ARP Rheumatology 2025;4:154-162
https://doi.org/10.63032/YVYO6106

CASE BASED REVIEWS

Wunderlich syndrome as an unusual presentation of microscopic polyangiitis: a case report with review of literature

Jana B[1], Bhowmick K[1], Chattopadhyay A[2], Das U[3], Sen I[1], Bhadury S[1]

ABSTRACT

Wunderlich syndrome, characterized by spontaneous perinephric hematoma with subcapsular extension has been scarcely reported in microscopic polyangiitis (MPA). We report the case of a 45-year-old woman, who presented with constitutional symptoms, left-eye episcleritis, and rapidly progressive glomerulonephritis. She developed sudden, severe left flank pain with hemoglobin drop two days after admission. Both computed tomography (CT) and non-contrast magnetic resonance imaging revealed large left-sided perinephric hematoma. CT angiography failed to demonstrate intrarenal aneurysms. A remarkable reduction in size of her perinephric hematoma was observed after three and a half months of treatment with glucocorticoids and intravenous cyclophosphamide (IV CYC) following the international guidelines. A literature review on renal vessel involvement in antineutrophil cytoplasmic antibody-associated vasculitis revealed 26 case reports and one case series with 20 cases of renal aneurysms. Eighteen cases in the case reports (69.2%) and nine in the case series (45%) ruptured their renal arteries. The majority (44.4%) were managed with IV CYC and high-dose glucocorticoids. Angioembolization, renal replacement therapy, and plasma exchange were used as adjuvant measures. Only three patients (16.7%) underwent nephrectomy, while the majority (63.6%) fully recovered.

Keywords: Microscopic Polyangiitis; Wunderlich syndrome; Medium-sized vessel; Renal artery aneurysms.

INTRODUCTION

Microscopic polyangiitis (MPA) is an uncommon, systemic, necrotizing vasculitis typically associated with antineutrophil cytoplasmic antibodies (ANCA). This rare primary vasculitis predominantly affects the small vessels, namely the arterioles, venules, and capillaries[1]. In contrast, medium-sized vessel vasculitis characterized by the presence of aneurysms that may rupture is the hallmark of polyarteritis nodosa (PAN). Thus, glomerulonephritis is the typical renal manifestation of ANCA-associated vasculitis (AAV) rather than vasculitis of intrarenal vessels. AAV with medium-sized vessel rupture leading to visceral hemorrhage is scarcely reported in the literature. In this case-based review, we detail an unusual presentation of MPA with spontaneous left perinephric hemorrhage, with an extensive literature review of the cases with renal artery involvement in AAV, focusing on their demographics, clinical presentation, management, and long-term outcomes.

CASE REPORT

A previously healthy 45-year-old married North-East Indian woman presented in the emergency department with a low-grade fever and polyarthralgia for the last 2 months. The fever was intermittent with an evening rise in temperature and a maximum recorded fever spike of 100.5°F. The fever subsided with antipyretics, which she used to take regularly. The polyarthralgia was insidious in onset, and symmetric, with involvement of the small joints of her hands and feet, and an early morning stiffness that lasted for around an hour. Over this period, she also experienced loss of appetite and unintentional weight loss of around 5 kg. For the last week, she developed redness and dull discomfort in her left eye. She had no history of nasal congestion, hearing loss, ear blockade, tinnitus, epistaxis, long-standing dry cough, wheezing, shortness of breath, hemoptysis, palpitation, paroxysmal nocturnal dyspnea, pedal-swelling, tingling, numbness, or weakness in the extremities, or

[1] Department of Internal Medicine, North Bengal Medical College and Hospital, Sushrutranagar, Darjeeling, West Bengal, India;
[2] Department of Rheumatology, North Bengal Medical College and Hospital, Sushrutranagar, Darjeeling, West Bengal, India;
[3] Department of Radiology, North Bengal Medical College and Hospital, Sushrutranagar, Darjeeling, West Bengal, India

Submitted: 13/01/2025
Accepted: 30/04/2025

Correspondence to: Kaustav Bhowmick
E-mail: silirony@gmail.com

gastrointestinal symptoms like post-prandial abdominal pain, chronic diarrhea, hematemesis, melena, or hematochezia.

She was admitted for evaluation of her symptoms and further investigations. Following admission, she was found hemodynamically stable but with persistent new-onset hypertension. Her average blood pressure (BP) was recorded as 160/100 mmHg in her left arm, with no discrepancies in BP or pulse across her limbs. Musculoskeletal examination revealed multiple tender metacarpophalangeal, metatarsophalangeal, and interphalangeal joints of hands and feet with a tender joint count of 16, but without swelling. She had redness in the temporal sector of her sclera on direct torch light examination. Slit-lamp evaluation confirmed the presence of episcleritis. Chest and cardiac examinations were non-contributory. Initial complete hemogram revealed anemia with a hemoglobin of 9.6 g/dl, leukocytosis with a total leucocyte count (TLC) of 18.9 X 10^3/µL with neutrophils 70%, lymphocytes 26%, monocytes 3%, eosinophil 1% and thrombocytosis with platelets of 772 X 10^3/µL. Her absolute eosinophil count at the baseline was 189/µL. Renal function showed raised serum creatinine levels at 2.02 mg/dl. Urinalysis showed active sediments with protein '+', white blood cells (WBCs) 4-5/high power field (hpf), red blood cell (RBC) casts 5-6/hpf, and granular casts 2-3/low power field (lpf). She also had sub-nephrotic range proteinuria with a 24-hour urine protein of 743 mg. She had a remarkably high serum C-reactive protein of 28.7 mg/dL (<0.3 mg/dL). Liver function tests revealed hypoalbuminemia of 2.7 g/dl, which was partially attributed to proteinuria and partially to a negative acute-phase reactant. [Table. 1]. She tested negative for tropical infections, endemic to her area, like malaria, enteric fever, scrub typhus, leptospirosis, and brucellosis. On further workup for infections as part of the evaluation of the above symptoms, she tested negative for hepatitis B surface antigen, hepatitis C, and human immunodeficiency virus (HIV). A 2D Echocardiography done as a part of the work-up

