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Case Report

Myocarditis: A rare manifestation of acute Q fever infection

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ABSTRACT

Myocarditis is a rare disease manifestation of acute Q fever caused by infection with *Coxiella burnetii*, an infectious Gram-negative proteobacteria. *C. burnetii* has a large animal reservoir and is often transmitted to humans during animal birth. Acute Q fever has a nonspecific disease presentation leading to delayed treatment and potentially worsened clinical outcomes. We describe a case of an otherwise healthy adult man with angina, ST elevations, and positive cardiac troponins—all findings suggestive of acute coronary syndrome. Cardiac catheterization revealed no significant coronary blockages or abnormalities. On echocardiography he was found to have heart failure with reduced ejection fraction. The patient's social history included several risk factors for Q fever. Serologic testing returned positive for anti-*C. burnetii* antibodies, and a diagnosis of acute Q fever myocarditis was made. The patient was appropriately treated with a course of doxycycline and clinically improved.

<**Learning objective:** Q fever has a nonspecific presentation often leading to a delayed or missed diagnosis, resulting in worsened morbidity and mortality. Patients with angina-like chest pain and risk factors for Q fever should promptly be tested for infection with *C. burnetii*. Cardiac magnetic resonance imaging is a useful tool to improve diagnostic accuracy, with positive serology confirming the diagnosis. Treatment includes a course of antibiotics—often doxycycline.>

Introduction

Q fever myocarditis is a rare disease caused by infection with *Coxiella burnetii*, a Gram-negative, obligate intracellular proteobacteria [1,2]. The "Q" in "Q fever" initially stood for "query" because the cause was unknown when originally recognized in Australia in 1935 [3]. *C. burnetii* is found in many domestic animals, including cattle, goats, sheep, dogs, and cats. Q fever antibodies have been found in wild animal hosts as well: deer, rabbits, coyotes, rodents, and birds [1]. Animals infected with *C. burnetii* can appear healthy. Transmission to humans often occurs while animals are giving birth. The bodily fluids (feces, urine, milk, birth products) expressed from the infected animal contaminate the air and are breathed in. Proteobacteria can survive for long periods and be carried long distances via the wind [3,4]. Thus, direct contact with an infected animal in not necessary for contraction of Q fever [2]. Rarely, cases of infection have been reported after patients have consumed contaminated, unpasteurized dairy products [4]. Q fever myocarditis has a nonspecific presentation, often delaying diagnosis and resulting in worsened morbidity and mortality. Diagnosis is routinely achieved after ruling out more common causes of cardiomyopathy, followed by confirmatory serologic testing for *C. burnetii*. We describe a case of nonischemic cardiomyopathy, subsequently diagnosed as Q fever myocarditis, in an otherwise healthy patient.

Case report

A 45-year-old white man sought care at a near-by hospital for chest tightness, chronic lower extremity wounds (Fig. 1), and shortness of breath on exertion that had begun approximately 4 days previously. He also reported fatigue, decreased appetite, abdominal discomfort, and darkened urine. His initial pertinent laboratory test results were obtained: creatinine, 1.2 mg/dL; total bilirubin, 4.2 mg/dL; alkaline phosphatase, 330 U/L; aspartate aminotransferase, 49 U/L; alanine aminotransferase, 169 U/L; total protein, 7.4 g/dL; albumin, 7.3 g/dL; white blood cell count, 11.3 × 10^9/L; hemoglobin, 14.0 g/dL; and international normalized ratio, 1.1. A chest X-ray revealed no acute cardiopulmonary findings. Initial electrocardiogram (ECG) revealed sinus rhythm with premature atrial complexes and ST elevations in anteroseptal leads (Fig. 2). Troponin T returned positive at 0.17 ng/mL with a B-

