A Case of Culture-Negative Endocarditis Due to *Bartonella henselae* and Cat Scratch Disease

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ABSTRACT

This report describes the case of a 73-year-old female with a history of a prosthetic mitral valve and breast cancer who presented with fever and confusion. Brain imaging revealed multiple ischemic infarcts, and abdominal imaging demonstrated splenic infarcts. Workup with transesophageal echocardiogram revealed a vegetation on the aortic valve, but several blood cultures had no bacterial growth. Further history revealed a recent exposure to a stray cat, and the patient was found to have positive antibodies for Bartonella henselae, the organism implicated in cat scratch disease. She was treated with the appropriate course of antibiotics, and she made a full recovery to her baseline functional status. This report emphasizes the importance of a comprehensive patient history and a broad differential diagnosis.

KEYWORDS: endocarditis, cat scratch disease, prosthetic valve

BACKGROUND

Infective endocarditis (IE) is defined as a microbial infection that causes inflammation within the endocardium of the heart. Severity varies by causative agent, valvular anatomy or pathology, and pathological presentation of the untreated disease. The characteristic lesion, a vegetation, is composed of a collection of platelets, fibrin, microorganisms, and inflammatory cells.[1] If the causative agent cannot be determined after three independent attempts to grow it in blood culture, it is termed "blood-culture negative".[2] Blood culture negative endocarditis is estimated to make up anywhere between 2.5–70% of all endocarditis cases depending on the country.[3] Difficulty in its detection contributes to the wide variability of incidence. Risk factors for this class of endocarditis include exposure to zoonotic sources such as cats, sheep, goats, as well as an underlying valvular heart disease or implanted cardiac devices such as pacemakers.[4–6] Confirmation requires both a high degree of clinical suspicion based on presentation and advanced microbiological diagnostic tools due to its ability to elude standard culture methods.[3,7,8]

While endocarditis can arise from various bacterial and viral sources, a relatively rare cause is Bartonella henselae. B. henselae is part of the Bartonella genus of Gram-negative bacilli that can cause a range of human complications including bacteremia, angiomatosis, myocarditis, and endocarditis.[2] Here we report a case of cat scratch disease due to Bartonella henselae that caused vegetations on a native aortic valve. This case adds to the growing body of literature regarding a rare causative agent and improve awareness of the management of culture-negative endocarditis.

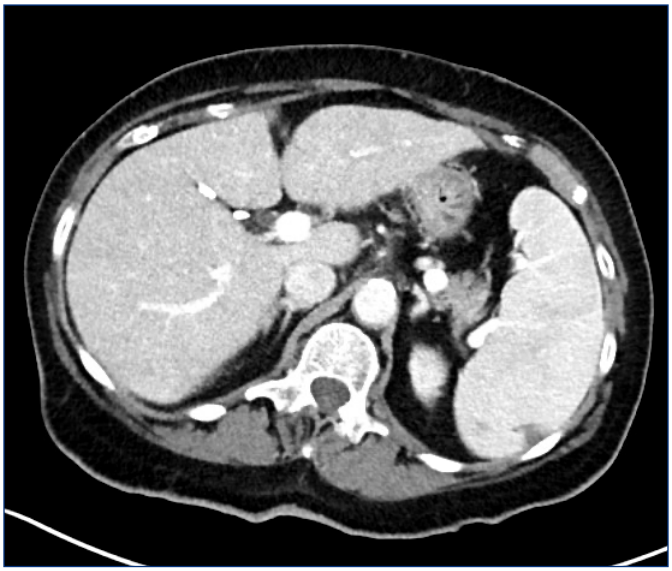
CASE REPORT

A 73-year-old female with a history of hypertension, mitral regurgitation status post prosthetic mitral valve on warfarin, vasculitis on steroids, and breast cancer post-excision and radiotherapy presented to the emergency room with acute onset confusion and a three-day history of fever. She denied any chest pain, shortness of breath, palpitations, cough, nausea, vomiting, abdominal pain, lightheadedness, dizziness, or syncope. Of note, she was recently hospitalized for a lower extremity purpuric rash and acute kidney injury. A kidney biopsy had revealed IgA deposits consistent with IgA nephropathy versus Henoch-Schönlein purpura, and she was discharged on a steroid taper, which she was currently still completing.

