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The Effects of Plasma Exchange on Diffuse Alveolar Hemorrhage in Severe Vasculitis – A Case Study

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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Case Study

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ABSTRACT

Introduction: Rapidly progressive glomerulonephritis (RPGN) and widespread alveolar hemorrhage define ANCA-associated vasculitis (AAV), a rare, life-threatening illness (DAH).
Case Presentation: An elderly female came with lower limb weakness and oliguria had features suggestive of RPRF and fluid overload. She developed hemoptysis with respiratory failure despite hemodialysis and intravenous steroids. The diagnosis of patients was pulmonary-renal syndrome–DAH in the setting of ANCA and based on the HRCT chest and positive p-ANCA report. She had excellent responses to intravenous pulse steroids, cyclophosphamide, and plasma exchange.

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Conclusion: Based on observation showed the importance of immediate intervention in potentially fatal disease DAH in AAV.

Keywords: ANCA; AAV-ANC; DAH; PE; RPGN.

1. INTRODUCTION

Pulmonary, renal syndrome (PRS), antineutrophil cytoplasmic antibody (ANCA)-associated small vessel vasculitis (ASVV), cryoglobulinemia, systemic lupus erythematosus, environmental factors, and certain drugs are among the causes of pulmonary renal-syndrome (PRS), which is characterized by a combination of diffuse alveolar hemorrhage (DAH) and rapidly progressive glomerulonephritis (RPGN [1]. Around 70% of PRS cases are caused by AAV, caused by microscopic polyangiitis (MPA), Wegener's granulomatosis, and Churg-Strauss disease. Antiproteinase-3anti myeloperoxidase and antimyeloperoxidase (anti-MPO, p-ANCA) antibodies, linked to ASSV pathophysiology, are present in 70–90% of patients and help in diagnosis [2,3]. Because the commercial serologic investigation proved positive, our current patient may be placed into a recognized subgroup. However, a renal biopsy could not be performed to confirm the diagnosis. PRS was diagnosed based on clinical manifestations and serological reports but without histopathological findings [4].

2. CASE PRESENTATION

A 60-year-old lady was admitted to our hospital with moderate grade fever off and on for the past four months. For the last 15 days, she had weakness in both legs with tripping while walking, tingling, and numbness. She had reduced urine output for five days. She denied any history of rash, cutaneous nodules, arthritis, or hemoptysis. A month before her admission, she had visited a general practitioner locally, had normal serum creatinine (0.98 mg/dl) and was given symptomatic treatment. She had pulmonary tuberculsevensis seven years back and took a complete anti-tuberculosis treatment course. On admission, a physical examination revealed pale conjunctiva, bodyweight of 45.0 kg, a body temperature of 36.7℃, pulse rate of 80 beats/min, blood pressure of 162/94 mmHg, and bilateral 2+ pitting edema in lower extremities. Her percutaneous oxygen saturation was 96% on atmospheric air with a respiratory rate of 12-16 breaths/min, and her Birmingham Vasculitis Activity Score was 24.

Her systemic examination for respiratory, cardiovascular & abdomen was unremarkable. Neurological examination revealed lower motor neuron involvement in lower limbs with grade 3 power distally and sluggish deep tendon reflexes in both lower limbs. She suffered a sensory loss in her lower limbs below the knees and patchy sensory loss in her upper limbs. There was no respiratory muscles involvement. Cranial nerves and coordination were normal. As shown in Table, on admission, the serum creatinine level was 7.6 mg/dL, metabolic acidosis, and normocytic anemia. Immediately she was started on hemodialysis support. Chest x-ray showed a fibrotic patch in the correct upper zone. Her sputum for Acid-fast bacilli & Quantiferon gold was negative & ruled out active tuberculosis.

An echocardiogram revealed an ejection fraction of 62%, type I diastolic dysfunction, mild to moderate mitral regurgitation without evidence of tamponade or pulmonary artery hypertension. Her ultrasound abdomen revealed bilaterally normal size kidneys with raised echotexture bilaterally. Urinary findings and increasing loss of renal function were used to diagnose rapidly progressive glomerulonephritis (RPGN); thus, we scheduled a percutaneous renal biopsy once her overall state improved.

