

Rare case of chronic Q fever myocarditis in end stage heart failure patient: A case report

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Abstract

BACKGROUND

Q fever myocarditis is a rare disease manifestation of Q fever infection caused by *Coxiella burnetii*. It is associated with significant morbidity and mortality if left untreated. Prior studies have reported myocarditis in patients with acute Q fever. We present the first case of chronic myocarditis in an end-stage heart failure patient with chronic Q fever infection.

CASE SUMMARY

A 69-year-old male was admitted with dyspnea on exertion, hypotension and bilateral lower extremity edema for a few months. He has a past medical history of ischemic cardiomyopathy with left ventricular ejection fraction of 25%, implantable cardioverter defibrillator in place, bioprosthetic aortic valve and mitral valve replacement. He continued to have shortness of breath despite diuresis along with low grade fevers. Initial infectious work up came back negative. On further questioning, the patient was found to have close contact with farm animals and the recurrent fevers prompted the work-up for Q fever. Q fever serologies and cardiac positron emission tomography confirmed the diagnosis of chronic Q fever myocarditis. He was then successfully treated with doxycycline and hydroxychloroquine for 18 mo.

CONCLUSION

Chronic Q fever myocarditis, if left untreated, carries a poor prognosis. It should be kept in differentials, especially in patients with recurrent fevers and contact with farm animals.

Key Words: Chronic Q fever; Myocarditis; *Coxiella burnetii*; Heart failure; Farm animals; Case report

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Core Tip: Q fever myocarditis is a rare disease (< 1% of cases) caused by infection with *Coxiella burnetii* (gram-negative proteobacteria). Q fever normally has a pleomorphic and non-specific clinical presentation which leads to delayed diagnosis and treatment, which can lead to worse outcomes. Q fever myocarditis should be kept in differentials not only in patients with acute Q fever but also with chronic Q fever infection, like in our case. Q fever serologies help in making a diagnosis of acute and chronic Q fever. Cardiac positron emission tomography and magnetic resonance imaging can be utilized to diagnose myocarditis in the setting of Q fever. Hydroxychloroquine and doxycycline, in combination, are used for treatment of Q fever myocarditis.

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INTRODUCTION

Q fever is caused by infection with gram-negative proteobacteria, *Coxiella burnetii*[1]. *Coxiella burnetii* is found in many domestic animals like deer, rabbits, rodents, birds, horses and even in arthropods like ticks[2]. Q fever is a zoonosis and is transmitted to humans *via* inhalation of contaminated aerosols[1]. *C. burnetii* can survive for extended periods of time and can be carried long distances *via* wind, hence direct animal contact may not be required for transmission[3]. Disease presentation is variable, ranging from asymptomatic, flu like symptoms to intensive care admission. The variability is mostly due to host factors, bacterial virulence factors and extent of exposure[1]. Myocarditis is a rare disease manifestation of acute Q fever (< 1% of cases)[1]. To the best of our knowledge, less than 30-35 isolated cases of myocarditis with *Coxiella* have been reported in the literature. However, no case of chronic myocarditis in Chronic Q fever infection has been reported. We present an interesting and rare case of chronic Q fever leading to chronic myocarditis in a patient with a prior history of ischemic cardiomyopathy and valvular heart disease.

CASE PRESENTATION

Chief complaints

A 69-year-old male presented with chief complaints of shortness of breath, fatigue, and intermittent fevers for the last 6 mo which were treated with antibiotics twice.

History of present illness

The patient's symptoms of dyspnea and fatigue had been ongoing for the last few months with severe hypotension, bilateral lower extremity edema and dyspnea on exertion. He denied any chest pain or pressure.

History of past illness

The patient had several comorbidities including ischemic cardiomyopathy with left ventricular ejection fraction (LVEF) of 25%, prior ST-elevation myocardial infarction status post (s/p) stent to proximal left anterior descending artery, s/p implantable cardioverter defibrillator (ICD) in 2018 for primary prevention, bicuspid aortic valve s/p aortic valve replacement with 25 mm Carpentier-Edwards bioprosthetic prosthesis in October 2012 followed by transcatheter aortic bioprosthetic valve in valve (26 mm Sapien S3) in April 2019, mitral valve repair with 32 mm seguin ring repair in October 2012 and subsequent transcatheter bioprosthetic mitral valve replacement with 29 mm Sapien 3 bioprosthetic valve for mitral regurgitation in June 2019, hyperlipidemia, chronic kidney disease stage III and atrial fibrillation.

