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Queensland tick typhus: three cases with unusual clinical features

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Abstract

Queensland tick typhus (QTT), caused by *Rickettsia australis*, is usually a relatively mild illness but can occasionally be severe. We describe three cases of probable QTT with unusual clinical features, namely splenic infarction, fulminant myopericarditis and severe leukocytoclastic vasculitis. QTT may present with uncommon clinical features in addition to the more common manifestations. A high index of suspicion enables specific antibiotic therapy that may hasten recovery.

A 25-year-old man presented with fevers and a widespread rash. He had been working in forestry immediately prior to becoming unwell, felling trees in the Nelson Bay area, New South Wales (NSW). Nine days prior to admission, the illness began with fevers to 40°C and rigors. A widespread rash developed, involving the trunk and limbs. Other symptoms included arthralgias, nausea, vomiting and headache. On presentation, there was a fever of 38.5°C, hepatosplenomegaly, cervical and inguinal lymphadenopathy, and a widespread macular petechial rash involving the trunk, limbs, palms and soles. No eschar was visible. Blood test results included neutrophilia with a left shift, thrombocytopenia, hyponatraemia, acute renal failure (urea 24.8 mmol/L; normal range (NR) 2.7–7.7, creatinine 257 µmol/L; NR 60–120), deranged liver function tests and elevated C-reactive protein (335 mg/L; NR < 3.1). Blood cultures were negative. Initial treatment included doxycycline for a presumed rickettsial illness, ibuprofen and paracetamol/codeine. From day 3, pleuritic left upper quadrant abdominal pain developed which radiated to the left shoulder. An upper abdominal ultrasound showed hepatosplenomegaly and a focal heterogeneous area in the spleen. A computed tomography (CT) scan on day 8 confirmed hepatosplenomegaly with a large hypodensity, consistent with a splenic infarct. Intermittent fevers resolved by day 5, and the abdominal pain improved slowly. A 10-day course of doxycycline was completed, with discharge on day 13. Antibody titres against spotted fever group rickettsiae rose from 256 (on 5 April 2011) to 8192 (on 12 April), confirming the diagnosis as one of the Australian rickettsial spotted fevers.

A 52-year-old woman who lived near Port Stephens, NSW, was previously well other than mild chronic obstructive pulmonary disease. She had been unwell for 6 days, with fevers, rigors, sore throat, headache, muscle and joint pains, and an itchy rash. Severe central chest pain developed *en route* to hospital. On arrival, her temperature was 34.9°C, blood pressure 120/85 and oxygen saturation 98% on oxygen 4 L/min. Examination showed a generalised maculopapular rash involving the trunk and lower limbs; there was no pericardial rub. Investigations of note included thrombocytopenia (platelet count 46 × 10^9/L; NR 150–400), renal impairment (urea 18.8; NR 3.5–7.2, creatinine 206; NR 60–100), C-reactive protein 257.6 mg/L (NR < 3.1) and troponin 0.95 (NR < 0.1). The chest X-ray showed a patchy right lower zone infiltrate. The initial electrocardiography showed marked ST segment elevation in lead V_6 and lesser ST elevation in leads I, II, III and aVF. An echocardiogram showed normal left ventricular size and

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contraction without pericardial effusion or thickening. Initial treatment consisted of ceftriaxone, azithromycin and oral prednisone. The next day, the patient was dyspnoeic, tachypnoeic and hypoxaemic (O_2 saturation 86–91% on oxygen 3 L/min). A progress chest X-ray showed an extensive bilateral pulmonary infiltrate, and the troponin rose to 59.2 (creatine kinase (CK) 1539; NR 1–125), then to >99 on day 2. The patient required intensive care unit admission because of respiratory failure needing intubation and mechanical ventilation and shock requiring inotropic support. Subsequently, atrial flutter and junctional tachyarrhythmias required cardioversion and amiodarone, thrombocytopenia worsened (nadir platelet count 14×10^9/L), and fevers persisted. Treatment included broad spectrum antibiotics (vancomycin/ceftriaxone/azithromycin), corticosteroids and intravenous immunoglobulin (for possible toxic shock syndrome). An echocardiogram on day 3 showed global hypokinesia with left ventricular ejection fraction (LVEF) of 20%. On day 4, intravenous tigecycline was commenced for possible rickettsial infection. Polymerase chain reaction (PCR) for rickettsial DNA from blood taken on day 3 was reported as positive, but DNA sequencing was unable to be performed. There was slow improvement over the following 4 days, with cessation of inotropes, extubation and defervescence. Serology for spotted fever and murine typhus group rickettsiae from day 20 showed antibody titres >1024 for both agents, compared with titres of <128 from day 3. Antibiotic treatment was completed with oral doxycycline. The patient was transferred to a rehabilitation ward on day 27 and was discharged on day 41. The LVEF improved to 53% on echocardiogram 11 months post-illness.

