Case Report

# Reversible pancytopenia: An unusual presentation of leptospirosis


*Abstract*

Leptospirosis, a zoonotic disease, may present with cardiovascular, gastrointestinal, neurological, hematological, and ocular manifestations apart from the classical presentation of renal failure and jaundice. In this report, we present a case of leptospirosis with pancytopenia as the prevailing manifestation, which reversed completely with intravenous cephalosporins. In conclusion, this case study suggests that Leptospira infection should be included in the differential diagnosis of febrile pancytopenia, even in the absence of classical signs of severe disease such as jaundice, meningitis, renal failure, and pulmonary infiltrates.



**Key words:** Cephalosporins, leptospirosis, pancytopenia



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## INTRODUCTION

Leptospirosis is a zoonotic disease caused by pathogenic spirochetes of the genus Leptospira. In 1907, Stimson described the microorganism in the renal tubules of a patient who died of the so-called yellow fever. The spirochete was first isolated in Japan by Inada and co-workers in 1915, nearly 30 years after Weil described the clinical disease in 1886. The relatively recent discovery of leptospirosis belies its long history, which was probably known much earlier in China and Japan by names such as "rice harvest jaundice" and "autumn fever".[1]

Leptospirosis classically manifests as a biphasic illness. The first phase is characterized by high fever and coincides with leptospiremia. This is followed by a brief period when the patient is afebrile. Fever returns heralding the second phase of illness that may be accompanied by jaundice and renal failure. During this period, leptospires are not found in the blood but are excreted in the urine.[2] Unfortunately, classical presentation is not synonymous with the most common presentation. Leptospirosis has protean manifestations and rare and unusual presentations should be kept in mind in relevant epidemiological scenario. The commonly identified complications of acute renal failure and jaundice have been widely described and reviewed extensively in literature. Severe cases of leptospirosis often present not only with renal failure and jaundice but also with other organ involvement including myocarditis, aseptic meningitis, and hemorrhagic diathesis.[3] Apart from the classical manifestations, leptospirosis may rarely occur with erythroid hypoplasia and/or pancytopenia. In this study, we report a case of leptospirosis with pancytopenia as the prevailing manifestation.

## CASE REPORT

A 60-year-old man with no significant medical history presented to the *tertiary care centre in* Haryana (North India) in mid-September with a history of fever, myalgias, and severe bilateral calf pain that began a few days prior. He had a 30 pack-year history of cigarette smoking, denied recent travel, did not own pets, and was engaged in farming and animal husbandry.

Vital signs in the emergency department were notable for a temperature of 39.3 degree centigrade, pulse of 110/min and blood pressure of 150/60 mmHg. The patient was alert and oriented. Ocular examination was notable for scleral icterus. The skin appeared jaundiced; the lungs revealed unilateral crepitations in the right lower zone; the abdomen was tender with mild hepatomegaly; and bilateral lower extremity tenderness was noted.

Initial laboratory study results were notable for a hemoglobin of 11.8 g%, white blood cell count of 3.5 × $10^3$ cells/cumm, absolute platelet count of 70,000/cumm, total bilirubin of 4.3 mg%, direct bilirubin of 2.6 mg%, alkaline phosphatase (ALP) of 332 IU, aspartate aminotransferase (AST) of 242 IU, alanine aminotransferase (ALT) of 246 IU, and serum creatinine of 1.2 mg%. Urine analysis showed moderate hematuria but no proteinuria. The following day, the patient's hyperbilirubinemia, anemia, leucopenia, and thrombocytopenia worsened. Serologic test results for acute hepatitis A, B, and C and HIV infections were negative. The NS1Ag (for Dengue virus) and Dengue serology were reported negative. Blood cultures taken before initiating antibiotics were reported to be sterile.

On the third day, the hematological parameters and liver function tests continued to deteriorate, but the renal parameters remained within normal limits. Serum leptospira antibodies and rickettsia serology were sent, and the patient was started on intravenous broad spectrum antibiotics. On the fourth day, hemoglobin was 8.1 mg%, the leucocyte count was 1.1 × $10^3$ cells/cumm, the absolute platelet count was 30,000/cumm, serum bilirubin was 5.2 mg%, serum ALP was 597 IU, and serum AST/ALT was 412/215 IU. Enzyme-linked immunosorbent assay (*ELISA*) for IgM leptospira antibody titers were reported to be more than 1:100 and the rickettsia serology was negative. As a result urine cultures for Leptospira were sent. After initiating intravenous cephalosporins, the hematological parameters and liver function tests returned to normal in a few days. Subsequently, the urine cultures were returned positive for Leptospira.

