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Case Report

Granulomatosis with Polyangiitis Presenting as Gross Hematuria Followed by Anuria

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Abstract

Granulomatosis with polyangiitis is a rare disorder characterized by the necrotizing granulomatous lesions of both the upper and lower respiratory tract and glomerulonephritis. Rapidly progressive renal failure in GPA is not an uncommon presentation and always requires urgent intervention. A 25-year-old male patient who presented with fever, hematuria, hemoptysis, and decreased urine output with an abnormal renal function was found to have high titers of anti-PR3 antibody on evaluation. His prolonged hematuria followed by an anuric state during the hospital stay improved with multiple sessions of hemodialysis, and then he was started on immunosuppressive therapy with resolution of fever based on high clinical suspicion. A dramatic improvement of ongoing gross hematuria and hemoptysis was noted following a week of immunosuppression. Progression of GPA can be prevented by early diagnosis and initiation of treatment.

Keywords: GPA, Vasculitis, ANCA, Wegener's granulomatosis.

INTRODUCTION

Granulomatosis with polyangiitis (GPA) is an uncommon immunologically mediated multisystemic small vessel vasculitis that occurs in the upper and lower respiratory tract and kidneys and also involves multiple other organs. It was formerly known as Wegener's granulomatosis. It is characterized by necrotizing granulomatous inflammation of the respiratory tract with necrotizing, pauci-immune glomerulonephritis and occasionally vasculitis involving other organs also [1]. Consistent with the revised Chapel Hill Consensus Conference Nomenclature of vasculitides, it belongs to AAV(ANCA-associated vasculitides) which is associated with the presence of circulating autoantibodies (ANCA) that are usually directed against proteinase 3 (PR3) or myeloperoxidase (MPO). PR3-ANCA account for the majority of ANCA with cytoplasmic immunofluorescence patterns (cANCA) in 60-80% of the cases [2]. The disease onset has a wide age distribution, with a peak incidence between the ages of 41 and 68 years, and a very rare occurrence in childhood and young adults [3]. If left untreated, GPA is potentially lethal and has a low survival rate of only 20% [4]. We report a catastrophic presentation of GPA in a young-aged man who presented with goss hematuria followed by anuria, hemoptysis, and GTCS.

CASE HISTORY

A 25 years old male patient presented to us with reddish discoloration of urine with generalized body swelling and decreased urine output for the last 15 days. There were episodes of productive cough with blood-tinged sputum for the last 10 days. It was also been associated with high-grade unrecorded fever with chills. During the hospital stay patient also developed two episodes of generalized tonic-clonic seizures.

On examination his pulse rate was 84 per minute, his blood pressure was 180/110 mm Hg with a respiratory rate of 24 per minute, and oxygen saturation of 87% at ambient room air. Urobag showed grossly reddish-coloured urine after foley's catheterization. Respiratory examination showed decreased air entry on the right side along with crepitation on the left basal lung fields. Abdominal examination showed free fluid

in the peritoneum, however, there was no evidence of any organomegaly. The central nervous system examination and cardiovascular system examination didn't show any abnormalities. Skin, oral cavity and eyes examination was also normal.

Routine investigations showed leucocytosis (19500 per mm^3) with granulocytosis (P78 L20) and severe anaemia (Hb 4.2 g/ dL). Renal functions were abnormal showing Blood Urea of 100 mg/dL and Creatinine of 3.4 mg /dL. A urine routine and microscopy examination showed a large number of RBCs along with few RBC casts and 2+ proteinuria. Serum electrolytes and liver functions including coagulation profile and serum proteins were normal. Common tropical fever workups for malaria, dengue, and leptospirosis were negative. Peripheral blood smear examination didn't show any evidence of hemolysis and serum LDH was normal. Serum complements levels of C3 and C4 were normal and an ASO (Anti Streptolysin O) titer was negative.

Chest x-ray revealed right-sided pleural effusion. Ultrasonography of abdomen and KUB showed bilaterally enlarged kidneys (Right kidney-120 × 57 mm, Left kidney- 118×59 mm) with maintained corticomedullary differentiation along with moderate free fluid in inter bowel spaces. Diagnostic tapping of the pleural fluid showed a transudative picture. Sputum Gram staining showed Gram-positive cocci in chains and its culture was positive for *Streptococcus Pneumoniae*. Sputum was negative for acid-fast bacilli (AFB).

