A case with acute kidney injury, thrombocytopenia and hyperbilirubinemia due to Leptospirosis

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Abstract

Introduction: Leptospirosis is a zoonosis not frequently encountered in the daily clinical practice. It is associated with thrombocytopenia, acute kidney injury (AKI) and other vital organ dysfunction. Its clinical spectrum can range from subclinical cases in mild forms to fulminant disease leading to death. Most of the time, patients have a history of exposure to contaminated materials with urine shedding of the infected rodent.
Case presentation: A 76-year old man presented at the emergency room due to fever, malaise, myalgia, and loss of appetite. He was admitted to the hospital for further workup. Blood tests showed severe thrombocytopenia, markedly elevated creatinine, bilirubin level and anemia. ELISA testing confirmed the clinical suspicion of leptospirosis. His clinical course was marked by acute kidney injury and episodes of bloody stool and mild hemoptysis with no other major hemorrhagic phenomena. He received antibiotic, supportive therapy and one session of dialysis was performed with good final clinical result.
Conclusion: This case should alert physicians to include leptospirosis in the top list of differential diagnosis in patients with fever, thrombocytopenia, AKI and hyperbilirubinemia. Early diagnosis, antibiotic therapy and supportive measures are the treatment mainstay of this condition.

Keywords: leptospirosis, zoonosis.

Introduction

Leptospirosis is a zoonosis not frequently encountered in the daily clinical practice. It is caused by Leptospira strains, a spirochete, from which Leptospira interrogans is the only one causing this condition in human beings. Humans are infected by chance when they get exposed to materials infected with animal urine (1). Its clinical spectrum can range from subclinical cases in mild forms to fulminant disease leading to death. Its most severe form is known as Weil disease hallmarked by jaundice, kidney injury, hemorrhage, myocarditis with arrhythmias (3). The mean incubation period is 15 days after exposure. The clinical course can manifest two phases: initial one lasting from three to seven days, characterized by fever, chills, marked headache followed by nausea, anorexia, diarrhea, and myalgia. This is the right timing to detect leptospira in the blood stream, but with low microbiological yield in less than 50% of cases, hence serological tests are commonly used for confirmation. The second phase can be clinically more severe with the occurrence of meningitis and uveitis. The specific antibodies can be detected in this period. Studies have shown correlation of disease severity with the intensity of host humoral response to infection (2,4).

Case presentation

A 76-year-old man presented to our emergency department due to fever, malaise, dyspnea, myalgia, loss of appetite, nausea, blood stained sputum, cough, abdominal pain, dark urine, edema and jaundice. One week before admission, he was on a hunting trip in Martanesh, North-East of Albania, and stayed there overnight. When he came back at home, he reported chills, fever and malaise, for seven days. He does not recall being bitten by rodents or getting exposed to supposedly infected materials. On physical examination there was no sign of wounds or scars.

Previous medical history is notable for high blood pressure and diabetes mellitus type II. He receives ACE-inhibitors, beta blockers and diuretics. His blood sugar is well controlled with diet and no oral therapy. He had no history of kidney disease. His family history was unremarkable. He smoked for 20 years and quitted 5 years ago.

On physical exam the patient's body temperature was 37.8^0C, respiratory rate 20/min, heart rate 95/min, blood pressure 125/81 mmHg, SpO_2 93% on room air, pitting peripheral edema +1/+2, had icteric sclera, injected conjunctivae and palatine hemorrhagic spots. The skin was icteric as well. Lung auscultation revealed coarse respiratory sounds. The rest of the objective examination was unremarkable. Laboratory investigation data on admission are shown below. Routine blood tests were drawn. The tests were remarkable for high bilirubin level, direct component predominated, elevated creatinine and BUN, low platelet count as well. Nephrologic consultation was ordered after which the clinical suspicion of leptospirosis and hemorrhagic fever with renal syndrome topped the differential diagnosis list. ELISA test for leptospirosis and hemorrhagic fever was ordered. Empirical antibiotic therapy and supportive measures were started. Patient had bloody stool and minor hemoptysis episodes. No other major hemorrhagic phenomena were noted. The platelet count nadir was 25x103/l on the second day of stay. He was transfused 5 units of pooled platelets. Urine output was preserved during the whole length of stay. One session of dialysis was performed on the second day due to high BUN level causing diminished level of consciousness. The polyuric phase started the next day with a maximal volume of approximately 7 l/day. The peak bilirubin and creatinine level were 32.4/dl, 7.2 mg/dl respectively. Low potassium levels, typical for leptospirosis, were noted. His general condition improved gradually. ELISA test confirmed the diagnosis of leptospirosis. Initial antibiotic treatment with ceftriaxone was not changed. Diuretic therapy was administered only the first day of admission and then stopped. Electrolyte imbalances were corrected as needed.

