

Case Report

Interstitial lung disease unmasked as myeloperoxidase-antineutrophil cytoplasmic antibody-associated vasculitis following acute kidney injury

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ABSTRACT

Small-vessel vasculitis driven by antineutrophil cytoplasmic antibodies (ANCA) is a severe, systemic autoimmune condition whose clinical behavior can be notoriously unpredictable. When the offending antibody targets myeloperoxidase (MPO), the disease most commonly manifests as microscopic polyangiitis (MPA), a necrotizing vasculitis that, unlike its granulomatous counterparts, destroys vessel walls without forming granulomas. We report a 49-year-old woman who had been living with what appeared to be idiopathic interstitial lung disease (ILD) for a full year before presenting to our emergency department in florid acute respiratory failure. She required emergent intubation for severe metabolic acidosis and, within 48 hours of admission, her kidneys, previously unaffected, collapsed into acute kidney injury (AKI) necessitating hemodialysis (HD). Serological testing came back strongly positive for MPO-ANCA, and renal biopsy showed crescentic glomerulonephritis (GN) in a pauci-immune pattern, confirming the diagnosis. We initiated plasmapheresis, high-dose pulse methylprednisolone, and cyclophosphamide, with rituximab planned as sequential therapy. Despite a brief biochemical response at three weeks, her clinical trajectory proved irreversible and she died. A high index of suspicion for underlying vasculitis is essential in any patient with established pulmonary fibrosis who develops sudden, unexplained renal deterioration.

Keywords: ANCA-associated vasculitis, Myeloperoxidase, Interstitial lung disease, Crescentic glomerulonephritis, Acute kidney injury, Microscopic polyangiitis

INTRODUCTION

MPO-ANCA-associated vasculitis occupies a peculiar niche in the autoimmune disease spectrum, being simultaneously destructive and diagnostically elusive.^{1,2} Its most common clinical expression, microscopic polyangiitis (MPA), produces necrotizing inflammation of small vessels without the granuloma formation that distinguishes it from granulomatosis with polyangiitis (GPA) or eosinophilic granulomatosis with polyangiitis (EGPA). This single histological difference carries enormous diagnostic weight, yet the distinction is often made only after biopsy in practice, frequently once an organ has already been damaged.³

Pulmonary and renal involvement, the two organs most commonly affected, do not always declare themselves simultaneously. In some patients, lung disease smolders quietly for months or even years before the kidneys become involved; in others, the reverse holds true. The patient described here exemplifies the former pattern: a year of seemingly stable, presumably idiopathic interstitial lung disease, followed by a renal event that unmasked the underlying vasculitis only when it was already far advanced.^{1,4}

CASE REPORT

A 49 year old woman with a one-year history of interstitial lung disease was brought to our emergency department

reporting a dry, non-productive cough of ten days' duration that had, in the 24 hours prior to arrival, progressed to breathlessness at rest. On examination she was markedly tachypneic. Arterial blood gas (ABG) analysis showed severe metabolic acidosis: pH 7.27, partial pressure of carbon dioxide (PaCO₂) 17.8 mmHg, partial pressure of oxygen (PaO₂) 132 mmHg, bicarbonate (HCO₃) 8 mmol/L, and oxygen saturation (SpO₂) 99% on supplemental oxygen. Given the severity of her respiratory distress, she was intubated and placed on mechanical ventilation without delay. The working impression at that point was acute exacerbation of her known ILD, and she was started empirically on antibiotics alongside antifibrotic therapy.

Initial bloodwork revealed a hemoglobin (Hb) of 4.9 g/dl, severe enough to warrant packed red blood cell (PRBC) transfusion, with a total leukocyte count (TLC) of 10,790/mm³ and platelets of 214,000/mm³. Renal function was entirely normal on admission: serum urea 37.8 mg/dl and creatinine 0.73 mg/dl. That changed within 48 hours. Repeat testing showed creatinine had risen to 12.04 mg/dl and urea to 364.1 mg/dl, a trajectory consistent with rapid-onset intrinsic renal failure. Hemodialysis was started the same day. All laboratory findings are summarized in Table 1.

Table 1: Summary of key laboratory investigations with reference values.