TABLE. I Laboratory Parameters on admission and at week 14

Parameters (reference values)	On admission	Week 14
RBC (3.8–6.5 X 10^6/µL)	3.7	5.5
Hemoglobin (12-15 g/dl)	9.6	11.3
WBC (4.5-11 X 10^3/µL)	18.9	8.7
Neutrophil (50 %- 70%)	70.0	56.7
Lymphocyte (25%-35 %)	26.0	35.3
Monocyte (4% - 6%)	3.0	5.0
Eosinophil (1% - 3%)	1.0	3.0
Platelet (150 -450 X 10^3/µL)	772	344
ESR (< 20 mm/hr)	95 in 1st hour	45
Total protein (6.0 – 8.3 g/dL)	6.4	6.8
Albumin (3.5 – 5.5 g/dL)	2.7	3.7
Total bilirubin (0.3 – 1.3 mg/dL)	0.4	0.5
AST (< 40 U/L)	19	15
ALT (< 40 U/L)	14	13
Urea (15-45 mg/dL)	40	26
Creatinine (0.6 – 1.1 mg/dl)	2.0	1.2
Urinalysis	Protein + RBC casts: 5-6/hpf WBC: 4-5 /hpf Granular casts: 2-3 /lpf	Protein + RBC casts: 2-3 WBC: 2-3 Granular casts: Nil
24-hour urine protein (0 -150 mg)	743	120
CRP (< 0.3 mg/dL)	28.7	0.5
Anti-MPO (0-20 U/ml)	120	< 20

ALT, Alanine aminotransferase; Anti-CCP, Anti-Cyclic citrullinated peptide; Anti-MPO, Anti-Myeloperoxidase; aPTT, Activated partial Thromboplastin Time; AST, Aspartate aminotransferase; CRP, C-Reactive Protein, ESR, Erythrocyte Sedimentation Rate; hpf, high power field; INR, International Normalized Ratio; lpf, low power field; PT, Prothrombin time, RBC, Red blood cells; WBC, White blood cells

for infective endocarditis did not reveal any vegetation. A baseline abdominal ultrasound showed normal sized kidneys with raised cortical echogenicity and an intact corticomedullary differentiation. Chest Computed Tomography (CT) done as a part of the evaluation of a long-standing fever was non-contributory. A workup for polyarthritis revealed a high-titer serum rheumatoid factor of 111 IU/ml (0-20 IU/ml) with a negative anti-citrullinated antibody test. She tested negative for anti-nuclear antibody in the Hep2 cell line by indirect immunofluorescence at 1:80 titer.

On Day 2 of admission she developed a sudden severe cramping pain over the left, lumbar region without history of antecedent trauma, or recent high-grade spiking of fever. On examination, a postural drop in blood pressure was noted with a resting tachycardia of 120 beats/min. She had tenderness over her left costovertebral angle without swelling or fever. A repeat laboratory examination showed a significant drop in hemoglobin levels from 9.6 to 7 g/dl. This was associated with a rapid rise in serum creatinine from 2.02 mg/dl to 4.2 mg/dl. Her basic coagulation screening tests like the prothrombin time and the activated partial thromboplastin time were within the normal range. An abdominal ultrasound on the same date revealed a 10 cm × 5 cm heterogenous splenorenal collection. On the next day, the non-contrast abdominal CT scan revealed a large area of hyperdensity in the perinephric area which extended into the pararenal space and compressed the adjoining left renal parenchyma with subcapsular extension. The CT finding pointed towards the possibility of either a hematoma or an abscess. Subsequently, on non-contrast abdominal magnetic resonance imaging, the T1 and T2 weighted images (Figure 1) showed a heterogeneously hypointense area measuring 11 X 2.6 X 7.8 cm in size in the left perinephric space, interspersed with areas of scattered hyperintensity, with subcapsular extension and pararenal space encroachment. Diffusion-weighted imaging (DWI) revealed restricted diffusion in the periphery of this large area with facilitated diffusion in the center. The above findings were compatible with a subacute perinephric hematoma. There was no evidence of cysts, or mass lesions adjoining the hematoma. However, a CT Angiography did not reveal aneurysms in the abdominal aorta or its major branches. The perinephric hematoma, arising from the left kidney, with subcapsular and pararenal extension, was therefore a spontaneous one, also known as Wunderlich syndrome[2]. She was tested for ANCA by Indirect Immunofluorescence (IIF) at 1:10 dilution, which showed a perinuclear staining pattern (p-ANCA) with a 3+ intensity. Myeloperoxidase-antineutrophil cytoplasmic antibody (MPO-ANCA) titers by Enzyme-Linked Immunosorbent Assay (ELISA) was 120 U/ml (0-20 U/ml). MPA was diagnosed based on the presence of episcleritis, rapidly progressive glomerulonephritis (RPGN), constitutional symptoms, and MPO-ANCA positivity in high-titers on ELISA[3]. She was immediately administered intravenous methylprednisolone (IV MP) 1 g for 3 days followed by a switch to oral prednisolone 1mg/kg/day along with doses of IV Cyclophosphamide (CYC) 15 mg/kg as per the European Vasculitis Society (EUVAS) protocol[4].

