The Importance of Exposures in Culture-negative Endocarditis in an IV Drugs Abuser

Ensiyeh Rahimi1*, Sara Gaderkhani1, Arash Seifi1, Mahsa Azadbakhsh Kanafgorabi1, Bahar Haghdooost2, Amirhossein Eghbal1, Saharnaz Sazgarnejad4, Saber Esmaili5

1Department of Infectious Diseases and Topical Medicine, Tehran University of Medical Sciences, Iran
2National Institute of Health Research, Tehran University of Medical Sciences, Iran
3Students’ Scientific Research Center, Tehran University of Medical Sciences, Iran
4School of medicine, Tehran University of Medical Sciences, Iran
5Department of Epidemiology and Biostatistics, Research Centre for Emerging and Reemerging infectious diseases, Iran

ABSTRACT

Background: Infective Endocarditis (IE) is a severe and life-threatening disease worldwide. Approximately 5% of IE cases have negative blood cultures. Risk factors are exposure to slow-growing bacteria and exposure to Bartonella species. Most patients have nonspecific symptoms such as fever, fatigue, and weight loss.

Case presentation: A 38 years old male with a history of addiction was referred to our center with severe dyspnea, high fever, chest pain, and shortness of breath. He went under CT angiography for pulmonary thromboembolism and TTE. According to the findings, the first diagnosis was right-side endocarditis, which led to septic embolism, so we started empiric antibiotic therapy with vancomycin plus ceftriaxone. After two weeks of constant fever despite broad-spectrum antibiotic therapy and pleural effusion drainage, we changed the antibiotic regimen to vancomycin plus meropenem, and re-sended blood cultures, which were negative 3 times, we considered Q fever, Bartonella, and Brucellosis as possible causes of culture-negative endocarditis according to the history of staying in the camp. We sent serology tests and blood PCRs to the laboratory of the Pasteur Institute of Iran. All of them were negative, but a serology test confirmed Bartonella henselae with a 1: 2048 titer. In the meantime, we changed the patient’s drug regimen to doxycycline, plus rifampin, due to the high level of creatinine, and warfarin was switched to enoxaparin. Clinically, the patient recovered with no breathing difficulties or chest pain after two weeks of treatment, and the result of the B. henselae IgG follow-up serology was 1:512. Four weeks after admission, the patient was discharged from the hospital with instructions to see a cardiologist, quit abusing IV drugs, and continue taking doxycycline and enoxaparin.

Conclusion: The patient’s social history regarding IV-drug abuse and low socioeconomic status are the most important considerations. Because of the increased risk factors in these patients, organisms such as Bartonella Henselae, Coxiella Burnetii and Brucella should also be investigated when cultures are negative.

Keywords: Culture-negative endocarditis; IV-drug abuse; low socioeconomic status; Bartonella henselae

INTRODUCTION

Infective Endocarditis (IE) is a severe and life-threatening disease worldwide [1]. However, because of non-specific clinical presentations, confirmation and prescription of effective treatment are sometimes not simple tasks. History may help significantly in the diagnosis of IE; For example, it is more common among drug addicts, particularly Intravenous

Received: 04-June-2024 Manuscript No: ipqpc-24-19859
Editor assigned: 06-June-2024 PreQC No: ipqpc-24-19859 (PQ)
Reviewed: 20-June-2024 QC No: ipqpc-24-19859
Revised: 25-June-2024 Manuscript No: ipqpc-24-19859 (R)
Published: 02-July-2024 DOI: 10.36648/1479-1064.32.3.15

Corresponding author Ensiyeh Rahimi, Department of Infectious Diseases and Topical Medicine, Tehran University of Medical Sciences, Iran, E-mail: erij.yh@yahoo.com

Citation Rahimi E, Gaderkhani S, Seifi A, Kanafgorabi MA, Haghdooost B, et al. (2024) The Importance of Exposures in Culture-negative Endocarditis in an IV Drugs Abuser. Qual Prim Care. 32:15.