Further workup with blood serology was positive for cANCA (Serine proteinase-3, PR-3 antibody). However, Anti-Nuclear Antibody (ANA), pANCA (anti myeloperoxidase, MPO antibody) and anti Glomerular Basement Membrane (anti-GBM) antibodies were negative.

HRCT thorax was carried out which showed bilateral multiple variable-sized nodular lesion with central cavitation within and bilateral pleural effusion (Figure-1). HRCT evaluation of paranasal sinuses was normal. MRI brain performed showed edema in bilateral parietooccipital lobe (Figure-2).

The patient was admitted to the medical ICU and was put on antibiotics in renal dose (piperacillin-tazobactam and moxifloxacin) along with oxygen therapy. Urinary bladder continuously irrigated with 3% glycine solution anticipating bladder clots. The patient was also treated with levetiracetam for ongoing seizure episodes. Within two days of hospital admission patient's urine output markedly reduced and went into the anuric state and generalised body swelling with a rise of serum creatinine to 9.4 mg/dl. He was then planned for serial sessions of heparin-free hemodialysis with multiple blood transfusions and three liters of ultrafiltrate taken out in the initial two sessions. His fluid intake was restricted to insensible loss and daily requirements. The patient was then managed on the lines of vasculitis with immunosuppressive therapy. High dose steroid pulse therapy with 500 mg of intravenous methylprednisolone was given for three consecutive days which is then followed with oral prednisolone of 50 mg daily dose. Following three sessions of hemodialysis his output improved to more than 1.5 litres per day and his serum creatinine decreased to 2.8 mg/dl, also he came out of oxygen support.

A marked improvement of ongoing gross haematuria and hemoptysis was noted following a week of steroid initiation. Due to the fear of flare of ongoing respiratory infection, he could not be put on further induction immunosuppressive therapy with cyclophosphamide. The patient's condition further improved and was managed with oral azathioprine of 75 mg daily without giving induction therapy as the patient has already achieved remission. The patient was discharged in a stable condition and followed twice monthly with a hemogram, liver function test, and urine routine-microscopy examination and kidney function test. An interval renal biopsy was planned after three months considering the general physical condition of the patient. During the follow up his oral steroid tapered to 5 mg daily dose and azathioprine continued in the same dose. His serum creatinine settled to 0.8 mg/dl over a period of four weeks and urine microscopic examination was not showing any RBCs and casts.

Renal biopsy performed after three months showed fibrous crescents with features of secondary focal and segmental glomerulosclerosis in 5/25 (20%) glomeruli with increased tubulointerstitial chronicity (Figure-3). There was no evidence of crescent or granuloma formation. The tissue for DIF was not showing any immune deposit.

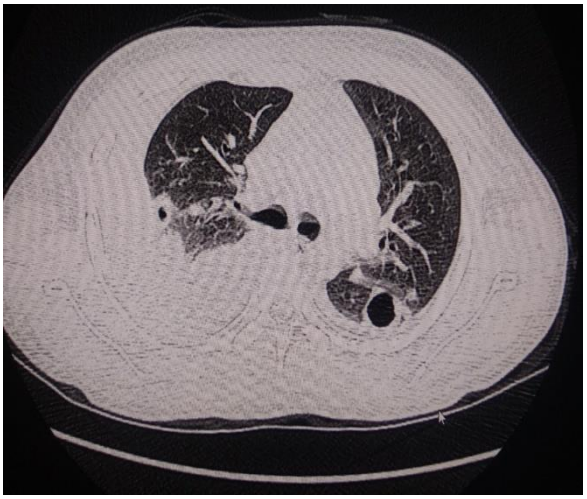

Figure-1: HRCT thorax showing few bilateral variable shaped nodular lesions, most of them showing central cavitation

