Ruptured renal artery in microscopic polyangiitis: a case report and literature review

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Abstract

Medium-vessel hemorrhage is a rare occurrence in ANCA-associated vasculitis, and has been previously described in only a few patients with microscopic polyangiitis. We report a case of renal hemorrhage in a patient with microscopic polyangiitis that was successfully managed by transcatheter arterial embolization of the active bleeding sites. The early clinical findings included necrotizing arteritis, as indicated by skin biopsy; rapidly progressive glomerulonephritis; mononeuritis multiplex; positive screening for myeloperoxidase-specific antineutrophil cytoplasmic antibody. Corticosteroid therapy was initiated. The patient's health deteriorated at 1 week, with rapidly progressing anemia. Computerized tomography identified a large, right-sided, perirenal hematoma, with active bleeding. Bleeding was successfully managed via segmental embolization of the renal artery. The patient was treated with steroid therapy and MZR, and subsequently underwent maintenance hemodialysis treatment for end-stage renal disease. Spontaneous renal hemorrhage is a rare but fatal clinical condition. A ruptured renal artery should be considered in a patient with microscopic polyangiitis, even in the absence of previous trauma and renal biopsy, when unexplained anemia or signs of shock occur.

Keywords Antineutrophil cytoplasmic antibody (ANCA) · Artery embolization · Microscopic polyangiitis · Perirenal hematoma · Renal hemorrhage

Introduction

Microscopic polyangiitis (MPA) is a rare, systemic, necrotizing vasculitis that typically occurs in the presence of anti-neutrophil cytoplasmic antibody (ANCA), affecting small vessels, such as arterioles, venules, and capillaries [1]. In contrast, aneurysm formation and rupture of medium-sized vessels are typically associated with polyarteritis nodosa (PAN). Arterial aneurysm rupture or medium-vessel hemorrhage is a rare occurrence in ANCA-associated vasculitis (AAV), and has been previously described in only a few patients with granulomatosis with polyangiitis (GPA) [2–5] and MPA [6]. We describe the clinical presentation, assessment, and diagnosis of a ruptured renal artery in a patient with MPA.

Case report

An 82-year-old Japanese woman presented to her primary physician with a 1-week history of general fatigue and arthralgia, and a 4-day history of lower extremity edema. She had been diagnosed with cellulitis and treated with cephalosporin. Her condition did not improve, and 2 days after the initiation of the antibiotics, she developed dyspnea and lower extremity hyperesthesia and numbness. She was transferred to our inpatient nephrology ward. The patient had a history of hypertension and depression. Current medication use included amlodipine, mirtazapine, mianserin, lansoprazole, and magnesium oxide. Before this episode, the patient had been physically active, and did not smoke, drink alcohol, or use illicit drugs. The patient reported fatigue, weight loss, shortness of breath, joint pain, and a decreased volume of urination over the previous 5 days. She did not have a cough, chest pain, hemoptysis, epistaxis, fevers, headaches, visual loss, dry eyes, or dry mouth.

Upon admission, the following vital signs were obtained: blood pressure, 145/66 mmHg; pulse rate, 87 beats per minute and regular; body temperature, 36.8 °C; respiratory rate,

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24 breaths per minute; an oxygen saturation of 90% while breathing oxygen (10 L per minute) via a face mask. Her skin and conjunctivae were pale, and examination of her lower extremities revealed the presence of purpura, edema, and hyperesthesia. On auscultation, bibasilar coarse crackles were heard in both lungs. The remainder of the physical examination was unremarkable.

