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CASE REPORT

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Massive hemoptysis with end stage renal disease (ESRD): An initial symptom of rare disease

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Key Clinical Message

Microscopic polyangiitis is a rare autoimmune vasculitis, that could present with renal-pulmonary symptoms, posing diagnostic challenges in patients with preexisting kidney disease. Timely diagnosis is crucial to improve patient outcomes.

KEYWORDS

diffuse alveolar hemorrhage, end stage renal disease, massive hemoptysis, microscopic polyangiitis, p-ANCA, vasculitis

1 | INTRODUCTION

Microscopic polyangiitis (MPA) is an uncommon autoimmune vasculitis primarily affecting small blood vessels. It is characterized by inflammation and damage to these vessels, particularly in the kidneys and lungs. The pathophysiology involves neutrophil-mediated inflammation and the formation of cytokines, leading to endothelial damage.[1] This damage exposes surface antigens, including myeloperoxidase, triggering the production of anti-myeloperoxidase antibodies, also known as perinuclear antineutrophilic cytoplasmic antibodies (p-ANCA).[1] Being a pauci-immune disease, p-ANCA vasculitis does not often present with IgA nephropathy. This report presents a case of a 21-year-old male with advanced IgA nephropathy, who presented with massive hemoptysis and was finally diagnosed with MPA.

2 | CASE PRESENTATION

A 21-year-old male had been on peritoneal dialysis due to end-stage renal disease secondary to advanced IgA nephropathy diagnosed by renal biopsy 2 years ago.

He presented to the emergency room with shortness of breath, cough, and chills for the past 3 days. Symptoms included upper respiratory tract symptoms with fever and malaise off and on for approximately 1 year after being diagnosed with IgA nephropathy. However, this time he reported having blood-tinged sputum associated with a cough and need for oxygen supplementation. The patient also noted arthralgia a few weeks before this. Other medical illnesses included hypertension, heart failure with preserved ejection fraction, and a generalized seizure disorder due to posterior reversible encephalopathy syndrome. His renal biopsy performed 2 years ago showed 75% globular

glomerulosclerosis and no crescent, necrotizing lesions or endocapillary hypercellularity noted; immunofluorescence and ultrastructural studies demonstrated immune deposit with IgA, IgM, IgG, C3, and lambda light chain. Tubular interstitial fibrosis involved approximately 75% of the cortex. He tested negative for ANCA, ANA, HIV, and viral hepatitis at that time (Table 1).

3 | METHODS

During this hospitalization, his laboratory investigations revealed bi-cytopenia with a hemoglobin of 6.7 g/dL and platelets of 23 K/μL. No significant change in renal function. Multifocal pulmonary infiltrates were noted on chest x-ray. He received packed red cells and platelet transfusion and was started on antibiotics for suspected pneumonia. Computed tomography (CT) chest angiogram and venogram later demonstrated extensive patchy consolidation throughout both lungs most pronounced in both lower lobes and right middle lobes. Differential diagnoses include severe multifocal pneumonia, pulmonary edema, or alveolar hemorrhage (Figure 1).

Infectious workup, including influenza and COVID-19, was negative. The patient tested positive for anti-myeloperoxidase antibodies (p-ANCA) and negative for anti-proteinase-3 antibodies (c-ANCA) and anti-GBM. His overall clinical picture was highly suggestive of MPA.

Despite medical interventions with methylprednisolone 1 g intravenously daily, rituximab 1 g intravenously one time for the treatment of MPA, and inhaled tranexamic acid, his symptoms continued to deteriorate. He developed respiratory failure from persistent hemoptysis, which required transfusions, necessitating intubation.

The patient's mode of dialysis was switched to hemodialysis for convenience while intubated. A bronchoscopy was done, which showed normal airway anatomy with serosanguinous secretion more prominent in the right lung—serial aliquots were collected and confirmed diffuse alveolar hemorrhage (DAH). Two more medications were added for the treatment of MPA, mycophenolate mofetil 3 g daily and cyclophosphamide 4 mg/kg/day for 3 days.

