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A Rare Manifestation of Leptospirosis: Long-Term Elevation in Liver Enzymes

Nadir Bir Leptospirozis Kliniği: Karaciğer Enzimlerinde Uzun Süreli Yükseklik

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ABSTRACT

Leptospirosis is a bacterial zoonosis that is endemic in many tropical and subtropical regions. The disease is transmitted to humans by contact with the urine or an environment contaminated with the urine of infected animals. The clinical manifestations of leptospirosis vary from subclinical infection to severe illness with multiorgan dysfunction. This case report aimed to present a leptospirosis case diagnosed with detailed anamnesis and progressed with long-term elevation in liver function tests, in a non-endemic region. A 28-year-old male patient was admitted with complaints of weakness, fever, and vomiting. As a result of the detailed anamnesis, it was learned that the patient with hyperbilirubinemia, elevated liver enzymes, and kidney failure had contact with polluted water in a rural area, and the patient was followed up with a preliminary diagnosis of leptospirosis. Leptospirosis may present with different clinical presentations and be confused with many diseases, risk factors should be carefully questioned.
Keywords: Acute kidney failure; leptospirosis; liver function tests.

ÖZ

Leptospiroz, birçok tropikal ve subtropikal bölgede endemik olan bakteriyel bir zoonozdur. Hastalık insanlara enfekte hayvanların idrarıyla veya idrarıyla kontamine olmuş bir ortamla temas yoluyla bulaşmaktadır. Leptospirozun klinik belirtileri subklinik enfeksiyondan çoklu organ fonksiyon bozukluğu ile seyreden ağır hastalık tablosuna kadar değişkenlik göstermektedir. Bu vaka raporunun amacı, endemik olmayan bir bölgede, detaylı anamnez ile tanı konulan ve karaciğer fonksiyon testlerinde uzun süreli yükselme ile seyreden bir leptospirosis olgusunu sunmaktır. 28 yaşında erkek hasta, halsizlik, ateş ve kusma şikayetleriyle başvurdu. Hiperbilirubinemi, karaciğer enzim yüksekliği ve böbrek yetmezliği olan hastanın ayrıntılı anamnez sonucu kırsal bölgede kirli su ile teması olduğu öğrenildi ve hasta leptospiroz ön tanısı ile takip edildi. Leptospirosis farklı klinik bulgularla ortaya çıkabildiği ve birçok hastalıkla da karışabildiği için risk faktörlerinin dikkatle sorgulanması gerekir.
Anahtar kelimeler: Akut böbrek yetmezliği; leptospirozis; karaciğer fonksiyon testleri.

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INTRODUCTION

Leptospirosis is a zoonotic infection caused by spirochetes of the genus of *Leptospira*. Although the disease is commonly seen in tropical and subtropical regions, it is a serious cause of mortality in low-income countries (1). The infection is transmitted not only from rodents but also from wild or domestic animals, especially from rodents. The disease is transmitted to humans by direct contact with

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the urine of infected animals or by contact with an environment contaminated with the urine of infected rodents. The clinical manifestation of leptospirosis varies from mild and self-limited illness to severe illness with multiorgan dysfunction. A mild, anicteric, and self-limiting febrile disease is seen in 90% of the cases. Weil's disease, the most severe form of illness, is characterized by jaundice, renal failure, and hemorrhage (2). The symptoms of leptospirosis can mimic other unrelated infections such as hepatitis, sepsis, hantavirus, and other viral hemorrhagic fevers. Thus, a significant amount of leptospirosis cases may go undetected or be misdiagnosed. The liver is not the main target of spirochetes infections. Hepatic dysfunction in leptospirosis usually presents with isolated direct hyperbilirubinemia with mild elevation transaminases and lever function usually improves without complications (3). Herein, we presented a case of leptospirosis with long-term elevation in liver function tests which was diagnosed by detailed anamnesis and serology.

CASE REPORT

A 28-year-old male patient with no medical history was admitted to the Infectious Diseases and Clinical Microbiology outpatient clinic with weakness, fever, and vomiting. Vital signs on admission were a fever of 39.2 °C, heart rate of 132 beats per minute, blood pressure of 110/60 mmHg, and respiratory rate of 22 breaths per minute. On physical examination, he was oriented and cooperative. He had scleral icteric and jaundiced skin. Other system examinations were normal. Upon further questioning, the patient was a teacher, who lived in the city center. He had no history of liver disease. He denied any recent travel, use of herbal supplements, or alcohol use. He had no contact with ticks and rodents. However, he reported that three days before the presentation, he was drinking natural spring water in rural settings near Mount Ararat.

