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Coxiella burnetii Endocarditis in a Patient with Systemic Lupus Erythematosus: A Case Report of a Diagnostic Challenge

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Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

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Patient: Male, 43-year-old
Final Diagnosis: Q-fever endocarditis
Symptoms: Lower limb edema • shortness of breath
Medication: —
Clinical Procedure: —
Specialty: General and Internal Medicine

Objective: Rare co-existance of disease or pathology

Background: There is a close association between Q fever and autoimmune disease, with some case reports in the literature of Q fever presenting as systemic lupus erythematosus (SLE) and others documenting their coexistence. However, making the correct diagnosis remains challenging and Q fever often is overlooked. Therefore, it is essential to review such a rare presentation to help in accurate diagnosis in future cases. This report is of a case of endocarditis due to *Coxiella burnetii* in a patient with Q fever and a history of SLE.

Case Report: We report the case of a 43-year-old man with a history of SLE and rheumatic heart disease, status post-valve replacement. The patient initially presented with an acute kidney injury in the setting of a history of full-house lupus membranous nephropathy, which was diagnosed on kidney biopsy. The patient had been on immunosuppressive therapy for 2 years. Shortly after he was admitted, echocardiography was ordered because the patient had progressive dyspnea, revealing infective endocarditis involving multiple valves. He underwent valve repair surgery and was placed on an extended course of antibiotic therapy. His symptoms gradually resolved, with normalization of his immunological markers. The patient's immunosuppressive regimen was eventually discontinued. He remains on lifelong antibiotic suppression therapy.

Conclusions: This case highlights the importance of awareness of infectious causes of endocarditis in patients with underlying autoimmune diseases such as SLE. This rare case of *C burnetii* endocarditis may have been associated with underlying valvular SLE.

MeSH Keywords: Endocarditis • Lupus Erythematosus, Systemic • Q Fever

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/926699

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Background

Q fever (Query fever), a zoonotic infectious disease caused by *Coxiella burnetti*, has a worldwide distribution, including in the Arabian Peninsula [1,2]. *C burnetii* is an intracellular gram-negative bacterium, found in ticks, birds, and mammals [3]. The primary sources of human infection are goats, sheep, and cattle. The most common modes of acquisition are by inhalation or ingestion of unpasteurized milk. The symptoms of Q fever are nonspecific and variable. Asymptomatic infection may occur in up to 60% of exposed individuals [4]. Q fever is most prevalent in men aged 30 to 70 years [5].

Two broad clinical syndromes characterize the clinical manifestation of Q fever: acute and chronic. Acutely, patients most commonly present with a self-limited influenza-like illness with associated fever, chills, fatigue, headache, cough, pneumonia, hepatitis, and maculopapular rash. In the chronic phase, which is thought to be a sequela of acute infection in up to 5% of infected individuals, endocarditis is the primary manifestation. Patients with a known history of valvular heart disease, congenital heart disease, immunosuppression, or chronic kidney disease are particularly susceptible to chronic Q fever infection [6–8]. It is worth noting that Q fever has been estimated to cause up to 5% of all cases of endocarditis worldwide [6]. Other manifestations of the chronic phase include aneurysms, osteomyelitis, hepatitis, interstitial pulmonary fibrosis, and chronic wound infections [9–11].

Q fever is primarily diagnosed based on serology, using immunofluorescent antibodies [12]. Two antigenic phases occur, causing different antibody responses that aid in differentiating the acute from the chronic form of the disease. Antibodies in response to antigens of phase II are predominant in the acute form of the disease. In contrast, phase I antibody titers are more prevalent in the chronic stage of the disease. Definitive diagnosis is made with positive polymerase chain reaction (PCR) testing in tissue specimens or serum [12–14].

The first-line treatment for acute Q fever is tetracycline. Alternative options include macrolides, fluoroquinolones, and trimethoprim-sulfamethoxazole. In cases of chronic infection or endocarditis, treatment typically consists of a course of doxycycline and hydroxychloroquine for at least 18 months or until phase I immunoglobulin (Ig) G is <1: 200 [12–14].

This report is of a case of endocarditis due to *C burnetii* in a patient with Q fever and a history of systemic lupus erythematosus (SLE). We aim to highlight complications due to delayed diagnosis because of the misleading presentation of this infectious disease.

