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A Race Against Time: Tocilizumab Rescue in Life-Threatening Antineutrophil Cytoplasmic Antibody (ANCA)-Associated Diffuse Alveolar Haemorrhage

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Abstract

Diffuse alveolar haemorrhage (DAH) is a potentially life-threatening manifestation of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), particularly when accompanied by glomerulonephritis. The role of interleukin-6 receptor blockade in AAV-associated DAH remains uncertain.

We report a previously healthy 24-year-old woman who presented with haemoptysis, dyspnoea, severe anaemia, acute kidney injury, haematuria, and bilateral pulmonary ground-glass opacities, raising strong clinical suspicion of DAH. Renal biopsy demonstrated necrotizing glomerulonephritis with focal crescent formation, and C-ANCA was positive at a titre of 1:80. Despite intravenous methylprednisolone (500 mg daily, Days 0-2), her respiratory condition deteriorated on Day 3, with oxygen saturation declining to 88% on room air. Cyclophosphamide was proposed but declined by the patient. Intravenous tocilizumab 400 mg was subsequently administered off-label, followed by rapid respiratory improvement, with oxygen saturation increasing to 96% on room air within 24 hours. However, renal dysfunction continued to progress, necessitating additional treatment with mycophenolate mofetil, plasma exchange, and rituximab. Serum creatinine improved to 150 µmol/L by discharge on Day 25.

At the latest follow-up in July 2026, the patient remained clinically well without relapse, with serum creatinine of 75 µmol/L, normal urinalysis, negative ANCA testing, and no immunosuppressive therapy since December 2025. This case highlights a striking temporal association between tocilizumab administration and rapid pulmonary improvement despite ongoing renal deterioration. IL-6 receptor blockade may have contributed to control of the acute inflammatory pulmonary process; however, causality cannot be established from a single case, and further investigation is warranted.

Categories: Rheumatology, Pulmonology, Nephrology
Keywords: anca-associated vasculitis (aav), diffuse alveolar haemorrhage, necrotizing glomerulonephritis, plasma exchange therapy, pulmonary renal syndrome, rituximab, tocilizumab

Introduction

Diffuse alveolar haemorrhage (DAH) is an uncommon but potentially fatal manifestation of systemic small-vessel vasculitis. In antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), DAH may occur together with rapidly progressive glomerulonephritis as part of a pulmonary-renal syndrome and can result in severe hypoxaemic respiratory failure [1].

The clinical significance of DAH is highlighted by its association with increased mortality in patients with AAV. In a 2024 analysis of the PEXIVAS trial involving 704 patients with severe AAV, DAH was identified in 191 patients (27.1%). One-year mortality was 12.0% among patients with DAH compared with 6.6% among those without DAH. These figures reflect the population enrolled in the PEXIVAS trial rather than the overall prevalence of DAH among all patients with AAV [2].

The diagnosis requires rapid integration of clinical, laboratory, radiological and, when appropriate, bronchoscopic findings. Haemoptysis, acute reduction in haemoglobin, hypoxaemia, and diffuse pulmonary infiltrates should raise immediate concern for DAH, particularly when associated with haematuria and acute kidney injury [3].

For organ- or life-threatening granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA), current international recommendations support remission-induction therapy with high-dose glucocorticoids in combination with either rituximab or cyclophosphamide [4,5]. The 2022 EULAR (European Alliance of

Associations for Rheumatology) recommendations also state that intravenous methylprednisolone pulses may be considered in patients with severely active disease, particularly those with severe renal involvement and/or DAH [4].

Tocilizumab is a humanized monoclonal antibody targeting the interleukin-6 receptor. Although IL-6 blockade has demonstrated efficacy across several immune-mediated inflammatory disorders, tocilizumab is not currently an established remission-induction therapy for GPA or MPA, and evidence supporting its use in AAV-associated DAH remains extremely limited [5].

Interest in IL-6 blockade as a rapidly acting anti-inflammatory intervention increased substantially during the COVID-19 pandemic. In the RECOVERY trial, tocilizumab, when added to usual care, most commonly including systemic corticosteroids, reduced 28-day mortality and the composite outcome of invasive mechanical ventilation or death among hospitalized patients with hypoxia and systemic inflammation [6]. These findings provided further clinical experience with IL-6 receptor blockade in selected severely ill patients, although careful assessment of infectious complications and treatment-related risks remains essential.

These findings, however, relate to COVID-19-associated hyperinflammation and cannot be directly extrapolated to immune-mediated pulmonary capillaritis or vasculitic alveolar haemorrhage.

We report a young woman with C-ANCA-positive necrotizing glomerulonephritis and life-threatening, clinically suspected DAH who received tocilizumab after cyclophosphamide was declined by the patient. The case is notable for rapid improvement in pulmonary manifestations temporally associated with tocilizumab administration despite continued deterioration of renal function, subsequently requiring plasma exchange and rituximab.

Case Presentation

A 24-year-old previously healthy woman presented to Jahra Hospital on 2 November 2023 (Day 0) with acute shortness of breath at rest, haemoptysis, and epistaxis. Ten days before hospital admission, she had developed an upper respiratory tract illness characterized by fever, sore throat, arthralgia, and myalgia, for which she had received antibiotic therapy without clinical improvement.

