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Case Report

Q Fever - An Unexpected Case Report

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Abstract

We present a case of Q fever in a 77-year-old autonomous male with a complex medical history. The patient, immunocompromised due to azathioprine and prednisolone use for myasthenia gravis, also suffered from diabetes mellitus, heart failure, and severe asthma. Despite no history of animal contact or travel to endemic regions, the patient developed flu-like symptoms followed by high fever and prostration.

Multiple courses of antibiotics were administered without clinical improvement, and cultures of blood, urine, and stool were negative. Serological testing for Coxiella burnetii confirmed the diagnosis, with positive IgG and IgM phase II antibodies. The patient received doxycycline therapy and experienced rapid clinical improvement, with sustained apyrexy and no recurrence of symptoms at a 2-week follow-up.

This case highlights the diagnostic challenges of Q fever, particularly in immunocompromised individuals with multiple comorbidities. Despite the absence of typical exposure history, serological testing was crucial for confirming the diagnosis. The timely initiation of doxycycline therapy was essential for a favourable outcome.

Keywords: ***Coxiella burnetii; Q fever; Doxycycline; Immunocompromised; Cultures.***

Introduction

Q fever, a zoonotic infection caused by Coxiella burnetii, is often underdiagnosed due to its wide-ranging and non-specific clinical presentation [1]. The bacterium, primarily transmitted through inhalation of contaminated aerosols, can survive for extended periods in the environment, making transmission possible even without direct contact with livestock or rural settings, the typical reservoirs of infection [2]. In clinical practice, this disease can mimic other respiratory and systemic infections, especially in patients without clear risk factors [3]. The diagnosis becomes particularly challenging in immunocompromised individuals, where atypical presentations and overlapping symptoms with other infections can obscure the clinical picture [4].

In this report, we present the case of a 77-year-old man with a history of multiple comorbidities, including Myasthenia Gravis, severe asthma, ischemic heart disease, and long-term immunosuppressive therapy, who developed acute Q fever. The patient presented with prolonged flu-like symptoms and subsequent high fever, leading to an initial diagnosis of pneumonia. Despite broad-spectrum antibiotic treatment, his condition failed to improve, prompting further investigation.

Acute Q fever often manifests with non-specific symptoms such as fever, cough, myalgia, and fatigue, making early diagnosis difficult, particularly when classical risk factors like contact with livestock or rural exposure are absent [5]. The delayed response to conventional antibiotics in this patient, along with the persistent fever spikes, raised the suspicion of an atypical infectious etiology. Serological testing eventually confirmed the diagnosis of acute Q fever, with positive phase II IgG and IgM antibodies [3].

This case underscores the diagnostic difficulties associated with Q fever, particularly in immunocompromised patients where the risk of severe disease and complications, such as chronic Q fever, is heightened [6]. Furthermore, it highlights the importance of considering Q fever in the differential diagnosis of prolonged febrile illnesses, even in the absence of classical epidemiological exposures [7]. Prompt recognition and treatment with doxycycline were crucial for the resolution of symptoms in this patient, preventing further complications such as endocarditis [8]. This case also emphasizes the need for heightened clinical awareness of Q fever in diverse clinical settings, especially in patients with prolonged fever unresponsive to standard antibiotic therapy.

Case Report

A 77-year-old man presented with flu-like symptoms such as low fever, cough, myalgia, fatigue, sneezing and runny nose for 3 weeks, followed by high fever of up to 41ºC and prostration on the day before going to the Emergency Department. The day before admission he was evaluated by a primary care physician and was prescribed Amoxicillin/Clavulanic Acid 875mg/125mg every 12 hours, with no improvement. His past medical history included Myasthenia Gravis with previous thymectomy; Severe restrictive and obstructive Asthma; Ischemic and Hypertensive Myocardiopathy with Heart Failure; Heart Failure with preserved left ventricle ejection fraction and Non-insulin-dependent Diabetes Mellitus. He also had a pacemaker and had undergone radical

prostatectomy for Prostate Adenocarcinoma a few years earlier. The patient was chronically medicated with immunosuppressants, including Azathioprine 50mg daily and Prednisolone 10mg daily. He had no significant family history, no history of contact with animals, or trips to rural areas.