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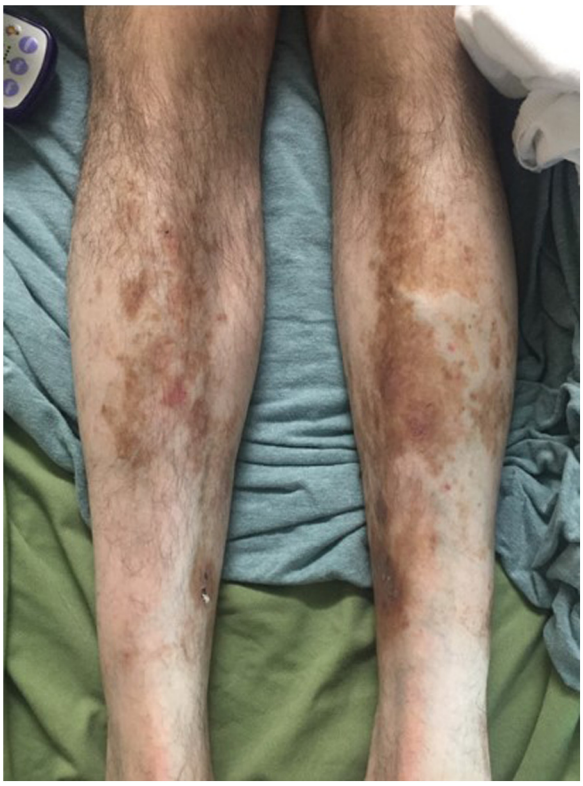

Fig. 1. Chronic lower extremity lesions.

type natriuretic peptide concentration of 4380 pg/mL. The patient was given aspirin, nitroglycerin, and was started on a heparin drip for acute coronary syndrome. He was transferred to our facility for further evaluation. On arrival he was dyspneic, diaphoretic, and continued to complain of angina-like chest tightness. Cardiac catheterization revealed no significant coronary abnormalities or blockages. A transthoracic echocardiogram (TTE) revealed left ventricular ejection fraction (LVEF) of 25.9% with global hypokinesis and no evidence of vegetations (Supplemental Videos 1 and 2). While undergoing TTE, the patient converted into atrial fibrillation with rapid ventricular rate and was started on carvedilol and apixaban. The patient began to complain of worsening abdominal discomfort. A computed tomography (CT) scan of the abdomen/pelvis revealed cardiomegaly and hepatomegaly with likely congestive hepatopathy etiology. Our patient responded well to initiation of intravenous (IV) furosemide. Results of toxicology screen and testing for human immunodeficiency virus antibodies were both negative, however C-reactive protein returned positive at 20.4 mg/dL. Scheduled cardiac magnetic resonance imaging (MRI) was postponed due to machine malfunction. Upon further investigation into the patient's history, it was found that he lived and worked on his family dairy farm where he was exposed to livestock (cows and goats) and field cats, and he often drank unpasteurized milk. Furthermore, the patient reported that his father, who had no previous history of cardiovascular disease, had been recently diagnosed with cardiomyopathy, as well.

A repeat TTE was completed 4 days following admission, revealing a LVEF of 32.4%. Further investigations included testing for eosinophilia, HFE gene, Lyme, and toxoplasmosis serology, the results of which were all negative. The patient's Q fever serology found no immunoglobulin (Ig) M antibodies to *C. burnetii* phase I or II; however, IgG returned positive (Table 1). The patient was diagnosed with acute Q fever myocarditis and started on oral doxycycline 100 mg twice daily for 14 days. He passed physical therapy/occupational therapy evaluation and was discharged home on lisinopril, carvedilol, and apixaban. He was instructed to have minimal exertion with return to farming. At his scheduled follow-up appointment two weeks later, cardiac MRI was completed that revealed LVEF 55%, without systolic dysfunction, infiltration, or inflammation (Fig. 3). It was also discovered that he had converted to normal sinus rhythm, thus apixaban was discontinued. His Q fever serology was also repeated, revealing decreased phase I IgG and unchanged phase II IgG (Table 1). He has since returned to farming without functional limitation.

