ANCA- associated vasculitis with pulmonary-renal syndrome in the elderly: A case report and review

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SUMMARY

We present a case of a 67-year-old Chinese male who presented with acute kidney injury and nephrotic syndrome. The patient subsequently developed pulmonary hemorrhage, and his serum myeloperoxidase and proteinase 3 tests were positive, indicating ANCA-associated vasculitis. Due to the rapid progression of his clinical condition, treatment was initiated with plasma exchange and intravenous immunoglobulin, alongside induction therapy with high-dose glucocorticoids. Renal biopsy was not performed due to multiple challenges. During his two-month hospital stay, the patient required hemodialysis at least twice a week and received standard treatment of care. Despite the aggressive treatment approach, the patient continued to exhibit signs of renal insufficiency, necessitating ongoing supportive care and monitoring.

INTRODUCTION

Anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) represents a group of rare, potentially life-threatening autoimmune diseases characterized by inflammation and destruction of small to medium-sized blood vessels. The primary subtypes of AAV include granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA). These conditions are hallmarked by the presence of ANCA, which target components of neutrophil cytoplasm, most commonly myeloperoxidase (MPO) and proteinase 3 (PR3).[1]

In elderly patients, AAV presents unique challenges. The pathogenesis remains complex and multifactorial, involving genetic predisposition, environmental factors, and dysregulation of the immune system. Clinical manifestations in this population can be particularly diverse and may be confounded by age-related comorbidities. Symptoms can range from mild manifestations such as fatigue and arthralgia to severe, life-threatening conditions like rapidly progressive glomerulonephritis and pulmonary haemorrhage. Moreover, the elderly are more susceptible to the adverse effects of immunosuppressive therapy, complicating treatment strategies.

This case report aims to present a detailed account of an elderly patient diagnosed with ANCA vasculitis, highlighting the clinical presentation, diagnostic challenges, therapeutic interventions, and outcomes. Through this case, we seek to contribute to the growing body of literature on AAV in the elderly and underscore the importance of a tailored, multidisciplinary approach in the management of this complex disease in older adults.

CASE PRESENTATION

A 67-year-old Chinese man with no prior medical history or known drug allergies presented with a one-month history of frothy urine, increased frequency of micturition, incomplete voiding, epigastric discomfort, and intermittent bilateral lower limb cramping. He had been using traditional medicine for abdominal discomfort during this period. He denied dysuria, haematuria, fever, joint pain, malar rash, oral ulcers, skin rash, sore throat, cough, altered bowel habits and no constitutional symptoms. He is a non-smoker and does not consume alcohol. He weighed about 66 kg.

His investigations during his early admission is tabulated on Table I.

Urinalysis showed proteinuria (3+) and haematuria (3+). Renal ultrasound showed mild right hydronephrosis without evidence of calculi. He was managed as acute kidney injury (AKI) with nephrotic syndrome and started on intravenous hydrocortisone 50 mg three times a day as we were cautious in view of his age together with his anaemia and complaint of epigastric discomfort. Additional workups for glomerulonephritis were sent, including C3, C4, serum electrophoresis, urine free light chain, serum ANA, serum ANCA, serum PLA2R antibody, and serum anti-GBM came back negative. On May 21, 2024, he had a two-hour haemodialysis via the right internal jugular catheter (IJC) in preparation for renal biopsy.

Unfortunately, his condition deteriorated with the development of fever, desaturation, and significant haemoptysis. He was electively intubated for airway protection and urgent CTA of the thorax revealed diffuse pulmonary haemorrhage (see Figure 1). Biochemical investigations showed positive ANA (titre 1:160, speckled pattern), MPO (titre >221.94 IU/ml), and PR3 (titre 23.5 IU/ml). He was treated for ANCA-associated vasculitis with pulmonary and renal involvement, hence underwent seven sessions of plasma exchange with fresh frozen plasma as the

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Table I: Investigations during early admission

	10 Nov 2022	9 May 2024	10 May 2024
Haemoglobin (12-15 g/dL)		7.1	
Urea (3.5- 8.5 mmol/L)	3.4	25.4	25.5
Sodium (136-145 mmol/L)	137	137	137
Potassium (3.5-5.1 mmol/L)	3.9	4.3	4.0
Creatinine (62-115µmol)	84	527	560
Albumin (32-48 g/L)		30	
Total Cholesterol (<5.2 mmol/L)		5.8	
Calcium (2.18-2.6 mmol/L)		1.82	
Phosphate (0.78-1.65 mmol/L)		0.75	
24-hour urine PCR (<15 mg/mmol)		284.21	
Random blood sugar (<6.7 mmol/L)		5.1	

