a substantial contributor to death. Age and delayed admission can be considered additional factors that contribute to an increased risk of mortality. The presence of diffuse or extensive radiological involvement has been identified as an additional significant factor contributing to a catastrophic prognosis.^{30,31}

The described case exhibits atypical characteristics that have not been previously documented in the existing literature, hence offering valuable insights for healthcare practitioners. One notable characteristic is the unique radiologic pattern characterized by bilateral linear interstitial marks and the presence of pleural effusions. Contrary to the aforementioned observation that bronchoalveolar lavage consistently discloses hemorrhage in all patients exhibiting respiratory symptoms, the bronchoalveolar lavage findings in this particular case solely indicated the presence of lymphocytosis, without any discernible evidence of hemorrhage. Furthermore, our examination of the diagnostic evaluation scores has yielded a result of 34 points, above the established threshold of 18 points for a conclusive diagnosis of leptospirosis. This outcome provides a precise and unambiguous final diagnosis, leaving no room for uncertainty. Conducting a comprehensive study that facilitates timely diagnosis of leptospirosis not only enables precise identification of the disease but also has the potential to mitigate the substantial death rates, which can reach up to approximately 15% in severe instances, through the initiation of early intervention measures.

Conclusions

The differential diagnosis of leptospirosis encompasses a range of conditions, including viral, autoimmune, neoplastic, and organ illnesses affecting the lungs, liver, or kidneys. Clinicians face significant challenges when dealing with leptospirosis due to its wide range of presentations, involving multiple organs, and its unpredictable patterns in diagnostic components, particularly in laboratory and radiologic manifestations. However, even among individuals exhibiting a disease profile that is consistent with the condition, the process of diagnosis might provide a challenge or difficulty, mostly because of the frequent involvement of several systems in the disease. A diagnostic challenge arises from the inclusion of several disorders, such as autoimmune, vasculitic, infectious, malignant, or other organ diseases, within the differential diagnosis, given their involvement in multiple bodily systems. Moreover,

when the results of leptospirosis investigations primarily indicate an association with a certain organ, particularly the lungs, the process of diagnosing the condition becomes significantly more challenging. From this perspective, it is evident that the diagnostic assessment scoring analysis we have proposed seems to be an essential instrument for physicians. While this analytic technique may not be sufficient for diagnosis on its own, it offers a precise pathway and a valuable differential diagnostic analysis, especially in cases when there are single organ presentations relevant to leptospirosis. The progression of disease and the emergence of major complications are consequences that arise from a delay in diagnosis. The application in question possesses significant utility by offering an early diagnosis, so potentially preventing the occurrence of life-threatening complications associated with leptospirosis, including renal failure, ARDS, and pulmonary bleeding. The proposed diagnostic score analysis not only offers significant advantages to clinicians in accurately identifying leptospirosis, but also serves as a vital tool for definitively diagnosing patients with atypical presentations or unusual clinical profiles. This is particularly relevant in cases where microbiological or serological findings are negative, and when pulmonary involvement manifests with an abnormal radiological pattern, as observed in our patient.

References

1. Gulati S, Gulati A. Pulmonary manifestations of leptospirosis. *Lung India* 2012;29:347-53.
2. Carvalho CRR, Bethlem EP. Pulmonary complications of leptospirosis. *Clin Chest Med* 2002;23:469-78.
3. Lomar AV, Diament D, Torres JR. Leptospirosis in Latin America. *Infect Dis Clin North Am* 2000;14:23-39.
4. Seguro ER, Ganoza CA, Campos K, et al. Clinical spectrum of pulmonary involvement in leptospirosis in a region of endemicity, with quantification of leptospiral burden. *Clin Infect Dis* 2005;40:343-51.
5. Levett PN. Leptospirosis. *Clin Microbiol Rev* 2001;14:296-326.
6. O'Neil KM, Rickman LS, Lazarus AA. Pulmonary manifestations of leptospirosis. *Rev Infect Dis* 1991;13:705-9.
7. Tanomkiat W, Poonsawat P. Pulmonary radiographic findings in 118 leptospirosis patients. *Southeast Asian J Trop Med Public Health* 2005;36:1247-51.
8. Chacko CS, Lakshmi S, Jayakumar A, et al. A short review on leptospirosis: clinical manifestations, diagnosis and treatment. *Clin Epidemiol Global Health* 2021;11:100741.
9. Pavli A, Maltezou HC. Travel-acquired leptospirosis. *J Travel Med* 2008;15:447-53.
10. Katz AR, Ansdell VE, Effler PV, et al. Assessment of the clinical presentation and treatment of 353 cases of laboratory-confirmed leptospirosis in Hawaii, 1974-1998. *Clin Infect Dis* 2001;33:1834-41.
11. Wasinski B, Dutkiewicz J. Leptospirosis--current risk factors connected with human activity and the environment. *Ann Agric Environ Med* 2013;20:239-44.
12. Sugunan AP, Vijayachari P, Sharma S, et al. Risk factors associated with leptospirosis during an outbreak in Middle Andaman, India. *Indian J Med Res* 2009;130:67-73.
13. Morgan J, Bornstein SL, Karpati AM, et al. Outbreak of leptospirosis among triathlon participants and community residents in Springfield, Illinois, 1998. *Clin Infect Dis* 2002;34:1593-9.
14. Puca E, Pilaca A, Kalo T, et al. Ocular and cutaneous manifestation of leptospirosis acquired in Albania: A retrospective

