Leptospirosis: a re-emerging infection
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1. Introduction

Leptospirosis is a worldwide zoonosis of great public health importance in the tropics[1–4]. It is considered primarily a disease that affects sewage workers, or encountered as a disease that threatens mankind during and after floods. Infection may be asymptomatic, but 5 to 15% of cases can be severe and fatal[4]. Most cases go undiagnosed because symptoms and signs are non-specific, and may resemble any other acute febrile illness. Failure to diagnose leptospirosis is particularly unfortunate as even severely ill patients often recover completely with prompt treatment, but if therapy is delayed or denied due to lack of diagnosis, death is likely. The presented case highlights the need for a high index of suspicion of leptospirosis in patients presenting with acute febrile illness with jaundice and organ failure, particularly in urban areas during and after monsoon.

2. Case report

A middle aged housewife presented with a febrile illness for 20 d, accompanied by jaundice for 15 d, swelling of lower limbs for 5 d, a rash on both lower limbs for 3 d and altered sensorium for 2 d. Fever was documented to be 102–103 °F. Jaundice was gradual in onset, progressive, associated with dark yellow colored urine but no pruritus. Edema in legs was symmetric and pitting, and progressed to involve abdomen. Altered sensorium was sudden in onset and associated with bowel and bladder incontinence. Although, there was a petechial rash on lower limbs for 3 d, there was no history of bleeding from any other site. There was no previous history of significant illness or hospitalization, therapeutic drug intake (except for the present illness), blood transfusion, drug abuse, or sexual promiscuity. Personal, family, menstrual & obstetric histories were non-contributory. On examination, patient was in a state of altered sensorium (E2V3M5), febrile (102 °F), jaundiced and had bilateral symmetrical pitting pedal edema. There was no cyanosis, clubbing or lymphadenopathy. A symmetrical petechial rash was present on both lower limbs up to the knees. Blood pressure was 130/86 mmHg, pulse rate was 76/min. Abdomen was distended with free fluid, but there was no tenderness or organomegaly. Pupils were
3. Discussion

Leptospirosis is a zoonosis with protean manifestation caused by the spirochete, *Leptospira interrogans*. Leptospirosis infection is transmitted to humans through direct or indirect contact of mucous membranes or skin abrasions with urine from infected animals or contaminated freshwater surfaces, including mud or water in lakes, rivers, and streams. Ingestion or inhalation of contaminated water or aerosols may also result in infection [5-8]. Leptospirosis manifests with a wide clinical spectrum from asymptomatic infection to severe form of Weil’s disease. Most infections are asymptomatic or mildly symptomatic and self-limiting[9,10]. Clinical leptospirosis typically manifests with a biphasic course, with an acute phase (anicteric form) lasting approximately 1 week followed by the immune phase characterized by antibody production and leptospiruria. However, only a minority of patients develop such biphasic illness. Patients present with fever of abrupt onset, headache, myalgias localized mainly in calves, conjunctival suffusion, photophobia, nausea, and vomiting[11,12]. Icteric leptospirosis (Weil’s disease) develops in 5%-10% of clinical leptospirosis cases. This multisystem illness has a rapidly progressive and often fulminating course characterized by jaundice, hemorrhage, and acute renal failure. In many cases, two phases of the disease are not apparent. In addition many patients present only with onset of the second phase of illness.

Serology is the most commonly used diagnostic method for leptospirosis worldwide. The microscopic agglutination test (MAT) is the reference method. MAT is time consuming, requires significant expertise, and may be subjected to performance variations among laboratories and personnel[13,14]. An increase in liver enzymes (up to five times normal) with a disproportionately high total bilirubin has been described as a prognostic indicator in leptospirosis[15]. The immunoglobulin (Ig) M enzyme-linked immunosorbent assay offers the advantage of providing results rapidly; however, IgM antibodies are detected 5 to 7 d following the onset of illness. As a rule, both conventional and rapid antibody detection tests are of limited value during the first week of illness; however, they diagnose leptospirosis afterward with a sensitivity of at least 85%[16]. Polymerase chain reaction (PCR) may acutely and rapidly diagnose leptospirosis using sera and urine specimens from the first week of illness, including cases with antibiotic administration. Recently, a real-time PCR assay was developed targeting the *lipL32* gene conserved among pathogenic *Leptospira* serovars and was associated with high sensitivity and specificity for detecting leptospiral DNA in sera and urine[17]. Culture of leptospires in clinical specimens takes several weeks and is of low sensitivity and thus of no value in the management of cases.

