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Mitral Valve Culture Negative Endocarditis Complicated by Severe Mitral Regurgitation and Chordae Tendinea Rupture

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Abstract

Infective endocarditis has a high mortality rate. Criterion for diagnosis is a positive blood culture, however, some cases present with negative blood culture. We present a 65-year-old male complaining of palpitations. EKG showed atrial fibrillation with RVR. Transthoracic echocardiogram showed severe mitral regurgitation and possible vegetation. Transesophageal echocardiogram revealed endocarditis with ruptured chordae and vegetation on the posterior leaflet. All obtained blood cultures remained negative. Cardiothoracic surgery and infectious disease specialties were consulted. Patient was started on broad spectrum antibiotics. Patient underwent a mitral valve replacement and pathology showed focal myxoid degeneration with no inflammation and cultures of the specimen were negative. The hospital course was complicated by hemopericardium, treated by pericardial window, and drain placement. The patient was ultimately discharged to an acute rehabilitation center. Culture-negative endocarditis presents a diagnostic and therapeutic dilemma for clinicians and should be promptly identified and treated to avoid complications.

Keywords: Infective endocarditis, Chordae rupture, Echocardiography

Learning Objectives

1. To identify vegetation on transthoracic and transesophageal echocardiography.
2. To identify blood culture negative endocarditis as a differential diagnosis and create work-up for it.

Introduction

Infective endocarditis (IE) is an extremely serious disease with a high mortality rate. The diagnosis of infective endocarditis is based on Duke's Criteria, the major criteria of which is a positive blood culture [1]. However, approximately 20% of cases of infective endocarditis have a negative blood culture (blood culture negative endocarditis [BCNE]) [2], which presents clinicians with a challenge of proper diagnosis and treatment. The most common causes of culture-negative endocarditis are previous administration of antimicrobials and the presence of unculturable organisms [3]. Infective endocarditis has a high rate of complications, such as heart failure, valve insufficiency or abscess, and neurological or septic [4].

Case Presentation

History of presentation

A case of 65-year-old male originally presented to a different hospital with a complaint of palpitations for 3 days prior to presentation to the emergency department. The patient reported that prior to the 3 days he has never experienced chest pain, orthopnea, dyspnea on exertion, lower extremity edema, however, he did reports experiencing palpitations in the past, but was never diagnosed with a rhythm disturbance.

His medical history is significant for hypertension, diabetes, and hyperlipidemia. Family history was significant for heart failure in both parents and a valve replacement in the mother.

The patient reported remote tobacco use, denied alcohol or illicit drug use, including intravenous drug use. Home medications were aspirin 81 mg, atorvastatin 40 mg, losartan/hydrochlorothiazide 100-12.5 mg, nifedipine ER 60 mg, metformin 500 mg.

On admission patient was normotensive, afebrile, saturating 99% on room air and tachycardic to 130s beats/min. Physical examination revealed a 3/6 systolic murmur at the apex radiating to the mid-axillary line.

Investigations

Complete blood count (CBC) and comprehensive metabolic panel (CMP) as well as thyroid-stimulating hormone (TSH) were within the normal limit, brain natriuretic peptide (BNP) was elevated to 164 pg/ml.

ECG was done and showed atrial flutter with rapid ventricular response (RVR) and variable block.

Transthoracic echocardiogram (TTE) showed ejection fraction (EF) 60-65% and thickening of the anterior leaflet and posterior leaflet, consistent with myxomatous proliferation. Prolapse, involving the posterior leaflet, malcoaptation of the valve leaflets. Severe regurgitation, with a single jet, directed eccentrically, anteriorly, and toward the septum. Shaggy posterior valve leaflet with severe mitral regurgitation, consider vegetation (**Figure 1**).

Transesophageal echocardiogram (TEE) revealed flail motion involving the medial and middle scallop of the posterior leaflets of the mitral valve, suggestive of possible endocarditis with ruptured chordae and possible vegetation on the posterior leaflet (**Figure 2**).

