Received: 11 March 2024 | Revised: 1 April 2024 | Accepted: 15 April 2024

DOI: 10.1002/ccr3.8883

CASE REPORT

Clinical Case Reports Open Access WILEY

Leptospirosis in a patient with cardiac manifestation: A case report study and literature review

Narges Lashkarbolouk[1,2] | **Mahdi Mazandarani**[1,2]

[1]Infectious Diseases Research Center, Golestan University of Medical Sciences, Gorgan, Iran

[2]Endocriniology and Metabolism Research Center, Endocrinology and Metabolism Clinical Sciences Institute, Tehran University of Medical Sciences, Tehran, Iran

Correspondence
Mahdi Mazandarani, Infectious Diseases Research Center, Golestan University of Medical Sciences, Gorgan, Iran.
Email: mahdi_mazandarani@yahoo.com

Key Clinical Message

Common cardiac arrhythmias seen in patients with leptospirosis are usually atrial fibrillation or first-degree atrioventricular block, with bradyarrhythmia being rare in this group. It is essential to prioritize the examination of the patient's medical background, clinical symptoms, and comprehensive physical evaluation in order to promptly identify and address the patient's condition.

Abstract

Leptospirosis, a zoonotic disease that is widespread worldwide, has a significant impact on tropical areas and can affect various organs throughout the infection. During the initial stage, symptoms are typically non-specific. Although cases of all three cardiac layers being affected have been reported, issues with the conduction system are especially significant in the early phase of the disease. The most frequent discoveries in these patients are atrial fibrillation or first-degree atrioventricular block, with bradyarrhythmia being rare. We describe a 37-year-old male farmer who initially sought medical attention for general symptoms that had been deteriorating despite receiving outpatient treatment for 3 days for a presumed diagnosis of influenza. During his initial assessment, he exhibited sinus bradycardia, anemia, leukocytosis, elevated levels of direct and total bilirubin, and abnormal liver function test results. Through thorough history-taking, physical examination, and laboratory analyses, a diagnosis of leptospirosis was conclusively established for him. Focusing on the patient's medical history, clinical manifestations, and thorough physical assessment is crucial for promptly diagnosing and treating patients. This becomes particularly significant for individuals who exhibit atypical symptoms, exemplified by our patient presenting with nonspecific indications and cardiac issues manifested as bradycardia.

KEYWORDS

arrhythmia, bradycardia, infectious diseases, leptospirosis

1 | INTRODUCTION

Leptospirosis, a significant zoonotic illness caused by *Leptospira* species, is transmitted through direct contact with the pathogen or contaminated water sources.[1] According to the World Health Organization (WHO), leptospirosis incidence varies from 0.01 to 1 case per 100,000 individuals in non-endemic temperate regions from 10 to 100 cases per 100,000 in endemic tropical areas.[2] The bacteria primarily infect a range of animals, particularly rodents, and human infections typically occur through accidental contact with contaminated water or soil carrying the urine of infected animals.[1] Iran is an endemic region for human leptospirosis. A 2020 study, involving a systematic review and meta-analysis, found that the prevalence of human leptospirosis in Iran is 19.71% with the microscopic agglutination test (MAT) and 27.84% with the ELISA test.[3]

The typical incubation period for leptospirosis ranges from 1 to 2 weeks, and it progresses through two distinct clinical forms, including anicteric and icteric forms, with the latter being more severe and exhibiting greater cardiac implications compared to the former. The majority of cases manifest as relatively mild, characterized by abrupt onset of symptoms such as fever, headache, nausea, vomiting, abdominal pain, conjunctival suffusion, and myalgia. Complications of leptospirosis encompass a range of serious conditions including renal failure, hepatitis, thrombocytopenia, pulmonary hemorrhage, acute respiratory distress syndrome, myocarditis, neuroleptospirosis, ocular issues, meningitis, hypotension, and hypokalemic paralysis.[2,4]

As stated in studies, the most common electrocardiographic anomalies observed in leptospirosis are atrial fibrillation or first-degree atrioventricular block, which is followed by atrial flutter, second-degree atrioventricular block, bundle-branch blocks, junctional rhythm, ST-segment deviations either downwards or upwards, T-wave reversal primarily in the anterior or lateral leads, prolonged corrected QT-intervals, premature ventricular contractions, and ventricular tachycardia.[5] Nonetheless, instances of severe bradycardia complicating leptospirosis have been infrequently reported thus far.[5,6]

In this case report study, we describe a patient with leptospirosis who exhibited cardiac symptoms in the form of bradycardia.

