Aneurysmal rupture in microscopic polyangiitis: a case-based review

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Abstract

Microscopic polyangiitis (MPA) affects small and medium vessel, which sometimes leads to arterial aneurysms. In English database, only 15 reports refer to ruptured aneurysms in MPA. We experienced a fatal case with MPA who developed multiple visceral aneurysms, resulting in rupture of the hepatic aneurysm. For the better knowledge of aneurysmal rupture in MPA, we reviewed the feature of 16 cases, including our case. Organ involvement observed was glomerulonephritis; 100%, pulmonary involvement; 25%, peripheral neuropathy; 25%, purpura; 12.5%. Locations of ruptured aneurysms were left gastric artery; 31.25%, renal and hepatic artery; 18.75% each, intracranial and splenic artery; 12.5% each, gastroepiploic and mesenteric artery; 6.25% each. Median time to rupture was 45 days after systemic symptom onset, and 15 days after immunosuppressive treatment induction. Symptoms at rupture were visceral pain; 68.75%, hemodynamic instability; 62.5%. Pathological findings of ruptured aneurysms were acute vasculitis in 5, no evidence of active inflammation in 3. Causes of death were aneurysmal rupture in 5, treatment complications in 3, total mortality rate was 50%. In conclusion, the initial presentation of MPA resulting in ruptured aneurysms tends to be renal-limited vasculitis. Aneurysms of abdominal medium-sized arteries tend to rupture, from 4 weeks after systemic symptom onset to 2 weeks after immunosuppressive treatment induction. Most aneurysms are less than 10 mm in diameter, develop asymptomatically in a few days, and are recognized when they rupture. Early induction of immunosuppressive treatment has the potential to shrink aneurysms and prevent rupture.
Keywords: microscopic polyangiitis, aneurysm, rupture, medium vessel vasculitis

Introduction

Symptoms of vasculitis are characterized by the size of the involved vessels. Medium vessels are defined as main visceral arteries and veins and their initial branches [1]. Medium vessel vasculitis sometimes present only with nonspecific systemic symptoms and suddenly develop life-threatening complications of organ ischemia and hemorrhage [2]. Small vessels are defined as all intraparenchymal vessels beyond the medium vessels [1]. Microscopic polyangiitis (MPA) is a form of ANCA-associated vasculitis, affecting small vessels predominantly [3]. MPA often involves the kidney, lung, nerve, and skin, which is characterized with organ-specific symptoms such as progressive renal dysfunction, interstitial pneumonia, peripheral neuropathy, and palpable purpura [4]. Aneurysms in medium-sized arteries are reminiscent of polyarteritis nodosa (PAN) [2], while several cases with aneurysms have been reported in MPA and a few of them result in aneurysmal rupture followed by fatal outcome. In our study, we reviewed the case reports of MPA with ruptured aneurysms. Our aim is to clarify the clinical features, prognosis, and management of ruptured aneurysms in MPA.

