

## Case Report

# Coinfection of Leptospirosis with Scrub Typhus: A Case Report

Rayeed Anan Surontee<sup>1</sup>, Mohammad Mahfuzul Hoque<sup>2</sup>, Tahsina Tasneem<sup>3</sup>, Md. Fariduzzaman<sup>4</sup>,  
Md. Mehedi Hasan<sup>5</sup>, Md. Shafiqul Bari<sup>6</sup>

### Abstract:

*Leptospirosis and scrub typhus are common zoonotic illnesses in tropical countries. Leptospira, a spirochaete, can cause leptospirosis when a patient comes in contact with contaminated water. Following a period of bacteraemic illness, leptospirosis may progress to a more severe form. Weil's disease is a severe form of leptospirosis characterised by jaundice, haemorrhage and acute kidney injury. Scrub typhus, a rickettsial disease, common in South-East Asia is caused by Orientia tsutsugamushi occurs due to bite of Trombicula mite. An eschar forms at the site of the bite. Here we present a case of a 60-year-old gentleman, hailing from Savar who was diagnosed as a case of coinfection of scrub typhus and leptospirosis. Patient presented with an eschar, high grade fever and features of Weil's disease. He didn't initially respond to Ceftriaxone and then Doxycycline was added after which he became afebrile.*

**Keywords:** *Leptospira, Weil's disease, eschar, Rickettsia*

**DOI:** <https://doi.org/10.3329/jom.v25i2.74660>

**Copyright:** © 2024 Surontee RA. This is an open access article published under the Creative Commons Attribution-Non Commercial-No Derivatives 4.0 International License, which permits use, distribution and reproduction in any medium, provided the original work is properly cited, is not changed in any way and it is not used for commercial purposes.

**Received:** 10.06.2024;

**Accepted:** 16.06.2024.

### Introduction:

Leptospirosis is a common zoonotic disease which occurs worldwide. However, it is more common in tropical countries, especially during monsoon season. It is caused by the spirochaete, *Leptospira* which can penetrate intact skin or mucous membranes when water contaminated with urine of an infected host come in contact with humans.<sup>1</sup>

Following an incubation period of 2 to 20 days, there is an acute leptospiremic phase which is then followed by an immune leptospiruric phase.<sup>2</sup> Bacteraemic leptospirosis can produce influenza-like illness with high-grade fever, myalgia, intense headache, photophobia, diarrhoea, vomiting and

conjunctival congestion. The patient spontaneously improves after about 1 week or merges into aseptic meningitis/neuroleptospirosis, Weil's disease characterised by fever, haemorrhage, jaundice and acute kidney injury or pulmonary syndrome which includes pulmonary haemorrhage and acute respiratory distress syndrome.<sup>3</sup>

Rickettsia are intracellular Gram-negative organisms which are responsible for two types of fever: typhus and spotted fevers. Scrub typhus caused by *Orientia tsutsugamushi* is common in South-East Asia and is transmitted by *Trombicula* mites. An eschar, which is a black, necrotic crusted sore, is common in rickettsial fevers and occurs at the site of insect bite. On the 5th – 7<sup>th</sup> day, patients may develop a maculopapular rash. Other symptoms include fever, headache, malaise, myalgia, cough and gastrointestinal symptoms.<sup>2</sup> The disease is usually self-limiting but may progress to more severe forms.<sup>1</sup> These include pneumonitis, cardiac failure, renal failure, delirium and deafness.<sup>2</sup>

According to the Centers for Disease Control and Prevention (CDC), around 1 million cases of leptospirosis occur globally with a mortality rate of 60,000/annum.<sup>3</sup> More than 1 million cases of scrub typhus occur annually in Asia which is more common among farmers in endemic regions.<sup>4</sup>

In a study done in Bangladesh, 2 – 8% of patients accounted for leptospirosis in febrile illness of unknown origin presenting to outpatient departments.<sup>5</sup> Another study done in 2019 in Bangladesh showed leptospirosis in 1.6% and