We ruled out multiple myeloma. A nerve conduction study and electromyography were performed, which revealed severe sensorimotor neuropathy. It was an asymmetrical, mixed type involving lower limbs more than upper limbs. MRI Lumbosacral spine revealed left subarticular annular tear and broad-based central disc protrusion at L4-L5 level; however, being trivial, was not contributing to the neurological deficit. Her blood and urine culture showed no growth. 3rd Day of admission: In addition to hemodialysis and maintaining euvolemia, intravenous methylprednisolone pulse therapy was administered 500mg every 24 hours.

On the next day, she had worsening her respiratory condition in the form of dyspnea, hypoxia, and hemoptysis. By this time, her ANCA results were obtained, and she was found to be pANCA positive with negative ANCA. Diffuse alveolar hemorrhage was diagnosed based on

Chest X-ray finding of diffuse infiltrative opacification pattern, and HRCT chest showed bilaterally more on the left side. We diagnosed AAV, microscopic polyangiitis with RPGN, and diffuse alveolar hemorrhage with this. 5th Day of admission: Plasma exchange was initiated a total of 5 times with approximately one time the predicted plasma volume (estimated by the following formula: [0.065×body weight (kg)]×[1-hematocrit]) 11 per session, using freshly frozen plasma as the replacement solution. During this period, pulse cyclophosphamide 500mg dose was administered intravenously.

6th Day of admission: Some improvement in lower limb weakness, anuria, and chest shadows persisted

After three pulse doses of IV methylprednisolone, she was switched to oral prednisone 40 mg once a day. After four sessions of plasma exchange were performed, her respiratory condition improved, and she was successfully weaned off the ventilator on Day 7. Her urine output improved significantly to 1200ml in 24 hours. Her hemodialysis was stopped.

Table 1. Laboratory findings on admission

Test Descriptions	Value	Test Descriptions	Value
Haemogram		**Thyroid profile**	
White blood cell (/µL)	10,80	TSH (mIU/ml)	4.68
Neutrophil	70	T3(ng/dl)	112
Lymphocyte	24	T4(µg/dl)	17.45
Monocyte (%)	03	**Serology**	
Eosinophil (%)	3.6	Antinuclear antibody (dilution)	1:1000
Basophil (%)	0.4	DNA	(-)
Hemoglobin (g/d/)	8.3	C3 complement (mg/d/)	98
Hematocrit (%)	30.8	C4 complement (mg/d/)	13.9
Platelet (10^4/ɜ/)	654	cANCA (AU/ml)	(--)
ESR	140	pANCA (AU/ml)	33.0
INR	1.12	Anti-GBM antibody	(–)
Serum Chemistry		**Arterial Blood Gas (room air)**	
Blood Urea (mg/d/)	203	pH	7.23
Creatinine (mg/d/)	7.6	pO_2 (mmHg)	104.0
eGFR(ml/min/1.73 m^2)	5.79	pCO_2 (mmHg)	21
Sodium (mEq/L)	120	HCO_3^i (mEq/L)	13
Potassium (mEq/L)	5.2	Base excess (mEq/L)	10.6
Chloride (mEq/L)	104	Anion Gap (mEq/L)	7.5
Calcium (mg/d/)	8.2	**Urinalysis**	
Phosphorus (mg/d/)	5.2	Gravity	1.009
C-reactive protein (mg/d/)	5.84	pH	5.5
Uric acid (mg/d)	8.9	Proteinuria	3+
Total Proteins	6.8	UPCR (g/GCR)	3.06
Albumin	3.1	Hematuria	3+
		Red blood cell (/HPF)	6-7
		RBC casts (/HPF)	4-6

Table 2. Laboratory workup

Sr. No.	Test Description	Test Result
1.	Peripheral smear	Mild anisopoikilocytosis, micrrocytes present with mild hypothermia
2.	Bone Marrow Aspiration	Inadequate erythroid response to anemia and mild plasmacytosis in bone marrow
3.	Serum protein electrophoresis	No abnormality detected
4.	Urine protein electrophoresis	No abnormality detected
5.	Electromyogram/Nerve conduction velocity study	Severe sensorimotor neuropathy asymmetrical, mixed type, involving lower limbs more than upper limbs

Table 3. Investigations flowchart during hospitalization

Day of Investigation	One month before admission	Day 1	Day 3	Day 7	Day 10	Day 12
White blood cell (/µL)	13100	8500		10,400	14,900	
Platelets	284	6.54		5.80	210	
Blood Urea		203	201	61	67	78
Sr Creatinine	0.98	7.6	7.5	3.9	1.9	2
eGFR		5.79				
Sodium		120	119	135	146	138
Potassium		5.7	5.2	4.1	3.4	4

10th Day of admission: She remained off dialysis for three days, and now her serum creatinine level has come down to 1.9 mg/dL. She continued to pour a good amount of urine. Now, we wanted to do a kidney biopsy; however patient, and her relatives did not consent and could not be convinced. 12th Day of admission: She left the hospital on oral prednisone and oral cyclophosphamide.