## DISCUSSION

Leptospirosis is a zoonosis of worldwide distribution. The organism infects a variety of animals, especially rodents and animals associated with farming. Humans represent only incidental infection usually through work-related contact through skin or mucous membranes, typically after exposure to water or soil contaminated with urine from an infected animal or via drinking of or bathing in contaminated water. The main occupational groups at risk are farm workers, field agricultural workers, plumbers, sewer workers, sanitation workers, and military troops.

Leptospirosis classically presents as a biphasic illness. The first phase of the disease is commonly referred to as the septicemic phase. It is characterized by fever, headache, myalgia, conjunctival congestion, and a host of non-specific features that may include mild cough, lymphadenopathy, rash, anorexia, nausea, and vomiting. This phase is followed by a brief afebrile period of variable duration that, in turn, is followed by the immune phase of illness. The common organs involved during this phase are the liver and kidneys. Both organ derangements are reversible. The severe form of leptospirosis, also known as Weil's disease, is characterized by a fulminant course with rapid onset of hepatic and renal failure and high mortality.[2] In a retrospective report of 34 patients with leptospirosis, the common clinical features included fever (100%), headache (75%), myalgia (55%), arthralgia (45%), and vomiting (39%).[4] Among the unusual manifestations of leptospirosis are hemorrhagic pneumonitis,[5] aseptic meningitis, myelopathy, and cerebellar dysfunction,[6] pancreatitis,[7] panuveitis,[8] myocarditis, pericarditis, arrhythmias,[9] rhabdomyolysis,[10] reactive arthritis,[11] male hypogonadism,[12] and pancytopenia.[13] Although thrombocytopenia has been extensively reported, along with renal and hepatic involvement, pancytopenia secondary to leptospirosis has been scarcely mentioned in literature.

The pathogenesis of pancytopenia in leptospirosis has been poorly understood. Some authors postulated that this could possibly be attributed to disseminated intravascular coagulation (DIC), a toxin, or cytotoxin-mediated mechanism as a direct complication of leptospiral vasculitis or as a general phenomenon of septicemia.[14] Whether either of these mechanisms is operating alone or in combination is uncertain and merits extensive investigation.

Pancytopenia was associated with a higher incidence of complications. Although associated with acute renal failure and jaundice, the more fatal complications of pulmonary hemorrhage, myocarditis, and acute respiratory distress syndrome (ARDS) were seen in the pancytopenic patients. It also follows that mortality rate is higher in the pancytopenic patients because of the increased frequency of these fatal complications. From these findings, it has been surmised that the presence of pancytopenia could be an indicator of the severity of the disease. It is important for clinicians to be aware and recognize the various ways in which leptospirosis can present. Although classically occurring as an acute febrile illness with renal failure and jaundice, the other less common manifestations may predominate. The changing pattern of the virulence of the disease could have been better explained by identifying the serovars involved. It has been speculated that a new strain of leptospires may be responsible for the more severe presentation in some patients.[13] Our poor yield in culture studies for Leptospira, and the unavailability of specific antigens for the different serovars makes this difficult.

The possibility of a novel infectious agent mimicking the presentation of severe leptospirosis should also be entertained. Hantavirus, which is the etiologic agent for the hemorrhagic fever with renal syndrome, and hantavirus pulmonary syndrome may be difficult to differentiate from leptospirosis in some instances. The reservoir of hantavirus is likewise similar to leptospirosis — the urban and rural rats. However, the possibility of hantavirus as causing the infection or causing a co-infection with leptospirosis could not be established at this point.[15] In an endemic area, leptospirosis is often confused with dengue fever due to the similarities of clinical features. LaRocque and colleagues summarized the data regarding clinical presentations of the two illnesses comparing 938 patients of dengue fever with 63 patients of leptospirosis. Presence of rash, pruritus, and a positive tourniquet test was significantly associated with dengue fever.[16] Karande and colleagues in their report of a concurrent epidemic

of leptospirosis and dengue fever in Mumbai noted that clinical features such as conjunctival suffusion, hemorrhage, abdominal pain, hepatosplenomegaly, and edema were significantly associated with leptospirosis, while arthralgia was significantly associated with dengue fever.[17]

The diagnosis of leptospirosis requires a high degree of clinical suspicion because the numerous manifestations of the disease can mimic other tropical infections or other nonspecific febrile illnesses, as well as noninfectious diseases such as small vessel vasculitides, systemic lupus erythematosus, or even malignancies. The initial diagnosis of leptospirosis remains a clinical one, a presumed analysis in the appropriate epidemiologic and clinical context. Routine laboratory testing is nondiagnostic but may show elevated erythrocyte sedimentation rate, peripheral leukocytosis, variable degrees of cytopenias, mildly increased aminotransferases and increased serum bilirubin and ALP. Isolation of the organism by culture of clinical specimens (blood, CSF, urine) during the first seven to 10 days of the illness is considered the gold standard of diagnosis. However, this method is difficult, requires longer than 16 weeks because initial growth may be slow, and has a low sensitivity and specificity. The majority of leptospirosis cases are diagnosed by serologic testing of which MAT is most common.