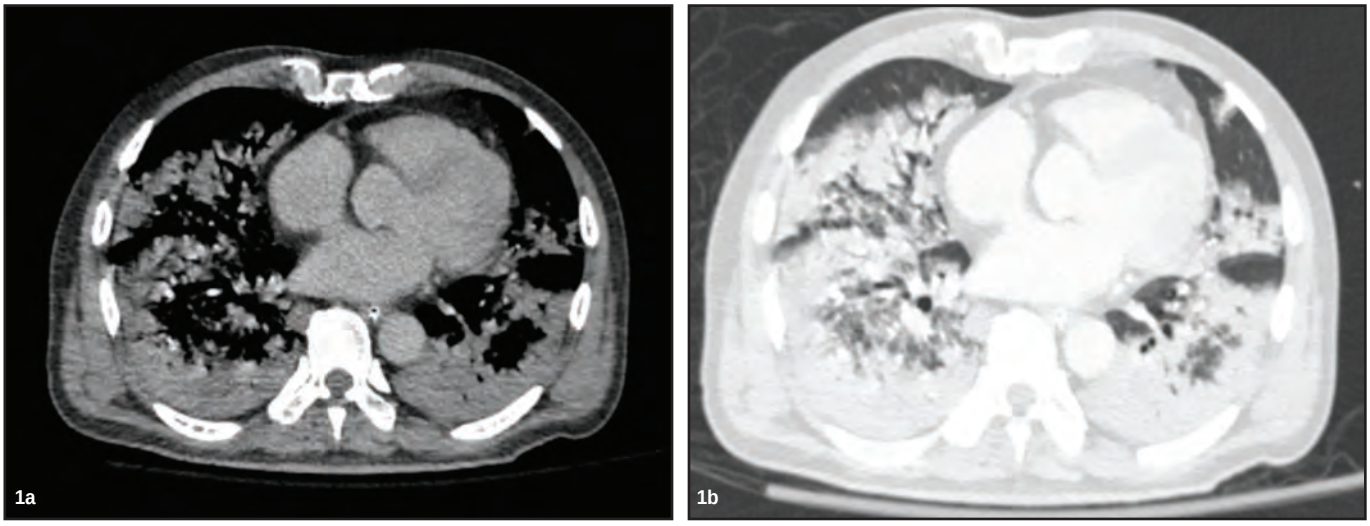

Fig. 1: CTA Thorax; axial images in soft tissue window (1a) and lung window (1b) respectively showed diffuse consolidative changes at both lung fields, predominantly at the dependent aspect associated with surrounding ground glass changes, likely to represent diffuse pulmonary haemorrhages in this case. Other differential diagnosis could be diffuse pulmonary infection / diffuse pneumonia No evidence of active bleeding (not shown in these images).

replacement fluid. He was also given 0.4 mg/kg intravenous immunoglobulin (IVIG) for five days and had his intravenous hydrocortisone increased to 100 mg three times a day. His stay in ICU was complicated with Methicillin-Resistant Staphylococcus Aureus (MRSA) bacteraemia, needing his IJC was removed, and a 14-day course of intravenous vancomycin. He showed clinical improvement and was extubated after 5 days.

Despite clinical improvement and good urine output of 1L-1.2L per day, his renal profile did not show much improvement. His urea ranged between 25-51 mmol/L, and creatinine persisted between 420-600 µmol/L, with blood gases showing mild metabolic acidosis (pH 7.34, HCO3 17.3 mmol/L). A renal biopsy was again planned but due to anaemia (haemoglobin ranging 6.5-7.9 g/dL) and thrombocytopenia (platelet range 90-100 x 10^9/L), this was not done. Full blood picture was sent showing functional iron deficiency anaemia with peripheral platelet consumption. Not only that, he went to develop frank haematuria needing bladder irrigation. There was positive leukocyte and nitrite in his urine analysis but negative urine cultures. A repeat ultrasound of the kidneys showed similar findings to previous imaging, and a subsequent CT urogram revealed a right ureteric calculus measuring 0.8 cm x 0.8 cm x 0.9 cm, causing mild right obstructive uropathy. He was empirically treated for a urinary tract infection , and an outpatient follow up was given for his ureteric stone.

Despite his 54-day-long stay with little improvement in his renal function, the renal biopsy was not performed as it was deemed too risky. He was then referred to rheumatology for extra-renal treatment for his AAV. Using the protocol as per EULAR guidelines, induction treatment was initiated: two-weekly cyclophosphamide for three cycles, followed by three-weekly for three cycles 2. Considering his previous history of severe infection, the initial cyclophosphamide dose was reduced by 30%, using a dose of 8.75 mg/kg. Full actual dose of 10 mg/kg was planned for subsequent cycles if he did not show any signs of infection. However, despite two cycles of induction treatment, his renal profile remained static with no improvement. His urea maintained 25-35 mmol/L and his creatinine between 450-600 µmol/L. Given this static trend, he was counselled for long-term renal replacement therapy, and he opted for haemodialysis. Upon discharge, he was planned for another four cycles of cyclophosphamide on an outpatient basis with weekly pre-haemodialysis blood monitoring. He was discharged with oral prednisolone at a dose of 1 mg/kg, with plans to taper the dose accordingly, and continued twice-weekly haemodialysis.

