Case Report

Recovery from Leptospira-Related Acute Liver Failure and Acute Kidney Injury –A Case Report from Bangladesh

Akmat Ali[1], Richmond Ronald Gomes[2], Khadiza Begum[3]

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Abstract

Leptospirosis is a zoonosis with protean manifestation caused by the spirochete, Leptospira interrogans. Here we report a 60-year-old male who presented with sudden onset of fever, rigors, myalgia and headache occasionally accompanied by nausea, vomiting and diarrhea. Later during the course of treatment he developed encephalopathy with fulminant hepatic failure and acute kidney injury and was diagnosed as a case of leptospirosis. A timely workup combined with early initiation of antibiotics and hemodialysis led to effective treatment for this patient.

Key words*: Weil's disease; Encephalopathy; Acute liver failure; Acute kidney injury*

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Introduction

Leptospirosis is the most widespread zoonosis with complex clinical features varying from subclinical infection and self-limiting anicteric illness to multiple organ failure (MOF) and death. Although considered as a re-emerging infectious disease throughout the world, leptospirosis is ignored in many cases.[1] Severe disease presenting with acute renal failure (ARF) is associated with acute liver failure (ALF) in up to 70% of cases and leads to MOF and death in one-third of the patients despite standard medical treatment.[2,3]

Case report

A 60-year-old non-diabetic, normotensive man presented with history of high grade, continued fever (highest recorded temperature was 104^0 F) with chills and rigor, minimally responded to antipyretic for five days. He had leg and back pain and for this he had taken ketorolac. He was passing high colored urine. He did not consume alcohol or take any illicit drugs. He was initially treated by the local doctor in district hospital with some antibiotics the name of which he could not mention. In spite of initial treatment, he developed confusion and became subconscious at the seventh day. Then he was transferred to a Private Medical College Hospital in Dhaka and was immediately shifted to intensive care unit. His physical examination revealed mild anemia, marked jaundice, temperature 100^0 F, pulse 100 beats/minute, blood pressure 173/100 mm of Hg and GCS 10/15. He lived in rural area of Bangladesh and gave no history of recent travel or taking street food or any operation or blood transfusion. There are many rats in his house including bed room. At the 8^{th} day he became fully unconscious. His urine output was reduced. On the day of admission (10.8.16) Hb was 9.4 gm/dL, WBC 9000/cu mm, neutrophil 76%, platelet count 65000/cu mm, aspartate transaminase (AST) 89 U/L, alkaline phosphatase (ALP) 215 U/L, serum albumin 2.1gm/dL, serum calcium 7.8 mg/dL, alanine transaminase (ALT) 70U/L, CRP 46, s. bilirubin 11.6 mg/dL, serum creatinine 7.9 mg/dL, blood urea 279 mg/dL, arterial ammonia 133mg/dL, gamma glutamase 49, serum sodium 141 mmol/L and potassium 3.5 mmol/L. Routine microscopic examination of urine showed that albumin was present and pus cells were 15–20/HPF. Coagulation profile showed that international

1. *Associate Professor, Department of Hepatology, Ad din Women's Medical College and Hospital, Dhaka*
2. *Associate Professor, Department of Medicine, Ad din Women's Medical College and Hospital, Dhaka*
3. *Associate Professor, Department of Medicine, Ad din Women's Medical College and Hospital, Dhaka*

Correspondence *Richmond Ronald Gomes, Email:rrichi.dmc.k56@gmail.com*

normalized ratio (INR) was 2.76, activated partial thromboplastin time (aPTT) was 72.11 seconds. Tests for hepatitis C virus antibody (anti-HCV), hepatitis B (HBsAg, HBeAg, IgM anti-HBc and anti-HBs), and hepatitis A antibody, hepatitis E antibody were negative, as were tests for antibodies against Dengue, human immunodeficiency virus (HIV) types 1 and 2, anti-nuclear (ANA) antibody. Echocardiography was normal and USG of whole abdomen reported contracted gall bladder. Anti Leptospira IgM was positive (IgM>1:80) and IgG was negative.

In ICU he was treated with IV fluid, broad spectrum antibiotics ceftriaxone, linezolid and nasogastric tube feeding, lactulose and rifaximine. Transfusion of packed red blood cells, fresh frozen plasma and glucose were given. At the 10th day his condition improved after two sessions of hemodialysis. On 13.8.16 WBC was 22000/cu mm, Hb 9.7 gm/dL, platelet count 160000/cu mm, s. creatinine was 2.8 mg/dL. At the 11th day of fever he became fully conscious and oral diet was resumed. His fever subsided and urine output increased. On 14.8.16, serum bilirubin was 6.8 mg/dL, serum creatinine 2.2 mg/dL, blood urea 50 mg/dL, Hb 10.9 gm/dL, WBC 13000/cu mm, neutrophil 78% and platelet count 180000/cu mm.