TABLE 1 Laboratory trend this visit compares with 2 years ago.

	2 years ago	This visit	Normal range
Hemoglobin (g/dL)	8.8	6.7	11.2–15.7
Hematocrit	26.5	19.5	44.1–44.9
MCV (fL)	88	88.2	79.4–94.8
White blood cells (k/μL)	10.2	13.35	4.23–9.07
Platelets (k/μL)	153	23	2.3–15.9
Prothrombin time (PT) (s)	13.4 (H)	10.4	10.1–12.5
Partial thromboplastin time (PTT) (s)	34.5	27.7	25.1–36.5
International normalized ratio (INR)	1.19	0.92	Critical high>5
BUN (mg/dL)	40	78	6–20
Creatinine (mg/dL)	13.6	14.6	0.5–1.2
Lactic acid (mmol/L)	NA	1.0	0.5–2.2
Total bilirubin (mg/dL)	0.4	0.3	0–1.0
Anti-HIV	Negative	Negative	Negative
Viral hepatitis panel	Negative	Negative	Negative
ANA	Negative	Positive	Negative
C3 level (mg/dL)	NA	61 (L)	90–180
C4 level (mg/dL)	NA	16	10–40
Antiproteinase-3 Ab (c-ANCA)	NA	<0.2	0.2–1.0
Antimyeloperoxidase Ab (p-ANCA)	NA	1.5 (H)	0.2–1.0

Abbreviations: H, high; L, low; NA, not available.

4 | RESULTS

After 6 days of the above specific treatment, with a decrease in pulmonary infiltrates and hemoptysis, the patient was successfully extubated. Methylprednisolone gradually tapered down; the patient was discharged on mycophenolate mofetil 2 g daily and prednisone 20 mg daily. At a 2-week follow-up, the patient no longer had shortness of breath; the prednisone dose was tapered down and he remained on 2 g of mycophenolate mofetil.

5 | DISCUSSION

DAH is not an uncommon life-threatening pulmonary manifestation in MPA.[1] With bilateral pulmonary infiltrations and a drop in hemoglobin, pulmonary hemorrhage should be taken into concern. The gold standard to confirm alveolar hemorrhage is bronchoalveolar lavage (BAL). The challenging part is the diagnosis of ANCA-associated systemic vasculitis as patients typically present with nonspecific prodromal symptoms—fever, malaise, myalgia, weight loss, and arthralgia[1]—which may last for weeks to months before developing specific organ involvement.[2] Similarly, our patient had some nonspecific symptoms prior to developing hemoptysis which led to further investigation, which included CT chest and BAL. Altogether with a positive p-ANCA and negative anti-GBM, the diagnosis of MPA was made in our patient

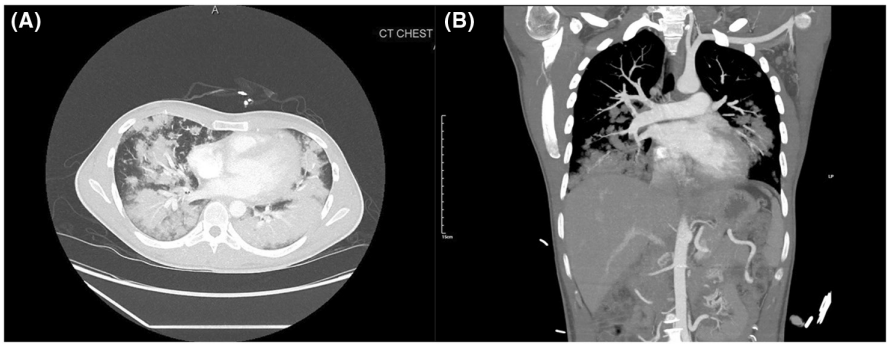

FIGURE 1 Initial computed tomography angiography (CTA) of the chest (A) axial view and (B) coronal view revealed severe patchy consolidative infiltrations throughout both lungs most pronounced in lower lobes right middle lobe.

based on 2022 American College of Rheumatology (ACR) classification criteria.

