A Rural South Indian Experience with Weil’s Syndrome: Case Report and Review

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ABSTRACT

Leptospirosis caused by bacteria of genus Leptospira has recently come to international attention as a globally important re-emerging infectious disease. Our case is unusual given the season, location and setting in which leptospirosis occurred. According to previous studies, leptospirosis was first reported from the Andaman Islands in 1929, and has since affected all parts of India. The highest positivity rate of 25.6% has been reported from southern India. A 45-year-old healthy rural man presented to our hospital with fever of intermittent type, with associated chills and rigor, vomiting, burning maturation, general muscular pain and multi-organ failure. The patient was treated initially with empirical antibiotics and other symptomatic medicines for suspected diagnoses with similar symptoms, diseases such as viral hepatitis, dengue fever, malaria, typhoid and leptospirosis. On the day of admission, the patient’s hemoglobin was 10.1 gm/dl but fell to 6.2 gm/dl after three days. The patient did not respond to antibiotics and his multi-organ failure worsened. The diagnosis was confirmed based on physical and laboratory investigations, which included blood tests, liver function tests, and kidney function tests. He responded to doxycycline and cofopodoxime proxitil and recovered after a course of these antibiotics. The case of Weil’s syndrome presented here should serve to alert health care providers and the general public to the clinical importance of this severe, sometimes fatal, disease. Leptospirosis should be considered early in the diagnosis of any patient with acute, non-specific febrile illness with multi-organ system involvement or high fever in a returning traveler.

KEYWORDS: Leptospirosis, Weil’s syndrome, zoonotic disease
INTRODUCTION

Leptospirosis is a zoonotic disease (1). It is also known by different names such as Weil's syndrome, canicola fever, canefield fever, nanukayami fever, 7-day fever, Rat Catcher's Yellows, Fort Bragg fever, black jaundice. It is caused by a bacteria belonging to the genus Leptospira (2). It has been diagnosed in humans for over a century and is responsible for significant morbidity and mortality globally (3). The most common medium for its spread is primarily water containing the urine of the infected animals. Soil and food are other vehicles responsible for the spread of infection. The main carriers of bacteria are rodents, livestock and dogs. Its associated symptoms include acute febrile illness, occurring secondary to a subclinical infection which might progress to severe syndrome of multi-organ dysfunction (Weil’s disease), especially during the monsoon season which warrants screening of such patients. Symptoms of Weil’s disease comprise of fever, jaundice, renal failure, cardiovascular collapse, hepatic necrosis, pulmonary problems, neurologic changes and hemorrhagic diathesis due to multiple organ failure (2, 3). Sero-diagnosis by a microagglutination test (MAT) is an ideal test to be employed as a detection test. However, its availability is limited. Other tests that help in the easy detection are the latex agglutination test and IgM ELISA (4).

In India, leptospirosis has been primarily reported in the southern and western part of India in the states of Gujarat, Maharashtra, Kerala, Tamil Nadu, Andhra Pradesh, Karnataka and Andamans. Some cases have also been witnessed in Goa and Orissa (5, 6). It is not age or gender specific. India has a very long coastline (8,129 km) with abundant natural resources that supports the agrarian economy. The ecosystem along the coast is not very stable and the emergence of various zoonotic diseases is a consequence. This emergence in the form of epidemics leads to fatality in large numbers. Some of the important factors induced by humans that have brought about changes in the ecosystem causing reemergence of leptospirosis from time to time are afforestation, use of modern agricultural and irrigation techniques and reuse of wastelands (4).

