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Do we care if you have a cat? Bartonella infection related glomerulonephritis with no endocarditis

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SUMMARY

Bartonella infection has been associated with culture negative endocarditis and in rare cases immune complex medicated rapidly progressive glomerulonephritis (RPGN). Most of the previously reported cases of RPGN are associated with endocarditis. We report a case of RPGN with no endocarditis secondary to *Bartonella* infection. Good social history, high index of suspicion, diagnosis with polymerase chain reaction and treatment with antibiotics is the key for treatment.

Keywords: Kidney disease, Bartonella infection, glomerulonephritis.

INTRODUCTION

Rapidly progressive glomerulonephritis (RPGN) is a clinical syndrome characterized by features of glomerular disease (positive dysmorphic red blood cells) in the urinalysis and by progressive loss of renal function over a comparatively short period of time. Pathologically, it is characterized by cellular crescents in the glomerular space from extracapillary proliferation [1]. Although more common in adults, it can be seen in any age group. It can be divided into 3 categories, anti-glomerular basement membrane (anti-GBM) antibody disease, immune complex mediated disease (for example; immunoglobin (Ig) A disease, lupus nephritis, mixed cryoglobulinemia, post-streptococcal disease and other infectious causes) and pauci-immune glomerulonephritis (GN) associated with anti-neutrophil cytoplasmic antibodies (ANCA) [1]. Various infections are associated with RPGN like hepatitis C virus, *Staphylococcus*, *Streptococcus* etc. Many of these are associated with endocarditis. The most common organism in endocarditis associated GN is *Staphylococcus aureus*, which is seen in 56 percent of cases; *Streptococcus* species are the next most common. Less common organisms include *Bartonella henselae, Coxiella burnetii, Cardiobacterium hominis,* and *Gemella* [2]. Majority of previously reported cases of *Bartonella* associated GN has been associated with "culture negative" endocarditis. Herein, we report a case of *Bartonella* infection associated with myeloperoxidase antibody positive RPGN with no endocarditis.

CASE REPORT

A 32-year-old male with past medical history of truncus arteriosus status post aortic valve replacement presented to the hospital emergency room with fatigue, fever, bilateral lower extremity edema and non-pruritic rash for couple of weeks. He did not have any history of illicit drug use; Chinese herbal supplement use or any other medications. His social history was positive for having a cat at home. Examination was positive for a petechial rash involving the lower and upper extremities, multiple cat scratches and lower

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extremity edema till mid-leg. It was negative for lymphadenopathy. His lungs were clear on auscultation and pulse was regular. He did not have any abdominal tenderness. Laboratory indices showed sodium of 134 mEq/L, potassium of 4.2 mEq/L, serum bicarbonate of 19 mEq/L, blood urea nitrogen of 19 mg/dL, serum creatinine of 5.4 mg/dL (baseline was 1.2 mg/dL 12 weeks before admission), lactate dehydrogenase 347 U/L, haptoglobin <10 mg/dL and pancytopenia. His urine microscopy was positive for dysmorphic red blood cells. He had non-nephrotic range proteinuria. Further laboratory workup was ordered to narrow our differential diagnosis of RPGN (anti-GBM disease, lupus nephritis, ANCA associated disease, IgA nephropathy, post-streptococcal disease or other infection related GN, hepatitis C related cryoglobulinemia and myeloma). Complement C3 and C4 were low and myeloperoxidase antibody was strongly positive. Anti-GBM antibody, antinuclear antibody, HIV, cytomegalovirus, Epstein Barr virus, parvovirus, antistreptococcal, hepatitis panel, cryoglobulin and blood cultures were negative. Serum protein electrophoresis and kappa/lambda light chains were normal. Ultrasound showed normal kidneys with no hydronephrosis. To investigate his kidney injury further, kidney biopsy was performed which showed active segmental crescents (Figure 1) and glomerular capillary wall deposition of IgG, IgM, C3, C1q, Kappa and Lambda which were positive on immunofluorescence. Electron microscopy showed glomerular, mesangial, para-mesangial and subendothelial deposits suggestive of a secondary process of kidney disease. On further exploration and with his social history of being a cat owner and examination findings of cat scratches, *Bartonella* polymerase chain reaction (PCR) test was sent which came out to be positive confirming *Bartonella* infection. He was diagnosed with RPGN secondary to *Bartonella* infection. Due to its association with endocarditis, echocardiogram was performed and was negative for vegetations. He was started on rifampin (300 mg twice daily) and doxycycline (100 mg twice daily). Due to severe acute kidney injury, he was also started on renal replacement therapy (hemodialysis) on day 3 of hospitalization. Although his clinical symptoms of fatigue and lower extremity edema improved with antibiotics and other supportive treatment, but his kidney function unfortunately did not improve, and he ended up on dialysis.

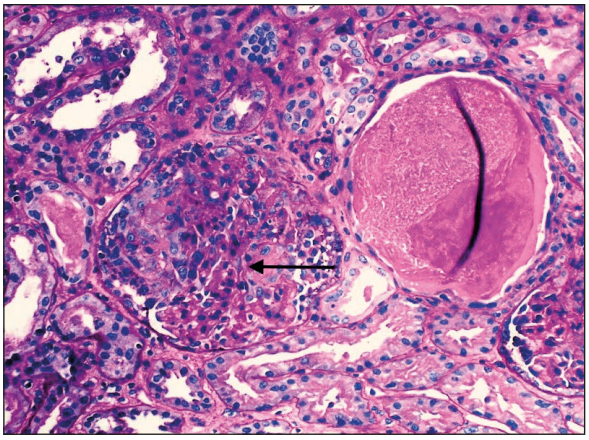

Figure 1 - Kidney biopsy showing active crescents in the glomerulus (arrow) suggestive of rapidly progressive glomerulonephritis.

DISCUSSION

Bartonella species are fastidious, Gram-negative bacteria that cause a range of manifestations, including cat scratch disease. It is one of the leading causes of culture-negative endocarditis [3,4]. Epidemiologic evidence suggests that cats serve as a major reservoir for *Bartonella henselae* human infections [5]. Most of the cases were reported in men and patients with preexisting cardiac valvular disease are considered at-high risk [4, 6]. Patients with *Bartonella* infection can also present with immune complex GN and can have positive ANCA [7-10]. Importantly, most of the previously reported cases of *Bartonella* related immune complex GN are present in the patients with endocarditis. We herein, report a rare case of a young male who had a contact with cat and had history of cardiac valvular disease presenting with acute kidney injury and was diagnosed with *Bartonella* infection related GN with echocardiogram findings negative for endocarditis.

RPGN is associated with pathological findings of active crescents in glomerular space. Crescents are usually formed due to release of proinflammatory cytokines, such as interleukin-1 and tumor necrosis factor-alpha [11, 12]. Workup of RPGN include identifying the cause of kidney disease after initial laboratory test showing elevated serum creatinine and urine analysis positive for dysmorphic red

blood cells. It is advisable to order autoimmune panel like antinuclear antibody, anti-GBM, ANCA and complements. To rule out infection related RPGN, antistreptococcal, HIV, hepatitis viral panel and blood cultures are commonly ordered. In few cases, the workup of renal failure can lead to identification of primary etiology like *Bartonella* infection in our patient.

Blood cultures have low yield in isolating *Bartonella* as it requires specific laboratory conditions like incubation in blood tubes containing ethylenediamine tetraacetic acid (EDTA) or extending the incubation period for 21 days [4]. It also replicates inside the RBCs which complicates its detection even more [13]. Hence, serologic testing can play a supportive role. A titer of ≥1:800 for IgG antibodies to *Bartonella* is considered as the cutoff for a positive test in patients with suspected Bartonella infection [14, 15]. There is limited data on use of IgM antibodies. Indirect immunofluorescence assays (IFA) and enzyme-linked immunosorbent assays (ELISA) are the two most commonly used serologic methods. PCR testing is performed by amplifying a 296 base pair fragment of the 16S ribosomal RNA which demonstrated a sensitivity and specificity of 58 and 100 percent, respectively [16].

Tetracyclines are a key component of therapy for *Bartonella* infection and aminoglycosides are also recommended to add for bactericidal effect [17-20]. In our patient, due to his severe acute kidney injury, we could not administer aminoglycosides and hence, rifampin was administered. The prognosis of kidney disease depends on the percentage of glomeruli with crescents and in patients with more than 80% glomeruli involvement and presence of circumferential crescents, prognosis can be worrisome. In contrast, patients with crescents in <50% of the glomeruli may follow a more indolent course or undergo remission [21]. Our patient's serum creatinine did not improve, and he unfortunately required renal replacement therapy. A good knowledge of patient's social condition, thorough examination, diagnosis with *Bartonella* PCR and treatment with antibiotics is the key to manage these patients.

Author contributions

G.S. saw the patient, prepared the manuscript and did literature review, N.S. reviewed the manuscript and literature.

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REFERENCES

[1] Couser W.G. Rapidly Progressive Glomerulonephritis: classification, pathogenetic mechanisms, and therapy. *Am. J. Kidney Dis.* 8, 11, 449-464, 1988.

[2] Boils C.L., Nasr S.H., Walker P.D., Couser W.G., Larsen C.P. Update on endocarditis-associated glomerulonephritis. *Kidney Int. Nature Publishing Group* 87, 1241-129, 2015.

[3] Spach D.H., Kanter A.S., Daniels N.A., et al. Bartonella (Rochalimaea) species as a cause of apparent "culture-negative" endocarditis. *Clin. Infect. Dis.* 20, 1044-1047, 1995.

[4] Raoult D., Fournier P.E., Drancourt M., et al. Diagnosis of 22 new cases of Bartonella endocarditis. *Ann. Intern. Med.* 125, 646-652, 1996.

[5] Koehler J.E. *Rochalimaea henselae* infection. A new zoonosis with the domestic cat as reservoir. *JAMA* 1994 [cited 2019 Aug 28]; 271, 531-535.

[6] Fournier P.E., Lelievre H., Eykyn S.J., et al. Epidemiologic and clinical characteristics of *Bartonella quintana* and *Bartonella henselae* endocarditis: A study of 48 patients. *Medicine* (Baltimore). 80, 245-251, 2001.

[7] Vercellone J., Cohen L., Mansuri S., Zhang P.L., Kellerman P.S. Bartonella endocarditis mimicking crescentic glomerulonephritis with pr3-anca positivity. *Case Reports Nephrol.* 1-4, 2018.

[8] Van Haare Heijmeijer S., Wilmes D., Aydin S., Clerckx C., Labriola L. Necrotizing ANCA-positive glomerulonephritis secondary to culture-negative endocarditis. *Case Reports Nephrol. J.* 2015; 2015 doi: 10.1155/2015/649763. Epub 2015 Dec 27.

[9] Khalighi M.A., Nguyen S., Wiedeman J.A., Palma Diaz M.F. Bartonella endocarditis-associated glomerulonephritis: A case report and review of the literature. *Am. J. Kidney Dis.* 63, 1060-1065, 2014.

[10] Raybould J.E., Raybould A.L., Morales M.K., et al. Bartonella endocarditis and pauci-immune glomerulonephritis: a case report and review of the literature. *Infect. Dis. Clin. Pract.* 254-260, 2016.

[11] Bonsib S.M. Glomerular basement membrane necrosis and crescent organization. *Kidney Int.* 33, 966-974, 1988.

[12] Atkins R.C., Nikolic-Paterson D.J., Song Q., Lan H.Y. Modulators of crescentic glomerulonephritis. *J. Am. Soc. Nephrol.* [Internet]. 1996 [cited 2019 Aug 28]; 7, 2271-2278. Available at: http://www.ncbi.nlm.nih.gov/pubmed/8959617 [Accessed 15th, May 2019].

[13] van Tooren R.M., van Leusen R., Bosch F.H. Culture negative endocarditis combined with glomerulonephritis caused by *Bartonella* species in two immunocompetent adults. *Neth. J. Med.* [Internet]. 2001 [cited 2019 Aug 28]; 59, 218-224.
[14] Edouard S., Nabet C., Lepidi H., Fournier P.E, Raoult D. Bartonella, a common cause of endocarditis: a report on 106 cases and review. *J. Clin. Microbiol.* [Internet]. 2015 [cited 2019 Nov 14]; 53, 824-829.
[15] Fournier P.E., Mainardi J.L., Raoult D. Value of microimmunofluorescence for diagnosis and follow-up of Bartonella endocarditis. *Clin. Diagn. Lab. Immunol.* 9, 795-801, 2012.
[16] Zeaiter Z., Fournier P.E., Greub G., Raoult D. Diagnosis of Bartonella endocarditis by a real-time nested PCR assay using serum. *J. Clin. Microbiol.* 41, 919-925, 2003.
[17] Foucault C., Brouqui P., Raoult D. *Bartonella quintana* characteristics and clinical management. *Emerg. Infect. Dis.* 12, 217-223, 2006.
[18] Foucault C., Raoult D., Brouqui P. Randomized open trial of gentamicin and doxycycline for eradication of *Bartonella quintana* from blood in patients with chronic bacteremia. *Antimicrob. Agents Chemother.* 47, 2204-2207, 2003.
[19] Angelakis E., Raoult D. Pathogenicity and treatment of Bartonella infections. *Int. J. Antimicrob. Agents* 16-25, 2004.
[20] Raoult D., Fournier P.E., Vandenesch F., et al. Outcome and treatment of Bartonella endocarditis. *Arch. Intern. Med.* 163, 226-230, 2003.
[21] Baldwin D.S., Neugarten J., Feiner H.D., Gluck M., Spinowitz B. The existence of a protracted course in crescentic glomerulonephritis. *Kidney Int.* 31, 790-794, 1987.