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Neoehrlichia mikurensis Infection in Immunocompromised Patient, the Netherlands, 2024

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We report a case of *Neoehrlichia mikurensis* infection from a tick bite in a 69-year-old immunocompromised man with non-Hodgkin lymphoma in the Netherlands. Because of increasing use of immunosuppressive therapies and frequent tick bites, *N. mikurensis* should be recognized as a potential cause of recurrent fever in immunocompromised patients.

Neoehrlichia mikurensis is a gram-negative tick-borne bacterium increasingly identified in Europe and Asia (*1*). Clinical manifestations of infection are fever, chills, night sweats, and systemic inflammatory responses, particularly in immunocompromised patients. We describe the case of *N. mikurensis* infection in a man who had recurrent, cyclical fever over a 1-year period.

A 69-year-old man with indolent non-Hodgkin lymphoma was undergoing immunochemotherapy consisting of rituximab, a CD20 monoclonal antibody that depletes B lymphocytes, along with cyclophosphamide, vincristine, and prednisolone (R-CVP regimen); treatment began in April 2024. He was admitted to Elisabeth-TweeSteden Hospital, Tilburg, the Netherlands, on July 23, 2024, with nonneutropenic fever, chills, night sweats, and mild bilateral edema of the legs. Apart from hiking in a national park in the Netherlands, he reported no other risk factors for infectious diseases (e.g., tick bite, travel abroad). Standard investigations,

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including chest radiograph, urine analysis, and blood cultures, were unremarkable. However, laboratory results showed the presence of leukocytosis (10.1×10^9 cells/L; reference range $4.0–10.0 \times 10^9$ cells/L) and a C-reactive protein level of 124 mg/L (reference <20 mg/L), which led to empirical treatment with cefuroxime.

The fever persisted for >5 days, prompting a positron emission tomography scan, which showed no infectious or inflammatory foci but did show good response to his lymphoma treatment. The patient felt unwell during fever episodes but was symptom free between those episodes (Figure). We discontinued cefuroxime and discharged him after 10 days.

After discharge, night sweats and edema began subsiding, and the patient had mostly recovered. However, during the last 2 therapy cycles for his lymphoma, night sweats returned, along with edema, chills, and fever. During follow-up on November 19, he was readmitted with a fever (40.3°C) and treated again with cefuroxime. We found no cause for the edema; echocardiography and chest radiograph showed no signs of right heart failure. Further diagnostic tests, including those for serum albumin and urine protein levels, were unremarkable. During hospital stays, each episode of chills and fever led to intercurrent systemic inflammatory response syndrome accompanied by severe hypotension and tachycardia, necessitating fluid resuscitation (Figure).

