

DOI: 10.4274/mjima.galenos.2025.25480.17

Mediterr J Infect Microb Antimicrob 2025;14:25480.17

Erişim: <http://dx.doi.org/10.4274/mjima.galenos.2025.25480.17>

Chronic *Coxiella burnetii* Infection in a Patient with a Left Ventricular Assist Device: A Case Report

Sol Ventrikül Destek Cihazı Olan Bir Hastada Kronik *Coxiella burnetii* Enfeksiyonu: Olgu Sunumu

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Abstract

Chronic infection with *Coxiella burnetii*, the pathogen responsible for Q fever, presents considerable diagnostic and treatment difficulties, especially in individuals with implanted devices like left ventricular assist devices (LVADs). We describe the case of a 28-year-old man with an LVAD who experienced persistent fever, weight loss, night sweats, and a productive cough. Blood and sputum cultures returned negative, and transthoracic echocardiography did not indicate endocarditis. Nevertheless, serological tests showed elevated levels of *C. burnetii* immunoglobulin G Phase I antibodies, and positron emission tomography-computed tomography revealed increased metabolic uptake at the aortic insertion site of the LVAD. Initial therapy with doxycycline and hydroxychloroquine was switched to doxycycline and moxifloxacin due to recurrent fever. After more than 18 months of monitoring, the patient remained symptom-free with reduced inflammatory markers. This case highlights the need to consider Q fever in LVAD patients with prolonged fever, particularly those with animal-related occupational exposure, and emphasizes the diagnostic and therapeutic challenges of chronic *C. burnetii* infection in this group.

Keywords: *Coxiella burnetii*, Q fever, left ventricular assist device, device-associated infection

Öz

Q hummasının etkeni *Coxiella burnetii*, özellikle sol ventrikül destek cihazı (LVAD) gibi implante tıbbi cihaz taşıyan hastalarda tanı ve tedavi açısından önemli güçlükler neden olur. Bu yazıda, LVAD'si olan ve uzamış ateş, kilo kaybı, gece terlemesi ve balgamlı öksürük şikayetleriyle başvuran 28 yaşında erkek bir hastayı sunuyoruz. Kan ve balgam kültürleri negatif bulunmuş ve transtorasik ekokardiyografide endokardit bulgusu saptanmamıştır. Ancak, serolojik incelemede *C. burnetii* immünoglobulin G Faz I antikorlarında yüksek titrerler saptanmış; pozitron emisyon tomografi-bilgisayarlı tomografi ise LVAD'ın aort giriş noktasında artmış metabolik aktivite göstermiştir. Başlangıç tedavisinde tercih edilen doksisisiklin ve hidroksiklorokin ile ateş yüksekliklerinin tekrarlaması üzerine hastanın tedavisi doksisisiklin ve moksifloksasin kombinasyonu ile değiştirilmiştir. On sekiz aydan uzun takip süresinde hasta semptomsuz kalmış ve inflamatuvar belirteçlerinde azalma gözlenmiştir. Bu olgu, özellikle mesleki hayvan temas öyküsü olan ve uzamış ateşi bulunan LVAD hastalarında Q hummasının mutlaka akılda tutulması gerektiğini ve kronik *C. burnetii* enfeksiyonlarının tanı ve tedavi zorluklarını vurgulamaktadır.

Anahtar Kelimeler: *Coxiella burnetii*, Q humması, sol ventrikül destek cihazı, endokardit

Introduction

Coxiella burnetii, the organism responsible for Q fever, can manifest with both acute and chronic forms. It poses a notable occupational risk for those employed in animal-related work and is linked to contact with both domestic and wild animals^[1].

In humans, acute Q fever commonly appears as atypical pneumonia or acute febrile hepatitis. About 1-5% of patients with an acute infection may develop the chronic form, which can lead to endocarditis or vascular involvement and has an estimated mortality rate of 15%^[2]. Infections related to LVADs are generally categorized as driveline infections, bloodstream

Cite this article as: Kahraman H, Ölmezoğlu SF, Doyuk Kartal E. Chronic *Coxiella burnetii* infection in a patient with a left ventricular assist device: A case report. Mediterr J Infect Microb Antimicrob. 2025;14:25480.16.



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Received/Geliş Tarihi: 06.05.2025 Accepted/Kabul Tarihi: 10.07.2025

Epub: 22.07.2025

Published: 19.08.2025



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infections, pocket infections, and localized infections not directly involving the device, including cases with negative cultures, which create substantial diagnostic difficulties^[3,4]. This case report outlines the clinical course, diagnostic workup, and treatment of chronic *C. burnetii* infection in a patient with an LVAD. Written informed consent was obtained from the patient for this publication.

