Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Internal Medicine

Pauci-Immune form of Pulmonary Renal Syndrome with Negative ANCA and Anti-MBG: A Case Report

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DOI: 10.36347/sjmcr.2024.v12i03.025 | **Received:** 14.01.2023 | **Accepted:** 19.02.2024 | **Published:** 29.03.2024

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Abstract **Case Report**

Background*:** Pulmonary renal syndrome (PRS) is a diagnostic and therapeutic emergency defined by the association of alveolar haemorrhage and rapidly progressive glomerulonephritis. The primary causes of PRS are dominated by ANCA-associated vasculitis (60-70% of cases) and Goodpasture's syndrome. The pauci-immune variant of this syndrome (ANCA-negative) is rare, and its management lacking well-established guidelines. We herein present the case of a patient with renal and pulmonary manifestations of ANCA-negative vasculitis. ***Case presentation: A 42-year-old woman with no prior medical history presented with acute dyspnoea with hemoptysis associated with purpuric lesions on both lower limbs and macroscopic hematuria. Initial laboratory values revealed a normochromic normocytic anemia at 6.1 g/dL, CRP of 264 mg/L, renal failure with a GFR of 33 mL/min/1.73m², active urine sediment and 24-hour urine protein at 2.53g/24h. The anti-nuclear antibody was negative, and routine enzyme-linked immunosorbent assay (ELISA) were negative for MPO-ANCA, PR3-ANCA and anti-MBG. A thoracic angioscan revealed alveolar hemorrhage, while cardiac echocardiography indicated an acute cor pulmonale. Due to the patient's clinical instability, a kidney biopsy was not performed. The diagnosis of ANCA-negative vasculitis was suspected. Management of the patient required several stays in intensive care, including pulse therapy with a high dose of methylprednisolone at 1000 mg/daily for 3 days followed by oral prednisone 1 mg/kg per day, appropriate antibiothics, multiple transfusions, and plasma exchanges due to corticosteroid resistance. The patient's clinical status showed an initial moderate respiratory improvement before succumbing to an acute respiratory failure. ***Conclusion***: There is a pressing need to promptly establish a well-structured management approach to ensure a more favorable prognosis for this uncommon condition.

Keywords: Pulmonary renal syndrome (PRS), Goodpasture's syndrome, Anti-MBG.

INTRODUCTION

Pulmonary renal syndrome (PRS) is a diagnostic and therapeutic emergency defined by the association of alveolar haemorrhage and rapidly progressive glomerulonephritis. The primary causes of PRS are dominated by ANCA-associated vasculitis (60-70% of cases) and Goodpasture's syndrome [1]. The pauci-immune variant of this syndrome (ANCA-negative) is rare, and its management lacking well-established guidelines. We herein present the case of a patient with renal and pulmonary manifestations of ANCA-negative vasculitis.

CASE PRESENTATION

A 42-year-old woman with no prior medical history presented with acute dyspnoea with hemoptysis associated with purpuric lesions on both lower limbs and macroscopic hematuria. Initial laboratory values revealed a normochromic normocytic anemia at 6.1 g/dL, CRP of 264 mg/L, renal failure with a GFR of 33 mL/min/1.73m², active urine sediment and 24-hour urine protein at 2.53g/24h. The anti-nuclear antibody was negative, and routine enzyme-linked immunosorbent assay (ELISA) were negative for MPO-ANCA, PR3-ANCA and anti-MBG.

A thoracic angioscan revealed alveolar hemorrhage, while cardiac echocardiography indicated an acute cor pulmonale. Due to the patient's clinical instability, a kidney biopsy was not performed. The diagnosis of ANCA-negative vasculitis was suspected. Management of the patient required several stays in intensive care, including pulse therapy with a high dose of methylprednisolone at 1000 mg/daily for 3 days followed by oral prednisone 1 mg/kg per day, appropriate antibiotics, multiple transfusions, and plasma exchanges due to corticosteroid resistance. The

patient's clinical status showed an initial moderate respiratory improvement before succumbing to an acute respiratory failure.