On admission, she appeared pale, anxious, and unwell and was tachypnoeic. Her blood pressure was 100/60 mmHg, pulse rate 124 beats/min, temperature 37.8°C, and oxygen saturation 93% on room air. Chest examination revealed bilateral fine crackles. Bilateral knee and wrist arthritis was also present.

Initial investigations demonstrated severe normocytic, normochromic anaemia, with a haemoglobin concentration of 6 g/dL compared with a baseline of 12 g/dL measured 10 days before hospital admission. The white-cell count was 8.0×10^9/L, with eosinophils accounting for 10%. Serum creatinine was 160 µmol/L compared with a baseline of approximately 60 µmol/L. The erythrocyte sedimentation rate (ESR) was 80 mm/h, C-reactive protein (CRP) was 8 mg/dL, and procalcitonin was 0.5 ng/mL. Urinalysis demonstrated microscopic haematuria, as shown in Table *1*.

Laboratory parameter	Patient result	Unit	Reference range
Haemoglobin	6.0	g/dL	12.0–16.0
White blood cell count	8.0	$\times 10^9$/L	4.0–11.0
Eosinophils	10	%	0–5
Serum creatinine	160	µmol/L	45–90
Erythrocyte sedimentation rate (ESR)	80	mm/h	0–20
C-reactive protein (CRP)	8	mg/dL	0.0–0.8
Procalcitonin (PCT)	0.5	ng/ml	0.0–0.05
Cytoplasmic ANCA (C-ANCA)	Positive; titre 1:80	Titre (unitless)	Negative (less than 1/20)
Urinalysis: microscopic haematuria	Present	Qualitative	Absent/negative

TABLE 1: Laboratory findings at presentation

Note: C-ANCA testing was requested on Day 0; however, the result was not immediately available due to laboratory processing time. The positive result (titre 1:80) was reported later during hospitalization.

Abbreviations: ANCA, antineutrophil cytoplasmic antibody; C-ANCA, cytoplasmic ANCA; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; PCT, procalcitonin.

The combination of haemoptysis, severe acute anaemia, hypoxaemia, acute kidney injury, and haematuria raised immediate concern for a pulmonary-renal syndrome, with AAV among the leading diagnostic considerations. Empirical antibiotic therapy was initiated while infectious screening and autoimmune investigations were undertaken. Because of the rapidly progressive respiratory presentation and concern for DAH, intravenous methylprednisolone 500 mg was administered within several hours of hospital admission (Day 0).

Despite initiation of intravenous methylprednisolone on Day 0, hypoxaemia persisted, with oxygen saturation on room air measuring 92% on Day 1 and 91% on Day 2. The patient's shock index on admission was 1.24. Given the persistent hypoxaemia and risk of rapid respiratory deterioration, she was transferred to the medical intensive care unit (ICU) for close respiratory and haemodynamic monitoring and received supplemental high flow nasal oxygen at a flow rate of 12-15 L/min. She remained spontaneously breathing and did not require non-invasive ventilation, endotracheal intubation, or invasive mechanical ventilation.

Chest radiography demonstrated bilateral mid- to lower-zone air-space opacities, more pronounced on the right (Figure *1*).

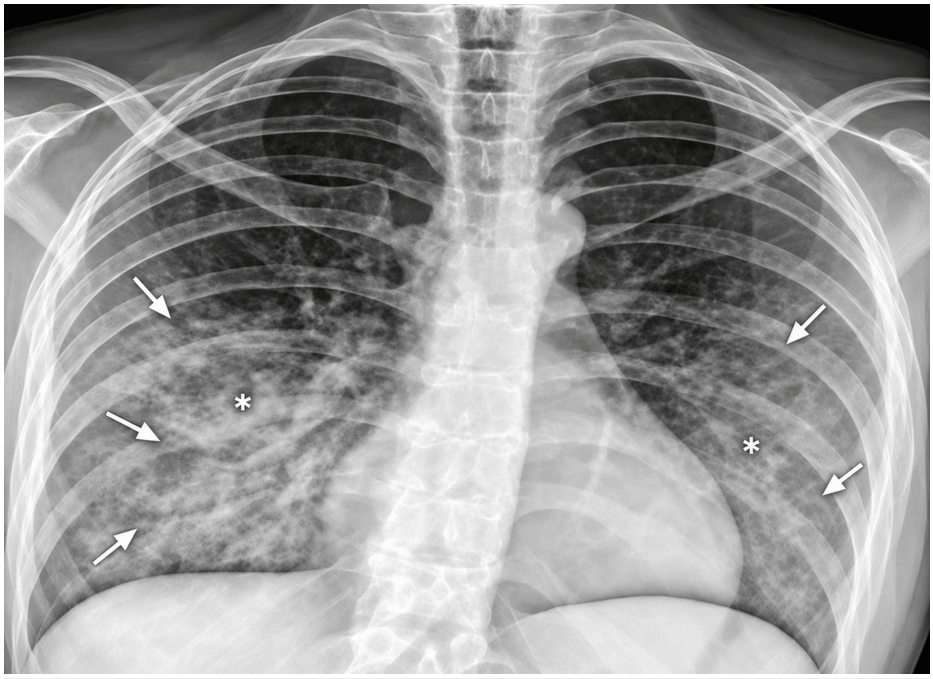


FIGURE 1: Admission chest radiograph.