Table 1. Laboratory data of the patient

Variable (normal range)	Day 1	Day 2	Day 3	Day 8	Discharge
Haemoglobin (14-18 g/dl)	11.4	9.5	10.7	9.4	10.1
PLT count (15-350x$10^3/\mu$l)	53x10^3	25 x10^3	35 x10^3	79 x10^3	372 x10^3
WBC count (4.8-10.8x$10^3/\mu$l)	14 x10^3	10 x10^3	13 x10^3	16 x10^3	9.8 x10^3
Creatinine (0.6-1.3mg/dl)	6.7	7.2	5.6	3.0	1.1
Urea (15-39mg/dl)	227	276	154	219	48
Total bilirubin (0.2-1mg/dl)	8.7	13.1	17	32.1	2.5
Direct bilirubin (0-0.2 mg/dl)	7.3	11.4	14.5	17.6	1.8
Indirect bilirubin (0-0.8mg/dl)	1.4	1.7	2.5	2.5	0.7
CK (39-308 U/L)	1847		290	85	16
LDH (105-330 U/L)	750	710	650	599	240
Alkaline phosphatase (50-136U/L)	114				
GGT (5-85U/L),	118				40
ESR (<15mm/h)	120		83		20
AST (15-37 UI/L)	89	59	50	47	30
ALT (12-78 UI/L)	61	56	58	55	35
HbA1C (4-6%)	6.5				
Albumin (3.4-5g/dl)	2.5		2.3	2.5	3.7
Total protein (6.4-8.2g/dl)	5.4				7.5
Bicarbonate (22-28mmol/L)	20.3	18.4	21.6		
Potassium (3.5-5.1mmol/L)	3.3	3.4	3.7	3.4	
Na^+ (135-145mmol/L)	131	134.1	139	144	
Cl^- (95-105mmol/L)	98	102	100		
Diuresis (ml/hour)	100	300	250		145
Ph (7.35-7.45)	7.39	7.40	7.38		

Discussion

Leptospirosis is a well-defined clinical condition, caused only by Leptospira interrogans. Its clinical manifestation can range from mild forms to full blown life-threatening condition. The kidney is one of the favorite target organs of this spirochetal infection, hallmarking the complicated scenarios of this disease (2,5). AKI is usually non-oliguric and hypokaliemic. Other vital organs affected by the infection are liver, lungs, brain, blood and rarely heart.

Fortunately, kidney injury is well managed with supportive measures, medical therapy and dialysis, in contrast to the other interested organs involved in the course of the disease, which can be treated only by conservative therapy. Thus, great importance is given to the renal therapy which can modify the natural history of the condition. It is well proven that AKI is a marker of severity and strongly correlates with increased mortality. Renal replacement therapy is a last resort measure to deal with the failing kidney (6,7). However, physicians involved in the complex management of this high risk patients should not hesitate to start early dialysis as needed. Oliguria, elevated BUN and creatinine on admission should prompt medical staff for the need of early renal therapy and take logistic measures accordingly. The approach to this condition is complex and requires multispecialty involvement, i.e. presence of an infectionist,

nephrologist and neurologist early in the course of the disease which helps for a timely diagnosis, appropriate treatment and avoidance of time consuming and expensive examinations.

Paradoxically, hypokalemia is a frequent feature of the condition even in the setting of acute kidney injury encountered in 45-74% of cases. The mechanism underlying this finding is explained by the potent inhibitory effect of the leptospira endotoxin on renal Na±K ATPase, which may subsequently affect the apical located Na±K±Cl co-transporter (8,9).

Antibiotic therapy is a mainstay of treatment with the third generation cephalosporin or ampicillin, which is equally effective in severe cases. Earlier treatment with antibiotic therapy is better. Doxycycline may be used in less severe cases or as oral prophylaxis.

Conclusion

This case should alert physicians to include leptospirosis in the top list of differential diagnosis in patients with fever, thrombocytopenia, AKI (acute kidney injury) and hyperbilirubinemia. Early diagnosis, antibiotic therapy, supportive measures and dialysis are the treatment mainstay of this condition. Patients should be referred to a tertiary care center with capabilities of managing several complications that can occur during the course of the disease.

Conflicts of interest: None declared.

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