CASE REPORT

A case report of antineutrophil cytoplasmic antibody-associated vasculitis and glomerular immune depositions

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Abstract

Background: Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a systemic disease leading to renal complications of pauci-immune focal and segmental necrotizing crescentic glomerulonephritis (PI-NCGN).

Case description: We present a 57-year-old female patient with rapidly progressive glomerulonephritis, multiple systemic infections [candidiasis and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)], severe weight loss, arthralgia, positive myeloperoxidase ANCA, acute deterioration of cardiac function and NCGN with heavy deposition of immunoglobulin (Ig) A and complement 3 (C3) in kidney biopsy. After two months of follow-up and appropriate treatments [methylprednisolone (60 mg/day), cyclophosphamide (15 mg/kg)], our patient recovered from multiple life-threatening infections, including candidiasis treated by fluconazole and SARS-CoV-2 treated by methylprednisolone and acute cardiac failure. In addition, she was saved from dialysis despite all poor prognostic factors.

Conclusion: AAV might lead to immune complex deposition in kidneys due to different pathogenetic mechanisms like complement activation and immune complex formation, apart from losing tolerance to neutrophil proteins. HIPPOKRATIA 2022, 26 (2):86-88.

Keywords: Acute kidney injury, antibodies, anti-neutrophil cytoplasmic, immunoglobulin A, heart failure

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Introduction

Whenever a patient has acute progressive kidney disease with glomerular hematuria and proteinuria, anti-neutrophil cytoplasmic antibody (ANCA) testing and kidney biopsy should be performed immediately[1]. Systemic forms of ANCA-associated vasculitis (AAV) affect cutaneous, nervous, gastrointestinal, musculoskeletal, cardiac, and pulmonary systems in addition to the renal manifestations. The typical kidney pathology observed in patients with AAV is pauci-immune focal and segmental necrotizing crescentic glomerulonephritis (PI-NCGN)[1,2].

Here, we present a 57-year-old female patient suffering from rapidly progressive glomerulonephritis with recurrent systemic infections, severe weight loss (20 kg in one month), arthralgia, a high titer (210 U/mL) of myeloperoxidase (MPO) ANCA, acute deterioration in cardiac function (ejection fraction decreased from 65 % to 40 % in two weeks), NCGN with deposition of immunoglobulin (Ig) A and complement 3 (C3) with severity degree of +3 in kidney biopsy.

Case Report

A 57-year-old female patient was admitted to our hospital with sudden dyspnea, fatigue, and diarrhea. She was normotensive and euvolemic in the physical examination without any pathological findings. In hematological and biochemical analysis, hemoglobin was 8.3 g/dL, serum albumin level was 2.6 g/dL, serum creatinine (Cr) level was 2.37 mg/dL, estimated glomerular filtration rate (eGFR) via Chronic Kidney Disease Epidemiology Collaboration equation (CKD–EPI-cre based) was 22 mL/minute/1.73m^2, C-reactive protein was 135 mg/L, serum C3 level was 0.87 g/L [normal range (NR): 0.9-1.8], IgA level was 5.05 g/L (NR: 0.7-4), proteinuria was 2,078 mg/day, albuminuria was 1,028 mg/day, and microscopic isomorphic hematuria was noted on admission (Figure 1). Ultrasonography revealed normal kidney size and echogenicity. On the 11th day of hospitalization, the pa-

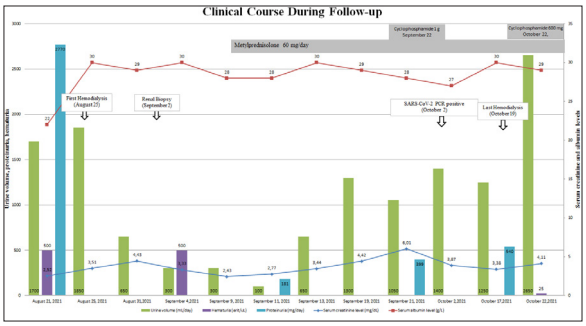

Figure 1: Clinical course of the reported patient with antineutrophil cytoplasmic antibody-associated vasculitis and glomerular immune depositions.

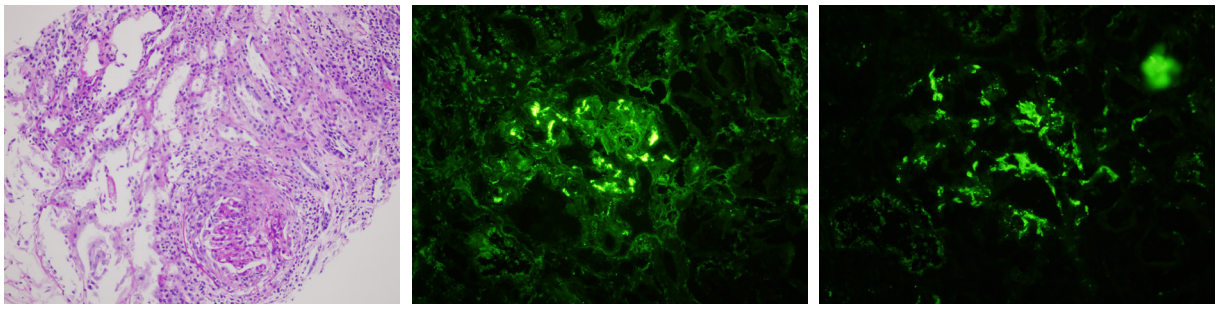

Figure 2: Histopathology images of the patient's kidney biopsy displaying a) necrotizing crescentic glomerulonephritis with severe tubulointerstitial inflammation by light microscopy (hematoxylin and eosin stain, ×400), b) glomerular mesangial severe (+3) immunoglobulin A deposition in granular pattern (immunofluorescence microscopy, ×400), and c) glomerular mesangial severe (+3) complement 3 deposition in granular pattern (immunofluorescence microscopy, ×400).