Her abdominal pain improved significantly from Day

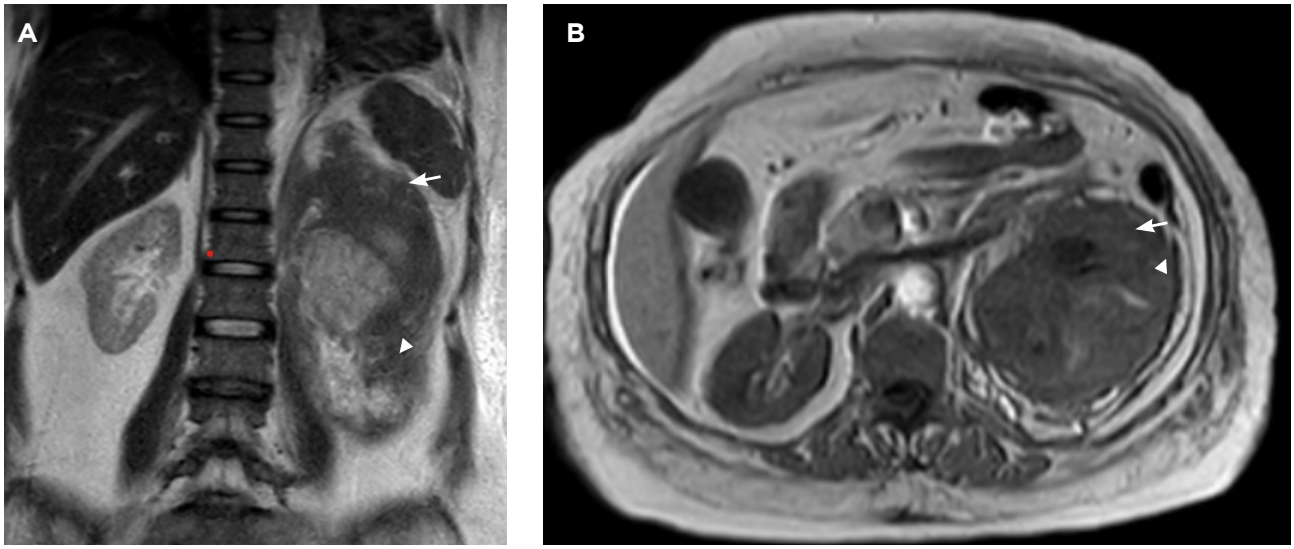

Figure 1. Non-Contrast T2 weighted magnetic resonance imaging of the left kidney shows a heterogeneously hypointense area (arrows) measuring 11 X 2.6 X 7.8 cm in size in the left perinephric space, interspersed with areas of scattered hyperintensity (arrowheads), with subcapsular extension and pararenal space encroachment on both coronal (a) and axial sections (b) suggestive of perinephric hematoma in the subacute stages.

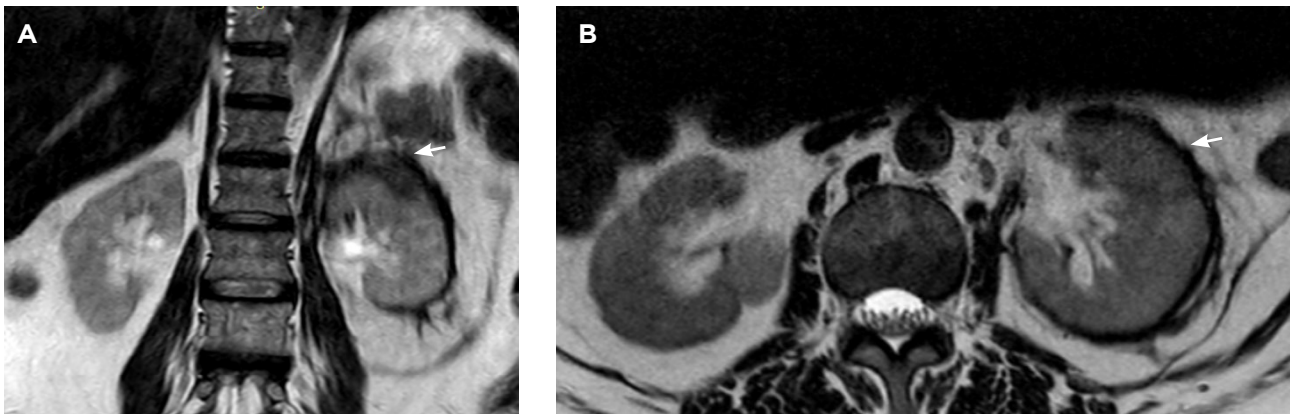

Figure 2. Non-Contrast T2 weighted magnetic resonance imaging of the left kidney shows a gross reduction in the size of perinephric hematoma measuring 5 X 2 X 3.5 cm and a thin rim of hypointense signal representing hemosiderin deposition on the renal contour (arrows) on both coronal (a) and axial sections (b).

7 of starting treatment. She has received 6 doses of CYC to date. There has been a decrease in serum creatinine levels from 4.2 mg/dl to 1.2 mg/dl after 14 weeks of starting treatment. She also had a remarkable reduction in the size of her left perinephric hematoma. with her current immunosuppressive therapy (Figure 2). The anti-MPO titer after 14 weeks of CYC doses is below 20 U/ml (Table I). She has been further planned for Rituximab maintenance therapy given the severe disease at the baseline.