Personal and family history

The patient denied pertinent family history.

Physical examination

On physical examination, the vital signs were as follows: T max of 100.04 degrees Fahrenheit, blood pressure of 91/61 mmHg, heart rate of 80/minute and oxygen saturation of 96% on room air. The patient's jugular venous pressure was elevated, and a diastolic murmur was heard at the aortic area, bilateral bibasilar crackles at the lung bases, and minimal bilateral lower extremity edema was present.

Laboratory examinations

Troponin-I level was 0.01 ng/mL (normal) and BNP was 1562 pg/mL. WBC count was normal and multiple blood cultures were negative.

Imaging examinations

ECG on admission showed atrial paced rhythm with left bundle branch block. Transthoracic echocardiogram (TTE) on admission showed LVEF of 20%-25% with global hypokinesis, mild to moderate aortic regurgitation, mitral valve mean gradient of 10 mmHg (@ HR of 72 bpm) with normal right ventricle size and function and no vegetation. His most recent TTE prior to admission was done at an outside facility on July 2019 and showed LVEF of 30%, no aortic valve or mitral prosthetic valve regurgitation, mean mitral valve gradient of 7 mmHg (@ HR of 67 bpm), and normal RV function. The chest X-ray on admission showed moderate cardiomegaly with central venous congestion and interstitial edema.

Further diagnostic work-up

To determine his cardiac hemodynamics, shock profile, and whether escalation to temporary mechanical support device is needed, an urgent right heart catheterization was done on admission that showed right atrial pressure 12 mmHg, right ventricular pressure 54/6 mmHg, pulmonary artery pressure 54/25 mmHg, mean pulmonary artery pressure 35 mmHg, pulmonary capillary wedge pressure 24 mmHg and cardiac index by Fick of 2 L/min/m² with pulmonary artery saturation of 57%. An infectious disease specialist was consulted. He underwent trans-esophageal echocardiogram to look for endocarditis. It showed a moderate paravalvular aortic valve regurgitation, the replaced mitral valve was functioning normally with no stenosis or regurgitation, and no definitive vegetation was noted on defibrillator leads and prosthetic material.

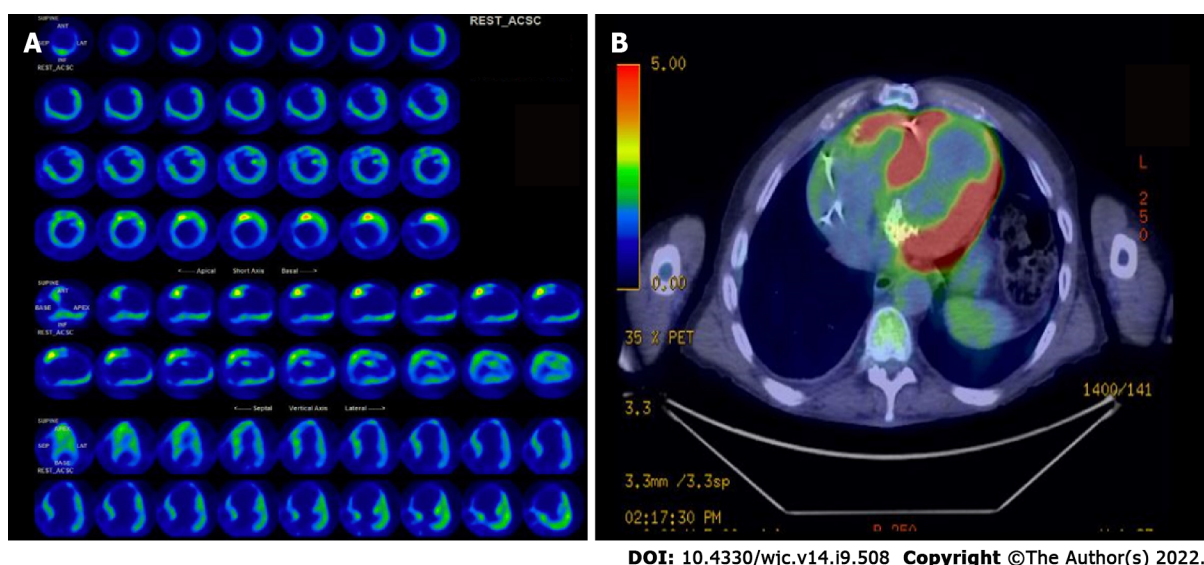
On further discussion with the patient's wife, his functional status decline was associated with intermittent fevers for the last 6 mo that were treated with antibiotics twice, but no source was identified. On further questioning, the patient reported that he raised horses for the last 30 years and has been in close contact with dogs and cats his whole life. Due to close animal contact, Q fever was suspected. Q fever titers were significantly high: Phase I IgG (1:16384), Phase II IgG (>1:32768), Phase I IgM (1:>2048), and Phase II IgM (>1:2048). 18-Fluorine fluorodeoxyglucose (FDG) cardiac positron emission tomography (PET) was preferred over magnetic resonance imaging (MRI) due to the presence of ICD. It revealed heterogenous areas of increased 18-F FDG uptake in the left ventricle raising the concern for myocarditis. The heterogenous uptake was identified in septal, lateral, and anterior walls of the left ventricle (Figure 1A). The basal anterolateral wall demonstrated maximum SUV of 6.9 and basal anteroapical demonstrated maximum SUV of 5.3. No increased uptake around the valvular structures was noted.

