

Neurological presentations caused by *Rickettsia felis* infection

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Introduction

Infection with *Rickettsia felis* can cause encephalopathy and status epilepticus. However, many cases continue to be misdiagnosed or remain undiagnosed, especially in non-endemic areas such as China. This article presents the case of a 24-year-old man who presented with refractory status epilepticus, persistent coma and recurrent febrile seizures. After ruling out other common infectious and autoimmune diseases the patient was diagnosed with *R. felis* encephalopathy with the help of metagenomic next-generation sequencing of the CSF. After treatment the patient's fever gradually disappeared and his limb twitches reduced. He was transferred from the intensive care unit to the general ward on the sixth day and was discharged home 6 days later.

Case report

A 24-year-old man who lived in Ningbo was admitted to hospital with sudden onset twitching of the extremities. His family reported that the patient was previously healthy and did not have any history of epilepsy; however, the patient was a pet lover who owned three dogs, and came into contact with stray dogs and cats. His temperature was 38.0°C, blood pressure 154/84 mmHg (without vasopressor support) and he had a regular pulse at 117/min. Examination revealed unconsciousness (Glasgow coma scale of 6), and a few inconspicuous maculopapular erythematous rashes on and around his neck (3–5 mm diameter). There were no focal neurological findings or neck stiffness. A routine blood test revealed a left shift with a high percentage of polymorphonuclear leukocytes (83.6%). The C-reactive protein level was 92.7 mg/litre (normal range 0–8 mg/litre), and the procalcitonin level was 0.229 ng/ml (normal range 0–0.046 ng/ml). Lumbar puncture was performed and the CSF was clear and colourless with a cell count of 8 cells/ μ l (two lymphocytes, six neutrophils), protein level 0.325 g/litre (normal range 0.15–0.45 g/litre), and glucose level 3.6 mmol/litre (normal range 2.5–4.5 mmol/litre). CSF and blood cultures were also performed, and no microorganisms were detected upon Gram staining or during routine culture. Serological testing and polymerase chain reaction for suspected microorganisms (such as *Escherichia coli*, *Vibrio cholerae*, *Rickettsia* and *Salmonella* spp.) were also conducted but provided no significant clues. A plain computed tomography scan of the head and a chest radiograph were normal. Renal function test values, liver function test values, and electrolyte levels were within the normal ranges. Treatment was initiated using valproate to treat status epilepticus and piperacillin-tazobactam combined with levofloxacin for suspected CNS infection.

On the second day of intensive care unit admission, the patient's CSF sample underwent metagenomic next-generation sequencing analysis. This identified eight sequence reads that uniquely corresponded to the *R. felis* genome, with 0.023% coverage. After removal of human reads, *R. felis* reads accounted for 0.8% of the microorganisms. *R. felis* DNA was further verified in the CSF using real-time polymerase chain reaction followed by Sanger sequencing. Based on these results and the past exposure to stray dogs and cats, the patient was diagnosed with *R. felis* encephalopathy. Oral doxycycline (0.1 g every 12 hours) was prescribed to replace piperacillin-tazobactam and levofloxacin. Subsequently the patient's fever gradually reduced, as did his limb twitches. He emerged from the coma on the fourth day of his intensive care unit admission and was discharged home 6 days later with no further limb twitches.

Discussion

R. felis infection is an arthropod-borne disease caused by a Gram-negative, obligate, intracellular bacterium (Valbuena et al, 2002). The cat flea, *Ctenocephalides felis*, is currently the only known biological vector of *R. felis*, although it has been found in a

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Learning points

- Despite the large number of potential vectors reported for *Rickettsia felis* infection, the only vector currently recognised is *Ctenocephalides felis*.
- In cases of unexplained status epilepticus combined with fever and cutaneous rashes, *R. felis* encephalopathy should be considered in the differential diagnosis.
- Metagenomic next-generation sequencing analysis of the patient's CSF facilitated the diagnosis of *R. felis* infection.

variety of arthropod species such as book lice and others such as mosquitoes (Dieme et al, 2015). In this case, fleas from the patient's pets as well as stray dogs and cats are highly likely to be the source of the infection.

In a review of 34 reported cases of *R. felis* infection, the clinical findings included fever (32 cases), cutaneous rash (24 cases, mostly maculopapular), cutaneous eschar (four cases), neurological signs (five cases), digestive symptoms, cough without pneumonia (three cases), and pneumonia (two cases) (Parola, 2011). If not treated in a timely manner, devastating manifestations such as myocarditis, meningoencephalitis and cerebral oedema can occur. In this case, *R. felis* was thought to be the cause of the patient's neurological presentations.

For patients with typical manifestations of rickettsia, the first-choice diagnostic inspection is real-time polymerase chain reaction. However, non-specific manifestations often lead to missed diagnosis. *R. felis* infection in this case was diagnosed following the metagenomic next-generation sequencing analysis of the patient's CSF. Metagenomic next-generation sequencing is an important addition to the diagnostic toolbox and improves the diagnostic yield of rare pathogens such as *R. felis*.

Doxycycline is the optimal treatment of *R. felis* infection. In this case, the patient's symptoms gradually improved after starting oral doxycycline treatment. Physicians should consider rickettsial infection (including *R. felis*) and be aware of potential neurological presentations, so that timely, effective therapy may be instituted.

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