CHAPTER

9

Leptospirosis in Current Status

Shobha Manish Itolikar

INTRODUCTION

India has taken giant strides in the field of medical science and we have cutting-edge technology available for the management of several ailments. But this advantage is restricted to non-communicable diseases; the same cannot be said about their communicable counterparts, which are posing a mammoth burden on our healthcare system. Compounding this problem is the re-emergence of long-forgotten diseases due to a conflux of environmental, socio-economic, and demographic factors like population pyramiding, poor sanitary infrastructure, deforestation, global warming and changing migration dynamics. One such disease which was sporadic till the eighties but subsequently became endemic in many Indian states and also caused major epidemics is leptospirosis.

CAUSATIVE ORGANISM

Leptospirosis is an acute anthropo-zoonotic disease of global importance. It is caused by the spirochete Leptospirosis interrogans complex which has 26 serogroups and over 250 pathogenic serovars. Even if most cases recover with mild infection, fulminant multi-organ dysfunction can occur in some cases. The causative pathogen belong to the class of spirochetes Leptospira which mainly consists of the species Leptospira interrogans and Leptospira biflexa.

EPIDEMIOLOGY

Leptospirosis, primarily a disease of animals, affects almost all mammalian species (wild, domestic, and farm animals): thus poses a significant veterinary burden. Rodents are the most important reservoir. Leptospires can persist in the host urogenital tract for years by establishing a symbiotic relationship. Soil salinity and alkaline pH favour survival of leptospires for several months and waterlogging favours dissemination of disease. Infection in humans occurs through contact of abraded skin and /or intact mucus membrane (especially conjunctiva and gut) with the urine, blood or tissue from infected animal, or with contaminated environment. Leptospirosis is more common in the 20-45 years age –group with male preponderance due to greater occupational exposure to infected animals and contaminated environment. Other high-risk groups are agriculture workers, sewer cleaners, livestock handlers, healthcare /veterinary professionals, military troops, sugarcane workers and those engaged in water-sports. According to the Modified Faine's Criteria (2004) search for epidemiological factors like rainfall, contact with contaminated environment and animal contact improves the diagnostic yield.

GLOBAL BURDEN

Leptospirosis occurs worldwide but is most common in tropical and subtropical areas which record high rainfall. Sporadic cases may be reported throughout the year. Incidences range from approximately 0.1–10 per 100 000 per year; it might reach over 50 per 10000 during outbreaks. Most cases have been reported from India, Indonesia, Thailand, Maldives and Sri Lanka. Epidemics in South-East Asia have been reported in the past in Jakarta (2003), Mumbai (2005) and Sri Lanka (2008).

INDIAN SITUATION

The endemic states are Gujarat, Maharashtra, Kerala, Tamil Nadu and Andaman-Nicobar Islands. Epidemic situations have arisen after natural calamities like flash floods (Mumbai 2005), cyclone (Orissa 1999) or due to spontaneous outbreaks like in Gujarat (2011). More recently, after the massive Chennai floods (2015), contrary to what was expected there was no significant spike in the number of case or deaths (1204 cases in 2015 compared to 3616 cases in 2011); attributable largely to the preparedness of authorities in the form of aggressive surveillance, prompt treatment, and initiation of chemoprophylaxis in exposed groups. Awareness and attitude of the healthcare provider is an important factor in controlling the magnitude of infection.

PATHOGENESIS

Weil's disease is the term employed for cases exhibiting a triad of bleeding, jaundice and renal failure, first described by a physician by the same name. Leptospira glycoprotein components or toxins could directly induce tissue damage by rapid induction of the inflammatory cytokine TNF-α. Host immunity also influences the disease outcome. In resistant hosts with mild symptoms, inflammatory responses occur rapidly to eradicate organisms and tissue damage is prevented. In those with inadequate immune response, inflammatory responses are delayed, leading to severe bacteremia. Such prolonged and massive immune response results in severe organ damage. After tissue invasion, the bacteria damage the microvascular endothelial linings leading to capillary leakage and severe hemorrhaging. Such damage results in injury to the proximal tubules (leading to renal interstitial nephritis), hepatocellular damage leading to jaundice, coagulopathy, liver failure and aseptic meningitis in the immune phase.

