

## CASE REPORTS

# Bartonella Henselae endocarditis mimicking ANCA associated vasculitis

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## ABSTRACT

*Bartonella* can cause a damaging endocarditis and patients typically need valve replacement. Infective endocarditis (IE) and small vessel vasculitis (SVV) can have similar clinical features and the presence of ANCA can be misleading and it is critical to differentiate between IE and SVV since their treatment are vastly different.

**Key Words:** ANCA, Vasculitis, *Bartonella*, Glomerulonephritis, Endocarditis

## 1. INTRODUCTION

*Bartonella* species are fastidious, gram negative rods, initially isolated in 1988.<sup>[1]</sup> The first case of *Bartonella* endocarditis was published in 1993<sup>[2]</sup> and accounts for 3% of all cases of infective endocarditis (IE)<sup>[3]</sup> but is the second most common (28%) cause of culture negative IE after *Coxiella burnetii*.<sup>[4,5]</sup> Of the 23 species identified, more than 14 causes zoonotic disease with arthropod vectors.<sup>[4]</sup> *Bartonella henselae* infection is a zoonotic disease with cats as the most important reservoir. It is the etiological agent of cat scratch disease, although transmission to humans does not always require being scratched by a cat.<sup>[6]</sup> ANCA (anti neutrophil cytoplasmic antibody) are typically associated with small vessel vasculitis (SVV), however they can also be present in patients with IE.<sup>[7]</sup> Since both can be ANCA positive and have similar signs and symptoms, it is crucial to differentiate between these two entities.

## 2. CASE REPORT

A 42-year-old white female with no significant past medical history presented with intermittent fevers up to 39°C associated with chills for two months which would improve with nonsteroidal agents and acetaminophen. Family history was significant for a sister with mitral valve replacement at a young age, details of which were not clear. Social history was significant for remote history of intravenous drug use (cocaine, methamphetamine) and half pack a day smoking. She also lived on a farm and was exposed to various animals including dogs, cats and chickens. Review of systems was notable for a 30 pound weight loss over the course of two months along with loss of appetite, nausea and bilateral inner thigh rash three weeks prior to presentation. She endorsed some generalized hair thinning, headaches, as well as burning sensation of hands and feet. Upon examination she was febrile with a temp of 38°C, blood pressure was 156/96 mmHg, pulse was 80 bpm. Besides having several tattoos over both arms her exam was unremarkable including no

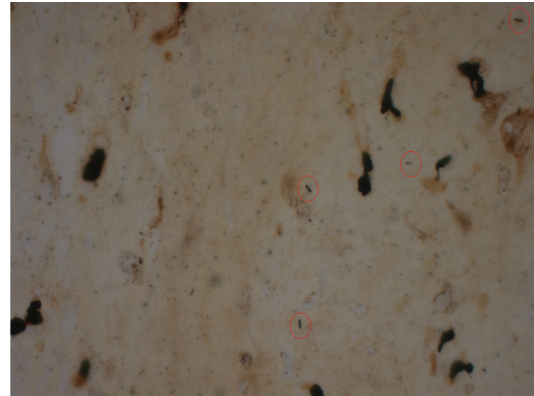
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murmurs on auscultation and no rashes.

Initial labs showed WBC  $3.5 \times 10^3$  ( $4.5-11 \times 10^3/\text{mm}^3$ ), Hemoglobin 6.1 g/dl 12-16 mg/dl, Platelets  $145 \times 10^3$  ( $150-400 \times 10^3/\text{mm}^3$ ), MCV 78.1 fL (80-98 fL), ESR 34 mm/hr (0-19 mm/hr), creatinine 2.29 mg/dl (0.6-1.60 mg/dl), with the rest of the metabolic parameters being within normal range. Urinalysis was notable for many RBCs, no casts, urine protein was 91 mg/dl and urine creatinine 73 mg/dl (ratio 1.3). A urine drug screen was negative. ANA was positive with 1:80 titer, homogenous, and 1:160 titer, speckled. C3 was low at 76 mg/dl (90-170 mg/dl) and C4 was normal at 17 mg/dl (12-36 mg/dl). Rheumatoid factor was 18 IU/ml (< 14 IU/ml), ASO titer was 152 U (0-530 U). Both C-ANCA and P-ANCA were positive with PR3 of 0.5 U (< 0.4 U) and MPO of 1.8 U (< 0.4 U). Blood and urine cultures again did not show any growth. A hepatitis panel and HIV test were also negative. A CT chest was unremarkable. A transesophageal echocardiogram (TEE) demonstrated thickened tricuspid valve with small vegetation with a hooded appearance which was consistent with myxomatous degeneration. Ejection fraction was 55%-60%. Renal US showed mildly echogenic kidneys and minimal left hydronephrosis. A renal biopsy was obtained which showed immune complex mediated focal proliferative glomerulonephritis that was not suggestive of any specific etiology. Immunofluorescence staining demonstrating extensive immune complex deposition that would be classic for lupus was not seen, however more deposition was present than would be seen in an ANCA associated pauci-immune glomerulonephritis. Under electron microscopy classic subepithelial humps that characterize infection were not seen although C3 and C1q were dominant. A diagnosis of a non specific immune complex mediated vasculitis was made and she was treated initially with high dose oral prednisone that improved her fevers as well as renal function.