Management

The patient was subsequently transferred to our institution for cardiothoracic surgery evaluation. Aerobic and anaerobic blood cultures were negative. Infectious disease specialists were consulted and were guiding antibiotic therapy throughout patients' hospitalization. The patient underwent coronary angiography, which revealed normal coronary vessels. Cardiothoracic surgery performed mitral valve replacement. Mitral valve pathology showed leaflets with focal myxoid degeneration, a fragment of cardiac myocardium with scarring and patches of pale myocardium, no inflammation seen. Two subsequent sets of blood cultures were negative. Autoimmune work-up was unrevealing and *Bartonella henselae* and *quintana* serologies are pending. Patient received a month of IV Vancomycin and 3 weeks of IV Cefepime. Large pericardial effusion and hemopericardium with pericardial window and pericardial drain placement, as well as pleural effusion with chest tube placement complicated the hospital course.

Outcome

Pericardial drain and chest tube were successfully removed, transaminitis with coagulopathy were corrected and patient was discharged to the acute inpatient rehabilitation center.

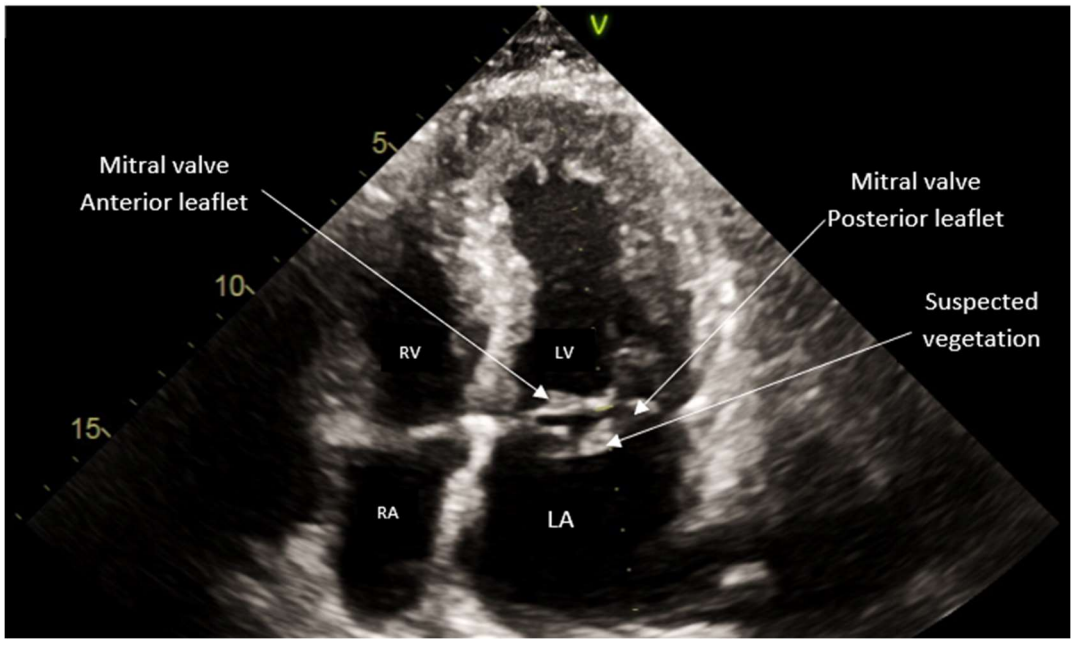

Figure 1. Transthoracic echocardiogram four-chamber view demonstrating mitral valve vegetation.

