

Case Report

Endocarditis Caused by *Coxiella burnetii*: A Case Report in Western Iran

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Abstract

Background: Q fever is a contagious zoonotic disease which is caused by a gram-negative and intracellular *Coccobacillus* known as *Coxiella burnetii* ticks play a role in its transmission. Endocarditis is the most common consequence of chronic Q fever.

Methods: Here we report a case of endocarditis caused by Q fever. The patient is a 67-year-old, and she had coronary artery bypass graft (CABG) and aortic valve replacement surgery.

Results: The result of echocardiography showed a suspicious mass (Vegetation) on the implanted valve. Based on laboratory and clinical assessments, endocarditis caused by *C. burnetii* was the final diagnosis.

Conclusion: Q fever is a tick-transmitted pathogen that has been known as an important cause of culture-negative endocarditis in Iran, and more attention needs to be paid to this disease in Iran by the healthcare system and physicians.

Keywords: Q fever; *Coxiella burnetii*; Endocarditis; Kurdistan; Iran

Introduction

Q fever is a contagious zoonotic disease caused by a gram-negative and intracellular *Coccobacillus* known as *Coxiella burnetii* (1). Common reservoirs of *C. burnetii* are cattle, goats, and sheep around the globe (2). Mainly, humans get infected through the inhalation of small aerosols carrying *C. burnetii* (3); however, other routes are, tick bites, person-to-person transmission, and consumption of contaminated dairy products as well (4). Farmers, veterinarians, slaughterhouse workers, livestock handlers, people in contact with raw milk and its products, and laboratory personnel are at higher risk of getting an infection (5).

Q fever mainly appears in acute or chronic forms. It is a self-limited and flu-like disease and approximately 60% of individuals are asymptomatic, and they may clinically manifest pneumonia, hepatitis, osteomyelitis, and cardiac involvement (3). The mortality rate due to acute Q fever is reported to be 1 to 2% (2). Chronic Q fever develops in only 5% of patients after symptomatic or asymptomatic acute Q fever (2). Chronic Q fever may cause vasculitis, prosthetic joint arthritis, osteoarticular infection, endocarditis, and lymphadenitis (1, 6). The most common form, endocarditis, accounts for 60–78% of all cases worldwide.

Patients with infective endocarditis (IE) are mainly men over 40 years of age (3). *Coxiella burnetii* endocarditis lesions may cause fibrosis, calcification, slight inflammation, and vascularization, and small or absent cardiac vegetation that is small and in some cases invisible, possibly due to the intracellular nature of the bacteria (7). The first cases with clinical symptoms diagnosed as acute Q fever were reported in 1952 in Iran. After that in a six-year period (1970 to 1976), 133 patients showing acute Q fever symptoms were added to the number (8). Unfortunately, since 1976, Q fever was neglected till occurring a large outbreak in the Netherlands (2007–2010)(6), at the same time *C. burnetii* antibodies were detected in febrile patients in the Kerman province (southeastern Iran) (16) and provoked the investigation for Q fever to be resumed. Various studies have shown that the prevalence of antibodies against Q fever in humans and animals is high in different regions of Iran (9). Surprisingly, a report showed over 30% of patients with infective endocarditis were caused by *C. burnetii* in Iran (10). Kurdistan Province has always been known as one of the native provinces for Q fever. A study of seroprevalence among high-risk individuals (hunters, butchers, and health workers) reported antibody levels against *C. burnetii* as high as 29% (11). Q fever cases in Iran are usually neglected due to late diagnosed, lack of experience among health care workers and lack of appropriate laboratory facilities. Here we report a case of endocarditis caused by *C. burnetii* in Kurdistan Province.

Case Presentation

Our case is a 67-year-old, illiterate, married woman with 5 children, from a village in Marivan County, Kurdistan Province. The patient has had a history of COVID-19 infection in the past two years and after that, she received two doses of COVID-19 vaccine. In addition, the patient had a history of neck ar-