2 | CASE PRESENTATION

2.1 | Medical history and examination

A 37-year-old man was admitted with symptoms of light-headedness, weakness, lethargy, general myalgia, low-grade fever, non-productive cough, nausea, and vomiting. These symptoms had onset 3 days prior to admission and had progressively worsened despite initial outpatient treatment proving ineffective.

The patient had no prior medical history or current medication use. He worked as a farmer in a rice field and denied consuming contaminated food or beverages. There was no reported history of substance abuse, unprotected sexual intercourse, recent travel or tattooing.

Upon admission, the patient was conscious with a blood pressure of 100/60, a heart rate of 40 beats/min, respiratory rate was 19/min, oxygen saturation at 95% without supplemental oxygen, and a normal body temperature of 37.2°C. Mild jaundice was observed during the sclera examination. Cardiopulmonary auscultation revealed normal findings, and there were no signs of hepatosplenomegaly or lymphadenopathy. During examination of the extremities, a clean 3 × 2 cm wound was noted on the right leg.

2.2 | Method (differential diagnosis, investigations and treatment)

As a result of the patient's bradycardia (Figure 1), an electrocardiogram was conducted, revealing sinus bradycardia. The patient underwent a cardiology assessment, which indicated an ejection fraction of 55% in the echocardiography examination, with no cardiac abnormalities detected. Recommendations were made to further investigate potential infectious and metabolic etiologies.

The admission test results outlined in Table 1 indicated the presence of anemia, leukocytosis, elevated direct and total bilirubin levels, and abnormal liver function tests in the patient. Additionally, normal troponin and CK-MB levels were observed. Renal and electrolyte tests yielded normal results, and abdominopelvic sonography revealed no abnormalities. Viral markers, including hepatitis C virus (HCV) antibody, hepatitis B surface (HBs) Antigen, hepatitis A virus (HAV) IgM antibody and antibody for hepatitis B core antigen (HBC) IgM, were negative. As a precaution during the COVID-19 pandemic, a PCR test for COVID-19 infection was administered, returning a negative result.

2.3 | Conclusion and results (outcome and follow-up)

Based on the patient's medical history, leg ulcer, occupational exposure in a rice field, and laboratory findings, a tentative diagnosis of leptospirosis was established, prompting the initiation of treatment with ceftriaxone