Case report

A patient in her 80s with a history of hypertension presented to our hospital with a fever of 38 degrees. Five weeks before admission, she visited her home doctor complaining of fever and fatigue, and observed with amoxicillin. Fifteen days prior to admission, screening test was performed because of her persistent fever: the data showed moderately elevated inflammatory makers and anemia, with normal creatinine level of 0.6 mg/dL. An upper gastrointestinal endoscopy showed a 70 mm-sized giant ulcer at the cardia of stomach four days before admission, with a prescription for bonoprazan 20 mg. She subsequently complained of increased fatigue with anorexia and was admitted to our hospital. Physical examination revealed her height 1.46 m, weight 35 kg, temperature 37.6 degrees, pulse rate 90 beats/min, blood pressure 143/81 mmHg, respiratory rate 20 breaths/min, and per cutaneous oxygen saturation 96% on ambient air. Abdominal examination revealed no palpable mass or tenderness. There were no respiratory, neurologic, ocular, otorhinolaryngologic, or cutaneous abnormalities. Initial blood and urinary tests are shown in Table 1. Chest and abdominal contrast-enhanced CT scan on admission showed no alveolar hemorrhage, interstitial pneumonia, or arterial aneurysms (Fig. 1A). Blood cultures, sputum mycobacterial culture, serology of hepatitis virus and tests for syphilis were negative. She was admitted with a diagnosis of partially treated urinary tract infection and received cefotiam 1 g every 8 hours. On the 4th day, myeloperoxidase (MPO)-ANCA was found to be positive. Since renal dysfunction was mild compared to her base line creatinine level, an elective renal biopsy was scheduled to diagnose MPA. On the 7th day, transaminase and biliary enzyme levels showed sudden elevation and anemia slightly deteriorated. She denied abdominal pain or abdominal tenderness. Abdominal ultrasound scan, plain CT scan and MR cholangiopancreatography image showed no abnormalities. On the 9th day, an upper gastrointestinal endoscopy revealed that the gastric ulcer (70 × 30 mm) entered the healing process with regenerative epithelium at the margins (Fig. 2). On the 11th day, her blood pressure decreased to 62/48 mmHg suddenly with right upper quadrant abdominal pain and with transaminase levels deterioration again. Resuscitative transfusion and continuous noradrenaline administration were initiated, and her systolic blood pressure recovered to 90 mmHg. Contrast-enhanced CT scan revealed a hepatic aneurysm (60 × 25 × 70 mm), a hematoma in the right liver lobe, hemorrhagic ascites (Fig. 1B), and multiple aneurysms in the hepatic, splenic, superior pancreaticoduodenal and ovarian arteries (Fig. 1C). Aneurysmal rupture of the right hepatic artery was diagnosed. Surgery or endovascular intervention was considered, but the patient preferred supportive care because of her poor general condition and passed away in 5 hours. Autopsy disclosed necrotizing vasculitis in pulmonary and renal small vessels, and glomerular tuft necrosis (Fig. 3B), consistent with MPA. Intra-abdominal aneurysms and submucosal arteries of the gastric ulcer lesion showed pathological findings of vasculitis: a specimen of the ruptured hepatic aneurysmal wall contained fibrinoid necrosis with neutrophil infiltration (Fig. 3A, 3C). NET staining was performed on the glomerular lesion and the ruptured hepatic aneurysm, both of which were positive (Fig. 3D, 3E).

Method

We conducted literature search in PubMed, Scopus, and DOAJ based on the title and abstract, using the terms “microscopic polyangiitis” AND (aneurysm OR artery) AND (rupture OR bleeding) for the period from January 1994 to July 2024. We included English-language case reports in which ruptured aneurysms were supposed to result from MPA. We collected and evaluated the data: age, gender, race, clinical presentation, clinical findings, blood test findings, treatment for MPA, timing, locations and pathological findings of ruptured aneurysms, interventions for ruptured aneurysms, and outcomes.

Results

Case identification

We identified 247 articles and excluded 165 duplicates, 7 non-English articles, 34 articles lacking case reports, 9 articles unrelated to MPA cases, 13 articles that did not report ruptured aneurysms, and 4 articles where the relationship between MPA and ruptured aneurysms was unclear. Finally, 16 articles, including our case, were evaluated [5-19].

Background of the patients

The median age was 72 (44-89) years. Eight patients (50%) were male, and eight patients (50%) were female. Eleven cases were reported from Japan, and one each from China, Spain, Scotland, the United States, and Germany. Hypertension was present in 5 cases (31.25%), and diabetes in 1 case (6.25%).

Clinical features of MPA

Clinical features observed in pre-rupture phase of aneurysms are shown in Table 2. The symptoms most frequently complained of were systemic symptoms (fever, fatigue, loss of appetite, weight loss, muscle/joint pain) followed by respiratory symptoms (coughing, dyspnoea) and neurologic symptoms (numbness of the extremities). The organ involvement most frequently observed was glomerulonephritis followed by pulmonary involvement and peripheral neuropathy. Seven patients (43.75%) had renal involvement concomitant with one or more other organ involvement, including lung, nervous system, skin, or gastrointestinal tract when diagnosed. Seven patients (43.75%) were diagnosed with pure renal involvement before the aneurysmal rupture. Two patients (12.5%) were diagnosed with MPA at autopsy.