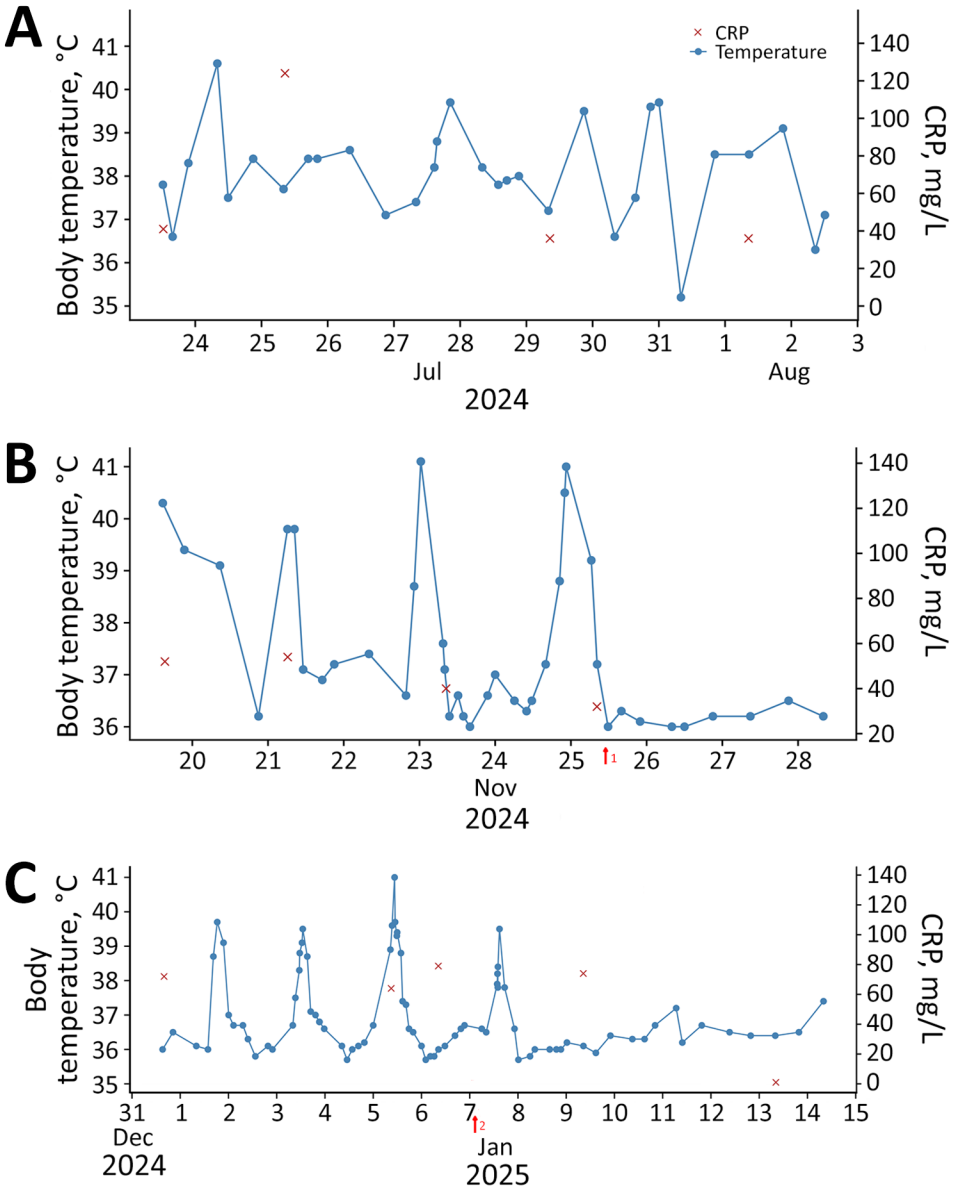


Figure. Body temperature course and blood CRP levels during hospital admissions in case study of *Neoehrlichia mikurensis* infection in immunocompromised patient, the Netherlands, 2024. A) First admission on July 23, 2024. B) Second admission on November 19, 2024. Red arrow 1 indicates initiation of naproxen treatment (250 mg 3×/d). C) Third admission on December 31, 2024. Red arrow 2 indicates initiation of doxycycline treatment (100 mg 2×/d). CRP, C-reactive protein.

We discontinued cefuroxime because of the absence of clinical response and negative blood cultures. After starting nonsteroidal antiinflammatory drugs on November 25, which seemed to reduce the fever, we discharged the patient on November 28.

On December 31, the patient was readmitted with similar symptoms. On January 2, 2025, a bone marrow biopsy was performed, which appeared to be reactive and did not show signs of lymphoma or other malignancies. The episodes of fever persisted with a noticeable cyclical pattern of ≈48 hours (Figure). Each episode began with chills, followed by fever up to 41.1°C and systemic inflammatory response syndrome reactions. Ultimately, broad-range PCR that targeted the 16S V3–V4 region of bacterial rRNA followed by sequencing revealed the presence of *N. mikurensis* DNA. An *N. mikurensis*–specific PCR of blood, performed at the National Institute for Public Health and the Environment in the Netherlands, confirmed the diagnosis. The patient started treatment with doxycycline on January 7 for 3 weeks, after which the fever and edema subsided within days. PCR of blood samples collected 3 and 6 months after doxycycline treatment were negative for *N. mikurensis*.

N. mikurensis is an emerging intracellular bacterium transmitted by ticks and is increasingly recognized as a major pathogen in immunocompromised populations. In a cohort study from Sweden, a substantial percentage of patients with *N. mikurensis* infections were undergoing immunosuppressive therapies that included rituximab and other B-cell–depleting agents (*1*). The epidemiology of *N. mikurensis* indicates that infections primarily occur in areas where ticks, particularly *Ixodes ricinus* ticks, are endemic. In western Europe, *N. mikurensis* has been detected in up to 24.2% of *I. ricinus* ticks (*2*). Clinical symptoms of *N. mikurensis* infection are diverse, ranging from mild fever and general malaise to more severe manifestations, such as vasculitis and thromboembolic events. Recognizing clinical manifestations of *N. mikurensis* is crucial, particularly because symptoms often do not align with typical infectious conditions and can lead to underdiagnosis (*3*). Moreover, incidence of clinically relevant *N. mikurensis* infections is likely to increase as use of immunosuppressive therapies rises (*4*).

Detection of *N. mikurensis* is diagnostically challenging. Current methods are limited to PCR that specifically tests for *N. mikurensis* or broadly tests for 16S rRNA; those methods are restricted to laboratories with appropriate resources (*5*). The recommended treatment for *N. mikurensis* infection is oral doxycycline at a dose of 100 mg 2×/day for 2–3 weeks, which has been shown to effectively eradicate the infection and lead to a rapid resolution of symptoms in patients. Shorter courses or lower doses of doxycycline might result in recurrence of infection, particularly in immunocompromised persons (*3*,*6*).

In conclusion, clinically relevant *N. mikurensis* infections in the Netherlands might increase because of the growing use of immunosuppressive therapies and frequent human *I. ricinus* tick bites. Further studies are needed, such as prospective studies of patients with fever after a tick bite (*7*). *N. mikurensis* should be recognized as a potential cause of recurrent fever in immunocompromised patients.

About the Author

Mr. Tjan was a resident in the Internal Medicine Department at the Elisabeth-TweeSteden Hospital during the treatment of the patient described in this case report. His interests focus on pathogenesis of diseases, particularly those in medical oncology.

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