DISCUSSION

AAV is predominantly a small vessel vasculitis affecting the ear, nose, throat, eyes, salivary glands, nerves, gastrointestinal tract, heart, lungs, and kidneys[5]. The predominant renal involvement is pauci-immune, crescentic, necrotizing glomerulonephritis. Renal vascular disease leading to multiple arterial aneurysms is classically described in Polyarteritis Nodosa (PAN), the prototype medium-vessel vasculitis[6]. In one of their papers, L. Guillevin *et al* [7] showed that ANCA positivity was associated with normal angiograms and concluded that renal and abdominal angiograms were undesirable in ANCA-positive patients with suspected vasculitis before undergoing diagnostic biopsies. Wunderlich syndrome, named after Carl Wunderlich, is characterized by spontaneous subcapsular, perinephric hematoma with or without para nephric extension. Renal neoplasms like angiomyolipomas and clear cell carcinomas contribute to most of the etiologies. Renal vascular diseases like aneurysms or pseudoaneurysms, renal vein thrombosis, arteriovenous malformations, and vasculitis stand as the next common group of diseases giving rise to the syndrome. The rarer causes are pyelonephritis, polycystic diseases, calculi, renal failure, and coagulopathies.[2]. AAV, a predominant small vessel vasculitis, can rarely present with large[8-12] and medium vessel vasculitis. Medium vessel vasculitis in AAV can affect both non-renal[13-20] and renal arteries[21-44,45]. Renal artery involvement in AAV can either present with asymptomatic aneurysms or with spontaneous perinephric hemorrhage due to aneurysmal or non-aneurysmal rupture of intrarenal arcuate and interlobar arteries[31]. The pathophysiology of the rupture of the renal arteries, stems from the weakening and damage to the vessel wall by the neutrophil extracellular traps (NETs), the reactive oxygen species (ROS), and several lytic enzymes released by the activated neutrophils. The entire process begins with the priming of the neutrophils, in the presence of the pro-inflammatory cytokines, such as the tumor necrosis factor (TNF), and Interleukin-1β (IL-1β). This is further facilitated by the C5a which binds to the C5a receptor on the surface of neutrophils. The primed neutrophils express MPO and proteinase 3 (PR3) on their plasma membrane. At the same time, prolonged exposure to the contents of NETs causes neutrophils to lose their tolerance to specific self-antigens, particularly MPO and PR3. These antigens are presented by dendritic cells to CD4+ T cells, leading to the production of ANCAs. The ANCAs bind the MPO and PR3 on the neutrophil surface, and at the same time the crystallizable fragment (Fc) region of these ANCAs binds to the Fcγ receptor on neutrophils. This binding induces excessive activation of neutrophils, leading to the release of ROS and lytic enzymes, along with the further generation of NETs. ROS, lytic enzymes, and NETs lead to vascular endothelial cell injury, propagating vessel injury, and damage[46].

In this case-based review, we intended to highlight the renal artery involvement in AAV which can coexist with pauci-immune necrotizing glomerulonephritis. We conducted an extensive search in English literature for renal artery involvement in AAV on MEDLINE

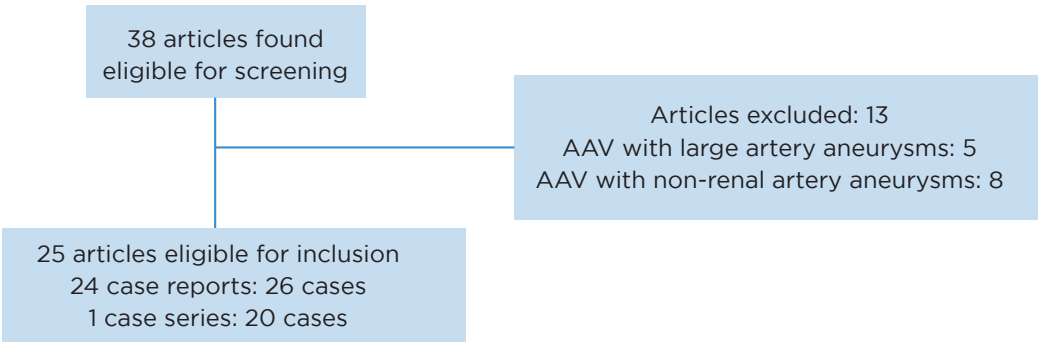

Figure 2. Non-Contrast T2 weighted magnetic resonance imaging of the left kidney shows a gross reduction in the size of perinephric hematoma measuring 5 X 2 X 3.5 cm and a thin rim of hypointense signal representing hemosiderin deposition on the renal contour (arrows) on both coronal (a) and axial sections (b).

(via PubMed), Web of Science, EMBASE, and Scopus up to December 2024. The MeSH terms or keywords used were 'ANCA associated vasculitis', 'spontaneous perinephric hematoma', and 'renal artery aneurysms'. A hand-picked Google search was also done to make the search complete[21-44,45]. We excluded articles of AAV with large vessel involvement[8-12] or non-renal medium vessel vasculitis[13-20]. Forty-six cases of renal artery involvement in AAV were identified. Of them, 26 cases had been reported from 24 case reports while 20 were reported from a French case series which reported cases of AAV combined with aneurysms (Figure 3).

According to published case reports (Table II), there was a male preponderance of renal artery involvement in AAV with a male-to-female ratio of 2.3: 1. Renal artery involvement associated with AAV was primarily diagnosed in the elderly age group, with the mean age being 56.7 years (SD ± 15.7 years). The interval between the diagnosis of AAV and the involvement of renal arteries has varied across studies with a median interval in the diagnosis of the latter being 14.5 days (range: 0-12 yrs). We report the case of a 45-year-old relatively younger woman in whom spontaneous perinephric hematoma was diagnosed simultaneously with AAV. Of the 26 reported cases, 21 cases (80.8 %) reported MPO-ANCA or PR3-ANCA antibodies by Enzyme-Linked Immunosorbent Assay (ELISA) or ANCA positivity by IIF. Of these 21 cases, eight cases (38.1 %) were MPO-ANCA positive by ELISA and the remaining 13 cases (61.9%) were either positive for PR3-ANCA by ELISA or had a cytoplasmic staining pattern of ANCA (c-ANCA) by IIF. Our patient was MPO-ANCA positive by ELISA.

Renal artery aneurysms were reported in 23 of the 26 case reports. Isolated renal aneurysms were reported in 15 cases (65.2 %). Eight (34.8%) reported aneurysms in other medium-sized vessels in the abdomen, in addition to renal aneurysms. Hepatic artery aneurysms were reported in seven cases (30.4%), mesenteric artery aneurysms in three cases (13.0%), pancreaticoduodenal artery aneurysms in two cases (8.7%), and celiac artery aneurysms in only one case (4.3 %).

Spontaneous perinephric hematoma arising from ruptured renal artery was reported in 18 cases (69.2 %). The majority (16; 88.9%) were unilateral perinephric hematoma while only two cases (11.1%) developed bilateral perinephric hematoma. The presenting symptom in all the patients with ruptured renal artery aneurysms was sudden-onset abdominal pain, while circulatory shock was associated in 10 of those 18 cases (55.6%) of spontaneous perinephric hematoma. We report our case with unilateral perinephric hematoma of the left kidney. We could not demonstrate any aneurysms by CT Angiography of the abdominal aorta and its major branches. However, non-aneurysmal vasculitic involvement of the small intra-renal arteries can also lead to the rupture of these arteries causing perinephric hematoma[31].