CLINICAL FEATURES

The incubation period ranges between 2-10 days. 85-90% of patients experience a self-limiting episode of influenza-like illness (anicteric leptospirosis). The

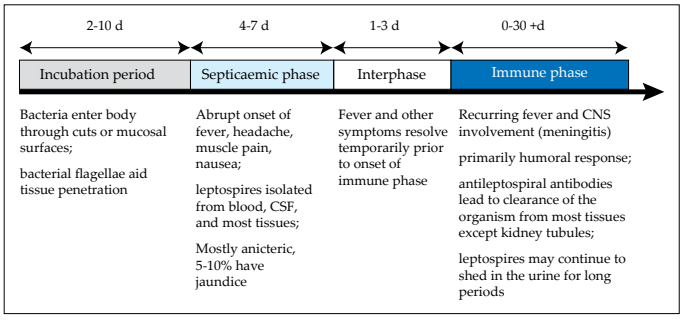
typical course consists of an acute septicaemic phase followed by the immune phase as shown in Figure 1. In the small proportion developing severe icteric leptospirosis or Weil's disease,, two phases are seen i.e. the leptospiremic phase characterized by remittent fever, headache, myalgia, vomiting, conjunctival suffusion and/or hepatosplenomegaly and an immune phase which coincides with the appearance of antibodies and is characterized by the onset of organ dysfunctions in the form of hepatocellular jaundice, acute interstitial nephritis, vascular collapse secondary to bleeding or myocarditis, acute lung injury or aseptic meningitis. Rarely encountered complications are cardiac arrhythmias, pericarditis, congestive heart failure, necrotising pancreatitis and uveitis.

Pulmonary haemorrhage, occurring as a consequence of vascular endothelial damage is almost always the cause of death.

DIAGNOSIS

Leptospirosis should be suspected in any patient presenting with an abrupt onset of fever, chills, conjunctival suffusion, headache, myalgia and jaundice. A high index of suspicion prompting elicitation of a detailed exposure history is critical and guides confirmatory testing.

Common hematologic abnormalities noted are leukocytosis (typical in severe disease), leukopenia, hemolytic anemia, mild to moderate anemia, and thrombocytopenia. Weil's disease is suggested by elevated levels of blood urea nitrogen and serum creatinine in conjunction with mixed hyperbilirubinemia with transaminase elevation (<200 U/L). Urinalysis may show abnormalities of sediments (leukocytes, erythrocytes, hyaline and granular casts). Elevation of the noncardiac isoform of creatine kinase may indicate skeletal muscle damage. On chest radiography, alveolar infiltrates predominate corresponding with hemoptysis but not purulent sputum. Other findings include diffuse interstitial infiltrate patterns suggesting acute respiratory distress syndrome and small nodular infiltrates and pleural-based densities representing hemorrhage. CSF shows elevated proteins, normal glucose and polymorph predominance (in early stages) and mononuclear cells (in the late stages).



Courtsey : Dr. Richard A. Collins, Hong Kong

Fig. 1: Typical course of Leptospirosis

SPECIFIC TESTS FOR LEPTOSPIROSIS

The various diagnostic approaches are depicted in Figure 2 with a brief description as follows:

1. Culture (Blood, Urine, CSF): Isolation of leptospires on culture gives definite proof of infection. It also helps in identifying the serovar. But it can be time-consuming, relatively insensitive, hence not useful for early diagnosis

2. Microscopy: Dark-field microscopy : This is useful for observing leptospires in culture, particularly when they are present in large numbers, and for observing agglutination in MAT. But this process demands good expertise to avoid false positive results due to fibrin threads.

3. Immunologic Methods:

a. Microscopic agglutination test (MAT)