Blood test results included the following: white blood cell count, 32,710/ μ L; neutrophils, 94.2%; eosinophils, 0.3%; lymphocytes, 3.1%; hematocrit, 32.5%; hemoglobin level, 10.3 g/dL; platelet count, 43.8×10^4 / μ L; prothrombin-time international normalized ratio, 1.09; activated partial-thromboplastin time (APTT), 48.1 s; fibrin/fibrinogen degradation products, 62.8 μ g/mL; D-dimer, 25.54 μ g/mL; MCV, 84.5 fL; MCHC, 31.5%; Fe, 41 μ g/dL; TIBC, 214 μ g/dL; and ferritin, 861 ng/mL. Renal function decreased significantly, with serum creatinine and blood urea nitrogen (BUN) levels of 5.29 mg/dL [estimated glomerular filtration rate (eGFR) of 6.5 mL/min/1.73 m²] and 65.9 mg/dL, respectively. 6 days earlier, the patient's serum creatinine level was 1.97 mg/dL (eGFR of 19 mL/min/1.73 m²), and she had never indicated renal dysfunction at her annual medical checkups. Urinalysis identified a hematuria of 3+ [> 100 per high-power field (HPF)] and a proteinuria of 2+, with many erythrocytes and 5–9 granular casts/HPF. Her 24-h urinary protein excretion was 0.474 g/day. C-reactive protein (CRP) level was 24.5 mg/dL, and sodium, potassium, and chloride levels were 130, 6.1, and 91 mEq/L, respectively. Immunoglobulin screening indicated levels of IgG, IgA, and IgM of 1637, 233 mg/dL, and 119 IU/mL, respectively. The myeloperoxidase (MPO)-ANCA titer was positive at 234 U/mL (normal < 3.5 IU/mL). All other immunological screenings were negative, including testing results for antinuclear antibody, anticyclic citrullinated peptide antibody, anti SS-A, proteinase 3 (PR3)-ANCA, antiglomerular basement membrane antibody, and cryoglobulin. Hepatitis B surface antigen and hepatitis C antibody screening were negative.

A chest radiograph and computed tomography (CT) scan, performed upon admission, indicated pulmonary congestion and bilateral pleural effusion, without the presence of nodules or alveolar hemorrhage. A skin biopsy of the lower extremity purpura revealed necrotizing vasculitis, which included fibrinoid necrosis of capillaries, neutrophilic infiltration of small-sized arteries, leukocytoclasia, and fibrin thrombus (Fig. 1). A nerve conduction study identified severe motor and sensory axonal neuropathy. Screenings for sinusitis and intracranial aneurysm were negative.

Lower extremity purpura, rapid progressive glomerulonephritis (RPGN), mononeuritis multiplex, and histological findings of necrotizing vasculitis were consistent with MPA, according to a previously reported classification algorithm [7]. The patient's Birmingham vasculitis activity score (BVAS) was calculated to be 37 points [8].

Fig. 1 Skin biopsy taken from the lower extremity purpura that is indicative of leukocytoclastic vasculitis. Fibrinoid necrosis of vessels (white arrow), neutrophilic infiltration of vessel walls, and leukocytoclasia (black arrow) were identified

Due to rapid progression of renal failure, pulmonary congestion, and hyperkalemia, hemodialysis was initiated on the day of admission. The patient was treated with intravenous high-dose methylprednisolone therapy (500 mg/day for 3 days), followed by prednisolone at 40 mg (1 mg/kg/day). Although WBC and CRP were elevated, systemic investigations for infection, including tuberculosis and blood culture, were unremarkable. Bacterial pleuritis or pneumonia could not be ruled out and, therefore, tazobactam/piperacillin was administered. Heparinization therapy (heparin 10,000 units per day) was also administered due to the high risk for venous thromboembolism associated with MPA and steroid therapy, despite her APTT not being prolonged.

1 week after the initiation of medical treatment, the patient complained of nausea and a decrease in urinary volume. These symptoms were associated with a sudden decline in hemoglobin level, from 9.8 to 5.8 g/dL. An abdominal CT scan revealed a large hematoma in the right perirenal space, with extravasation of the contrast agent (Fig. 2a), through which active bleeding was suspected. Blood transfusion, fluid resuscitation, and the discontinuation of heparin were not sufficient to stabilize the patient. Emergency arterial angiography was performed, which showed active bleeding from the superior segmental renal artery (Fig. 2b) and the interlobular artery of the right kidney, and a microaneurysm was suspected at the site of bleeding. Embolization of the right segmental renal artery was performed using microcoils, and follow-up aortic angiography confirmed occlusion of the embolized arteries.