The treatment for renal artery involvement in AAV was determined by the type of involvement of the renal arteries or the concurrent involvement of other medium vessels. Of the 26 case reports of renal artery involvement in AAV, eight (30.8%) had incidentally diagnosed unruptured renal aneurysms. These cases were managed with immunosuppressives targeting the underlying clinically involved organ system. Three of the 18 cases (16.7%) of perinephric hematoma required nephrectomy for intractable renal bleeding. The remaining 15 cases (83.3%) were treated with immunosuppressive agents, angioembolization (AE), renal replacement therapies, and therapeutic plasma exchanges in varying combinations. AE was used in half of the cases (9; 50.0%) of perinephric hematoma. AE was used in the majority of these cases (8; 88.9%) in conjunction with immunosuppressive therapy. Only one reported isolated AE (11.1%) to control the perinephric bleed-

TABLE II. Literature review of renal artery involvement in ANCA-associated vasculitis with and without perinephric hematoma

Author, Year	Sex/age (years)	Diagnostic confirmation	Duration between AAV diagnosis and perinephric hematoma	Involved artery(ies) on Angiography	Ruptured artery	Aneurysmal symptoms	Therapy	Outcome
Baker et al.[21], 1978	M/24	Paranasal sinus biopsy	Simultaneously	Renal	Yes (Renal)	Right flank pain, shock	Gel foam embolization, oral steroids, Oral CYC	Recovered
Moutsopoulos et al.[22], 1983	M/30	Maxillary sinus, nasal mucosa biopsy	4 months	Renal	No	NA	Oral Steroids, Oral CYC	NA
Moutsopoulos et al.[22], 1983	F/53	Clinical	1 month	Renal	No	NA	Oral Steroids, Oral CYC	NA
Inatsu et al.[23], 2002	M/78	Clinical, MPO-ANCA	Simultaneously	Renal	No	Right abdominal pain	High-dose oral prednisolone, dipyridamole	Recovered
Senf et al.[24], 2003	M/35	Clinical, PR3-ANCA, bronchoscopic biopsy	24 days	Hepatic, renal, splanchnic	Yes (Renal)	Sharp left flank pain, shock	Pulse steroids, Pulse IV CYC, HD	ESKD on HD
Daskalopoulos et al.[25], 2004	M/62	NA	NA	NA	Yes (Renal)	Flank pain	Radical nephrectomy	Deceased
Arlet et al.[26], 2007	M/29	Clinical picture, NGV, PR3-cANCA + PICG	5 years	Pancreatic-duodenal, Hepatic, renal	No	Abdominal pain, weight-loss, vomiting	AE coil hepatic artery, IV MP, IV MMF, IVIg	Recovered
Tamei et al.[27], 2008	M/55	Clinical picture, MPO-ANCA + PICG	8 months	Renal, hepatic	Yes (Renal)	Sharp left-sided abdominal pain, circulatory shock.	IVMP, oral steroids	ESKD on HD
Carron et al.[28], 2011	M/79	Clinical, cANCA-PR3	4 weeks	Celiac and superior mesenteric arteries and both renal arteries	Yes (Superior mesenteric arteries)	Hemorrhagic shock due to left colon hematoma	PE, IV CYC, Prednisolone.	Recovered
Boersma et al.[29], 2013	F/51	Clinical, PR3-ANCA	15 years	Renal	Yes (Renal)	Circulatory shock with tenderness in the lower abdomen.	Arterial embolization	Recovered
Dhaun et al.[30], 2013	M, 56	Clinical, MPO-ANCA	Simultaneously	Renal, Hepatic, Mesenteric	Yes (Renal)	B/L loin pain	Oral Steroids, PE, IV CYC	Recovered
Dhaun et al.[30], 2013	M, 60	Clinical, PR3-ANCA	Simultaneously	Renal	No	B/L flank pain	Oral steroids, IV CYC	Recovered
Nakashima et al.[31], 2015	F/77	Clinical, MPO-ANCA	14 days	NA	Yes (B/L Renal)	RPGN, left flank pain	High-dose oral steroids	Recovered
Kim et al.[32], 2017	M/71	Clinical, Biopsy, PR3-ANCA	Simultaneous	Renal	No	NA	CYC, Steroids	Recovered
Ishiwatari et al.[33], 2018	F/82	Clinical picture, Necrotizing vasculitis, MPO-ANCA	7 days	Renal	Yes (Renal)	Nausea, Shock	Coil embolization, steroids, mizoribine	ESKD on HD