Frontal chest radiograph obtained on admission (Day 0), demonstrating bilateral patchy air-space opacities predominantly involving the middle and lower lung zones, more pronounced on the right. White arrows indicate representative areas of pulmonary opacification, while asterisks (*) highlight more confluent regions of pulmonary involvement. These findings are consistent with an acute bilateral pulmonary process.

High-resolution computed tomography (HRCT) of the chest demonstrated diffuse bilateral ground-glass opacities with superimposed interlobular septal thickening, producing a crazy-paving appearance (Figure *2*). Although these findings are nonspecific and may also be encountered in pulmonary oedema, infection, or acute respiratory distress syndrome (ARDS), they were considered compatible with clinically suspected DAH in the context of haemoptysis, severe acute anaemia, hypoxaemia, and pulmonary-renal syndrome.

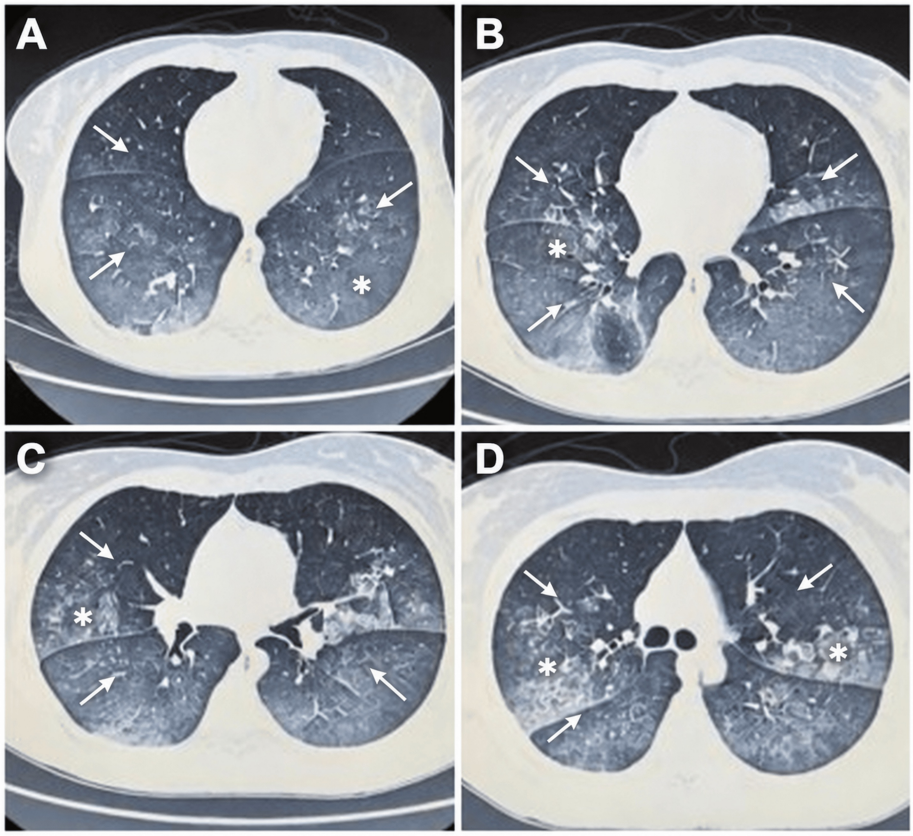


FIGURE 2: High-resolution computed tomography of the chest at presentation (Day 0).

Representative axial high-resolution computed tomography (HRCT) images demonstrating bilateral multifocal ground-glass opacities with superimposed interlobular septal thickening. (A) Bilateral ground-glass opacities predominantly involving the lower lung regions. (B) Multifocal ground-glass opacities with bilateral pulmonary involvement. (C) Ground-glass opacities with superimposed interlobular septal thickening, producing a crazy-paving appearance. (D) Bilateral patchy ground-glass opacities with heterogeneous pulmonary involvement. White arrows highlight representative areas of ground-glass opacification and interlobular septal thickening, while asterisks (*) indicate more confluent regions of pulmonary involvement. These findings are compatible with diffuse alveolar haemorrhage in the appropriate clinical context.

The patient received intravenous methylprednisolone 500 mg daily for three consecutive days (Days 0-2). Haemoptysis ceased, and the inflammatory arthritis improved; however, hypoxaemia persisted, with oxygen saturation on room air measuring 92% on Day 1 and 91% on Day 2. Renal function deteriorated concurrently, with serum creatinine rising from 160 µmol/L on admission to 202 µmol/L on Day 1 and 220 µmol/L on Day 2. The patient received two units of packed red blood cells (PRBCs) on Day 2, with no additional PRBC transfusions throughout hospitalization.

On Day 3, the patient's respiratory condition deteriorated further, with oxygen saturation declining to 88% on room air and serum creatinine increasing to 240 µmol/L. Arterial blood gas analysis confirmed hypoxaemia, with a PaO_2 of 55 mmHg on room air. Nephrology consultation was obtained because of worsening acute kidney injury, microscopic haematuria, and suspected glomerulonephritis. A 24-hour urine collection demonstrated proteinuria of 1.2 g/24 hours (reference range: 0-0.150 g/24 hours), and renal biopsy was subsequently performed. Cyclophosphamide was discussed with the patient as an established remission-induction option for severe organ- or life-threatening AAV; however, she declined this treatment.