Clinical features of ruptured aneurysms

Thirteen patients had one ruptured aneurysm, two patients had two ruptured aneurysms, and one patient had two ruptures from one location. All ruptured aneurysms were located in medium-sized arteries, which were left gastric artery; 5 cases (31.25%), the renal artery; 3 cases (18.75%), the hepatic artery; 3 cases (18.75%), the intracranial artery; 2 cases (12.5%), the splenic artery; 2 cases (12.5%), the gastroepiploic artery; 1 case (6.25%), and the mesenteric artery; 1 case (6.25%). Two patients (12.5%) experienced aneurysmal rupture before admission. Twelve patients (75%) experienced aneurysmal rupture during hospitalization; four patients had not yet received immunosuppressive treatment, eight patients were undergoing treatment. Two patients (12.5%) experienced aneurysmal rupture after discharge. The median time to admission from systemic symptom onset was 32.5 (7-120) days. The median time to aneurysmal rupture from admission was 10.5 (2-90) days: 15 (4-90) days with immunosuppressive treatment, 3 (2-11) days without. The median time to aneurysmal rupture from systemic symptom onset was 45 (14-180) days: 81.5 (14-180) days with immunosuppressive treatment, 33 (28-46) days without. The median time to aneurysmal rupture from immunosuppressive treatment induction was 15 (2-90) days. The symptoms or signs of aneurysmal rupture were pain of the targeted organ (visceral pain or headache); 11 cases (68.75%), hemodynamic instability; 10 cases (62.5%). The median size of ruptured aneurysms was 8.5 (5-15) mm. Diagnostic procedures detecting ruptured aneurysms were contrast-enhanced CT or CT angiography; 10 cases (62.5%), catheter angiography; 9 cases (62.5%). Among 8 patients with pathological findings of ruptured aneurysms, 5 patients showed active vasculitis findings (inflammation cell infiltration and fibrinoid necrosis), 1 patient showed fibrinoid degeneration without inflammatory cell infiltration,1 patient showed destruction of the internal elastic lamina without inflammatory cell infiltration or fibrinoid necrosis, and 1 patient showed a segmental arterial mediolysis (SAM)-like finding.

Treatment and outcomes

Glucocorticoid was administered in 14 cases (87.5%), 8 of which received steroid pulse therapy (intravenous infusion of 1-3 g of methylprednisolone). Cyclophosphamide was administered in 5 cases (31.25%). Rituximab was administered in 2 cases (12.5%). Azathioprine and mizoribine were administered in 1 case (6.25%) each. Plasma exchange was performed in 1 case (6.25%). Renal replacement therapy was performed in 7 cases (43.75%). Four patients (25%) died directly of aneurysmal rupture. Five patients (31.25%) received emergency surgery (laparotomy or craniotomy) owing to limited access for endovascular intervention or contraindications for elective treatment based on their general condition. Five patients (31.25%) received endovascular treatment. Two patients (12.5%) received conservative treatment. Of the 5 patients who received surgical treatment, 1 patient died from hemodynamic instability despite perioperative care, 3 patients died from subsequent nosocomial infections, and 1 patient survived. All 5 patients who were decided to be indications for endovascular treatment survived, albeit 3 of them had unstable hemodynamics. The 2 patients who were selected for conservative treatment owing to their good general condition survived. Eventually, the mortality rate was 50%. Fig. 4 summarize the clinical courses of the cases reviewed.

Discussion

In our review, MPA complicated with ruptured aneurysms had a lower frequency of involvement of lung, nervous system and skin, except for kidney. Ruptured aneurysms showed typical acute vasculitis findings or no evidence of active inflammatory findings, with a tendency to occur from 4 weeks after systemic symptom onset to 2 weeks after immunosuppressive treatment induction. Aneurysms in MPA were usually below 10 mm in size, were asymptomatic until rupture, and located in various abdominal medium-sized arteries, sometimes in cerebral arteries. Intra-abdominal or biliary hemorrhage due to ruptured aneurysms required for emergency intervention.

Hankard et al. reported the clinical features, rupture rate, and mortality rate in ANCA-associated vasculitis complicated with aneurysms, while the majority of the cases included were granulomatosis with polyangiitis [20]. The review did not discuss the pathological findings or treatment options of ruptured aneurysms.