Case Report

A 28-year-old man presented with fever, chills, night sweats, marked weight loss (6–7 kg over 2 weeks), and a productive cough persisting for 2 months. His symptoms had started 2 months before admission, with episodes of high-grade fever and chills that had worsened during the preceding 10 days. Although he had visited several outpatient clinics and had been prescribed empirical antibiotics including moxifloxacin, amoxicillin–clavulanate, and cefixime, his symptoms did not resolve. He was therefore admitted for further evaluation of his prolonged fever.

His medical history included LVAD implantation and aortic valve replacement in 2021 due to advanced heart failure. There was no notable family medical history. He resided in a rural area, worked in livestock farming, and regularly consumed raw milk and dairy products.

On physical examination, his vital signs were as follows: body temperature 38.4 °C, pulse rate 115 beats per minute, blood pressure 85/50 mmHg, respiratory rate 20 breaths per minute, and peripheral oxygen saturation of 94% on room air. He appeared pale and diaphoretic. Cardiovascular examination was limited due to the mechanical sound from the LVAD. Petechial rashes were noted on both lower limbs. Examination of other systems revealed no abnormalities.

Initial laboratory investigations showed a white blood cell count of 5,120/mm³, with neutrophils at 3,340/mm³ and lymphocytes at 1,420/mm³. The hemoglobin level was 10.2 g/dl, and the platelet count was 164,000/mm³. Liver enzymes were slightly elevated, with aspartate aminotransferase at 63 U/l and alanine aminotransferase at 52 U/l. Renal function was normal, with a creatinine level of 0.78 mg/dl. Inflammatory markers were raised, with a C-reactive protein (CRP) of 80 mg/l and a procalcitonin level of 1.37 ng/ml. The international normalized ratio was 2.22.

Chest X-ray and high-resolution computed tomography scans did not identify any abnormalities that could explain the patient's symptoms. Blood and sputum cultures were negative for bacterial growth. Further serological tests, including *Brucella* tube agglutination and Human Immunodeficiency Virus 1/2 antibody-p24 antigen tests, were negative. The purified protein derivative test was anergic.

Transthoracic echocardiography (TTE) performed twice over a 2-week period showed no vegetations on intracardiac structures. However, transesophageal echocardiography could not be done due to the presence of the LVAD. Serological testing revealed a positive *C. burnetii* immunoglobulin G (IgG) Phase I immunofluorescence assay (IFA) with a titer of 1:2048. Real-time polymerase chain reaction (PCR) for *C. burnetii* was negative. Positron emission tomography-computed tomography (PET-CT) indicated increased metabolic uptake at the LVAD's aortic entry point (SUV_{max} 3), suggestive of infection.

Doxycycline (100 mg twice daily) and hydroxychloroquine (200 mg three times daily) were started. A consultation with cardiovascular surgery determined that replacing the LVAD was not an option. After a 26-day hospital stay, the patient was discharged with ongoing doxycycline and hydroxychloroquine treatment.

One month after discharge, the patient was re-admitted due to recurrent fever and elevated CRP levels. Moxifloxacin was started at another facility, and he was then referred back to our clinic for further care. With the addition of moxifloxacin (400 mg daily), both his symptoms and inflammatory markers improved. Hydroxychloroquine was subsequently stopped because of possible drug interactions, and therapy was continued with doxycycline and moxifloxacin.

At the third month of follow-up, the patient remained symptom-free, with a positive *C. burnetii* IgG Phase I IFA titer of 1:8192. Moxifloxacin was completed at that point, and treatment continued with doxycycline and hydroxychloroquine.

During follow-up visits every 3 months, the patient stayed clinically stable. At the 1-year follow-up, the *C. burnetii* IgG Phase I IFA titer was 1:16,384, and the Phase II titer was 1:32,768. A repeat PET-CT showed minimal residual metabolic activity at the LVAD entry site, with decreased intensity and area compared to earlier imaging.

By the 18-month follow-up, serology showed a further drop in the *C. burnetii* IgG Phase I IFA titer to 1:8192, while the Phase II titer remained at 1:32,768. The patient stayed asymptomatic and continues treatment with doxycycline and hydroxychloroquine. Another PET-CT is planned at the 2-year follow-up to reassess disease activity.

Discussion

Q fever is a zoonotic infection caused by *C. burnetii*, most commonly spread through inhalation of contaminated aerosols or consumption of unpasteurized animal products^[5]. Infection with *C. burnetii* presents notable diagnostic and treatment difficulties, especially when it progresses to a chronic form. Chronic Q fever is uncommon, occurring in less than 5% of

people following an acute infection, and can appear months or even decades after the initial exposure. Those with underlying valvular heart disease, vascular grafts, or arterial aneurysms are at the highest risk. Endocarditis is the predominant presentation of chronic Q fever, accounting for 60–78% of cases, followed by vascular infections^[6,7]. In this patient's case, classic signs of chronic Q fever were observed, including prolonged fever, marked weight loss, and night sweats, further complicated by a history of LVAD implantation and aortic valve replacement.