Pros: Gold standard serologic test with a high specificity

Useful for epidemiologic surveillance

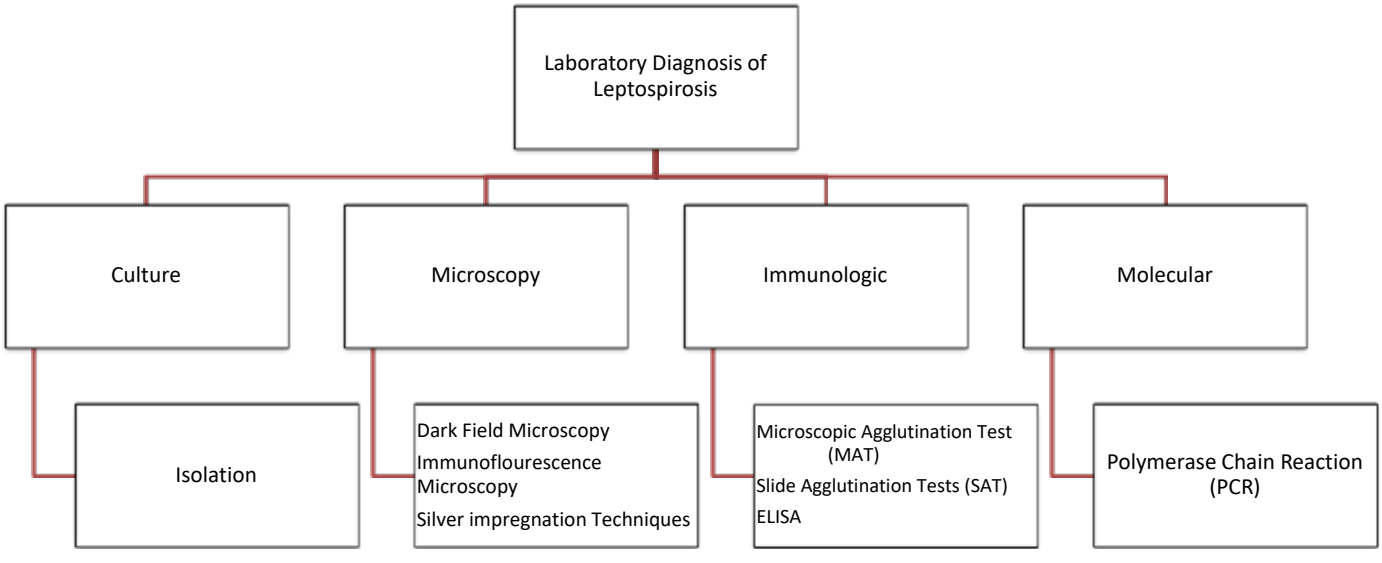


Fig. 2: Approach to laboratory diagnosis of Leptospirosis

Cons: MAT-detectable antibodies usually do not develop before seven days of illness.

Paired serum samples are needed often, which delays the diagnosis.

Less sensitive than MSAT and ELISA

b. Macroscopic Slide agglutination Test (MSAT)

Pros: More sensitive as initial screening test.

Simple, easy to perform

Cons: Less specific than MAT

c. IgM ELISA:

Pros: Simple, sensitive rapid test

Cons: Poor specificity

Not useful in early diagnosis

Cannot detect re-infection due to persistence of antibodies

4. Molecular diagnosis: Polymerase Chain Reaction

Pros: PCR can rapidly confirm the diagnosis in the early phase of the disease before antibodies are detectable.

Cons: It requires special equipment and skilled personnel.

Conventional PCR may give false-positive results in the presence contaminants and false-negative results due to the presence of inhibitors

DIFFERENTIAL DIAGNOSIS

When fever and severe myalgia predominate, influenza is often considered; other important possibilities include malaria, rickettsial diseases, arboviral infections (e.g., dengue and chikungunya), typhoid fever, Hantavirus infection (hemorrhagic fever with renal syndrome or Hantavirus cardiopulmonary syndrome), and viral hepatitis.

TREATMENT

Leptospires are susceptible to all clinically useful antibiotics expect chloramphenicol and rifampicin. Oral therapy with penicillin, doxycycline and azithromycin is recommended in mild cases. In severe cases, in addition to treatment with intravenous penicillin or ceftriaxone, specific therapy should be directed towards correction of organ dysfunction i.e. dialysis for renal injury, lung protective ventilation for ARDS, and fluid resuscitation for hypovolemic shock. Timely initiation of dialysis and lung-protective ventilation are associated with a favourable outcome. Chemoprophylaxis with oral doxycycline (200 mg weekly) throughout the period of exposure is recommended in high risk individuals.

IMMUNISATION

Immunization by means of vaccines seems to provide a certain degree of protection. Vaccines are, in principle, suspensions of killed leptospires of particular serovars only. Hence protection is largely serovar-specific.

CONCLUSION

It is ironic that despite the progress we have made on other fronts, we are losing our fight against infectious diseases. The constant threat of a leptospirosis epidemic looms large whenever there is heavy flooding. Adherence to recommended guidelines, as well as urgent implementation of appropriate surveillance and control measures is the need of the hour.

REFERENCES

1. Sambasiva RR, Naveen G, Bhalla P and Agarwal SK. Leptospirosis in India and rest of the world. *Braz J Infect Dis* 2003; 7:178–193.
2. Bharti AR, Nally JE, Ricaldi JN, Matthias MA, Diaz MM, Lovett MA et al. Leptospirosis: a zoonotic disease of global importance. *Lancet Infect Dis* 2003; 3:43–489.
3. Shivakumar S. Leptospirosis: Current Scenario in India. Medicine Update Edition 18, Chapter 106, Publisher : The Association of Physicians of India, 2008: 799-809.
4. John TJ. The prevention and control of Human leptospirosis. *J Post Grad Med* 2005; 57:205-209.
5. Shivakumar S. Indian Guidelines for the Diagnosis and Management of Human Leptospirosis. Medicine Update 2013. Publisher : The Association of Physicians of India. Available at < www.apiindia.org/medicine_update_2013/chap07.pdf>
6. Shivakumar S, Shareek PS. Diagnosis of leptospirosis utilizing modified Faine's criteria. *JAPI* 2004; 52:678-79.
7. Leptospirosis Fact Sheet. Available at http://www.searo.who.int/about/administration_structure/cds/zoonoses/leptospirosis. Accessed on 23rd October 2016
8. Bhatia M, Umapathy B L, Navaneeth B V. Evaluation of diagnostic utility of modified Faine's criteria in leptospirosis- experience from a tertiary care hospital. *Natl J Integr Res Med* 2015; 6:20-26.
9. National Guidelines for Diagnosis, Case Management, Prevention and Control of Leptospirosis (2015). Available at www.ncdc.gov.in