thritis and stomach disease. The patient was introduced by a cardiologist as a possible case of endocarditis due to severe weakness, fever, chills, sweating, and anorexia in May 2022. She was referred to an infectious disease specialist, and due to the symptoms was admitted to Tawheed Hospital in Sanandaj. At the initial examination, the blood pressure was 120/80 mmHg, the heart rate was 80 beats per minute, the respiratory rate was 18 times per minute, the body temperature was 36 °C, and oxygen saturation was 94%. In the ophthalmic examination, the conjunctiva was pale, but there were no sarcastic signs. In the chest examination, a 12 cm long surgical scar was observed, and no deformity was observed. The expansion was normal and systemic, and there was no murmur on auscultation of the heart, and she did not use the accessory muscles for breathing. The abdomen was soft and distended, and striate were observed on the abdomen. The patient has no history of using alcohol or smoking. The patient's symptoms at the time of hospitalization were weakness and lethargy, cold sweat, myalgia, blurred vision, headache, loss of appetite, photophobia, and weight loss. The patient had a history of contact with non-pasteurized animals and cattle. The results of the patient's para-clinical tests are shown in Table 1.

The patient had a history of coronary artery bypass graft (CABG) and aortic valve replacement surgery four months ago, following the surgery she was hospitalized for a month. During hospitalization, she had oral candidiasis due to the prescription of broad-spectrum antibiotics. Notably, the valve implanted for this patient was of the bioprosthetic type.

At the time of hospitalization, the patient has taken Omeprazole 20 mg, Clindium C, Aspirin 80 mg, Fluoxetine 20 mg (due to low mood), Domperidone 10 mg, Atrostatin 40 mg (due to heart problems) and Warfarin 5 mg. In June 2022, the patient expressed weakness and lethargy, and she was nominated for transesophageal echocardiography. The result of echocar-

diography showed a suspicious mass (Vegetation) on the implanted valve and ejection fraction was 40%. In the initial investigations regarding the involvement of the aortic valve, the spiral HRCT (High-resolution CT) scan of the chest showed the presence of multiple suspicious nodular lesions with peripheral expansion in the parenchyma of both lungs with GGO (Ground-glass opacification), which had the possibility of septic emboli, and this simultaneous heart and lung involvement increased the probability of diagnosis in favor of Q fever endocarditis because cases of Q fever endocarditis mostly involve the right heart.

Abdominal and pelvic ultrasonography results showed a normal-sized liver, and the echogenicity of the liver parenchyma increased slightly, which was primarily indicative of grade 1 and 2 fatty liver. In addition, in the right lobe, a hyperechoic lesion with a diameter of 44 mm was seen in the vicinity of the gallbladder, which is in favor of hemangioma. Additionally, splenomegaly was seen (Span: 144 mm) and the patient had anemia, weakness, and lethargy. The patient underwent several stages of endoscopy and no serious findings were reported. According to the vegetation state of the observed mass, the patient was introduced as a suspected case of endocarditis and required to perform para-clinical tests. Due to the patient's stable hemodynamics and living in the endemic area of brucellosis, serial bacterial blood cultures and serological tests were performed for the patient to check brucellosis and all the results were negative. Considering the serology tests, negative culture of brucellosis, the clinical course of the disease, and pulmonary involvement the suspicion of Q fever infection were increased. To follow diagnostic procedure, the patient's blood and serum samples were sent to the National Reference Laboratory for Plague, Tularemia and Q fever of Pasteur Institute of Iran to be checked for *C. burnetii* infection. The result of the real-time PCR test was negative for *C. burnetii*. Phase I and II IgG antibody against *C. burnetii* was inves-

tigated using the IFA (Indirect Fluorescent Antibody) technique (IFA *Coxiella burnetii* IgG, Vircell, Spain) and their values were reported as 1:512 and 1:128, respectively. Based on these results, endocarditis caused by *C. burnetii* was the final diagnosis. The standard antibiotics for patients with Q fever endocarditis were doxycycline and chloroquine, but levofloxacin was prescribed instead due to the intolerance of doxycycline. Due to valve replacement, the patient has been prescribed warfarin for 6 months, which the patient had refused to take for some time. As the patient was old and had a long-term history of using antibiotics, she was at high risk of urinary symptoms and underwent dialysis three times a week due to kidney complications and increased blood creatinine levels. In the consultation with the ophthalmologist, the patient had moderate cataracts and the Roth spot, which is a common complication of endocarditis, was not observed in the retina. The patient was finally discharged from the hospital in August 2022 with personal consent and was referred for valve replacement. Contact made with the patient, the valve was replaced again, the general condition has improved, the weakness and lethargy, nausea and fever have been disappeared, and she still being treated with the antibiotics ciprofloxacin, doxycycline and chloroquine, and dialysis has been stopped due to normal blood creatinine level.