Continues on the next page

TABLE II. Continuation

Author, Year	Sex/age (years)	Diagnostic confirmation	Duration between AAV diagnosis and perinephric hematoma	Involved artery(ies) on Angiography	Ruptured artery	Aneurysmal symptoms	Therapy	Outcome
Mahmudpour et al.[34], 2018	M/60	Clinical, c-ANCA	NA	Renal	Yes (Renal)	Rt. flank pain, shock	Right Nephrectomy	Deceased from renal failure
Yu et al.[35], 2018	M, 61	Clinical, Biopsy, MPO-ANCA	Simultaneously	Renal, Hepatic, Mesenteric	Yes (Renal)	Left Lumbago	Left Nephrectomy, Retroperitonal hematoma removal	NA
Skonieczny et al.[36], 2019	M/50	Clinical features, PR3-ANCA	15 days	Renal	Yes (Renal)	Rt. flank pain, shock	Arterial embolization, IV MP, Pulse CYC	Deceased from septic shock
Zhang et al.[37], 2019	F/57	Clinical, MPO-ANCA	7 days	NA	Yes (Renal)	Chills, fatigue, dyspnea, lumbago, delirium	IV MP, oral steroids	Recovered
Andrew et al.[38], 2020	F/50	Clinical features, MPO-ANCA	Simultaneous	Renal, Hepatic	Yes (B/L Renal)	Abdominal pain, circulatory shock	B/L percutaneous drainage of hematoma, IVMP, CYC	NA
Schneider et al.[39], 2021	M/58	Clinical, Biopsy, PR3-ANCA	Simultaneous	Renal	Yes (Renal)	Abdominal pain	Arterial embolization, high-dose oral steroids, CYC, RTX	Recovered
Gravos et al.[40], 2021	M/63	Clinical, PR3-ANCA	1 month	Renal, hepatic, and pancreaticoduodenal arteries	Yes (Pancrea-ticoduodenal)	Acute abdominal pain	Arterial embolization, CVVHDF, IV MP, Pulse CYC	Deceased from septic shock
Matsunaga et al.[41], 2021	F/75	Clinical features, PR3-ANCA	20 days	Renal	Yes (Renal)	Abdominal pain, shock	Arterial embolization, Steroids, RTX	Recovered
Tong et al.[42], 2022	M/50	Clinical, Biopsy pulmonary capillaritis, PR3-ANCA	7 days	Renal	Yes (Renal)	Sharp, sudden left abdominal pain	Arterial embolization, IV CYC, oral steroids, PE	Deceased from renal failure
Nunes et al.[43], 2022	F/52	Clinical, PICG	15 days	Renal	Yes (Renal)	Severe abdominal pain, hemorrhagic shock	Arterial embolization , CVVHDF, IVMP, Pulse CYC	Recovered
Shaker et al.[44], 2023	M/Late fifties	Biopsy, c- ANCA	12 years	Renal	Yes (Renal)	Severe abdominal pain, circulatory shock	Arterial embolization, immunosuppressives	Recovered
Current study, 2025	F/45	Episcleritis, Glomerulonephritis, Polyarthritis, Constitutional, MPO-ANCA	Simultaneously		Yes (Renal)	Severe abdominal pain, drop in hemoglobin	IV MP, Oral steroids, IV CYC	Recovered

AE, Angioembolization; c-ANCA, cytoplasmic Antineutrophil cytoplasmic antibody; CVVHDF, Continuous Venovenous Hemodiafiltration; CYC, Cyclophosphamide; ESKD, End Stage Kidney Disease; F, Female; HD, Hemodialysis; IVMP, Intravenous Methylprednisolone; M, Male; MPO-ANCA, Myeloperoxidase Antineutrophil cytoplasmic antibody; NA, Not Applicable; NGV, biopsy proven Necrotizing Granulomatous Vasculitis; PE, Plasma Exchange; PICG, biopsy-proven Pauci-immune Crescentic Glomerulonephritis; PR3-ANCA, Proteinase 3 Antineutrophil cytoplasmic antibody.

ing. Therapeutic plasma exchange support was used in two cases (11.1%), whereas hemodialysis and continuous venovenous hemodiafiltration supports were required in one each (5.6 %), in addition to immunosuppressive therapy. Among the immunosuppressives used, high-dose glucocorticoids and CYC were the mainstay of therapy in eight cases (44.4%). Three (16.7 %) were managed with high-dose glucocorticoids only. Rituximab was used as a steroid-sparing agent in two cases with renal artery rupture (11.1%), whereas mizorabine was used in a single case of spontaneous perinephric hematoma (5.6%).

Of the 26 reported cases of renal artery involvement in AAV, long-term outcomes were available in only 22 cases. Five of these 22 cases died. Three succumbed to renal failure and septic shock following perinephric hematoma, giving rise to a mortality rate of 22.7 %. Among the 17 cases who survived, three (13.6 %) required long-term hemodialysis, whereas the remaining 14 cases (63.6 %) fully recovered. Our patient responded well following treatment with high-dose glucocorticoids and 6 doses of IV CYC with a substantial reduction in the size of perinephric hematoma and a decrease in serum creatinine levels.

A case series of 51 patients by Hankard *et al* in 2023 on AAV with aneurysms described 20 cases (39%) of renal aneurysms[45]. Of these 20 cases, nine ruptured their aneurysms (41% cases) while 11 (38%) cases remained stable with immunosuppressive treatment.

After an extensive literature review, we found that most cases with renal artery involvement in AAV demonstrated aneurysms. Twenty-three out of the 26 case reports and the 20 cases of the single case series demonstrated renal aneurysms[21-44,45]. We have tried to highlight the magnitude of the renal artery involvement in AAV, as depicted in Table II. We could not demonstrate renal aneurysms in our case. However, non-aneurysmal rupture of the intrarenal arteries was the most plausible mechanism of spontaneous perinephric hematoma in our case, as also described by Nakashima *et al.*[31] and Zhang *et al.*[37] The present case report has tried to emphasize the fact that the involvement of renal artery, commonly associated with PAN, when accompanied with glomerulonephritis in AAV, can lead to catastrophic consequences.

In conclusion, spontaneous perinephric hematoma or Wunderlich syndrome in AAV could be the consequence of medium-vessel vasculitis involving the intra-renal vessels. Wunderlich syndrome in AAV should be considered when in the absence of recent trauma or renal biopsy, a patient present with flank pain, unexplained anemia, or signs of shock. Based on our literature review, immunosuppressive therapy for AAV was found to be the mainstay of treatment for this condition. Angioembolization for aneurysmal bleeding, renal replacement therapy, and plasma exchange can be used as supportive measures. Prompt and aggressive immunosuppression with pulse glucocorticoids and IV CYC without any other ancillary measures facilitated the control of perinephric bleeding and the recovery of renal function in our case.