Given the progressive, potentially life-threatening pulmonary involvement despite high-dose corticosteroid therapy, an individualized rescue strategy was considered following multidisciplinary discussion. Tocilizumab 400 mg was administered intravenously on Day 3 while corticosteroid therapy was continued. Its administration in this setting was off-label and was not intended to replace established AAV remission-induction therapy.

Within 24 hours following tocilizumab administration (Day 4), marked improvement in respiratory status was observed. Oxygen requirements decreased substantially, respiratory symptoms resolved, and oxygen

saturation increased from 88% on room air on Day 3 to 96% on room air on Day 4. Notably, this early pulmonary improvement occurred despite continued deterioration in renal function, with serum creatinine rising from 240 µmol/L on Day 3 to 300 µmol/L on Day 4 and subsequently reaching 320-325 µmol/L (reference range: 45-90 µmol/L). This contrasting pulmonary and renal course represented a striking clinical observation (Table 2).

Day/assessment	SpO_2 room air (%)	HR (beats/min)	Hb (g/dL)	Creatinine (µmol/L)	Steroid (mg/day)*	Clinical/imaging	Main intervention
Day 0	93	124	6.0	160	500	Dyspnoea, haemoptysis, epistaxis; bilateral infiltrates on CXR/HRCT	IV methylprednisolone 500 mg; admission
Day 1	92	92	5.7	202	500	Dyspnoea; urinalysis: RBCs 10–15/HPF, blood +++	IV methylprednisolone 500 mg
Day 2	91	95	6.2	220	500	Dyspnoea; persistent microscopic haematuria	IV methylprednisolone 500 mg; PRBC ×2 (only transfusion)
Day 3	88	130	10.8	240	60	Respiratory deterioration; room-air ABG PaO_2 55 mmHg; P/F 262	Tocilizumab 400 mg IV; nephrology review
Day 4	96	92	11.4	300	60	Rapid respiratory improvement; asymptomatic	Ongoing corticosteroid therapy
Day 5	97	85	7.8	320	60	Asymptomatic; Hb decline	Ongoing corticosteroid therapy
Day 6	97	82	9.9	317	60	Respiratory stability	MMF 1 g twice daily initiated
Day 7	97	88	8.3	325	60	Respiratory stability	PLEX session 1; MMF
Day 8	99	80	7.3	320	50	Asymptomatic	MMF
Day 9	99	79	7.5	317	50	Asymptomatic	PLEX session 2; MMF
Day 10	99	80	8.0	320	50	Asymptomatic	Rituximab 500 mg IV, dose 1; MMF
Day 11	—	—	—	—	—	Follow-up HRCT: mildly regressive bilateral opacities; residual GGO	Follow-up HRCT (Figure 3)
Day 12	99	80	8.2	317	50	Asymptomatic	PLEX session 3; MMF
Day 13	99	76	9.3	280	50	Asymptomatic	MMF
Day 14	—	—	—	—	—	—	PLEX session 4
Day 16	—	—	—	—	—	—	PLEX session 5
Day 17	—	—	—	—	—	—	Rituximab 500 mg IV, dose 2
Day 19	—	—	—	—	—	—	PLEX session 6
Day 21	—	—	—	—	—	—	PLEX session 7 (final session)
Day 22	—	—	—	—	—	—	Rituximab 500 mg IV, dose 3
Day 25	—	—	—	150	50	Discharged; respiratory symptoms resolved	Prednisone 50 mg/day taper; MMF 1 g twice daily; prophylaxis dose of septrin
After discharge: ~ Day 29	—	—	—	—	—	Fourth rituximab infusion administered approximately one week after the third dose.	Rituximab 500 mg IV, dose 4 (day-case unit)
i.e., 13 months after presentation, 04 Dec 2024	—	—	12.0	78	—	Clinically well; urinalysis negative; CRP/ESR normal; C-ANCA negative	MMF 1 g twice daily
Jul 2026	—	—	—	75	—	No relapse; normal urinalysis/inflammatory markers; ANCA negative	Off immunosuppression since Dec 2025

TABLE 2: Serial clinical and laboratory course, key interventions, and follow-up

Notes: Day 0 represents the date of hospital admission (2 November 2023). A dash (—) indicates that a measurement was unavailable and does not imply a normal result.

Corticosteroid therapy: Intravenous methylprednisolone 500 mg daily was administered on Days 0–2, followed by oral prednisone 60 mg daily on Days 3–7 and 50 mg daily from Day 8. At discharge on Day 25, prednisone 50 mg once daily was prescribed, with a planned gradual taper over four months.

Reference ranges: Haemoglobin 12.0–16.0 g/dL; serum creatinine 45–90 µmol/L. Two units of packed red blood cells were transfused on Day 2, with no additional transfusions during hospitalization.

Plasma exchange: Seven sessions were performed on Days 7, 9, 12, 14, 16, 19, and 21. Each session involved the exchange of one plasma volume (40 mL/kg), using 5% albumin and fresh frozen plasma as replacement fluids.

Rituximab: Four intravenous infusions of 500 mg each were administered. The first three doses were given on Days 10, 17, and 22, respectively, and the fourth was administered one week after the third dose in the outpatient day-case infusion unit.

