Lecture: Leptospirosis

Urinary Module-Phase II

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Leptospirosis

Leptospirosis is an emerging infectious disease and one of the most widespread zoonoses in the word.

It is a bacterial disease caused by spirochaetes of the genus *Leptospira* that affects humans and other animals

It was described by Adolf Weil in 1886. Also known as

Weil's disease

Swineherd's disease

Sugarcane grower's disease

Swamp fever

Mud fever

Canicola fever

Leptospirosis has a broad spectrum of clinical manifestations varying from in-apparent infection to fulminant fatal disease.

Mild form: influenza-like illness with headache and myalgia

Severe form : characterized by jaundice, renal dysfunction & hemorrhagic diathesis – Weil's syndrome

ETIOLOGY

Causative organisms : Leptospires . Leptospires belong to

Order : Spirochaetales

Family : Leptospiraceae

Genus : Leptospira

Pathogenic : *Leptospira interrogans*

Non pathogenic : Leptospira biflexa (saprophytic)

Leptospira interrogans has over 20 **serogroups** & > 200 **serovars.**

MORPHOLOGY

The Leptospira appear tightly coiled thin flexible Spritochetes 5 – 15 microns long.

Fine spiral of 0.1 – 0.2 microns. One end appears bent forms a hook.

Actively motile. Seen best with dark field Microscopy.

EPIDEMIOLOGY

Rodents, domestic & wild animals form the reservoir of infection

Temporary carriers: domestic animals like cattle, dogs & pigs

Permanent carriers: rodents

Leptospires are excreted in the urine of these animals.

Apart from humans, at least 160 mammalian species are infected – rats, cattle, pigs, dogs, cats, squirrels, raccoons, bandicoots.

Transmission

Transmitted via infected urine.

Leptospires infect humans by invasion across mucous surfaces of eye, throat & gut or non intact skin . Infection may occur via direct contact with urine or contact with contaminated water / soil following monsoon rains.

Occurs both in urban & rural areas.

Urban areas of developing countries due to overcrowded slums, inadequate drainage and sanitary facilities, presence of stray dogs, cattle, pigs, domestic rats, poor condition of slaughter houses.

In rural areas, high risk groups are workers in rice fields, cane fields & other agricultural crops & animal husbandry staff

In addition sewer workers , miners, fishermen & those involved in water sports are at risk too.

Susceptability

All age groups & races

Adult men are at higher risk

More common in tropics , rainy season

Number of cases vary every year due to factors like rainfall, floods & animal infections

Sri Lankan situation of leptospirosis

Leptospirosis is an endemic disease in Sri Lanka.

Climate, seasonal rainfall, humidity and other ecological factors have contributed to the maintenance of the disease.

Clustering of cases and occurrence of outbreaks in relation to rainfall and paddy field cultivation has been observed in many parts of the country.

During the last decade, there has been an increase in the reported number of Leptospirosis cases.

The recent outbreak was reported from Colombo, Gampaha, Kalutara, Matara, Anuradhapura, Kegalle, Ratnapura, Hambanthota, and Kandy districts.

Sustained outbreak since 2008.

Annual case incidence 22-34 per 100,000 population (2nd highest reported incidence worldwide)

Majority of the cases (49%) had been exposed in paddy fields.

Most of the affected cases were in the age group of 20-44 years.

The important factor during this outbreak was the reports of rapidly fatal cases among these patients mainly due to respiratory distress.

PATHOGENESIS

Incompletely understood.

Leptospires enter the host through abrasions in skin or intact mucous membranes (conjunctiva or oro- & nasopharynx)

After entry of organisms , leptospiremia develops, with subsequent spread to all organs.

Multiplication takes place in blood & tissues, leptospires can be isolated from blood & CSF during first 4 – 10 days of illness.

Damage the wall of small blood vessels leading to vasculitis with leakage & extravasation of cells, including Hemorrhage.

Mainly affect kidneys & liver.

In kidney, they migrate to interstitium, renal tubules causing interstitial nephritis & tubular necrosis. Hypovolemia due to dehydration or altered capillary permeability leads to renal failure.

In liver, Centrilobular necrosis with proliferation of Kupffer cells

Other sites ;

Pulmonary involvement is as a result of hemorrhage but not of inflammation.

Invasion of skeletal muscles results in swelling, vacuolation of myofibrils & focal necrosis.

In severe infection, vasculitis impairs the microcirculation & increased capillary permeability results in fluid leakage & hypovolemia.

Antibody response & Leptospires persistence

When antibodies are formed, leptospires are eliminated from all sites except eye, proximal renal tubules & brain where they persist from weeks to months. Persistence in aqueous humour leads to recurrent uveitis.

CLINICAL MANIFESTATIONS

Many remain asymptomatic.

In symptomatic cases, clinical manifestations vary from mild to serious or even fatal.

>90% of symptomatic have mild, anicteric form of leptospirosis with / without meningitis.

5-10% - Weil's syndrome

Incubation period : 7-12 days, can vary from 2 – 30 days.

The course of infection ; Typically characterized by

(1). Acute leptospiremic phase

(2). Immune leptospiruric phase.

Distinction between the 2 phases is not always clear and milder cases do not always include the 2nd phase.

Early non-specific leptospiraemic phase

Acute febrile, influenza like illness with chills, sore throat, headache, myalgia, back pain, anorexia, nausea & vomiting. Sometimes reactivation HSV – cold sore occurs.

When acute phase is severe, patient is exhaused & has persistently high fever with tender muscles, cough, dyspneoa, haemoptysis, vomiting & abdominal pain.

Immune leptospiruric phase

After the initial illness, a second phase begins, characteristically the patientt having developed antibodies, predominantly of IgM class.