Copyright © 2024 Rahimi E, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
drug users [2,3]. Approximately 5% of IE cases have negative blood cultures, and its risk factors are exposure to slow-growing bacteria such as Bartonella species, fastidious nonbacterial organisms, previous antibiotic use, underlying valvular heart disease, and intracardiac or vascular device or other foreign bodies in contact with the blood [4-6]. Most patients have nonspecific symptoms such as fever, fatigue, and weight loss. In a case series comprising 348 blood culture-negative endocarditis cases from France, almost all the patients had a fever as a presenting symptom. In contrast, about 50% to 70% had symptoms of heart failure, such as exertional dyspnea, and about 50% had insidious weight loss [7].

Bartonella species is a small, intracellular, gram-negative, and very fastidious rod mainly transmitted by vectors; they are the second most common cause of culture-negative endocarditis. Among the cases of Bartonella endocarditis, two species predominantly implicated in causing culture-negative endocarditis are B. henselae and B. Quintana [8]. These bacteria have been isolated from many mammalian species, including cats and dogs. It can cause mild infection to severe and life-threatening endocarditis in humans and dogs. In dogs, several Bartonella species have been identified; one of the most common ones is B. henselae. It should be mentioned that in recent years, more cases of culture-negative endocarditis have been reported from developing countries [9]. This report presents a case of a patient with culture-negative Bartonella endocarditis from Iran, diagnosed using a combined diagnostic approach that included clinical evaluation, imaging, epidemiology, serology, echocardiography, and Transthoracic Echocardiography (TTE).

CASE REPRESENTATION

Patient Information

The patient was a 38 years old male, single and unemployed with a history of addiction, who had received care from a treatment camp for 6 months. He was discharged when he was on methadone maintenance therapy just before his first hospital admission. He was an IV drug abuser with a history of regularly using amphetamine, cocaine, and heroin. He also smoked cigarettes for 20 years. He also exposed that he had unsafe sex and lost contact with dogs and cats.

Clinical Findings Timeline

The symptoms onset was 20 days before admission when he had fever and chills besides shortness of breath in the camp. The patient was hospitalized in another care center for five days as a suspected COVID-19 case and he was treated with Remdesivir, but his nasopharyngeal and oropharyngeal PCR tests were negative. Having been discharged from the hospital, he started using amphetamine again, which deteriorated his condition.

This time he was admitted to our center, as a referral center, with severe dyspnea, high fever (40°C), chills, chest pain, myalgia, and hemoptysis. The patient was ill and, on physical examination, he had tachycardia (Heart rate=107) and tachypnea (Respiratory rate=28), with low blood pressure (90/60), fluctuated oxygen saturation which was less than 92%, normal heart auscultation, no clubbing, no splenomegaly, and no lymphadenopathy. Table 1 summarizes the lab results.

Table 1: The results of main lab tests at the admission time

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>WBC</td>
<td>18,100 (normal range between 4,500-11,000)</td>
</tr>
<tr>
<td>Procalcitonin</td>
<td>More than 30 (normal range between 0.5-5)</td>
</tr>
<tr>
<td>Covid PCR test</td>
<td>Negative</td>
</tr>
<tr>
<td>CRP</td>
<td>174 (normal range: Less than 10 mg/L)</td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.1</td>
</tr>
<tr>
<td>Troponin</td>
<td>Negative</td>
</tr>
<tr>
<td>D-dimer</td>
<td>25.14 (normal range: Less than 0.50)</td>
</tr>
<tr>
<td>Blood culture (3 times)</td>
<td>Negative</td>
</tr>
<tr>
<td>HCV Ab</td>
<td>Positive</td>
</tr>
<tr>
<td>HCV PCR</td>
<td>Negative</td>
</tr>
</tbody>
</table>

