Case Report

Bartonella Endocarditis Mimicking Crescentic Glomerulonephritis with PR3-ANCA Positivity

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Bartonella henselae is a fastidious organism that causes cat scratch disease, commonly associated with fever and lymphadenopathy but, in rare instances, also results in culture-negative infectious endocarditis. We describe a patient who presented with flank pain, splenic infarct, and acute kidney injury with an active urinary sediment, initially suspicious for vasculitis, which was subsequently diagnosed as B. henselae endocarditis. Bartonella endocarditis may present with a crescentic glomerulonephritis (GN) and elevated PR3-ANCA antibody titers, mimicking ANCA-associated GN, with 54 cases reported in the literature. Unique to our case in this series is a positive PR3-ANCA antibody despite a negative IIF-ANCA. Thus, the presentation of Bartonella can mimic ANCA-associated GN, and renal biopsy showing immune complex deposition is critical for diagnosis and appropriate treatment.

1. Introduction

Bartonella henselae is a fastidious organism commonly known for causing cat scratch disease. Cat scratch disease had been described over 50 years ago, but the first causal evidence of disease was not documented until 1983 [1]. Cat scratch disease typically presents with cutaneous lesions at the site of infection that progresses to lymphadenopathy and fever approximately two weeks after exposure to the bacteria. Visceral organ involvement, albeit unusual, typically involves the liver and spleen with marked hepatomegaly and splenomegaly. Rarely, B. henselae results in culture-negative endocarditis, an illness that can be difficult to diagnose and a challenge to treat effectively and in a timely manner. Herein, we present a case of B. henselae with endocarditis, in a previous healthy male, causing crescentic glomerulonephritis with PR3-ANCA positivity mimicking an ANCA-associated vasculitis.

2. Case Report

A 47-year-old male with a past history of nephrolithiasis, irritable bowel syndrome, and mild depression presented to the emergency center with two weeks of flank pain and four days of cola-colored urine. He described a throbbing, stabbing pain in his left flank that persisted and progressively worsened, which was associated with dark urine, nausea, unmeasured fever, chills, and a 10-lb weight loss. He denied dysuria or urinary hesitancy.

On physical exam, vital signs showed a temperature of 37.2°C, blood pressure of 121/55 mmHg, pulse of 95 bpm, and respirations at 20 breaths per minute while saturating at 94% on room air. He was alert and oriented x 3, but in moderate distress from his left-sided flank pain. There was no cervical, axillary, or femoral lymphadenopathy present. On auscultation, he was noted to have bilateral, basilar crackles without rhonchi or wheezing. Cardiac exam showed a regular rate and rhythm, with a 2/6 systolic, crescendo-decrescendo murmur heard best over the left sternal border. There was severe, left CVA tenderness on exam, but his abdomen was soft, nondistended, and nontender. Extremities showed no edema, and skin exam showed no evidence of petechiae or rashes.

Initial laboratory data showed a WBC of 3.8 bil/L, Hgb of 7.7 g/dL, platelet count of 89 bil/L, sodium of 138 mmol/L,
ANCA was negative, but proteinase-3 (PR3-ANCA) anti-
got 97mg/DL. Urinalysis showed 3+ blood, 1+ protein,
BUN of 19mg/dL, creatinine of 2.36mg/dL, and glucose of
92mmol/L, calcium of 7.4mg/dL, phosphorus of 3.0mg/dL,
potassium of 4.4mmol/L, chloride of 114mmol/L, CO2 21
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Abdominal ultrasound showed a 12.6 cm right kidney,
12.4 cm left kidney with no hydronephrosis, and a spleen
with wedge-shaped areas suggestive of infarct. An MRI
showed splenomegaly of 17.9 cm and a wedge-shaped infarct
(Figure 1)

Further blood test results showed a haptoglobin of
159 mg/DL, LDH of 272 U/L, fibrinogen of 248 mg/dL, an
elevated CRP of 4.9 mg/dL, ESR of 25 mm/hr, C3 of 94 mg/dL,
C4 of 23 mg/dL, negative antibodies to hepatitis A, B, and
C, and negativeANA, ASO, and antcardiolipin antibodies.
ANCA testing was negative using an indirect immune-
fluorescent assay (IIF) with a positive lab test considered for
results greater than 1:20. Myeloperoxidase antibody (MPO-
ANCA) was negative, but proteinase-3 (PR3-ANCA) anti-
body titer was elevated at 160 units, using an enzyme-linked
immunosorbent assay (ELISA) with a positive result greater
than 21 units. Blood cultures were negative and remained so
after 5 days.

A renal biopsy was performed. Light microscopy (Fig-
ure 2, left) showed focal proliferative injury with two non-
necrotic crescents. Immunofluorescence was positive for
IgM, IgA, C3, and Clq located predominantly along the
glomerular capillary loops and rarely in the mesangial areas.
Electron microscopy (Figure 2, right) showed segmental foot
process fusion with mesangial and subendothelial immune
deposits with no subepithelial deposits, consistent with an
immune complex GN.

