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A 16-Year-Old Boy from Sri Lanka With Fever, Jaundice and Renal Failure

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Clinical Presentation

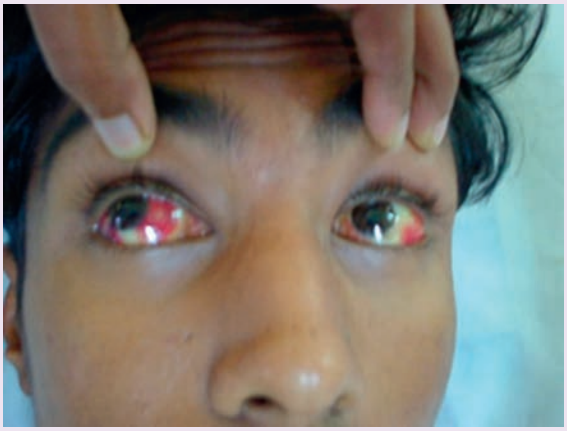
History

A 16-year-old Sri Lankan boy presents to a local hospital with fever, frontal headache and severe body aches for 2 days. He has vomited two to three times during the illness and has not passed any urine for the previous 12 hours. He does not have a cough, coryza or shortness of breath. He has been attending school until his illness. He had been fishing in an urban water stream 5 days before falling ill.

Clinical Examination

The boy appears ill and drowsy. He is jaundiced and has subconjunctival haemorrhages (Fig. 27.1). Temperature is 38.3°C (100.9°F), the pulse rate is 100 bpm (low in volume). The blood pressure is 90/60 mmHg.

There is no neck stiffness, however there is severe muscle tenderness, mainly involving the abdominal wall and the calves such that the patient finds it difficult to walk. There is no lymphadenopathy. The cardiac apex is not shifted and heart sounds are clear. Examination of the lungs is normal. The liver is palpable at 4 cm below the right costal margin and is tender. The spleen is not palpable. There is mild bilateral renal angle tenderness. Neurological examination is normal.



• **Fig. 27.1** Jaundice and subconjunctival haemorrhages

TABLE 27.1 Laboratory Results on Admission

Parameter	Patient	Reference
WBC ($\times 10^9$/L) (neutrophils: lymphocytes)	5.7 (68%: 31%)	4–10
Haemoglobin (g/dL)	14.8	12–16
Platelets ($\times 10^9$/L)	96	150–350
AST (IU/L)	64	13–33
ALT (IU/L)	58	3–25
ALP (IU/L)	246	40–130
Serum bilirubin total (μmol/L)	77	13.7–30.8
Serum bilirubin direct (μmol/L)	54.7	<5
Blood urea nitrogen (μmol/L)	20.7	2.5–6.4
Serum creatinine (μmol/L)	212.2	71–106
C-reactive protein (mg/L)	48	<5

Further Investigations

The laboratory findings are summarized in Table 27.1. The urine microscopy shows 20 red blood cells per high-power field, proteins '+' and granular casts '+'. A chest radiograph is normal. An ECG shows sinus tachycardia.

Questions

1. What is the most likely diagnosis and what are your differentials?
2. What tests are indicated to confirm the diagnosis?

Discussion

A Sri Lankan teenage boy presents with fever, severe body aches and a reduced urine output. He is jaundiced with subconjunctival haemorrhage and has a tender hepatomegaly. He has had contact with a water stream before his ill health.

His laboratory results show signs of cholestasis with only mildly elevated transaminases. The creatinine is increased twofold and there is thrombocytopenia. The leucocyte count is normal.

Answer to Question 1

What is the Most Likely Diagnosis and What Are Your Differentials?

An acute febrile illness accompanied by jaundice, renal failure and subconjunctival haemorrhage should raise the suspicion of leptospirosis, particularly in case of a history involving exposure to potentially contaminated water.

Scrub typhus is another very common infection in South Asia. It may present with an acute onset of fever, hepatomegaly and renal failure. There usually is lymphadenopathy; and on careful examination, one may spot an eschar. Subconjunctival haemorrhage has been described but is less common than in leptospirosis, and complications such as renal failure tend to occur late in the infection (after about 7 days).

Hantavirus infection may cause a haemorrhagic fever with renal syndrome. It has a similar epidemiology to leptospirosis and is also associated with contact with rodent excreta.