A 65-year-old patient was referred for investigation of an axonal sensorimotor neuropathy that has been evolving for 5 months. Possible infectious and neoplastic causes were ruled out by examination, laboratory tests and imaging. The patient reported ocular and oral dryness. Minor salivary gland biopsy highlighted the presence of focal lymphocytic sialadenitis with a focus score of 1 foci/mm³. Schirmer’s test was inferior to 5 mm/5 min in both eyes. Laboratory investigations revealed anterior pituitary failure including secondary adrenal insufficiency, central hypothyroidism and hypogonadotropic hypogonadism. Magnetic resonance imaging of the hypothalamo-pituitary region demonstrated signs of autoimmune hypophysitis. During hospitalization, the patient developed anemia and thrombocytopenia with schizocytes count at 4%. The diagnosis of TMA associated to SS, without renal failure was made. The patient was commenced on intravenous immunoglobulin, corticosteroids, azathioprine and pregabalin. An improvement was noticed in her neuropathic pain, anemia and thrombocytopenia. Schizocytes count was reduced progressively.

Diagnostic Assessment and Therapeutic Intervention

Due to fever, dyspnea, and an SpO₂ below 90%, a Computed Tomography (CT) was performed. The chest CT showed moderate pleural effusion and bilateral emphysema in the apex of the lungs and cardiomegaly. Pelvic and abdominal ultrasounds were normal. Because of dyspnea, tachycardia elevated D-dimer, and SpO₂ of less than 90%, we decided to take CT angiography for Pulmonary Thromboembolism (PTE). CT angiography showed PTE, moderate pleural effusion in the right lung compatible with empyema, and a blurred wedge in the Left Upper Lobe (LUL). We put the patient under anticoagulation therapy with warfarin, after PTE was diagnosed, and based on the localized pleural fluid in the CT scan, empyema pattern, and the patient’s fever, the effusion was tapped, and a chest tube was placed. The patient’s pleural fluid was analyzed, which was exudative with Alb=900, Pro=2400, LDH=1184, RBC=50, WBC=3400, Glucose=80, and negative culture. The lung field was found to have a septic embolism pattern, which led to an
echocardiogram. Upon echocardiography, small vegetation was detected; therefore, a Transthoracic Echocardiogram (TTE) was conducted to confirm. TTE showed severe tricuspid valve damage, 8 millimeter vegetation in place, increased pulmonary artery pressure (PAP=40), and Ejection Fraction (EF)=45%, confirming the vegetation on the atrial side of the tricuspid valve.

According to the findings, the first diagnosis was right-side endocarditis, which led to septic embolism, so we started empiric antibiotic therapy with vancomycin plus ceftriaxone. After 2 weeks of constant fever despite broad-spectrum antibiotic therapy and pleural effusion drainage, we changed the antibiotic regimen to vancomycin plus meropenem, and, re-evaluated our diagnosis by taking a detailed history, re-sending blood cultures, which were negative 3 times, performing abdominal ultrasound and investigating the possible causes of culture-negative endocarditis including Q fever, Bartonella, and brucellosis, according to the history of staying in the camp. The serology and blood PCRs were sent to the laboratory of the Pasteur Institute of Iran. The PCR and serology for Q-fever were negative. Serology Wright and 2-ME test for brucellosis were negative, but a serology test confirmed for Bartonella henselae with a 1:2048 titer. In the meantime, we changed the patient’s drug regimen to doxycycline (100 mg twice daily), instead of aminglycosides, plus rifampin (300 mg twice daily), due to the high level of creatinine (3 mg/dL-3.3 mg/dL), and warfarin was switched to enoxaparin due to rifampin and warfarin drug interactions and patient noncompliance. After 72 hours he responded to this drug combination significantly; Fever, tachycardia, and dyspnea improved, creatinine levels decreased and the pleural fluid test result was negative for Bartonella. After two weeks, rifampin was discontinued, but he received an extended course of doxycycline monotherapy. Also, due to severe tricuspid valve insufficiency, he underwent medical treatment, but because of his addiction, the cardiac surgery service did not recommend him for valvoplasty. A summary of the clinical practice of the patient is shown in Figure 1.

