

Recurrent culture-negative endocarditis and osteomyelitis caused by Q fever in Iran, a case report.

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Abstract

In this case report, we are presenting a man with intermittent fever for three months with a history of aortic and pulmonary valve replacement and also recurrent blood culture-negative endocarditis. After several evaluations based on endemic epidemiology, the Real-time PCR and IFA (indirect immunofluorescence assay) were positive for Q fever.

Introduction

Infective endocarditis (IE) is a serious diagnosis that occurs around 30 new cases per million worldwide, it is a challenging condition that requires the most attention for early diagnosis and proper treatment [1-3]. IE can occur following valvular problems and other heart surgeries and devices and leads to fatal cardiac and non-cardiac manifestations. Due to the multi-organ damages caused by IE, early detection with laboratory examinations, transesophageal echocardiography (TEE), imaging, and cultures are required and definite treatment with antibiotics or even surgery is critical [4-6]. One of the difficulties in IE diagnosis is blood culture-negative endocarditis (BCNE). Although BCNE is decreased due to advanced diagnostic methods, it is responsible for approximately 20% of infective endocarditis [7, 8]. Based on documented evidence, the organisms responsible for BCNE are mostly Bartonella, Coxiella, and Chlamydia species [7, 9]. among these organisms Bartonella species are responsible for the most number of BCNE in recent years [10].

Q fever is a zoonotic endemic disease caused by *Coxiella burnetii* which can cause BCNE in patients who underwent valvular surgeries and other chronic heart problems. Patients having Q fever are commonly asymptomatic, while others have different non-specific symptoms; therefore, its diagnosis depends on the patient's history of animal contact especially in endemic regions [11, 12].

Based on different surveys, Iran is one of the regions with *C. burnetii* endemicity, and due to the broad contact with domestic animals, Q fever has a high prevalence in our region; therefore, we should consider this domestic disease as a probable cause of BCNE [13, 14]. In this case report, we are presenting a patient with Q fever endocarditis with a history of chronic endocarditis and multiple valve replacement.

Case presentation

A 30-year-old man was admitted to the hospital with intermittent fever for three months. He had received antibiotics for 6 weeks due to the negative culture endocarditis 3 years ago. At admission, his temperature was 38 degrees centigrade with normal vital signs. Abnormalities in the physical examination were mild cyanotic lips, hyperpigmentation (lipodermatosclerosis) in both legs, splenomegaly, and a mid-systolic murmur in

the second left intercostal space. In his past medical history, he had blood culture-negative endocarditis twice in 25 and 27 years of age and also TOF early in his life. His past surgical history consists of Blalock-Taussig shunt in 1994, tetralogy of Fallot total correction (TFTC) in 2001, pulmonary valve replacement (PVR) with a bioprosthetic valve in 2010, and Bentall procedure for native aortic valve endocarditis (NVE) along with mechanical PVR in 2015. In all three surgeries, pathological results were positive for infection and endocarditis [15]. There was not a history of animal contact, recent travel, or any suspicious contact, he just mentioned eating local cheese occasionally and he was the only person with fever in his family.

According to the history of BCNE in our patient and a documented fever, we performed several examinations to rule out infective endocarditis. In early laboratory data, white blood cell count was $5700 \times 10^9/L$ ($4000-10000 \times 10^9/L$) with 58% polymorphonuclear leukocytes, hemoglobin level was 12.1 gr/dL (13-16 gr/dL), platelet cell count was 124000 (150,000 to 450,000 platelets per microliter), serum creatinine was 2 mg/dL (0.6-1.5 mg/dL), erythrocyte sedimentation rate was 120 mm/h (0-15 mm/h), and C-reactive protein was 31 mg/L (<6 mg/L).

Urine analysis, viral markers, Coomb's wright, and 2ME tests were all negative. Other examinations such as Covid-19 PCR and blood culture (six times) were also negative.

We found right axis deviation, first degree atrioventricular (AV) block, right bundle branch block (RBBB), and left posterior hemiblock on his electrocardiography (ECG). The chest spiral computed tomography (CT) scan was normal and without any pathologic findings. In TEE we didn't find any particular evidence regarding IE and his ejection fraction (EF) was 40%.

According to the former history of BCNE in this patient, the history of PET/CT scan involvement, and also the European heart association guidelines in endocarditis, PET/CT scan was performed. Hyper metabolic lesions were seen over the aortic and pulmonary prosthetic valves along with ascending aorta graft, aortic arch, and proximal root of pulmonary artery involvement, all in favor of infective endocarditis, diffuse increased metabolic activity of sternum which may represent osteomyelitis and also right sub-pectoral adenopathy (Figure 1). Based on modified Duke's Criteria in this patient, our suspicion was more towards endocarditis.

After the PET/CT scan report, we have performed other examinations to find the organism responsible for BCNE especially brucellosis and Q fever due to the region we practice. Blood and sera samples of this patient were referred to the National Laboratory for Plague, Tularemia, and Q fever of Pasteur Institute of Iran. The Real-time PCR and IFA (IgG phase I; 1:16384, IgG phase II; 1:16384) were positive for *C. burnetii* and Q fever endocarditis was confirmed. We also examined the previous samples from the last valve replacement for *C. burnetii*, which was also positive. After the diagnosis, the proper treatment with doxycycline 100mg every 12 hours and hydroxychloroquine 200mg every 8 hours was initiated and the patient's fever was resolved.