At the emergency department he was found to be febrile with a temperature of 40,2ºC, tachycardic at 116 beats per minute and physical examination revealed no significant findings. Arterial blood gas analysis was performed and showed low partial pressure of oxygen and he was started on oxygen therapy. Laboratory workup revealed elevated systemic inflammatory markers, including a C-reactive protein level of 82mg/L and procalcitonin level of 1.55ng/mL, with normal renal function. Chest X-ray showed what appeared to be pneumonia. Based on these findings, blood and urine cultures were collected, and the antibiotic regimen was maintained, with the addition of Azithromycin 500mg daily, assuming a diagnosis of pneumonia.

The patient remained in the emergency department for five days while waiting to be admitted to the ward, with no significant improvement in his condition. During this time, he had a daily fever spike, occurring each afternoon around 19 hours, with the temperature consistently above 40ºC, accompanied by episodes of altered mental status. A head CT scan was performed, which showed no abnormalities. Repeated blood tests revealed a marked increase in C-reactive protein levels to 350mg/L and thrombocytopenia (platelet count 78 x 10⁹/L).

Upon admission to the ward, new blood cultures were taken, and the antibiotic regimen was escalated to Piperacillin/Tazobactam 4,5g every 6 hours. On the fourth day of Piperacillin/Tazobactam, the treatment was switched to Ceftriaxone 2g daily and Vancomycin 1g every 12 hours due to signs of cholestasis. In total, the patient received 5 days of Amoxicillin/Clavulanic Acid and Azithromycin, followed by 4 days of Piperacillin/Tazobactam, and 4 days of Ceftriaxone and Vancomycin.

While on this antibiotic regimen, there was some clinical improvement; however, the patient continued to experience daily fever spikes in the evening around 19 hours. A comprehensive infectious workup was performed, testing for Hepatitis A, B, and C, HIV, Syphilis, Mycoplasma, Chlamydia, Rickettsia conorii, Cytomegalovirus, Epstein-Barr Virus, the Huddleson reaction, "Bengale violet" test, and Tuberculosis, all of which returned negative results. A nasal swab for respiratory viruses identified Rhinovirus. A CT scan of the thorax, abdomen, and pelvis with contrast was performed, showing no significant findings. Transthoracic and transesophageal echocardiograms revealed no suspicion of infective endocarditis. Multiple samples were taken for culture (6 blood, 1 urine, 1 stool), and urine antigen tests for Streptococcus pneumoniae and Legionella pneumophila were also negative.

Nine days after admission, serology results showed positive IgG phase II (1/200) and positive IgM phase II (1/100) for Coxiella burnetii, confirming the diagnosis of acute Q fever. The patient was then started on Doxycycline (200mg as a loading dose, followed by 100mg every 12 hours), with immediate clinical improvement and resolution of fever. He was discharged from the hospital asymptomatic and was reevaluated two weeks later, with no recurrence of symptoms. The patient remained under follow-up in Internal Medicine outpatient consultations and did not develop chronic Q fever. This case of Q fever was reported to SINAVE.

Discussion

Q fever, also known as Query fever, is a widespread zoonotic disease caused by the bacterium Coxiella burnetii. Originally classified as Rickettsia burnetii due to its similarity with other Rickettsiae, particularly in being an obligate intracellular Gram-negative organism, genomic sequencing has since demonstrated that it is more closely related to bacteria from the order Legionellales. Domesticated ruminants, particularly cattle, sheep, and goats, are the primary reservoirs of C. burnetii for humans. The microorganism is highly virulent and resistant to environmental inactivation, remaining viable in dust, soil, and feces for months. Human infection typically occurs through the inhalation of contaminated aerosols, often originating from infected livestock, with just a few bacteria sometimes as few as one capable of causing disease [1,2].