The vast majority of infections with leptospira are self-limiting, and it remains controversial if antimicrobials produce benefit in cases of mild leptospirosis without end-organ damage. The current choices of treatment for mild leptospirosis include oral doxycycline and amoxicillin. Parenteral high-dose penicillin G has long been considered the treatment of choice of fulminant leptospirosis. At present, the broad-spectrum third generation cephalosporins, cefotaxime, and ceftriaxone are also considered as acceptable agents for patients with severe leptospirosis.

The use of steroids in patients with leptospirosis has not been well established.[13] Several case reports have described the beneficial effects of glucocorticoids in severe leptospirosis with pulmonary hemorrhage, thrombocytopenia, and renal failure. In the present case, pancytopenia reversed completely with the use of intravenous cephalosporins. In conclusion, leptospirosis should be considered as a differential in febrile pancytopenia even in the absence of the usual manifestations of significant renal derangement, meningitis, and pulmonary involvement.

## REFERENCES


1. Terpstra W. Human Leptospirosis: Guidance for Diagnosis, Surveillance, and Control. Geneva: World Health Organization; 2003.
2. Jaureguiberry S, Roussel M, Brinchault-Rabin G, Gacouin A, Le Meur A, Arvieux C, *et al*. Clinical presentation of leptospirosis: A retrospective study of 34 patients admitted to a single institution in metropolitan France. Clin Microbiol Infect 2005;11:391-4.
3. Tantitanawat S, Tanjatham S. Prognostic factors associated with severe leptospirosis. J Med Assoc Thai 2003;86:925-31.
4. Bharadwaj R, Bal AM, Joshi SA, Kagal A, Pol SS, Garad G, *et al*. An urban outbreak of leptospirosis in Mumbai, India. Jpn J Infect Dis 2002;55: 194-6.
5. Yersin C, Bovet P, Merien F, Clement J, Laille M, Van Ranst M, *et al*. Pulmonary haemorrhage as a predominant cause of death in leptospirosis in Seychelles. Trans R Soc Trop Med Hyg 2000;94:71-6.
6. Panicker JN, Mammachan R, Jayakumar RV. Primary neuroleptospirosis. Postgrad Med J 2001;77:589-90.
7. Pai ND, Adhikari P. Painless pancreatitis: A rare manifestation of leptospirosis. J Assoc Physicians India 2002;50:1318-9.
8. Rathinam SR, Rathnam S, Selvaraj S, Dean D, Nozik RA, Namperumalsamy P. Uveitis associated with an epidemic outbreak of leptospirosis. Am J Ophthalmol 1997;124:71-9.
9. Trivedi SV, Bhattacharya A, Amichandwala K, Jakkamsetti V. Evaluation of cardiovascular status in severe leptospirosis. J Assoc Physicians India 2003;51:951-3.
10. Coursin DB, Updike SJ, Maki DG. Massive rhabdomyolysis and multiple organ dysfunction syndrome caused by leptospirosis. Intensive Care Med 2000;26:808-12.
11. Pappas G, Akritidis N, Christou L, Mastora M, Tsianos E. Unusual causes of reactive arthritis: Leptospira and Coxiella burnetii. Clin Rheumatol 2003;22:343-6.
12. Panidis D, Rousso D, Skiadopoulos S, Vavilis D, Kalogeropoulos A. Hypothalamic-pituitary deficiency after Weil's syndrome: A case report. Fertil Steril 1994;62:1077-9.
13. Bishara J, Amitay E, Barnea A, Yitzhaki S, Pitlik S. Epidemiological and clinical features of leptospirosis in Israel. Eur J Clin Microbiol Infect Dis 2002;21:50-2.
14. Kahn JB. A case of Weil's disease requiring steroid therapy for thrombocytopenia and bleeding. Am J Trop Med Hyg 1982;31:1213-5.
15. Markotic A, Kuzman I, Babic K, Gagro A, Nichol S, Ksiazek TG, *et al*. Double trouble: Hemorrhagic fever with renal syndrome and leptospirosis. Scand J Infect Dis 2002;34:221-4.
16. LaRocque RC, Breiman RF, Ari MD, Morey RE, Janan FA, Hayes JM, *et al* . Leptospirosis during dengue outbreak, Bangladesh. Emerg Infect Dis 2005;11:766-9.
17. Karande S, Gandhi D, Kulkarni M, Bharadwaj R, Pol S, Thakare J, *et al*. Concurrent Outbreak of Leptospirosis and Dengue in Mumbai, India, 2002. J Trop Pediatr 2005;51:174-81.


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