Dengue haemorrhagic fever (DHF) is another differential diagnosis to consider. It also presents with fever, severe myalgias, thrombocytopenia and haemorrhages. Acute kidney injury and jaundice are uncommon for DHF.

Answer to Question 2

What Tests Are Indicated to Confirm the Diagnosis?

The microscopic diagnosis of leptospirosis requires a dark-field or a phase-contrast microscope because the bacteria stain poorly. However, dark-field microscopy is of poor sensitivity and specificity and only yields positive results during the early bacteraemic phase of the disease.

Leptospira may be cultured from blood, CSF or urine. Isolation of the bacteria from blood or CSF is only possible during the first week of illness. Samples have to be incubated for at least 8 weeks and analysed weekly with a dark-field microscope. This technique is laborious and not routine practice in a standard microbiological laboratory.

Polymerase chain reaction (PCR) detection has been used on blood, CSF and urine. PCR performance varies between types of samples taken and depends on the time the sample was taken in relation to duration of illness. Sensitivity and specificity appear to be higher in urine than in blood and are better in blood samples taken early rather than later during the course of illness.

For indirect diagnosis, the historical reference serological test is the microscopic agglutination test (MAT). MAT relies on incubation of patient serum with *Leptospira* antigen suspension and determines agglutination with a dark-field microscope. This method requires a high level of expertise and is limited to expert centres.

The MAT cannot differentiate between current or past infections. Therefore two consecutive serum samples should be examined to look for seroconversion or at least a fourfold rise in titre. The significance of titres in single serum specimens is a matter of debate.

Various ELISA tests detecting anti-*Leptospira* IgM are now commercially available, facilitating the diagnosis outside reference centres. It appears that sensitivity of these tests is highly variable if blood is examined during week one of the illness, it improves (75% and 100%) if blood is taken after day 7. A positive IgM ELISA should be confirmed by MAT.

The Case Continued…

Severe leptospirosis was suspected and the patient was commenced on empirical benzylpenicillin. Despite rehydration he developed acute renal failure warranting haemodialysis (HD). He developed myocarditis and atrial fibrillation, but luckily tolerated further HD. He gradually recovered over 10 days with intensive care management.

SUMMARY BOX

Leptospirosis

Leptospirosis is a zoonotic disease that occurs worldwide. It is caused by pathogenic *Leptospira* species, which belong to the spirochaetes. The most common species causing disease in humans and animals are *L. interrogans* and *L. borgpetersenii.*

Humans become infected through direct contact with urine of infected mammalian hosts, contact with contaminated water or animal abortion products. The major reservoirs are rodents, canines, livestock and wild mammals. Most at risk are slum dwellers and people with an occupational or recreational exposure involving animal contact or immersion in water. Also, natural disasters such as hurricanes and floods may put people at risk.

The bacteria enter the human body through cuts or abrasions of the skin or through intact mucous membranes. The incubation period is 2 to 30 days. The spectrum of disease ranges from asymptomatic to severe infection.

The classical presentation of leptospirosis is that of a biphasic illness. The initial leptospiraemic phase usually starts abruptly. Symptoms are non-specific with fever, headache, sore throat, abdominal pain and a rash. Severe myalgias, most notably of the calves and the lumbar area, and subconjunctival haemorrhage have been mentioned as distinguishing physical findings. This first phase lasts for a week and is followed by a second phase dominated by immune-mediated pathology.

Five to ten per cent of those with clinical infection will develop severe leptospirosis with cholestatic jaundice, acute kidney injury and haemorrhagic diathesis (Weil's syndrome). Further complications include pulmonary involvement, aseptic meningitis and myocarditis.

Leptospirosis is usually treated with antibiotics, although the usefulness of antibiotic treatment in particular during the second phase of illness, which is immune-mediated, has been disputed.

For uncomplicated cases, oral doxycycline is the drug of choice. Alternatives include amoxicillin and azithromycin. In severe infection benzylpenicillin, IV doxycycline, ceftriaxone or cefotaxime seem to have similar efficacy. Doxycycline 200 mg weekly has been suggested as exposure prophylaxis.

Further Reading

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4. Eldin C, Jaulhac B, Bediannikov O, et al. Values of diagnostic tests for the various species of spirochetes. Med Mal Infect 2019;49 (2):102–11.