- analysis with implications for travel medicine. *Travel Med Infect Dis* 2016;14:143-7.
15. Rathinam SR, Rathnam S, Selvaraj S, et al. Uveitis associated with an epidemic outbreak of leptospirosis. *Am J Ophthalmol* 1997;124:71-9.
 16. Sanford JP. Leptospirosis--time for a booster. *N Engl J Med* 1984;310:524-5.
 17. Vanasco NB, Schmeling MF, Lottersberger J, et al. Clinical characteristics and risk factors of human leptospirosis in Argentina (1999-2005). *Acta Trop* 2008;107:255-8.
 18. Romero EC, Blanco RM, Yasuda PH. Aseptic meningitis caused by *Leptospira* spp diagnosed by polymerase chain reaction. *Mem Inst Oswaldo Cruz* 2010;105:988-92.
 19. Pamplona BE, Carvalho, CRR. Pulmonary leptospirosis. *Current Opinion in Pulmonary Medicine* 2000;6:436-41.
 20. Segura ER, Ganoza CA, Campos K, et al. Clinical spectrum of pulmonary involvement in leptospirosis in a region of endemicity, with quantification of leptospiral burden. *Clin Infect Dis* 2005;40:343-51.
 21. Hurst FP, Neff RT, Katz AR, et al. Acute kidney injury requiring hemodialysis in patients with anicteric leptospirosis. *Clin Nephrol* 2009;72:186-92.
 22. Dupont H, Dupont-Perdrizet D, Perie JL, et al. Leptospirosis: prognostic factors associated with mortality. *Clin Infect Dis* 1997;25:720-4.
 23. Bethlem EP, Carvalho CRR. Pulmonary leptospirosis. *Curr Opin Pulm Med* 2000;6:436-41.
 24. Im JG, Yeon KM, Han MC, et al. Leptospirosis of the lung: Radiographic findings in 58 patients. *AJR Am J Roentgenol* 1989;152:955-9.
 25. Allen P, Raftery S, Phelan D. Massive pulmonary haemorrhage due leptospirosis. *Intensive Care Med*. 1989;15:322-4. Poh SC, Soh CS. Lung manifestations in leptospirosis. *Thorax* 1970;25:751-5.
 26. Silva JJ, Dalston MO, Carvalho JE, et al. Clinicopathological and immunohistochemical features of the severe pulmonary form of leptospirosis. *Rev Soc Bras Med Trop* 2002;35:395-9.
 27. Pai ND, Adhikari PM. Haemorrhagic pneumonitis: A rare presentation of leptospirosis. *J Postgrad Med* 2001;47:35-6.
 28. Nery LE, de Paula AB, Nakatani J, et al. Clinical, radiological and functional pulmonary manifestations in patients with leptospirosis. *Rev Inst Med Trop Sao Paulo* 1977;19:366-73.
 29. Allen P, Raftery S, Phelan D. Massive pulmonary haemorrhage due leptospirosis. *Intensive Care Med* 1989;15:322-4.
 30. Marotto PC, Nascimento CM, Eluf-Neto J, et al. Acute lung injury in leptospirosis: Clinical and laboratory features, outcome, and factors associated with mortality. *Clin Infect Dis* 1999;29:1561-3.
 31. Spichler AS, Vilaça PJ, Athanazio DA, et al. Predictors of lethality in severe leptospirosis in urban Brazil. *Am J Trop Med Hyg* 2008;79:911-4.
 32. Budiono E, Sumardi, Riyanto BS, et al. Pulmonary involvement predicts mortality in severe leptospirosis patients. *Acta Med Indones* 2009;41:11-4.
 33. Yang J, Zhang Y, Xu J, et al. Serum activity of platelet activating factor acetylhydrolase is a potential clinical marker for leptospirosis pulmonary hemorrhage. *PLoS One*. 2009;4:e4181.
