

Acute Renal Failure in a Patient with both Leptospirosis and Dengue Fever

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Abstract

The spectrum of tropical nephropathies includes Acute Renal Failure (ARF) or Acute Kidney Injury (AKI) due to infective agents that are endemic in the tropics which include *Leptospira* (LS) and Dengue Viruses (DV). The major histological feature is Acute Tubular Necrosis (ATN).^{1,2}

We report the case of a patient who presented ARF with co-infection with both agents. The clinical manifestations were consistent with both diseases. A renal treatment was supportive and the outcome was positive.

We conclude that co-infection with these two tropical agents was possible. It may have been overlooked when the diagnosis of one

agent was confirmed, especially that aware of the possibility of co-infection, as the management may be different. Spontaneous full recovery in these circumstances is still possible with supportive treatment.

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Introduction

Leptospirosis is a widely distributed disease caused by several serotypes (over 250 serotypes) of *leptospira interrogans*. It is an uncommon cause of ARF in western countries,^{3,4} but is a major cause of in some tropical countries. It is reported to account for about 24% of all cases of ARF in South East Asia.^{5,6}

Leptospirosis is caused by pathogenic spiral bacteria belonging to the genus *leptospira*.^{7,8} The pathogen enters the body via the skin and/or mucosa. It multiplies in the blood and spreads to other parts of the body particularly the liver and kidneys.⁹ In the kidney it causes interstitial nephritis and/or tubular necrosis.¹⁰ Liver involvement consists of centrilobular necrosis with proliferation of Kupffer cells. Jaundice occurs as a result of hepatocellular dysfunction.^{11,12} The incubation period is usually 7-12 days.

Dengue fever is the most common arthropod-borne viral infection in humans: with approximately 150,000 deaths annually, dengue is now the tenth leading cause of death worldwide; there are approximately 80-100 million new cases annually worldwide¹³ and approximately 40% of the world's population live in area at risk for dengue.¹⁴⁻¹⁶ ARF Occurs in 5% of patients with dengue fever, it is mainly due to ATN.

We report the case of a patient with both infections. He had an excellent recovery with supportive measures.

Case report

A 41 year old gentleman presented to a private hospital with complaints of fever, generalized body aches, myalgia, fatigue and anorexia for a duration 3 days.

Investigations at that hospital showed deranged renal functions, deranged liver function tests and mild thrombocytopenia. Hemorrhagic fever was suspected and the patient was referred to our hospital for further investigations and treatment including hemodialysis.

He does not have history of a significant medical illness. The symptoms occurred one week after his return from trip to Thailand, where he stayed for 2 weeks. During his stay there, he undertook open air activities including kayaking.

On examination, the patient was conscious and oriented, he was looking mildly jaundiced. The temperature was 37.4 degree Celsius. The blood pressure was 150/70 mmHg. The pulse was 70/minute and regular. The examination of the chest, heart and abdomen was unremarkable.

Investigations showed hemoglobin of 12.6 g/dL (N: 14-18 g/dL), a platelet count of 122,000 cells/mm³ (N: 150-450 cells/mm³) and a leukocyte count of 9,300 cell/mm³ (N: 3.6-11.5 cell/mm³), renal functions were grossly deranged with a serum creatinine of 622 umol/L (N: 60-120 umol/L) and a blood urea of 19 mmol/L (N: 3.3-7 mmol/L). The liver functions were also deranged with a serum albumin of 22g/L (N: 35-50 g/L), a total bilirubin of 36umol/L (N: 3-17 umol/L) and alanine transpeptidase (ALT) of 116 iu/L (N: 10-60 iu/L). The coagulation screen was normal with prothrombin time of 10 secs. (N: 9.3-11.7 secs.), activated partial thromboplastin of 28.8 secs. (N: 27.2-39.1 secs.) And thrombin time of 13.2 secs. (N: 12-16 secs). Urine dipstick showed specific gravity of 1.015 (N: 1.003-1.03), mild leukocyturia 25+ leuco/ul., mild protein of 25+ mg/dl. with mild blood 10 Ery/ul and urobilinogen of 2+mg/dL.

Urine and blood cultures were negative. Serology for hepatitis B virus, hepatitis C virus, hepatitis A virus and HIV was negative. Serology for brucellosis was negative and a blood film for malaria was negative. The serology for Dengue Fever (DF) came as positive for IgM antibodies. The titres of the IgM antibodies were as follows: *Leptospira Icterohemorrhagiae* 100, *Leptospira Canicola* 400, *Leptospira Grippityphosa*, *Leptospira Pyrogens* <100, *Leptospira Pomona* <100, *Leptospira Hebdomadis* <100, *Leptospira Australis* 800, *Leptospira Sejroe* 800 and *Leptospira Patoc* 3200 (the positive threshold is set at 100).

The above investigations were diagnostic of DF and Leptospirosis with ARF, liver derangement and thrombocytopenia.

Treatment was supportive with good hydration, antibiotic, with a third generation cephalosporin, was added later. Dialysis and a kidney biopsy were contemplated but deferred then declined due to rapid clinical improvement of patient.

The condition of the patient started to improve, he became a febrile 2 days after admission, he was passing good amount of urine. The serum creatinine was 113umol/L. on the fourth day of admission, platelets normalized on the third day and liver function tests were normal on the fifth day.

The patient was discharged after 5 days of admission with almost normal condition, he was complaining of residual fatigue that further improved on subsequent control visits.

Discussion

Tropical Nephropathy is a generic term for a spectrum of pathology that occurs mainly and/or frequently in the tropics. LS and DF are seen worldwide but distributed diseases that occur more frequently in the tropics.