Abbreviations: ABG, arterial blood gas; CXR, chest X-ray; GGO, ground-glass opacity; Hb, haemoglobin; HR, heart rate; HRCT, high-resolution computed tomography; MMF, mycophenolate mofetil; P/F, PaO_2/FiO_2 ratio; PLEX, plasma exchange; PRBCs, packed red blood cells; SpO_2, peripheral oxygen saturation.

Further autoimmune investigations demonstrated positive C-ANCA at a titre of 1:80, negative P-ANCA (less than 1:20), positive antinuclear antibody (ANA) at a titre of 1:80 with a speckled pattern, and negative extractable nuclear antigen (ENA) testing. Complement levels (C3 and C4) were within normal limits, while anti-double-stranded DNA (anti-dsDNA), anti-glomerular basement membrane (anti-GBM) antibodies, and cryoglobulin testing were negative. Hepatitis B surface antigen and hepatitis C antibody testing were also negative. Antigen-specific PR3-ANCA and MPO-ANCA assays were unavailable. The initial eosinophilia subsequently normalized. Renal biopsy demonstrated necrotizing glomerulonephritis with focal crescent formation, providing histopathological evidence of active glomerular involvement consistent with an ANCA-associated vasculitic process. The retrospectively calculated Birmingham Vasculitis Activity Score (BVAS, version 3) at initial diagnosis was 19/63.

Bronchoscopy with bronchoalveolar lavage (BAL) was proposed for further diagnostic evaluation; however, the patient declined the procedure. An extensive infectious workup was performed. Blood, urine, and sputum cultures were negative. Additional investigations, including SARS-CoV-2 testing, *Pneumocystis jirovecii* PCR, *Aspergillus* galactomannan antigen, cytomegalovirus (CMV) PCR, Epstein-Barr virus (EBV) testing, parvovirus B19 testing, and HIV screening, were all negative. These findings reduced the likelihood of an infectious aetiology, although infection could not be completely excluded. The overall clinical, laboratory, radiological, and histopathological findings strongly supported an ANCA-associated pulmonary-renal syndrome with clinically suspected DAH.

Because renal dysfunction continued to progress despite sustained pulmonary improvement, further vasculitis-directed treatment was initiated. Mycophenolate mofetil 1 g twice daily was commenced on Day 6. Plasma exchange (PLEX) was initiated on Day 7, and seven sessions were performed on Days 7, 9, 12, 14, 16, 19, and 21. Each session involved the exchange of one plasma volume, calculated at 40 mL/kg of body weight, with an average duration of two hours. A combination of 5% albumin and fresh frozen plasma (FFP) was used as replacement fluid because of the associated pulmonary haemorrhage.

Rituximab was administered as an individualized regimen of four intravenous infusions of 500 mg each, following multidisciplinary discussion between the rheumatology and nephrology teams. The first three doses were administered on Days 10, 17, and 22, respectively. The timing of rituximab was coordinated with PLEX, with the first rituximab infusion administered after the second PLEX session on Day 9 and the subsequent PLEX session performed on Day 12. Similarly, the second rituximab infusion on Day 17 was followed by PLEX on Day 19. The third infusion was administered after completion of all PLEX sessions.

Her respiratory status remained stable, with complete resolution of respiratory symptoms and oxygen saturation reaching 99% on room air. Follow-up HRCT performed on Day 11 demonstrated interval regression of the previously observed bilateral pulmonary abnormalities, with residual ground-glass opacities (Figure *3*). The official radiology report described a mildly regressive course of the pulmonary findings, raising the possibility of resolving DAH in the appropriate clinical context.

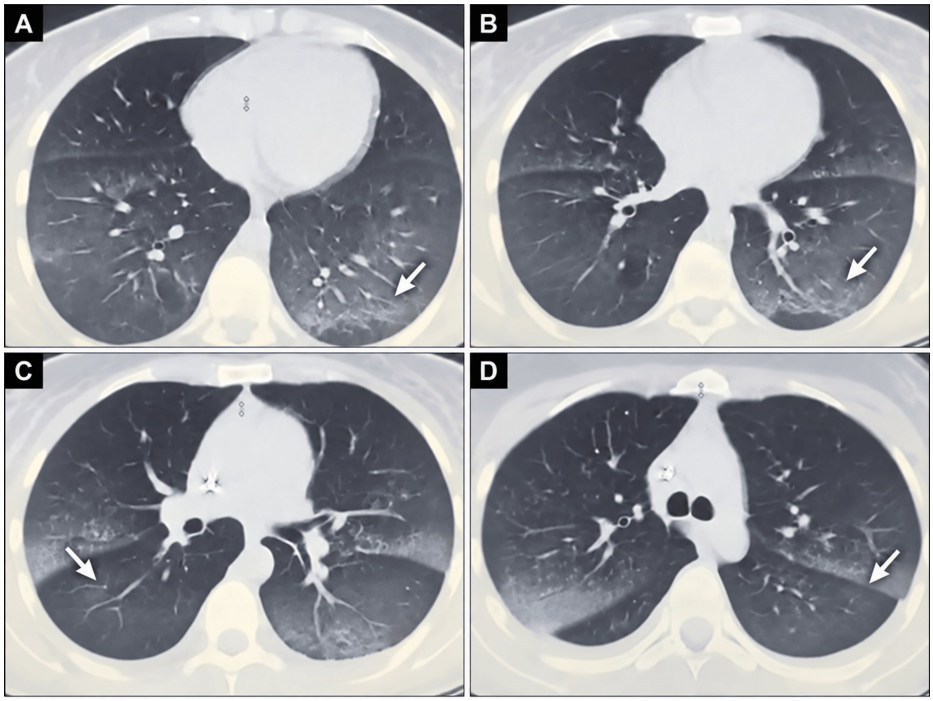


FIGURE 3: Follow-up high-resolution computed tomography of the chest on Day 11.

