

Neoehrlichiosis Associated With Arteriovenous Fistula Thrombosis: A Case Report



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We report on a case of a 55-year-old female with therapy-refractory myasthenia gravis (MG) receiving immunosuppressive treatment and weekly plasma exchange via a stented brachiocephalic arteriovenous fistula. She presented with recurrent thromboses and central stenoses of her arteriovenous fistula, as well as recurrent fever, shivering, malaise, and a localized skin rash. Blood cultures, serological testing, and untargeted next-generation sequencing (NGS) for common pathogens were negative. Histopathology of a skin biopsy demonstrated partial small-vessel thrombosis but no evidence of an infectious agent. Positron emission tomography-computed tomography (PET-CT) revealed increased metabolic activity around the implanted stent. During a subsequent percutaneous transluminal angioplasty, blood was sampled directly from the affected fistula segment after dilatation, and 16S ribosomal RNA gene polymerase chain reaction (PCR) with amplicon NGS demonstrated the presence of *Neoehrlichia mikurensis*. Antimicrobial therapy with rifampicin was initiated for 6 weeks. Clinical and laboratory indicators of infection normalized, and follow-up PET-CT demonstrated resolution of the previously increased metabolic activity. Neoehrlichiosis is an emerging tick-borne disease prevalent in Eurasia. Clinical manifestations of neoehrlichiosis include fever, myalgia, arthralgia, thrombotic events, and cutaneous lesions; and are most frequently observed in immunocompromised individuals. Because this intracellular bacterium is detectable only through molecular methods, the infection is likely underrecognized. Our case demonstrates that neoehrlichiosis should be considered in immunosuppressed patients presenting with fever and vascular access complications. A high index of clinical suspicion is required, because untargeted NGS from peripheral blood may fail to detect the pathogen, whereas local sampling can increase the likelihood of diagnosis.

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KEYWORDS: arteriovenous fistula thrombosis; fever of unknown origin; *Neoehrlichia mikurensis*; neoehrlichiosis

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INTRODUCTION

N. mikurensis is an intracellular bacterium and an emerging human pathogen causing neoehrlichiosis. Transmission in Europe occurs predominantly through

bites of the *Ixodes ricinus* tick. Infection rates in ticks vary regionally, with particularly high prevalence reported in Scandinavia.^{1–4} In Norway, a study found a 25.5% infection rate in ticks, whereas another identified *N. mikurensis* in 7 of 70 individuals presenting with erythema after a tick bite.^{5,6} By contrast, the prevalence in ticks in Denmark was reported to be only 0.1%.² Beyond humans, *N. mikurensis* has been detected in wild rodents, including mice and rats.^{7,8}

In humans, symptomatic infection has almost exclusively been observed in immunocompromised

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patients and B-cell depletion in particular appears to be strongly associated with development of clinical disease.^{9–12} Typical clinical manifestations of *N mikurensis* infection include fever, myalgia, arthralgia, and skin rashes. Beyond these nonspecific symptoms, various thrombotic events have been described in the context of *N mikurensis* infection.^{11,13} Human vascular endothelial cells have been identified as target cells of the bacterium, which may explain the occurrence of thrombotic events and the reported cutaneous manifestations, including small-vessel thrombosis.¹⁴ Neoehrlichiosis is likely underdiagnosed, because the pathogen is difficult to detect.⁴ As an intracellular bacterium, it was first cultivated only in 2019, when successful propagation was achieved in human endothelial cells.¹⁴ At present, diagnosis relies on specific PCR assays or 16S ribosomal RNA gene sequencing from blood or bone marrow, whereas serological tests remain unavailable.^{2,15} In most reported cases, doxycycline has been used successfully for antimicrobial therapy, usually resulting in rapid clinical improvement.^{1,9,12} Here, we report on the first case of neoehrlichiosis-associated arteriovenous fistula thrombosis.

