Leptospirosis: an unusual presentation

Jane H Thomas and Dianne P Stephens

ABSTRACT

Leptospirosis is a common zoonosis that is endemic in the tropical Top End of the Northern Territory. Disease ranges from mild to very severe. We report a patient with anicteric leptospirosis who became critically ill, challenging the view that anicteric leptospirosis is less severe than the icteric form. Despite a typical but non-specific presentation and recreational high-risk activities, diagnosis of leptospirosis was delayed. The patient developed respiratory failure, resulting from pulmonary haemorrhage, and acute renal failure. This case highlights the multiple factors that should prompt health care workers to consider the diagnosis of leptospirosis in non-classical presentations.

Crit Care Resusc 2006; 8: 215–218

We describe a patient with severe leptospirosis who was treated in the intensive care unit of Royal Darwin Hospital in the Northern Territory. The patient made a relatively rapid and full recovery considering the severity of his illness in the early stages of hospitalisation. The presentation did not have all the classical symptoms of severe leptospirosis, which may have delayed diagnosis and treatment.

Leptospirosis is a common, emerging, worldwide zoonosis caused by spirochaetes of the genus *Leptospira*.[1] In Australia, the number of reported cases has varied over the past 10 years from 120 to 320 per annum, with 128 cases in 2005.[2] Most cases occur in Queensland, where the incidence was recently reported as 3.1 per 100 000 population.[3] However, cases occur in every Australian state and territory.[2] The species that causes leptospirosis in humans is *Leptospira interrogans,* which includes over 200 serovars. Primary reservoirs of the bacteria are small mammals, especially rodents, which transfer infection to larger animals and humans.[1] Transmission is through direct or indirect exposure to urine of the infected animal.[4] This usually occurs during specific recreational or occupational activities where humans come into contact with contaminated water, soil or vegetation.[4] Those at risk of direct contact include farmers, veterinarians and abattoir workers, while those at risk of indirect contact include sewerage workers, miners, soldiers and gamekeepers.[1] In Queensland, most cases occur through occupational exposure in farm workers, with recreational exposure accounting for 18% of cases.[3] Leptospires gain entry to the body via mucous membranes, skin wounds, and even intact skin if exposure is protracted.[5]

Leptospirosis is endemic in the Northern Territory and is most commonly found in the tropical regions of the Top End. Leptospires are able to survive longer in a warmer climate, resulting in greater endemicity in tropical regions.[1] The bacteria may survive for weeks to months in favourable environmental conditions.[4]

The incubation period for leptospirosis ranges from 4 days to 4 weeks.[6] Common initial symptoms are non-specific and generally include gastrointestinal complaints, headache, fever, chills, myalgia and conjunctival congestion. Progression to more severe manifestations depends on the serovar, inoculum magnitude, host factors and timing of appropriate medical management. Leptospirosis may produce anything from a mild infection to fulminant septic shock with multiple organ failure.[1] The mortality rate is 3%–5%.[7] However, in 85%–90% of cases, leptospirosis is a mild self-limiting disease, with the severity depending on the causative serovar. Two distinct forms of leptospirosis are recognised: the less severe anicteric form and the severe icteric form, also known as Weil's syndrome.[4] The icteric form of leptospirosis is characterised by jaundice, acute renal failure and pulmonary haemorrhages, but may also present with primary respiratory pathology.[1]

Clinical record

A previously healthy 31-year-old white man presented to the emergency department complaining of fevers, aching joints and back, and intermittent diarrhoea and vomiting. A history of excessive alcohol use was noted. The patient had been prescribed tramadol and celecoxib by his general practitioner, with no relief of symptoms. Screening for Ross River and Barmah Forest viruses by the GP gave negative results.

The patient was temporarily in Darwin working on the annual horticultural and agricultural show circuit. Two weeks previously, he had been pig-hunting on a quad bike in a rural area on the outskirts of Darwin, and had sustained multiple mosquito bites on his legs, and multiple bruises on his left side in a fall from the bike.

On presentation, the patient was alert and orientated. He had a heart rate of 90 beats per min, blood pressure of 110/60 mmHg, temperature of 39.5°C, and oxygen satu-

Table 1. Results of laboratory investigations, key observations and therapy over the course of the patient's stay in the intensive care/high dependency unit