tient required hemodialysis as she developed oliguria and melena. Gastroscopy revealed esophageal candidiasis, so fluconazole was administered orally. Auto-antibodies such as antinuclear (ANA), anti-double-stranded deoxyribonucleic acid (anti-dsDNA), and anti-glomerular basal membrane antibody (anti-GBM) were negative except for perinuclear-ANCA (p-ANCA), and serum C3 was low (complement 4 was normal). Renal biopsy revealed NCGN with deposition of IgA and C3 (Figure 2).

Methylprednisolone 60 mg/day was commenced as soon as the control gastroscopy was normal, while fluconazole treatment was ongoing. Increased movement capacity, appetite, urine volume (up to 1,300 mL/day), and serum albumin levels were observed immediately after steroid therapy. Cyclophosphamide (15 mg/kg) was administered intravenously after fluconazole treatment was completed in two weeks. Unfortunately, urinary infection (caused by *Escherichia coli*) and catheter-related septicemia (caused by *Staphylococcus aureus*) were documented a week later. Plasmapheresis could not be performed because of sepsis. In the meantime, positive nucleic acid amplification tests detected Coronavirus disease 2019 (COVID-19) infection. After she had recovered from COVID-19 (treated by methylprednisolone and parenteral nutrition) and bacterial infections (*Escherichia coli* treated by removal of catheters and sulfamethoxazole and trimethoprim combination), she was started on a reduced dose of intravenous cyclophosphamide (10 mg/kg) and sulfamethoxazole and trimethoprim combination 60 mg/800 mg tablet three times per week[1]. After one month of hemodialysis dependence, her urine output started to increase. Her cardiac functions improved (ejection fraction increased from 40 % to 50 %), and she did not require dialysis since then. After six monthly courses of cyclophosphamide therapy, the ANCA antibody test was negative, and the patient's serum creatinine level was 1.7 mg/dL. Methylprednisolone (4 mg/day) and azathioprine (2 mg/kg/day) were administered for maintenance treatment for 18 months.

Discussion

According to the draft classification criteria for AAV, the patient was classified as microscopic polyangiitis (MPA) due to a high titer of p-ANCA positivity with a diagnostic sensitivity of 87 %[3]. In addition, the presence of characteristic multiorgan involvement (cardiac and renal) with constitutional symptoms supported this diagnosis[2]. Kidney biopsy findings (fibrinoid necrosis, fibrocellular crescents, proliferative glomerulonephritis) were compatible with renal pathology of MPA except intense and codominant IgA and C3 depositions rather than pauci-immune glomerulonephritis (GN)[2]. Kidney biopsies of AAV patients usually present no or few depositions of immune complexes defined as pauci-immune (<2+ intensity of immune deposition)[2]. However, we have found immune complex (IC) (IgA and C3) deposition on an intensity scale of 3+. Based on these codominant IgA and C3 depositions, our differential diagnosis included the following entities: i) coexistent AAV and IgA nephropathy (dual glomerulopathy), ii) IgA nephropathy with ANCA positivity, iii) a novel form of AAV with glomerular IgA and C3 deposition, and iv) glomerular diseases with infections developing ANCA[4-7].

There are some cases of IgA nephropathy with ANCA positivity in the literature[8,9]. To define our case as this clinical entity, the typical diagnostic findings for IgA nephropathy should have been present; mesangial proliferation with predominant or codominant IgA deposition in kidney biopsy and normal serum complement levels with normal or increased serum IgA levels[1,8,9]. Hence, we discarded all forms of IgA nephropathy in our patient based on the absence of mesangial proliferation.

Could our patient's diagnosis be AAV with glomerular intense IgA and C3 deposition? Recently, studies have reported that AAV cases do not always present with pauci-immune GN. Instead, severe immune depositions could accompany them, and these IC depositions are associated with a poor prognosis in these patients[10]. Along with the unclear mechanism of IC depositions in AAV, the alternative complement pathway activation observed in the chronic phase might play a role in IC depositions of MPO-ANCA-associated GN. At the time of renal biopsy, our patient suffered from candida infection, which might have led to infection-related glomerulonephritis resulting in IC deposits superimposed on AAV-related NCGN[11]. More information and biomarkers are needed in the lit-

erature to distinguish these entities.

Does the diagnosis of our case AAV with strong deposition of IgA and C3 or dual glomerulonephritis of AAV and post-infective glomerulopathy exist? Future studies are needed to clarify this question, or a second biopsy might give additional information about her disease if complete recovery cannot be attained after treatments are completed. We administered cyclophosphamide and methylprednisolone along with appropriate antifungal and antibacterial treatment. After two months of follow-up, our patient recovered from multiple life-threatening infections, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and acute cardiac failure. She was also saved from dialysis despite all poor prognostic factors.

This case report is unique for demonstrating the good outcome by treatment in a patient diagnosed with AAV with severe IC depositions in kidney biopsy associated with a poor prognosis.

Conflict of interest

Authors declare no conflicts of interests.

Acknowlegment

Informed consent was obtained from the patient.

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