1. Honorary Medical Officer, Department of Medicine, Dhaka Medical College Hospital
2. Assistant Professor, Department of Medicine, Dhaka Medical College Hospital
3. Indoor Medical Officer, Department of Medicine, Dhaka Medical College Hospital
4. Indoor Medical Officer, Department of Medicine, Dhaka Medical College Hospital
5. Honorary Medical Officer, Department of Medicine, Dhaka Medical College Hospital
6. Professor, Department of Medicine, Dhaka Medical College Hospital

**Corresponding author:** Dr. Rayeed Anan Surontee, Honorary Medical Officer, Dhaka Medical College Hospital, Mobile: 01759355096, Email: surontee\_28@live.com

rickettsiosis in 8.8% of patients with febrile illness. *Orientia tsutsugamushi*, which is responsible for scrub typhus, is the most common among rickettsiosis.<sup>6</sup>

Leptospirosis is usually confirmed by microscopic agglutination test (MAT) which can become positive by the end of the first week. IgM ELISA is easier to perform but has less sensitivity. Blood cultures are usually positive if taken before day 10 of illness. Detection of leptospiral DNA by polymerase chain reaction (PCR) is possible in blood in early symptomatic disease and in urine from day 8 of illness.<sup>2</sup>

In mild cases of leptospirosis, oral treatment with tetracycline, doxycycline, ampicillin, or amoxicillin is usually given. For severe cases of leptospirosis, intravenous administration of penicillin G, amoxicillin, ampicillin, or erythromycin is recommended.<sup>1</sup>

Diagnosis of Rickettsial infections is usually clinical, but serological tests or polymerase chain reactions are confirmatory. Weil-Felix is a nonspecific agglutination test. It tests for three different antigens; OX 2, OX 19 and OX K. Scrub typhus is positive against OX K.<sup>7</sup> Treatment is with tetracycline, doxycycline or chloramphenicol.<sup>2</sup>

#### Case History:

A 60-year-old, normotensive, non-diabetic gentleman, hailing from Noakhali presented with high-grade fever associated with chills and rigor, jaundice, anorexia and vomiting for 18 days. He also developed high coloured urine and pale stool for the same duration. 5 days before admission, he developed bipedal oedema. He had a history of showering in a lake every day.

On examination, the patient was icteric, had subconjunctival haemorrhage, and had bipedal oedema. His pulse was 88 beats per minute, which was normal in volume. His blood pressure was 110/70 mmHg, temperature was 40°C, and spO<sub>2</sub> was 97% with room air. Examination of the chest revealed an eschar present on the left side of his chest. On query, the patient revealed that the eschar had been present on his chest for 1 month. Examination of other systems revealed no abnormalities.

Investigation revealed anaemia with raised erythrocyte sedimentation rate, normal white blood cell counts with a neutrophil predominance and a normal platelet count. Serum creatinine was mildly raised, and serum electrolytes were normal. Liver function tests revealed hyperbilirubinaemia, mildly raised alanine aminotransferase with a markedly raised alkaline phosphatase. The patient had hypoalbuminemia, but prothrombin time was normal. Rapid test for IgM antibodies to *Leptospira* was found positive, and Weil-Felix test revealed OXK increased fourfold to a titre of 1:320.

On admission, the patient was started on injectable Ceftriaxone 2 gm. However, the fever did not subside. Therefore, he was started on Doxycycline and gradually became afebrile. After improvement, he was discharged on the 9<sup>th</sup> day after admission.

**Table 1.** Table of investigations

Investigation	Findings
Complete Blood Count:	
Haemoglobin	10.7 g/dl
Erythrocyte Sedimentation Rate	45 mm/1 <sup>st</sup> hour
Whole Blood Count	10.9x10 <sup>9</sup> /L
Neutrophil	63%
Lymphocyte	
Platelets	175x10 <sup>9</sup> /L
Serum creatinine	1.45 mg/dl
Serum bilirubin	8.18 mg/dl
Alanine aminotransferase	190 U/L
Alkaline phosphatase	595 U/L
Serum albumin	1.5 g/L
Prothrombin time	15.1 seconds
HbsAg	Negative
IgM antibodies to <i>Leptospira</i>	Positive
Weil Felix test	
OXK	1:320
OX19	<80
OX2	<80



**Figure 1:** Picture showing an eschar on the chest

### Discussion:

In this study, we present a 60-year-old gentleman from Noakhali who presented with a coinfection of leptospirosis and scrub typhus. Although cases of coinfection in Bangladesh are rare, a significant number of cases of coinfection have been found in South-East Asia.<sup>8</sup> Even though leptospirosis occurs worldwide, it is more common in tropical climates, especially during monsoon season when the patient comes in contact with contaminated water. Scrub typhus, caused by *Orientia tsutsugamushi*, occurs due to bites by *Trombicula* mite. This is also more common during monsoon season.<sup>2</sup> Our patient was admitted in November with a history of high-grade fever, jaundice and vomiting for 18 days.