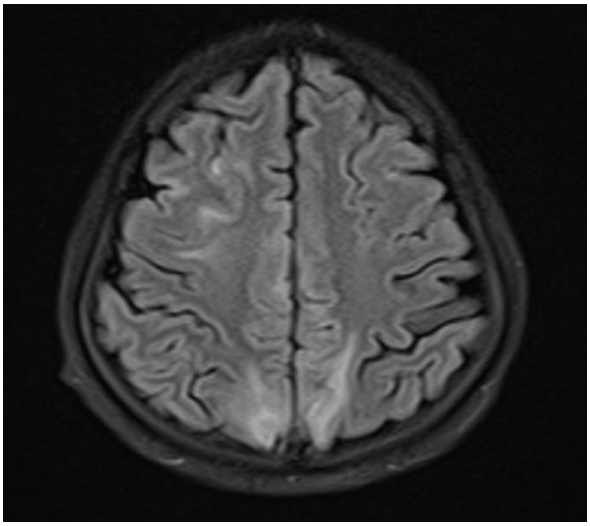

Figure-2: MRI brain T2 FLAIR sequence suggestive of hyperintense signal located in bilateral occipital lobe suggestive of oedema

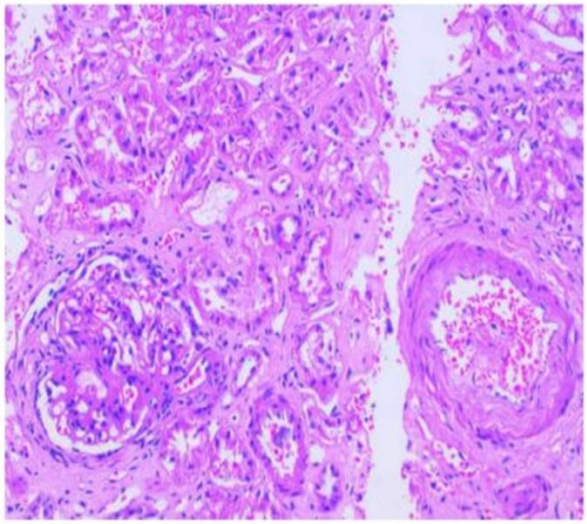

Figure-3: Interval renal biopsy showing fibrous crescents with features of secondary focal and segmental Glomerulosclerosis after three months of immunosuppressive therapy

DISCUSSION

The prevalence of GPA is about 3 in 100,000 with a slight male preponderance (3:2) [5]. The classic clinical triad of the disease consists of upper airway involvement, lower respiratory tract involvement, and glomerulonephritis with pulmonary and renal involvement in 90% and 80% cases respectively [6]. Kidney involvement most often manifests as microscopic hematuria with RBC or mixed cellular casts, proteinuria, and an abnormal serum creatinine level [7]. Oliguria and anuria are relatively rare renal presentation of GPA [8]. However macroscopic hematuria is not commonly reported. Proper diagnosis and initiation of appropriate immunosuppressive therapy are essential for optimal patient outcomes.

A chest X-ray helps in detecting underlying pathology in patients with pulmonary symptoms although CT has a higher sensitivity in detecting pulmonary nodules, cavities, and alveolar opacities. A positive ELISA test for PR3-ANCA has high diagnostic specificity for AAV in the appropriate clinical setting. However, renal and lung tissue biopsy is often important in establishing the diagnosis [9].

Treatment of GPA involves a 2-stage approach. First, the induction phase for initial 3-6 months has the goal of rapidly reducing the inflammatory process and minimizing tissue damage. Second, the maintenance phase for the next 24-48 months has the aim of preventing disease relapse. The standard of care for induction therapy in severe GPA includes a combination of glucocorticoids with either cyclophosphamide or rituximab. Glucocorticoids are a central component in the management of ANCA-associated vasculitis, especially in the context of renal involvement [10]. The maintenance treatment of GPA includes the combination of oral corticosteroids with azathioprine (2 mg/kg/day orally) or rituximab (500 mg every 6 months) [11].

The management should be individualized based on the clinical profile of the patient. Considering the general physical aspects and overwhelming infections, performing a renal biopsy at admission was difficult for this patient. So, we could not elicit a granuloma on renal biopsy as it was performed later following treatment with immunosuppressants and probably all th granulomatous lesions were healed with fibrous crescents and secondary focal and segmental sclerosis. However, tissue DIF was negative for immune deposits. As our patient responded well to initial pulse and oral steroid therapy and remission achieved, also there was possibility of flare of lower respiratory tract infection, we avoided further induction with cyclophosphamide and put him directly on maintenance therapy with azathioprine and steroids.

In conclusion we report a rare case of aggressive GPA with gross haematuria followed by anuria which responded dramatically on standard care of therapy and subsequently recovered fully.

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