In mild cases the 2nd phase is associated with minimal signs & symptoms.

Severe infections – meningeal & hepatorenal manifestations predominate.

Important feature of immune phase is development of ASEPTIC MENINGITIS.

Anicteric Leptospirosis

Fever with chills

Frontal headache / retroorbital pain

Nausea, vomiting

Myalgia (calf muscles, back, abdomen)

Sore throat

Cough, occasionally haemoptysis.

On examination

Fever with conjunctival suffusion

Muscle tenderness

Lymphadenopathy

Throat congestion

Macular, maculopapular, erythematous, utricarial & haemorrhagic rash

Hepatomegaly

Rarely splenomegaly

Most become asymptomatic within 1 week.

After 1-3 days , illness reccur & the start of this immune phase & symptoms are more variable.

WEIL'S SYNDROME (Severe Leptospirosis) ; Commonly due to serovar *icterohaemorrhagiae*

Characterized by jaundice, renal dysfunction & hemorrhagic diathesis

Pulmonary involvement in many cases

Mortality – 5 -15 %

Onset same as anicteric leptospirosis

After 4-9 days, jaundice, renal & vascular dysfunction develop.

Hepatomegaly

Tenderness Right Upper quadrant

Splenomegaly – 20 % cases

Renal failure – often in 2nd week

Hypovolemia & decreased renal perfusion

acute tubular necrosis with oliguria or anuria.

Pulmonary involvement : cough, dyspnea, chest pain & blood stained sputum .

Sometimes haemoptysis / resp failure / ARDS

Hemorrhagic : epistaxis, petechiae, purpura, ecchymosis, rarely Subarachnoid hemorrhage (SAH) & GI bleed.

Rhabdomyolysis

Hemolysis

Myocarditis

Pericarditis

ARDS

Necrotizing Pancreatitis

Multi organ dysfunction

Differential diagnosis of leptospirosis

Viral hepatitis

Hantavirus infection

Dengue

Malaria

Enteric fever

Hemolytic uremic syndrome – *Shigella , E.coli*

Meningococcemia

Laboratory Investigations

- WBC : leukocytosis
- ESR : raised
- Mild thrombocytopenia (50 % cases)
- Urine : urinary sediment changes (leukocytes, erythrocytes, hyaline / granular casts)

  mild proteinuria (anicteric form)

  renal failure (severe form)
- LFT : raised bilirubin

  raised alkaline phosphatase

  mild rise in transaminases (up to 200 U/L)
- Bleeding time prolonged & bleeding is due to capillary fragility
- Clotting time normal
- Later rise in PT – Hepatocyte failure
- S.CPK – in 1st week of illness (differentiate from viral hepatitis)

Meningeal involvement :

initially PMNs & later mononuclear

CSF protein – elevated

Pulmonary : radiographic abnormalities more than physical findings.

CXR : Most common : patchy alveolar pattern

Diagnosis of leptospirosis

(1). Clinical features

(2). Laboratory investigations

A definite diagnosis - Isolation of organism from the patient or on seroconversion (> 4 fold rise in antibody titre in MAT).

TESTS :

1. **Microscopic agglutination test (MAT)**

gold standard for definitive evidence of infection.

2. Darkfield Microscopy: lack sensitivity and specificity (104 organisms per mL are needed to allow for the detection of one cell per field).

3. Culture: Isolation is not a commonly used laboratory tool due to the need for specialised media and resources required to maintain the cultures for up to eight (8) weeks for weekly viewing by darkfield microscopy.

4. PCR

5. SEROLOGY

SEROLOGY

Serovar Specific tests :

Microscopic Agglutination Test (MAT)

Genus Specific tests :

ELISA

Latex Agglutination

Dipstik Tests

CULTURE

Cultures: Blood & CSF – during first 10 days

Urine – after 10 days for several weeks

Cultures become positive after 2-4 weeks, with range of 1 week to 6 months

Medium: Ellinghausen-McCullough-Johnson-Harris (EMJH) Medium

Fletcher Medium

Korthof Medium

Culture is the most definite way of confirming leptospirosis, but they do not contribute to early diagnosis.

Genus specific tests: Tests of choice for diagnosis of current infection

Simple

More sensitive

Become positive earlier than MAT (5^{th} – 6^{th} day of illness)

Detect genus specific antibodies, which are shared by pathogenic & saprophytic leptospira.

Detect specific IgM antibody

Laboratory Criteria for diagnosis

<u>Confirmed</u>

- ✓ Culture : positive
- ✓ MAT : seroconversion / 4 fold rise in titer

<u>Probable</u>

- ✓ Rapid tests : positive
- ✓ MAT : high titer (single sample)
- ✓ *Leptospira* (EIA) IgM: positive result

Treatment:

Severe infections:

Should be managed with IV benzyl penicillin and will require hospital admission.

In patients with penicillin allergy, a program of erythromycin can be used.

In mild to moderate cases

Oral medication using amoxycillin, erythromycin, doxycycline or ampicillin can be used, subject to contraindications and age limits.

Chemoprophylaxis:

Doxycycline 200 mg One Dose once a week

Control of rodent sources of transmission

Reduce reservoir density

Pesticides

Deny access to human living environment

Deny access to food and water

Remove food sources and ecological habitats

Limitations

Pesticides are costly

Can not control by chemical interventions alone. i.e. pesticide resistance

Prevent exposure to transmission sources

1. Disinfecting areas of contaminated environment (hypochlorite)

2. Protective clothing (boots, gloves)

3. Cleaning wounds after exposure

4. Prevent contact with dead or ill animals.

5. Health education on risk exposure