In this case, we considered rupture of the renal artery to be a possible manifestation of active vasculitis; however, MPO-ANCA titer was decreased to 109 U/mL in the first 2 weeks, and no other organ symptoms indicating active

Fig. 2 **a** Abdominal CT scan, indicating a large hematoma in the right perirenal space, with extravasation of contrast agent (black arrow). **b** Arterial angiography, indicating active bleeding from the

superior segmental and interlobular renal artery of the right kidney (black arrow). Disseminated arterial microaneurysms are evident

vasculitis were detected. Therefore, the patient was maintained on prednisolone alone. Considering that the patient was elderly, and on maintenance hemodialysis, we believed that a relatively low dose of steroids would be desirable to minimize the adverse effects, and strong immunosuppressive agents, such as cyclophosphamide and azathioprine, would be harmful rather than beneficial. 6 weeks after the initiation of steroid therapy, we administered mizoribine (MZR), 50 mg after each dialysis, as maintenance therapy to taper prednisolone promptly without recurrence. After 2 years of follow-up, the patient is currently stable on maintenance hemodialysis, with oral prednisolone 2.5 mg/day and mizoribine 50 mg/day after each dialysis. Her BVAS has improved from 37 to 0 points, and the MPO-ANCA titer is within the normal range.

Discussion

In this case report, we present a rare case of renal hemorrhage in a patient with MPA that was successfully managed by transcatheter arterial embolization of the active bleeding sites. The patient was treated with steroid therapy and MZR, and subsequently underwent maintenance hemodialysis treatment for end-stage renal disease. We did not perform

a renal biopsy, because the patient already had severe renal dysfunction and the risk for additional hemorrhage was high.

Rupture of medium-sized vessels is a rare feature of AAV [9]. To the best of our knowledge, renal artery aneurysms have previously been reported in only two cases of MPA and seven cases of GPA in the English literature [2–6, 10–12]; the salient characteristics of these cases are summarized in Table 1. Of these, one case of MPA and four cases of GPA included rupture of a renal artery aneurysm, with one case of GPA requiring coil embolization [4]. The duration from the diagnosis of AAV to the aneurysm formation varies widely, from simultaneously to 15 years.

Renal vascular disease is usually described as a complication of classic PAN. The occurrence of multiple arterial aneurysms is a classical feature of PAN and is identified in 50–60% of cases, with kidney involvement 80–90% of cases [13–15]. Spontaneous renal hemorrhage is a rare but fatal clinical condition. In addition to PAN, malignant and benign neoplasms, vascular disease, renal vein thrombosis, and polycystic kidney disease are common etiologies of spontaneous perirenal hemorrhage [16]. In patients on hemodialysis, spontaneous renal hemorrhage can occur due to anticoagulation therapy during hemodialysis [17]. In our clinical case, the rapid progression of glomerulonephritis and high serum titer of MPO-ANCA were consistent with

Table 1 Reports of perirenal hemorrhage in patients with ANCA-associated vasculitis

