CASE REPORT

The dangers of living in a tent in London

Richard Frederick De Butts, Anna Li, James Goodhand, Eleanor Wood

Department of Gastroenterology,
Homerton University Hospital,
London, UK

Correspondence to
Dr Richard Frederick De Butts,
richdebuts@hotmail.com

Accepted 23 April 2014

SUMMARY

A middle-aged patient was admitted severely unwell with acute liver and renal failure of unknown cause. After extensive investigation the patient was found to have leptospirosis. We examine the investigations and management and discuss the disease itself.

BACKGROUND

Leptospirosis is a very uncommon cause of acute liver failure in the UK but one that should be considered in those presenting with acute liver and renal failure and living in environments where this zoonosis is likely to be prevalent.

CASE PRESENTATION

A previously healthy middle-aged patient presented feeling generally unwell with diarrhoea and vomiting for 4 days. A friend had noticed that he looked increasingly jaundiced and was no longer able to walk, so an ambulance was called.

There was no medical, surgical or contributory family history. The patient denied taking any medications, including over-the-counter paracetamol. The patient did not drink alcohol, use illicit drugs and was a life-long non-smoker. He had not travelled abroad.

The patient had been living in a tent in a large grassed area in London, UK, for the last 3 years. The patient had previously lived with friends but after losing his job had become homeless. Recently, the patient had been forced to relocate to a tow path next to one of the local canals. On detailed history the patient revealed that he had never swum or washed in the canal but had washed in the sprinklers which utilised water from the canal.

On examination the patient was jaundiced but there were no signs of chronic liver disease. The patient was tachypnoeic (respiratory rate 24 bpm), hypotensive (blood pressure 89/60 mm Hg) and tachycardic (heart rate 120 bpm); however, the remainder of the cardiorespiratory examination was normal. The patient had a tender epigastrium, with no rebound tenderness or guarding. There was hepatomegaly, but no splenomegaly or lymphadenopathy. Urogenital examination was normal, however the patient was found to be anuric when a urethral catheter was passed. The neurology examination was unremarkable, there was no conjunctival suffusion noted and the patient had no skin lesions.

The patient was transferred to the intensive therapy unit on admission on account of the hypotension and anuria.

INVESTIGATIONS

Investigations showed an acute kidney injury, serum urea 45.2 mmol/L, creatinine 669 μ mol/L and the estimated glomerular filtration rate 8 mL/min. The blood results also showed hyponatraemia, Na 116 mmol/L but the remainder of the electrolytes was normal. The liver function tests were abnormal: bilirubin 267 μ mol/L, albumin 17 g/L, alanine transaminase 85 μ mol/L and alkaline phosphatase 103 μ mol/L. The International Normalised Ratio was 1.1. The patient was thrombocytopenic with platelets of 24×10^9 /L. Haemoglobin was unremarkable at 12.6 g/L but the white cell count was raised at 19.2×10^9 /L. C reactive protein was 180 mg/L.

An arterial blood gas showed a metabolic acidosis: pH 7.34, partial pressure of carbon dioxide 4.3 kPa, base excess 7 mmol/L and lactate 2.8 mmol/L.

Urine toxicology screen was unremarkable.

A liver screen including serological testing for hepatitis A, B, C, HIV, cytomegalovirus and Epstein-Barr virus (EBV) was negative. Paracetamol levels were less than 10 mg/L. Ceruloplasmin, α -1-antitrypsin, ferritin and an autoimmune screen were all negative.

Abdominal ultrasound scanning showed a thickened gallbladder with the pericholecystic fluid. The liver was enlarged with a normal echotexture and no mass lesions. The intrahepatic ducts and the common bile duct were of normal dimensions with no gallstones. There was no splenomegaly or ascites. The renal tract was normal with no hydronephrosis. Chest X-ray was normal.

The initial leptospirosis ELISA serology (performed in the Hereford leptospirosis reference laboratory) was negative.

As the aetiology of the acute liver and renal injury remained unclear a liver biopsy was performed (figure 1). This showed the preserved liver

Figure 1 Liver biopsy with Warthin-starry stain. The black elongated structures are thought to represent leptospira.

CrossMark

To cite: De Butts RF, Li A, Goodhand J, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201654

architecture with moderate canalicular and hepatocyte cholestasis. Some lymphocytes and occasional neutrophils were seen within the sinusoidal spaces but there was no significant portal, interface or lobular inflammation. There was no evidence of confluent necrosis. Many hepatocytes were mitotically active and occasional apoptotic hepatocytes were also noted.