CASE PRESENTATION

We report on the case of a 55-year-old female patient with treatment-resistant, generalized seronegative MG, who was undergoing plasma exchange via a brachiocephalic fistula 3 times/wk at the Department of Nephrology and Medical Intensive Care, Charité Universitätsmedizin Berlin, Germany. Previous therapies for MG had included multiple cycles of rituximab (anti-CD20 monoclonal antibody), efgartigimod alfa (anti-FcRn monoclonal antibody), intravenous immunoglobulins, mycophenolate mofetil, immunoadsorption, and thymectomy, none of which had resulted in sustained clinical improvement. In addition, she carried a diagnosis of polyglandular autoimmune syndrome type 2a, type 1 diabetes, Hashimoto thyroiditis, and adrenal insufficiency.

The patient presented with recurrent episodes of fever of up to 38.8 °C, shivering, and malaise persisting for >2 weeks, but reported no other symptoms. In recent months, she had experienced multiple complications of her forearm arteriovenous fistula, including recurrent central (type 4) stenoses requiring repeated percutaneous transluminal angioplasties and stent implantation, followed by in-stent restenoses and shunt occlusions necessitating several further percutaneous transluminal angioplasties and open shunt revision. On physical examination, an erythematous rash was noted

on the upper arm near the brachiocephalic fistula (Figure 1a).

Laboratory tests revealed a mildly elevated C-reactive protein of 20 mg/l and a normal white blood cell count with a slight relative monocytosis (15%). Multiple sets of blood cultures remained sterile, and serologies for *Borrelia*, *Brucella*, *Coxiella*, cytomegalovirus, Epstein–Barr virus, HIV, and *Bartonella henselae* were negative. Transesophageal echocardiography showed no evidence of endocarditis. Histopathological examination of a skin biopsy demonstrated partially thrombosed small vessels with superficial and deep perivascular lymphohistiocytic infiltrates; however, no pathogen was identified (Figure 1b). NGS of cell-free DNA of a peripheral blood sample did not detect microbial sequences.

A fluorodeoxyglucose PET-CT scan revealed increased metabolic activity in the region of the implanted subclavian vein stent, raising suspicion of a stent-associated infection (Figure 1c). Secondary findings included splenomegaly without increased fluorodeoxyglucose uptake.

Multidisciplinary consultation was obtained from the departments of vascular surgery, infectious diseases, neurology, and interventional radiology. Because of the symptomatic recurrence of the in-stent stenosis, another angioplasty was performed, which provided the opportunity to obtain blood samples directly from the suspected site of infection (Figure 1d).

In this sample, *N mikurensis* was detected by pan-bacterial 16S ribosomal RNA gene PCR and amplicon sequencing (100% identity over 398/398 base pairs). The pathogen was further confirmed through concurrent detection of multiple specific genetic markers by multilocus sequence analysis targeting the heat shock protein gene (*groEL*), lipase gene (*lipA*), adenosine triphosphatase-dependent chaperone gene (*clpB*), cell division protein gene (*ftsZ*), and galactitol-specific phosphotransferase system component gene (*gatB*). The multilocus sequence analysis approach used in this study was performed according to a protocol previously described in Grankvist *et al.*¹⁶

Only after molecular confirmation of *N mikurensis* did the patient recall multiple tick bites without erythematous skin changes, occurring approximately 8 weeks before symptom onset.

The case was subsequently discussed in a local interdisciplinary board, including specialists from neurology, nephrology, and infectious diseases. The patient was treated with rifampicin 600 mg once daily for 6 weeks, because of the concern that doxycycline could aggravate MG. Clinical improvement was noted after 1 week, and C-reactive protein levels had