The laboratory tests showed a white blood cell (WBC) count of 7060 /mm^3 (normal range, 4500-11000 /mm^3), aspartate aminotransferase (AST) level of 128 U/L (normal range, 10-40 U/L), alanine aminotransferase (ALT) level of 247 U/L (normal range, 10-40 U/L), alkaline phosphatase (ALP) level of 153 U/L (normal range, 44-147 U/L), gamma-glutamyl transferase (GGT) level of 1160 U/L (normal range, 0-65 U/L), total bilirubin level of 3.5 mg/dl (normal range, 0.2-1.2 mg/dl), direct bilirubin level of 1 mg/dl (normal range, 0.0-0.3 mg/dl), platelet count (PLT) of 240 x10^3/uL (normal range, 150-400 x10^3/uL), and creatinine level of 2.4 mg/dl (normal range, 0.5-1.2 mg/dl). Hepatobiliary ultrasonography (USG) showed normal liver size and no biliary dilatation. Anti-HAV IgG was positive, while anti-HAV IgM, Hbs-Ag, anti-HBc IgG, and anti-HCV were negative. Hence, antibiotic empiric treatment was initiated with ceftriaxone 2-gram IV once daily for preliminary diagnosis of leptospirosis. The highest values in the follow-up were as follows; AST: 1126 U/L, ALP: 245 U/L, GGT: 1716 U/L, total bilirubin: 10.6 mg/dl, and creatinine: 5.9 mg/dl. The examination results of the patient are shown in Table 1. On the fourth day, the fever regressed, and hyperbilirubinemia and renal function improved. Serum *Leptospira* PCR was positive, confirming the suspected diagnosis of leptospirosis. Hantavirus IgM and IgG were negative. In the follow-up, hemodialysis was not necessary due to acute renal failure, as a resolved renal function. The patient gradually improved and was discharged on the 10th day. The elevation in liver function tests continued for 6 weeks and completely regressed to normal values.

DISCUSSION

Leptospirosis is endemic in various parts of the world. Transmission to humans usually occurs as a result of contact with the urine or tissues of infected animals, which are long-term carriers, or contact with contaminated soil and water. Mice are the most commonly known reservoir of the disease. Shepherds, slaughterhouse workers, butchers, sewer and mine workers, hunters, veterinarians, and laboratory workers who are likely to come into contact with these reservoirs are risky occupational groups in terms of leptospirosis (3). Although he was not in the occupational risk group in our case, leptospira was transmitted as a result of contact with contaminated water in the rural area.

The clinical manifestation of leptospirosis in humans varies from an asymptomatic, self-limiting mild disease to severe illness with, hepatic dysfunction and acute renal failure. About 90% of leptospirosis is a subclinical and self-limiting febrile illness, while the severe form is presented by multiorgan dysfunction. The most severe form of leptospirosis is Weil's disease, characterized by jaundice, acute renal failure, and hemorrhage and can be fatal without treatment (4).

Hepatic involvement in leptospirosis can vary from an asymptomatic rise in transaminases to severe icteric hepatitis. However, detailed data on the frequency and type of hepatic dysfunction in leptospirosis are limited. Studies aiming to elucidate the pathogenesis of *Leptospira*

Table 1. Laboratory findings on admission and days later

Days	AST (U/L)	ALT (U/L)	ALP (U/L)	GGT (U/L)	TBIL (mg/dL)	PLT (x10^3/uL)	Cr (mg/dL)
1st	128	247	153	1160	3.5	140	2.4
3rd	979	712	197	1340	7.8	82	3.2
5th	1126	918	245	1716	10.6	53	5.9
7th	878	754	179	1236	8.2	76	2.5
10th	500	357	161	886	5.2	97	2.0
21st	274	91	158	534	3.5	158	1.0
42nd	98	76	142	256	2.1	175	1.0

AST: aspartate aminotransferase, ALT: alanine aminotransferase, ALP: alkaline phosphatase, GGT: gamma-glutamyl transferase, TBIL: total bilirubin, PLT: platelet, Cr: creatinine

induced jaundice and hepatic disorders have shown that hyperbilirubinemia in leptospirosis matched with a cholestatic pattern, rather than hepatocellular injury or hemolysis (5,6). They have shown that conjugated bilirubinemia seen in leptospirosis could be due to hepatic infiltration of leptospires (6). Penetration of cells such as endothelial cells, kidney cells, and macrophages by leptospires was reported in in vitro studies (7). In a study based on this, it was investigated whether leptospires localized in hepatocytes, but couldn't find leptospires localized in hepatocytes. This finding suggests that pathogenic leptospires invade host hepatocytes intercellularly rather than intracellularly and hepatocytes are not the main target of leptospires (6). Also, some studies reported that *Leptospira* induced apoptosis of hepatocytes.

Studies investigating clinical manifestation and laboratory test abnormalities in patients who had severe leptospirosis and case reports reported in the literature confirm that elevated liver enzymes in leptospirosis usually resolve without long-lasting effects (8). In our case, high liver enzyme elevation for a long time is remarkable. Transaminases, which were elevated 10 times in the first week, continued to be elevated 2–3 times in the 6th week. By the eighth week, it was completely normal.

While spontaneous recovery is observed in most mild leptospirosis cases, it has been shown that early antibiotic treatment in severe leptospirosis cases reduces mortality (9). Doxycycline or amoxicillin is generally recommended in moderate cases, and penicillin or ceftriaxone is recommended in severe cases (10). In our case, the patient who applied with fever, weakness, and nausea was accepted as having leptospirosis with clinical findings and anamnesis, and antibiotic treatment was started with a preliminary diagnosis of Weil's disease. A fever response was obtained on the fourth day of treatment, and clinical symptoms and urea and creatinine values became completely normal. Hemodialysis was not necessary for acute renal failure although there was a serious increase in urea and creatinine, This suggested that it may be due to early antibiotic treatment and supportive treatment.

Our case is important in terms of early diagnosis as a result of detailed anamnesis in the non-endemic region. Leptospirosis may present with different clinical presentations and may be confused with many diseases with similar clinical presentations. Therefore, risk factors should be carefully questioned in the anamnesis. Our case is interesting in that the elevation in liver function tests is a case of leptospirosis that lasts for a very long time.

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