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Case Report

A Leptospirosis Case Presenting with Thrombotic Thrombocytopenic Purpura

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ABSTRACT

Background: Leptospirosis is a zoonotic disease caused by spirochetes of the genus Leptospira. While the majority of leptospirosis cases occur in the tropics, some cases are also observed in temperate regions of developing countries. The disease has various clinical presentations ranging from a mild influenza-like form to a severe potentially fatal illness accompanied by multi-organ failure. However, atypical presentations of leptospirosis have occasionally been described. Here, a case of leptospirosis presenting as thrombotic thrombocytopenic purpura (TTP) is reported.

Case Report: A 58-years-old male presented with fever, oliguria, darkening of urine, and visual hallucinations. Laboratory investigations revealed anaemia, severe thrombocytopaenia, elevated total bilirubin with indirect predominance, high lactate dehydrogenase, and increased urea (293 mg/dL) and creatinine (7.6 mg/dL) levels. He was diagnosed with TTP. Patient was thought leptospirosis due to atypical clinical manifestations. Leptospirosis was confirmed by strongly positive Microscopic Agglutination Test. Patient recovered completely with antibiotics and plasmapheresis.

Conclusion: Leptospirosis may be accompanied by thrombotic thrombocytopenic purpura in particular subtropic regions.

Key Words: Leptospirosis, Weil's disease, thrombotic thrombocytopenic purpura

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Introduction

Leptospirosis is a zoonotic disease caused by spirochetes of the genus *Leptospira*. The genus *Leptospira* consists of two species, *L. Biflexia* and *L. interrogans,* which can be grown in vitro from clinical specimens including blood, urine, and cerebrospinal fluid (1).

Although the disease can sporadically be observed in temperate regions, it is more frequent in tropical regions. It can be encountered both endemically and epidemically in developing countries, as outbreaks may occur from common source exposures. The natural hosts for the organism are various mammals including mice, dogs, wild rodents, farm animals, and cats (2). Infection can be acquired either through direct contact with animals or through environmental contamination by animal urine. Portals of entry for microorganisms include abraded skin, mucous membranes, or conjunctiva. The infection is rarely acquired by ingestion of contaminated food with urine or via aerosols (3). Leptospirosis is associated with variable clinical courses ranging from a mild influenza-like infection to a severe multi-organ disease. Weil's syndrome is defined as severe leptospirosis with multi-organ dysfunction, which can present with fever, jaundice, hepatorenal failure, and coagulation impairments (4, 5).

Thrombotic thrombocytopenic purpura (TTP) is a haematological disorder that is characterised by fever, neurological disorders, renal failure, anaemia, and thrombocytopaenia (6). It may be either idiopathic or secondary to autoimmune diseases, some drugs, cancer, and various infections (6, 7). Leptospirosis in association with TTP has so far been rarely reported in the literature. We describe a case of leptospirosis with presenting features suggestive of TTP.

Case Report

A previously healthy 58-year-old male worker visited the emergency unit with a 1-week history of fatigue, fever, oliguria, darkening of urine, and visual hallucinations. The exposure to sewage 10 days ago was retrieved from the history. On physical examination, he was found to be jaundiced, and had a fever of 38.2°C. Laboratory investigations revealed anaemia (haemoglobin: 10.3 g/dL, corrected reticulocyte of 4%), thrombocytopaenia (33.000/mm^3), elevated total bilirubin (24 mg/dL) with indirect predominance (10 mg/dL), high lactate dehydrogenase (LDH; 932 IU/L), and increased urea (293 mg/dL) and creatinine (7.6 mg/dL) levels. Coombs tests were negative. The laboratory test results on admission are shown in Table 1.

Urinalysis revealed haematuria, bilirubinuria, and trace proteinuria. Serology for viral hepatitis was negative. Serological tests for anti-nuclear antigens (ANA) and against the Toxoplasma, Rubella, Cytomegalovirus, Herpes (TORCH) panel were all negative. Blood, throat, and urine cultures were negative. On abdominal ultrasonographic examination, the gall bladder wall thickness was found to be increased, intra- and extra-hepatic bile ducts were normal, and renal echo-

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Table 1. Initial laboratory results of the patient

Parameter	On admission	Normal range
Leukocyte (mm^3/L)	4.800	4.000-10.000
Haemoglobin (g/dL)	10.3	12-16
Thrombocyte (mm^3/L)	33.000	150.000-450.00
Reticulocyte (%)	4	0.5-2.5
Activated partial thromboplastin time (aPTT, sec)	22.4	22.8-31
Prothrombin time (sec), (INR)	10.1 (0.9)	11.2-14.4 (0.85-1.15)
Direct and indirect Coombs	negative	
Fasting blood glucose (mg/dL)	77	70-105
Urea (mg/dL)	293	10-43
Serum creatinine (mg/dL)	7.6	0.4-1.2
Alkaline phosphatase (ALP, IU/L)	105	<258
Alanine aminotransferase (ALT, IU/L)	102	<40
Aspartate aminotransferase (AST, IU/L)	158	<45
Gamma-glutamyl peptidase (GGT, IU/L)	39	1-50
Creatinine kinase (CK, IU/L)	370	<195
Total bilirubin (mg/dL)	24	0.3-1.2
Direct bilirubin (mg/dL)	14	0-0.4
Indirect bilirubin (mg/dL)	10	0-0.4
Lactate dehydrogenase (LDH, IU/L)	932	0-247
Sodium (Na, mEq/L)	123	136-147
Potassium (K, mEq/L)	5.1	3.6-5.1
Calcium (Ca, mg/dL)	8.2	8.8-10.8
Phosphorus (P, mmol/L)	2.7	2.5-5.0

genicities were increased by grade 1-2. Blood film examination showed fragmented red cells.