Representative axial HRCT images (A–D), obtained at levels comparable to the admission study, demonstrating interval regression of the previously observed bilateral ground-glass opacities and interlobular septal thickening, with residual patchy ground-glass abnormalities bilaterally, more evident in the posterior lower lung regions. White arrows indicate representative residual areas of pulmonary involvement. These findings indicate interval radiological improvement compared with the admission HRCT.

Renal function gradually improved following additional vasculitis-directed treatment, with serum creatinine decreasing from 320-325 µmol/L to 150 µmol/L by hospital discharge on Day 25 (Table *2*). The fourth rituximab infusion was administered one week after the third dose, following hospital discharge, in the outpatient day-case infusion unit. A subsequent retrospective BVAS assessment following completion of the fourth rituximab infusion yielded a score of 3/33 using the persistent-disease scoring category.

At hospital discharge on Day 25, serum creatinine had improved to 150 µmol/L. The patient was prescribed prednisone 50 mg once daily, with a planned taper over four months, mycophenolate mofetil 1 g twice daily, calcium and vitamin D supplementation, and trimethoprim-sulfamethoxazole (Septrin) prophylaxis. The fourth rituximab infusion (500 mg) was subsequently administered one week after the third dose, following hospital discharge, in the outpatient day-case infusion unit.

Her respiratory status remained stable, with complete resolution of respiratory symptoms and oxygen saturation of 99% on room air. A subsequent follow-up chest radiograph demonstrated near-complete resolution of the previously observed bilateral pulmonary opacities (Figure *4*).

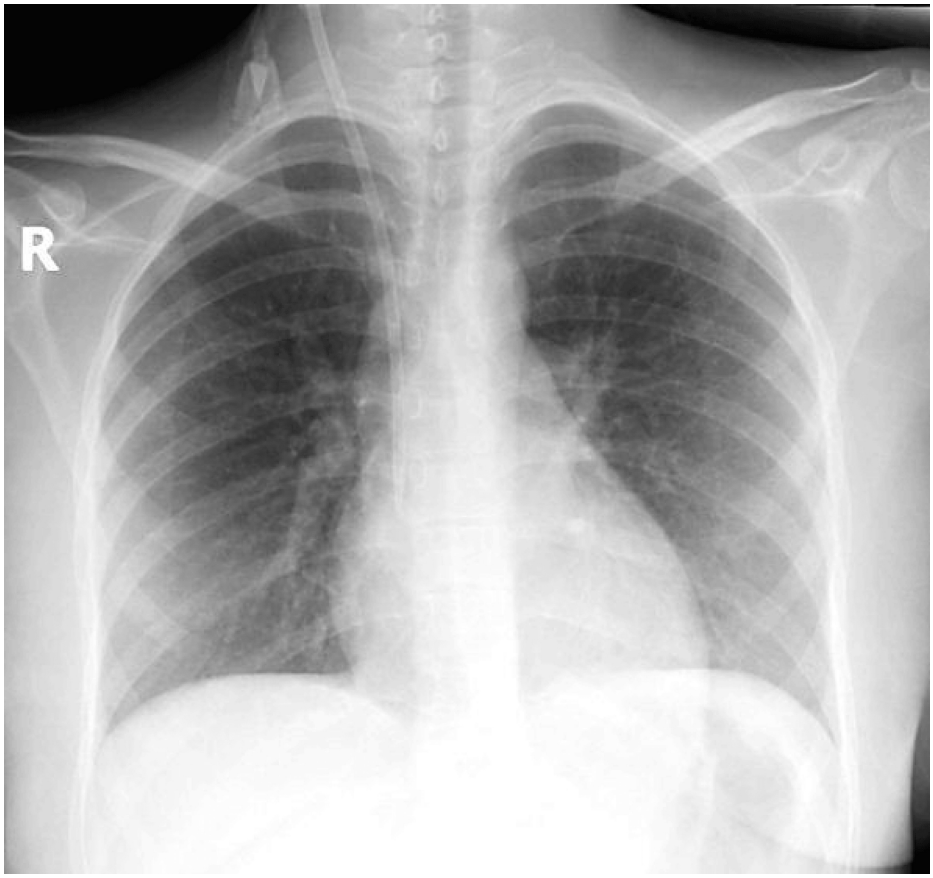


FIGURE 4: Follow-up chest radiograph demonstrating marked radiological improvement.

Follow-up frontal chest radiograph showing near-complete resolution of the previously observed bilateral mid- to lower-zone pulmonary opacities compared with the admission radiograph (Figure 1), consistent with substantial interval radiological improvement.

Following hospital discharge, the patient continued rheumatology follow-up, with sustained clinical stability and progressive improvement in renal function.