Her temperature on admission to the hospital was 101.7°F (38.7°C) and she was tachycardic with a heart rate of 115 beats per minute. Physical exam revealed that she was oriented to herself but not to place or time. The rest of her neurologic exam was normal. Her mucous membranes were dry. Auscultation of the heart revealed tachycardia with a regular rhythm, and a mid-systolic click. Her abdomen was soft, nontender, and nondistended, without evidence of hepatosplenomegaly. Inspection of the lower extremities revealed a palpable purpuric rash bilaterally.

International normalized ratio (INR) was 2.4, below the goal INR of 2.5–3.5 for patients with prosthetic mitral valves. Troponin was elevated at 1.831 and trended down. Electrocardiogram showed sinus tachycardia with a rate of 107, without evidence of AV block or ischemia. Computed tomography angiography (CTA) of the abdomen, and pelvis revealed mild splenomegaly and peripheral hypoattenuating regions

Figure 1. CT angiogram of the abdomen and pelvis reveals mild splenomegaly and peripheral hypoattenuating regions in the spleen consistent with splenic infarcts.



in the spleen consistent with splenic infarcts (**Figure 1**). Magnetic resonance imaging (MRI) of the brain showed multiple punctate ischemic infarctions in the left insula, left cerebellum, and right parieto-occipital lobe, with no evidence of metastasis (**Figure 2**).

Transthoracic echocardiogram revealed no evidence of endocarditis. Transesophageal echocardiogram (TEE) revealed a 6-millimeter vegetation on the ventricular side of the aortic valve (**Figure 3**). There was a trace to mild aortic insufficiency. However, five sets of blood cultures, including cultures drawn prior to antibiotic administration, revealed no growth.

Infectious disease specialists were consulted for further evaluation. Further history revealed recent exposure to a stray cat in which she pet the cat on multiple occasions in the several weeks before presentation. Coxiella burnetii serology, Bartonella PCR and serologies, and fungal blood cultures were sent. Antibodies were positive for Bartonella Henselae, with an IgG titer of 1:1024, which was strongly suggestive of Bartonella as the etiology for culture negative infective endocarditis.

Figure 2. MRI brain demonstrates multiple punctate ischemic infarctions in the [**A**] left insula, [**B**] left cerebellum, and [**C**] right parieto-occipital lobe.

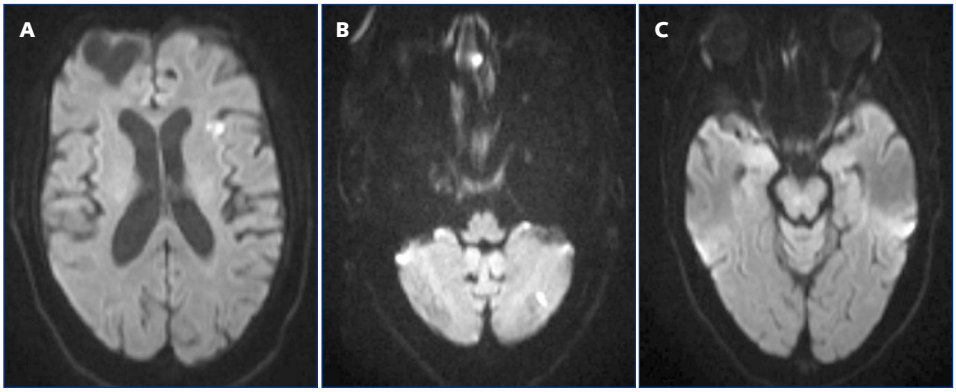
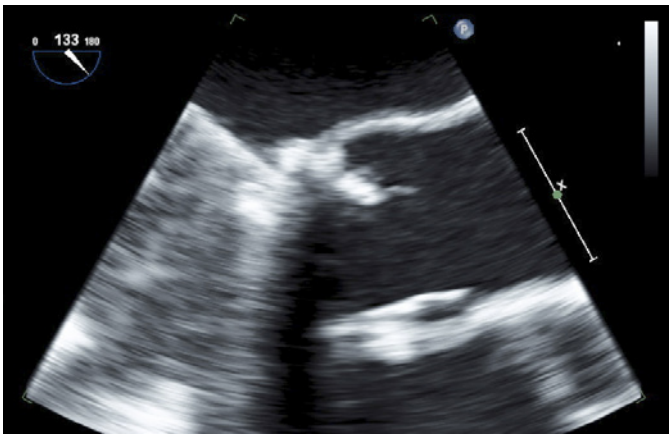


Figure 3. TEE reveals a 6-millimeter vegetation on the ventricular side of the aortic valve.