Case Report

A 43-year-old man with a history of SLE and rheumatic heart disease, status post-mitral valve valvuloplasty and aortic valve replacement was admitted to our institution in August 2016 with postural hypotension and dizziness. Echocardiography at the time showed no evidence of vegetation or masses (Limban-Sacks endocarditis was not documented at this time). Initial workup revealed gross proteinuria and microscopic hematuria. Initial laboratory tests showed positivity for antinuclear antibody (ANA) and anti-double-stranded DNA antibodies (anti-ds DNA Ab), and low levels of C3 and C4. In light of these findings, the patient underwent a kidney biopsy. Histopathology was consistent with lupus membranous nephropathy, and immunofluorescence detected full-house nephropathy.

In January 2018, the patient was readmitted with progressive shortness of breath, bilateral lower-extremity edema, and elevated liver enzymes. The possibility of a lupus flare was a concern. Echocardiography revealed severe tricuspid regurgitation with a mass on the tips of the anterior leaflets. In addition, there was moderate aortic and mitral regurgitation. However, there was no evidence of pulmonary embolism. At this point, the differential diagnosis was infective endocarditis, given the patient's history of immunosuppression, and valvulopathy or a lupus flare. No tests for *Coxiella* were sent preoperatively, as the diagnosis was overlooked.

The patient underwent debridement of the aortic valve root, pulmonary and mitral valve replacement, aortic valve replacement with homograft, pulmonary valve replacement with autograft, and mitral valve repair with removal of the old ring. Intraoperative transesophageal echocardiography revealed vegetative lesions along the mitral valve ring and the aortic valve. Several pockets of pus-filled collection were observed. The postoperative diagnosis was infective endocarditis involving the pulmonic valve, mitral valve ring, aortic valve, and the aortic graft; therefore, samples were taken to detect the causative organism (Figures 1–4). Intraoperative bacterial, *Brucella*, and acid-fast bacilli cultures were negative. Fungal culture for Candida also was negative. *Bartonella quintana* PCR was negative. However, quantitative *C burnetii* PCR was positive and detection was with 16S rDNA PCR. The final diagnosis was Q fever infective endocarditis.

The patient is a civil engineer and he denied exposure to animals. He was started on treatment with doxycycline and hydroxychloroquine. Immunosuppressive therapy, which consisted of mycophenolate mofetil and prednisone, was stopped. The plan was to keep the patient on lifetime suppressive antimicrobial therapy, in light of his immunocompromised status and the burden of his disease process.

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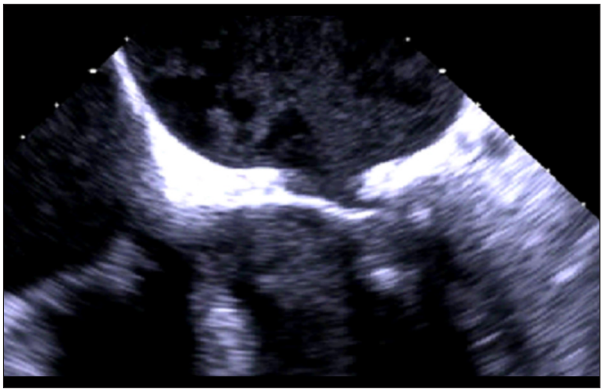

Figure 1. Preoperative transesophageal echocardiogram (TEE) showing mitral valve vegetation in a 43-year-old man with a history of systemic lupus erythematosus (SLE) who presented with endocarditis associated with Q fever due to infection with *Coxiella burnetii*. The TEE was performed in 2018 and shows impaired closure of the mitral valve leaflets (malcoaptation) associated with valve vegetation.

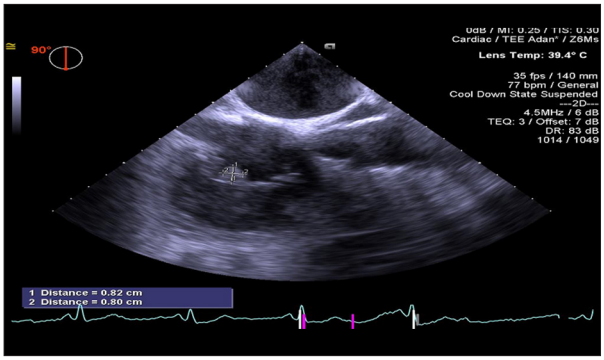

Figure 3. Preoperative transesophageal echocardiogram (TEE) of a 43-year-old man with a history of systemic lupus erythematosus (SLE) who presented with endocarditis associated with Q fever due to infection with *Coxiella burnetii*. The image, which shows a mass on the repaired tricuspid valve, was taken in 2018.