At rheumatology follow-up on 4 December 2024, the patient remained clinically well without evidence of disease relapse. Serum creatinine was 78 µmol/L, haemoglobin was 12 g/dL, and ESR, CRP, and liver function tests were within normal limits. Urinalysis was negative, and repeat C-ANCA testing was also negative. She remained on mycophenolate mofetil 1 g twice daily.

At the latest documented follow-up in July 2026, approximately 32 months after the initial presentation, the patient remained clinically well without evidence of relapse. She had discontinued immunosuppressive treatment in December 2025. Serum creatinine was 75 µmol/L, urinalysis was normal, inflammatory markers remained within normal limits, and ANCA testing was negative, indicating sustained clinical remission without ongoing immunosuppressive therapy.

Discussion

This case illustrates the diagnostic and therapeutic complexity of severe AAV presenting as a pulmonary-renal syndrome, with clinically suspected DAH occurring alongside rapidly progressive glomerular injury.

The combination of haemoptysis, severe anaemia, hypoxaemia, bilateral pulmonary infiltrates, acute kidney injury, and microscopic haematuria strongly suggested DAH associated with systemic small-vessel vasculitis. Subsequent renal biopsy demonstrating necrotizing glomerulonephritis with focal crescent formation, together with positive C-ANCA, provided additional support for an AAV process. DAH is among the most serious pulmonary manifestations of AAV and is associated with substantial morbidity and mortality, particularly in patients developing respiratory failure [7]. The overall diagnosis was supported by the combined clinical, laboratory, radiological, and renal histopathological findings, rather than chest imaging alone.

The initial peripheral eosinophilia also warranted consideration of eosinophilic granulomatosis with polyangiitis (EGPA) in the differential diagnosis. However, the absolute eosinophil count was 800 cells/µL, and the patient had no history of bronchial asthma or nasal polyps. Furthermore, the clinical presentation was dominated by severe pulmonary-renal involvement with necrotizing glomerulonephritis. These findings made EGPA less likely, although it could not be definitively excluded. The subsequent normalization of eosinophilia must also be interpreted in the context of corticosteroid administration. Antigen-specific PR3-ANCA and MPO-ANCA assays were unavailable, limiting further serological characterization of the vasculitic phenotype.

Current international recommendations support remission induction with glucocorticoids in combination with either rituximab or cyclophosphamide for organ- or life-threatening AAV [4,5,8]. In our patient, cyclophosphamide was discussed as an established treatment option but was declined by the patient. This necessitated an individualized therapeutic strategy developed through multidisciplinary collaboration between the rheumatology, nephrology, and intensive care teams.

The decision to administer tocilizumab was made in the context of progressive, potentially life-threatening pulmonary involvement despite initial high-dose corticosteroid treatment. The patient had received intravenous methylprednisolone 500 mg daily for three consecutive days (Days 0-2). Although haemoptysis ceased and inflammatory arthritis improved, respiratory function deteriorated further on Day 3, with oxygen saturation declining to 88% on room air. Arterial blood gas analysis demonstrated a PaO_2 of 55 mmHg and a calculated PaO_2/FiO_2 ratio of 262. Tocilizumab was therefore administered as an individualized, off-label rescue intervention while additional established vasculitis-directed treatment was being arranged.

Previous experience with interleukin-6 (IL-6) receptor blockade in severe inflammatory pulmonary conditions provided a potential biological rationale for this approach. In the RECOVERY trial, tocilizumab improved clinical outcomes in hospitalized patients with COVID-19-associated hypoxia and systemic inflammation when added to usual care, including corticosteroids [6]. Similar evidence emerged from the REMAP-CAP trial in critically ill patients with COVID-19 [9]. Nevertheless, COVID-19-associated inflammatory lung injury differs substantially from immune-mediated pulmonary capillaritis, and these findings cannot be directly extrapolated to AAV-associated DAH.

Evidence supporting tocilizumab in AAV remains limited. Sakai et al. described a small prospective case series and reviewed previously reported experience with tocilizumab in AAV, suggesting a possible therapeutic role while highlighting important safety concerns and the need for further investigation [10]. Tocilizumab is not currently an established remission-induction treatment for GPA or MPA, and its administration in our patient should not be interpreted as a substitute for rituximab or cyclophosphamide.

The most striking observation in our case was the temporal association between tocilizumab administration and rapid respiratory improvement. Despite deterioration in oxygenation on Day 3 following three days of intravenous methylprednisolone, oxygen saturation increased from 88% to 96% on room air within 24 hours of tocilizumab administration. This improvement was accompanied by a substantial reduction in oxygen requirements and resolution of respiratory symptoms, with subsequent oxygen saturations remaining between 97% and 99% on room air.

The possible contributions of preceding corticosteroid therapy, blood transfusion, supportive care, and the natural evolution of DAH must be considered when interpreting this observation. Delayed corticosteroid effects cannot be excluded, even though respiratory deterioration was documented after completion of pulse methylprednisolone. Similarly, the two units of PRBCs administered on Day 2 may have improved oxygen-carrying capacity and overall clinical stability but do not directly explain the subsequent improvement in oxygen saturation on room air. Moreover, the fluctuations in haemoglobin, including the decline to 7.8 g/dL on Day 5, prevent definitive conclusions regarding the precise timing of cessation of alveolar bleeding.