We discharged our patient with the stable condition, suggested to follow up his status with intermittent serological testing every three months and PET/CT scan, a consultant with cardiologist and infectious disease specialist and prescribed doxycycline 100mg every 12 hours and hydroxychloroquine 200mg every 8 hours for 2 years due to the prosthetic valve with a regular eye examination.

In three months, follow-up patient's inflammatory indices such as ESR and CRP were within normal ranges, *C. burnetii* serologic test, and sternum uptake in PET/CT scan were decreased.

Discussion

Q fever, a zoonotic infectious disease, can present with chronic manifestations rather than intermittent fever. The most common chronic complication is endocarditis with a high rate of morbidity and mortality. In addition to endocarditis, osteomyelitis is another chronic Q fever complication [16-18]. *C. burnetii* grows on the abnormal cardiac valve along with the prosthetic valve and causes Q fever non-specific manifestations, therefore chronic Q fever is hardly diagnosed and because of several antimicrobial treatment resistance, it is hardly treated too. One of the risk factors for chronic Q fever is valvular surgeries which our patient underwent several times [19, 20].

Due to the high prevalence of *C. burnetii* in our country, we should consider it as an important agent for BCNE [21, 22].

Despite the great medical development, infective endocarditis is still a concern in both diagnosis and treatment and the best option for early diagnosis and immediate treatment is to consider IE as a possible diagnosis [23, 24]. Even nowadays the mortality rate caused by IE reaches 30% annually [25]. Echocardiography is a non-invasive diagnostic evaluation in IE which can detect the vegetation accurately without a significant difference from the surgical view. In some cases like ours, there is no evidence suggesting IE in echocardiography, therefore normal ECG cannot rule out IE diagnosis [26].

To identify extra cardiac IE manifestations, classification, and also management, PET/CT scan is helpful. In our patient all the studies except PET/CT scan couldn't reveal the IE evidence, therefore we should declare that performing PET/CT scan is a necessary evaluation in IE cases or even in those with suspicious IE diagnosis [27, 28].

Conclusion:

As we understood Q fever-induced endocarditis usually does not present with specific clinical manifestations and echocardiographic evidence, therefore early diagnosis and proper treatment are generally delayed. This mismanagement leads to different complications and increases the morbidity and mortality rate. According to the endemic distribution of Q fever in various regions, clinicians must consider any suspicious animal contact and keep this diagnosis in mind. We can decrease the diagnostic delay by making the laboratory tests available and performing rapid diagnostic tests for those with a history of animal contacts or other complicated underlying conditions.

Declaration

We have no conflict of interest to declare.

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Detailed author's contribution

M.M has wrote the paper, M.A has collected the data, F.L has contributed the data, F.Gh and S.E have conceived the data and S.Gh has supervised the whole process.

Availability of data

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Consent for PublicationWritten informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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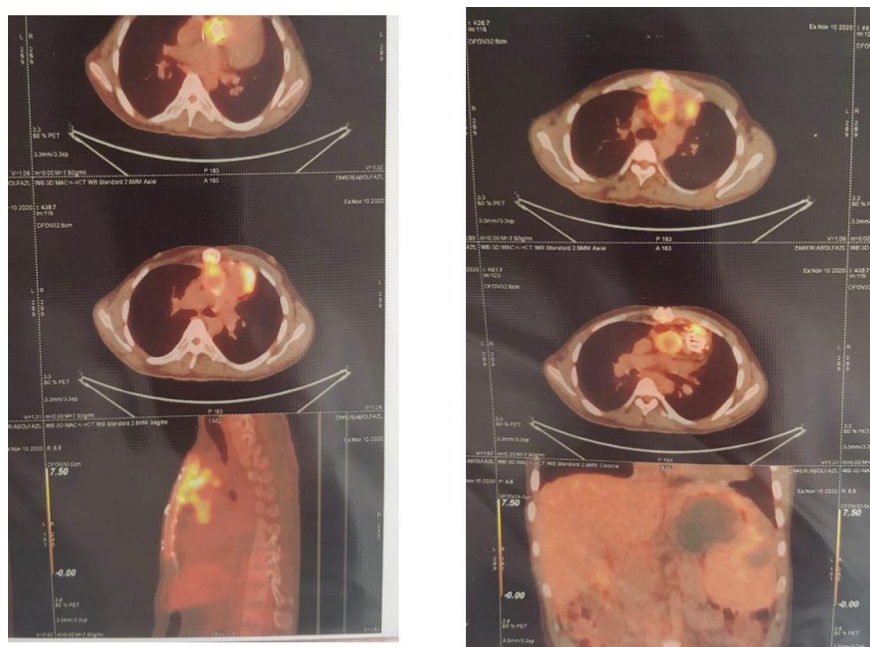


Figure 1. Patients PET/ CT scan

Findings: Hypermetabolic lesions over the prosthetic aortic valve with involvement of ascending and aortic arch. Huge splenomegaly with loss of normal metabolic activity in favor of perfusion defect and massive infarct. Splenic hilar adenopathies were also seen.

Abbreviations: PET/CT scan= positron emission tomography-computed tomography scan.