Generally, pulmonary involvement is seen in 25-55% of MPA cases, neurologic involvement in 37-72%, and cutaneous involvement in 30-60% [3]. In our review, pulmonary, neurologic, and cutaneous involvement were relatively uncommon, with 25%, 25%, and 12.5% of cases, respectively. The involvement reported was pulmonary parenchymal involvement, peripheral neuropathy and purpura, all of which are manifestations specific to small vessel vasculitis (pulmonary parenchyma, peripheral nerves and dermis are all supplied by small vessels) [21-23]. Conventional MPA is small vessel dominant, while some cases are poor in small vessel lesions. Sano et al. reported that MPA has two clinical phenotypes: one that shows significant capillaritis of glomeruli and lung, and one that shows glomerular capillaritis without pulmonary involvement. The former had a low frequency of arteritis and the latter tended to affect small to medium-sized arteries [24]. This may mean that MPA with few small vessel lesions has an intermediate spectrum between small and medium vessel vasculitis. However, it is unclear why a high frequency of renal glomerular lesions is consistently observed, regardless of other organ involvement. The subgroup of MPA with only renal involvement is called renal-limited vasculitis (RLV), which accounts for one-quarter to one-third of MPAs [25, 26]. Compared to non-renal-limited

MPA, RLV is characterized with lower C-reactive protein levels (median 1.3 mg/dL, interquartile range 0.4-3.1 mg/dL) [26]. 43.75% of the patients in our review were initially diagnosed with RLV, whose C-reactive protein levels were high and ranged from 2.9-21.1 mg/dL (median 7.4 mg/dL). Fig. 5 shows the C-reactive protein levels of the group initially diagnosed with RLV and the non-renal-limited MPA group in our review. Although the early clinical presentation of MPA with ruptured aneurysms resembles that of RLV, a higher C-reactive protein level may serve as a differential point from conventional RLV.

Arkin classified the stages of necrotizing arteritis into the degenerative stage, acute inflammatory stage, granulation tissue stage, and healed granulation tissue stage [27]. In MPA, arterial aneurysms form mainly in the acute inflammatory stage, leading to rupture following the progressive dilation of necrotic vessel walls [28]. Among the 5 patients whose pathological findings of ruptured aneurysms showed vasculitis in the acute inflammatory stage, no patient had pulmonary, neurologic, and cutaneous involvement; the time to rupture after systemic symptom onset was 44-46 days; the time to rupture after immunosuppressive treatment induction was 2-15 days. These features were well consistent with the overall trend of this review. The situation of the 3 patients without active vasculitis findings were as follows; case 12 of reference [16] experienced rupture of a mesenteric aneurysm due to severe hypertension during the remission period three months after the induction of immunosuppressive treatment; case 3 of reference [7] experienced re-rupture of a posterior inferior cerebellar aneurysm after receiving surgical clipping; case 4 of reference [8] experienced rupture of a left gastric aneurysm with the SAM-like pathological finding, before the onset of MPA symptoms. Two mechanisms of aneurysmal rupture in MPA are considered: rupture originated directory from vasculitis during the acute stage of MPA, occurring from a month after the disease onset to within 2 weeks of treatment induction, and rupture unrelated to the course of vasculitis, which is caused by secondary factors such as hypertension.

The treatment indication for visceral aneurysms depends on the size, location, etiology of the aneurysms, or complications of rupture [29, 30]. Visceral aneurysms larger than 20 mm in diameter have a risk of rupture and are indicated for prophylactic treatment, whereas microaneurysms smaller than 10 mm are prone to rupture if caused by vasculitis [20, 29]. In the pancreaticoduodenal, gastroduodenal and hepatic artery, false aneurysms (inflammatory, traumatic, genetic) are more common than true aneurysms, meaning the aneurysms in these arteries have a potentially higher risk of rupture [30, 31]. Multiple (more than 4) aneurysms or irregular aneurysmal walls with perivascular inflammation on imaging are suggestive of inflammatory aneurysms [30, 32]. Practically, precise identification of the etiology requires pathological examination [31]. The standard treatment for visceral aneurysms is either open surgery or endovascular intervention, which should be decided based on the ability to tolerate the procedure, aneurysmal shape, and collateral circulation [33, 34]. Aneurysms due to vasculitis may regress with immunosuppressive agents alone [20]. In PAN, medical treatment precedes surgical or endovascular treatment for unruptured aneurysms [35]. However, the risks of aneurysmal rupture are significantly different between MPA and PAN (43% vs 9%, respectively) [20, 36]. Aneurysms of MPA should not be treated equally with those of PAN. Our patient's initial contrast-enhanced CT scan, performed 11 days before rupture of the hepatic aneurysm, did not detect any aneurysms. In case 14 of reference [18], where a splenic aneurysm ruptured 10 days after rupture of a gastroepiploic aneurysm, the splenic aneurysm was not detected on the initial catheter angiography. The gold standard procedure for detecting microaneurysm is catheter angiography [37], while CT angiography is considered to be less invasive with almost the same detection ability [12, 30]. These may suggest that new aneurysms form in a short period of time in MPA, rather than that microaneurysms are easily missed on angiography. Eventually, early detection of visceral aneurysms is difficult in MPA. In contrast to PAN, the use of angiography as a screening tool for microaneurysms seem to be unfeasible. PET-CT scanning allow the detection of inflammation in arterial walls before aneurysmal formation and is expected to be useful not only for the evaluation of large vessel vasculitis, but also for the medium vessel vasculitis [38].