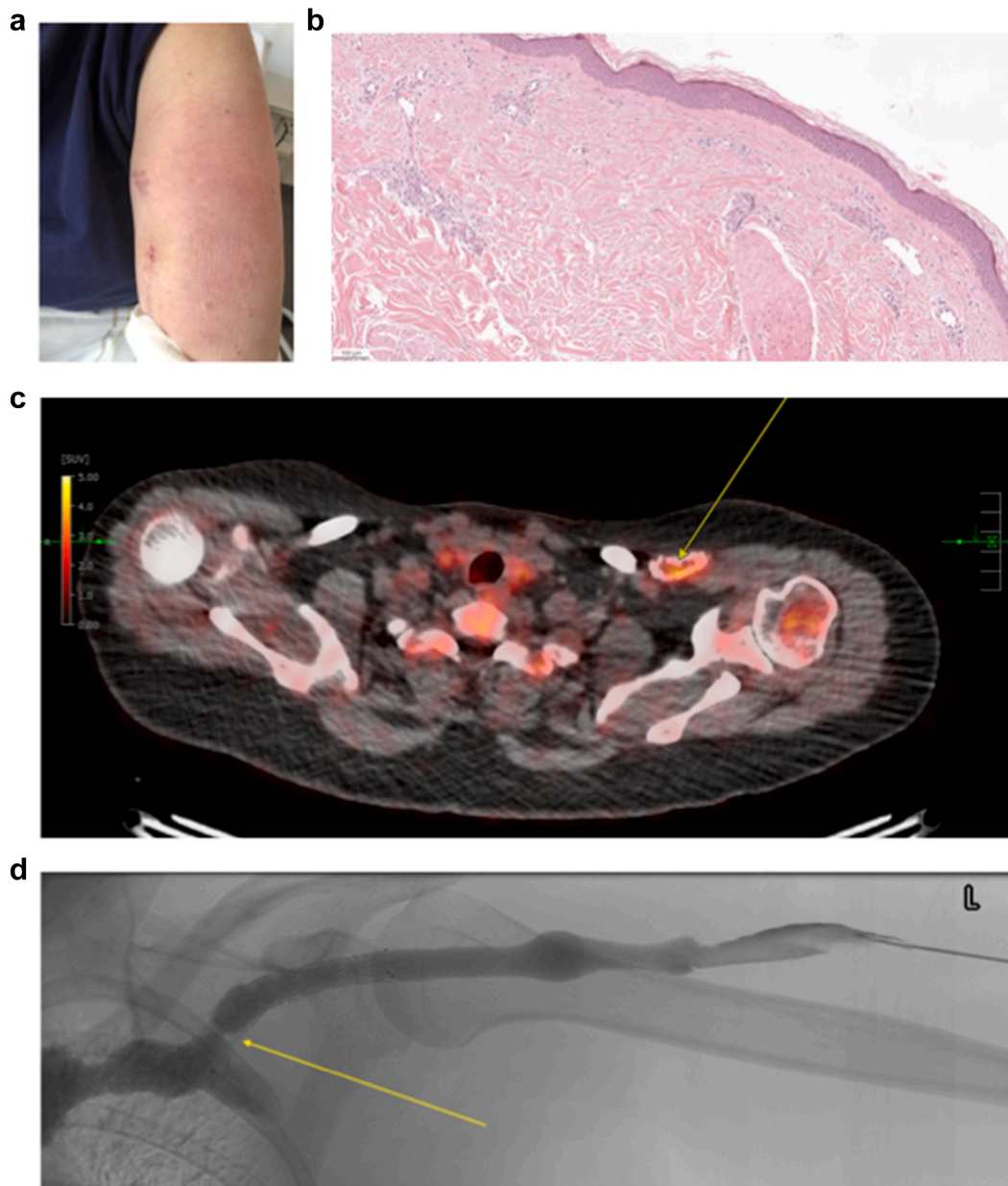


Figure 1. (a) Erythematous rash on the upper arm at the site of the brachiocephalic fistula. (b) Hematoxylin eosin staining of the skin biopsy. (c) ^{18}F -fluorodeoxyglucose positron emission tomography–computed tomography (transverse plane) at the level of the stenotic shunt vein at the junction of the brachiocephalic and subclavian veins, demonstrating increased focal metabolic activity along the stent in the left subclavian vein raising suspicion of prosthetic infection (yellow arrow). The color scale corresponds to uptake of the ^{18}F -fluorodeoxyglucose tracer in standardized uptake value units. (d) Angiography of the brachiocephalic fistula on the upper arm showing the shunt vein and the stent with an in-stent restenosis (yellow arrow) before angioplasty.

normalized. A follow-up PET-CT at the end of therapy showed resolution of the localized tracer uptake.

DISCUSSION

To our knowledge, this is the first case report of neoehrlichiosis associated with recurrent shunt thrombosis. Awareness of this pathogen remains limited, likely due to both its rarity and the diagnostic challenges it poses.