Table 1: Pulmonary-Renal Syndrome with Negative ANCAs: literature review

	Author, year	Sex, age	Renal involvement	Pulmonary involvement	Treatment	Response
1	Wang CC, 2009 [8]	M, 66	creatinine, 5.8 mg/dl, active urine sediment KB: necrotizing vasculitis with glomerular crescent IFD: negative	Hemoptysis CT: (DAH) Bronchoscopy: confirmation of DAH	3 MP pulses 500 mg/d and ATB 6 sessions of Plex Maintenance: prednisone 60 mg/d + MMF	Improvement of hemoptysis Stabilization of renal function
2	Sandhu, 2010 [9]	F,76	Renal failure + nephritic Syndrome KB: pauci-immune proliferative GN + necrosis	Hemoptysis + severe hypoxemia X-ray: bilateral infiltrations Bronchoscopy: confirmation of DAH	ICU and intubation 3 MP pulses 1 g/d Hemodialysis and ATB 6 sessions of Plex CYC+ prednisone	Extubation Improvement of renal function
3	Yamaguchi, 2013 [10]	F,76	Creatinine: 4.04 mg/dl, active urine sediment KB: proliferative GN and glomerulosclerosis	Hemoptysis CT: DAH	ICU and intubation 3 MP pulses of 500 mg/d followed by 3 MP pulses of 250mg/d followed by 3 MP pulses of 125mg/ 3j followed by prednisolone 60 mg/ Hemodialysis, transfusion and ATB	No relapse within the first year
4	Saladi, 2018 [4]	M,85	renal failure KB: pauci-immune necrotizing glomerulonephritis	Hemoptysis CT: diffuse bilateral ground-glass opacities Bronchoscopy: confirmation of HAH	ICU and intubation MP pulses Hemodialysis and ATB 7 sessions of Plex CYC+ prednisone	Improvement followed by relapse and initiation of palliative care
5	Our case, 2020	F,42	acute renal failure active urine sediment KB: not performed due to clinical instability	Hemoptysis CT: DAH	ICU and intubation 3 MP pulses 1g/d followed by prednisone 1mg/kg/d 2 sessions of Plex ATB + transfusion	Death

DAH: diffuse alveolar hemorrhage, MP: Methylprednisolone, ATB: antibiotics, plex: Plasma Exchange treatment, MMF: Mycophenolate mofetil, KB: kidney biopsy, ICU: intensive care unit, CYC: cyclophosphamide, GN: glomerulonephritis

DISCUSSION

PRS was first described by Goodpasture in 1919 in a patient presenting with alveolar hemorrhage and rapidly progressive glomerulonephritis.

Studies have shown that up to 70% of cases of PRS had anti-ANCA antibodies while anti-MBG antibodies were positive in 20% of cases [1]. Others studies have demonstrated that patients with ANCA-negative vasculitis exhibit a rapidly progressive glomerulonephritis akin to those with ANCA-positive vasculitis, while pulmonary signs are less frequent [2].

The pauci-immune variant of this syndrome is rare, its pathogenesis is not yet fully understood and its clinical presentation tend to be non-specific. Hemoptysis may be absent in 35% of patients with diffuse alveolar hemorrhage, and half of these patients may require mechanical ventilation [3].

Renal impairment usually revealed by hematuria and proteinuria, occasionally progressing to the advanced stage of end-stage renal failure [4].

Optimal management of ANCA-negative PRS has not been established, however immunosuppressive therapy is can be used, as it is the case for its ANCA-positive counterpart. Methylprednisolone pulse therapy has been utilized to achieve remission, either as a standalone treatment or in association with cyclophosphamide [5]. While plasmapheresis seems to be useful in an acute setting, its long-term efficacy in ANCA-negative patients is uncertain, though it is believed to have advantages due to the presence of unidentified serum antibodies [6, 7].

CONCLUSION

Our case underscores the similarity of the clinical presentation of PRS in both its ANCA-associated and pauci-immune forms. Further research is needed to develop a more in-depth therapeutic strategy for this particular entity.

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