Table 1: Summary of organs affected in Weil’s syndrome

<table>
<thead>
<tr>
<th>Organ</th>
<th>Clinical features</th>
<th>Investigations revealed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney</td>
<td>Decrease in urine output, features of uraemia.</td>
<td>Increase in serum creatinine and blood urea.</td>
</tr>
<tr>
<td>Liver</td>
<td>Jaundice, hepatomegaly</td>
<td>Increase in serum bilirubin with normal or mildly elevated SGPT (ALT) and SGOT (AST) and increased CPK</td>
</tr>
<tr>
<td>Lungs</td>
<td>Cough, haemoptysis, dyspnoea with increase in respiration rate and basal creps</td>
<td>X ray chest showed lower and mid zone opacities.</td>
</tr>
<tr>
<td>Heart</td>
<td>Hypotension, irregular pulse</td>
<td>ECG revealed type of arrhythmia</td>
</tr>
<tr>
<td>Blood</td>
<td>Bleeding tendencies</td>
<td>Decrease in platelet count</td>
</tr>
<tr>
<td>Brain</td>
<td>Altered consciousness with neck rigidity</td>
<td>CSF showed increase in cells, protein, normal sugar</td>
</tr>
</tbody>
</table>
EPIDEMIOLOGY OF LEPTOSPIROSIS (WORLD AND AN INDIAN SITUATION)

The current incidence of leptospirosis is not completely known. According to estimates, 0.001% people develop leptospirosis in temperate climate whereas 0.01% people in tropical climate develop it. In case of an epidemic, the incidence can go as high as 0.1% (3, 4). The first case of leptospirosis was reported in the Andaman Islands in 1929 and since then, it has been reported in different parts of the country. Leptospirosis is a health concern in India and different parts of India have different positivity rates with the highest being in South India (25.6%) followed by north (8.3%), west (3.5%), central (3.3%) and east (3.1%) India.

National incidence data are not available but leptospirosis has been recognized as a major health problem. The highest positivity rate of 25.6% has been reported in southern India. The reported positivity rates are 8.3%, 3.5%, 3.1% and 3.3% in northern, western, eastern and central India, respectively (8). In Chennai, a city in the southern state of Tamil Nadu, among the cases getting treated for pyrexia of unknown origin (PUO) in healthcare facilities, the incidence of leptospirosis can go as high as 38% during the monsoon season (1).

CASE REPORT

On 28 October 2011, a 45-year old male patient came to the department of medicine, an outpatient department (OPD) in RMMC and H Annamalai University located in Chidambaram, Tamil Nadu. The patient came with the following symptoms: intermittent-type fever associated with chills and rigor, vomiting, burning micturation and general body pain. His fever was high grade at the time of admission with general weakness and inability to walk. The patient had a medical history of fever and rigors for the past 3 days and was being treated for it without his medication history being known. Upon examination on the date of admission, the following observations were made: patient was conscious, oriented, ran a temperature of 104 °F, blood pressure of 120/90 mm Hg, with pulse of 80/min. Hemoglobin was 10.1 gm/dl on 28 October 2011, which went down to 6.2 gm/dl by 2 November 2011.

At the time of admission, the patient was empirically treated with ceftriaxone 2 gm and paracetamol 650 mg tablets, as well as injections of pantaprazole 40 mg and ondansetron 4 mg. On the next day (29th October, 2011) the patient was treated with chloroquine 500 mg and intravenous fluid (IVF) consisting of dextrose and normal saline. On the 30th October, 2011, a suspected diagnosis of viral hepatitis and leptospirosis were made. On the 31st October, 2011, since leptospirosis was suspected, doxycycline 100 mg was added to the therapy. On the 2nd November, 2011; pyrimethamine 25 mg and sulfadoxine 500 mg were added to the treatment regimen as well. Sonogram report showed splenomegaly. Test for typhoid, malaria and hepatitis were negative. The final diagnosis of leptospirosis was made on the 3rd November, 2011 based on decreasing platelets counts, increased serum urea serum creatinine, bilirubin and alkaline phosphate (ALP) levels. Hence, tablets cefopodoxime proxitiil, doxycycline, pantaprazole, capsules B. complex and paracetamol 650 mg and syrup sucralfate were prescribed for 7 days.
Table 2: Showing laboratory investigation of the patient and reference value

