

# Cat Scratching Your Valve: An Elusive Case of *Bartonella* Endocarditis

Ritu Nahar, MD and Evan Caruso, MD

## INTRODUCTION

*Bartonella Henselae* is an uncommon, but significant cause of "culture-negative" endocarditis. While six *Bartonella* species have reportedly caused infective endocarditis (IE) in humans, the vast majority of cases are secondary to either *B. quintana* or *B. henselae*. The epidemiologic features of patients predisposed to *Bartonella* endocarditis are varied. Alcoholism, body lice infestation, and homelessness have been associated with *B. quintana* endocarditis, while *B. henselae* endocarditis has been linked to prior valvular disease and cat exposure.<sup>1-4</sup> Patients with *Bartonella* endocarditis have clinical manifestations similar to those seen with traditional forms of subacute bacterial endocarditis. However, the rarity of the disease compounded by limitations of diagnostic testing make this entity a diagnostic challenge. This case exemplifies a classic presentation of *Bartonella* endocarditis while highlighting the systemic repercussions of inadequate source control and challenges associated with surgical intervention.

## CASE PRESENTATION

A 53-year-old female with a history of dysautonomia status post pacemaker over 10 years ago, membranoproliferative glomerulonephritis (MPGN), and chronic pulmonary embolism (not on anticoagulation) presented to an outside hospital with two years of fatigue, weakness, and weight loss complicated by unexplained fevers for 2 weeks. The patient was initially treated with broad spectrum antibiotics, but fevers persisted. Infectious work-up at outside hospital was negative. Upon delving further into her social history, the patient endorsed extensive contact with cats, assisting in kitten birthing 6 months prior to presentation. Physical exam revealed a 2/6 systolic murmur at the left lower sternal border that was louder with inspiration. On transthoracic echocardiography, a 2.2 x 1.9 echodensity was visualized adjacent to the tricuspid valve in close proximity to the right ventricular (RV) pacemaker lead with smaller echodensities on the atrial side of the RV pacemaker lead. Broad-spectrum antibiotics were initiated but the patient continued to spike fevers as high as 104° F. Blood cultures remained sterile despite prolonged incubation periods. Transesophageal echocardiography 5 days later demonstrated progression of lesions, now revealing a 3.9 x 2.5 cm mass stemming from the RV pacemaker

lead. On the 5th hospital day, the patient developed severe pleuritic chest pain. Computed tomography (CT) of the chest demonstrated wedge shaped peripheral opacities suspicious for lung infarct from septic emboli versus thromboemboli.

## DIFFERENTIAL DIAGNOSIS

Patients with valvular/pacemaker vegetations in the absence of overt bacteremia typically result from marantic endocarditis secondary to a noninfectious etiology or culture-negative endocarditis from an infectious source.<sup>5</sup> Marantic vegetations (nonbacterial thrombotic endocarditis) refers to a spectrum of lesions generally seen in the setting of hypercoagulable states, malignancy, and rheumatologic conditions including systemic lupus erythematosus (Libman-Sacks endocarditis). Interestingly, our patient had a history of pulmonary embolism diagnosed the year prior in the setting of antithrombin deficiency which, compounded by her biopsy proven MPGN, raised concern for a possible thrombotic endocarditis or verrucous endocarditis.

The leading causes for negative cultures in infective endocarditis include prior antimicrobial treatment as seen with our patient and insufficient microbiological techniques. While HACEK organisms (*Haemophilus aphrophilus*; *Actinobacillus actinomycetemcomitans*; *Cardiobacterium hominis*; *Eikenella corrodens*; and *Kingella kingae*) were conventionally believed to be culture-negative, they have since been more successfully cultured with the assistance of modern culture systems.<sup>6</sup> Instead, the predominating causative agents of blood culture-negative endocarditis are fastidious organisms such as zoonotic agents and fungi. *C. burnetii* and *Bartonella* species are two such pathogens with prevalence based on exposure to epidemiological risk factors. Of note, *T. whipplei* may also be an underappreciated source of culture-negative IE with *Mycobacteria* being a rarer cause.<sup>7</sup>

Our patient underwent a thorough rheumatologic and infectious work-up. Her extensive kitten exposure combined with iatrogenic interruption of her valve (pacemaker placement) significantly increased the risk for a possible *Bartonella* infection. Diagnostic tests for culture-negative endocarditis include unique culturing

techniques, molecular tests including polymerase chain reaction (PCR) and serologic assays, and lastly direct histopathology staining of valvular tissue. She was found to have positive *Bartonella* serology with an elevated *Bartonella henselae* immunoglobulin G (IgG) level at 1:512. Interestingly, her *B. Quintana* IgG was also 1:512 likely secondary to cross-reactivity, which is common between IgG among *Bartonella* species. Of note, the recommended cutoff for definitive positivity in patients with suspected *Bartonella* endocarditis is a titer of  $\geq 1:800$  for IgG antibodies to either *Bartonella henselae* or *Bartonella quintana*.<sup>8</sup> Diagnosis was eventually confirmed by positive blood PCR for *Bartonella*.