**Figure 1:** Timeline of symptoms onset and interventions

### Follow-up and Outcomes

After 2 weeks of treatment with doxycycline plus rifampin, clinically, the patient recovered with no difficulty in breathing and no chest pain. The results of the follow-up serology for *B. henselae* IgGs were 1:512. The patient was discharged from the hospital approximately four weeks after admission, with a recommendation to visit a cardiologist, stop his IV drug abuse, and continue doxycycline and enoxaparin. A controlled chest X-ray showed improvement, and the chest tube was discontinued. The patient left the hospital in good general condition, without fever, with a normal heart rate and acceptable SpO₂ (>94%).

### RESULTS AND DISCUSSION

Blood culture-negative IE has a high variation in prevalence among countries; the reports vary from 2.5%-70% of all infective endocarditis based on zoonotic agent exposure, antibiotic prescription pattern, and diagnostic tools [10]. *Bartonella* species are among the main microorganisms in culture-negative endocarditis. Meanwhile, among all 45 known *Bartonella* species, *B. henselae* is the second most common cause of culture-negative endocarditis [11]. While cats and cat-scratch are considered the main reservoir of *B. henselae*, dogs could also transmit infection as accidental hosts [12]. Moreover, although *Bartonella endocarditis* is a worldwide issue and there are case reports from all parts of the world, most reported cases are from European countries and the Americas [11].

In this article, we are reporting a case of *Bartonella endocarditis* in Iran; it is notable that since *Bartonella endocarditis* is not common in Iran, usually physician does not put this agent on the list of their differential diagnosis, which causes several challenges to achieving a timely diagnosis and treatment of *Bartonella endocarditis*. Besides, the final diagnosis is even more challenging due to non-specific symptoms, which are the same as other subacute endocarditis or infective syndromes. Moreover, the diagnosis is more challenging during the COVID-19 pandemic and the similarity between the typical symptoms of SARS-CoV-2 and *endocarditis* [13]. Nevertheless, several diagnostic tools are available; despite their limitations, such as low specificity and cross-reactions, serology is still considered valuable in diagnosing *Bartonella endocarditis* [14]. Also, PCR testing on whole blood or plasma specimen, with approximate sensitivity of 58% and specificity of 100%, is an effective diagnostic tool [15].

In this case, the patient had a history of contact with dogs, but based on previous studies, connection with cats is more common in most *B. henselae endocarditis* cases. Moreover, in the current case, one of the first complaints of the patient was exertional dyspnea, and heart failure manifestations are considered an acute coronary syndrome. At the same time, based on the study conducted by Okaro, et al., approximately 50% to 70% of *Bartonella* endocarditis presents symptoms of heart failure, including exertional dyspnea [11]. Low socioeconomic status is one of the underlying determinants of developing *B. Quintana endocarditis*. While in our patient, who was diagnosed with *B. henselae*, the patient’s social history regarding IV-drug abuse and low socioeconomic status were the most important considerations [11]. Also, prognosis and treatment must consider epidemiological exposure and alternate diagnoses for culture-negative endocarditis in individuals who don’t respond to therapy.

### CONCLUSION

The patient’s social history regarding IV-drug abuse and low socioeconomic status are the most important considerations. Because of the increased risk factors in these patients, organisms such as *Bartonella henselae*, *Coxiella burnetii* and
**Brucella** should also be investigated when cultures are negative.

**ETHICAL APPROVAL**

This study has been approved by the ethics committee of Tehran University of Medical Sciences, adheres to the Declaration of Helsinki and informed consent was taken. The patient has given a written informed consent for the publication. The authors confirm that written consent has been obtained from the patient for submission and publication. All the patient’s data and materials are provided in the manuscript.

**ACKNOWLEDGEMENT**

None.

**CONFLICT OF INTEREST**

The authors declare that they have no competing interests.

**REFERENCES**