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Leptospirosis with Severe Acute Kidney Injury & Jaundice: A Review of 2 Cases

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ABSTRACT

Introduction: Leptospirosis is a zoonosis of global significance due to infection with Leptospira spp., a motile, obligate aerobic, spiral bacteria from contaminated soil, water or rat urine. This infection may have variable and protean manifestations. We present two cases of severe acute kidney injury (AKI), hyperbilirubinemia in association with sepsis due to Leptospiral infection seen in Hamilton, Bermuda. In many cases the disease may be mild, but severe cases with AKI and hepatic involvement with jaundice (Weil's disease) require prompt diagnosis and institution of therapy to prevent morbidity and mortality. In some cases the diagnosis may be delayed. The aim of this paper is to report two cases in which rapid diagnosis and therapy led to good outcome and recovery. WE also review the literature on AKI in Weil's disease.

Case Presentation: We present two cases of AKI, & jaundice & hepato-renal syndrome with oliguria of unclear etiology, in which a clinical index of suspicion of possible rat exposure with the patient's social history led to subsequent testing that confirmed the diagnosis quickly. Both cases presented with sepsis, altered mentation and hyperbilirubinemia. The patients tested positive for Leptospira IgM antibodies suggesting likely recent exposure that precipitated the current illness. Both patients had very severe AKI, and marked conjugated hyperbiliribunimia, but only one required hemodialysis. Both patients received antibiotic therapy with third generation cephalosporins (Piperacillin-Tazobactam, Ceftazidime) & Doxycycline for 2 weeks, with improvement and resolution of AKI. One patient had residual chronic kidney disease (CKD).

Conclusion: Leptospriosis can present in severe cases with AKI and hyperbilirubinemia and organ failure (Weil's disease). This pattern may be seen in endemic areas and occasionally in non-endemic areas. A high index of suspicion and awareness is critical to facilitate early diagnosis and therapy. It should be considered in the differential diagnosis of AKI and conjugated hyperbilirubinemia and severe sepsis. Antbiotic therapy should be instituted early while waiting for serologic confirmation to improve outcome. Recovery from AKI may be incomplete in some cases.

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Introduction

When patients present with severe AKI and hepatic failure with hyperbilirubinemia, a rapid diagnosis and urgent institution of therapy is crucial to limit morbidity and reduce mortality. If specific therapy is not instituted and diagnosis is delayed, affected patients may suffer irreversible clinical deterioration and possibly death. We present two cases of severe leptospirosis presenting with severe AKI and jaundice (Weil's disease) in an Hamilton Bermuda.

Case Reports

Case - 1

A 72-year-old gardener presented with fever, muscle aches and nausea to the emergency room. He had felt weak and malaise for 3 days prior to presentation. He reported poor urine output. He had no chronic medical problems except for hypertension treated with hydrochlorothiazide 12.5mg daily. He denies any sick contacts at home. On examination, he was jaundiced, with a blood pressure of 110/86 , pulse of 106/min with hepatosplenomegaly. His admission laboratory tests showed: BUN of 53, serum creatinine of 5.1mg/dl, 2+ proteinuria on urinalysis with 10-15rbc/hpf, thrombocytopenia of 20,000; and conjugated hyperbilirubinemia of 12mg/dl. Intravenous Ceftazidime and Doxycycline were started after admission. Renal function worsened over time as shown in table 1 & figure 1, but dialysis was not required as oliguria improved by day 6. Hepatitis B antigenserology and Hepatitis C antibodies were negative. A rapid Leptospira test was positive by day 2 and IgM antibodies were confirmed by microscopic agglutination test (MAT) by day 5.

Case - 2

A 70-year-old, homeless man presented to hospital with leg pain, myalgias, nausea, weakness and fever, and confusion. On physical exam, patient was disoriented to place and time, with BP of 126/73, pulse of 98/min. While in emergency department he had a tonic clonic seizure. His labs showed BUN of 168mg/dl, creatinine of 14.5mg/dl, CPK of 16,000 IU/ml, ALT was 290IU/dl, AST was 384IU/dl, admission bilirubin was 21 mg/dl. Intravenous

Ceftriaxone & Doxycycline were started for sepsis. Urgent hemodialysis was initiated, and after 4 dialysis sessions, oliguria improved and renal function continued to recover as shown in Table 1 Figure 1. Hepatitis B, C and Human immunodeficiency virus (HIV) antibodies were negative. Leptospira IgM antibodies by MAT assay were positive by day 4.