REFERENCES

1. Jennette JC, Falk RJ, Bacon PA, et al. 2012 revised international Chapel Hill consensus conference nomenclature of vasculitides. Arthritis Rheum 2013;65:1–11. https://doi.org/10.1002/art.37715.
2. Jignesh NS, Darshan G, Srinivasa RP, et al.Wunderlich Syndrome: Comprehensive Review of Diagnosis and Management. Radiographics 2023;43:6. https://doi.org/10.1148/rg.220172.
3. Suppiah R, Robson JC, Grayson PC, et al. DCVAS INVESTIGATORS 2022 American College of Rheumatology/European Alliance of Associations for Rheumatology classification criteria for microscopic polyangiitis. Ann Rheum Dis 2022;81:321-326. https://doi.org/10.1136/annrheumdis-2021-221796.
4. de Groot K, Harper L, Jayne DR, et al. EUVAS (European Vasculitis Study Group) Pulse versus daily oral cyclophosphamide for induction of remission in antineutrophil cytoplasmic antibody-associated vasculitis: a randomized trial. Ann Intern Med 2009;150:670-680. https://doi.org/10.7326/0003-4819-150-10-200905190-00004.
5. Hunter RW, Welsh N, Farrah TE, Gallacher PJ, Dhaun N. ANCA associated vasculitis. BMJ 2020;369:m1070. https://doi.org/10.1136/bmj.m1070.
6. Nuzum JW., Jr Polyarteritis nodosa: statistical review of one hundred seventy-five cases from the literature and report of a "typical case". Arch Intern Med 1954;94:942–955. https://doi.org/10.1001/archinte.1954.00250060076007.
7. Guillevin L, Lhote F, Amouroux J, Gherardi R, Callard P, Casassus P.Antineutrophil cytoplasmic antibodies, abnormal angiograms and pathological findings in polyarteritis nodosa and Churg-Strauss syndrome: indications for the classification of vasculitides of the polyarteritis Nodosa Group. Br J Rheumatol 1996;35:958-964. https://doi.org/10.1093/rheumatology/35.10.958.
8. Sieber SC, Cuello B, Gelfman NA, et al. Pulmonary capillaritis and glomerulonephritis in an antineutrophil cytoplasmic antibody-positive patient with prior granulomatous aortitis. Arch Pathol Lab Med 1990;114:1223-1226.
9. Blockmans D, Baeyens H, Van Loon R, et al. Periaortitis and aortic dissection due to Wegener's granulomatosis. Clin Rheumatol 2000;19:161-164. https://doi.org/10.1007/s100670050038.
10. Carels T, Verbeken E, Blockmans D et al. p-ANCA-associated periaortitis with histological proof of Wegener's granulomatosis: case report. Clin Rheumatol 2005;24:83-86. https://doi.org/10.1007/s10067-004-0998-0.
11. Shitrit D, Shitrit AB, Starobin D, et al. Large vessel aneurysms in Wegener's granulomatosis. J Vasc Surg 2000;36:856-858. https://doi.org/10.1067/mva.2002.126088
12. Sasaki H, Yamazaki H, Kohsaka H. A Case of ANCA-associated Large Vessel Vasculitis with Multiple Saccular Aneurysms. J Rheumatol. 2016;43:179. https://doi.org/10.3899/jrheum.150435.
13. Aoki N, Soma K, Owada T, Ishii H. Wegener's granulomatosis complicated by arterial aneurysm. Intern Med 1995;34:790-793. https://doi.org/10.2169/internalmedicine.34.790
14. Famularo G, De Cata A, Bracci M, Minisola G, De Simone C, Nicotra GC. Fatal rupture of an inflammatory arterial aneurysm in a patient with Wegener's granulomatosis. Scand J Rheumatol