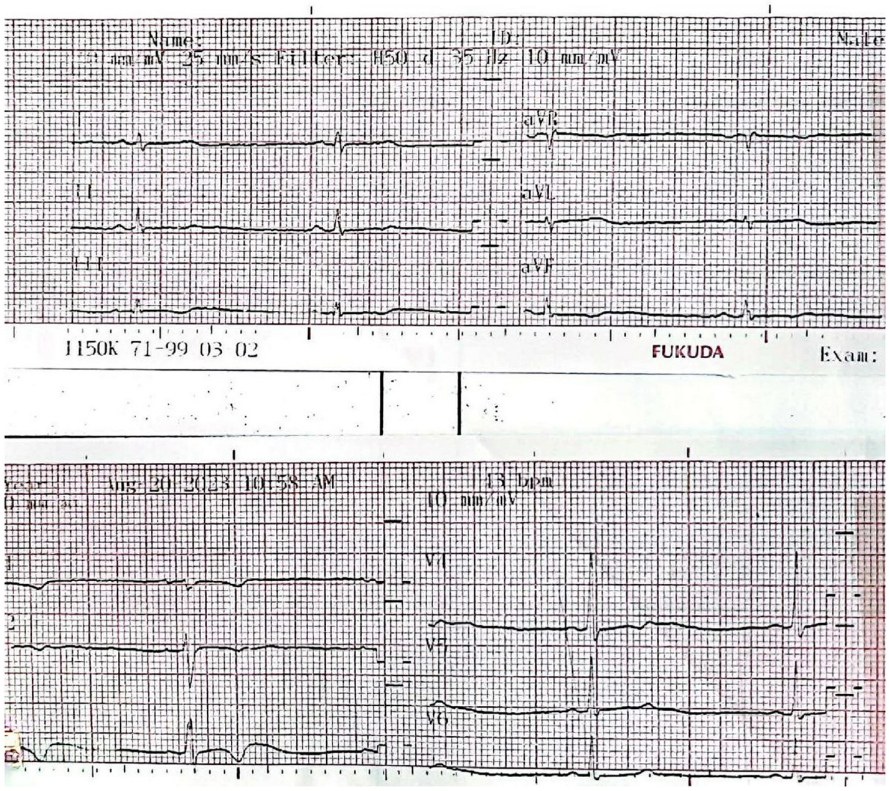

FIGURE 1 Shows an electrocardiogram of the patient. It demonstrates sinus bradycardia with normal QTc. T invert in V1 to V3. Normal PR interval, good R wave progression with no ST segment changes.

and doxycycline. Subsequent serological tests, including leptospirosis Ab IgM and the MAT, were performed and yielded positive results.

After starting standard regime with doxycycline 100 mg twice orally and ceftriaxone 1gr twice intravenous for 7 days, the laboratory results and bradycardia improved and he was discharge a week later with good condition.

3 | DISCUSSION

Leptospirosis represents a significant resurfacing global health challenge, with an approximate 1.03 million new cases reported worldwide.[7] The spirochetes responsible for the disease find their natural reservoirs in both wild and domestic animals, with occupational activities potentially facilitating indirect exposure to the infectious agent. Human transmission occurs through contact with infected urine from carrier mammals, either directly or through contamination of water or soil.[7] In our case report, our patient had new onset ulcer on his leg and he worked as a farmer on rice field, which was believed as a source of leptospirosis for him.

The typical clinical presentation of leptospirosis follows a two-phase pattern, with an initial acute or septicemic phase lasting approximately 1 week, succeeded by the immune phase marked by antibody production. Severe forms of the disease, characterized by jaundice, often indicate a poor prognosis and are termed Weil's disease, denoting severe leptospirosis with liver and kidney dysfunction. However, the acute phase of non-jaundice-causing leptospirosis typically spans from 2 to 9 days and is characterized by a sudden onset of fever caused by bacteria in the blood. Symptoms include abrupt fever, chills, muscle aches, and headaches. Around half of the patients also experience nausea, vomiting, and diarrhea, while 25%–35% may have a nonproductive cough.[8]

Our patient presented with nonspecific symptoms, including weakness, lethargy, nausea, vomiting, myalgia, and fever, leading to an outpatient treatment for influenza. During the examination, notable findings such as scleral icterus, leg ulcer, a history of working in rice fields, and the presence of constitutional symptoms prompted consideration for a diagnosis of acute phase leptospirosis.

Lab findings during the acute phase include neutrophilia, although the overall white blood cell count can be within the normal range, low, or high. Thrombocytopenia and anemia are not as commonly observed. The erythrocyte sedimentation rate (ESR) is typically elevated, and liver enzymes may slightly rise. Elevated levels of creatine kinase may be present in around half of patients. Proteinuria, pyuria, granular casts, and occasionally microscopic hematuria were observed in urine analysis. Acute kidney injury is a rare occurrence during this stage. Our patient had elevated ESR, CRP, liver function tests, leucocytosis, and thrombocytopenia in the initial laboratory evaluation. Cardiac biomarkers were normal. (Table 1).[7,8]

TABLE 1 Initial laboratory findings of the patient.

Variables	Laboratory findings	Normal range
WBC	12.3	$4.5–11 \times 10^9$/L
Hb	11.7	14–17.5 g/dL
Plt	28,000	$150–450 \times 10^9$/L
AST	222	20–60 IU/L
ALT	288	5–40 IU/L
Alkp	479	40–129 IU/L
Bili		
Total	1.5	0.1–1.3 mg/dL
Direct	1	0.1–0.4
Cr	0.7	0.5–1.2
LDH	588	<480
CPK	65	Up to 195
CK-MB	10	Up to 25
Troponin	Negative	0.00–0.08 ng/mL
PT	12	11–14 s
PTT	32	26–31 s
INR	1	1–1.4
ESR	36	Age/2
CRP	+1	N.A.