False positive p-ANCA results could be from several causes including SLE patient with positive ANA, infection such as subacute bacterial endocarditis and other forms of bacteremia, drug-induced ANCA-associated vasculitis including propylthiouracil, methimazole, carbimazole, hydralazine, minocycline. At the time of the initial diagnosis, the patient was not on any of these medications, and there was no evidence of infection eventually from blood cultures and respiratory cultures.[3]

The question in our patient lies in whether he developed the pulmonary-renal syndrome. The syndrome is defined as the combination of DAH and rapidly progressive glomerulonephritis (RPGN).[4] The mortality rate can be as high as 50% even with treatment.[5] ANCA-associated vasculitis, including MPA, is one of the major causes of the syndrome. Acute respiratory failure occurs in approximately 50% of cases.[5] However, our patient had been on peritoneal dialysis for over a year for ESRD secondary to advanced IgA nephropathy, negating a clinical benefit to a renal biopsy beyond diagnostic confirmation.

Although renal involvement in MPA is pauci-immune glomerulonephritis, some studies showed that IgA deposition can be observed in MPA.[6,7] There have also been reports of coexistence or concomitance of IgA nephropathy with both negative and positive ANCA-associated systemic vasculitis (GPA, MPA, and EGPA).[8–10]

In patients with asymptomatic hematuria with normal kidney function, ANCA-positive glomerulonephritis diagnosis may be delayed; they may have been diagnosed with IgA nephropathy. However, ANCA-positive patients have a higher risk of progressing to ESRD.[8] With the previous renal biopsy interpretation, our patient most likely has coexisting IgA nephropathy and p-ANCA-positive systemic vasculitis (MPA) that presented with hemoptysis. However, some studies report kidney-limited vasculitis patients are part of GPA/MPA spectrum because the renal histopathologic results are undifferentiated from those of the glomerulonephritis in GPA/MPA and because some patients, who present with disease limited to the kidney could eventually exhibit extrarenal manifestation of either GPA/MPA. The active delayed extra-renal disease could occur during chronic renal failure or dialysis.[11]

The mainstay treatment of MPA involves systemic corticosteroids and other immunosuppressive agents.[1,4,5] Due to the possibility of having pulmonary-renal syndrome from MPA, our patient was treated accordingly with pulse methylprednisolone for remission induction (1000 mg for 3–5 days) and rituximab. Conforming to the Remission in AAV trial (RAVE trial), rituximab showed comparable results to cyclophosphamide in achieving remission.[1] Plasmapheresis is also effective in cases of pulmonary hemorrhage and severe renal disease.[1,4] Low-dose glucocorticoids with azathioprine, rituximab, methotrexate, or mycophenolate mofetil are given for maintenance therapy.[5] Given the lower risk of relapse, rituximab is recommended by ACR for maintenance compared with azathioprine and methotrexate.[12]

6 | CONCLUSION

Unexplained hemoptysis in young patients with various constitutional symptoms should raise concerns for alveolar hemorrhage due to ANCA vasculitis. Clinicians should also keep in mind the possible diagnosis of pulmonary-renal syndrome and its rapid clinical deterioration. Prompt recognition is vital to improve patient outcomes and effectively manage the disease. Even though coexisting or co-occurrence of ANCA vasculitis and IgA nephropathy is rare, it is possible. This case underscores the challenges in diagnosing and managing MPA and emphasizes the need for a multidisciplinary approach to improve patient outcomes.

AUTHOR CONTRIBUTIONS

Sakditad Saowapa: Conceptualization; data curation; formal analysis; methodology; project administration. **Nattanicha Chaisrimaneepan:** Investigation; methodology; writing – original draft; writing – review and editing. **Yaw Adu:** Validation; writing – original draft; writing – review and editing. **Pitchaporn Yingchoncharoen:** Formal analysis; resources; validation. **Jerapas**

Thongpiya: Writing – review and editing. **Amanda L. Bell:** Validation; writing – review and editing. **Natchaya Polpichai:** Resources; software; supervision; validation. **Pharit Siladech:** Data curation; funding acquisition; methodology; project administration; resources. **J. Drew Payne:** Supervision; validation; visualization; writing – review and editing.