*Leptospira* can penetrate intact skin and mucous membrane; however, human infection occurs easily in areas of cuts and abrasion.<sup>2</sup> The eschar at the site of a mite bite facilitates infection by *Leptospira*.<sup>9</sup> Our patient presented with an eschar one month before his symptoms started.

Bacteraemic phase of leptospirosis and scrub typhus present with initial symptoms of high-grade fever associated with chills and rigour, headache, malaise, weakness, myalgia and gastrointestinal symptoms. Conjunctival suffusion is the only sign present in bacteraemic leptospirosis, which may also be present in scrub typhus.<sup>2</sup> However, eschar occurs in scrub typhus and is not a sign of leptospirosis.<sup>10</sup> This occurs due to an immunological reaction at the site of inoculation of the organism, which causes vasculitis.<sup>2</sup> Around 40% of patients of scrub typhus develop a maculopapular rash around 5<sup>th</sup> – 7<sup>th</sup> day of infection.<sup>1</sup>

At the end of 1<sup>st</sup> week, 10% of patients with bacteraemic leptospirosis may progress into one of the more severe forms of leptospirosis. This includes neuroleptospirosis, Weil's disease and pulmonary syndrome. Weil's disease is characterized by haemorrhage jaundice and acute kidney injury.<sup>2</sup> Following high grade fever, our patient developed jaundice and bipedal oedema. Scrub typhus may progress to pneumonitis, cardiac failure and renal failure if left untreated.

Laboratory investigations for leptospirosis reveal neutrophilic leucocytosis, raised erythrocyte sedimentation rate and mild thrombocytopenia.<sup>2</sup> Liver function tests show raised bilirubin, markedly raised alkaline phosphatase with only mildly raised aminotransferase. This maybe due to centrilobular necrosis of hepatocytes which is followed by disruption of hepatocyte junction. Leptospirosis doesn't cause severe hepatocellular necrosis.<sup>1</sup> Therefore, jaundice in leptospirosis maybe obstructive in nature as presented in our patient.

IgM antibodies are specific but have moderate sensitivity.<sup>2</sup> However, confirmatory investigation is microscopic agglutination test (MAT) or isolation of organism from the patient.<sup>1</sup> Our patient had a positive IgM antibody against *Leptospira*.

Diagnosis of Rickettsial infections is usually clinical, but serological tests or polymerase chain reaction are confirmatory. Weil-Felix is a nonspecific agglutination test. It tests for three different antigens; OX 2, OX 19 and OX K. A fourfold rise of titre of OX K is positive for scrub typhus.<sup>7</sup> Our patient had a titre of 1:320 for OX K antigen.

Leptospirosis and scrub typhus are both common in tropical and subtropical region with rodents as reservoir, common during monsoon and in areas with poor sanitation. However, coinfection with leptospirosis is not common. [8] In a study done in India, 25% of patients with leptospirosis were coinfecting with scrub typhus.<sup>10</sup>

In severe cases of leptospirosis, intravenous administration of penicillin G, amoxicillin, ampicillin, or erythromycin is recommended. Studies demonstrated equal efficacy between intravenous ceftriaxone and intravenous penicillin G for the treatment of severe leptospirosis.<sup>11</sup> Treatment of scrub typhus is with tetracycline, doxycycline or chloramphenicol.<sup>2</sup> Rickettsial infection doesn't respond to treatment with ceftriaxone or penicillin.<sup>1</sup> Therefore, despite starting treatment with Ceftriaxone, our patient didn't initially respond. However, he became afebrile after adding Doxycycline.