Abbreviations: Alkp, alkaline phosphatase; ALT, alanine transaminase; AST, aspartate aminotransferase; Bili, Bilirubin; CK-MB, creatine phosphokinase-MB; CPK, creatine phosphokinase; Cr, creatinine; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; INR, the international normalized ratio; LDH, lactate dehydrogenase; N.A, not applicable; Plt, platelet; PT, prothrombin time; PTT, partial thromboplastin time;WBC, white blood cell.

Upon reviewing the patient's current presentation, physical examination, laboratory tests, and positive leptospirosis serological test, we confirmed the diagnosis of acute leptospirosis for him.

The cardiac manifestations observed in cases of leptospirosis infection are diverse, encompassing arrhythmias and abnormalities in electrocardiographic readings, pericarditis, myocarditis, congestive heart failure, aortitis, acute coronary arteritis, and involvement of heart valves.[6] Based on the studies, various causes for cardiac involvement in leptospirosis have been stated. Recent studies propose that systemic complications involve the activation of innate immunity through a Toll-like receptor 2 (TLR2)-dependent pathway. Research in TLR2-deficient mice has demonstrated that TLR2-mediated signaling in the heart is linked to heightened expression of tumor necrosis factor, interleukin-1β, and nitric oxide.[5,9] Interleukin-1 and tumor necrosis factor-α have been shown to induce arrhythmogenic effects in cultured cardiomyocytes, and their excessive presence in the perisinoatrial nodal region has been associated with the attenuation of sinoatrial node control over the heart and potential disruption of normal impulse transmission from the sinoatrial node to other parts of the heart. Moreover, it has been suggested that a glycoprotein component of the leptospiral cell wall may hinder the Na-K ATPase, potentially leading to arrhythmias.[1,5,8,10]

Common electrocardiographic alterations seen in leptospirosis include conduction abnormalities, nonspecific ST-T changes, and atrial arrhythmias.[5] Furthermore, myocarditis and endocardial inflammation consistent with vasculitis can further complicate the cardiac manifestations of the disease.[5] According to the Trivedi et al.'s study which conducted on 25 seropositive patients of leptospirosis revealed cardiovascular complications in 56% of the patients. Electrocardiographic alterations were detected in 52% of the patients, with first-degree AV block being the most prevalent arrhythmia observed in 44% of cases. The presence of cardiac involvement, whether identified through electrocardiographic changes or clinical symptoms, was associated with a poor prognosis.[11] Our patient showed heart complications of leptospirosis in the form of bradycardia. Which, according to the study of Assimakopoulos SF, et al., is uncommonly seen in patients. In this study, they presented a patient diagnosed with leptospirosis who developed sinus bradyarrhythmia during hospitalization.[2,6] In the study conducted by Mathew et al., encompassing 105 leptospirosis patients, various acute ECG changes were observed. These were include sinus tachycardia (34.2%), sinus bradycardia (16.2%), ST-segment elevation (13.2%), atrial fibrillation (AF) (6.31%), ST-segment depression (5.66%), first-degree atrioventricular (A-V) block (4.76%), left bundle branch block (LBBB) (4.76%), incomplete right bundle branch block (RBBB) (4.76%), atrial and ventricular ectopic beats (2.83%), T-wave inversions (2.83%), junctional rhythm (1.90%), low voltage QRS (1.90%), and abnormal QRS-T angle (1.90%).[7]

Standard therapy using ceftriaxone and doxycycline was administered to the patient. Thankfully, after 48 h, the symptoms improved, and bradycardia resolved. Following a progressive recovery, the patient was discharged in a week in good health with no complications.

We presented a patient with nonspecific symptoms initially treated as an outpatient for suspected influenza without improvement, which manifested light-headedness and bradycardia at the time of admission. Notably, our study's robustness lies in the timely identification of leptospirosis, enabling prompt administration of appropriate treatment, resulting in the patient's discharge without complications and in good overall health. However, a key drawback of our investigation was the prolonged duration required for diagnostic tests, causing a delay in confirming the disease diagnosis.