3. DISCUSSION

We successfully treated an elderly female patient with severe AAV and DAH with the immediate institution of haemodialysis, induction regimen of plasma exchange (PE) combined with intravenous methylprednisolone (CS) and cyclophosphamide (CYC) [5]. ANCA-associated vasculitis is a multisystem disease with more than 75% of patients with renal involvement presenting with rapidly progressive glomerulonephritis (RPGN). The etiology and pathogenesis of AAV are multifactorial and individuals are predisposed by genetics, environmental factors including drugs, and responses of the innate and adaptive immune system [6]. Randomized controlled trials in the past two decades have advanced the therapy of AAV and transformed AAV from a fatal disease to a chronic disease with relapsing course and concomitant morbidity. The mortality of AAV is very high in cases of acute disease. Strong predictors of increased mortality after admission are mechanical ventilation and admission to the intensive-care unit (ICU) [7]. Although our patient required ICU admission, mechanical ventilation, and hemodialysis, survived and had a remarkable renal recovery. It is essential to institute immediate therapies for severe AAV. Microscopic polyangiitis is the most prevalent cause of the P-ANCA pattern. A positive P-ANCA (or MPO) level in the blood confirms the diagnosis and can help differentiate MPA from WG. The P-ANCA test is positive in 50 percent to 75 percent of patients. The functional impairment of key organs, such as severe renal disease (creatinine>5.7 mg/dL), DAH, or another life-threatening disease, is described as a severe disease. DAH with pathologic capillaritis is the most common manifestation in patients who develop lung disease. Joint, skin, peripheral nervous system, and gastrointestinal involvement are also relatively common.

Hemoptysis, anemia, widespread lung infiltration , and sudden respiratory failure are symptoms of DAH, a unique clinicopathologic syndrome of pulmonary bleeding originating from pulmonary microcirculation. The most common cause of DAH is pulmonary capillaritis, linked to systemic vasculitis and findings like anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis, anti-GBM disease, systemic lupus erythematosus (SLE), and collagen vascular diseases. It can also occur due to other factors, such as the use of certain medicines or transplantation. Congestive heart failure, pneumonia, localized pulmonary bleeding, and other acute manifestations of diffuse parenchymal lung disease were all ruled out [8-10].

Clinical circumstances suggestive of vasculitis in this case were: 1) DAH, 2) RPRF, 3) pulmonary-renal syndrome, 4) peripheral neuropathy and 5) multisystem disease [11,12]. Although a confident diagnosis can sometimes be reached without a tissue biopsy, a suggestive biopsy is still required for a definitive diagnosis; however, we could not get a kidney biopsy done as the patient was not willing [11]. Because DAH is a medical emergency, a careful and systematic approach to DAH diagnosis is essential for proper therapy, to establish the diagnosis and determine the underlying cause. DAH was diagnosed based on particular clinical, laboratory, radiologic, and pathologic characteristics.

Patients with systemic vasculitis had a 75% death rate before immunosuppressive treatment was introduced. Despite significant advances

over the previous two decades, individuals with systemic vasculitis who get therapy still have a high death rate. Patients with severe illness may benefit from a combination of CYC, CS, and PE treatment, according to recent research [12,13]. In patients with severe renal impairment and DAH, adding plasma exchange treatment to the conventional cyclophosphamide plus corticosteroid regimen has been demonstrated superior to high-dose, pulsed, intravenous steroids in restoring renal function. In this patient, the disease was controlled with plasma exchange and CYC plus CS, and we succeeded in weaning the patient quite early and achieving renal recovery with stoppage of hemodialysis support, sound urine output, and serum creatinine 2 mg/dl on discharge [14-18].

4. CONCLUSION

Our present findings suggest that immediate treatment of severe AAV with DAH with plasma exchanges and intravenous steroids and cyclophosphamide is effective and lifesaving and induced remission of severe AAV in our elderly patient and rendered remarkable renal recovery.

CONSENT

As per international standard or university standard, patients' written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical approval has been collected and preserved by the author(s).

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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