Leptospirosis and scrub typhus are significant causes of acute febrile illness in tropical climates, especially Southeast Asia. Both diseases have similar epidemiological patterns. If left untreated, the case fatality rate of leptospirosis is 7.9%, and that of scrub typhus is 7%.<sup>1</sup> Therefore, they must be diagnosed early and treated.

### References:

1. Kasper, Dennis L, Fauci, Anthony S. *Harrison's Infectious Diseases*. 2nd ed., New York, Mcgraw-Hill Education, Inc., 2013, pp.660–4.
2. Penman, Ian D, Ralston, Stuart H., Strachan, Mark W. J., Hobson, Richard P. *Davidson's Principles and Practice of Medicine*. 24th ed., Edinburgh, Elsevier Limited, 2022, pp. 305–6.
3. Centers for Disease Control and Prevention (U.S.). "Leptospirosis Fact Sheet for Clinicians." *Stacks.cdc.gov*, 2018, [stacks.cdc.gov/view/cdc/52537](https://stacks.cdc.gov/view/cdc/52537).
4. Nicholson, William, Christopher Paddock. "Rickettsial Diseases| CDC Yellow Book 2024." *wwwnc.cdc.gov*, 2024, [wwwnc.cdc.gov/travel/yellowbook/2024/infectionsdiseases/](https://wwwnc.cdc.gov/travel/yellowbook/2024/infectionsdiseases/)

- ricketts al-diseases#:~:text=More%20people%20 worldwide %20are%20at. Accessed 6 May 2024.
5. Kendall, Emily A., Galloway, Renee, Breiman, Robert F., Bui, Duy M., Brooks, W. Abdullah, Goswami, Doli, et al., "Leptospirosis as a Cause of Fever in Urban Bangladesh." *The American Journal of Tropical Medicine and Hygiene*, vol. 82, no. 6, 1 June 2010, pp. 1127–30, [https://doi.org/10.4269/ajtmh.2010.09\\_0574](https://doi.org/10.4269/ajtmh.2010.09_0574). Accessed 24 Nov. 2020.
  6. Das, Pritimoy, Rahman, M. Ziaur, Banu, Sayera, Rahman, Mahmudur, Chisti, Mohammad Jobayer, Chowdhury, Fahmida et al. "Acute Febrile Illness among Outpatients Seeking Health Care in Bangladeshi Hospitals prior to the COVID-19 Pandemic." *PLOS ONE*, vol. 17, no. 9, 1 Sept. 2022, <https://doi.org/10.1371/journal.pone.0273902>.
  7. Felix A. Technique and Interpretation of the Weil-Felix Test in Typhus Fever. *Transactions of the Royal Society of Tropical Medicine and Hygiene*. 1944 Mar;37(5):321–41.
  8. Labib Imran Faruque, Rashid Uz Zaman, Gurley ES, Massung RF, Alamgir M, Galloway RL, et al. Prevalence and clinical presentation of Rickettsia, Coxiella, Leptospira, Bartonella and chikungunya virus infections among hospital-based febrile patients from December 2008 to November 2009 in Bangladesh. *BMC Infectious Diseases*. 2017 Feb 13;17(1).
  9. Arora, Tarun, Malik, Yogender Kumar, Kala, Vikram, Singh, Navtej, Panjeta, Prerna. "Leptospira and Scrub Typhus Co-Infection: An Unusual Presentation with Delirium." *International Multispecialty Journal of Health*, vol. 5, no. 1, Jan. 2019, pp. 14–16, <https://zenodo.org/doi/10.5281/zenodo.2553953>.
  10. Biswajyoti Borkakoty, Aniruddha Jakharia, Biswas D, Jagadish Mahanta. Co-infection of scrub typhus and leptospirosis in patients with pyrexia of unknown origin in Longding district of Arunachal Pradesh in 2013. *Indian journal of medical microbiology*. 2016 Jan 1;34(1):88–91.
  11. Panaphut, T., Domrongkitchaiporn, S., Vibhagool, A., Thinkamrop, B., Susaengrat, W. "Ceftriaxone Compared with Sodium Penicillin G for Treatment of Severe Leptospirosis." *Clinical Infectious Diseases*, vol. 36, no. 12, 15 June 2003, pp. 1507–13, <https://doi.org/10.1086/375226>. Accessed 5 June 2020.