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A Rare Cause of Hyponatremia and Acute Kidney Injury: Leptospirosis

Hiponatremi ve Akut Böbrek Hasarının Nadir Bir Nedeni: Leptospirozis

Mürşide Esra DÖLARSLAN[1]
Simge BARDAK[2]
Kenan TURGUTALP[1]
Serap DEMİR[1]
Ahmet Alper KIYKIM[1]

1 Mersin University Faculty of Medicine, Department of Internal Medicine, Division of Nephrology, Mersin, Turkey
2 Batman State Hospital, Department of Nephrology, Batman, Turkey

ABSTRACT

Leptospirosis is a zoonotic infection, caused by Leptospira interrogans. Clinical presentation may vary from asymptomatic infection to Weil disease characterized by multiple organ failure. We described a 22-year-old case who had renal, hepatic and pulmonary involvement with leptospirosis. He presented with hyponatremia and recovered by the treatment with penicillin G. We emphasized that early diagnosis and management will be life saving.

KEY WORDS: Acute kidney injury, Hyponatremia, Leptospirosis

ÖZ

Leptospirozis, Leptospira interrogans tarafından oluşturulan zoonotik bir enfeksiyon hastalığıdır. Asemptomatik klinik tablodan Weil Hastalığı olarak da adlandırılan çoklu organ yetmezliği tablosuna kadar farklı klinik şekillerde görülebilir. Yazıda böbrek, karaciğer ve akciğer tutulumu ile birlikte hiponatremi ile prezante olan ve penisilin G tedavisi ile tamamen iyileşen 22 yaşındaki bir leptospirozis olgusu sunulmuştur. Aynı zamanda erken tanı ve uygun tedavinin hayat kurtarıcı olduğu vurgulanmıştır.

ANAHTAR SÖZCÜKLER: Akut böbrek hasarı, Hiponatremi, Leptospirozis

INTRODUCTION

Leptospirosis is an acute, febrile zoonotic infection, caused by *Leptospira interrogans*. Patients with leptospirosis may present with jaundice, renal dysfunction and hemorrhagic diathesis. A total of 5-10% of patients may present with Weil disease which is a severe form of leptospirosis characterized by multiple organ failure (1). It may eventually be fatal unless diagnosed and treated early. We described a case with leptospirosis who presented with hyponatremia and acute kidney injury. We pointed out that leptospirosis may present with hyponatremia besides its known classic triad, and emphasized the importance of prompt diagnosis and management.

CASE PRESENTATION

Informed consent was taken from the patient. A 22-year-old farmer presented to our hospital with complaints of fever, weakness, pain, white colored sputum, nausea, and vomiting.

Physical Examination

Arterial blood pressure: 75/45 mm Hg, respiratory rate: 32/min, pulse: 125/min. Jaundice was observed. Rough rales were heard over the lung bases. He had neither jugular venous distension nor pretibial edema. He was normovolemic.

Laboratory

Hemoglobin: 12.4 gr/dL, white blood cell: 12.940/mm^3, platelet: 126.000/mm^3. Serum creatinine: 4.3 mg/dL, aspartate aminotransferase: 94 U/L, alanine aminotransferase: 38 U/L, creatine kinase: 1012 U/L, C-reactive protein: 406 mg/L, sodium: 119 mEq/L, potassium: 6.14 mEq/L, reticulocyte: 0.75%, total bilirubin: 8.3 mg/dL, direct bilirubin: 5 mg/dL, alkaline phosphatase: 71 U/L, gamma glutamyl transferase: 26 U/L, lactate dehydrogenase:

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Correspondence Address:
Mürşide Esra DÖLARSLAN
Mersin Üniversitesi Tıp Fakültesi,
İç Hastalıkları Anabilim Dalı,
Nefroloji Bilim Dalı, Mersin, Turkey
Phone : +90 324 241 00 00
E-mail : esradolarslan@hotmail.com

401 U/L, uric acid: 4.1 mg/dL, urine sodium: 60 mEq/d. Urine analysis: density, 1018; pH, 5; and 8 leukocytes and 9 erythrocytes per high-power field, protein, 150 mg/dL; bilirubin, 2+. Serologic tests for hepatitis were negative. No schistocyte was observed on peripheral blood smear. Abdominal ultrasonography was normal. Reticular infiltrates were seen on chest X-ray and chest CT revealed bilateral areas of consolidation. All other causes of hyponatremia were excluded. Leptospirosis was considered in the differential diagnosis, and treatment with penicillin G started. Antibodies against *L. biflexa serovar patoc* at a titer of 1/200 was found by Enzyme-Linked ImmunoSorbent Assay (ELISA). Then, microscopic agglutination test (MAT) was performed for *Leptospira icterhaemorrhagicae*, and the test result was 1/400, so the diagnosis was confirmed. In addition to hyponatremia, all clinical and laboratory parameters were improved after penicillin G treatment. Laboratory parameters at hospital admission and after treatment are shown in Table I. The patient was discharged after 7 days following penicillin G treatment. The hyponatremia had therefore been related to inappropriate ADH syndrome due to leptospirosis.

DISCUSSION

This case is important as leptospirosis may rarely present with hyponatremia, and should take place in the differential diagnosis of hyponatremia. By this report, we demonstrated that hyponatremia may be associated with severe leptospirosis.