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Investigation</th>
<th>Test Value</th>
<th>Normal Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Platelet</td>
<td>$73 \times 10^{-3}$</td>
<td>$150-450 \times 10^{-3}$</td>
</tr>
<tr>
<td>2</td>
<td>ALP</td>
<td>222 U/L</td>
<td>35-45 U/L</td>
</tr>
<tr>
<td>3</td>
<td>Serum urea</td>
<td>50 mg/ dl</td>
<td>15-40 mg/dl</td>
</tr>
<tr>
<td>4</td>
<td>Serum Creatinine</td>
<td>1.45 mg/dl</td>
<td>0.6-1.2 mg/dl</td>
</tr>
<tr>
<td>5</td>
<td>Hemoglobin</td>
<td>6.2 gm/ dl</td>
<td>13-17 gm/dl</td>
</tr>
</tbody>
</table>

Abbreviations: mg/dl = milligrams per deciliters, gm/dl = grams/deciliters, U/L = units per liter

**DISCUSSION**

The sero-prevalence of leptospirosis in patients with acute febrile illness has been studied less often in northern as compared to southern India. Leptospirosis is a very rare disease. Weil’s syndrome is considered the most common zoonotic infections in the world and has recently been recognized as a re-emerging infectious disease among animals and humans and has the potential to become more prevalent with anticipated global warming (1,2).

Traditionally considered to be a disease of sewage workers, miners and farmers, leptospirosis is now recognized as one of the common causes of acute febrile illness in the general population. Deodhar et al, found that 31% patients had serological evidence of leptospirosis (9). Leptospirosis peaks during the monsoon and post-monsoon months, and occurs more commonly where poor sanitation and low hygienic conditions are prevalent (9). In the past decade, it has been reported from all parts of urban and rural India (10). This patient was admitted in the month of October which is rainy season in Tamil Nadu and mainly works as a farmer and he has several cattle at home. The patient’s home also is close to coastal area, and frequently boating and swimming in the sea. The transmission of human leptospiral infections results primarily from direct or indirect exposure to the urine of infected animals. Moisture is an important factor for the survival of the leptospires in the environment. Other modes of transmission of infection, such as handling infected animal tissues and ingestion of contaminated food and water, are also possible (3, 9). The patient’s history was taken according to the Leptospirosis Case Report form provided by the State of California Health and Human Services Agency, United States of America (11).

Leptospira are flagellated thin, motile organisms having spiral shape. The most common serovars which are usually found in rats (Rattus norvegicus) are Licterohaemorrhagiae. Most significant source of Leptospira sp. is the urinary shedding of organisms from infected animals because the spirochetes can persist for long periods of time in the renal tubules (12).

The natural course of leptospirosis comprises of two distinct clinical phases: septicemia and immune. Humans typically become ill seven to twelve days post exposure to leptospires. During the first stage, bacteria may be isolated from
blood cultures and cerebrospinal fluid (CSF) therefore; it is referred to as septicemia phase (leptospiremic phase). This phase is characterized by a nonspecific flu-like illness with sudden onset of high fever, headache, myalgias (classically involving the paraspinal, calf and abdominal muscles) and conjunctival suffusion (12). Conjunctival suffusion (reddening of the eye surface) is a characteristic physical finding in leptospirosis, and its presence in a patient with a nonspecific febrile illness should raise suspicion for diagnosis.

In the second stage circulating antibodies can be detected and the bacteria can be isolated from the urine therefore, it is called as immune phase (leptospiruric phase). This stage occurs as a result of the body’s immunologic response which leads to production of immunoglobulin M antibodies and duration can be of more than one month. Specific organ damage can be observed during this stage. During the immune phase, one of the most important clinical syndromes that can occur in 80% of patients is aseptic meningitis. Renal symptoms, including uremia, azotemia, pyuria and hematuria, may occur. Pulmonary manifestations can range from minor issues such as chest pain, cough and dyspnea to serious issues such as pulmonary hemorrhage and acute respiratory distress syndrome. The important prognostic indicator in leptospirosis is the increase in liver enzymes (up to five times normal) with a disproportionately high total bilirubin (13). Therefore jaundice, pancreatitis, hepatomegaly and myocarditis of varying degree can also occur.