 34. Shenoy VV, Nagar VS, Chowdhury AA, et al. Pulmonary leptospirosis: An excellent response to bolus methyl prednisolone. *Postgrad Med J* 2006;82:602-6.
 35. Trivedi SV, Vasava AH, Bhatia LC, et al. Plasma exchange with immunosuppression in pulmonary alveolar haemorrhage due to leptospirosis. *Indian J Med Res* 2010;131:429-33.
 36. Nicodemo AC, Duarte MI, Alves VA, et al. Lung lesions in human leptospirosis: Microscopic, immunohistochemical, and ultrastructural features related to thrombocytopenia. *Am J Trop Med Hyg* 1997;56:181-7.
 37. Sonthayanon P, Chierakul W, Wuthiekanun V, et al. Accuracy of loop-mediated isothermal amplification for diagnosis of human leptospirosis in Thailand. *Am J Trop Med Hyg* 2011;84:614-20.
 38. Koizumi N, Nakajima C, Harunari T, et al. A new loop-mediated isothermal amplification method for rapid, simple, and sensitive detection of *Leptospira* spp. in urine. *J Clin Microbiol* 2012;50:2072-4.
 39. Cermakova Z, Kucerova P, Pliskova L, Kubickova P. Real-time PCR method for the detection of the gene encoding surface lipoprotein LipL32 of pathogenic *Leptospira*: use in the laboratory diagnosis of the acute form of leptospirosis. *Scand J Infect Dis* 2013;45:593-9.
 40. Waggoner JJ, Pinsky BA. Molecular diagnostics for human leptospirosis. *Curr Opin Infect Dis* 2016;29:440-5.
 41. Schreier S, Doungchawee G, Chadsuthi S, et al. Leptospirosis: current situation and trends of specific laboratory tests. *Expert Rev Clin Immunol* 2013;9:263-80.
 42. Levett PN. Usefulness of serologic analysis as a predictor of the infecting serovar in patients with severe leptospirosis. *Clin Infect Dis* 2003;36:447-52.
 43. Johnson WD Jr, Silva IC, Rocha H. Serum creatine phosphokinase in leptospirosis. *JAMA* 1975;233:981-2.
 44. Nery LE, de Paula AB, Nakatani J, et al. Clinical, radiological and functional pulmonary manifestations in patients with leptospirosis. *Rev Inst Med Trop Sao Paulo* 1977;19:366-73.
 45. Fontes AP, Ribeiro DP, Jesus LS, et al. Respiratory functional characteristics of human leptospirosis. *Rev Soc Bras Med Trop* 2010;43:161-5.
 46. Lee RE, Terry SI, Walker TM, Urquhart AE. The chest radiograph in leptospirosis in Jamaica. *Br J Radiol* 1981;54:939-43.
 47. Matos ED, Costa E, Sacramento E, et al. Chest radiograph abnormalities in patients hospitalized with leptospirosis in the city of Salvador, Bahia, Brazil. *Braz J Infect Dis* 2001;5:73-7.
 48. Chawalparit O, Charoensak A, Niwattayakul K, et al. Radiographic chest findings and clinical correlations in leptospirosis. *J Med Assoc Thai* 2007;90:918-24.
 49. Marchiori E, Müller NL. Leptospirosis of the lung: High resolution computed tomography findings in five patients. *J Thorac Imaging* 2002;17:151-3.
 50. Yang J, Zhang Y, Xu J, et al. Serum activity of platelet activating factor acetylhydrolase is a potential clinical marker for leptospirosis pulmonary hemorrhage. *PLoS One* 2009;4:e4181.