DISCUSSION

AAV represents a group of rare, potentially life-threatening autoimmune diseases characterized by inflammation and destruction of small to medium-sized blood vessels.[1,3,7] The kidney lesion associated with these conditions is pauci-immune, focal and segmental necrotizing crescentic glomerulonephritis (NCGN).[1] A severe manifestation of AAV is pulmonary-renal syndrome, which involves concurrent pulmonary hemorrhage and glomerulonephritis. This condition presents unique challenges in the elderly due to age-related comorbidities, altered immune responses, and potential treatment complications.[6]

The incidence of AAV increases with age, peaking in the seventh decade of life.[1,3] Elderly patients often exhibit a different ANCA profile compared to younger individuals, with a higher prevalence of MPO-ANCA positivity.[2,7] The pathogenesis involves autoantibodies targeting neutrophil components, leading to neutrophil activation, endothelial damage, and subsequent inflammation in various organs, predominantly the kidneys and lungs.[9]

In elderly patients, the clinical presentation of pulmonary-renal syndrome can be atypical and nonspecific, often delaying diagnosis. Common symptoms of renal involvement include haematuria, proteinuria, and rapidly progressive glomerulonephritis, often leading to renal insufficiency. Pulmonary involvement can include alveolar hemorrhage, presenting as hemoptysis, dyspnea, and diffuse alveolar infiltrates on imaging. Systemic symptoms such as fever, weight loss, and arthralgias are also frequent but may be attributed to other age-related conditions, complicating the clinical picture.[1,5,8]

Diagnosing AAV with pulmonary-renal syndrome in the elderly requires a high index of suspicion and a thorough workup. Laboratory tests often reveal elevated serum creatinine, active urinary sediment with red blood cell casts, and positive ANCA testing.[2] Imaging studies, such as chest radiographs or CT scans, may show diffuse pulmonary infiltration or ground-glass opacities suggestive of alveolar haemorrhage such as this patient. Renal biopsy is the gold standard for diagnosis as it is important for both the primary diagnosis and recurrent disease. However, in some patients, such as the one discussed, renal biopsy may not be feasible due to underlying issues such as anemia and thrombocytopenia, the presence of ureteric stone and its reason for hematuria. Furthermore, in the context of positive MPO or PR3-ANCA serology and clinical features compatible with small vessel vasculitis, an immediate biopsy may not be necessary and should not delay the initiation of treatment.[2]

Managing AAV with pulmonary-renal syndrome in the elderly involves balancing effective disease control with minimizing treatment-related adverse effects. The mainstays of therapy include induction therapy with high-dose corticosteroids combined with cyclophosphamide or rituximab to achieve remission.[1,2] The choice of agent depends on patient comorbidities and overall health status. Following induction therapy, maintenance therapy involves low-dose corticosteroids with azathioprine or rituximab to maintain remission and prevent relapses. Supportive management includes temporary hemodialysis in severe kidney involvement, plasma exchange for patients with rapidly increasing serum creatinine and those with diffuse alveolar hemorrhage who have hypoxemia, management of comorbid conditions, monitoring for infections, and addressing treatment-related complications such as osteoporosis or diabetes.[1,2,5-6]

The prognosis of elderly patients with AAV and pulmonary-renal syndrome is generally poorer compared to younger patients, primarily due to delayed diagnosis, treatment toxicity, and underlying comorbidities. However, the prognosis improves with immunosuppressive treatment.2,4 Atypical presentation and overlapping symptoms with other geriatric conditions can delay diagnosis and initiation of appropriate therapy. Furthermore, elderly patients are more susceptible to adverse effects of immunosuppressive therapy, requiring careful monitoring and dose adjustments.6 The presence of other chronic diseases can complicate management and worsen outcomes.[1,6] For the patient discussed, the diagnosis was fully established upon developing pulmonary hemorrhage and positive serum MPO/PR3 results. He was treated with plasma exchange and IVIG, but his condition was complicated by MRSA bacteremia, urinary tract infection and haematuria. His induction therapy was delayed due to infection and plans for renal biopsy, which ultimately could not be performed due to multiple challenges.

CONCLUSION

ANCA-associated vasculitis with pulmonary-renal syndrome in the elderly is a complex and challenging condition requiring a multidisciplinary approach for optimal management. Early recognition, appropriate therapeutic strategies, and vigilant monitoring for complications are crucial to improve outcomes in this vulnerable population. Further research is needed to develop age-specific treatment protocols and improve the quality of life for elderly patients with AAV.

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DECLARATION

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