CASE REPORT

Life-threatening Q fever infection following exposure to kangaroos and wallabies

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SUMMARY

A 28-year-old woman, a park ranger, developed acute Q fever with associated sepsis, profound jaundice, disseminated intravascular coagulation and multiorgan failure necessitating prolonged admission to the intensive care unit for ventilatory support. She recovered fully and remains well 4 years later.

BACKGROUND

Q fever can be found in all regions of the world except New Zealand and Antarctica. Most Q fever infections are asymptomatic, but pneumonia and hepatitis are the most commonly recognised clinical manifestations of disease. Chronic Q fever occurs as Q fever endocarditis in a small proportion of cases. Severe life-threatening Q fever sepsis syndrome appears to be rare (or rarely recognised).

CASE PRESENTATION

A 28-year-old woman, a park ranger in Central Queensland, developed a mild influenza-like illness with a headache. Two days later, her general practitioner prescribed oral oseltamavir and amoxycillin/clavulanate 875/125 mg two times a day.

The patient developed nausea, vomiting, anorexia and generalised abdominal discomfort. She presented to a regional hospital 8 days after the onset of symptoms, with abdominal pain localised to the right upper quadrant. Her temperature was 37.8°C, pulse rate 120 bpm and blood pressure 87/51 mm Hg with an O_2 saturation of 98% on room air. She became hypotensive with haemodynamic instability requiring 8 L of intravenous crystalloid. Abdominal ultrasound scan at this time showed an oedematous gallbladder 1.8 cm thick, no cholelithiasis, no dilation of the hepatic ducts, with the common bile duct measuring 8.2 mm. Three sets of blood cultures were negative. The remainder of her initial treatment consisted of single doses of intravenous ampicillin, metronidazole and gentamicin as empiric therapy for suspected biliary sepsis. She was stabilised and transferred by air to a tertiary intensive care unit (ICU). While being transported, she became oliguric and required inotropic support.

On arrival at the tertiary centre (day 8 of illness), she was in vasodilatory shock with an escalating noradrenalin requirement and metabolic acidosis with preserved gas exchange. On examination, she had evidence of mucosal bleeding, but no petechial rash. Her right upper quadrant was tender without hepatomegaly. Her cardiovascular and respiratory examinations were normal, without cardiac murmurs. The neurological examination was normal. There were no visible tick bites. Other issues at this time were an acute kidney injury (estimated glomerular filtration rate 25 mL/min/1.73 m^2, creatine 210 μmol/L), worsening liver impairment with hypoglycaemia, disseminated intravascular coagulation and profound thrombocytopenia (lasting 14 days), with platelets 15×10^9/L, prothrombin time 25 s, Echis time 22 s, fibrinogen 0.9 g/L and international normalised ratio 2.5. Liver enzyme abnormalities reached their peak between days 8 and 11. The patient became deeply jaundiced (peak total/conjugated bilirubin were 310/194 μmol/L). Hepatitis was evident with peak alanine aminotransferase transaminase of 274 U/L (relative range (RR) <34), gamma glutamyl transferase 250 U/L (RR<38), aspartate aminotransferase 607 U/L (RR<31) and lactate dehydrogenase 1170 U/L (RR 150–280). Ammonia level was 74 μmol/L (RR<50). Lipase was normal.

She had been previously fit and well. She smoked 20 cigarettes per day and drank 60–80 g ethanol daily. Her regular medications included levelen (combined ethinyloestradiol-levonorgestrel) and metamucil. She had no known allergies or adverse drug reactions. Her work included park maintenance including disposing of road-kill animals, which were mostly kangaroos and wallabies. The carcases were dragged from the road or collected and deposited into long drop toilets. Her most recent contact with dead kangaroos was 3 weeks prior to presentation. She had no recent travel and no recent history of tick bites, but regularly had mite bites during her work. Three of her work colleagues were recently unwell with self-limiting influenza-like illnesses. She lived approximately 2 km away from a paddock with cattle.

Scrub typhus was considered a possibility given the severity of illness, mite exposure and possible geographical proximity to known foci of scrub typhus.[1] Other diagnoses included Gram-negative bacterial sepsis, toxic shock syndrome, Q fever, brucellosis and leptospirosis. Doxycycline and meropenem (total daily dose of 3 g for 7 days) were started empirically. The meropenem was ceased on confirmation of Q fever diagnosis. Doxycycline treatment continued for 14 days. While the diagnosis was unconfirmed in this septic patient, other antimicrobial agents prescribed included vancomycin 1000 mg intravenously two times a day for 2 days (empiric treatment for community-acquired methicillin-resistant *Staphylococcus aureus*, which accounts for 15% of *S. aureus* isolates in the region) and single doses of azithromycin 500 mg

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Table 1 Q fever serology

Q fever tests	Day 8	Day 11	Day 18	Day 50	Day 162	Day 1365
Ph 2 EIA IgG	NR	NR	RE	RE	RE	RE
Ph 2 EIA IgM	RE	RE	RE	RE	EQUIV	NR
Ph 1 IgG IF	<10	<10	10	80	≥1280	320
Ph 2 IgG IF	<10	160	≥1280	≥1280	≥1280	640
Ph 2 IgM IF	40	320	≥1280	≥1280	80	40

EIA, enxyme immunoassay; EQUIV, equivocal; IF, immunofluorescence; NR, not reactive; RE, reactive.

intravenously and ciprofloxacin 400 mg intravenously as empiric therapy for atypical pathogens including *Legionella pneumophila/longbeachae*.

Q fever results showed acute seroconversion (table 1). Q fever DNA was detected on two blood specimens taken 13.7 h apart on day 9 of illness.[2] The C reactive protein (283 mg/L on admission) and the procalcitonin (7.3 µg/L) were consistent with systemic bacterial infection with sepsis.

