Q fever following a tick bite

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CASE

A man aged 41 years was brought by his wife to the Gold Coast University Hospital with fever, sweats, headache, myalgia, arthralgia and increasing confusion of six days' duration.

He worked as a fly-in-fly-out coal miner inland from Mackay, Queensland, and had been bitten by ticks 10 days previously.

There was no significant past medical history, regular medication or known medication allergies. Specifically, he had no known valvulopathy or aneurysm.

On examination he was febrile with no rash, eschar or lymphadenopathy and no stigmata of infective endocarditis. Cardiovascular and respiratory examinations were normal. A smooth liver edge was palpable below the costal margin. An engorged tick was detected crawling out from between his bed sheets. It was sent for laboratory testing.

A diagnosis of an infection by a tick-transmitted pathogen was suspected (*Rickettsia* spp. or *Coxiella burnetii*), and he commenced doxycycline orally 100 mg twice daily.

Laboratory tests showed abnormal liver function (alanine aminotransferase [ALT] 388 IU/L [reference range 10–50 IU/L] and aspartate aminotransferase [AST] 265 IU/L [reference range 10–35 IU/L]), thrombocytopenia (platelet count 76×10^9/L [reference range $150–400 \times 10^9$/L]), lymphopenia (0.8×10^9/L [reference range $1.0–4.0 \times 10^9$/L]), neutropenia (1.3×10^9/L [reference range $2.0–8.0 \times 10^9$/L]) and a raised C-reactive protein (69 mg/L [reference range <5 mg/L]). Cerebrospinal fluid and mid-stream urine were normal, and two sets of blood cultures showed no growth. Serology and real-time quantitative polymerase chain reaction (qPCR) for Q fever were both negative. Serology was negative for rickettsial infection, human immunodeficiency virus and cytomegalovirus but positive for Epstein–Barr virus, consistent with past exposure.

The patient continued to improve and was discharged after seven days and instructed to continue a 10-day course of doxycycline.

He was reviewed in the outpatient department one week after discharge, at which time he was well apart from significant ongoing fatigue, limiting his ability to return to work. A transthoracic echocardiogram was normal. Serum taken at this time showed seroconversion to *C. burnetii* over the nine-day period, confirming the diagnosis of acute Q fever. The phase II immunoglobulin (Ig) M titre was ≥1280 and the phase II IgG titre was 320 (determined by microimmunofluorescence), but the phase I IgG was negative, a result consistent with acute Q fever.

The tick was damaged, so while it could be partially identified as *Amblyomma* spp., full species identification (based on mouthpart morphology) was not possible. It was most likely *A. triguttatum*, the ornate kangaroo tick. The tick was strongly positive for DNA from *C. burnetii* by qPCR based on two unique genes: *com1* and *htpAB*.

QUESTION 1

Is this the manner by which people usually contract Q fever?

QUESTION 2

Is this a typical presentation for Q fever?

QUESTION 3

Is ongoing fatigue a common problem with acute Q fever?

QUESTION 4

Why were the Q fever qPCR and serology both negative when tested early in the illness?

QUESTION 5

Could this infection have been prevented?

ANSWER 1

Q fever is typically contracted from infected parturient animals (eg goats, cattle, sheep) that contaminate the soil with 'spores' (small cell variant) of *C. burnetii*. The microbe remains viable in the soil for months, and potentially for years,[1] and is dispersed by the wind, especially in dry conditions. Humans inhale the pathogen, and infection is

initiated in the lungs but becomes systemic by haematogenous and lymphatic spread into many organs. Q fever was first recognised in Australia,[2] and the microbe initially identified as a *Rickettsia* spp. prior to its reclassification.[3] Several species of Australian ticks are known to carry *C. burnetii*, including two species that regularly bite humans: *Ixodes holocyclus*, the paralysis tick, and *A. triguttatum*, the ornate kangaroo tick.[1,4–6] A tick-transmitted case of Q fever was reported in Western Australia in 1989.[7]

ANSWER 2

This is a typical presentation for Q fever, even though it was transmitted by tick bite rather than aerosol inhalation. The transmission of Q fever has been reported via a crushed tick[8] and a tick bite.[7] It is uncommon for a rash or eschar to be present in Q fever, unlike in rickettsial infections. Fever and headache associated with a transaminitis, thrombocytopenia and lymphopenia is common. There may be respiratory symptoms, ranging from a mild cough to atypical pneumonia, mimicking influenza.

ANSWER 3

Ongoing fatigue is a problem in 15–20% of patients with acute Q fever.[9] This may be a serious problem for some patients, with ongoing economic and psychological impact. Post–Q fever fatigue is a post-infectious syndrome with a likely immunological basis. It differs from chronic Q fever (also known as persistent, localised Q fever), which is an ongoing infection usually presenting as endocarditis or endovascular infection and requires prolonged antibiotic therapy and specialist advice.

ANSWER 4

The negative Q fever qPCR and serology were both false-negative results. The qPCR assay is often positive early in the illness while the patient is bacteraemic, with a sensitivity of approximately 30–50% during the first seven days.[10] In this patient, the initial seven-day period had already passed, and hence the qPCR was negative. The development of antibodies (positive serology) usually takes between one and two weeks after the onset of illness.[10] The first serum, taken early in the illness, is often negative; however, repeat serum testing later in the illness or after recovery is usually positive as the patient's immune system has now produced antibodies.[10] This is known as seroconversion and is a reliable marker of recent infection. This highlights the importance of performing paired serology (at least seven days between the acute and convalescent specimens), even if the initial serology and qPCR results are negative.

ANSWER 5

Q fever vaccination would likely have prevented this infection. This vaccine, which is approximately 95% effective, became available in 1989, only in Australia.[11–13] Prior to vaccination with the Q fever vaccine, individuals must undergo pre-vaccination evaluation with both serum antibody testing and skin testing to ensure they have not previously been exposed to the organism. Administration of Q fever vaccine after exposure to Q fever can lead to significant adverse reactions to the vaccine given the development of hypersensitivity to the organism. Similarly, individuals with a previous history of Q fever infection should not be vaccinated.

The authors recommend this vaccine for persons living or working in rural and regional Australia, especially in Queensland and New South Wales where Q fever is a problem, and who have exposure to high-risk animals.[13] The Australian Immunisation Handbook recommends Q fever vaccination for individuals aged ≥15 years who have close contact with animals, including abattoir workers, farmers, veterinarians, professional dog and cat breeders, wildlife and zoo workers and animal refuge workers.[13] Its use with at-risk children is also recommended, with caution.[14]

Key points

- Q fever, caused by the bacterium *C. burnetii*, is usually acquired by inhalation of an aerosol from an infected animal but may be rarely acquired by tick bite or by crushing a tick.
- The infection is more common in regional and rural parts of Australia, especially Queensland and New South Wales.
- The diagnosis is difficult on clinical grounds alone, although it should be suspected in a patient with fever associated with acute liver enzyme abnormalities and thrombocytopenia. Key laboratory investigations are Q fever qPCR and serology on blood; however, it is important to be alert to the possibility of false-negative results.
- Treatment of acute Q fever is with doxycycline, 100 mg orally twice daily for 14 days. If the patient has already become afebrile when the diagnosis of Q fever is made, some experts recommend a seven-day course of doxycycline to prevent the 5% risk of the patient developing chronic Q fever.
- Q fever can be prevented by vaccination.

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