Investigation	Admission value	Repeat (48 hours)	Reference range
Hemoglobin (Hb) (g/dl)	4.9	-	12-16
Total leukocyte count (TLC) (/mm³)	10,790	-	4,000-11,000
Platelet count (/mm³)	214,000	-	150,000-400,000
Serum urea (mg/dl)	37.8	364.1	15-40
Serum creatinine (mg/dl)	0.73	12.04	0.5-1.1
Urine albumin-to-creatinine ratio (mg/g)	750	-	Less than 30
Urine sodium (mEq/l)	83	-	40-220
Fractional excretion of sodium (FeNa) (%)	18.4	-	Less than 1 (prerenal)
Erythrocyte sedimentation rate (ESR) (mm/hour)	120	-	Less than 20
C-reactive protein (CRP) (mg/l)	322.74	-	Less than 5
Serum ferritin (ng/ml)	1096	-	12-150
pH (arterial blood gas)	7.27	-	7.35-7.45
PaCO₂ (mmHg)	17.8	-	35-45
HCO₃ (mmol/l)	8	-	22-26
MPO-ANCA index	4.37 (+++) Positive	-	Negative (less than 1.0)
PR3-ANCA index	0.37 Negative	-	Negative (less than 1.0)
Anti-GBM antibody index	0.21 Negative	-	Negative (less than 1.0)
Anti-nuclear antibody (ANA) by immunofluorescence	3+ Speckled	-	Negative
ANA blot (U1-RNP)	Positive	-	Negative
Serum urea at week 3 (mg/dl)	-	25.7	15-40
Serum creatinine at week 3 (mg/dl)	-	1.18	0.5-1.1

Hb: hemoglobin; TLC: total leukocyte count; FeNa: fractional excretion of sodium; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; PaCO₂: partial pressure of carbon dioxide; HCO₃: bicarbonate; MPO-ANCA: myeloperoxidase anti-neutrophil cytoplasmic antibody; PR3-ANCA: proteinase-3 ANCA; anti-GBM: anti-glomerular basement membrane; ANA: anti-nuclear antibody; U1-RNP: U1 ribonucleoprotein.

Urinalysis showed abundant red cells, triple-positive hematuria, trace glycosuria, and proteinuria; the urine albumin-to-creatinine ratio was markedly elevated at 750 mg/g. Random urine sodium was 83 mEq/l and the fractional excretion of sodium (FeNa) reached 18.4%, both findings pointing toward intrinsic renal pathology rather than a prerenal state. Inflammatory markers were substantially elevated: erythrocyte sedimentation rate (ESR) 120 mm/hour, C-reactive protein (CRP) 322.74

mg/l, and ferritin 1096 ng/ml. Abdominal ultrasonography and echocardiography were both normal. High-resolution computed tomography (HRCT) of the thorax showed a usual interstitial pneumonia (UIP) pattern, with bilateral subpleural reticular opacities, honeycombing, and traction bronchiectasis (Figure 1).

The autoimmune panel was central to establishing the diagnosis. Anti-nuclear antibodies (ANA) by immunofluorescence were positive at 3+ in a speckled

pattern, with a positive ANA blot for U1 ribonucleoprotein (U1-RNP). The ANCA line blot assay demonstrated the following results: flow control (FC) and cutoff control (Cut) bands were both valid, confirming assay integrity. Proteinase-3 ANCA (PR3-ANCA) returned negative at an index of 0.37. Myeloperoxidase ANCA (MPO-ANCA) returned strongly positive at an index of 4.37, reported as triple-positive (+++). Anti-glomerular basement membrane (anti-GBM) antibody was negative at an index of 0.21. Strongly positive MPO-ANCA together with negative PR3-ANCA and negative anti-GBM pointed toward MPO-ANCA-associated vasculitis rather than GPA or anti-GBM disease.



Figure 1: High-resolution computed tomography (HRCT) of the thorax in lung window settings demonstrating a usual interstitial pneumonia (UIP) pattern. Arrow A indicates honeycomb cysts within the right lower lobe with subpleural predominance. Arrow B indicates traction bronchiectasis within the fibrotic parenchyma of the right lung mid-zone. Arrow C indicates dense honeycomb cysts within the reticular opacities of the left upper lobe. Arrow D indicates cystic honeycombing in the left lower lobe. Patient-identifying information has been redacted.

Despite supportive management, renal function continued to deteriorate, necessitating daily hemodialysis. Renal biopsy demonstrated crescentic glomerulonephritis (Figure 2), and immunofluorescence of the biopsy specimen revealed a pauci-immune pattern (Figure 3). These clinical and histopathological findings confirmed the diagnosis of MPO-ANCA-associated vasculitis.