FINAL DIAGNOSIS

Based on the history above, physical examination, laboratory findings, and discussions with our infectious disease colleagues, the most likely etiology of the patient's presentation was chronic myocarditis secondary to chronic Q fever infection. Patient met criteria of both chronic Q fever and chronic myocarditis[4,5].

TREATMENT

The patient was started on milrinone 0.125 mcg/kg/min and intravenous diuresis for his acute presentation of acute on chronic heart failure; however, it was stopped after a few days due to ventricular ectopies. Moreover, he did not feel any improvement in symptoms with milrinone. For the Q fever myocarditis, treatment with doxycycline 100 mg twice daily and hydroxychloroquine 200 mg three times daily was initiated for an 18-mo course. Prolonged treatment course was utilized due to his history of prosthetic valves. Due to the patient's significant underlying comorbidities, our advanced heart failure therapy committee meeting deemed him an unsuitable candidate for advanced heart failure therapies at the time of admission. Due to his hypotension, he could not be discharged on guideline directed medical management.



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Figure 1 18-Fluorine fluorodeoxyglucose positron emission tomography scan. A: Heterogenous areas of increased uptake involving septal, lateral as well as basal and anterior wall of left ventricle suggestive of myocarditis; B: Whole body positron emission tomography obtained after 1 mo with focus on cardiac structure showing no evidence of residual myocarditis.

OUTCOME AND FOLLOW-UP

On subsequent follow up clinic visits, the patient was noted to have significant improvement in his heart failure symptoms and his fevers resolved. Repeat Cardiac PET after 1 mo showed complete resolution (**Figure 1B**). The patient was doing better at 1 wk post discharge follow-up and his blood pressure improved. He was started on dapagliflozin 10 mg daily, losartan 25 mg daily and metoprolol XL 100 mg daily. At the patient's 6-month routine follow up, he was doing well and repeat phase I and phase II titers were significantly down: Phase I IgG (1:16384), Phase II IgG (1:16384), Phase I IgM (1:256), and Phase II IgM (1:16) (**Table 1**). Repeat echocardiogram at 6 mo showed no change in the LVEF, no aortic regurgitation and no stenosis or regurgitation of the mitral valve. He will continue doxycycline and hydroxychloroquine for 18 mo.

