ABSTRACT
A 56 year old female a known diabetic, hypertensive and hypothyroid was diagnosed with acute kidney injury secondary to urosepsis or contrast induced nephropathy due to febrile illness and a positive urine culture. During the ongoing treatment in hospital with antibiotics, fever was still persistent and patient developed worsening renal functions and decreasing trend in the hemoglobin levels. To rule other differential diagnosis, further blood and urine investigations were done in which P-ANCA was found to be strongly positive. After analysing the reports which revealed rapidly progressive renal failure with proteinuria, microscopic hematuria and a positive ANCA, a clinical diagnosis of vasculitis was made. A renal biopsy helped to ascertain final diagnosis of P-ANCA associated vasculitis and crescentic glomerulonephritis emphasizing that early biopsy and aggressive treatment is a must in a suspected case of vasculitis. Treatment with IV steroids followed by oral steroids and IV Endoxan helped the patient to recover with improved renal function.

Keywords: Antineutrophil cytoplasmic antibody, vasculitis, renal biopsy, crescentic glomerulonephritis.

P-ANCA Associated Vasculitis and Crescentic Glomerulonephritis in Patient with Type 2 Diabetes

1Pankaj Aneja, 2Yogesh Chhabra, 3Gaurav Bhalla, 4Neeti Parvesh, 5Blessy Sehgal Bhalla
1,3,4Consultant, 2Senior Consultant, 5Hony. Consultant
1Department of Diabetes and Metabolic Diseases, 2Department of Nephrologist, 3,4Department of Diabetologist, 5Department of Nephrology
1,2Max Super Speciality Hospital, Shalimar Bagh, New Delhi, India
3,4Max Healthcare Institute, New Delhi, India
5Action Balaji Hospital, New Delhi, India

Mrs V, a 56 years old female a known diabetic, hypertensive and hypothyroid presented to the emergency room (ER) from a nursing home with complaints of low grade fever since 3 months and vomiting since 2-3 days. She had no complaint of decreased appetite but had history of significant weight loss of about 5 kg since past 3 months. She did not report any history of cough, expectoration or hemoptysis. Patient had no history of loose stools or constipation, no urinary complaints like dysuria, graveluria, hematuria or pyuria. She never had any complaints of rashes on her body, joint pains or oral ulcers or bleeding from any site. Patient underwent some basic blood and urine investigations outside the hospital setup. Hemoglobin was 9.8 gm/dL, total leucocyte count came out to be 13000 cells/mm³ and the platelet count was 4.68 lakhs per microliter in her complete blood count reports. In her renal function tests, the level of blood urea was found out to be elevated to 44 mg/dL and serum creatinine levels were within normal range (1.04 mg/dL). Patient’s liver function tests were found within normal limits. Her blood sample was negative for malarial parasites and typhoid too (test performed was typhidot). Culture sensitivity report was negative. Routine microscopy for urine revealed increased WBC count of 20-30 cells/hpf, while urine culture sensitivity reports revealed the growth of E. coli species. Patient was also radiologically investigated for CECT Abdomen
which suggested hepatomegaly with bilateral renal concretions. CECT chest findings were normal. Patient was reinvestigated for blood and urine samples on 03/07/19 (Table 1).

From the above investigations and their findings, patient was diagnosed as a case of urosepsis which was inadequately treated outside in a patient with diabetes, hypertension and hypothyroidism. Also, a preliminary diagnosis of acute kidney injury secondary to urosepsis or contrast induced nephropathy was made. Accordingly, the treatment strategy for Mrs V was planned. Angiotensin receptor blockers (ARBs) were stopped. Antibiotics were optimized (colistin). Patient was started on tablet amlodipine and thyroid supplements were increased. Blood investigations were further monitored for 5 days during her hospitalization (Table 2).

During the ongoing treatment, patient was febrile persistently with fever spikes in between. During the hospital stay patient developed worsening renal functions and decreasing trend in the hemoglobin levels. Considering the worsening condition of the patient, differential diagnosis of malignancy, tuberculosis and fungal infections, autoimmune condition was also taken into consideration. For ruling out the above differentials, some more blood and urine investigations were sent and bone marrow aspiration and biopsy was done (Table 3 and Table 4).

After analyzing the reports which revealed rapidly progressive renal failure with proteinuria, microscopic hematuria and a positive ANCA, a clinical diagnosis of vasculitis was made and a renal biopsy was planned. Inspite of deranged renal parameters and coagulopathy which posed a technical problem in performing a renal biopsy, patient underwent renal biopsy on 23/07/19. Findings were 14 glomeruli, 13/14 glomeruli showed crescents (10 cellular; 3 fibro cellular) and IFTA (Interstitial fibrosis and tubular atrophy) was 15-20%. Immunofluorescence findings were negative for C3/ IgA/ IgM/IgG/kappa/lambda. Final diagnosis of P-ANCA associated vasculitis and crescentic glomerulonephritis was made. Patient was started on IV steroids followed by oral steroids and IV Endoxan. The patient responded well to the treatment and has recovered renal function and is doing well on low dose oral steroids and Mycophenolate mofetil (MMF) along with septran for Pneumocystis carinii pneumonia (PCP) prophylaxis.