Following confirmation of the diagnosis, intravenous methylprednisolone pulse therapy was initiated, followed by oral corticosteroids and intravenous cyclophosphamide. The patient also underwent one cycle of plasmapheresis. Intravenous rituximab was planned as sequential B-cell-depleting therapy following rheumatology consultation. Renal parameters showed transient biochemical improvement by the third week (urea 25.7 mg/dl; creatinine 1.18 mg/dl). Despite this renal recovery, however, her respiratory status continued

to deteriorate, and she died of progressive respiratory failure shortly thereafter, an outcome consistent with the poor prognosis of MPO-ANCA vasculitis when pulmonary and rapidly progressive renal involvement occur simultaneously at presentation.

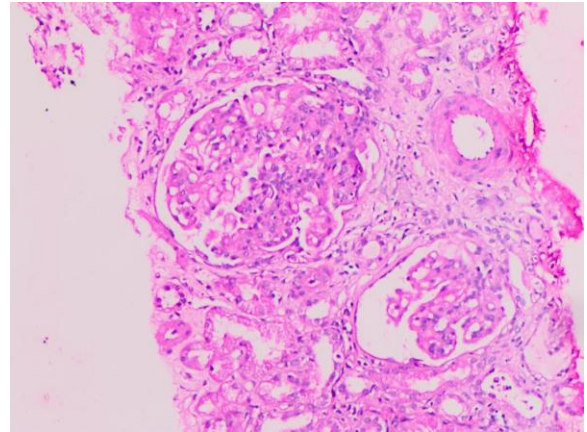


Figure 2: Renal biopsy showing crescentic glomerulonephritis. Hematoxylin and eosin (H&E) stain, 40x magnification. Cellular crescent formation compressing the glomerular tuft is evident, consistent with rapidly progressive glomerulonephritis. Sections were additionally evaluated using periodic acid-Schiff (PAS), Masson Trichrome, and Silver methenamine stains

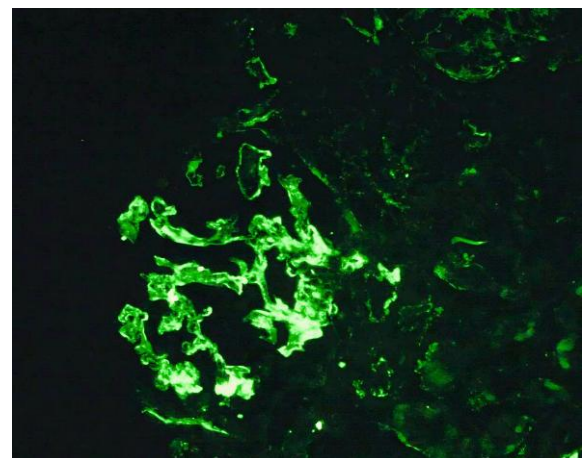


Figure 3: Immunofluorescence microscopy of the renal biopsy specimen, 40x magnification, using fluorescein isothiocyanate (FITC)-conjugated antisera. The image demonstrates a pauci-immune pattern with absent or minimal immunoglobulin and complement deposition along glomerular capillary walls, the hallmark finding of ANCA-associated glomerulonephritis.

DISCUSSION

The diagnostic course in this case is not unusual. MPO-ANCA vasculitis has a well-established tendency to present first with pulmonary involvement, and when it

does, the lung disease can mimic idiopathic pulmonary fibrosis closely enough that no further workup is pursued for months or years. This patient carried a diagnosis of ILD for a full year before her kidneys revealed the underlying systemic process. The literature documents this pattern repeatedly: pulmonary disease, particularly ILD, preceding the renal manifestations of vasculitis, sometimes by a significant interval.¹⁻³ A 2024 cohort study by Salvati et al. demonstrated that MPO-ANCA titers measured at the time of ILD diagnosis significantly predicted subsequent renal involvement, suggesting that ANCA levels in patients with unexplained pulmonary fibrosis should be monitored longitudinally rather than tested once and forgotten.¹ Practically, this means MPO-ANCA testing belongs in the standard workup for unexplained pulmonary fibrosis, not reserved as an afterthought for when kidney function deteriorates.³