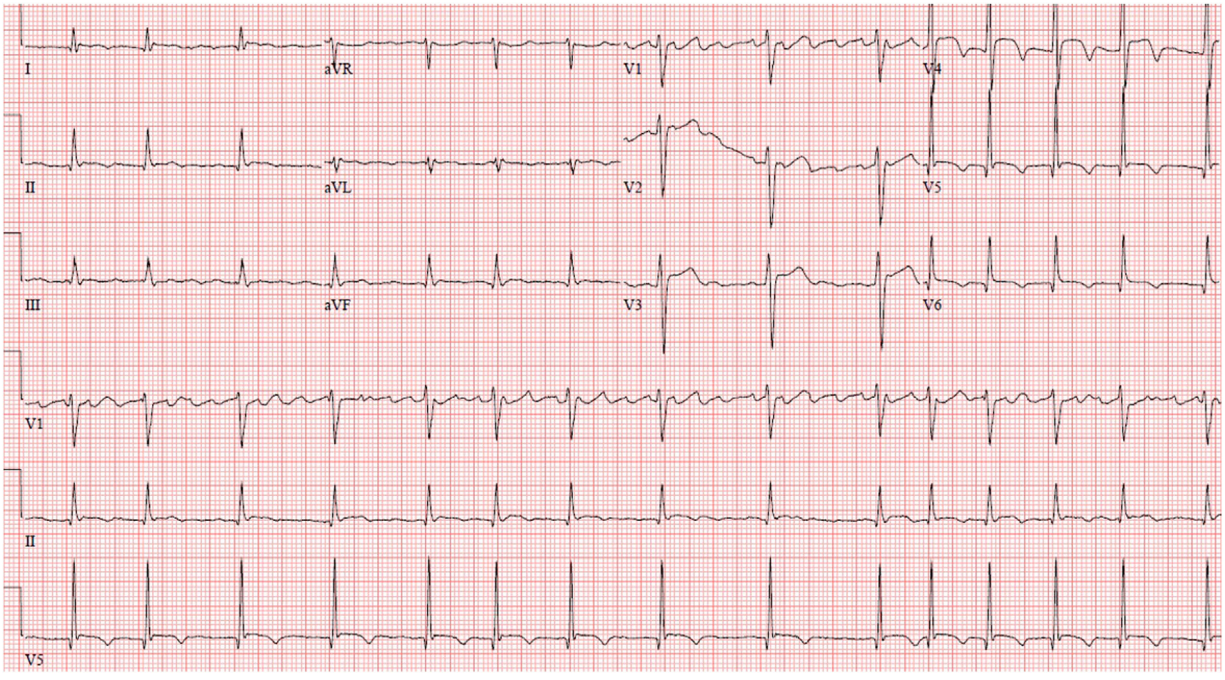

Fig. 2. Electrocardiogram tracing revealing sinus rhythm with premature atrial complexes, ST elevation to anterior leads with a prolonged QTc (464 ms).

Table 1 Q fever serology, with results indicating acute Q fever infection. Ig, immunoglobulin.

	Reference range	06/13/2018	06/27/2018
Phase 1, IgG	<1:16	1:64	1:32
Phase 2, IgG	<1:16	1:256	1:256
Phase 1, IgM	<1:16	<1:16	<1:16
Phase 2, IgM	<1:16	<1:16	<1:16

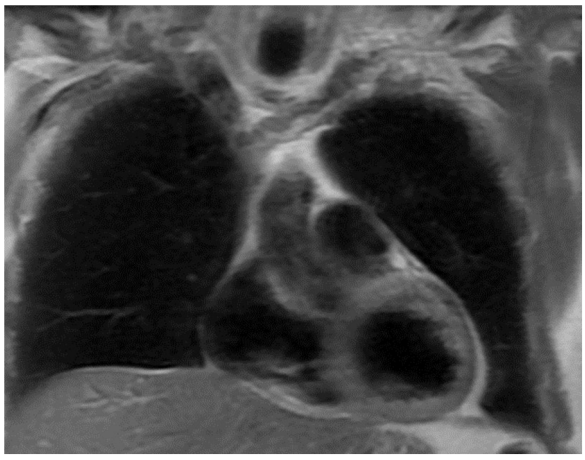

Fig. 3. Cardiac magnetic resonance image revealing normal left and right ventricular size and function, left ventricular ejection fraction of 55%, and no evidence of intramyocardial fibrosis/scar, infiltration, inflammation, or hemodynamically significant valvular pathology.

