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SHORT REPORT

Q fever endocarditis in Iran: A case report



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Summary In this report, we describe the first chronic case of Q fever endocarditis in a 72-year-old woman in Iran. The patient developed radiation-associated heart disease status post (s/p) coronary artery bypass surgery, mitral and aortic valve replacements, and tricuspid valve repair. Endocarditis was also suspected due to a history of heart valve surgery. Blood cultures were negative, but a diagnosis of Q fever endocarditis was confirmed based on serologic titers (IgG phase I 1:32,768). The patient was treated with doxycycline and hydroxychloroquine.
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Case report

The patient was a single 72-year-old Iranian woman had migrated to the United States at the age of 24 years. She had worked as a nurse in Chicago and

traveled to Iran for 2–3 months each year to visit her family. The patient returned to Iran in 2009 living in a suburb in Tehran. She recently had contact with wild pigeons, and there was a farm located in her neighborhood. Pastures for grazing sheep and goats were located approximately 2 km from the patient's house, and animals have been observed to travel near her home.

The patient had a history of hypertension, breast cancer, mastectomy, radiotherapy with cobalt (Co) for 5 weeks (1970), atrial fibrillation (1996),

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Table 1 Biochemical and hematological laboratory test results on the first day of admission.

WBC	5700
Serum cr	0.74
Pleural fluid protein	4.3
Serum protein	7.2
Pleural fluid LDH	121
Serum LDH	227
Pleural fluid WBC	1485 (84% lymph)
Pleural fluid cytology	Negative
Blood cultures 6×	Negative
Urine culture	10,000 ≤ Gram negative rod
Pleural fluid culture	Negative
PPD	Positive

hypothyroidism (2005), bilateral knee arthroscopy, cholecystectomy, aortic valve replacement (AVR), mitral valve replacement (MVR), aortic arch bypass graft surgery (2007), tricuspid valve repair (2007), osteoporosis, atrial fibrillation, proximal aortic calcification, severe stenosis of aortic valve, stenosis and failure of the mitral valve, and coronary heart disease. The patient had been immunized with the Bacillus Calmette-Guérin (BCG) vaccine and was a smoker during 1978–1996 and for a few months in 2007. The patient had drug sensitivity to simvastatin, atorvastatin, heparin, and narcotic drugs. In the USA, she had consumed a small amount of alcohol per year and consumed pasteurized dairy products.

The patient was hospitalized in Iran on February 9, 2012 due to fever, chills, cold swelling, ascites, and clay-colored bowel movement. She had fever for the first 3 days of hospitalization, after which her condition improved for 3 days; however, the fever relapsed. On initial examination, the blood pressure, heart rate, and oxygen (O₂) saturation at room ambience were 103/53 mmHg, 80 beats/min, and 92%, respectively. A pleural tap was carried out and she underwent cardiac catheterization. Due to a urinary tract infection, she was treated with a course of Ciprofloxacin for 10 days. There was no leukocytosis, the pleural fluid was exudative, and blood cultures were negative (Table 1).

She traveled to the United States 10 days after hospital admission in Iran. On February 23, 2012, she was hospitalized in Boston due to shortness of breath and coughing, followed by the development of intermittent fever for 1 week. The fever was accompanied by night sweats and chills without shivering; there was no daytime fever. Several weeks prior to this incident, she had a mild nonproductive cough. She did not have dysuria or urgency. She experienced 2–3 kg weight loss several months before hospitalization.

According to a CT scan of the lungs, pleural effusion in the right lower lobe (scattered opacity with ground glass appearance), centrilobular emphysema in the superior lobe, and scattered osteopenia in the thoracic vertebrae were observed. No evidence of endocarditis was present on echocardiography.

The patient was hospitalized and treated for decompensated heart failure attributed to severe tricuspid regurgitation as the primary diagnosis, but the fever and dry cough persisted. On February 28, a pleural tap was performed and she underwent cardiac catheterization on March 1, which revealed occlusions of her vein grafts to the right coronary artery (RCA) and left anterior descending artery (LAD) and elevated right atrial pressures attributed to severe tricuspid regurgitation. According to the transthoracic echocardiogram, severe tricuspid regurgitation was confirmed, and well situated mitral and aortic bioprosthetic valves with no evidence of valvular vegetation were observed. Infection was considered a precipitating factor for decompensated heart failure. However, viral pneumonia was also a suitable differential diagnosis according to the affected region in the lung and the duration of disease. Tuberculosis was unlikely due to the pattern of pulmonary involvement. Lung infarction was a possibility according to the differential diagnosis based on the computed tomography scan. We isolated the patient, and a sputum test for tuberculosis, diagnostic panel of respiratory viruses, and repeated blood cultures were conducted.