Because the interval between tick exposure and clinical manifestation is often prolonged (6–16 weeks),

the association can usually be established only when clinical suspicion is high.² In our patient, multiple tick bites without local erythema had occurred approximately 2 months before symptom onset—an important detail in view of the nonstandard diagnostic methods required. Another challenge highlighted by this case is that untargeted NGS of cell-free DNA from peripheral blood failed to detect *N mikurensis*; confirmation was only achieved through targeted sampling from the suspected site immediately after angioplasty and subsequent 16S ribosomal RNA gene PCR with amplicon

sequencing. Whether untargeted shotgun NGS from a sample taken from the focus of infection might have detected *N mikurensis* in this case as well remains unclear. However, the case presented here clearly shows that choosing the most sensitive detection method is key for the diagnosis of *N mikurensis* infections.

Reported clinical features of neoehrlichiosis include fever, myalgia, arthralgia, skin rash, and thrombosis.¹ In a Swedish cohort, >60% of patients experienced thromboembolic events.¹³ Our patient exhibited the full spectrum of these manifestations, including large-vessel involvement with recurrent thrombosis of the arteriovenous fistula and local inflammatory changes demonstrated using PET-CT. A similar case of an immunosuppressed patient with fever, multiple venous thromboses, and increased fluorodeoxyglucose uptake in thrombotic areas has been reported.¹¹ The strong tropism of *N mikurensis* for vascular endothelial cells may account for these thrombotic complications and associated local inflammation.¹⁴

Nearly all published cases have been treated successfully with doxycycline, typically 100 mg twice daily for 3 weeks.² However, in our patient, doxycycline was contraindicated because of the risk of precipitating myasthenic crisis. Instead, guided by a previous case report, rifampicin was chosen as an alternative therapy, leading to complete clinical recovery.¹⁷

Severe neoehrlichiosis has been observed almost exclusively in immunocompromised patients, particularly those with hematologic malignancies or undergoing immunosuppressive treatment for autoimmune disease.^{1,2} More specifically, impaired B-cell immunity appears to be the major risk factor, with severe cases described after B-cell depletion, B-cell lymphoma, or splenectomy.^{9,10,12} Consistent with this, our patient had received multiple cycles of rituximab for MG and was further immunocompromised by chronic plasma exchange and efgartigimod treatment. How B-cell-mediated immunity contributes to the defense against *N mikurensis* remains an important question for future research.

Neoehrlichiosis is a rare infectious disease that requires both a high index of clinical suspicion and the use of molecular diagnostic techniques. The combination of fever of unknown origin, B-cell-depleting therapy, and thrombotic events should prompt consideration of *N mikurensis* infection. In some cases, targeted blood sampling from the site of infection together with PCR may be necessary to establish the diagnosis. Rifampicin was successful in the treatment of neoehrlichiosis in this case.

DISCLOSURE

All the authors declared no competing interests.

PATIENT CONSENT

The patient gave her written consent for publication of this case report.

Declaration of AI and AI-Assisted Technologies in the Writing Process

Claude Opus 5 (Anthropic, PBC) was used to assist with language editing and stylistic refinement. The authors take full responsibility for the content of this manuscript.

CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

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SUPPLEMENTARY MATERIAL

Supplementary file (PDF)

CARE-checklist.

REFERENCES

1. Gynthersen RMM, Stensvold CR, Nielsen SL, et al. Neoehrlichia mikurensis-An emerging opportunistic tick-borne infection in immunosuppressed patients. *J Intern Med*. 2023;293:782–790. <https://doi.org/10.1111/joim.13638>
2. Portillo A, Santibáñez P, Palomar AM, Santibáñez S, Oteo JA. ‘Candidatus Neoehrlichia mikurensis’ in Europe. *New Microbes New Infect*. 2018;22:30–36. <https://doi.org/10.1016/j.nmni.2017.12.011>