Discussion

Myocarditis is a rare manifestation of acute Q fever, reported in less than 1% of all cases [5]. The early disease course can be complicated with nonspecific symptoms, making the diagnosis difficult and often delayed. Patients may present with signs of congestive heart failure and fever, although fever is not always present. Initial evaluations often include ECG and TTE testing. ST elevations have been documented on ECG during acute Q fever infection (often diffuse ST elevations), with resolution of ECG changes several weeks following symptom onset [6,7]. Echocardiographic findings can be nonspecific and range from normal ventricular function to wall motion abnormalities with severe systolic dysfunction [6].

Following an in-depth interview, it was discovered that our patient's father was recently diagnosed with nonischemic cardiomyopathy and that both patients carried risk factors for the development of Q fever. Common risk factors for development of Q fever include being male; more than 40 years old; immunocompromised; underlying cardiac valvular damage; pregnant; exposed to animal reservoir; living downwind from a livestock farm; exposed to contaminated manure, straw, or dust; working with *C. burnetii* in a laboratory; travelling to endemic areas; working in a slaughterhouse; and consuming unpasteurized dairy products [3,4].

Often, the primary source of a Q fever transmission cannot be identified [7]. Our patient likely contracted his infection from one of several elements of his dairy farming career: close contact with cows and sheep, and consumption of unpasteurized dairy products.

Diagnosis of Q fever myocarditis can be difficult as *C. burnetii* does not routinely grow in blood cultures. Thus, serology is often used for diagnostic purposes. Ideally, two serum samples should be obtained: the first at symptom onset, and the second at 2 to 4 weeks after antibiotic initiation. *C. burnetii* exhibits a two-phase antigenic variation that is caused by change 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 of Q fever. Screening is positive for acute disease when anti-phase II IgG anti-immunoglobulins return active at a dilution of ≥1:200 or IgM ≥1:50 [3]. 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 ≥1:800 [1].

Cardiac MRI can be a helpful tool in the diagnosis of myocarditis. Findings on T_1-weighted and T_2-weighted images have been recorded as subepicardial abnormalities indicating myocardial edema and inflammation. The pericardium often demonstrates a normal appearance [5].

Endomyocardial biopsy is another modality effective in the diagnosis of myocarditis. Biopsy has become a relatively safe procedure with a reported less than 1% complication rate. Obtaining a biopsy has been shown useful when presented with a clinical scenario, including; idiopathic heart failure of under two weeks' duration unresponsive to conventional therapy [8]. With our patient, after suspicion for myocarditis was raised, cardiac MRI was planned but unattainable due to machine failure. As his Q fever serology returned positive, antibiotic treatment was initiated. However, if testing had returned indeterminate, endomyocardial biopsy would have been an appropriate next diagnostic step.

Per Centers for Disease Control and Prevention recommendations, treatment often consists of 100 mg doxycycline twice daily for 14 days [2,4]. However, if the patient has preexisting valvular disease with an increased disposition for the development of chronic Q fever, hydroxychloroquine is often included at a dosage of 600 mg daily for 12–18 months [4]. Hydroxychloroquine is used mainly to prevent the development of chronic Q fever endocarditis. We treated our patient with a 14-day course of 100-mg doxycycline twice daily. Upon repeat evaluation, his symptoms had resolved. Although his serology markers had remained elevated, they had not increased. Thus, we did not add antibiotics to his initial regimen because he had not progressed to chronic Q fever. He is scheduled to have repeat serology in 3 months.

When patients present with findings of myocarditis, Q fever caused by the zoonosis *C. burnetii* should be on the differential. A delay in diagnosis and treatment can result in worsened morbidity and mortality.

The authors declare that they have no conflicts of interest to declare.

Conflict of interest

The authors declare no conflict of interest.

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Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.jccase.2019.03.012.

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