Clinical Management of Leptospirosis

Introduction

Leptospirosis is a zoonosis caused by pathogenic spirochetes of the genus *Leptospira* which are spiral-shaped and highly motile. Approximately 90% of cases are asymptomatic or mild with a favorable outcome. 5% to 15% of cases present a severe form with multiple organ dysfunction and a high mortality rate without prompt treatment.

Epidemiology

Leptospirosis is most prevalent in tropical regions but also occurs in temperate regions. The incubation period can range from 2 to 30 days.

Rodents are the most important reservoirs for maintaining transmission in most settings. In addition to rodents, the organism infects a variety of both wild and domestic mammals, especially cattle, swine, dogs, horses, sheep, and goats. It rarely occurs in cats. Organisms can survive for days to months in urine-contaminated soil and fresh water.

Human exposures that lead to infection include contact with urine-contaminated soil or water (eg, floodwater, ponds, rivers, streams or sewage), ingestion of food or water contaminated by urine or urine-contaminated water, or direct contact with the urine or reproductive fluids from infected animals.

Risk Factors

Persons at increased risk of catching leptospirosis include farmers, abattoir workers or sewer workers, and those who enjoy freshwater swimming, gardening, walking barefoot or who are often exposed to water recreationally.

Outbreaks tend to occur after heavy rainfall or flooding in endemic areas, especially in areas with poor housing and sanitation conditions.

Signs and Symptoms

Most cases are mild and self-limited or asymptomatic. The majority of symptomatic patients with leptospirosis have the anicteric form of disease. Anicteric leptospirosis has been described as a biphasic illness, with an acute phase and an "immune" phase which occurs about a week later.

Symptoms during the acute phase include fever, rigors, myalgias, headache, nausea, vomiting, diarrhea, nonproductive cough, arthralgia, bone pain, sore throat, abdominal pain, and rash. Noteworthy signs are hepatosplenomegaly, conjunctival hyperemia ('suffusion') and petechiae.

In the immune phase, patients present with aseptic meningitis and/or uveitis.

Icteric leptospirosis occurs in approximately 5 to 10 percent of symptomatic leptospirosis cases and is a rapidly progressive multisystem illness associated with mortality rates of 5 to 15 percent. Usually, icteric leptospirosis is accompanied by fever, jaundice, and renal failure, a syndrome known as "Weil's disease."

Complications

- Acalculous cholecystitis
- Pancreatitis

- Rapidly progressive pulmonary hemorrhage
- Acute respiratory distress syndrome
- Myocarditis
- Rhabdomyolysis
- Renal failure (which may be oliguric or polyuric)
- Heart failure or cardiogenic shock
- Encephalitis
- Guillain-Barré syndrome
- Transverse myelitis

Diagnosis

Diagnosis should be suspected based on a clinical assessment – once suspected, empirical treatment must be started promptly without waiting for the results of tests.

4ml of clotted blood should be sent to the Central Health Laboratory for a complement fixation test; in addition, 4ml in an EDTA tube should also be sampled for a *Leptospira* polymerase chain reaction (PCR) test.

The diagnosis is confirmed by a positive PCR of blood or by positive serologic testing. The diagnosis is not ruled out by negative test results, because the sensitivity of leptospirosis testing is suboptimal.

PCR is most sensitive during the bacteremic phase (i.e., the first week) of infection, with antibodies becoming detectable by serology after the first week.

To diagnose leptospirosis by serologic testing, one blood sample should be obtained upon presentation (i.e., an acute sample) and a second sample should be obtained 7 to 14 days after the first test is sent (i.e., a convalescent sample). A four-fold change in titer confirms infection.

Triage

All patients suspected of having leptospirosis should be admitted to a regional hospital for a work-up.

Initial investigations can include full blood count, urea, electrolytes, creatinine, urinalysis, liver function tests, INR / PTT, chest x-ray (CXR) and electrocardiogram.

Transfer the patient to the High Dependency Unit or an Intensive Care Unit (if available) if:

- CXR is abnormal, or the patient is hypoxic (O_2 sat < 90% on 6L of O_2 by mask) or respiratory rate > 30/min;
- Moderate to severe bleeding or coagulopathy or platelets < 50,000/mm^3;
- Acute renal failure requiring hemodialysis;
- Hypotension with systolic blood pressure < 90mmHg or mean arterial pressure < 60mmHg;
- Seizures

- Malignant cardiac arrhythmias; or
- Glasgow Coma Scale ≤ 12.

Treatment

A Jarisch-Herxheimer reaction may occur following antimicrobial therapy for leptospirosis; this is an acute inflammatory response to clearance of spirochetes from the circulation and is characterized clinically by fever, rigors, and hypotension.

Doses shown in this section are for adults and for a normal renal function. Adjustments may be required for pediatric populations or for patients in renal failure.

Mild to moderate disease

- Doxycycline 100mg PO BD x7d (avoid in pregnant women and in children)
- Azithromycin 500mg PO OD x3d – if not available, substitute with clarithromycin 500mg PO BD x7d; however, note that few studies are available on the efficacy of clarithromycin in the treatment of leptospirosis.
- Amoxicillin 500mg PO TDS x7d

Severe disease

- Penicillin 1.5 million units IV Q6h x7d
- Doxycycline 100mg IV BD x7d (avoid in pregnant women and in children)
- Ceftriaxone 2g IV OD x7d
- Cefotaxime 1g IV Q6h x7d

If complications occur, supportive treatment should be provided after appropriate referrals to the concerned departments e.g., patients in respiratory failure can be intubated and patients in shock should be placed on inotropes.

Supportive renal replacement therapy (eg, hemodialysis) may be required for survival in up to half of patients with Weil's disease, but complete renal recovery is typical after discontinuation of renal replacement therapy. Electrolyte imbalances are common, including hypokalemia and hyperkalemia, which should be treated accordingly.

While admitted, the following tests should be ordered every 24 to 48 hours based on the patient's clinical condition: platelets, INR/PTT, urea, electrolytes, creatinine and bilirubin.

Discharge

Patients can be discharged when all complications and danger signs have resolved. Of note, mild cases may not require more than 24-48 hours of admission – such patients can be discharged on outpatient oral therapy with instructions to return to the hospital if their condition deteriorates.

Jaundice can persist for many weeks – it is not necessary to wait until jaundice is resolved before discharging a patient if all else is satisfactory.

References

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