Then he was shifted from ICU to a cabin and continued conservative management and discharged on 15th day of illness with stable mentation and hemodynamics. He was advised to come for follow-up at OPD with repeat liver and renal function tests after one week.

Discussion

Leptospirosis is a worldwide zoonotic infection due to *Leptospira* spp. Animals, specifically rodents are the primary vectors of disease. Human infection results from exposure to the urine of infected animals or through contact with contaminated soil or water.[4] Regions prone to hurricanes and floods are at higher risk of exposure.[5-7] The diagnosis is challenging for several reasons: i) its low incidence in the United States, ii) its highly variable clinical symptoms and iii) its mimicry of common diseases such as viral hepatitis. Typically, leptospirosis has a biphasic disease course. The first phase lasts up to seven days and presents with nonspecific symptoms such as fever, headache and myalgia. The second phase can be categorized into anicteric and icteric forms. Most patients undergo the milder anicteric form. Rarely, leptospirosis presents with a severe icteric form with multiple organ involvement called Weil's disease. Weil's disease can lead to acute kidney failure, acute liver failure, rhabdomyolysis and thrombocytopenia with possible hemorrhagic diathesis. In our patient there were acute kidney injury, thrombocytopenia and acute liver failure as evidenced by presence of coagulopathy and encephalopathy. The mortality rate in the course of combined acute renal failure and acute liver failure is reported to be 70–80% despite optimal medical therapy.[8]Acute liver failure results in an endogenous accumulation of toxins involved in the impairment of cardiovascular, kidney and cerebral function. Moreover, these toxins have been shown to damage the liver itself by inducing hepatocellular apoptosis and necrosis, thus creating a vicious cycle of hepatic injury. Transaminase levels are moderately elevated with a mild increase of alkaline phosphatase.[9] An AST:ALT ratio of >3 may indicate a poorer prognosis.[8] Serum bilirubin may rise as high as 30 to 40 mg/dL.[9] Jaundice as a result of septic cholestasis typically appears during day 5 to 9 of the disease course. Liver function usually returns to normal without complications, as observed in this patient. The diagnosis can be confirmed by serological tests detecting leptospiral antibodies or through polymerase chain reaction assay.[10] Our patient was positive for IgM anti-Leptospira antibody. Pathologists may also perform leptospiral immunohistochemistry staining on liver biopsies for diagnosis, but this must be specifically requested.[10]

Treatment of leptospirosis with antibiotics remains controversial.[11] A Cochrane review of seven randomized clinical trials was inconclusive on the role of antibiotics (penicillin) in leptospirosis, regardless of severity.[12] Nearly 90% of cases are considered mild and oral doxycycline or amoxicillin may be used. For severe cases, parenteral high-dose penicillin G or ceftriaxone is recommended.[13] As there were logistic constraints, our patient was managed conservatively with broad spectrum antibiotics, gut sterilizer and temporary renal replacement therapy and improved significantly.

Molecular adsorbent recirculating system is a modified dialysis that uses an albumin containing dialysate which is recirculated and perfused online through charcoal and anion exchange columns. This procedure is able to remove the protein-bound toxins, such as bilirubin, phenols or ''false'' neurotransmitters and thus it allows the temporary replacement of the hepatic detoxification function. Therefore, albumin dialysis has been used as a bridge to liver transplantation in patients with fulminant hepatic failure. It has shown efficacy in the treatment of ALF of various etiologies, hepatorenal syndrome, primary nonfunction after liver transplantation, or an acute decompensation of a chronic liver insufficiency.[14] As there was no scope for albumin dialysis in Bangladesh yet, our patient received two sessions of hemodialysis as temporary renal replacement therapy and improved.

The new extracorporeal liver support methods are capable of removing water-solved and albumin-bound toxins including single-pass albumin dialysis (SPAD), molecular adsorbent recirculating system (MARS) and the Prometheus system. Literature data indicate that albumin dialysis with MARS and fractionated plasma separation with Prometheus system might have a favorable effect in treatment of acute or acute-on-chronic liver failure and also provide renal support in case of renal failure.[15,16] After the implementation of MARS therapy clinical and biochemical parameters significantly improved in a patient with Leptospira-related acute fulminant hepatic failure and acute kidney injury, suggesting this was a decisive therapeutic option for survival and complete recovery of hepatic and renal functions.[17]

Conclusion

Leptospirosis has complex clinical features, including, in severe cases, acute renal failure and acute liver failure. Renal replacement therapy with other supportive treatment appears to be effective in patients with severe FHF due to Leptospirosis. Further studies are necessary to confirm the efficacy of extracorporeal liver support in Leptospirosis-induced ALF.

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