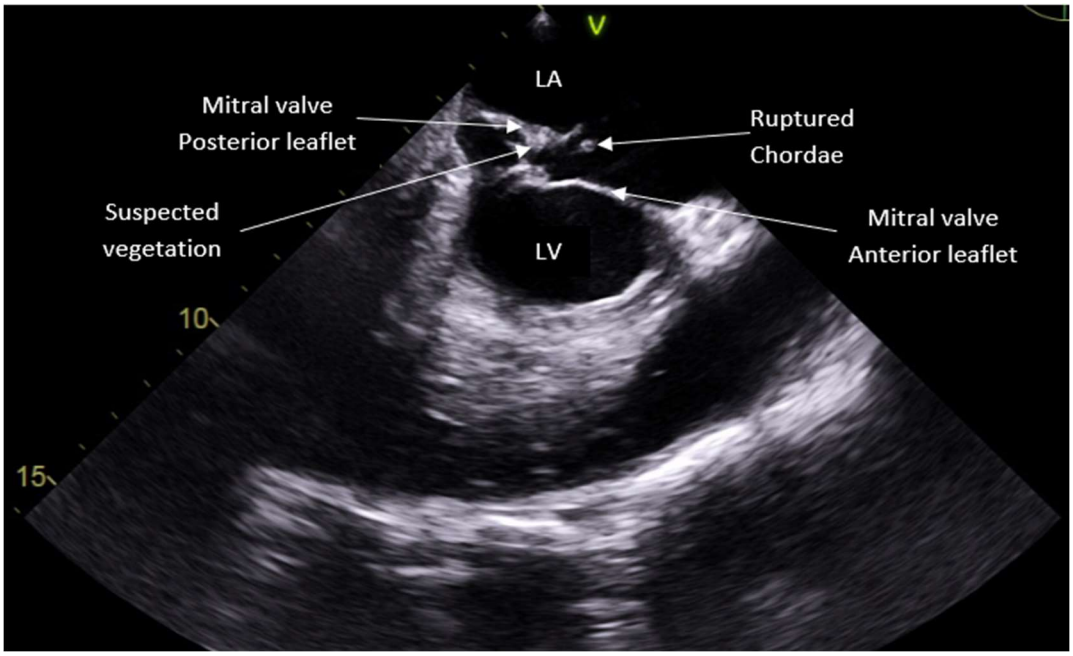

Figure 2. Transesophageal echocardiogram demonstrating mitral valve vegetation and ruptured chordae.

Discussion

Infective endocarditis (IE) is defined as a microbial infection of the endocardial surface of the heart, native, prosthetic heart valve, or cardiac device [5,6]. Infection is a source of high morbidity and mortality, and it is estimated to have an annual incidence of 30 cases per million inhabitants in population-based studies performed in Western countries [7] . Almost any infective agent can be a cause of IE, however the most common pathogens are gram positive bacteria such as *Staphylococcus* and Streptococcus [8].

A very rare but especially challenging type of IE, with serious and life-threatening repercussions, is blood culture-negative endocarditis (BCNE). This type accounts for up to 35% of all cases of infective endocarditis, with an observed increase in rate over the past few years (IE) [9]. Culture-negative endocarditis can be related to sterilized blood due to previous antibiotic use [10]. Culture techniques factors like suboptimal specimen collection, inadequate volume are also common culprits [9]. Important cause are fastidious organisms that require longer incubation periods (HACEK group: *Haemophilus* spp., *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, and *Kingella kingae*) and intracellular bacteria that do not grow in traditional methods, like *Coxiella burnetii*, *Bartonella* species, and *Tropheryma whipplei* [10].

As for our patient, it was not clear whether the cause of endocarditis was an intracellular bacterium as cultures were still pending.

Very often, the presentation is subtle, with insidious onset, contributing to delay in the diagnosis and treatment. Traditionally, Duke's criteria (**Table 1**), provides a guidance that along with clinical suspicion contributes to the diagnosis of IE. Given the mainstream workup of echocardiogram findings and blood culture, in the case of infective BNCE, a broader approach is needed, that ranges from demographics to new molecular/ histopathologic techniques.

Newer culture methods allow the culture of fastidious organisms in 5 days or less. Molecular methods of common organisms are used to aid in the diagnosis. Given major microorganism load, excised heart tissue has a higher yield probability than blood PCR [10]. This technique has their highest yield when blood culture has resulted negative. In the case of our patient, the mitral valve was sent for pathology however, no inflammation or microorganisms were seen.

Multimodal approach, with multidisciplinary team is key in the diagnosis, and multiple step designs have been formulated over the years. The first step continues to be cultures and imaging. In the setting of negative culture, further serologic studies were the next step proposed, especially for common pathogens such as *Coxiella burnetii*, *Bartonella* spp., *Aspergillus* spp., *Mycoplasma pneumonia*, *Brucella* spp., and *Legionella pneumophila*, along with PCR for *Tropheryma whipplei*, *Bartonella* spp and fungi. If the culprit pathogen is still unclear and surgery is performed, histopathologic and molecular analysis of the excised valve has the highest yield in detection of organisms [8].