	Reference range	Initial	Day in ICU/HDU 1	2	3	4	5	6	7	8	9	10
Investigations												
White cell count ($\times 10^9$/L)	4–11	13.6	15.5	28.6	29.4	33.5	29.4	25.5	17.2	15.9	10.1	–
C-reactive protein (mg/L)	0–8	–	–	323	–	143	103	–	40	56	35	7
Urea (mmol/L)	3–8	12	15	14	20.3	24.4	17.7	16.9	21.4	26	22.3	16.6
Creatinine (μmol/L)	50–120	125	252	396	423	254	220	235	253	243	193	149
Bilirubin (μmol/L)	0–20	9	29*	41*	12	11	11	9	8	11	9	–
ALP (U/L)	39–117	145	91	97	99	91	78	73	73	85	80	–
GGT (U/L)	0–60	135	123	141	107	89	83	75	79	89	70	–
Albumin (g/L)	35–45	28	25	23	22	23	22	22	22	29	31	–
Haemoglobin (mg/L)	135–185	164	133	125	121	104	101	88	80	103	103	–
Platelets ($\times 10^9$/L)	>150	207	129	135	77	119	110	165	234	403	611	–
Observations												
Temperature (°C)†		39.5	39.6	39.8	39.3	38.8	37.9	37.5	37.1	37.4	37	36.8
Mean arterial BP (mmHg)‡		83	58	70	71	72	67	63	70	82	82	82
Heart rate (beats per min)†		116	140	145	130	110	98	102	100	98	90	90
PaO_2/FIO_2‡		228	89	57	208	176	181	170	196	–	–	–
Therapy												
Inotropes		–	Yes	Yes	Yes	Yes	Yes	Yes	–	–	–	–
Renal replacement therapy		–	–	–	Yes	Yes	–	–	–	–	–	–
Ventilation		–	Yes	Yes	Yes	Yes	Yes	Yes	Yes	–	–	–
Prone positioning		–	Yes	Yes	–	–	–	–	–	–	–	–

* Bilirubin rise considered to be related to pulmonary haemorrhage. † Highest value for that day. ‡ Worst value for that day.
ALP = alkaline phosphatase. GGT = γ-glutamyl transferase. BP = blood pressure. PaO_2 = partial pressure of oxygen, arterial. FIO_2 = fraction of inspired oxygen.

ration of 98% breathing room air. On examination, there was left renal angle tenderness and slight hepatomegaly. A rash was noted on the upper body, and numerous insect bites on the lower legs and ankles. There was no jaundice. Urinalysis showed large amounts of blood and protein. Blood tests revealed a raised white cell count (13.9×10^9/L; reference range [RR], $4–11 \times 10^9$/L), neutrophil count (13.6×10^9/L; RR, $1.8–7.5 \times 10^9$/L), and serum levels of γ-glutamyl transferase (135 U/L; RR, 0–60 U/L), alanine aminotransferase (145 U/L; RR, 5–44 U/L), urea (12 U/L; RR, 3–8 U/L) and creatinine (125 μmol/L; 50–120 μmol/L) (Table 1). All other results were unremarkable. Abdominal computed tomography gave normal results.

The patient was admitted to the short-stay unit with suspected renal contusion secondary to his fall and viral infection. His condition deteriorated over the next 36 hours, with increasing tachycardia, hypotension, fever, shortness of breath and chest tightness. Blood tests revealed worsening renal function and increasing white cell count. Chest x-ray showed bilateral nodular opacities, and an echocardiogram showed a small pericardial effusion. The patient was transferred to the ICU for respiratory and haemodynamic monitoring and support.

On ICU admission, he was commenced on intravenous piperacillin–tazobactam and azithromycin to cover typical and atypical respiratory pathogens. However, his condition deteriorated further, and he required intubation and ventilation because of severe respiratory distress. At intubation, suction yielded a large amount of blood-stained tracheal aspirate. Chest x-ray revealed diffuse bilateral infiltrates, which progressed to complete left-sided "whiteout" on ICU Day 2 (see Figure 1). He required prone positioning for worsening gas exchange despite optimal mechanical ventilation. Haemodynamic monitoring confirmed septic shock with a high cardiac output and low systemic vascular resistance. Inotrope support was required for haemodynamic instability. The haemoptysis and chest x-ray appearance led to a clinical suspicion of pulmonary haemorrhage and leptospirosis and, 12 hours after ICU admission, doxycycline was started.

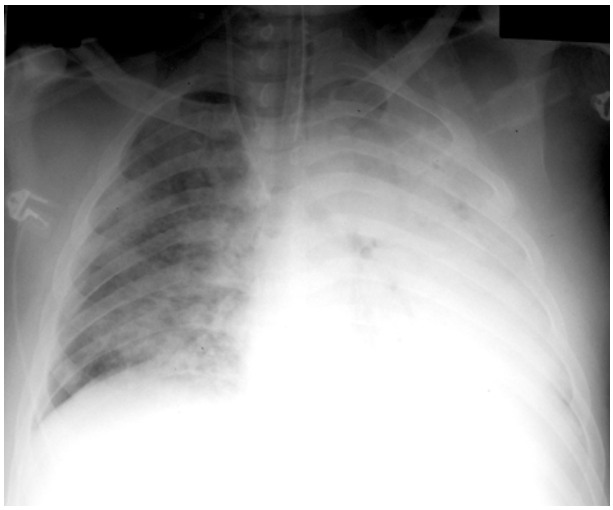
On ICU Day 3, the patient was commenced on continuous renal replacement therapy because of worsening renal function. This was continued for 48 hours. Haemoptysis continued for several days. Inotropic support was discontinued after 6 days, and ventilation therapy was weaned by Day 7.

Results of laboratory investigations, key observations and therapy over the course of the patient's stay in the intensive care/high dependency unit are shown in Table 1.