The disease course can move quickly once renal involvement appears, as it did here. Rapidly progressive glomerulonephritis with pauci-immune crescentic changes on biopsy, combined with a UIP pattern on HRCT and MPO-ANCA positivity, constitutes one of the highest-risk clinical phenotypes in the ANCA disease spectrum.^{2,4} A long-term follow-up study by Kim et al, published in 2023, reported 5-year and 10-year overall survival rates of only 73.5% and 42.0% respectively among patients with MPA-associated ILD, with older age and elevated bronchoalveolar lavage (BAL) neutrophil counts emerging as independent predictors of mortality.⁴ Similar findings have been corroborated by Zhao et al and Song et al, who described comparable trajectories of isolated pulmonary disease progressing to severe renal failure, with the UIP pattern on HRCT consistently emerging as a marker of poor prognosis.^{5,6} A 2021 systematic review and meta-analysis by Zhou et al further confirmed that the presence of ILD significantly worsens mortality outcomes in ANCA-associated vasculitis.⁷ Our patient's course illustrates this dissociation starkly: although her renal parameters recovered with treatment, she succumbed to progressive respiratory failure, underscoring that in MPA-associated ILD it is often the lung, rather than the kidney, that ultimately determines survival.

Current guidelines for severe ANCA-associated vasculitis recommend high-dose corticosteroids combined with either rituximab or cyclophosphamide for treatment. The landmark Rituximab versus Cyclophosphamide for ANCA-Associated Vasculitis (RAVE) and Rituximab versus Cyclophosphamide in ANCA-Associated Renal Vasculitis (RITUXVAS) trials, both published in 2010, established that rituximab achieves remission at rates comparable to cyclophosphamide.^{8,9} The 2021 American College of Rheumatology (ACR) and Vasculitis Foundation (VF) guidelines, the most current evidence-based framework for managing ANCA-associated vasculitis, conditionally recommend rituximab over cyclophosphamide for remission induction in most patients with severe GPA and

MPA, citing comparable efficacy with a more favorable toxicity profile.¹⁰ In our patient, given the rapidity of multi-organ deterioration and resource availability at our center, cyclophosphamide was initiated alongside pulse steroids, with rituximab held in reserve as sequential therapy.

Plasmapheresis, or therapeutic plasma exchange (TPE), is one of the more contested interventions in this disease. Historically it was used in severe cases to remove circulating pathogenic antibodies and to allow time for immunosuppression to take effect, but the 2020 Plasma Exchange and Glucocorticoids in Severe ANCA-Associated Vasculitis (PEXIVAS) trial challenged this practice directly, finding that routine plasma exchange did not significantly reduce mortality or end-stage renal disease (ESRD) progression in most patients with severe ANCA-associated vasculitis.¹¹ This negative result changed practice in many centers, but a 2025 post-hoc analysis of the PEXIVAS dataset by Odler et al demonstrated that patients receiving plasma exchange showed greater improvement in estimated glomerular filtration rate (eGFR) in the early weeks after initiation of therapy, suggesting that selected patients with severe renal impairment may still derive early kidney benefit from this intervention.¹² A further consideration in our patient was the concurrent positivity for anti-U1 ribonucleoprotein (U1-RNP) antibodies in association with a speckled ANA pattern, a serological profile characteristic of mixed connective tissue disease and overlap syndromes. This was not regarded as an incidental finding; the coexistence of MPO-ANCA-associated vasculitis with connective-tissue-disease-related autoimmunity signaled a broad, antibody-mediated disease process and directly informed the decision to initiate therapeutic plasma exchange, with the aim of clearing circulating pathogenic antibodies while immunosuppression took effect. With crescentic glomerulonephritis and rapidly escalating organ failure compounding this rationale, plasma exchange was undertaken. It did not alter the eventual outcome, but within the framework of available evidence, it remained a defensible decision.

CONCLUSION

In conclusion, a diagnosis of idiopathic interstitial lung disease should always be regarded with some degree of caution. When such a patient subsequently develops acute kidney injury, particularly one that progresses as rapidly as described here, ANCA-associated vasculitis must be considered urgently and pursued aggressively. The gap between pulmonary onset and renal involvement is not a diagnostic reprieve; it represents a window of opportunity that, once closed, may not reopen. Early serological testing including MPO-ANCA, renal biopsy without undue delay, and prompt initiation of immunosuppressive therapy are essential, as in this disease, they may represent the difference between a chance at remission and a preventable death.

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