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CONFLICT OF INTEREST STATEMENT

None declared.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

ETHICS STATEMENT

All subjects gave their informed consent for inclusion before they participated in the study. The study was conducted in accordance with the Declaration of Helsinki.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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REFERENCES

1. Hashmi MF, Jain V, Tiwari V. Microscopic Polyangiitis. *StatPearls [Internet]*. StatPearls Publishing; 2023. https://www.ncbi.nlm.nih.gov/books/NBK531484/
2. Falk RJ, Hogan S, Carey TS, Jennette JC. Clinical course of anti-neutrophil cytoplasmic autoantibody-associated glomerulonephritis and systemic vasculitis. The glomerular disease collaborative network. *Ann Intern Med*. 1990;113(9):656-663. doi:10.7326/0003-4819-113-9-656
3. Lionaki S, Blyth ER, Hogan SL, et al. Classification of antineutrophil cytoplasmic autoantibody vasculitides: the role of antineutrophil cytoplasmic autoantibody specificity for myeloperoxidase or proteinase 3 in disease recognition and prognosis. *Arthritis Rheum*. 2012;64(10):3452-3462.
4. Papiris SA, Manali ED, Kalomenidis I, Kapotsis GE, Karakatsani A, Roussos C. Bench-to-bedside review: pulmonary-renal syndromes—an update for the intensivist. *Crit Care*. 2007;11(3):213. doi:10.1186/cc5778
5. Boyle N, O'Callaghan M, Ataya A, et al. Pulmonary renal syndrome: a clinical review. *Breathe (Sheff)*. 2022;18(4):220208. doi:10.1183/20734735.0208-2022
6. Haas M, Eustace JA. Immune complex deposits in ANCA-associated crescentic glomerulonephritis: a study of 126 cases. *Kidney Int*. 2004;65(6):2145-2152. doi:10.1111/j.1523-1755.2004.00632.x
7. Bantis C, Stangou M, Schlaugat C, et al. Is presence of ANCA in crescentic IgA nephropathy a coincidence or novel clinical entity? A case series. *Am J Kidney Dis*. 2010;55(2):259-268. doi:10.1053/j.ajkd.2009.09.031
8. Yang YZ, Shi SF, Chen YQ, et al. Clinical features of IgA nephropathy with serum ANCA positivity: a retrospective case-control study. *Clin Kidney J*. 2015;8(5):482-488. doi:10.1093/ckj/sfv078
9. Kucuk A, Solak Y, Gaipov A, et al. Co-existing proteinase 3-antineutrophil cytoplasmic antibody-associated vasculitis with immunoglobulin a nephropathy. *Korean J Intern Med*. 2016;31(1):194-196. doi:10.3904/kjim.2016.31.1.194
10. Endo Y, Minato H, Taki R, et al. Myeloperoxidase-antineutrophil cytoplasmic antibody-negative microscopic polyangiitis with pulmonary haemorrhage and IgA nephropathy. *Case Rep Dermatol*. 2011;3(1):22-27. doi:10.1159/000324422
11. Woodworth TG, Abuelo JG, Austin HA 3rd, Esparza A. Severe glomerulonephritis with late emergence of classic Wegener's granulomatosis. Report of 4 cases and review of the literature. *Medicine*. 1987;66(3):181-191. doi:10.1097/00005792-198705000-00002
12. Chung SA, Langford CA, Maz M, et al. 2021 American College of Rheumatology/Vasculitis Foundation guideline for the management of antineutrophil cytoplasmic antibody-associated vasculitis. *Arthritis Rheumatol*. 2021;73(8):1366-1383. doi:10.1002/art.41773

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