Bartonella Henselae Endocarditis: A Serological Dilemma

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Serology has a key role in the diagnosis of infectious diseases in medicine. Bartonella henselae is a slow-growing, fastidious gram-negative bacillus, was first identified as a cause of endocarditis in 1993. It is responsible for approximately 6% cases of culture negative endocarditis. Serology, detection of DNA and cultures are utilized in the diagnosis of Bartonella infection. We faced an interesting situation where serology created more confusion than assisting the diagnosis.

An 81-year-old Caucasian man with a history of prosthetic aortic valve replacement 10-years back, presented with a 4-month history of increasing fatigue, dyspnea, unintentional weight loss of 20 pounds and intermittent fevers with chills. He was seen 3 weeks back in the hospital for similar complaints, where work up of infective endocarditis (IE) was performed. Negative blood cultures and absence of vegetation on transesophageal echocardiogram (TEE) had warranted discharge with improvement in his symptoms. He was withdrawn from empiric antibiotics, which had been begun after the initial 6 or 7 sets of blood cultures had been obtained. Prior to being discharged the patient had a large number of serologic studies performed to look for the so-called “culture-negative” causes of IE. Prolonged blood cultures came positive for gram-negative bacillus suspicious for Hemophilus, actinobacillus, cardiobacterium, eikenella, kingella (HACEK) group.

Patient was hence readmitted. He did report having a 15-year-old declawed cat with recent infestation of fleas. Physical examination was pertinent for a grade II/VI systolic murmur at the right upper sternal border and diffuse splinter hemorrhages on the distal extremities. Screening labs were significant from white count of 16,600/mm3 and erythrocyte sedimentation rate of 50. Serological studies were interesting and significant for Ehrlichia chaffeensis antibodies positive at 1:256 for IgG antibodies but IgM antibodies were negative. Anaplasma phagocytophila antibodies were greater than or equal to 1:1024, again IgG class only. Coxiella burnetii antibody titers were positive for phase 2 IgG titers, which were 1:64. Phase 1 titers were negative, as were IgM titers and IgA titers. Chlamydia antibodies revealed titers of 1:512 for Chlamydia pneumoniae, 1:128 for Chlamydia trachomatis, and 1:128 for Chlamydia psittaci. Brucella antibodies were also positive but were not expressed in a titer but rather in ELISA units, definitely outside of the normal range. Bartonella henselae antibodies were positive at a titer of 1:1024, again IgG class only. DNA polymerase chain reaction (PCR) testing of the blood was positive for Bartonella henselae, negative for Bartonella quintana. (Table 1)

Multiple blood cultures had shown slow growing fastidious, tiny, gram-negative rods that grow well on chocolate agar. He was started on ceftraixone, doxycycline, gentamicin and rifampin to cover all possible organisms.

A TEE was performed which revealed a mobile, soft echodensity mass originating from the left atrial side of the posterior mitral leaflet, about 8 x 8 mm, shaggy and thickened anterior mitral leaflet of possible infectious etiology and a thickened prosthetic aortic valve without any evidence of vegetation with a peak gradient of 60 mmHg. A computed tomography of abdomen was performed revealing splenomegaly and splenic infarcts consistent with embolic phenomena.

Blood cultures later did come back positive for Bartonella hensalae and ceftriaxone was withdrawn. Cardiothoracic surgery was consulted for valve replacement. Intra-operatively, the aortic bioprothesis showed significant calcification and vegetation in the form of pinkish color deposit on the ventricular aspect of non-coronary cusp. The aortic valve was replaced using #29 mosaic porcine valve. Exploration of the mitral valve revealed possible vegetation of non-infectious etiology on the anterior and posterior leaflets, which were excised and cultured which came later as negative for any growth.

Patient was continued on 4 weeks of intravenous Gentamicin. At his outpatient appointment, negative Bartonella henselae PCR warranted stopping rifampin and doxycycline after completing 6 weeks of the therapy. He recovered well when evaluated at his outpatient follow up appointments with no evidence of endocarditis recurrence.

Bartonella species are gram-negative fastidious growing intracellular bacilli, responsible for about 2% of culture negative IE[1, 2]. Few case reports of Bartonella henselae induced prosthetic valve IE have been described before even though it is uncommon. Bartonella quitana is the causative agent in about 75% of Bartonella induced IE affecting immunocompromised individuals and Bartonella henselae accounts for the other 25%[1].

Bartonella is a slow-growing organism, hence it is challenging to have blood cultures positive for it. Molecular diagnostic testing with direct DNA sequencing and PCR amplification from the blood and resected specimens provide 100% specificity for its diagnosis. In our case blood cultures were positive for Bartonella henselae growing on chocolate agar medium and PCR amplification confirming the diagnosis[1-4].

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Table 1:

Name of the organism	Result/Titer
Ehrlichia chaffeensis	IgG 1:256 IgM negative
Anaplasma phagocytophila	IgG ≥1:1024
Bartonella henselae	Ig G 1:1024
Bartonella quintana	Negative
Coxiella burnetii	IgG Phase 1 negative Phase 2- 1:64 IgM, IgA-negative
Brucella	IgG Positive
Chlamydia pneumonia	1:512
Chlamydia trachomatis	1:128
Chlamydia psittaci	1:128

Serologic testing can provide more questions than answering them with Bartonella species cross-reactivity with chlamydia and Coxiella species as was apparent in our case[5]. Studies have also shown an immunogenic protein, dihydrolipoamide succinyltransferase protein (SucB) causing cross-reactivity between Bartonella species and Brucella melitensis, Mycoplasma pneumoniae, Franscisella tularensis, Coxiella burnetii and Rickettsia typhi resulting in false positive immunologic diagnostic tests[6]. In addition, there was positive serology for Anaplasma, Brucella and Ehrlichia in this particular case, which has not been reported before to the best of our knowledge. The confirmatory diagnostics test should always be PCR amplification for this reason, which helps in not only identifying the causative agent but also helps directing the antibiotic treatment in the right direction.

There are no precise treatment guidelines. Ideal choice of antibiotic treatment per the infectious disease society of America is intravenous aminoglycosides for at least 2 weeks in immunocompetent patients with IE[7]. They also recommend the use of more than one antibiotic. From our experience, a 4-week course of intravenous aminoglycoside with 6-weeks total of oral rifampin (in cases of prosthetic valve involvement) and doxycycline helps in eradicating the organism.
Bartonella hensenlae should always be considered as a causative organism in patients with cats at their home for IE. This report emphasizes that we need to be aware of the Bartonella cross reactivity leading to multiple positive serological studies causing diagnostic dilemma. There should be no hesitation to perform definite diagnostic modalities such as PCR amplification and/or DNA sequencing to confirm the diagnosis of Bartonella infection.

Statement of ethical publishing

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Conflict of interest:

There is no conflict of interest for any of the authors.

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