Test	Patient 1	Reference Range	Patient 2
Hemoglobin (g/dL)	11.9	13–15.9	10.4
WBC (cells ×10^9/L)	17.0	3.7–10.1	15.6
Platelets (cells ×10^9/L)	238	155–380	110
Blood Urea Nitrogen (mg/dL)	155	10–20	53
Creatinine (mg/dL)	7.1	0.7–1.0	5.1
Sodium (mmol/L)	138	135–145	140
Potassium (mmol/L)	5.4	3.5–5.4	4.8
Total Bilirubin (mg/dL)	21	1.1	12
Direct Bilirubin (mg/dL)	18	0.8	9
AST (IU/L)	586	10–38	384
ALT (IU/L)	484	10–38	290
Serum Amylase (IU/L)	140	100–150	126
Prothrombin Time (INR)	1.9	0.8–1.2	1.5
Albumin (g/dL)	3.2	3.5–4.9	2.8
Total Protein (g/dL)	5.8	6.0–8.2	5.4
Leptospira IgM	**Positive (+)**	**Negative**	**Positive (+)**

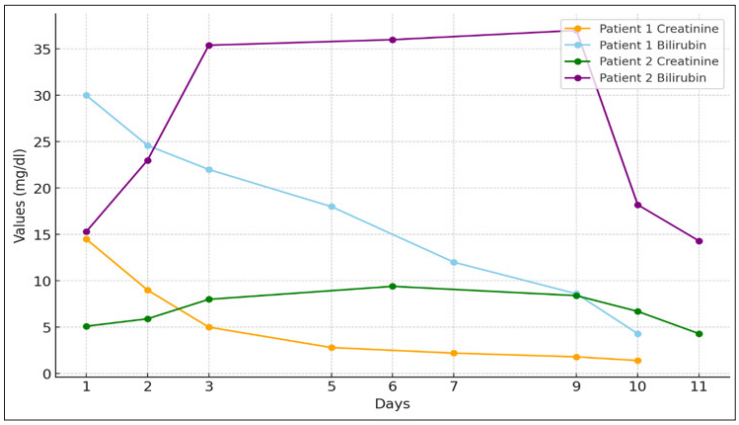

Figure 1: Evolution of Renal Function x Hyperbilirubinemia (Days 1-10)

Discussion

The occurrence of severe AKI, jaundice and raised liver function tests (transaminitis) may be a diagnostic challenge in critically-ill patients. The differential diagnosis in this case would include toxic hepatitis, viral hepatitis, severe sepsis, malaria and hepatorenal syndrome with cirrhosis, and cholemic nephropathy [1-3]. Leptospirosis may also present with this picture, as illustrated by these 2 cases presented in our report [4]. Jaundice with AKI in leptospirosis is a severe disease that can run an aggressive clinical course. Our patients presented with symptoms mimicking severe septic shock, with severe AKI and jaundice. Because of the social history of the 2 patients (gardener & homeless pt sleeping in destitute quarters) the occurrence of AKI and jaundice elicited concern to exclude leptospirosis which is endemic in Bermuda. Both patients presented with severe oliguria, although leptospirosis-associated AKI is thought to be more commonly non-oliguric [4]. One patient required hemodialysis, while the other did not. Renal function recovered with therapy, although there was still residual renal dysfunction at discharge.

Icteric leptospirosis with severe organ dysfunction (Weil's disease) that present late may be associated with high morbidity and mortality [2,5,6].

About 10% of Leptospirosis cases develop severe AKI and jaundice [3]. Leptospirosis is an important zoonosis of global importance in both endemic areas and non-endemic areas where frequent global travel may lead to infection in non-endemic areas. A report from Israel shows that the disease may be associated with jaundice in as much as 71% of cases [7]. In one report, features of vasculitis was shown [8].

Mortality rate has been shown in areas where diagnosis is made late in the course of the illness, such as in rural india [9].

Serological tests play a critical role in the diagnosis of leptospirosis. The microscopic agglutination test (MAT) is still considered the gold standard, although rapid assay tests may complement this [8].

In some cases, leptospiral infection has been suggested to affect kidney transplant function, with possible contribution to dysfunction and rejection of allografts [10].

Conclusion

In conclusion, early diagnosis and therapy may be life-saving in leptospirosis presenting with AKI and jaundice. beta-lactam

antibiotics and tetracyclines help eradication of infection. A high index of suspicion and history of possible exposure to soil, contaminated water and rats, should elicit a high index of suspicion.

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