**DISCUSSION**

The kidneys are vascular organs and therefore are rendered as targets for different types of systemic vasculitis, specifically those affecting small vessels. The most common presentation is with glomerulonephritis as the primary renal sites for small-vessel vasculitides.
are the glomeruli. The characteristic kidney lesions in these conditions are pauci-immune necrotizing and crescentic glomerulonephritis (NCGN).\(^1\) Pauci-immune crescentic glomerulonephritis (PICG) represents up to 80% of cases of rapidly progressing glomerulonephritis (RPGN). Incidence of PICG is estimated to be 7–10 cases per million people per year in the United States. PICG has a predilection for whites compared to blacks, with roughly equal representation in men and women.\(^2\)

Active pauci-immune small vessel vasculitis is typically associated with circulating Anti-Neutrophil Cytoplasmic Antibodies (ANCA) antibodies.\(^1\)

Glomerulonephritis (GN) and vasculitis caused by ANCAAs is the most common form of new-onset GN in adults >50 years.\(^3\) The 2012 Chapel Hill Consensus Conference Nomenclature of Vasculitides (CHCC 2012) defines ANCA-associated vasculitis as necrotizing vasculitis, with few or no immune deposits, predominantly affecting small vessels (i.e., capillaries, venules, arterioles, and small arteries).\(^4\) ANCA Associated vasculitis (AAV) is characterized by a focal necrotizing vasculitis in any organs with varying severity, particularly affecting small vessels. The lungs and kidneys are the most commonly involved organs, in about 70-80% of patients.\(^1\) Patients with ANCA associated glomerulonephritis usually present with rapidly progressive glomerulonephritis with proteinuria, serum creatinine elevation and hematuria. Typical necrotizing and crescentic glomerulonephritis will be the clinical presentation in such patients.\(^5\)
Serologic detection of ANCA is an important diagnostic marker for AAV. ANCA has two major Immunofluorescence (IFA) patterns: The C-ANCA and P-ANCA pattern. C-ANCA is characterized by diffuse cytoplasmic staining due to antibodies against Proteinase-3 (PR3). P-ANCA is characterized by perinuclear staining pattern around the nucleus due to antibodies against Myeloperoxidase (MPO). Initially patient should be investigated with complete blood count, Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP). Renal function workup also is a mandatory investigation and should be evaluated immediately. Renal function tests with eGFR, urinalysis for proteinuria and hematuria, quantification of proteinuria with a 24-hour urine protein collection has to be performed. Measurement of complement level is useful since it might be low in patients with other forms of vasculitis as immune complex vasculitis.¹

Conventional treatment of ANCA disease is high-dose cyclophosphamide and glucocorticoids, which has remission in approximately 75% of patients at 3 months and up to 90% at 6 months.³ Treatment of AAV can be divided into three phases, initial immunosuppression and subsequent maintenance and third is treatment of relapse. The initial phase of immunosuppression includes intravenous pulse therapy or oral Cyclophosphamide, glucocorticoids like Prednisone which has to be tapered down in the maintenance phase and chimeric monoclonal anti-CD20 antibody Rituximab intravenously as a pulse therapy. Role of plasmapheresis is unclear, but the likely mechanism is rapid removal of ANCA and the circulating inflammatory cytokines and complement. The second phase of maintenance includes glucocorticoids as prednisolone, Azathioprine, Mycophenolate mofetil or methotrexate. With the advances in understanding of the underlying disease mechanisms, Abatacept (dimeric fusion protein), Eculizumab and Pexelizumab (monoclonal antibody agents to C5a) and Natalizumab are some of the potential novel therapies for AAV.¹

**CONCLUSION**

Our patient was a diagnostic challenge as she being a diabetic female who presented with febrile illness and a positive urine culture and looked like a clear case of urosepsis, which is a common presentation in middle aged diabetic females. But as she developed worsening symptoms and was not responding to antibiotics, we kept a high index of suspicion and started the search of other causes of rapidly progressive renal failure and were able to make the diagnosis of crescentic glomerulonephritis on the basis of renal biopsy and were able to treat the patient appropriately. Again emphasizing the fact that all that glitters is not gold and we should keep a high index of suspicion and early biopsy and aggressive treatment is a must in a suspected case of vasculitis.

**REFERENCES**