INTRODUCTION

Leptospirosis is a spirochetal zoonosis of significant epidemiological importance to a country like India. It is presumed to be the most widespread zoonosis in the world. It is a tropical infection which leads to great degree of morbidity and mortality among the productive population of the country. There have been spurts of leptospirosis cases during the rainy seasons which have lead to epidemics and thus this disease warrants as much importance as any other tropical infection.

In the city of Mumbai post the deluge of 2005, leptospirosis has been constantly affecting the population in large numbers. In the tertiary care hospital of KEM hospital we see around 200 to 250 patients in each monsoon, with high mortality varying from 10-25%.

EPIDEMIOLOGY

Leptospirosis is caused by different serovars of spirochete Leptospira namely; Leptospira interrogans, icterohemorrhagica, grippotyphosa, biflexa, pomona, ballum, canicola, copenhagenii etc. These different serovars are found in different animals who act as reservoirs for them. These organisms shed the bacteria in their urine and contact of urine contaminated media with humans lead to infections in humans. Such media include animal bedding, soil, mud, water and aborted tissue. The presence of cattle in the house, drinking stream water, contact with garbage, walking barefoot and standing in water while working were identified as significant factors associated with leptospirosis.2,3

The organism enters the body via abraded skin or mucous membranes, such as the conjunctiva or alimentary tract. Occasionally, the organism may even enter the body through intact skin. Infection has also occurred after animal and rodent bites, after contact with abortion products of infected animals, and after ingestion of contaminated food and water. In Mumbai most patients are affected due to the exposure to contaminated water while wading through it in monsoon.

A case control study to explore the risk factors for acquisition of leptospirosis in Surat city, after flood by Bhardwaj et al4 factors identified associated with leptospirosis was walking barefoot in flood waters. They concluded that prompt and vigilant fever surveillance activities, intensive public messages, rodent control programs and improvement of environmental sanitary conditions may help to greatly reduce the incidence of leptospirosis.

CLINICAL FEATURES

Leptospirosis causes varied manifestations, in majority of affected people it leads to a subclinical infection. The classical picture of Weil's syndrome occurs only in severe cases.

It is a biphasic infection with initial acute phase of bacterimia which lasts for a week followed by immune phase characterized by antibody production and excretion of leptospires in the urine. This occurs in the second week of the infection.

The major number of patients who have subclinical infection usually do not seek any care and recover on its own. The rest manifest the disease in the form of an acute febrile illness. The fever may be associated with chills, severe myalgias, headache and conjunctival suffusion. Myalgia usually affects the lower back, thighs, and calves, is often intense and lead to local tenderness.

Severe cases often present late in the course of the disease, and this contributes to the high mortality rate, which ranges between 5 and 15%. This clinical stage of leptospirosis is also referred as the icteric phase. Jaundice may be severe with high bilirubin levels and may take weeks to recover, but only mild to moderate increase in transaminase levels is observed.

The complications observed in leptospirosis are usually multisystem. It can lead to acute renal failure (ARF), which can have both a prerenal and renal component. Diverse mechanisms are implicated in leptospiral nephropathy and new data supports the role of peculiar ion transport defects. The prerenal ARF responds to hydration. While the renal type might require hemodialysis for management.

Thrombocytopenia and other bleeding complications have also been observed in leptospirosis.

Most of the patients of leptospirosis who have pulmonary involvement have a very high mortality. The occurrence of pulmonary symptoms in cases of leptospirosis was first noted...
by Silverstein.\textsuperscript{14} The patient can have breathlessness, hemoptysis, cough and in severe cases acute respiratory distress syndrome (ARDS). Patients can have intraalveolar hemorrhages due to alveolitis which can be severe enough to lead to death. In a study by Paganin et al\textsuperscript{14} out of 169 patients with a laboratory-confirmed diagnosis of leptospirosis 134 patients had pulmonary involvement. Univariate analysis found the following factors related to severe pulmonary leptospirosis: dyspnoea, pulmonary crepitations, abnormal chest X Ray with alveolar shadowing, oliguria/anuria, hepatomegaly, shock, ICU admission, dialysis, mechanical ventilation and development of nosocomial infection. The mortality rate was significantly different between severe (40\%) and non-severe (5.3\%) pulmonary forms.\textsuperscript{14} In a study by Maneewatch et al,\textsuperscript{24} it was found that out of 53 patients treated with cyclophosphamide, 22 (66.7\%) survived, while in the control group out of 32 patients, three (9.4\%) survived.