Currently, doxycycline, ampicillin, amoxicillin, erythromycin, and azithromycin are recommended for less severe cases, whereas penicillin G, ampicillin, cefotaxime, and ceftriaxone are the drugs of choice for severe disease.

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**Table 1**

<table>
<thead>
<tr>
<th>Summarized investigations during course of illness.</th>
<th>Day 1</th>
<th>Day 4</th>
<th>Day 9</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb (gm/dL)</td>
<td>10.0</td>
<td>9.0</td>
<td>8.3</td>
</tr>
<tr>
<td>TLC (/mm$^3$)</td>
<td>6800</td>
<td>7400</td>
<td>16200</td>
</tr>
<tr>
<td>DLC (N/L/M) %</td>
<td>70/26/4</td>
<td>63/36/1</td>
<td>90/10</td>
</tr>
<tr>
<td>PLT (/mm$^3$)</td>
<td>100000</td>
<td>120000</td>
<td>100000</td>
</tr>
<tr>
<td>RBS (mg/dL)</td>
<td>81</td>
<td>126</td>
<td>75</td>
</tr>
<tr>
<td>Urea/Creatinine (mg/dL)</td>
<td>49/1.2</td>
<td>108/1.0</td>
<td>210/2.1</td>
</tr>
<tr>
<td>Bilirubin (T/D) (mg/dL)</td>
<td>16 (12/4)</td>
<td>18.5 (15/3.5)</td>
<td>23 (14/9)</td>
</tr>
<tr>
<td>AST/ALT/ALP (U/L)</td>
<td>206/98/237</td>
<td>165/80/137</td>
<td>117/53/164</td>
</tr>
<tr>
<td>Protein (T/A/G) (g/dL)</td>
<td>6.3/3.0/3.3</td>
<td>6.1/2.6/3.5</td>
<td>5.2/2.6/2.6</td>
</tr>
<tr>
<td>Na/K (meq/L)</td>
<td>130/5</td>
<td>140/3.3</td>
<td>150/5.6</td>
</tr>
<tr>
<td>Ca/P (mg/dL)</td>
<td>8.9/2.3</td>
<td>8.1/3.5</td>
<td>7.5/5.6</td>
</tr>
</tbody>
</table>

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Symmetrical and reacting to light. There were no signs of meningeal irritation or focal neurological deficit. Rest of general and systemic examinations was normal.

Investigations (Table 1) showed anemia, thrombocytopenia, altered liver and renal function and deranged coagulation profile (PT: 46.3 s, INR: 3.89, APTT: 68 s s). Ultrasound of abdomen showed only free fluid that was a transudate. A plain CT scan of head was normal. CPK was raised (605 U/L). Blood culture and urine culture were sterile; viral markers, ANA, RF, Malaria Antigen and Dengue serology were negative but Leptospira serology (IgM) was positive. Severe leptospirosis with liver and failure and encephalopathy was diagnosed and treated with ceftriaxone and other supportive measures. However, on the fourth day of admission, the patient developed acute respiratory failure and her condition worsened. Patient was given methyl prednisolone and provided ventilator support. A liver transplant was advised and considered but could not be done due to numerous constraints. Patient died on the ninth day of hospitalization.
Ceftriaxone and penicillin G appear to be equally effective for the treatment of severe leptospirosis; however, the former offers the advantage of once-daily administration compared with every 6 h administration of penicillin[4,18,19]. Several case reports have described the beneficial effects of glucocorticoids in severe leptospirosis with pulmonary hemorrhage, thrombocytopenia and renal failure[20–23]. It is important that family physicians have a high index of suspicion, especially during monsoon, and in urban areas with poor drainage. The present patient was a resident of Eastern part of the city, notorious for flooding every year during monsoon. A high index of suspicion should not however be considered as an excuse for empirical use of the mentioned antimicrobials, except in life threatening situations. Rather, possibility of exposure should be part of historical exercise in all febrile cases during the monsoon season, and clinical work-up of such cases should include investigations for leptospirosis.

**Conflict of interest statement**

We declare that we have no conflict of interest.

**References**