Reminder of important clinical lesson

Leptospirosis: a globally increasing zoonotic disease

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Summary

A 27-year-old previously healthy man was admitted to the intensive care unit with severe jaundice, dyspnoea with haemoptysis, anaemia, thrombocytopenia and acute renal injury. He had no recent history of foreign travel but had been building a shed in his back garden in Cork, Ireland, for the preceding week. The patient's history, clinical observations, haematological and radiological results were all consistent with icteric leptospirosis or Weil's disease. This was confirmed on serological testing. He completed 7 days intravenous ceftriaxone and made a complete recovery. While endemic in tropical climates, leptospirosis incidence is increasing in temperate climates. Recent cases seen in temperate climates can be severe, particularly with pulmonary manifestations. The report of this case serves to increase awareness of this re-emerging potentially fatal infectious disease.

BACKGROUND

Leptospirosis is increasingly prevalent in temperate climates such as Ireland due to anticipated global warming. We present the case of a previously healthy 27-year-old man who required intensive care management secondary to severe Weil's disease. We decided to highlight this case as it is important to increase awareness of this potentially fatal re-emerging infectious disease. Severe pulmonary manifestations, rather than renal manifestations previously seen, presenting as haemoptysis and chest infiltrates are a cause of morbidity and mortality in this group. Early recognition and instigation of antibiotic treatment may help decrease complications.

CASE PRESENTATION

A 27-year-old civil engineer presented to his general practitioner with myalgia, headache, fever and sore throat. He was given oseltamivir to treat pandemic H1N1 influenza virus. His symptoms improved for a period of 2 days followed by increasing myalgia, particularly of his lumbar and calf muscles, shortness of breath with haemoptysis, nausea, vomiting and diarrhoea. On re-presentation he was hypotensive, tachycardic, tachypnoeic and icteric. Further examination revealed abnormal chest auscultation bilaterally, tender right upper quadrant and small mucosal breaks on his lower limbs consistent with recent gardening.

This patient had many poor prognostic features associated with Weil's disease, including pulmonary haemorrhage, dyspnoea, abnormal chest x-ray, oliguria, thrombocytopenia, leucocytosis and abnormal ECG.

He worked as a civil engineer in the rural south west of the country. This involved him working on construction sites where he wore gloves on-site. The week prior to his illness he spent in his back garden making a shed. There was a stream at the back of the garden. He had no involvement in water sports. He had no recollection of being exposed to any animal urine but his father reports setting traps to catch

rats after seeing them in the garden. He had a pet dog as well. The dog had two 'Vanguard 7' vaccinations (containing inactivated *Leptospira canicola* and inactivated *L. icterohaemorrhagiae*) as a puppy and had received annual boosters since. Microscopic agglutination testing (MAT) on the dogs serum was negative for L serotypes at a cut off of 1:100.

INVESTIGATIONS

Blood parameters showed bilirubin of 117 µmol/l (ref 2–20 µmol/l), with relatively preserved transaminases, elevated urea of 30.2 mmol/l (ref 2.5–7 mmol/l) and creatinine 410 µmol/l (ref range 50–130 µmol/l), elevated creatine kinase 21 U/l (40–180 U/l), anaemia haemoglobin 8.5 g/dl (ref 14–17.4 g/dl) and thrombocytopenia platelets 74×10⁹/l (140–440×10⁹/l). His chest x-ray and non-contrast CT thorax showed diffuse infiltrates bilaterally consistent with pulmonary haemorrhage (figures 1 and 2). ECG showed diffuse T wave inversion consistent with myocarditis (figure 3). Influenza A H1N1 was considered and ruled out using the Roche H1N1 swine origin reverse transcriptase-PCR assay on a throat swab.

Leptospira ELISA immunoglobulin M (IgM) was positive at 1:2560 (using antigen detected from *L. interrogans*) and MAT, considered gold standard, was also positive at 1:320. Infecting serogroup was confirmed as *L. icterohaemorrhagiae*—the causative serogroup for Weil's disease. The leptospira IgM ELISA is an 'in house' assay of the Leptospira reference unit, Hereford, UK. When compared to MAT, it has a sensitivity of 96% and a specificity of 93%. There was no cross-reactivity with antibodies to nine other antigens.¹ The patient had a serum tested for leptospira total antibodies using the Focus Diagnostics leptospirosis indirect haemagglutination assay 2 weeks after the initial positive result and it was again positive. However this specimen was not sent to the reference unit for 'rising titre' by ELISA IgM and MAT as it was felt that the diagnosis was made and the patient had responded to treatment.

Figure 1 Chest x-ray showing extensive alveolar densities throughout mid and lower zones bilaterally.

Figure 2 CT thorax showing extensive bilateral alveolar haemorrhage.

Figure 3 ECG showing diffuse T wave inversion.

TREATMENT

He started intravenous ceftriaxone for presumptive Weil's disease, which was subsequently confirmed on serum and microscopic agglutination testing. Before receiving his first intravenous dose of ceftriaxone, he had an episode of acute fever and tachycardia consistent with a Jarisch–Herxheimer reaction.