DISCUSSION

To the best of our knowledge, this is the first case of chronic myocarditis in a patient with chronic Q fever. Our patient suffered from chronic Q fever infection which ultimately led to chronic myocarditis. Certain conditions like immunosuppression, pregnancy, vascular abnormalities and heart valve conditions predispose individuals to chronic Q fever infection[1]. Our patient had significant valvular heart disease which may have been a predisposing factor for this chronic infection. Myocarditis secondary to *Coxiella burnetii* is a rare manifestation (< 1%)[6,7]. Chronic Q fever diagnosis can often be delayed for months due to nonspecific symptoms and pleomorphic presentation. Endocarditis is the most commonly reported cardiac pathology in chronic Q fever cases[5]. Myocarditis has been almost always reported in the setting of acute Q fever[8,9].

Myocarditis is most likely underestimated in this population due to non-specific signs and symptoms, and a high index of suspicion is required for diagnosis. The diagnosis of Q fever myocarditis is challenging as *C. burnetii* does not grow in routine cultures. Thus, serology is used in most cases for diagnosis[3,10]. *C. burnetii* displays a two-phase antigenic variation due to changes in lipopolysaccharide C antigens: Phase I (often seen in chronic Q fever) and phase II (often seen in acute Q fever). Indirect immunofluorescent assay is used for serological detection. Cut-off for serological titers varies between countries, but the screening test is generally considered positive for acute disease when anti-phase II IgG anti-immunoglobulins return active at a dilution of $\geq 1:200$ or IgM $\geq 1:50$ [8]. These positive tests are then diluted and tested for presence of anti-phase I IgG and IgM. Chronic Q fever is found when phase I IgG $\geq 1:800$, usually in the presence of anti-phase II antibodies[3,11]. Cardiac MRI and 18 F-DG-PET scan have been used before to diagnose Q fever myocarditis[12]. Another point worth mentioning is the negative troponin-I in our patient. Prior studies have shown negative troponin-I with biopsy proven myocarditis. The lack of troponin-I release does not rule out myocarditis[13]. There have been a few cases in the past showing Q fever infection leading to valvulitis[14], and this may explain the aortic regurgitation in our patient which got better with treatment of Q fever.

Table 1 Q fever serology

Variables	Reference range	Admission	3 months	6 months
Phase I IgG	<1:16	1:16384	1:32768	1:16384
Phase II IgG	<1:16	>1:32768	1:131072	1:16384
Phase I IgM	<1:16	>1:2048	1:1024	1:256
Phase II IgM	<1:16	>1:2048	1:2048	1:16

IgG: Immunoglobulin G; IgM: Immunoglobulin M.

The prognosis of Q fever myocarditis is uncertain, but it has worse prognosis compared to other forms of Q fever diseases. In some studies, mortality with Q fever myocarditis has been reported to be up to 30% [8,15]. Patients with chronic *C. burnetii* are usually unable to eradicate the infection without utilizing antibiotics [1]. Center for Disease Control and Prevention recommends doxycycline 100 mg twice daily and hydroxychloroquine 200 mg three times a day for ≥ 18 -24 mo as the treatment of choice for Q fever myocarditis, endocarditis or vascular infection [16,17]. Hydroxychloroquine is used mainly to increase the efficacy of doxycycline and prevents the development of chronic Q fever endocarditis. Although this regimen seems long, the addition of hydroxychloroquine has reduced the treatment time from 5 years to 18-24 mo [17]. Our patient was started on the long course of antibiotics to prevent endocarditis due to significant valvular abnormalities. Both doxycycline and hydroxychloroquine can cause photosensitivity, and patients should be warned to avoid excessive sun exposure. Regular heart and eye examinations are needed due to the risk of hydroxychloroquine induced retinopathy [16].

CONCLUSION

Q fever myocarditis is a rare disease, and a high index of suspicion is required for diagnosis. Given the poor prognosis of Q fever myocarditis and the presence of reliable therapy, it should be kept in differentials for patients with fevers and cardiomyopathy, especially in patients with a history of animal exposure. Multimodality imaging like echocardiogram, cardiac MRI and cardiac PET can be utilized in diagnosing myocarditis in patients with Q fever.

FOOTNOTES

Author contributions: Goyal A and Dalia T have contributed equally to the manuscript writing, editing, and data collection; Bhyan P and Farhoud H have assisted with writing and edits; Shah Z and Vidic A have contributed to conceptualization and supervision; all authors have read and approved the final manuscript.

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