Concerned with the heart murmur and renal biopsy
results, a transthoracic echocardiogram was performed and
was negative for valvular vegetations. A subsequent trans-
eosophageal echocardiogram showed a bicuspid aortic valve
with a vegetation. Culture-negative endocarditis was diag-
nosed and valve replacement performed with pathology
showing necrosis, neutrophils, and B. henselae on tissue
culture and specialized stains.

The patient received 6 weeks of antibiotic therapy with
doxycycline and rifampin and clinically improved with
decrease in flank pain. Urinalysis also improved showing 4-
10 RBC/HPF, 0-5 WBC/HPF, and no visible casts. Creatinine
decreased to 1.4 mg/dL, and ESR and CRP normalized within
2 months to 3 mm/hr and <0.4 mg/dL respectively. Repeat
proteinase-3 antibodies remained elevated at 121-163 units
despite antibiotic therapy.

3. Discussion

Initial testing for ANCA-associated vasculitis typically uses
IIF-ANCA. The specificity of ANCA testing is very high,
with a very low false negative rate, but measurement of PR3-
ANCA or MPO-ANCA antibodies with a positive IIF-ANCA
improves sensitivity by ruling out false positive tests.

Positive tests for IIF-ANCA, PR3-ANCA, and MPO-
ANCA antibodies may be found in patients with subacute
bacterial endocarditis. Common organisms include Viri-
dans streptococci, Staphylococcus aureus, and other staph
species. The association of infectious endocarditis with these
antibodies has led to postulated causal mechanisms for
vasculitis. Unmethylated CpG is a constituent of bacterial
DNA and has been shown to stimulate ANCA production
in B cells of ANCA-associated vasculitis patients. Staph
aureus tsst-1 superantigen nasal carriage carries a high rate
of relapse in granulomatous polyangiitis patients. Diseases
with barrier dysfunction to microbes, such as inflammatory
bowel disease, show increased incidence of ANCA positivity.
Neutrophil extracellular traps (NETs), which play a role in
extracellular killing of microbes, may also release ANCA-
associated antigens [2].

On the other hand, a retrospective review of patients with
IIF-ANCA-negative, positive MPO-ANCA, or PR3-ANCA
antibody testing such as that found in this case, showed that
only 1 of 38 of these patients actually developed ANCA-
associated vasculitis. There is evidence for cross-reactivity
in the assays, as PR3-ANCA-positive antibodies have also
been found in nonvasculitic inflammatory conditions such
as rheumatoid arthritis, inflammatory bowel disease, and SLE
[3]. Most relevant to our case, in contrast to ANCA-associated
vasculitis, endocarditis-associated ANCs typically show
immune complex deposits in the kidney and resolution of
kidney disease with treatment of the infection. Thus, although
there is argument for bacterial endocarditis antigens being
causal for renal vasculitis, current evidence favors ANCA
antibody production as a nonpathologic result of bacterial
endocarditis.

We present a case of culture-negative endocarditis and
acute kidney injury due to glomerulonephritis, due to Bar-
tonella henselae cardiac valve infection. Culture-negative
infectious endocarditis is estimated to comprise 3-48% of
all endocarditis cases. A literature search revealed 54 cases
of Bartonella-induced infective endocarditis associated with
glomerulonephritis reported in 14 publications, with 77%
of cases presenting with serologic positivity of either IIF-
ANCA, PR3-ANCA, or both. Unique to our case is a high
titer positive PR3-ANCA antibody with a negative IIF-ANCA
(Figure 3). A review of glomerular light-microscopy findings
associated with the aforementioned 54 cases of Bartonella-
induced infective endocarditis demonstrated similar find-
ings of focal proliferative injury with both necrotic and
nonnecrotic crescents in both ANCA-positive and ANCA-negative cases [4–17]. Of the cases describing pathology in more detail, all but one showed positive immunofluorescence indicative of immune complex disease.

In summary, this case highlights how *Bartonella henselae* endocarditis may present with a crescentic and proliferative GN and elevated PR3-ANCA antibodies, thus mimicking an ANCA-associated GN. Because *Bartonella* is fastidious and often does not grow in blood cultures, as opposed to more typical endocarditis microbes such as *Staphylococcus aureus* and Viridans streptococci, clinical symptoms and lab results may lead to an incorrect diagnoses of ANCA vasculitis. An incorrect diagnosis may expose patients to immunosuppressive regimens potentially hazardous to patients with bacterial endocarditis. Thus, a kidney biopsy showing immune complex deposition is critical to establishing appropriate therapy.

**Disclosure**

This research was presented in poster format at the American Society of Nephrology’s (ASN) Kidney Week 2017 in New Orleans, Louisiana, on November 1, 2017.

**Conflicts of Interest**

The authors declare that they have no conflicts of interest.

**References**


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