2004;33:277-279.
https://doi.org/10.1080/03009740410005908.
15. Den Bakker MA, Tangkau PL, Steffens TW, Tjiam SL, van der Loo EM. Rupture of a hepatic artery aneurysm caused by Wegener's granulomatosis. Pathol Res Pract 1997;193:61-66. https://doi.org/10.1016/s0344-0338(97)80096-9.
16. Takei H, Komaba Y, Kitamura H, Hayama N, Osawa H, Furukawa T. Aneurysmal subarachnoid hemorrhage in a patient with Wegener's granulomatosis. Clin Exp Nephrol 2004;8: 274-278. https://doi.org/10.1007/s10157-004-0280-4
17. Cheung CK, Tan J, Lowe RA, Gouldesbrough D, Stoves J. ANCA-associated vasculitis complicated by haemoperitoneum. NDT Plus 2010;3:142–144. https://doi.org/10.1093/ndtplus/sfp187.
18. Takamasu E, Hattori S, Yokogawa S, Shimada K. Multiple Aneurysms in Granulomatosis with Polyangiitis. The Journal of Rheumatology 2024;51:97. https://doi.org/10.3899/jrheum.2023-0510
19. Koh E, Kang N, Lee JY, et al. Multiple hepatic aneurysms and dry gangrene of fingertips in eosinophilic granulomatosis with polyangiitis: a case report. Allergy Asthma Clin Immunol 2020;16:90. https://doi.org/10.1186/s13223-020-00484-4
20. Htun, P., Horger, M., Gawaz, M., Fateh-Moghadam. Clinical Images: Giant Coronary Artery Aneurysms and Eosinophilic Granulomatosis With Polyangiitis. Arthritis & Rheumatism 2013;65:1406-1406. https://doi.org/10.1002/art.37898.
21. Baker SB, Robinson DR. Unusual renal manifestations of Wegener's granulomatosis. Report of two cases. Am J Med 1998;64:883-889. https://doi.org/10.1016/0002-9343(78)90532-6.
22. Moutsopoulos HM, Avgerinos PC, Tsampoulas CG, et al. Selective renal angiography in Wegener's granulomatosis. Ann Rheum Dis 1983;42:192-195. https://doi.org/10.1136/ard.42.2.192.
23. Inatsu A, Shimizu J, Ooshima S, et al. Antineutrophil cytoplasmic antibody (ANCA)-associated glomerulonephritis with intrarenal aneurysms and renal arteriovenous fistulaes. Intern Med 2002;41:853-858. https://doi.org/10.2169/internalmedicine.41.853
24. Senf R, Jürgensen JS, Teichgräber U, et al. Ruptured arterial aneurysm of the kidney in a patient with Wegener's granulomatosis. Nephrol Dial Transplant 2003;18:2671-2673. https://doi.org/10.1093/ndt/gfg380
25. Daskalopoulos G, Karyotis I, Heretis I, Anezinis P, Mavromanolakis E, Delakas D. Spontaneous perirenal hemorrhage: a 10-year experience at our institution. Int Urol Nephrol 2004;36:15-19. https://doi.org/10.1023/b:urol.0000032680.65742.9a
26. Arlet JB, Le Thi Huong D, Marinho A, et al. Arterial aneurysms in Wegener's granulomatosis: case report andliterature review. Semin Arthritis Rheum 2008;37:265-268. https://doi.org/10.1016/j.semarthrit.2007.07.004
27. Tamei N, Sugiura H, Takei T, Itabashi M, Uchida K, Nitta K. Ruptured arterial aneurysm of the kidney in a patient with microscopic polyangiitis. Intern Med 2008;47:521-526. https://doi.org/10.2169/internalmedicine.47.0624
28. Carron PL, Malvezzi P, Thony F. Finding of kidney arterial aneurysms in a case of Wegener's granulomatosis. Ther Apher Dial 2011;15:509-510. https://doi.org/10.1111/j.1744-9987.2011.00975.x
29. Boersma HE, Nap RH, Haanstra WP, et al.A rare cause of spontaneous perirenal haemorrhage in a patient with ANCA associated vasculitis. Neth J Med 2013;71:318-322.
30. Dhaun N, Patel D, Kluth DC.Computed tomography angiography in the diagnosis of ANCA-associated small- and medium-vessel vasculitis. Am J Kidney Dis 2013;62:390-393. https://doi.org/10.1053/j.ajkd.2012.12.035.
31. Nakashima, Y., Ohura, M., Mima, T. et al.Successful non-surgical treatment on bilateral spontaneous perirenal giant hematomas in rapidly progressive glomerulonephritis with MPO-ANCA positive. Ren Replace Ther 2015;1:8. https://doi.org/10.1186/s41100-015-0006-y.
32. Kim YR, Lee YH, Lee JH, et al. Contrast-enhanced ultrasound and computed tomography findings of granulomatosis with polyangiitis presenting with multiple intrarenal microaneurysms: a case report. Clin Imaging 2017;43:144-147. https://doi.org/10.1016/j.clinimag.2017.03.003
33. Ishiwatari A, Endo M, Wakai S. Ruptured renal artery in microscopic polyangiitis: a case report and literature review. CEN Case Rep 2018;7:301-306. https://doi.org/10.1007/s13730-018-0347-9
34. Mahmudpour M, Esmaili A, Abbasi MZ, et al. Spontaneous perinephric hematoma in a patient with granulomatosis with polyangiitis. Urol Case Rep 2018;17:26-28. https://doi.org/10.1016/j.eucr.2017.11.003
35. Yu Y, Li J, Hou H. A rare case of spontaneous renal rupture caused by anca - associated vasculitides. Int Braz J Urol 2018;44:1042-1043. https://doi.org/10.1590/s1677-5538.ibju.2018.0119
36. Skonieczny P, Heleniak Z, Liberek T, et al. Life-threatening bleeding from an aneurysm in the arcuate artery of the kidney as a rare complication of granulomatosis with polyangiitis. Pol Arch Intern Med 2019;129:930-931. https://doi.org/10.20452/pamw.15028
37. Man-Yu Z, Ding-Ping Y, Jun-Ke Z, Xue-Yan Y, Jun-Yun L, Ding-Wei Y. Spontaneous rupture of kidneys triggered by microscopic polyangiitis. Int J Clin Exp Med 2019;12:2883-2887.
38. Andrew D, Shyam K, Johny J. Microscopic polyangiitis presenting with bilateral spontaneous perinephric haematoma. BMJ Case Rep 2020;30;13:e239282. https://doi.org/10.1136/bcr-2020-239282
39. Schneider J, Venhoff N, Walz G. Ruptured Intrarenal Arterial Aneurysm in a Patient With Granulomatosis With Polyangiitis. J Rheumatol 2021;48:615. https://doi.org/10.3899/jrheum.190986
40. Gravos A, Katsifa K, Tselioti P, et al. Ruptured arterial aneurysm in Wegener's granulomatosis: a case report. J Med Case Rep 2021;15:343.
41. Matsunaga K, Tsurukiri J, Kato T, et al. Rupture of Renal Artery Aneurysm in a Patient with Granulomatosis with Polyangiitis. JMA J 2021;4:434-438. https://doi.org/10.31662/jmaj.2021-0027
42. Tong J, Zhou ZY, Liu X, Wang DX, Deng W. Antineutrophil cytoplasmic antibody-associated vasculitis with alveolar hemorrhage and ruptured renal aneurysm: a case report and literature review. Medicine 2022;101:1(e28543). https://doi.org/10.1097/md.0000000000028543
43. Nunes TF, Marchiori E, Motta-Leal-Filho JM. Spontaneous Rupture of Renal Pseudoaneurysm in Microscopic Polyangiitis: A Case Report and Literature Review. J Urol Ren Dis 2022;07: 1251. https://doi.org/10.29011/2575-7903.001251.
44. Shaker G. Rare case of spontaneous rupture of renal artery secondary to wegner granulomatosis. Urol Case Rep 2023;52:102631. https://doi.org/10.1016/j.eucr.2023.102631
45. Hankard A, Puéchal X, Martin SN, et al. Characteristics of ANCA-associated vasculitis with aneurysms: Case series and review of the literature. Autoimmun Rev 2023;22(5):103293. https://doi.org/10.1016/j.autrev.2023.103293.
46. Nakazawa D, Masuda S, Tomaru U, Ishizu A. Pathogenesis and therapeutic interventions for ANCA-associated vasculitis. Nat Rev Rheumatol. 2019 Feb;15:91-101. https://doi.org/10.1038/s41584-018-0145-y.