Case Report

Bartonella henselea Prosthetic Valve Endocarditis Mimicking Vasculitis: A Case Report With Literature Review

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Abstract

Description

We present one of the first reported cases of *Bartonella henselae* prosthetic valve endocarditis, which mimicked p-antineutrophil cytoplasmic autoantibody (p-ANCA), an anti-proteinase 3 positive necrotizing glomerulonephritis caused by a cat scratch resulting in temporary dialysis. Documentation of such infections is necessary as zoonotic infections are becoming more prevalent with early identification essential for proper treatment. Although pauci-immune patterns are not a unique finding in bacterial endocarditis associated with glomerulonephritis, they are an atypical finding in *Bartonella henselae* endocarditis. Furthermore, p-ANCA-associated vasculitis can also be responsible for renal and cardiac disease. Because of the similar disease presentation of different etiologies (autoimmune and infectious), it can make the diagnosis much more challenging. Our patient's presentation is unique as there are no documented cases in the medical literature of *Bartonella henselae* resulting in temporary hemodialysis from previously healthy kidneys with recovery. Our case documents the success of early identification and appropriate treatment.

Keywords

Bartonella henselae; glomerulonephritis; endocarditis; kidney diseases; nephropathy; acute kidney injury; cat-scratch disease; warfarin

Introduction

Bartonella henselae is a gram-negative, intracellular facultative bacterium commonly transmitted to humans from zoonotic carriers. The incidence of Bartonellosis or "cat-scratch disease" is reported to be about 6.4 per 100,000 adults globally.[1] In typical infections, the disease is self-limited to cutaneous and lymph node disorders near the site of inoculation. Exceptions to typical infections would be in patients who are already immunocompromised such as patients with chronic kidney disease or patients on immunosuppressant medications who would be more at risk of systemic disease.[2] Rarely, it can cause culture-negative, infective endocarditis, which can be more challenging to diagnose and treat.

Glomerulonephritis secondary to endocarditis is uncommon and is usually associated with valvular infection by blood culture-positive bacteria.[3] This case focuses on the importance of early detection and treatment of *Bartonella* infection, which can mimic a p-antineutrophil cytoplasmic autoantibody (p-ANCA)-associated vasculitis and glomerulonephritis, to prevent life-threatening complications.[4,5]

Case Presentation

A 43-year-old male with a past medical history of a congenital bicuspid aortic valve with an ascending aortic aneurysm status post aortic valve replacement and aneurysm repair (3 years prior) on warfarin therapy along with hypertension presented to our facility with a chief com-

Table 1. Selected Labs from Vasculitis Evaluation (Abnormal Results Are Bolded)

Lab	Value	Reference
IgG (mg/dL)	**2146** (mg/dL)	700-1600 (mg/dL)
IgA (mg/dL)	110.8 (mg/dL)	70-400 (mg/dL)
IgM (mg/dL)	**254** (mg/dL)	40-230 (mg/dL)
ANA	Negative	Negative
c-ANCA (titer)	x < 1:20 (titer)	x < 1:20 (titer)
Anti-proteinase 3 (U/mL)	**58.7** (U/mL)	0.0-3.5 (U/mL)
p-ANCA (titer)	**1:160** (titer)	x < 1:20 (titer)
Ro/La antibodies (AI)	x < 0.2 (AI)	0.0-0.9 (AI)
Smith antibody (AI)	x < 0.2 (AI)	x < 0.2 (AI)
Double stranded DNA (IU/mL)	2 (IU/mL)	0-4.9 (IU/mL)
Thyroid peroxidase (IU/mL)	**111** (IU/mL)	0.0-35 (IU/mL)
Complement C3 (mg/dL)	**63** (mg/dL)	90-180 (mg/dL)
Complement C4 (mg/dL)	16.50 (mg/dL)	14-44 (mg/dL)

plaint of shortness of breath and abdominal pain. He initially presented to our emergency department (ED) where the patient was found to be pancytopenic with acute kidney injury (AKI). He also had a non-pruritic, palpable purpura on his bilateral lower extremities. He received an abdominal ultrasound (US), which revealed enlarged, mildly heterogeneous, echogenic kidneys bilaterally, suggesting acute renal disease with an incidental finding of a spleen measuring 20 cm in length. Blood cultures were taken and the patient was admitted for further workup.

During his hospitalization, his evaluation for AKI included obtaining lab work to evaluate for vasculitis (**Table 1**). A renal biopsy was obtained because of the concern for vasculitis-induced glomerulonephritis, which was read as "immune complex-mediated acute proliferative glomerulonephritis with the possibility of warfarin nephropathy because of extensive red blood cell cast formation" (**Figure 1**). This outcome was thought to be from an infectious process. A subsequent workup included obtaining a transesophageal echocardiogram (TEE), which did not show any vegetations on the patient's prosthetic or native valves. Sever-

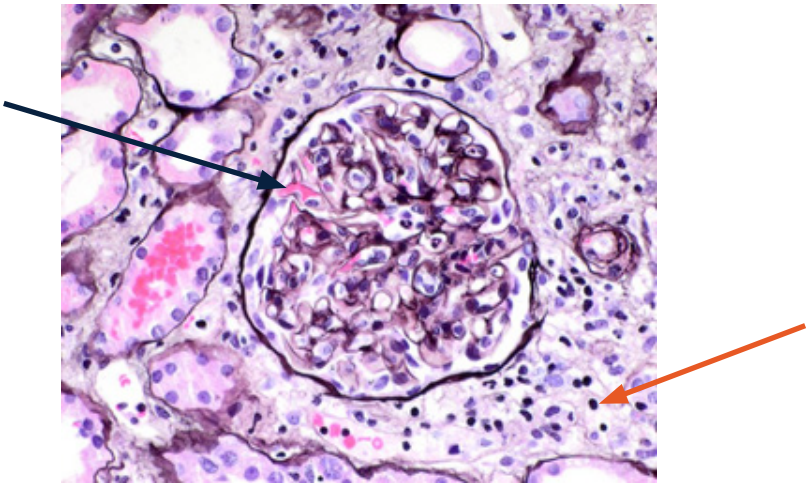

Figure 1. Light microscopy of the glomerulus shows no crescent formation or necrotizing lesions, the mesangium is not expanded and the capillary loops do not show spikes, bubbles, or double contours. There is severe interstitial edema (orange arrow). The inflammatory cell infiltrate is composed of lymphocytes, plasma cells, and eosinophils, and numerous red blood cell casts (black arrow) are present. No vasculitis was seen.

Table 2. Select Results from PCR Panel (Abnormal Results Are Bolded)

Lab	Value	Reference
Syphilis serology	x < 0.2	0.0-0.9
A. phagocytophilum serology	Negative	Negative
Bartonella henselae IgG	**1:2560**	Negative, x < 1:320
Bartonella henselae IgM	**1:400**	Negative, x < 1:100
Bartonella henselae DNA	**Positive**	Negative
Bartonella quintana IgG	**1:640**	Negative, x < 1:320
Bartonella quintana IgM	Negative	Negative
Lyme serology	Negative/Absent	Negative/Absent
COVID-19 polymerase chain reaction (PCR)	Negative	Negative
Cytomegalovirus PCR	Negative	Negative
Ehrlichia chaffeensis serology	Negative	Negative
Epstein Barr virus serology	Negative	Negative
Hepatitis serology	Negative	Negative
Herpes PCR	Negative	Negative
Human immunodeficiency virus serology	Not detected	Not detected
Parvovirus PCR	Negative	Negative
Q-fever antibodies	Negative	Negative
Tuberculosis serology	Negative	Negative

al bacterial and viral panels were evaluated for underlying causative organisms (**Table 2**), and blood cultures consistently returned negative results with the exception of one bottle, which was contaminated with skin flora (*Corynebacterium* species). The patient's Duke Criteria for infective endocarditis was scored as "possible endocarditis" with 4 minor criteria being met (fever, predisposing heart condition, vascular phenomenon, and immunologic phenomena). A bone marrow biopsy was obtained and returned as slightly hypercellular without any evidence of infection, leukemia, lymphoma, myeloma, or fibrosis. The patient was initially treated with pulse dose steroids, which resulted in clinical improvement of his lower extremity purpura. The results of the bacterial panel discussed above were as follows: *Bartonella henselae* IgG was 1:2560, IgM was 1:400, *Bartonella henselae* DNA was positive, and *Bartonella quintana* IgG was 1:640 (**Table 2**). After further questioning, the patient admitted that he lived on a farm with many cats and that he was "often scratched" by the cats. The patient was started on doxycycline and rifampin prior to discharge with improvement in his abdominal pain. Warfarin was replaced with dual antiplatelet therapy because of the possibility of warfarin-induced nephropathy.

Two months after hospitalization, the patient was no longer on hemodialysis and liver function tests returned to his baseline. His creatinine was elevated at 2.7 mg/dL, and his estimated glomerular filtration rate was 26.7 mL/min/1.73 m^2, which is thought to be his new baseline.

Discussion

Culture-negative endocarditis is a difficult diagnosis to make and is made more challenging by elusive organisms such as *Bartonella henselae*. Seven species of *Bartonella* (*B. quintana*, *B. henselae*, *B. elizabethae*, *B. vinsonii* subsp. *berkhoffii*, *B. koehlerae*, *B. bacilliformis*, and *B. alsatica*) have been shown to cause human disease with the first case of infective endocarditis being described in 1993.[5] *B. quintana* accounts for roughly 75% of cases of endocarditis and *B. henselae* accounts for another 20%. The

remaining species of *Bartonella* rarely cause endocarditis. *B. bacilliformis* is responsible for the famous Carrion's disease causing "Peruvian Warts." It carries a high mortality rate but does not generally cause endocarditis.[6] *B. henselae* has a predilection for the aortic valve with up to 75% of *B. henselae* endocarditis cases affecting the aortic valve.[7] Furthermore, *B. henselae* has a higher incidence of affecting native valves compared to prosthetic valves, with prosthetic valve involvement having worse outcomes.[8,9] Our patient's epidemiology differs from these studies, as no vegetation was identified on TEE, and his prosthetic valve is thought to be the infectious source.

It is important to consider *B. henselae* as a causative organism of culture-negative endocarditis as studies have shown that about 40% of domesticated cats in the United States have been shown to harbor *B. henselae*, and missing the diagnosis will delay treatment, causing increased morbidity.[8] As demonstrated in our case, it can also cause glomerulonephritis presenting with AKI, which ultimately leads to hemodialysis in previously healthy kidneys. The pathophysiology of renal failure in the setting of endocarditis has been debated in the medical literature and was originally attributed to emboli from the vegetation[10], but our case would support the idea that there is a primary immune complex (IC) deposition component (**Figure 2**). This component could stem from the passive trapping of IC that is already in circulation or from the reactivity of IgG antibodies with an endogenous component of the glomerulus itself seen in membranous nephropathy or anti-glomerular basement disease. Several variables determine the clinical consequences of the IC depositions, including where the deposit forms, the biological properties of the antibody, the mechanism of deposition, and the amount of complexes deposited.[11]

Correct identification of the cause of AKI is imperative for patient outcomes, as demonstrated above. Anticoagulation-induced nephropathy should be considered in patients receiving warfarin or heparin products with findings of IC-mediated acute proliferative glomerulonephritis on renal biopsy. The pathophysiology behind this phenomenon is glomerular hemorrhage stemming from over anticoagulation with the blood causing an obstruction in the renal tubules, which may ultimately lead to acute tubular necrosis.[12] Treatment for anticoagulation-induced nephropathy is meant to stop the offending agent and add steroids.

Vasculitis can mimic endocarditis (and vice-versa) both serologically (with high p-ANCA) and clinically.[13,14] Certain infections and drugs can induce the production of p-ANCA in endocarditis and glomerular disease. However, proteinase 3-ANCA are specifically found in patients with endocarditis.[15] Some mechanisms linked to the production of these antibodies include barrier dysfunction and superantigens, as seen in patients with p-ANCA-associated endocarditis.[15] It is imperative to do a renal biopsy with light microscopy and immunofluorescence studies to detect p-ANCA-associated vasculitis

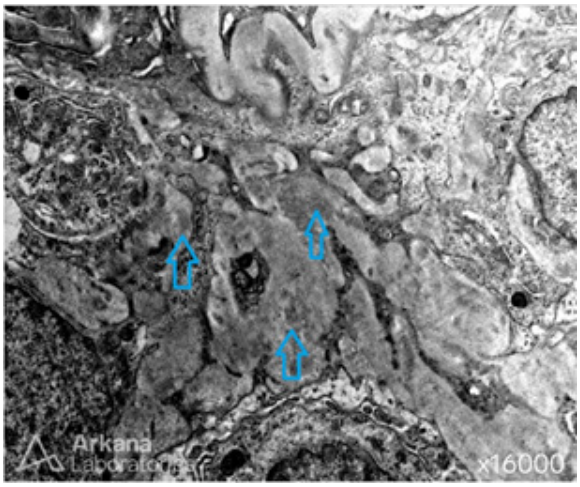

Figure 2. Electron microscopy of the renal biopsy shows mesangial deposits (blue arrows) of immune-complexes.

and glomerular disease, which can be a part of other vasculitis phenomena such as Wegener's granulomatosis, to ensure the proper diagnosis is made.[15]

Conflicts of Interest

The authors declare they have no conflicts of interest.

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