Table 1. Biochemical, hematological, and serological laboratory test results of a 67-year-old patient suspected for Q fever on the first day of admission, Tohid Hospital, Sanandaj City, Kurdistan Province, 2022

Biochemistry			
Test Name	Result	Unit	Flag
B.U.N	8	Mg/dl	
Cr	1.25	Mg/dl	Hi
Ca	8.9	Mg/dl	
Na	136	Meq/dl	
K	3.9	Meq/dl	
SGOT	22	IU/l	
SGPT	12	IU/l	
Alk.P	110	IU/l	

Table 1. Continued ...

CPK	30	IU/l	
LDH	360	U/l	
Troponin I	Negative		
BS	125	Mg/dl	Hi
Hematology			
WBC	6.5	$\times 10^3$	
RBC	3.67	$\times 10^6$	Lo
Hb	9.9	Gr/dl	Lo
Hct	31.2	%	Lo
MCV	85	fl	
MCH	27	pg	
MCHC	31.7	g/dl	
Plt	190	$\times 10^3$	
Serology			
P.T.T	26	Sec	
PT	17.8		
INR	1.4		
PT control	13	%	

Discussion

Q fever endocarditis is a serious complication of Q fever, a zoonotic disease caused by the bacterium *C. burnetii*. In this condition as occurs in our case, the bacterium infects the heart valves, leading to inflammation and damage. This case had been challenged to diagnose and treat by prolonged antibiotic therapy which no cure had been achieved and finally led to surgical intervention. Having diverse landscape and significant agricultural sector, prone Iran potentially be a region where Q fever occurs. In Iran, as in other parts of the world, individuals at higher risk for Q fever endocarditis include those who work closely with livestock, such as farmers, veterinarians, and slaughterhouse workers. Additionally, people with underlying heart conditions or compromised immune systems, same to our case, may be more susceptible to developing endocarditis if they contract Q fever. The patient had been continuously treated with antibiotics after the valve replacement surgery and after being re-hospitalized due to following complications, and this could be one of the reasons for the negative molecular tests.

Kurdistan Province has always been known as one of the native provinces for Q fever as the seroprevalence antibody levels against *C.*

burnetii were reported as high as 29% among high-risk groups (11). Various studies have shown that the prevalence of antibodies against Q fever in humans and animals is high in different regions of the country (9), and the prevalence of *C. burnetii* in the milk of domestic cattle and aborted fetuses of these animals are reported to be very high (12, 13). The transmitting-role of ticks in Q fever has been controversial, although previous studies have demonstrated *C. burnetii* in ticks. It has been shown infection by *C. burnetii* is systemic, and the midgut, hemolymph, malpighian tubules, salivary glands, and ovaries were the most infected organs(14). Moreover, ticks excrete notable numbers of *C. burnetii* in their body fluids. The infection of *C. burnetii* has been reported in Iranian ticks. As among the collected tick from livestock *Ixodes ricinus*, *Hyalomma anatolicum*, *Hy. marginatum*, *Rhipicephalus bursa*, *Rh. sanguineus*, and *Rh. turanicus* were infected by *C. burnetii*. Importantly, the specimens collected in Kurdistan Province were the most infected ticks having a 92.5% infection rate(15). Based on the available data four species of hard ticks including *Rh. sanguineus sensu lato*, *Haemaphysalis concinna* and *Dermacentor marginatus* have been reported infected by *C. burnetii* in Kurdistan Province(15,16), suggesting that these species might act as potential vectors of Q fever in the region. Considering the contact of our patient with non-pasteurized dairy and cattle in the endemic area of the disease, it is very likely that she was infected through non-pasteurized dairy or an infected bite of a tick. As the implanted valve was bioprosthetic, which has favorable conditions for the establishment of infection, posed the patient a high risk for endocarditis caused by Q fever infection.

Conclusion

Q fever cases in Iran are usually not detected early, it is probably due to the lack of clinical diagnosis experience and appropriate

laboratory facilities. As Q fever has been known as an important cause of culture-negative endocarditis in Iran, thus more attention needs to be paid to this disease in Iran by the healthcare system and physicians.

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This research has been approved by the ethical research committee of Kurdistan University of Medical Sciences (IR.MUK.REC.1402.049).

Ethical considerations

Informed consent was obtained from the patient for the reporting. The patient's identity was protected by removing name, date of birth, and medical record number. No images of the patient have been illustrated.

Conflict of interest statement

The authors of this report have declared that they have no conflict of interest.

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