4 | CONCLUSION

According to the nature and progression of the illness, leptospirosis can present a diverse array of non-specific to severe and life-threatening symptoms. Cardiac complications, such as cardiac conduction abnormalities, may manifest in various forms within this condition. Diligent consideration of medical history, clinical assessment, and timely intervention can help mitigate the severity and progression of detrimental outcomes in affected individuals.

AUTHOR CONTRIBUTIONS

Narges Lashkarbolouk: Conceptualization; project administration; writing – original draft; writing – review and editing. **Mahdi Mazandarani:** Conceptualization; investigation; methodology; project administration; supervision; writing – original draft; writing – review and editing.

ACKNOWLEDGMENTS

Not applicable.

FUNDING INFORMATION

The authors declare that no funds, grants, or other supports were received during the preparation of this manuscript.

CONFLICT OF INTEREST STATEMENT

The authors declare that they have no competing interests.

DATA AVAILABILITY STATEMENT

The datasets used during the current study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

This case report was performed in line with principles of the Declaration of Helsinki.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

ORCID

Narges Lashkarbolouk https://orcid.org/0000-0001-9443-3453
Mahdi Mazandarani https://orcid.org/0000-0001-8972-6171

REFERENCES

1. Jesrani G, Gupta S, Gaba S, Gupta M. Electrocardiographic abnormalities in prevalent infections in tropical regions: a scoping review. *J Acute Dis*. 2022;11(2):45-51.
2. Warrier R, Singh SK, Singh S, et al. Junctional rhythm: a rare sign in leptospirosis. *Indian J Crit Care Med*. 2018;22(12):889-891.
3. Khalili M, Sakhaee E, Amiri FB, Safat AA, Afshar D, Esmaeili S. Serological evidence of leptospirosis in Iran; a systematic review and meta-analysis. *Microb Pathog*. 2020;138:103833.
4. Chin VK, Basir R, Nordin SA, Abdullah M, Sekawi Z. Pathology and host immune evasion during human leptospirosis: a review. *Int Microbiol*. 2020;23:127-136.
5. Swarath S, Maharaj N, Seecheran R, et al. Leptospirosis-induced myocarditis and arrhythmias. *J Investig Med High Impact Case Rep*. 2023;11:1-5.
6. Assimakopoulos SF, Michalopoulou S, Papakonstantinou C, Lekkou A, Syrokosta I, Gogos C. A case of severe sinus bradycardia complicating anicteric leptospirosis. *Am J Med Sci*. 2007;333(6):381-383.
7. Mathew A, Shanks M, Punnoose E, et al. Cardiac involvement in critically ill patients with leptospirosis: a prospective study using myocardial deformation imaging. *Eur Heart J Acute Cardiovasc Care*. 2020;9(8):975-983.
8. Gomes AP, Gazola DM, Braga LM, da Motta OJ, Gazineo JL. Leptospirosis: an update-part 1 of 2: etiology, ecology, epidemiology, prophylaxis and Contro Leptospirose: Uma actualização-parte 1 De 2: Etiologia, Ecologia, Epidemiologia, Profilaxia e Controlo. *Braz J Health Rev*. 2022;5(3):11361-11372.
9. Vernel-Pauillac F, Werts C. Recent findings related to immune responses against leptospirosis and novel strategies to prevent infection. *Microbes Infect*. 2018;20(9–10):578-588.
10. Chin VK, Lee TY, Lim WF, et al. Leptospirosis in human: biomarkers in host immune responses. *Microbiol Res*. 2018;207:108-115.
11. Trivedi SV, Bhattacharya A, Amichandwala K, Jakkamsetti V. Evaluation of cardiovascular status in severe leptospirosis. *J Assoc Physicians India*. 2003;51:951-954.

How to cite this article: Lashkarbolouk N, Mazandarani M. Leptospirosis in a patient with cardiac manifestation: A case report study and literature review. *Clin Case Rep*. 2024;12:e8883. doi:10.1002/ccr3.8883