On ICU Day 6, the diagnosis of leptospirosis was confirmed. The differential diagnoses considered were Q fever, mycoplasma infection, rickettsial disease and legionellosis. Blood, sputum and urine cultures were negative, but serological testing with the microscopic agglutination test gave positive results, with a titre of 1:3200 for *Leptospira* serovar Australis.

The patient was discharged home from the high dependency unit on Day 10, with oral doxycycline to continue for 5 days and paracetamol.

Figure 1. Chest-ray on Day 2 in the ICU



Chest x-ray showing bilateral alveolar and interstitial infiltrates consistent with pulmonary haemorrhage.

Discussion

This severe case of anicteric leptospirosis challenges the traditional view that the anicteric form of the disease is less severe than the icteric form. This patient required maximal supportive therapies to survive. Scharfetter et al[7] reported three critically ill patients with leptospirosis, noting that the only patient with icterus had the best clinical course. That patient did not require mechanical ventilation or renal replacement therapy. Our case further demonstrates that jaundice does not necessarily help define severity of illness in leptospirosis.

Our patient presented to the hospital with many non-specific signs and symptoms that are well reported as characteristic of leptospirosis.[1,4,7] The non-specific nature of the clinical features and laboratory findings means that health care workers must maintain a high index of suspicion for leptospirosis to avoid missing the diagnosis.[7] The most important feature of this patient's recent history was pig-hunting in an endemic area, combined with multiple abrasions. High-risk activities combined with skin abrasions are strongly associated with leptospirosis and are well reported in the literature.[1,4,7] However, leptospirosis is an emerging disease and is occurring in urban areas and not always linked to high-risk recreational or occupational activities.[1,7] This urbanisation of leptospirosis may be a result of rodent infestation in urban areas.[7]

Pulmonary haemorrhage in leptospirosis may be a source of diagnostic confusion, and radiographic abnormalities must alert practitioners to consider the diagnosis of leptospirosis with pulmonary haemorrhage. Pulmonary symptoms are more common in anicteric than icteric cases.[1] Further, in both forms of the disease, mortality rates are higher in patients with pulmonary symptoms.[1] In our patient, the pulmonary manifestations were so severe that not only was mechanical ventilation required, but also prone positioning, as an adjunctive therapy to ameliorate severe gas exchange abnormalities.

Leptospirosis commonly produces acute renal failure and, in severe cases, may necessitate renal replacement therapy.[4] Acute renal failure with oliguria is associated with increased risk of mortality.[1] Pre-renal failure associated with azotaemia may respond to rehydration therapy.[1]

The diagnosis of leptospirosis in our patient was based on serological testing with the microscopic agglutination test. Despite its complexity, this test is the most appropriate.[1] In this case, blood cultures were negative, demonstrating the need for the clinician to consider serological testing when blood cultures are negative. Rapid diagnostic tests for leptospirosis are currently being developed.[1] Royal Darwin Hospital outsources the microscopic agglutination test to an interstate laboratory, and time from testing to reporting of the result was 5 days. This delay highlights the need to consider testing for leptospirosis early in the diagnostic process.

The recommended antibiotic treatment for leptospirosis is doxycycline.[4] In this case, the patient was not commenced on doxycycline until 48 hours after presentation to the hospital, as leptospirosis was considered unlikely at initial presentation in the absence of significant liver impairment with raised serum bilirubin levels.

Conclusion

Leptospirosis can be life-threatening and may have an atypical presentation. This case is a reminder to consider the diagnosis of leptospirosis in high-risk groups in endemic areas, such as tropical northern Australia, even in the absence of jaundice or other classical features.

Author details

Jane H Thomas, Research Coordinator
Dianne P Stephens, Director
Department of Intensive Care, Royal Darwin Hospital, Darwin, NT.
Correspondence: Jane.thomas@nt.gov.au

References

1 Levett PN. Leptospirosis. *Clin Microbiol Rev* 2001; 14: 296-326.

2 National Notifiable Diseases Surveillance System. Canberra: Australian Government Department of Health and Ageing, May 2006. Available at: www1.health.gov.au/cda/Source/CDA-index.cfm (accessed 2006).

3 Slack AT, Symonds ML, Dohnt MF, Smythe LD. The epidemiology of leptospirosis and the emergence of *Leptospira borgpetersenii* serovar Arborea in Queensland, Australia, 1998-2004. *Epidemiol Infect* 2006; May 11: 1-9.

4 Lomar AV, Diament D, Torres JR. Leptospirosis in Latin America. *Infect Dis Clin North Am* 2000; 14: 23-39.

5 Kobayashi Y. Clinical observation and treatment of leptospirosis. *J Infect Chemother* 2001; 7: 59-68.

6 Weir E. The challenge posed by leptospirosis. *CMAJ* 2000; 163: 1501.

7 Scharfetter A, Muhlhans M, Payer S, Wenisch C. Three cases of leptospirosis requiring intensive care. *Eur J Clin Microbiol Infect Dis* 2004; 23: 905-8. ❑