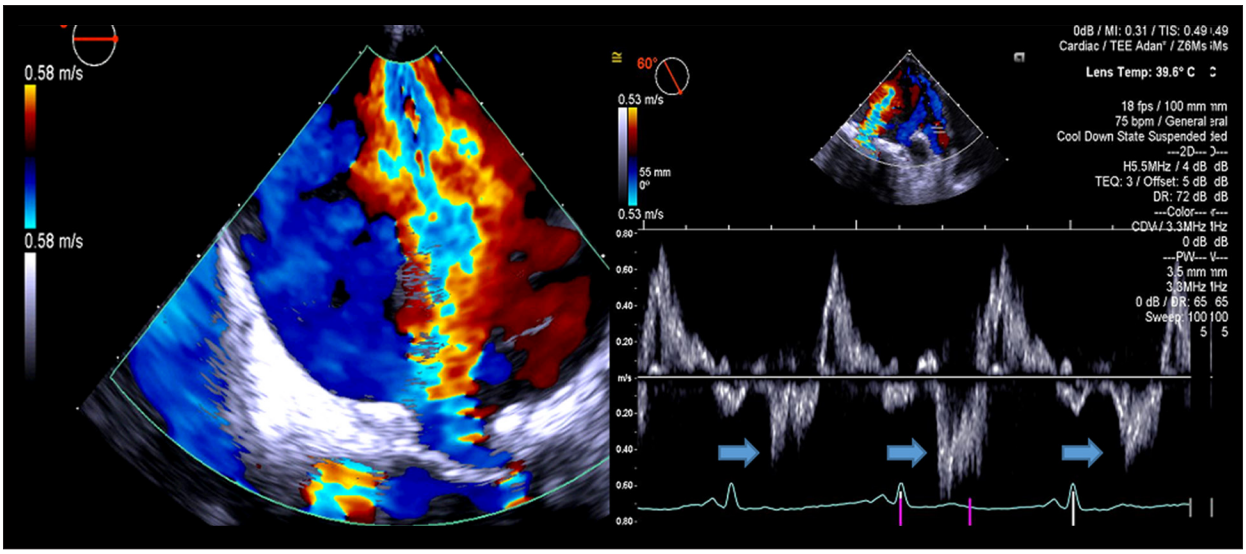

Figure 2. Preoperative transesophageal echocardiogram (TEE) showing severe mitral regurgitation with color Doppler and systolic flow reversal of the pulmonary vein in a 43-year-old man with a history of systemic lupus erythematosus (SLE) who presented with endocarditis, which was later diagnosed to be an infection with *Coxiella burnetii*. The TEE was performed in 2018.

Discussion

This case highlights the elusive presentation of Q fever, particularly the relationship between it and autoimmune disease. Multiple studies have postulated a close association between Q fever and autoimmune disease [5,15]. A unique manifestation of Q fever is the presence of autoimmune antibodies, including ANA, antiphospholipid antibody, and anti-smooth muscle antibody [15,16]. The presence of these autoimmune biological abnormalities may point toward a vasculitis, systemic inflammatory disease, or autoimmune disease instead of Q fever infection as the diagnosis [17,18].

It is well established that immunological phenomena are associated with the later stages of subacute forms of untreated infective endocarditis [19,20]. It is postulated that the pathogenesis of chronic Q fever infective endocarditis is related to circulating immune complexes [21]. In one study, the autoantibody profile found in Q fever was similar to those found in autoantibody diseases [22]. The most common autoimmune syndromes associated with Q fever infection are SLE and antiphospholipid syndrome [23]. Several case reports in the literature suggest that Q fever should be considered as a cause of fever in patients with SLE [24–27]. Indeed, as illustrated in