There was no significant portal or pericellular fibrosis. The native bile ducts were identified in all portal areas and appeared normal. There was no evidence of duct damage or ductular reaction. No granulomas or fungal organisms were identified. Warthin-Starry staining was carried out for spirochaetes. Some slender long structures which were thought to represent leptospira were noted.

Ten days after admission, repeat leptospirosis ELISA testing was positive with a titre of 1:640. A leptospirosis microscopic agglutination test (MAT) was then performed which confirmed the diagnosis.

DIFFERENTIAL DIAGNOSIS

On admission paracetamol overdose and acute alcoholic hepatitis seemed less likely given the patient's history. Leptospirosis was considered high on the list of differentials but the initial ELISA test did not confirm this. Severe sepsis, including biliary sepsis, was also considered. Thrombotic thrombocytopenic purpura was another remote possibility but there were a number of features of this including significant anaemia and neurological symptoms which were not present. Other infectious diseases including dengue fever and malaria were ruled out due to the patient's lack of foreign travel.

TREATMENT

Because of the presentation with two-organ dysfunction the patient was managed in the intensive care unit (ICU). Initially, vasopressors and renal replacement therapy with continuous venovenous haemofiltration (CVVHF) were required.

Empirically, for presumed leptospirosis, the patient was treated with a 1-week course of ceftriaxone 1 g once daily followed by a 1-week course of doxycycline 100 mg twice daily.

Bleeding occurred post liver biopsy which was sufficiently managed with blood transfusion alone.

OUTCOME AND FOLLOW-UP

After 10 days in ICU the patient was moved to the gastroenterology ward. There was gradual improvement over 6 weeks, and on discharge liver and kidney functions had returned to the baseline.

A gastroenterology follow-up was organised but the patient unfortunately did not attend on two occasions.

DISCUSSION

Leptospirosis is a zoonotic disease caused by the spirochaete *Leptospira interrogans*. The incidence is uncertain but it is uncommon in temperate zones. In endemic tropical zones, for example, the Caribbean the incidence ranges from 0.1–1/100 000 to 10–100/100 000 per year.¹ However, because of under-reporting, it is highly likely that this is an under-estimate. Data from a single centre in Peru found that 51% of inpatients with fever of unknown cause had serological evidence of acute leptospirosis.² Outbreaks have also been reported; 44% of athletes competing in a swimming event in Malaysia in 2000 were found to have contracted the infection.³ In the UK it is far less common with only 301 cases confirmed in the 5 years from 2006 to 2010 and 25.9% of these thought to have been contracted abroad.⁴ However, due to the low clinical index of

suspicion for this disease in the UK this figure will not represent the asymptomatic carriers and those with mild disease who were never tested.

The infection is spread through contact with the urine of infected animals, most commonly rodents, but cattle, dogs, sheep and goats can act as reservoirs. The organism can survive in neutral pH soil for months and is thought to enter the body through small abrasions and mucus membranes and less commonly via ingestion or inhalation.⁴ Whether the spirochaete can penetrate the intact human skin is more controversial.

The exact pathogenesis is poorly understood, but probably relates to damage of endothelial lining of small blood vessels. This can affect any organ, explaining the wide range of clinical manifestations. These include most commonly a mild-influenza-like self-limiting illness with fever, rigors and myalgia in the majority of cases and less commonly cough, diarrhoea, vomiting, abdominal pain and arthralgia.⁵

Examination findings may include hepatosplenomegaly, lymphadenopathy and rashes. One finding that is more specific to leptospirosis is conjunctival suffusion but this only occurs in roughly 28% of patients.^{5 6}

Rarely leptospirosis presents with multiorgan involvement including liver failure which can be life threatening. This condition is known as Weil's syndrome and can also involve acute renal failure, myocarditis, meningitis, haemorrhage, pulmonary complications and rhabdomyolysis.⁴

Clinical investigations are non-specific. Raised bilirubin is seen only in Weil's syndrome.

Specific laboratory tests for leptospirosis include:

1. **Serology:** This is the most common test used to confirm the diagnosis. The MAT test is the gold standard but is difficult to perform as it requires significant expertise as well as the need for a large panel of different leptospira to be subcultured relatively frequently. ELISA tests, looking for IgM antibodies, are more commonly performed as the initial screening test as they are easier, however they are less specific. A MAT test can then be used to confirm the diagnosis. It can take 3–4 weeks for IgM antibodies to be produced, although most patients seroconvert in the first 10 days. Because of this the test should be repeated every 5–7 days if the diagnosis is suspected but the initial tests are negative, as in this case. A fourfold increase in titre over this time is also suggestive of an acute infection. In our case the initial test was negative but the second test came back positive 10 days later. Significant titres of the IgM antibody will remain for many months after infection so high titres do not guarantee acute infection.^{4 7}
2. **Culture:** *Leptospira interrogans* can be grown in vitro from the blood, urine and cerebrospinal fluid (CSF) but only on specific media and thus laboratories need to be informed that this diagnosis is suspected in advance.⁵ Cultures of blood and CSF usually become positive in only 50% of cases and can take up to 3 months although normally are positive by 10 days. This makes this a less useful or reliable method of diagnosis.^{4 5}
3. PCR has been developed and could be useful in rapid diagnosis but is not currently widely available.⁴
4. Demonstrating the presence of leptospirae in tissues using antibodies labelled with fluorescent markers. This requires tissue samples and is not as practical or reliable as serology.

Management

Early diagnosis is essential in the treatment of leptospirosis, with evidence supporting the best prognosis if antibiotics are

started before the fifth day of presentation. However, clinicians often start antibiotic therapy regardless of the date of the symptom onset.

Antibiotics such as ceftriaxone, penicillins, doxycycline or erythromycin can all be used in the treatment of leptospirosis. Randomised controlled trials have shown no significant difference in efficacy of any the antibiotics listed above.^{8 9} In developing countries doxycycline is commonly used as it also treats other infections which cause similar symptoms such as scrub typhus. In those who have organ failure associated with the infection supportive treatment is the mainstay of care.

Leptospirosis is characterised by great clinical variability, ranging from general flu-like illness to acute multiorgan failure, and so mortality rates vary widely between 4% and 10%.¹

Learning points

- ▶ Leptosporosis serology ELISA and microscopic agglutination tests may take weeks to become positive so a negative test in the context of a high clinical index of suspicion does not rule out the condition and tests should be repeated every 5–7 days. In this case a negative ELISA test resulted in a liver biopsy being performed which was complicated by a bleed. As the patient was improving, arguably it may have not been necessary to perform the liver biopsy and merely send for leptosporosis PCR and repeat an ELISA test 7 days later.
- ▶ Presents with a wide range of presentations from mild flu-like illness to acute liver and renal failure as in this case.
- ▶ Management is with an appropriate antibiotic use (ceftriaxone, doxycycline, amoxicillin) and supportive care.

Acknowledgements The authors would like to acknowledge Dr V Sheshappanavar for providing the pathology slides.

Contributors AL wrote the initial summary from the case notes. RFDeB wrote up the case report and performed the literature review and wrote the discussion. He also obtained the pathology slides, coordinated and submitted the report. JG reviewed the case report and advised alterations. EW then reviewed the case report and advised further alterations.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Levett PN. Leptospirosis: re-emerging or re-discovered disease? *J Med Microbiol* 1999;48:417–18.
- 2 Segura ER, Ganoza CA, Campos K, *et al*. Clinical spectrum of pulmonary involvement in leptospirosis in a region of endemicity, with quantification of leptospiral burden. *Clin Infect Dis* 2005;40:343–51.
- 3 Centers for Disease Control and Prevention. Update: outbreak of acute febrile illness among athletes participating in Eco-Challenge-Sabah 2000—Borneo, Malaysia, 2000. *MMWR Morb Mortal Wkly Rep* 2001;50:21–4.
- 4 Forbes AE, Zochowski WJ, Dubrey SW, *et al*. Leptospirosis and Weil's disease in the UK. *Q J Med* 2012;105:1151–62.
- 5 Katz AR, Ansdell VE, Effler PV, *et al*. Assessment of the clinical presentation and treatment of 353 cases of laboratory-confirmed leptospirosis in Hawaii, 1974–1998. *Clin Infect Dis* 2001;33:1834–41.
- 6 Berman SJ, Tsai CC, Holmes K, *et al*. Sporadic anicteric leptospirosis in South Vietnam. A study in 150 patients. *Ann Intern Med* 1973;79:167–73.
- 7 Silva MV, Camargo ED, Batista L, *et al*. Behaviour of specific IgM, IgG and IgA class antibodies in human leptospirosis during the acute phase of the disease and during convalescence. *J Trop Med Hyg* 1995;98:268–72.
- 8 Panaphut T, Domrongkitchaiporn S, Vibhagool A, *et al*. Ceftriaxone compared with sodium penicillin G for treatment of severe leptospirosis. *Clin Infect Dis* 2003;36:1507–13.
- 9 Suputtamongkol Y, Niwattayakul K, Suttinont C, *et al*. An open, randomized, controlled trial of penicillin, doxycycline, and cefotaxime for patients with severe leptospirosis. *Clin Infect Dis* 2004;39:1417–24.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow