Case Report

# Infective endocarditis mimics ANCA associated glomerulonephritis

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## *Abstract*

***Background:*** Sub-acute bacterial endocarditis (SBE) rarely presents with features of a small vessel vasculitis. Patients with SBE can also develop multiple serological abnormalities including ANCA. In this report, we present a case of infective endocarditis mimicked ANCA associated glomerulonephritis.

***Case presentation:*** A 57-year old male with a clinical picture of rapidly progressive renal failure (RPGN) and positive seology for PR3-ANCA (C-ANCA) was referred to our hospital. The renal histology findings were compatible with focal and segmental glomerular necrosis. After receiving corticosteroid therapy, the patient became febrile and his general condition worsened. Cardiac ultrasound echocardiographic study disclosed multiple large vegetations on the aortic valve. After appropriate antibiotic therapy and valvular surgery, the patient's condition improved and his serum creatinine reached 1.7 mg/d**.**

***Conclusion:*** Misdiagnosis of SBE as ANCA-associated vasculitis and an inappropriate immunosuppressive therapy can have catastrophic consequences.

***Keywords:*** Sub-acute, Endocarditis, ANCA, Vasculitis, Glomerulonephritis

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Sub-acute bacterial endocarditis (SBE) can rarely manifest with features of small vessel vasculitis. It is usually attributed to microembolism and the effects of circulating immune complexes on the vascular endothelium (1). The differentiation between SBE induced vasculitis and primary small vessel vasculitis can be difficult sometimes especially if the heart murmur is absent. The minor criteria for SBE including fever, glomeruloneohritis and purpura are similar to the clinical manifestations of primary ANCA (antinuclear cytoplasmic antibody) associated vasculitis. Osler's nodes, Janeway lesions, and splinter hemorrhages typical for SBE may mimic cutaneous vasculitis (1-3). Interestingly, non-infectious endocarditis sometimes is a part of a clinical spectrum of systemic vasculitis (1). The differential diagnosis is much more difficult when a culture-negative SBE has positive laboratory test results for ANCA (4). Misdiagnosis of SBE as ANCA-associated vasculitis and an inappropriate immunosuppressive therapy can have catastrophic consequences.

## Case presentation

A-57-year old male was admitted to nephrology unit because of renal dysfunction and severe anemia. One month before admission, he was in a relatively good general health. During the last 4 weeks, he started complaining of polyuria and nocturia.

Physical examination on admission revealed blood pressure, 140/100, body temperature, 37.3ºC and apical systolic murmur was found in cardiac examination.

Early laboratory examination revealed serum creatinine: 2.8 mg/dl, blood urea nitrogen: 94 mg/dl, urinalysis; 2+ proteinuria / hematuria, fasting blood sugar: 90 mg/dl, WBC; 8700/µl, hemoglobin: 7.3 g/dl, MCV: 72.5 (76-96), MCHC: 30.4% (32-36), LDH: 780 (<250IU/L) M.C.H: 22.1 pg (28-32), ESR: 110 mm/h, C.P.K (Creatin phosphokinase): 89 IU/L (24-170), ALT: 12 U/L, serum calcium: 9.5 mg/dl, serum phosphorus: 3.6 mg/dl, serum sodium; 138 meq/l, serum potassium: 4.6 meq/l, CRP:4+, 24 hours urine collection revealed 800 mg/day proteinuria. Future laboratory examination revealed negative results for hepatitis B and hepatitis C infections. CKMB (creatine kinase-MB) 3U/L (0-24), serum complement C3: 53 mg/dl (90-180), C4: 15 mg/dl (10-40), CH50: <50 (70-150U), anti-GBM antibody: 5.8 U/ml (< 15), PR3-ANCA: 45 U/ml (<0.4), MPO. ANCA: 0.1 U/ml (<3.1i/ml), Rheumatoid factor (RF): 2+ positive, anti-nuclear antibody (ANA):1+ positive, anti-double stranded DNA (anti-dsDNA) and anti-cardiolipine antibodies were negative. Brucella agglutination test was negative. Ultrasound examination disclosed increased renal parenchymal echogenicity, right kidney size was measured; 112mm and left kidney size: 116 mm. Renal biopsy was performed and with the suspicion of renal limited ANCA associated rapidly progressive glomerulonephritis (RPGN), methylprednisolone pulse therapy, 500 mg daily for two consecutive days was started. A histological study of the renal biopsy revealed focal and segmental glomerular necrosis with an increase in mesangial matrix, capillary lumen narrowing and closure without hypercellularity (figure 1). An immunofluorescent study showed IgG, IgM, and C3 deposit in the mesangial regions.

Three days after receiving corticosteroid therapy the patient's general condition worsened and started chilling with high grade fever. Blood culture was performed and empiric antibiotic therapy with third generation cephalosporin and vancomycin were started. Cardiac ultrasound echocardiographic study disclosed normal left ventricular ejection fraction without any pericardial effusion, there were multiple large vegetations on the aortic valve, severe aortic regurgitation with pseudoaneurysm formation with systolic bulging.

Transesophageal echocardiography confirmed the conventional echocardiography findings, aortic valve annulus was: 2.31cm and vegetation size was 3×0.85 cm. Mitral valve was also involved by infective process. Tricuspid and pulmonic valves were normal.

The patient became afebrile after the start of intravenous antibiotic therapy with ampicilin, ceftriaxone, gentamicin and vancomycin. His fever dropped within 72 hours, then he underwent cardiac surgery and aortic valve replacement. After two months, the patient's general condition improved dramatically and his (serum creatinine level reach to 1.7 mg/dl hemoglobin level reached 12 mg/dl, LHD: 257 IU/L). The results of PR3-ANCA, RF and ANA negative and complement C3 serum level level returned to normal.

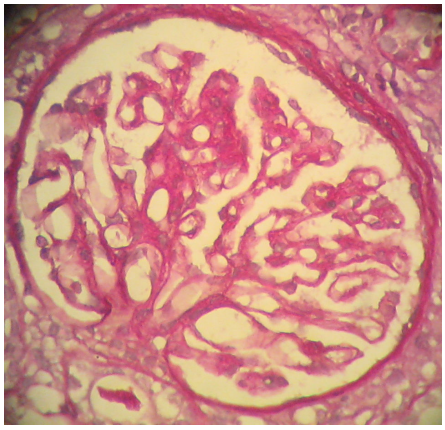
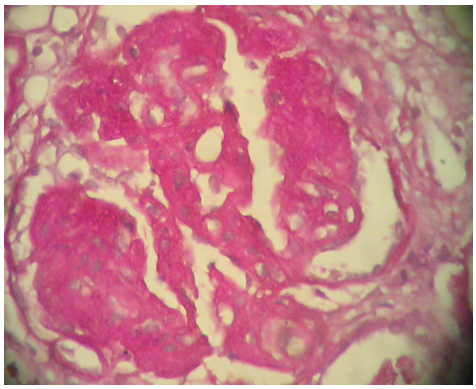


**Figure 1. A: Mild mesangial matrix expansion and segmental necrosis without endocapillary cellular infiltration or extracapillary crescent formation. PAS staining 10×40**



**B: Global necrosis and severe mesangial matrix expansion and capillary lumen closures. Without endocapillary cellular infiltration or extracapillary crescent formation. PAS staining 10×40**

## Discussion

In this study we report a patient with RPGN-like clinical course and positive serology for PR3-ANCA. With profound deterioration of clinical condition after

corticosteroid therapy, infective nature of disease came under consideration. From its early presentation, low C3 complement level and elevated LDH level were incompatible with a primary system vacuities. The severity of anemia was also incompatible with the degree of renal dysfunction. Severity of anemia and elevated LDH level were also unexplained by renal failure itself. Then we explained the severity of anemia by an infective endocarditis induced hemolytic process. Because the renal pathological findings of infective endocarditis are not specific, they do not lead us to the definitive etiological diagnosis even after renal biopsy. Acute renal failure can complicate the course of SBE as infectious induced interstitial nephritis, acute tubular necrosis, glomerulonephritis and antibiotic related interstitial nephritis. In the present case, renal biopsy findings did not have the pathological features of infectious glomerulonephritis.

Focal and segmental glomerular necrosis rather was in favor of glomerular vasculitis or thrombosis. The patients with prolong infections can develop multiple serological abnormalities. Viral infections can trigger the production of antinuclear antibodies (ANA), anticardiolipin antibodies (aCL), Cryoglobulins, and antineutrophil cytoplasmic antibodies (ANCA). The associations between HBV infection with polyarteritis nodosa and HCV infection with cryoglobulinemia have been discussed extensively. protozoal and fungal infections have also been reported as a cause of auto-antibody production (1-8).

In a review of 17 patients with infectious induced ANCA production, 11 patients had bacterial infections (streptococcus viridans, enterococcus, coagulase-negative staphylococcus, staphylococcus aureus) and six patients had positive serology for Hepatitis C Virus (HCV) and Hepatitis B Virus (HBV) infections (9). In patients with double ANCA positivity (PR3- and/ MPO-ANCA), SBE and HCV infection should be excluded (7). Usually, the infection-associated auto-antibodies are transient, lower titers and more often of the IgM type (8).

Bacterial infections are also a trigger for Wegener's granulomatosis (WG) as the relapse rate is higher in S. aureus nasal carriers. a marked increase in the expression of T cell receptor V ß 2.1, which recognizes superantigens found in patients with WG (10). B cells can produce ANCA antibodies after being stimulated by bacterial unmethlylated oligodeoxynucleotides via toll-like receptor 9 (TLR9) (11). Binding of ANCA to PR3 and MPO, expressed on the surface of neutrophils induces the secretion of TNF-α, IL-8, IL-1 and production of oxygen radicals (7). In the eleven reported patients with bacterial endocarditis and positive ANCA test, seven patients had positive c-ANCA (PR3-ANCA), and 4 patients had positive P-ANCA (MPO-ANCA). Low levels of serum complement and positive serological results for RF, ANA, cryoglobulins and anticardiolipin antibodies were also detected frequently among them. Like in our study, sometimes endocarditis is diagnosed after a wrong treatment with immune-suppressives (12).

In infectious associated ANCA positivity, there are no skin manifestations of vasculitis (7, 9). The patients with primary ANCA associated vasculitis have higher rate of nasal and sinus involvement. In patients with infectious induced vasculitis, the presence of cryoglubulin and hypocomplementemia are associated with more severe clinical course and higher possibility of renal dysfunction (7). After the appropriate treatment of the infection, ANCA titer decreased but it might take two years for it to completely disappear (13).

In conclusion, SBE induced glomerulonephritis with false positive serology for ANCA can mimic the clinical features of ANCA associated glumerulonephritis. Intense immunosuppressive therapy in this situation can disseminate the infection and have catastrophic consequences. We recommend a systemic approach and consider the possibility of SBE particularly in those patients who do not match the full clinical features of ANCA.

**Conflict of interest:** There was no conflict of interest.

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