CLINICAL WORKUP

Initially, the differential diagnosis for fever and confusion in this woman with breast cancer and a prosthetic mitral valve was broad. Brain infarcts and splenic infarcts were concerning for thromboembolism, especially given the presence of a prosthetic valve and possible hypercoagulable state of malignancy. Infective endocarditis was another possibility, although the source was not immediately evident. Prosthetic valve endocarditis from bacterial species including Enterococcus, Staphylococcus, and Streptococcus tend to be common culprits. Marantic endocarditis was also possible, given her history of vasculitis and malignancy. Brain metastasis was on the differential for confusion. Other possible diagnoses included brain abscess, meningitis, and encephalitis.

While hospitalized, the patient had a repeat brain CT after her brain MRI which showed intraparenchymal hemorrhage. She was transferred to the intensive care unit where her warfarin was held, and heparin was started. Intravenous heparin was started due to her prosthetic mitral valve. She then developed a right frontal hemorrhage seen on a subsequent CT. Heparin drip was discontinued until repeat MRI and neurological exams were stable, and then resumed in 48 hours. The patient was discharged from the hospital once

neurologically stable and therapeutic on warfarin. She was initially treated with broad-spectrum antibiotics, vancomycin and piperacillin-tazobactam. These were discontinued when Bartonella henselae antibodies returned positive and culture-negative endocarditis was established. She was then started on ceftriaxone, doxycycline, and rifampin with plans for a four-week treatment course. Aminoglycosides were avoided in view of her recent renal dysfunction due to vasculitis. Cardiothoracic surgery was consulted, but surgery was not indicated due to the absence of significant valvular abnormalities. She did not complete the ceftriaxone course due to concerns for an allergic reaction; however, the rifampin and doxycycline courses were completed, and the patient remained off antibiotics without signs of further infection or complications at 2 months. She received physical rehabilitation services at home, and she returned to her baseline functional status in about 2 months.

DISCUSSION

Culture-negative induced endocarditis is typically caused by fastidious organisms such as Bartonella spp. and other zoonotic agents and fungi and accounts for around 10% of all IE.[9–11] Some reports estimate the Bartonella spp. accounts for 2-–28% of culture-negative endocarditis depending on geographical region.[2,8,9] Especially in the cases driven by Bartonella spp., underlying valvular and congenital heart disease appear to be significant risk factors as highlighted in several recent case reports.[12–15]

Among patients with reported bartonella endocarditis, some reports estimate that cat exposure such as owning a cat (or being in regular contact with strays) can result in a seroprevalence of between 28.9–40% depending on the country where the studies were conducted.[10,16,17] These patients usually present with constitutional non-specific symptoms such as fever, fatigue, weakness, and weight loss. In many cases, they will have evidence of a murmur on cardiac auscultation, but in some cases, the key findings of endocarditis, including elevated white blood cell count (WBC) and erythrocyte sedimentation rate (ESR), may be lacking.[18] In addition, some studies have shown that when compared to native valvular disease, prosthetic valve disease leads to a more aggressive disease course with rapid deterioration in hemodynamics, valvular perforation, and eventual heart failure.[13,19] Adding to the sequelae, patients may also develop an immune-complex glomerulonephritis as reported in several studies[20-22] including the patient presented in this report.

CONCLUSION

While several Bartonella spp. have been described to cause infective endocarditis, in patients with epidemiological exposure to cats and underlying valvular disease or prosthetic valves, B. henselae should be considered high on the differential diagnosis. Patients with clinical and echocardiographic evidence of endocarditis that have negative blood cultures after 72 hours should be suspicious of Bartonella endocarditis or any of the slow-growing bacteria such as the HACEK bacteria group. Patients with subacute constitutional symptoms, with murmurs on auscultation, and immune-complex glomerulonephritis should also raise clinical suspicion of a Bartonella induced endocarditis. Clinical suspicion of culture-negative endocarditis followed by confirmatory tests such as ELISA and PCR can prevent the rapid decline of these patients and need for operative repairs by interceding with rapid antimicrobial treatment courses. Vigilance and obtaining a comprehensive patient history are key in maximizing favorable outcomes.

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