The patient's work involving livestock and regular intake of unpasteurized dairy products were significant risk factors for *C. burnetii* infection^[8]. Diagnosis of chronic Q fever depends on identifying an elevated or rising Phase I IgG titer, generally $\geq 1:1024$, along with clinical evidence of an ongoing infection focussuch as endocarditis, a vascular infection, or osteomyelitis^[7]. For this patient, diagnosis was challenging because of persistent symptoms despite several outpatient antibiotic treatments. Blood and sputum cultures stayed negative, and TTE showed no vegetations. However, serology revealed markedly elevated *C. burnetii* IgG Phase I titers, and PET-CT showed increased metabolic uptake at the LVAD's aortic entry site, indicating localized infection.

Infection is the most frequent complication among LVAD recipients, and a considerable number of these infections are culture-negative, creating specific diagnostic and treatment difficulties. In the MOMENTUM 3 trial, out of 1,213 major infection events reported in 585 patients, bacterial pathogens were found in 66% of cases, fungal in 2%, viral in 3%, and polymicrobial in 2%, while in 26% of cases, no causative organism was identified. When broken down by infection type, culture negativity was highest in localized non-device-related infections (33%), followed by driveline infections (20%), and was lowest in bloodstream infections (14%). In LVAD patients, culture-negative infections often require empiric antimicrobial treatment based on clinical suspicion and known risk factors, including the patient's immune status and any prior use of antibiotics. Having an implanted device and heart failure-related immune system dysfunction may further increase susceptibility to atypical pathogens and subtle clinical presentations. Therefore, clinicians should keep a high level of suspicion for culture-negative infections in LVAD patients and apply multiple diagnostic approaches, including advanced imaging and serologic tests, as illustrated in this case^[3].

The standard treatment for chronic Q fever generally involves doxycycline (100 mg twice daily) together with hydroxychloroquine (200 mg three times daily), with treatment duration adjusted depending on the infection's location and severity^[7]. Alternative options, such as moxifloxacin,

clarithromycin, trimethoprim-sulfamethoxazole, and rifampin, may be used for patients unable to tolerate doxycycline^[8]. In this case, treatment was begun with doxycycline and hydroxychloroquine according to current recommendations^[7]. Within the first month of therapy, the patient developed recurrent fever, and moxifloxacin was started at another facility. After being referred back to our clinic, moxifloxacin was continued alongside doxycycline, while hydroxychloroquine was stopped due to possible drug interactions^[9]. Treatment continued with doxycycline and moxifloxacin^[10] for 3 months. Afterward, since the patient had no active symptoms, the regimen was switched back to doxycycline and hydroxychloroquine.

The main treatment goal in chronic Q fever is to achieve at least a fourfold drop in Phase I IgG antibody titers or reach a titer of $\leq 1:1024$ before stopping antibiotic therapy^[11]. However, the prognostic significance of serologic follow-up remains debated. Some studies have shown higher mortality rates in patients who do not reach a fourfold reduction in Phase I IgG titers after 1 year of treatment. Furthermore, persistent Phase II IgM antibodies at 1 year have also been linked to increased mortality, as shown by Million et al.^[12].

Conversely, although elevated Phase I IgG titers during and after treatment have been associated with treatment failure in certain reports^[13], other studies, including one involving 337 patients, did not find a significant link between serologic titers and negative clinical outcomes^[14]. These results indicate that serological testing alone may not reliably predict treatment success in chronic Q fever. Therefore, management decisions should be based on clinical evaluation, PCR results, and imaging, while research continues to identify better prognostic indicators^[14]. In this case, despite persistently high Phase I and Phase II IgG titers at the 1-year follow-up, the patient remained clinically stable, and repeat PET-CT at that time showed reduced metabolic activity at the device insertion site. By the 18-month follow-up, the Phase I IgG titer had declined further, which supported the overall favorable clinical progress.

Conclusion

To the best of our knowledge, this is the first reported case of *C. burnetii* infection in a patient with an LVAD, illustrating the distinctive diagnostic and treatment challenges involved. Although IgG titers remained elevated during early follow-up, successful management was achieved through careful clinical assessment, serologic testing, and advanced imaging. This case highlights the need to consider Q fever in LVAD patients with prolonged fever and occupational exposure to animal products and points to the necessity for further research to improve diagnostic and treatment approaches for this specific patient group.

Ethics

Informed Consent: Written informed consent was obtained from the patient for this publication.

Footnotes

Authorship Contributions

Surgical and Medical Practices: H.K., S.F.Ö., E.D.K., Concept: H.K., S.F.Ö., E.D.K., Design: H.K., S.F.Ö., Data Collection or Processing: H.K., S.F.Ö., Analysis or Interpretation: H.K., E.D.K., Literature Search: H.K., Writing: H.K., S.F.Ö., E.D.K.,

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study received no financial support.

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