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Case Report: Two Cases of Acute Q Fever from the Same Family Who Returned from Malawi to Japan

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Abstract. In July 2018, acute Q fever (AQF) was diagnosed in two Japanese individuals from the same family. They returned to Japan from Malawi, where the epidemiology of AQF is unknown. A child presented to the hospital with high-grade fever without any symptoms, and a mother presented with fever and dry cough. Paired serum antiphase II IgM and IgG significantly elevated in the convalescent phase in both cases. *Coxiella burnetii* gene (*IS1111*) was detected from the mother's blood sample. They had no reported direct animal contact, but the onset of symptoms coincided with the dry season in Malawi, which may have facilitated environmental dispersal. These cases may serve as an alert for high-risk people to possible AQF spread and underdiagnosis in Malawi.

Acute Q fever (AQF), a zoonosis which transmits by inhalation of aerosols contaminated with *Coxiella burnetii*, has been reported worldwide.[1] It is challenging to diagnose because most patients are asymptomatic or develop nonspecific and self-limited symptoms.[2,3] High-risk patients may develop chronic infections, such as endocarditis.[1] Despite its clinical importance, limited AQF information is available in resource-limited countries, especially Eastern Africa.[4] We report two Japanese patients with AQF from the same family, who returned from Malawi.

In July 2018, a 4-year-old previously healthy Japanese boy developed high-grade fever without any symptoms the day he returned to Japan for summer vacation. He had lived in Malawi with his family since 2016. Although their house was located in a suburban area of Lilongwe, where livestock, especially cattle, were raised, he had no direct contact with them. His parents took him to a clinic, and his liver function tests were abnormal (aspartate aminotransferase [AST]: 57 U/L and alanine aminotransferase [ALT]: 68 U/L). He was clinically diagnosed with a viral infection; his fever continued for 7 days and spontaneously subsided.

Two days after his recovery, his 40-year-old mother developed fever with a dry cough. Two days after onset, she presented to the National Center for Global Health and Medicine (Tokyo, Japan). She worked as an office worker in Malawi and had a history of Kawasaki disease without cardiac complications. On admission, she had fever (38.7°C) with relative bradycardia (85 bpm, regular). Blood tests revealed bicytopenia (white blood cell count 2,510/mm^3 and platelet count 13.9 × 104/mm^3) and mildly elevated liver transferase levels: AST 60 U/L and ALT 42 U/L. Blood smear and rapid diagnostic test for malaria and blood culture were negative. She was suspected of having AQF because of her relative bradycardia and her indirect livestock contact in Malawi. Nucleic acids were extracted from whole blood obtained on the fourth hospital day. Multiplex real-time polymerase chain reaction, including *IS1111* gene primers and probes (FTD Tropical fever Africa, Fast Track Diagnostics, Luxembourg, Belgium), revealed that the blood sample was *C. burnetii* positive.[5] By indirect fluorescent antibody test, serum antiphase II IgM was positive (1:64) and antiphase II IgG and antiphase I IgG were negative (1:64 and < 1:16, respectively). She was diagnosed with AQF and completely recovered with oral doxycycline (100 mg bid for 14 days). In the convalescent phase, the paired serum sample phase II IgG titers were significantly raised (1:256). A transthoracic echocardiogram showed no valvular heart disease, and a contrast chest computed tomography revealed only a small pure ground-glass nodule in the right upper lobe, which was suspected to be a malignant tumor, rather than pneumonia. The lesion did not change after 2 weeks and required follow-up.

After the mother's diagnosis, her son was also suspected of having had AQF, and thus, we examined him on the seventh day after his recovery. His blood tests showed higher liver transferase levels than the previous test: AST 110 U/L and ALT 177 U/L. Serum antiphase II IgM and IgG were positive (1:64 and 1:514, respectively) and antiphase I IgG was negative. Transthoracic echocardiogram revealed no valvular heart disease. After 2 weeks, the paired antiphase II IgG became higher than that of previous tests (1:1,024). Based on these results, he was diagnosed with AQF with spontaneous recovery, without any complications.

The epidemiology of *C. burnetii* infection in eastern Africa, such as Malawi, has been unclear. A systematic review reported *C. burnetii* infection epidemiologies in Africa and showed that AQF accounted for 2–9% of hospital admissions due to febrile illness.[4] In Eastern Africa, few reports are available about human AQF in northern Tanzania.[6,7] Among admitted febrile patients, 3% of children and 8% of adults were diagnosed with AQF, and AQF may be associated with livestock parturition during the dry season.[6] Q fever in travelers returning from Africa has also been reported, mainly from European countries.[8–15] However, to the best of our knowledge, no study has reported patients returning from Malawi. In Malawi, the serological prevalence of Q fever in cattle was reported as 6.5%,[16] and the incidence of AQF in humans remains unknown. From June to July, it is dry season in Malawi, and it is possible that dust contaminated with *C. burnetii* from livestock easily spread by wind. Other family members might have been asymptomatically infected. We did not examine

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C. burnetii antibody titer because they had no symptoms or underlying risk factors and stayed in Japan for a limited time.

According to the patient, some of her neighbors also had fevers, and AQF is potentially underdiagnosed in Malawi. In conclusion, AQF should be considered an important differential diagnosis among residents in, and travelers returning from, Malawi, especially in the dry season. Pretravel counseling to high-risk groups, such as pregnant women, immunocompromised hosts, and patients with valvular diseases, is crucial.[1] More studies that investigate the epidemiology nationwide are needed to clarify *C. burnetii* infections in Eastern African countries, including Malawi.

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