

b Leptospirosis

A recent case of leptospirosis presenting as acute multisystem illness

Leptospirosis was the likely diagnosis in a 34-year-old resident of Gauteng, South Africa, who presented with an acute febrile illness with significant splenomegaly and multisystem pathology. He had travelled for business to Nairobi, Kenya and Addis Ababa, Ethiopia in the week prior but had not experienced any likely exposures to zoonotic diseases. On return to South Africa, he visited a number of game parks where he had close contact with a number of animals, and opportunity for exposure to *Leptospira* species. While visiting a game farm near Bela Bela he became ill.

The course of illness was rapidly progressive with the development of ARDS, renal failure, DIC, liver dysfunction with jaundice, and depressed level of consciousness. The patient required assisted ventilation, inotropic support and renal dialysis. A broad differential diagnosis was considered, he was isolated and was tested for a large number of infectious diseases including zoonotic infections: – viral haemorrhagic fevers including Crimean Congo haemorrhagic fever and Rift Valley fever, dengue, leptospirosis, Q fever, and arboviral infections, all of which were negative in the first week of illness. Malaria was actively sought despite his not having travelled to a known malaria transmission area, but all tests were negative. Blood cultures were repeatedly negative. An initial anaemia (Hb 8.8 g/dL), a WCC of $2.52 \times 10^9/L$ and thrombocytopenia ($28 \times 10^9/L$) were noted. A normal reactive bone marrow with eosinophil infiltration, and raised hepatic transaminases and bilirubin levels (AST 452 u/L ALT 178 u/L, total bilirubin 157 umol/L, direct bilirubin 107 umol/L, LDH 1748 u/L) was documented. The PT was 11.9 sec, PTT 32.4 sec, INR 1.2, D-dimers >10 mg/L with fibrinogen of 1.94 g/L, indicating a compensated DIC.

The patient received broad-spectrum antibiotic treatment with ceftriaxone, plus a quinolone and doxycycline for possible rickettsial infection or Q fever. The course of illness was biphasic, with an initial favourable response to treatment. The final, fatal event was likely a nosocomial infection.

Negative leptospiral antibodies in the first week of illness with a seroconversion (by Elisa, repeated on three occasions) in the second week of illness was highly suggestive of the diagnosis of leptospirosis, despite a negative PCR test in the first week. The source of the infection and the exact source remains unknown.

Leptospirosis as a human disease in South Africa

Leptospirosis has a worldwide distribution, but has been relatively rarely diagnosed in South Africa. In 1947 Buchanan reported that despite laboratory investigations on more than 200 jaundiced patients over a 20-year period, mainly on the Witwatersrand, no leptospiral infections were detected. Likewise, his examination of 231 rodents of various types revealed no instances of infection. It was not until 1952 that the first South African case of leptospirosis was diagnosed, in a Cape Town fish hawkler who died of typical Weil's disease due to *Leptospira icterohaemorrhagiae*, complicated by myocarditis. In 1958 Gear *et al* described 5 cases amongst persons that recovered from leptospiral meningoencephalitis in Johannesburg, and in the 1960s and 1970s further cases of leptospirosis were published from Cape Town, and one from KwaZulu-Natal Province. Several of these were dockworkers. Evidence of animal reservoirs of infection in South Africa dates from the 1950s, and the first isolation of *L. icterohaemorrhagiae* in Cape Town rats was reported in 1964, followed by isolation of *L. pomona* in pigs and dogs in the Western Cape. In the last study, 54% of Cape Town dogs had serological evidence of infection with *L. icterohaemorrhagiae* or *L. pomona* or both. The South African veterinary literature contains many data about leptospirosis in wild and domestic animals, but is not reviewed here. As part of a study of rodent-associated infections in rural and urban areas of South Africa, 2003-2006, serosurveys of rodents and humans in an urban informal settlement in Durban showed that, respectively, 10% and 20% of rodents and humans had serological evidence of exposure. More recently, three human cases, acquiring the infection in rural settings near Johannesburg (cases 1 and 2), and in an informal settlement in Windhoek, Namibia (case 3), were diagnosed by PCR on blood samples and were published in the Communiqué in 2007 (Vol. 6, No. 1, pp. 3-4), with an additional case in a Cape Town flower seller documented in 2008 (Communiqué Vol. 7, No. 5, p. 1).

Leptospirosis diagnostics

Leptospirosis is pathognomonic with variable clinical manifestations and clinical suspicion must be confirmed with laboratory tests. Findings on general laboratory studies include elevated erythrocyte sedimentation rate, thrombocytopenia, leucocytosis, hyperbilirubinaemia, elevated serum creatinine, elevated creatinine kinase and elevated serum amylase. On urinalysis, proteinuria may be

present. Leukocytes, erythrocytes, hyaline casts, and granular casts may be present in the urinary sediment.

Laboratory diagnosis of leptospirosis is usually carried out by culturing the bacteria from blood, urine or tissues, by detecting antibodies, or by demonstrating the presence of leptospires in tissues using antibodies labelled with fluorescent markers. Other methods include darkfield microscopy (the classic method but no longer recommended), polymerase chain reaction (PCR) and staining using monoclonal antibodies.

The definitive laboratory diagnosis of leptospirosis is made by isolation of leptospires from clinical specimens, but it is technically demanding, requiring rapid inoculation of special fresh medium that is not readily available. Routine microbiological laboratories are generally not equipped for leptospire culture, and it is time consuming and subject to contamination and high failure rates. Therefore, serological approaches are used commonly for diagnosis of leptospirosis. However, detection of antibodies is by itself no proof of a current infection as antibodies may persist for

months or even years after an infection. In general, seroconversion or a four-fold rise in titre in consecutive serum samples is considered to be diagnostic proof of current or recent infection. Seroconversion may occur as early as 5–7 days after the onset of illness, but sometimes only after 10 days or longer. In the acute phase, leptospires can be found in blood and CSF for 7-10 days and their presence can be confirmed by detecting and identifying specific segments of leptospiral DNA using PCR amplification. However, due to the small number of leptospires present in blood samples, very sensitive diagnostic tests are required and samples should be taken prior to antibiotic treatment. Leptospires are susceptible to most antibiotics, except chloramphenicol. Recommended treatments include high-dose penicillin G or a 3rd generation cephalosporin, alternatively doxycycline, azithromycin or ampicillin. Severe leptospirosis is associated with a cytokine storm and multiorgan failure, requiring skilled supportive treatment in

Source: Centre for Emerging and Zoonotic Diseases, Division of Public Health, Surveillance and Response, NICD-NHLS