Other rare complications in the form of acute demyelinating polyneuropathy, thrombotic thrombocytic purpura, acalculous cholecystitis, rhabdomyolysis etc. have also been reported.

LABORATORY DIAGNOSIS

Leptospirosis is mostly diagnosed with the help of serology, the formation of antibodies requires at least 5-7 days after symptom onset. Microscopic agglutination test (MAT) is the reference method for serological diagnosis. Because of the complexity of the MAT, rapid screening tests for leptospiral antibodies in acute infection have been developed, ELISA test to detect antibodies have mostly replaced MAT in clinical practice. IgM dot ELISAs are usually used as rapid diagnostic tests.

As is stated earlier these antibodies take at least a week to develop in the body of the patient, thus in patients with initial negative results if suspicion is strong newer molecular diagnostic tests to detect DNA by polymerase chain reaction (PCR) is of significant value.

The major drawbacks with molecular diagnostics are the cost and expertise required in these tests.

MANAGEMENT

Treatment of leptospirosis is determined by the clinical status of the patient. Patient with mild febrile illness can be managed on outpatient care with oral antibiotics and adequate rest. While patient with jaundice and other complications like ARDS, ARF, hepatic encephalopathy, myocarditis may require intensive care management.

Oral doxycycline in the dosage of 100 mg BD for 7 days has been shown to decrease duration of fever and most symptoms.

Hospitalized patients should be treated with intravenous penicillin G therapy which is the treatment of choice. The dose is around 20 lac units 6hourly for 7 days. Third-generation cephalosporins are as effective as doxycycline and penicillin in the treatment of acute disease.\textsuperscript{4} New options, such as ceftriaxone, have a superior safety profile to penicillin. In vitro studies have outlined potential antimicrobial candidates such as macrolides and ketolides.\textsuperscript{18,19} In case of complicated cases with multisystem involvement patient may require ICU care.

In ARF, patient might require hemodialysis. Dialysis is the standard supportive therapy even though recent evidence suggests clinical benefit from alternative treatments such as plasmapheresis and hemofiltration.\textsuperscript{20} ARDS may warrant lung protective ventilation, inotrope support in case of hypotension and platelet transfusions in case of thrombocytopenia with bleeding having a significant role.

Injectable bolus therapy of methylprednisolone within 12 hours of presentation in the dose of 1 gram iv for 3-5 days has shown significant benefit in patients with ARDS in case of leptospirosis.\textsuperscript{17,20-22} The above mentioned strategies of management have shown to help and thus are adopted by us in our protocol as well. Trivedi et al\textsuperscript{23} treated pulmonary involvement with cyclophosphamide (60 mg/Kg single dose) in addition to methylprednisolone. They found that out of the 33 patients treated with cyclophosphamide, 22 (66.7\%) survived, while in the control group out of 32 patients, three (9.4\%) survived.

Jarisch-Herxheimer reaction caused by toxic bacterial substances massively released as a result of the antibiotic mediated-bacterial lysis occurs in some patients which may aggravate the existing severe clinical manifestations. In a study by Maneewatch et al,\textsuperscript{24} a humanized-murine single-chain monoclonal antibody (HuScFv) was produced and tested as an alternative of antibiotics for treatment of leptospirosis.

Prophylactic therapy for high-risk individuals or prompt diagnosis and early treatment (before 4 days of symptoms) appear to be cost-effective approaches to prevent severe complications of leptospirosis.\textsuperscript{25}

Doxycycline is commonly advocated for prophylaxis of leptospirosis Systematic review assessed Brett-Major et al\textsuperscript{26} showed that regular use of weekly oral doxycycline 200 mg increases the odds for nausea and vomiting with unclear benefit in reducing Leptospira seroconversion or clinical consequences of infection. Oral penicillin has also been evaluated for prophylaxis.\textsuperscript{37}

REFERENCES

Leptospirosis: An Emerging Infection