However, repeatedly, as the prednisone was tapered to below 20 mg her fevers returned and she developed a vasculitic rash over bilateral lower extremities as well as bilateral MCP arthralgias, 1-2 hours of morning stiffness and requiring readmission. A repeat transthoracic echocardiogram did not show any vegetations, and with a higher dose of prednisone her symptoms again resolved. Patient continued to show significant hematuria. At this point *Bartonella* titers were obtained and *B. henselae* IgG: > 1:1024, *B. quintana* IgG titers 1:512. A repeat transesophageal echocardiogram (TEE) showed large partially calcified vegetations in two out of three valves in the tricuspid valve with significant valvular damage and moderate tricuspid regurgitation. She was then urgently referred to CT surgery and was admitted for tricuspid valve replacement and started on ceftriaxone, doxycycline, and

gentamicin. Tricuspid valve Steiner stain showed rare rod shaped organisms consistent with *Bartonella* (see Figure 1). The valve PCR later came back positive for *Bartonella*.



**Figure 1.** Steiner stain of aortic valve demonstrating rare rod shaped organisms (ovals) consistent with *Bartonella*

### 3. REVIEW

The patient discussed above posed a significant diagnostic challenge, supporting the fact that *Bartonella* endocarditis is grossly under recognized. It has a subacute, nonspecific presentation especially with asthenia and weight loss; and may also have embolic phenomenon, immune complex glomerulonephritis, rash consistent with SVV<sup>[8]</sup> and ANCA positivity. Furthermore initial infectious workup can be unrevealing.

In a published series from France *B. henselae* endocarditis was found to be associated with underlying valvular pathology<sup>[4]</sup> particularly involving the left sided valves, and most patients with *Bartonella* endocarditis had extensive valve damage requiring surgery.<sup>[4]</sup> Our patient did not have documented valvular damage, but may have had a damaged valve from previous IVDU or changes since birth as her sister also had received a valve replacement. *Bartonella* has a predilection for native aortic valve.<sup>[9,10]</sup> There are 2 other published cases of native tricuspid valve endocarditis.<sup>[11,12]</sup> Left sided endocarditis remains most common but right sided valves may be affected by *Bartonella* as in our patient. Reports in the literature demonstrate high levels of C-ANCA and less commonly p-ANCA, or both.<sup>[13]</sup> In fact there are several reports of *Bartonella* IE that were masquerading as vasculitis.<sup>[7,10]</sup> Although the prevalence of ANCA in all cause IE was 18% (total 109 patients),<sup>[13]</sup> *Bartonella* IE, in particular, appears to be associated with a much higher rate of ANCA positivity in up to 60%<sup>[14]</sup> in a recently published case series comprising of 47 patients. There are several hypotheses as to why PR3 antibody are induced during infection including presence of superantigens and molecular mimicry.<sup>[15]</sup> At present there are no guidelines for diagnosis of *Bartonella* IE

with only up to 20% with positive blood cultures.<sup>[4]</sup> Positive PCR from cardiac valve or blood specimen, and IgG titer of  $\geq 1:800$  have been recommended for diagnosis, and suggested to be included as a major Duke criteria by some investigators.<sup>[4]</sup>

In conclusion, IE and SVV can have a similar clinical spectrum including fevers, malaise, arthralgia, rash, renal disease, and valvular involvement. However, suspicion for infective

endocarditis should include dual ANCA positivity and, low C3<sup>[7]</sup> as SVV typically do not have low complements. Culture negative causes of IE including *Bartonella* must be pursued in the presence of ANCA positivity in the appropriate clinical setting.

## CONFLICTS OF INTEREST DISCLOSURE

The authors have declared no conflicts of interest.

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