Table 1. Modified Duke criteria for endocarditis. Definite infective endocarditis = two major, or one major and three minor, or five minor; possible infective endocarditis = one major and one minor, or three minor.

Major criteria
1. **Blood culture positive for IE**
a. Typical microorganisms consistent with IE from 2 separate blood culture • *Viridans streptococci*, *Streptococcus bovis*, HACEK group, *Stapylococcus aureus*; or • Community- acquired enterococci, in the absence of a primary focus; or
b. Microorganism consistent with IE from persistently positive blood cultures, defined as follows: • At least 2 positive cultures of blood samples drawn >12 h apart; or • All of 3 or a majority of ≥ 4 separate cultures of blood (with first and last sample drawn at least 1h apart)
c. Single positive blood culture for *Coxiella burnetii* or antiphase I Ig G antibody titer >1:800
2. **Evidence of endocardial involvement**
a. Echocardiogram positive for IE (TEE recommended in patient with prosthetic valves; rated at least "possible" IE by clinical criteria or complicated IE (paravalvular abscess); TTE as first test in other patients), defined as follows: • Oscillating intracardiac mass on valve or supporting structures, in the path of regurgitant jets, or on implanted material in the absence of an alternative anatomic explanation; or • Abscess; or • New partial dehiscence of prosthetic valve
b. New valvular regurgitation (worsening or changing of pre-existing murmur not sufficient)
Minor criteria
• Predisposition, predisposing heart condition or injection drug use
• Fever, temperature >38°C
• Vascular phenomena, major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, intracranial hemorrhage, conjunctival hemorrhages and Janeway's lesions
• Immunologic phenomena: glomerulonephritis, Osler's nodes, Roth's spots and rheumatoid factor
• Microbiological evidence: positive blood culture but does not meet a major criterion as noted above* or serological evidence of active infection with organism consistent with IE

Even though continuous efforts are being made to research the topic, the mortality rate has not improved in over two decades. Complications can involve almost any organ and are usually referred to as intracardiac and extracardiac. Extracardiac phenomena are most of the time related to infarct or infection foci from emboli dislodged of the infective material from the heart in the circulation. Cardiac manifestations are related to the local extension of the infected area causing local destruction. The most common complication is heart failure [5]. A less common but life-threatening complication is rupture of cardiac tissue causing valvular dysfunction, such as seen in our patient [11].

The mainstream treatment continues to be a long course of antibiotics, possibly tailored to the culprit pathogen. The timing and role of surgery is still controversial, a multidisciplinary and individualized approach is the best course.

Our case has some limitations, blood cultures were drawn after initiation of broad-spectrum antibiotics, therefore the diagnostic yield was lower. Another limitation is that PCR results of intracellular organisms, such as *Bartonella* were not obtained, therefore diagnosis was not complete. Despite these limitations, this case report demonstrates a rare entity, which needs further investigation, such as diagnostic criteria for blood culture-negative endocarditis as well as treatment.

Conclusion

This case presents a patient with blood culture-negative endocarditis with multiple intracardiac complications. Blood culture-negative endocarditis can present a diagnostic and therapeutic dilemma for clinicians. It should be part of the differential diagnosis when suspicion for IE is high, but blood cultures remain negative, as failure to treat can lead to high morbidity and mortality.

It was concluded that the treatment of BNCE may require

long-term antibiotics and, if clinically warranted, replacement of the affected valve.

Abbreviations

IE: Infective Endocarditis; BCNE: Blood Culture Negative Endocarditis; CBC: Complete Blood Count; CMP: Comprehensive Metabolic Panel; TSH: Thyroid Stimulating Hormone; RVR: Rapid Ventricular Response; TTE: Transthoracic Echocardiogram; TEE: Transesophageal Echocardiogram; EF: Ejection Fraction; CT: Computed Tomography; HACEK: *Haemophilus* spp, *Aggregatibacter* spp, *Cardiobacterium* hominis, *Eikenella* corrodens, *Kingella* spp; IgG: Immunoglobulin G

Disclosures

The authors have nothing to disclose.

Conflict of Interest

None.

Informed Consent

Patient has signed an informed consent form allowing for publication of clinical data related to his care.

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