References	Sex/age (years)	MPA/GPA	Auto-antibody	Diagnosis—aneurysm	Immunosuppressive therapy—aneurysm	Involved artery	Rupture	Presentation	Therapy	Outcome
[2]	M/24	GPA	ND	Simultaneously	Simultaneously	Renal	+	Right flank pain, shock	Gelform embolization, steroids, CYA	Survived
[3]	M/35	GPA	PR3	1 month	1 month	Hepatic, renal, splanchic	+	Left flank pain, shock	Blood transfusion, steroids, CYA, plasmapheresis	Survived, HD
[4]	M/29	GPA	PR3	5 years	5 years	Pancreatic-duodenal, hepatic, renal	+	Abdominal pain, vomiting	Coil embolization, steroids, CYA, IVIg, MMF	Survived
[5]	F/51	GPA	PR3	15 years	15 years	Renal	+	Abdominal pain, shock	Blood transfusion, fluid resuscitation	Survived, HD
[6]	M/55	MPA	MPO	20 days	26 days	Renal, hepatic	+	Abdominal pain, shock	Blood transfusion, steroids	Survived, HD
This case	F/82	MPA	MPO	7 days	7 days	Renal	+	Nausea, shock	Coil embolization, steroids, mizoribine	Survived, HD
[10]	M/30	GPA	ND	4 months	4 months	Renal	–	ND	Steroids, CYA	Survived
[10]	F/53	GPA	ND	1 month	1 month	Renal	–	ND	Steroids, CYA	Survived
[11]	M/79	GPA	PR3	4 weeks	ND	Renal	–	Hemorrhagic shock due to left colon hematoma	Plasmapheresis CYA, steroids	Survived
[12]	M/78	MPA	MPO	13 days	6 days	Renal	–	ND	Steroids	Survived, HD

CYA cyclophosphamide; *Duration* duration between aneurysms and diagnosis: *F* female; *GPA* granulomatous polyangiitis; *HD* hemodialysis; *IVIg* intravenous immunoglobulin; *M* male; *MMF* mycophenolate mofetil; *MPA* microscopic polyangiitis; *MPO* antineutrophil cytoplasmic antibody with myeloperoxidase; *ND* no data; *PR3* antineutrophil cytoplasmic antibody with anti-proteinase 3; *Ref* reference number

MPA, rather than PAN. Furthermore, there was no evidence of malignant and benign neoplasm, arteriovenous fistula, renal vein thrombosis, or polycystic kidney disease upon CT findings. Therefore, we inferred that the renal hemorrhage was due to a rupture of the renal artery caused by AAV. Disruption of the internal and external elastic laminae is noted, and may contribute to the development of aneurysmal dilation. In addition to arterial narrowing and thrombosis, inflammation can weaken the vessel wall and lead to aneurysm formation in AAV [6]. However, other etiologies, such as PAN, malignant and benign neoplasms, vascular disease, renal vein thrombosis, and polycystic kidney disease, could not be completely ruled out, and the risk for bleeding may have increased because of the use of anticoagulant therapy as a preventive measure for venous thromboembolism.

The treatment of AAV complicated by a ruptured renal artery should include supportive therapy, such as fluid resuscitation and transfusion, and transcatheter arterial embolization if active bleeding is suspected. There have been reported cases of renal artery rupture recurrence [4, 5]. Additional immunosuppression can be occasionally considered as a treatment option if vasculitis is considered the underlying cause. In the reported cases of AAV-associated ruptures of the renal artery listed in Table 1, all patients survived; however, in 50% of cases (i.e., 5 of 10 cases), regular hemodialysis for end-stage renal disease was required.

In this case, we administered MZR for maintenance therapy. MZR is an imidazole nucleoside and an immunosuppressive agent [18]. MZR is reportedly associated with a lower incidence of drug-related adverse events in comparison with cyclophosphamide (CPA) [19]. Recent reports have shown that MZR is safe and effective in maintaining remission and preventing relapse, even against AAV with elderly people and with renal insufficiency undergoing hemodialysis [19, 20]. The administration of MZR seemed to assist with the tapering prednisolone. We administered MZR, because the patient was old, end-stage renal disease on hemodialysis and in consideration of the balance between suppression of the disease activity and adverse effects of CPA treatment, such as myelosuppression and severe infection.

In conclusion, this case report describes an unusual complication of MPA. Although small-vessel vasculitis predominates in MPA, inflammation of medium-size arteries may also occur. A ruptured renal artery should be considered in a patient with MPA, even in the absence of previous trauma and renal biopsy, when unexplained anemia or signs of shock occur. Renal artery embolization provides an effective treatment option for such patients in the emergency setting.

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Compliance with ethical standards

Conflict of interest The authors have declared that no conflict of interest exists.

Ethical approval This article does not contain any studies with human participants performed by any of the authors.

Informed consent Informed consent was obtained from the participant included in the article.

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