## OUTCOME AND FOLLOW-UP

The patient was started on doxycycline (given continued symptomatic fevers) and deemed appropriate for pacemaker and lead removal. The decision was also made to initiate anticoagulation given evolving lung infarcts on CT. Management was complicated by heparin resistance requiring antithrombin concentrate pre- and intra-operatively. On hospital day 10, the patient underwent successful cardiopulmonary bypass surgery for pacemaker and associated mass removal. Of note, the patient was not a candidate for percutaneous lead extraction due to the size of her vegetation; thus, earlier detection may have precluded necessitating surgical intervention. Post-operatively she was initiated on a 6-week course of doxycycline, rifampin, and ceftriaxone. Gentamycin was avoided given her renal impairment from MPGN. Upon confirmation of *Bartonella* blood PCR, ceftriaxone was discontinued and the patient completed a 6-week course of oral doxycycline and rifampin.

## DISCUSSION

This case highlights the importance of eliciting epidemiologic risk factors when working up fevers of unknown origin. Systemic complications our patient endured from lack of prompt intervention include recurrent hospitalizations and septic lung emboli. Additionally, *Bartonella* endocarditis is associated with development of immune-complex glomerulonephritis.<sup>9</sup> Thus her MPGN may also in fact be a manifestation of her untreated endocarditis. Blood cultures for *Bartonella henselae* are seldom positive, potentially a result of intraerythrocytic sequestration of the pathogen. Therefore, specialized culturing, molecular assays, and histopathological evaluation of valvular tissue are generally required to establish the diagnosis.

Medical management for *Bartonella* endocarditis is comprised of dual therapy with doxycycline and gentamicin. Gentamicin may be replaced by rifampin if the patient has renal impairment. Ceftriaxone can be

added for additional coverage of culture-negative endocarditis if definitive diagnosis of *Bartonella* has not been established.<sup>10</sup> Of note, our patient had actively evolving lung infarction from septic emboli and recurrent symptomatic fevers resulting in hemodynamic instability, thus surgical removal of the pacemaker and leads was indicated. While endocarditis is an established predisposing factor for decreased heparin responsiveness during cardiopulmonary bypass, the mechanism of this phenomena and how this alters management pre and intra-operatively is an area of research requiring further evaluation.<sup>11</sup>

## KEY POINTS

Recognizing and appropriately diagnosing *Bartonella* endocarditis is critical in preventing systemic complications via earlier surgical intervention for source control augmented with adequate antibiotic coverage.

## REFERENCES

1. Raoult D, Fournier PE, Drancourt M, et al. Diagnosis of 22 new cases of *Bartonella* endocarditis. *Ann Intern Med* 1996;125:646-652.
2. Spach DH, Kanter AS, Daniels NA, et al. *Bartonella* (Rochalimaea) species as a cause of apparent "culture-negative" endocarditis. *Clin Infect Dis* 1995; 20:1044-1047.
3. Raoult D, Fournier PE, Vandenesch F, et al. Outcome and treatment of *Bartonella* endocarditis. *Arch Intern Med* 2003;163:226-230.
4. Fournier PE, Lelievre H, Eykyn SJ, et al. Epidemiologic and clinical characteristics of *Bartonella quintana* and *Bartonella henselae* endocarditis: a study of 48 patients. *Medicine (Baltimore)* 2001; 80:245-251.
5. Fournier PE, Thuny F, Richet H, et al. Comprehensive diagnostic strategy for blood culture-negative endocarditis: a prospective study of 819 new cases. *Clin Infect Dis* 2010; 51:131-140.
6. Petti CA, Bhally HS, Weinstein MP, et al. Utility of extended blood culture incubation for isolation of *Haemophilus*, *Actinobacillus*, *Cardiobacterium*, *Eikenella*, and *Kingella* organisms: a retrospective multicenter evaluation. *J Clin Microbiol* 2006; 44:257-259.
7. Fournier PE, Thuny F, Richet H, et al. Comprehensive diagnostic strategy for blood culture-negative endocarditis: a prospective study of 819 new cases. *Clin Infect Dis* 2010; 51:131-140.
8. Raoult D, Casalta JP, Richet H, et al. Contribution of systematic serological testing in diagnosis of infective endocarditis. *J Clin Microbiol* 2005; 43:5238-5242.
9. Van Haere Heijmeijer S, Wilmes D, Aydin S, et al. Necrotizing ANCA-Positive Glomerulonephritis Secondary to Culture-Negative Endocarditis. *Case Rep Nephrol* 2015; 2015:649763.
10. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis: diagnosis, antimicrobial therapy, and management of complications: a statement for healthcare professionals from the Committee on Rheumatic Fever, Endocarditis, and Kawasaki Disease, Council on Cardiovascular Disease in the Young, and the Councils on Clinical Cardiology, Stroke, and Cardiovascular Surgery and Anesthesia, American Heart Association: endorsed by the Infectious Diseases Society of America. *Circulation* 2005;111:e394-434.
11. Na S, Shim JK, Chun DH, Kim DH, Hong SW, Kwak YL. Stabilized infective endocarditis and altered heparin responsiveness during cardiopulmonary bypass. *World J Surg*. 2009;33:1862-1867.