The patient developed progressive respiratory failure and was intubated and ventilated. Ongoing resuscitation was administered, consisting of intravenous fluids, stress dose corticosteroids and vasopressors, which were able to be rapidly weaned after 48 h. Transthoracic echocardiogram showed no evidence of endocarditis, with normal heart valves, moderate to severe left ventricular dilation and global systolic dysfunction, and an ejection fraction of 35–40%. The patient remained thrombocytopenic with a platelet transfusion requirement. Her acute kidney injury improved over 4 days and her urine output improved rapidly. Ultrasonography of the renal and portal veins was normal. Haemolytic screen was negative. Liver function test abnormalities were predominantly hepatocellular. The patient was jaundiced with hepatomegaly (span 26 cm), and mildly increased echogenicity with no focal lesions. She remained febrile with temperatures >38.5°C daily during her 7 day ICU admission. There was a gradual improvement in clinical condition with normalisation of her liver enzymes, thrombocytopenia (duration 11 days) and jaundice (26 days). She was successfully extubated after 7 days. A follow-up transoesophageal cardiac echo was normal on day 23. The patient fully recovered, resumed work and remains well 4 years later.

INVESTIGATIONS

Patients with sepsis and jaundice have a broad differential diagnosis including infections and autoimmune diseases. In our case, relevant negative serological tests/antigen detection tests included typhoid, *Rickettsia*, *Orientia*, *Brucella*, dengue, leptospirosis, hepatitis A, B and C, *Burkholderia pseudomallei*, and HIV. *Legionella pneumophila* serogroup 1 and *Streptococcus pneumoniae* urinary antigens were not detected. An autoimmune screen was negative (antinuclear antibody, anti-double-stranded DNA) as was a vasculitis screen (c-ANCA (antineutrophil cytoplasmic antibody)/p-ANCA). Haemolysis screening tests were negative with normal haptoglobin, glucose-6-phosphate dehydrogenase levels and negative direct Coombs tests.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis of patients with sepsis and jaundice include local zoonotic infections, biliary sepsis from intra-abdominal infections, bacterial toxin-induced illnesses and autoimmune diseases.

TREATMENT

The patient was treated for sepsis syndrome with broad antibiotic cover, which was quickly rationalised to doxycycline for 14 days when the acute Q fever diagnosis was made. Recovery ensued with supportive management.

OUTCOME AND FOLLOW-UP

The patient recovered fully and remains well 4 years later.

DISCUSSION

This case describes an unusually severe presentation of Q fever associated with multiorgan failure, including shock, renal failure, profound hyperbilirubinaemia, disseminated intravascular coagulation and respiratory failure requiring mechanical ventilation.[3–5]

The greatest risks for infection with Q fever are to abattoir workers, people exposed to farm animals, typically cattle, sheep or goats, those living downwind from contaminated farming materials (dust, feed, hay, birth products) and workers at Q fever laboratories.[6]

The patient's work history may have been relevant to her illness. Our patient had frequent ongoing physical contact with dead grey kangaroos and wallabies in the course of her work. Previously described severe Q fever cases reported from southeast Queensland (Ipswich) occurred adjacent to high kangaroo density areas containing >5 kangaroos/km^2.[4 7] Q fever serosurveys of wild kangaroo populations in Australia have consistently shown high prevalence of Q fever antibodies in kangaroos and wallabies.[8–10] In Western Australia, grey and red kangaroos have had high Q fever seroprevalence (33%), higher than Q fever seroprevalence in sheep and cattle in the same area. *Coxiella burnetii* DNA in kangaroo faeces has commonly been detected (12%).[8] Similar high prevalence rates of Q fever were reported in 1960 in kangaroos in western Queensland.[10] Recent kangaroo seroprevalence studies reported in 2012 showed similar high prevalence rates (11% to 25% near Ipswich, and up to 40% in areas near our case).[9] Although association does not prove causality, our patient's repeated exposure to carcases of kangaroos and wallabies as part of her work was a potential source of infection. At least one of her work colleagues subsequently tested positive for Q fever. Although some ungulates (cattle, sheep, goats) are well-known zoonotic reservoirs for Q fever, parturient animals such as cats have been linked to Q fever outbreaks.[6] Bandicoots, kangaroos and wallabies (Australia) and three-toed sloths (French Guiana) may also be reservoirs for Q fever transmission.[6 8–11] The genotyping of PCR products detected in patients with Q fever could improve our understanding of epidemiology of Q fever in Australia and identify other occupations for which Q fever vaccination would be indicated.[12–15]

Learning points

- Sepsis syndrome with severe jaundice has a broad differential diagnosis including infections caused by toxin-producing pathogens, for example, *Clostridium perfringens* (gas gangrene) and *Streptococcus pyogenes* and *Staphylococcus aureus* (toxic shock syndrome).[16]
- Typhoid fever and severe bacterial pneumonias may be associated with sepsis and jaundice.[16]
- Zoonotic diseases including Q fever, leptospirosis and *Rickettsia*/*Orientia* infection can produce sepsis, jaundice and hepatitis, with leptospirosis often producing renal disease.[16]
- Doxycycline administration should be considered in the treatment of severely ill patients who may have risk factors for zoonotic infections.

Contributors SS wrote the first draft of the paper. JG was the intensive care specialist who oversaw the management of the patient and provided advice on the manuscript. ST provided advice regarding molecular testing for Q fever and testing of potential Q fever reservoirs. MW was responsible for editing and revising the initial draft of the manuscript and revisions, and for ongoing care of the patient.

Competing interests None declared.

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