A 59-year-old diabetic woman presented in October 2011 with vomiting, diarrhoea, myalgia, fever and rash. She had been bitten by a tick on the umbilicus 8 days previously in the mid-North Coast region of NSW. On examination, she was febrile with an erythematous rash around the umbilical area. Chest X-ray showed a left lower lobe pulmonary infiltrate. Antibiotic treatment was commenced, which included various beta-lactam antibiotics (ceftriaxone and ticarcillin + clavulanate) and gentamicin. The patient's condition worsened over the next 10 days with development of dyspnoea and atrial fibrillation. A generalised painful skin rash with generalised oedema developed, thought to be a drug eruption secondary to beta-lactam antibiotics, which were ceased, and doxycycline was started. The skin rash evolved to a painful retiform confluent rash on the trunk and limbs, with skin necrosis, bullae and purpura; tongue ulcers were also present. An inoculation eschar was noted at the site of the tick bite in the umbilical area. A presumptive diagnosis of Stevens–Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN) was made after dermatology consultation. The patient was treated with intravenous immunoglobulin, topical steroids, dressings and analgesics. The skin biopsy showed features of severe leukocytoclastic vasculitis, with infarction of the epidermis, skin appendages and subcutis, and partial infarction of the dermal interstitium, with nodules of nuclear dust and polymorphs. The eschar from the umbilicus was biopsied, from which rickettsial DNA was detected by PCR. Serology for rickettsial spotted fever group was negative (<128) on day 1, but became positive (>1024) on day 11. DNA sequencing, and hence confirmation of rickettsial species, was unable to be performed. Rickettsial DNA was detected by PCR on peripheral blood on both day 1 and day 3. A 7-day course of oral doxycycline was completed. The patient gradually improved and was discharged from hospital after a long rehabilitation period.

The most likely cause of the three cases on epidemiologic grounds was *Rickettsia australis*. However, it is possible that another rickettsial species that cross-reacts on serologic testing may have been the causative organism. The cases of rickettsial infection displayed unusual features, namely splenic infarction, fulminant myocarditis and severe leukocytoclastic vasculitis. The second case was successfully treated with intravenous tigecycline, which has not been previously used in this setting to the best of our knowledge. A previous study showed low minimum inhibitory concentration values when tigecycline was tested with *Coxiella burnetii* strains, although information relating to *Rickettsia* species is lacking.[1]

There are several reports of splenic infarction occurring in the context of a rickettsial infection. A 41-year-old man in Los Angeles with murine typhus (*R. typhi*) had several splenic infarcts, which necessitated splenectomy.[2] A 28-year-old woman in Israel with possible murine typhus experienced left upper quadrant abdominal pain with a large splenic infarct on CT scan.[3] The diagnosis was revised to *R. felis* infection after further PCR tests.[4] The pathogenesis of splenic infarction is thought to involve vasculitis with organisms invading endothelial cells of the blood vessel wall. Vasculitis involving large vessels has not been commonly described in rickettsial infection.

The second case was remarkable for the complication of fulminant myocarditis, which required inotrope infusions, intubation and mechanical ventilation for acute pulmonary oedema. The global reduction in LVEF was acute in onset but has improved significantly in follow-up. Myocarditis has been described in several rickettsial infections, including those caused by *R. rickettsii*,[5–8] *R. helvetica*,[9] *R. africae*,[10,11] *R. japonica*[12] and *R. conorii*.[13] Of the rickettsial diseases occurring in Australia, numerous cases of myocarditis related to scrub typhus have been

reported.[14–18] There is a single case report of fatal murine typhus (*R. typhi*) where myocarditis was found on autopsy.[19] Queensland tick typhus (QTT) caused by *R. australis* is generally a mild infection, although there are a few reports of severe illness[20,21] and one fatal case.[22] To the best of our knowledge *R. australis* infection complicated by severe myopericarditis has not been previously described.

The third case illustrated severe leukocytoclastic vasculitis with skin changes mimicking SJS or TEN, including bullous lesions and mucous membrane involvement. A murine model suggested that *R. australis* could cause disseminated infection of endothelial cells and highly invasive vascular damage, resulting in severe vasculitis in animals.[23] However, there have been only a few human case reports of severe cutaneous involvement in QTT with oral mucosal lesions[24] or bullae.[21]

In conclusion, QTT may present with complications, such as splenic infarction, myocarditis or leukocytoclastic vasculitis, in addition to the more common manifestations. A high index of suspicion enables specific antibiotic therapy that may hasten recovery.

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