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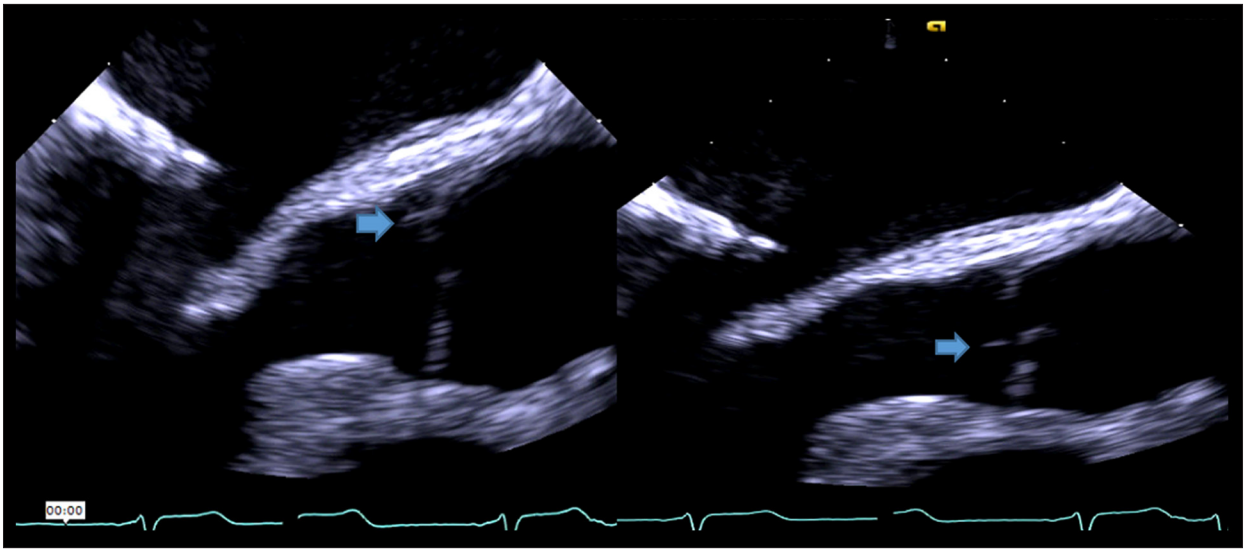

Figure 4. Transesophageal echocardiogram (TEE) showing multiple small, flickering masses post-Ross procedure on the aortic valve (native pulmonary valve) of a 43-year-old man with a history of systemic lupus erythematosus (SLE) who presented with endocarditis, which was later diagnosed to be an infection with *Coxiella burnetii*. The TEE was performed in 2019.

our case, a history of autoimmune disease can often mislead and obscure the diagnostic picture, resulting in a delay in diagnosis and potentially devastating consequences.

One patient in a recent case reportedly had Q fever endocarditis on top of SLE and associated Limban-Sacks endocarditis [28]. Our patient had a history of valvuloplasty due to rheumatic heart disease. However, no clear documentation was available of Limban-Sacks endocarditis prior to the episode Q fever endocarditis, but it is important to note that it is a possibility in our patient. This underscores the issue of Limban-Sacks endocarditis as a risk factor for Q fever endocarditis.

Renal biopsy findings are insufficient to establish a diagnosis of SLE. The pathologic features of lupus nephritis (LN) are characteristic but not pathognomonic. These include glomerular deposits of IgG and C3 with or without IgM, IgA, and C1q. Other findings suggestive of SLE are tubulointerstitial and vascular wall deposits, as well as endothelial tubuloreticular inclusions on electron microscopy. Similar findings are possible, however, with other autoimmune processes, such as rheumatoid arthritis and mixed connective tissue disease. Full-house staining is quite specific for LN but it is not necessarily present in all biopsy specimens from patients with SLE. Unfortunately, such full-house staining also occurs in other conditions, including IgA nephropathy, cryoglobulinemic glomerulonephritis (GN), and primary membranoproliferative GN.

Conclusions

This case adds to the multitude of studies that have shown an association between Q fever infective endocarditis and autoimmune diseases, particularly SLE. Several questions are unanswered and remain to be elucidated by future studies. First, in the immunocompromised host, should treatment be lifelong given the burden of the disease process? Also, should high-risk patients who are more susceptible to Q fever endocarditis – namely those with history of valvulopathy and autoimmune disease – undergo routine surveillance echocardiogram in regular fixed intervals? In addtion, research needs to clarify the role of continued immunosuppressive therapy following treatment of Q fever and resolution of immune markers. Although this case had devastating complications, it fortunately resulted in a favorable outcome. Several factors came together to make the perfect storm.

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