The most severe form of leptospirosis is the Weil’s disease. Patients can present with high fever (>40°C), significant jaundice, renal failure, hepatic necrosis, pulmonary involvement, cardiovascular collapse, neurologic changes and hemorrhagic diathesis, with a variable clinical course. Weil’s disease can occur at the end of the first stage and reach its peak during the second stage but can occur at any time during acute leptospirosis as a single, progressive illness (4, 12).

In developing countries, the major cause of death in patients with Weil’s disease is the particularly serious type of lung involvement called severe pulmonary hemorrhagic syndrome, with profuse lung hemorrhage dominating the clinical picture (14). Hepatic dysfunction is usually not severe in leptospirosis and reversible, but in severe leptospirosis, liver dysfunction can be seen as conjugated serum bilirubin levels may increase to above 80 mg/dl, accompanied by moderate elevations in transaminases, which rarely exceed 200 U/L (15). Thrombocytopenia of variable degree has been reported with leptospirosis, but the pathogenesis of thrombocytopenia and hemorrhagic diathesis in leptospirosis is not well understood. Overall, mortality rate by Weil’s syndrome is of 5% to 10%. The mortality is caused by mainly renal failure, cardiopulmonary failure and widespread hemorrhage (16).

The gold standard for diagnosis is isolation of the organism by culture of clinical specimens (blood, CSF, urine) during the first seven to 10 days of the illness. However, this method is tedious, requires more than 16 weeks because initial growth may be slow and has a low sensitivity and specificity. The majority of leptospirosis cases are diagnosed by serologic testing of which MAT is mostly used.

The benefit of antimicrobials in cases of mild leptospirosis without end-organ damage remains controversial, because of self-limiting nature of vast majority of infections with leptospira. The current treatment choice for mild leptospirosis includes oral doxycycline and amoxicillin. In cases of fulminant leptospirosis parenteral high-dose penicillin G has long been considered as the treatment of choice. Recent clinical trials have proved the acceptability of broad spectrum third
generation cephalosporins: cefotaxime and ceftriaxone agents for patients with severe leptospirosis (17, 18).

In order to prevent and reduce leptospirosis, public health measures should be taken which include identification of contaminated water sources, rodent control, prohibition of swimming in waters where the risk of infection is high, and informing persons of the risk involved in recreational water activities. In the case of our patient, the diagnosis of leptospirosis was not initially considered because at the beginning, potential risk factors were not identified. The majority of cases of leptospirosis occur in the tropical regions, with infrequent incidences in temperate regions.

The infection is often wrongly diagnosed due to the wide range of symptoms. This leads to a lower registered number of cases than exists. Symptoms of leptospirosis include high fever, severe headache, chills, muscle aches, and vomiting, and may include jaundice, red eyes, abdominal pain, diarrhea, and rash. Initial presentation may resemble pneumonia and viral hepatitis.

**CONCLUSION**

Leptospirosis is a reemerging disease in both the developing as well as the developed nations. Our case of fulminant leptospirosis presents information which will help healthcare providers learn more about the clinical nature of the disease. We recommend that patients with a fever for more than a week should get tested for leptospirosis. Leptospirosis associated mortality is a public health concern due to lack of rapid, reliable diagnostic test and prevalence of clinical suspicion. There is need for developing a quick and reliable diagnostic test for enhancing patient safety and public health. Antimicrobial treatment due to late detection of fulminant leptospirosis can decrease the severity and duration of the symptoms but this in turn, can lead to further increase in severity of fulminant leptospirosis.
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