In light of the patient's history with acute kidney injury, thrombocytopaenia, findings of intravascular haemolysis, and anaemia, a presumptive diagnosis of TTP was made and daily therapeutic plasma exchange (TPE) was initiated subsequently at a dose of 10 units/day with fresh frozen plasma for 14 days. Serological testing (microscopic agglutination test [MAT]) showed a high antibody positivity (1/600) against *Leptospira*. Antibiotic therapy with doxycycline 200 mg/day was initiated. After the end of the 14-day course of antibiotic treatment and plasmapheresis for a duration of a month, the clinical and laboratory signs returned to normal (Figure 1).

Discussion

Leptospirosis is a zoonotic infectious disease commonly encountered in farmers, veterinarians, sewer workers, and in people who swim in lakes and streams. It is caused by spiral microorganisms of the *Leptospira* serotype. Since neither the clinical features nor routine laboratory findings are specific for leptospirosis, a high index of suspicion must be maintained for the diagnosis (8, 9).

Coagulation disorders mostly reported as disseminated intravascular coagulation are well known in leptospirosis, but TTP is a very rare presentation (10). Although the majority of TTP cases are idiopathic, it may also develop due to secondary reasons like drugs, pregnancy, malignancies, bone marrow transplantation, and infections (6, 7, 11-13). Shiga toxin-producing *Escherichia coli*, HIV, and pneumococcal infection may be responsible for the aetiology of TTP (11-13). Leptospirosis complicated by TTP carries a high mortality rate. Laing et al. (14) reported a case of Leptospirosis complicated by TTP, who died, despite vigorous use of plasma exchange along with continued antibiotics, steroids, and high-dose intravenous immunoglobulin. We describe here an uncommon case of leptospirosis complicated by TTP that responded to plasma exchange and antibiotic therapy.

TTP and haemolytic uraemic syndrome (HUS) are acute haematological syndromes with abnormalities in multiple organ systems, and are characterised by microangiopathic haemolytic anaemia and thrombocytopaenia. In a few patients, neurological abnormalities are predominant and manifestations of renal failure are minimal or absent. These patients are considered by some to represent idiopathic or 'classical' TTP. When acute renal failure dominates the clinical picture, the

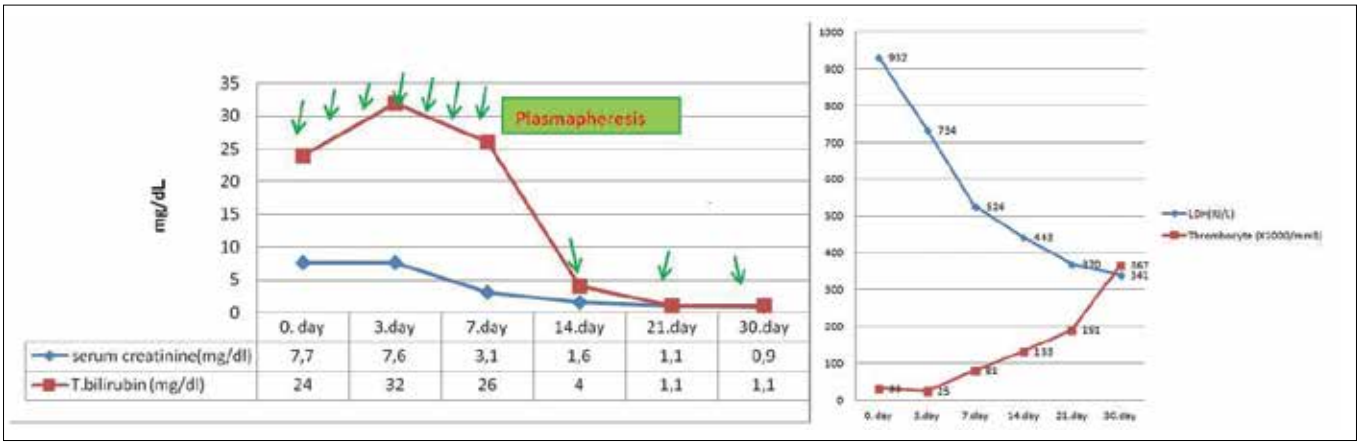

Figure 1. Laboratory parameters (Serum Creatinine,Lactate dehydrogenase, and Thrombocyte) of the patient during follow-up. The green arrows show plasmapheresis.

disorder is considered as HUS (15). In our case, the presence of neurological abnormalities and fever suggests TTP.

We excluded acute cholangitis and/or choledocholithiasis by the presence of indirect hyperbilirubinaemia, the absence of leukocytosis, and no biliary system stone in abdominal ultrasonographic imaging. Acute hepatitis was excluded due to negative viral hepatitis serological markers and TORCH panel. On admission, sepsis syndrome and disseminated intravascular coagulopathy were also considered because of the presentation of the case and accompanying thrombocytopenia. These were also excluded due to negative culture results, normal D-dimer level, and coagulation tests, and normal fibrinogen levels.

Leptospirosis may present with features of TTP and should be considered in any patient who lives in subtropical regions with a history of exposure to environmental sources. Early diagnosis and treatment can be lifesaving.

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