Leptospirosis was first recognized as an occupational disease of sewer workers in 1883, Inada et al identified the causal agent in Japan in 1916.⁷ Leptospirosis is caused by pathogenic spiral bacteria belonging to the genus *leptospira* which are finely coiled, thin, motile obligate, slow growing anaerobes. Leptospirosis is zoonoses that are provoked by a bacterium of the *leptospira* genus and of the interregna's species. The man is an incident host, the natural hosts being mammals, mainly rodents, cattle and dogs. Man is infected through the exposure to animal's urine. The bacteria penetrate the body through the skin and mucosa. Risk factors for contamination are occupational such as farmers and sewer workers. Household exposure and recreational activities in fresh water such as swimming. The patient under discussion had been to Thailand, a known endemic area, and had fresh water recreational activities (kayaking).

Dengue fever is an arthropod (*Aedes egypti* mosquito) born viral disease. The disease is widely distributed with predominance in the tropics mainly in Asia, Africa, central and south America. The disease is increasing in prevalence. The incubation period is 5-6 days. Usually it is a self limited disease but may have a complicated course in some patients. The patient under discussion returned to Oman one week before the appearance of the symptoms. It is a possible that the mosquito bite had taken place in Thailand. However, having the bite in Oman would also be quite possible, especially that the DF is reported in a patient who did not travel outside Oman. The clinical presentation of both diseases is similar in the vast majority of cases. It consists of fever, rigors, myalgia, fatigue, and headache. Conjunctival suffusion would be a sign that favors Leptospirosis while a skin rash would orient more towards DF. The patient presentation was dominated with the above mentioned elements without a rash or conjunctival suffusion. The initial laboratory investigations showed hepatic involvement with high serum bilirubin, high serum ALT and low albumin. The coagulation screen was normal. The platelet count was slightly low at 122×10^9 (N: $150-450 \times 10^9$) there was no hyperleucocytosis. As an opinion, the low albumin would indicate a disease of some day's duration and by that would be due to Leptospirosis. The low platelet count would rather be due to the DF. Nevertheless, both of these elements could occur in both diseases.

Acute renal failure secondary to acute tubular necrosis is reported in complicated cases of both Leptospirosis and DF. Other forms of acute kidney injury include interstitial nephritis and thrombotic microangiopathies. The patient under discussion presented with acute renal failure that improved before the biopsy was performed. He most probably had acute tubular necrosis or acute interstitial nephritis. The treatment in these circumstances includes supportive measures, antibiotics in the case Leptospirosis and hemodialysis. The patient condition improved with supportive measure. Hemodialysis was contemplated, but the improvement of the renal function abrogated this option. Antibiotic was administered after the diagnosis of Leptospirosis was confirmed. The recovery was complete.

The diagnosis of both infections was confirmed by serology. The high titer of *Leptospira Patoc* IgM indicates recent Leptospirosis. Also positive IgM for DF indicates a recent DF infection.

Polymerase chain reaction was not performed. We think that the serology, in spite of not being of an absolute value, is confirmatory in view of the epidemiological and clinical context of the patient.

Conclusion

In conclusion, the clinician should be aware that co-infection with DF, and Leptospirosis is possible. The condition may lead to

ARF. Recovery with supportive measures is still possible in these circumstances.

References

1. Nissenson AR. Acute Renal Failure: definition and pathogenesis. *Kidney Int* 1998;66:7-10.
2. Aboud O. Tropical Acute Renal Failure. *CIN* 2003.
3. Kennedy ND, Puesy CD, Rainford DJ, Higginson A. Leptospirosis and Acute Renal Failure in clinical experience and a review of literature. *Postgrad Med* 1979;55:167.
4. O'Neill PG, Christie M, Cahill J, Duffy B. Leptospirosis and renal failure—clinical experience over a one year period. *Ir J Med Sci* 1982 Nov;151(11):339-342.
5. Sitprija V. Renal involvement in human Leptospirosis. *Br Med J (Clin. Res)* 1968; 2:656.
6. Lai KN, Aarons I, Woodroffe AJ, Clarkso AR. Renal lesions in Leptospirosis. *Aust NZM Med* 1982;12:267.
7. Green J, Hshoff W. Leptospirosis in humans: E medicine. *Web Med*.
8. Cacciapuoti B, Ciceroni L, Maffei C, Di Stanislao F, Strusi P, Calegari L, et al. A waterborne outbreak of leptospirosis. *Am J Epidemiol* 1987 Sep;126(3):535-545.
9. Communicable disease surveillance and response. Clinical diagnosis, treatment, prevention and control. 2nd ed. Geneva, WHO, C 2004 (cited 2005 March 24).
10. Raoult D, Jeandel PL, Mailloux M, Rougier Y. Thrombocytopenia and renal failure in leptospirosis. *Am J Trop Med Hyg* 1983 Nov;32(6):1464.
11. Edwards CN, Nicholson GD, Everard CO. Thrombocytopenia in leptospirosis. *Am J Trop Med Hyg* 1982 Jul;31(4):827-829.
12. Pecchini F, Borghi M, Bodini U, Copercini B, Grutta d'Auria C, Romanini GL, et al. Acute renal failure from leptospirosis: new trends of treatment. *Clin Nephrol* 1982 Sep;18(3):164.
13. Barsoum R, Sitprija V. Tropical Nephrology. In *Disease of the kidney*. 6th Edtion. (City), 1996: p. 2221- 2268.
14. Chin J. Control of communicable diseases. Manual 17th Ed. Washington, DC: American public health association.
15. Jelinek T. Dengue fever in international travelers. *Clin Infect Dis* 2000 Jul;31(1):144-147.
16. World Health Organization. The world report 1998. Geneva: WHO.