The diagnosis of Q fever can be challenging due to its broad spectrum of clinical presentations and the lack of specific symptoms early in the disease course. Additionally, misdiagnosis is common, as many patients lack the classical exposure history, such as contact with livestock or travel to endemic areas. In our case, the patient did not have direct contact with animals or travel to rural areas, making the initial suspicion of Q fever low. Therefore, diagnosing Q fever requires careful consideration of epidemiological factors, clinical presentation, and, most importantly, serological testing [3,4,9].

The incubation period for Q fever typically ranges from 9 to 28 days. Most acute infections are either asymptomatic or self-limiting, manifesting with flu-like symptoms such as fever, fatigue, cough, and myalgia, which can easily be mistaken for other viral or bacterial infections. While the overall mortality rate in acute Q fever is low, about 50% of symptomatic patients may require hospitalization due to more severe manifestations such as pneumonia or hepatitis. In rare cases, acute Q fever can involve the central nervous system, manifesting as meningoencephalitis or encephalitis, which significantly complicates the clinical picture [5,7].

One of the most serious complications of Q fever is the development of chronic disease, which occurs in 1% to 5% of cases, particularly in patients with predisposing conditions such as valvular heart disease, vascular abnormalities, chronic renal insufficiency, or immunosuppression. In our case, the patient's immunosuppression due to chronic use of azathioprine and prednisolone, along with his pacemaker and history of ischemic heart disease, placed him at higher risk for more severe disease. Chronic Q fever, particularly in the form of endocarditis, represents the most severe manifestation of the disease and may require surgical intervention due to damage to the heart valves. Other chronic forms of Q fever, such as vascular infections, osteoarticular disease, and chronic hepatitis, are less common but similarly challenging to diagnose and manage [6,10].

The diagnosis of Q fever primarily relies on serological testing. The detection of IgM and IgG antibodies against phase II antigens typically occurs 2 to 3 weeks after infection. In acute Q fever, IgM antibodies to phase II antigens are predominant, while the presence of elevated phase I IgG titers (≥1:800) is indicative of chronic infection [11]. In this case, the patient's serology showed both positive IgG and IgM for phase II antibodies, confirming the diagnosis of acute Q fever.

Initial treatment in our case included broad-spectrum antibiotics such as amoxicillin/clavulanic acid, azithromycin, and piperacillin/tazobactam, which are generally ineffective against Coxiella burnetii. It was only after the serological diagnosis of Q fever that doxycycline, the recommended first-line treatment for acute Q fever, was started. According to the Sanford Guide to Antimicrobial Therapy [8], tetracyclines, including doxycycline, remain the cornerstone of treatment, with other agents like chloramphenicol, macrolides, and quinolones as alternative options. Our patient showed rapid clinical improvement following the initiation of doxycycline, with the resolution of fever and systemic symptoms, and was discharged asymptomatic.

Conclusion

This case report highlights the diagnostic challenges of Q fever, a zoonosis caused by the bacterium Coxiella burnetii. The atypical clinical presentation and the absence of a clear history of animal exposure made initial diagnosis difficult, leading to a delay in specific treatment. The importance of serology for diagnostic confirmation is evident, especially in cases with high clinical suspicion.

The delay in diagnosis and the initial use of ineffective antibiotics emphasize the need for a high index of suspicion for Q fever, especially in immunocompromised patients. The presence of multiple comorbidities and the use of immunosuppressants in this patient increased the risk of complications and disease severity.

The timely treatment with doxycycline was essential for the resolution of symptoms and the prevention of chronic complications such as endocarditis. This case highlights the importance of clinical suspicion for this disease, especially in patients with prolonged fever and signs of systemic infection, even in the absence of classic risk factors.

Declarations

Consent for Publication

Consent was given by the patient for the writing of this article.

Conflicts of Interest

The authors declare that there is no conflict of interest regarding the publication of this paper.