After 6 days of hospitalization, the patient was temporarily discharged because she did not have fever during the previous 2 days. After discharge, the fever recurred and shortness of breath increased. Furthermore, she was unable to climb the stairs for more than a half set of stairs. Blood cultures were found to be negative again. We were unable to detect *Bartonella henselae* immunoglobulin M and G, *Bartonella quintana* immunoglobulin M and G, brucellosis immunoglobulin M and G, tuberculosis (T-SPOT), or human immunodeficiency virus (HIV) infection using serologic analyses. At the second stage, phase I and II antibodies against *Coxiella burnetii* (IgM & IgG) were evaluated by indirect immunofluorescent assay (Focus Diagnosis, Cypress, CA, USA) and antibody titers of IgM and IgG phase I against *C. burnetii* were 1:2048 and 1:32,768, respectively. Furthermore, antibody titers of IgM and IgG phase II against *C. burnetii* were 1:128 and 1:32,768, respectively. According to these results, Q fever endocarditis was considered the final diagnosis for this patient, which is superimposed on radiation-associated heart disease.

Table 2 Serologic results for *Coxiella burnetii* using the immunofluorescent antibody (IFA) test.

Date	IgM I	IgM II	IgG I	IgG II
03/08/2012	1:2048	1:128	1:32,768	1:32,768
03/12/2012	—	—	1:32,768	1:16,384
03/16/2012	1:2048	1:256	1:32,768	1:32,768
04/06/2012	1:2048	1:256	1:32,768	1:32,768
07/03/2012	1:256	1:128	1:32,768	1:8192
01/08/2013	Negative	Negative	1:4196	1:1024
06/09/2013	Negative	Negative	1:2048	1:1024

The patient was asked to return to the hospital for further evaluation and treatment of Q fever. At this time, her blood pressure, heart rate, O₂ saturation at room temperature, and body temperature were 119/67 mmHg, 96 beats/min, 96%, and 37°C, respectively. Icterus and rash were not observed during the skin examination. The head, neck, and pharynx physical examination were normal. Lung auscultation indicated decreased pulmonary sounds at the base of both lungs, and no murmur sounds were present with cardiac auscultation. The physical examination of abdomen and extremities were normal. This patient was diagnosed with infective endocarditis using the modified Duke criteria, including a phase I IgG antibody titer >1:800 for *C. burnetii* (as major criteria) and minor criteria such as predisposing heart condition and fever. The patient was treated with doxycycline 100 mg twice daily and hydroxychloroquine 600 mg daily. She underwent a bioprosthetic tricuspid valve replacement in July 2012 for progressive tricuspid regurgitation and right sided heart failure. In addition, we monitored her treatment progress and antibodies against *C. burnetii* for several months (since October 2012) in the United States and Iran (Table 2).

Conclusion

We report a case of Q fever endocarditis in a patient from Iran. The first case of acute Q fever in Iran was reported in 1952 [1], and since then, human seropositive cases of Q fever have been reported from certain parts of the country [2,3]. No human cases have been reported in Iran since 1976 and the disease was ignored for many years [4]. In 2010, *C. burnetii* antibodies were reported in febrile patients in the Kerman province (southeast Iran) [5] and investigation for Q fever was resumed in Iran. However, there have been no reports of chronic Q fever in Iran until now. According to old and recent reports regarding the prevalence of Q fever among

domestic and wild animals, Q fever was endemic in Iran [3,4,6–10]. Q fever cases were not diagnosed in Iran for >35 years due to a lack of diagnostic facilities and the relatively low level of awareness within the Iranian health care system.

The present patient presented with congestive heart failure and a history of AVR/MVR, tricuspid valve repair, and coronary artery bypass graft. Initially, endocarditis was suspected due to the presence of fever, coughing, and radiographic changes in the lung, especially the right lung, and a history of heart valve surgery. There was no sign of vegetation on echocardiography, but the diagnosis of Q fever was confirmed by serologic titers (IgG phase I 1:32,768) and the serologic panel was applied during the following months (since March 2012 to June 2013).

Transmission of Q fever to humans occurs mainly through the exposure of infected animals and inhalation of contaminated aerosols [11]. Older and immunocompromised individuals are at a greater risk for developing chronic Q fever. Endocarditis is the most common manifestation of chronic Q fever, which predominantly occurs in patients with a history of valve disorders and/or valve replacement surgery. Pre-existing valvular heart disease and prosthetic valves are recognized as risk factors for Q fever endocarditis [12]. In a study on 408 patients with Q fever endocarditis, it was shown that underlying valvular heart disease was almost invariably present, and 38% of the patients had prosthetic valves [13].

In this case, the patient had been living in the United States until 2009 and returned to Tehran, Iran afterwards. Therefore, there is a possibility that the patient had been infected in the United States and presented with endocarditis after several years in Iran. However, the probability of getting an infection in the United States is low given the patient's history in the United States (i.e., not keeping livestock or pet animals and not consuming unpasteurized dairy products). However, the pasture used for grazing domestic animals, which was

located near the patient's home in Iran, was as an important reservoir of Q fever. Furthermore, the patient's symptoms appeared after living in Iran for a few years. Therefore, it is more likely that the infection occurred in Iran.

Q fever in the patient was not diagnosed early in Iran, probably due to a lack of experience in clinical diagnosis and appropriate laboratory facilities; however, the disease was diagnosed after evaluations in the United States. The lack of recent reports regarding acute or chronic forms of Q fever, especially endocarditis and the valvular form might be due to a lack of awareness of clinicians and the health care system in Iran.

Conflict of interest

The authors declare that they have no competing financial interests.

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