The World Health Organization (WHO) has reported the incidence of leptospirosis as 873.000, and 48.600 of them died (2). The risk groups for leptospirosis are farmers, veterinarians, sewer workers, wetland workers, hunters, fisherman, military personnel, laboratory workers, and people who perform water activities such as swimming, canoeing (1). The infection is transmitted by animal urine contacting breaks in the skin, eyes, mouth, or nose (1). Our patient was a farmer with low income, but did not have skin erosion or abrasion or a contact with mucous membrane.

Table I: Laboratory parameters of the patient at hospital admission and after treatment.

Laboratory parameters	At hospital admission	After treatment
Hemoglobin (gr/dL)	12.4	12.8
White blood cell (mm^3)	12.940	9.800
Platelet (mm^3)	126.000	135.000
Serum creatinine (mg/dL)	4.3	1.1
Aspartate aminotransferase (U/L)	94	45
Creatine kinase (U/L)	1012	45
C-reactive protein (mg/L)	406	5
Sodium (mEq/L)	119	138
Potassium (mEq/L)	6.14	4.35
Total bilirubin (mg/dL)	8.3	1.2
Direct bilirubin (mg/dL)	5	0.8
Alkaline phosphatase (U/L)	71	25
Lactate dehydrogenase (U/L)	401	170

A total of 75% of the patients may present with the complaints of fever, myalgia, jaundice, headache, conjunctival redness, and periorbital pain after the incubation period (2-26 days, mean: 10 days). Conjunctival redness is an important finding, and is prevalent in 55% of patients. Other symptoms and findings such as dry cough, nausea, vomiting, diarrhea, splenomegaly, lymphadenopathy, pharyngitis, hepatomegaly, muscle rigidity, abnormal respiratory findings, skin rashes, and less commonly arthralgia, bone, chest and abdominal pain may be present (3). Our patient had complaints of fever, myalgia, cough, nausea, vomiting, and jaundice. However, he had neither fever nor conjunctival redness. Patients with leptospirosis may have aseptic meningitis, pulmonary hemorrhage, acute respiratory distress syndrome, myocarditis, rhabdomyolysis, and uveitis (1,4). Hypokalemia is usually prevalent in patients with nonoliguric kidney injury (5). Hepatic insufficiency is usually reversible. Vasculitic lesions may be seen in the extremities (3).

Systemic vascular resistance is decreased, whereas cardiac output, and renal vascular resistance are increased in leptospirosis. Blood volume is increased initially, whereas it decreases in the follow up. There may be no response to fluid replacement (6). As our patient was hypotensive at hospital admission, he needed intravenous fluid replacement and vasopressor.

Kidney injury is usually associated with tubular dysfunction due to tubular dilatation, degeneration and necrosis in patients with leptospirosis. Direct toxic effects of leptospirosis together with hypotension, hypovolemia, hypoxemia, jaundice, immune complex glomerulonephritis, and rhabdomyolysis may all contribute to the renal injury (3,7). Çetin et al reported that 8 of 16 leptospirosis cases had renal failure, and 7 of them required hemodialysis (7). Afiri et al reported that 77.3% of 88 leptospirosis cases had acute kidney injury (8). Our patient might also have renal injury due to the direct tubular toxic effect of leptospirosis. His kidney functions recovered without need of hemodialysis.

Hyponatremia may be present in severe leptospirosis as well as leukocytosis, leucopenia, thrombocytopenia, hyperbilirubinemia, azotemia and/or increase in creatinine kinase (1,6). Alian et al reported that 7.6% of patients with leptospirosis had hyponatremia in Northern Iran. In the same report, 30.3% of the leptospirosis cases due to *L. Icterohemorrhagica* had acute kidney injury, mostly in the first week (1). However, why hyponatremia develops in leptospirosis was not explained in these studies. Our patient was the first reported case who presented with hyponatremia due to leptospirosis in Turkey.

Increased antidiuretic hormone level, increased sodium flux into cell, loss of sodium, and blockage of osmoreceptors are possible reasons of hyponatremia due to leptospirosis (6). In addition, Na-K-Cl co-transporter activity in the loop of Henle is inhibited by the outer membrane of the leptospirosis agent, and this leads to hypokalemia and sodium excretion (5). Electrolyte disorders are transient, and improve when the infection is controlled (6). The electrolyte imbalance in our patient improved as infection recovered.

Microscopic agglutination test, macroscopic hemagglutination test, indirect hemagglutination, and ELISA are serologic tests used in the diagnosis of leptospirosis. Main test for diagnosis is MAT, and a titer of ≥1/200 is accepted as a positive result (3,9). Our patient had a MAT titer of 1/400, which confirmed the diagnosis.

Doxycycline, azithromycin, penicillin, ceftriaxone or cefotaxime are suggested in the treatment of leptospirosis (9). Empiric treatment should be initiated if the clinical suspicion is high. Initiation of antibiotherapy within 2 days following symptoms of leptospirosis was found to be associated with better outcomes (9). Delay in initiation of antibiotherapy after the onset of symptoms may be fatal. Advanced age, male gender, oliguria, anuria, jaundice, meningitis, and multiorgan failure have been associated with mortality (10). Penicillin G was started in our patients, and a dramatic response was obtained.

In conclusion, leptospirosis may rarely present with hyponatremia instead of the classic triad which consists of fever, renal dysfunction and hemorrhagic diathesis. Prompt diagnosis and management may contribute to early recovery and decreased mortality and morbidity.

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