He required non-invasive ventilation with arterial and central venous cannulation for pressure monitoring. He required norepinephrine for ionotropic support. By day 4 of admission he was maintaining his blood pressure without ionotropes, did not require supplemental oxygen and was transferred for ward care. He completed 7 days intravenous ceftriaxone with excellent response.

OUTCOME AND FOLLOW-UP

He completed 10 days of intravenous ceftriaxone and his blood parameters, radiology and ECG returned to normal and he was discharged home well.

DISCUSSION

Leptospirosis is a febrile illness caused by infection with the spirochete *L. interrogans*. It is estimated that there are more than 500 000 cases of leptospirosis annually worldwide.² The actual figure may be higher with studies conducted in Thailand showing that leptospirosis may represent up to 20% of febrile illness of unknown origin.³ Although endemic in tropical climates, leptospirosis is increasing in temperate climates. There were six confirmed cases of leptospirosis in Dublin, Ireland, in November 2001. All were associated with canoeing on a particular stretch of the river Liffey. Four of the six cases required hospital admission but all recovered.⁴ Subsequent notifications have demonstrated a 57% increase in incidence of

leptospirosis in Ireland from 2004–2007.⁵ Other outbreaks in European temperate climates have been reported, including an epidemic in German strawberry harvesters in 2007.⁶ Leptospirosis has the potential to become increasingly prevalent in temperate climates such as Ireland due to anticipated global warming.

Clinical manifestations of leptospirosis vary between mild symptoms (anicteric leptospirosis; about 95% of cases) to potentially life-threatening illness (icteric leptospirosis or Weil's disease) as in this case. It has an incubation period of 4–14 days and can present as a biphasic illness with the first stage presenting as an influenza-like illness.⁷ This is illustrated in the our patient who was given treatment for circulating pandemic H1N1 influenza virus. Common symptoms of this first stage are myalgia, particularly in lumbar and calf muscles, arthralgia, pharyngitis, non-productive cough, abdominal pain, nausea, vomiting and diarrhoea, temperature and headache. Icteric leptospirosis can move directly into the second phase of illness bypassing the brief asymptomatic phase seen in anicteric disease. This second phase is characterised by aseptic meningitis, jaundice, renal failure, uveitis, pulmonary haemorrhage, acute respiratory distress syndrome, myocarditis and rhabdomyolysis, and if severe can be associated with mortality of up to 40%.⁸

Animals are more frequently affected by the spirochete leptospiral with humans accidental hosts. Humans most often become infected after exposure to environmental sources, such as animal urine, contaminated water or soil, or infected animal tissue. *Leptospira* can infect humans via breaks on the skin, conjunctiva or mucus membranes. Risk factors are mainly outdoor exposure to animal urine during recreational exposure such as canoeing, fresh water swimming or surfing.⁹ Those with occupation exposure such as

farmers, sewer workers and abattoir workers are also at increased risk. Household exposure, as in this case, with infestations of infected rodents or dogs can also be a risk.

Pulmonary involvement seems to be more prevalent in the re-emergence of leptospirosis. Alveolar haemorrhage, presenting as dyspnoea and haemoptysis, is the main pulmonary manifestation seen. The emergence of massive haemoptysis and acute respiratory distress syndrome has characterised the recent changes reported in the clinical patterns of leptospirosis. The pulmonary involvement has emerged as a serious life threat becoming the main cause of death due to leptospirosis in some countries.¹⁰ An Argentinean study between 1990 and 1999 showed no severe pulmonary haemorrhage in 276 cases diagnosis. However, in an outbreak of 93 cases in 2001 two patients died due to pulmonary haemorrhage. These 2001 were the first reported cases of severe pulmonary haemorrhage caused by leptospirosis in Buenos Aires.¹¹

The Cochrane Database of Systematic Reviews concluded that evidence from randomised controlled trials (RCTs) is insufficient to provide clear guidelines for the treatment of leptospirosis but some RCTs have shown similar outcomes in severe leptospirosis with parenteral penicillin G, doxycycline and cefotaxime.¹²

There is no human vaccination available against leptospirosis. The American Ammonal Hospital Association Canine Vaccine Task Force recommend *L. interrogans* (combined with serovars canicola and icterohaemorrhagiae)¹³ vaccination at 12 weeks and at 14–16 weeks with annual booster to those with reasonable risk of exposure. Other preventive measures include avoidance of potential sources such as swimming in freshwater ponds, wearing of protective clothing when working with wet soil, rodent control and protection of food from animal contamination.

Learning points

- ▶ This case report serves to increase awareness of this re-emerging potentially fatal infectious disease.
- ▶ This re-emergence is associated with severe pulmonary manifestations as demonstrated in this case, which can cause morbidity and mortality.
- ▶ Early recognition and instigation of appropriate antibiotics may decrease complication rate.

Competing interests None.

Patient consent Obtained.

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Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Rock C, Brady D, Forde P, Lucey P, Horgan M. Leptospirosis: a globally increasing zoonotic disease. *BMJ Case Reports* 2010;10.1136/bcr.04.2010.2947, date of publication

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