3. Quarsten H, Salte T, Lorentzen ÅR, et al. Tick-borne pathogens detected in the blood of immunosuppressed Norwegian patients living in a tick-endemic area. *Clin Infect Dis*. 2021;73:e2364–e2371. <https://doi.org/10.1093/cid/ciaa971>
4. Wennerås C, Wass L, Bergström B, Grankvist A, Lingblom C. Ten years of detecting Neoehrlichia mikurensis infections in Sweden: demographic, clinical and inflammatory parameters. *Eur J Clin Microbiol Infect Dis*. 2024;43:2083–2092. <https://doi.org/10.1007/s10096-024-04909-5>
5. Pedersen BN, Jenkins A, Paulsen KM, et al. Distribution of Neoehrlichia mikurensis in Ixodes ricinus ticks along the coast of Norway: the western seaboard is a low-prevalence region. *Zoonoses Public Health*. 2020;67:130–137. <https://doi.org/10.1111/zph.12662>
6. Quarsten H, Grankvist A, Høyvoll L, et al. Candidatus Neoehrlichia mikurensis and Borrelia burgdorferi sensu lato detected in the blood of Norwegian patients with erythema migrans. *Ticks Tick Borne Dis*. 2017;8:715–720. <https://doi.org/10.1016/j.ttbdis.2017.05.004>
7. Jahfari S, Fonville M, Hengeveld P, et al. Prevalence of Neoehrlichia mikurensis in ticks and rodents from North-West Europe. *Parasit Vectors*. 2012;5:74. <https://doi.org/10.1186/1756-3305-5-74>
8. Naitou H, Kawaguchi D, Nishimura Y, et al. Molecular identification of Ehrlichia species and ‘Candidatus Neoehrlichia mikurensis’ from ticks and wild rodents in Shizuoka and Nagano prefectures, Japan. *Microbiol Immunol*. 2006;50:45–51. <https://doi.org/10.1111/j.1348-0421.2006.tb03769.x>
9. Welinder-Olsson C, Kjellin E, Vaht K, Jacobsson S, Wennerås C. First case of human ‘Candidatus Neoehrlichia mikurensis’ infection in a febrile patient with chronic lymphocytic leukemia. *J Clin Microbiol*. 2010;48:1956–1959. <https://doi.org/10.1128/JCM.02423-09>
10. Wennerås C, Goldblatt D, Zancolli M, et al. Natural IgM antibodies in the immune defence against neoehrlichiosis. *Infect Dis (Lond)*. 2017;49:809–816. <https://doi.org/10.1080/23744235.2017.1347815>
11. Sjöwall J, Kling K, Ochoa-Figueroa M, Zachrisson H, Wennerås C. Neoehrlichia mikurensis causing thrombosis and relapsing fever in a lymphoma patient receiving rituximab. *Microorganisms*. 2021;9:2138. <https://doi.org/10.3390/microorganisms9102138>
12. Andréasson K, Jönsson G, Lindell P, et al. Recurrent fever caused by Candidatus Neoehrlichia mikurensis in a rheumatoid arthritis patient treated with rituximab. *Rheumatology (Oxford)*. 2015;54:369–371. <https://doi.org/10.1093/rheumatology/keu441>
13. Höper L, Skoog E, Stenson M, et al. Vasculitis due to Candidatus Neoehrlichia mikurensis: a cohort study of 40 Swedish patients. *Clin Infect Dis*. 2021;73:e2372–e2378. <https://doi.org/10.1093/cid/ciaa1217>
14. Wass L, Grankvist A, Bell-Sakyi L, et al. Cultivation of the causative agent of human neoehrlichiosis from clinical isolates identifies vascular endothelium as a target of infection. *Emerg Microbes Infect*. 2019;8:413–425. <https://doi.org/10.1080/22221751.2019.1584017>
15. Grankvist A, Jaén-Luchoro D, Wass L, Sikora P, Wennerås C. Comparative genomics of clinical isolates of the emerging tick-borne pathogen Neoehrlichia mikurensis. *Microorganisms*. 2021;9:1488. <https://doi.org/10.3390/microorganisms9071488>
16. Grankvist A, Moore ERB, Svensson Stadler L, et al. Multi-locus sequence analysis of clinical “Candidatus Neoehrlichia mikurensis” strains from Europe. *J Clin Microbiol*. 2015;53:3126–3132. <https://doi.org/10.1128/JCM.00880-15>
17. Wennerås C. Infections with the tick-borne bacterium Candidatus Neoehrlichia mikurensis. *Clin Microbiol Infect*. 2015;21:621–630. <https://doi.org/10.1016/j.cmi.2015.02.030>