Although these alternative explanations remain possible, the available clinical findings do not establish any single mechanism as the predominant cause of the rapid respiratory improvement. Equally, the temporal association does not prove that tocilizumab was solely responsible. Nevertheless, the documented sequence of respiratory deterioration followed by substantial improvement within 24 hours of IL-6 receptor blockade represents a clinically significant observation worthy of further investigation.

An additional distinctive feature was the marked dissociation between pulmonary and renal responses. While respiratory function improved rapidly, serum creatinine continued to rise from 240 µmol/L on Day 3 to 320-325 µmol/L during the subsequent days. This contrasting course suggests that improvement in the pulmonary manifestations did not necessarily represent adequate control of the underlying systemic vasculitic process. One possible interpretation is that IL-6 receptor blockade may have contributed to modulation of the acute inflammatory pulmonary response without providing sufficient control of the renal vasculitis. However, this hypothesis remains speculative and requires further investigation.

The subsequent management of renal involvement required additional immunosuppressive treatment and plasma exchange. The PEXIVAS trial did not demonstrate a significant overall reduction in death or end-

stage kidney disease with routine plasma exchange in severe AAV [11]. Additional evidence has similarly failed to establish a clear mortality benefit from plasma exchange specifically for AAV-associated DAH [12]. Current recommendations therefore favour selective rather than routine use of plasma exchange, particularly in patients with active glomerulonephritis and a substantial risk of progression to kidney failure [4,13]. In our patient, the decision to initiate plasma exchange was individualized in the setting of progressive renal dysfunction, with serum creatinine exceeding 300 µmol/L and biopsy-demonstrated active glomerular injury.

Rituximab was subsequently introduced as an established remission-induction agent. The landmark RAVE trial by Stone et al. demonstrated that rituximab was an effective alternative to cyclophosphamide for remission induction in AAV [14]. Although the trial excluded patients with alveolar haemorrhage requiring mechanical ventilation and those with serum creatinine exceeding 4.0 mg/dL, our patient did not require mechanical ventilation, and her peak creatinine remained below this threshold. More recent evidence, including the systematic review and meta-analysis by Watanabe et al. published in Modern Rheumatology in 2023, provides additional context regarding contemporary treatment strategies for AAV, including rituximab-based approaches [15]. Nevertheless, evidence remains less definitive for the most severe presentations of DAH.

The rituximab regimen in our patient consisted of four divided intravenous doses of 500 mg, selected following multidisciplinary discussion and coordinated with the plasma exchange schedule. Although this provided a cumulative dose of 2,000 mg, the regimen differed from conventional induction schedules and should be regarded as an individualized therapeutic approach rather than an established alternative dosing protocol.

Following the additional vasculitis-directed interventions, renal function gradually recovered, with serum creatinine decreasing to 150 µmol/L by hospital discharge and subsequently normalizing. Follow-up HRCT on Day 11 demonstrated regression of the pulmonary abnormalities, while subsequent chest radiography showed substantial resolution of the previously observed pulmonary opacities. These imaging findings provide objective evidence of pulmonary recovery during the overall treatment course but cannot independently establish the contribution of any single intervention.

The favourable clinical outcome was sustained during long-term follow-up. At the latest assessment in July 2026, approximately 32 months after presentation, the patient remained clinically well without relapse, with normal renal function, negative urinalysis, normal inflammatory markers, and negative ANCA testing. She had been off immunosuppressive treatment since December 2025.

The principal limitation of this report is its single-patient observational design. The absence of a comparator and the potential effects of preceding corticosteroid therapy and supportive interventions prevent definitive attribution of the early respiratory improvement to tocilizumab. Furthermore, BAL was not performed because the patient declined the procedure; consequently, DAH remained a clinically supported rather than bronchoscopically confirmed diagnosis. Although the targeted infectious investigations were negative, infection could not be excluded with absolute certainty. These limitations should be considered when interpreting the findings.

Despite these limitations, the striking temporal association between tocilizumab administration and rapid pulmonary improvement, occurring alongside continued progression of renal vasculitis, remains the central observation of this case. This discordant organ response raises an important hypothesis regarding the potential adjunctive role of IL-6 receptor blockade in selected patients with severe AAV-associated pulmonary involvement and supports further investigation of this therapeutic pathway.

Conclusions

This case highlights a striking temporal association between tocilizumab administration and rapid, sustained improvement in severe pulmonary manifestations of AAV, despite continued progression of biopsy-proven renal vasculitis. The discordant pulmonary and renal responses suggest that IL-6 blockade may have contributed to control of the acute inflammatory pulmonary process but was insufficient to suppress the underlying systemic vasculitic disease. Tocilizumab should therefore not be considered a substitute for established remission-induction therapy with rituximab or cyclophosphamide. Rather, this case raises a hypothesis that IL-6 blockade may have a potential adjunctive or rescue role in carefully selected patients with life-threatening AAV-associated pulmonary involvement when standard induction therapy cannot be administered immediately. Because causality cannot be established from a single case, further clinical investigation is required before this approach can be recommended in routine practice.

Beyond its therapeutic implications, this case emphasizes the importance of early recognition of pulmonary-renal syndrome, timely renal biopsy when clinically feasible, and prompt initiation of appropriate treatment. It also highlights the essential role of multidisciplinary collaboration and shared decision-making in developing individualized treatment strategies when patients decline standard induction therapy.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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Disclosures

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