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Authors' Contributions

PF was involved the patient care, collected and analysed the patient data and wrote the manuscript. SE and RS were involved in the patient care and a major contributor in reviewing the manuscript. AC, SC and AL were involved in the patient care. PN and VT were a major contributor in writing and reviewing the manuscript. All authors read and approved the final manuscript.

Availability of Supporting Data

The data supporting the findings of this case report are derived from previously published literature on Q fever, it's diagnosis, clinical management, and treatment strategies. Relevant sources include clinical reviews, epidemiological studies, and expert guidelines. Škultéty (2020) provides insights into the prevention of Q fever and the epidemiological challenges associated with controlling this zoonotic infection. Raoult et al. (2005) present a comprehensive review of Q fever, highlighting its pathogenesis, clinical features, and diagnostic challenges. Anderson et al. (2013) provides guidelines on the diagnosis and management of Q fever in the United States, which are aligned with international recommendations. Brouqui et al. (2004) discuss the diagnosis of tick-borne bacterial diseases in Europe, including Q fever, and offer recommendations relevant to clinical microbiology. Fournier et al. (1998) focus specifically on the diagnostic strategies for Q fever, emphasizing the role of serological testing. Several reviews by Parker et al. (2006) and Angelakis & Raoult (2010), as well as more recent works by Eldin et al. (2013, 2017), offer detailed analyses of Q fever's progression from acute to chronic phases, which informed the diagnostic and therapeutic approaches used in this case. The management of chronic Q fever and its impact on patients' long-term quality of life is explored in studies by Van Roeden et al. (2018). Lastly, the Sanford Guide (2023 edition) was consulted for current antimicrobial therapy recommendations, specifically the use of doxycycline in the treatment of acute Q fever.

All relevant data for this report were obtained from these peer-reviewed sources, which are available publicly or through institutional access to scientific databases.

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Not applicable.

References

[1] Raoult D, Marrie T, Mege J. "Q Fever." *Clinical Microbiology Reviews*, 18(4): 491-505, 2005.

[2] Škultéty L. "Q fever and prevention". Epidemiol Mikrobiol Imunol, 69(1): 6-10, 2020.

[3] Fournier PE, Marrie TJ, Raoult D. "Diagnosis of Q Fever." *Journal of Clinical Microbiology*, 36(7): 1823-1834, 1998.

[4] Anderson A, Bijlmer H, Fournier PE, et al. "Diagnosis and Management of Q Fever — United States, 2013." *MMWR Recommendations and Reports*, 62(RR03): 1-30, 2013.

[5] Parker NR, Barralet JH, Bell AM. "Q Fever." *The Lancet Infectious Diseases*, 6(11): 679-688, 2006.

[6] Eldin C, Mélenotte C, Angelakis E, et al. "From Acute Q Fever to Chronic Q Fever: A Formidable Tetrad." *Antimicrobial Agents and Chemotherapy*, 57(11): 4786-4795, 2013.

[7] Angelakis E, Raoult D. "Q Fever." Veterinary Microbiology, 140(3-4): 297-309, 2010.

[8] Gilbert DN, Chambers HF, Eliopoulos GM, et al. (eds). "*The Sanford guide to antimicrobial therapy*", 2023.

[9] Brouqui P, Bacellar F, Baranton G, et al. "Guidelines for the Diagnosis of Tick-Borne Bacterial Diseases in Europe." *Clinical Microbiology and Infection*, 10(12): 1108-1132, 2004.

[10] Van Roeden SE, Reukers DFM, Van Jaarsveld CHM, et al. "Chronic Q fever: patient and treatment-related factors influencing long-term quality of life." *QJM*, 111(4): 271-277, 2018.

[11] Eldin C, Mélenotte C, Mediannikov O, et al. "From Q Fever to Coxiella burnetii Infection: A Paradigm Change." *Clinical Microbiology Reviews*, 30(1): 115-190, 2017.