Ruptured visceral aneurysms typically induce gastrointestinal bleeding and intra-abdominal hemorrhage, with a high mortality rate of 25-70% [29]. The total mortality rate in our review was 50%. The 5 patients who underwent surgical treatment had the highest mortality rate of 80% (4 patients died), while all 5 patients who received endovascular treatment survived. The 12 patients of intracranial, intra-abdominal or biliary hemorrhage due to ruptured aneurysms were decided to be candidates for emergency intervention regardless of hemodynamics, none of whom survived with conservative treatment alone. The 2 patients who experienced rupture of renal aneurysms and subsequent retroperitoneal hematomas had stable hemodynamics maintained through conservative treatment alone, whose aneurysms regressed after 2-6 months of immunosuppressive treatment. One patient experienced a ruptured renal aneurysm and a large retroperitoneal hematoma with ascites, and survived with endovascular treatment owing to hemodynamic instability with conservative treatment. One patient experienced a ruptured hepatic artery aneurysm and was received with endovascular treatment for unspecified reasons. While endovascular treatment for ruptured visceral aneurysms has technical issues due to the difficulty of manipulating the device and identifying the target artery [39], it supersedes surgical treatment in situations where general anesthesia is difficult, such as hemodynamic instability [40]. Therefore, endovascular intervention is the first choice for ruptured aneurysms with gastrointestinal bleeding or intra-abdominal hemorrhage. When the hematoma is localized to the retroperitoneum, conservative treatment should be prioritized, and intervention should be considered if the effect is insufficient.

Our patient showed characteristic gastrointestinal involvement prior to aneurysmal rupture. In general, the gastrointestinal involvement of small vessel vasculitis is patchy mucosal erosions, ulcers, and bleeding, whereas medium vessel vasculitis manifests more extensive ischemia [41]. The giant gastric ulcer in our patient

corresponded to lesions of the later. Sano et al. reported that medium vessel lesions in MPA included cerebral hemorrhage, multiple small intestinal ulcers, and skin eruptions [24]. While only two cases with gastrointestinal involvement suggestive of medium vessel vasculitis were observed in our review, the presence of extensive ischemic lesions in the gastrointestinal tract raises the possibility of aneurysms in medium-sized arteries.

Both MPA and PAN show fibrinoid necrosis with neutrophil infiltration and are generally classified on the affected vessel size, although some cases involve a mixture of small and medium vessel vasculitis [42]. In cases with MPA accompanied with medium arteritis, the origin of the arteritis is hard to differentiate MPA from PAN. Neutrophil extracellular trap (NET) deposition in necrotizing vasculitis lesions is reported to be a characteristic feature of ANCA-associated vasculitis [43]. NETs are pathogenic agents responsible for vascular damage in ANCA-associated vasculitis [44]. The small vessel vasculitis and glomerular crescent lesions contain abundant NET formation [44]. A novel immunofluorescent staining method allows visualization of NET formation in tissues. This method targets the components of NETs: citrullinated histone H3, extracellular DNA and MPO [45]. Co-localization of these NETs markers with neutrophil infiltration is characteristics of MPA, although this finding is not prominent in medium arteritis of PAN [43]. NET staining might be an optimal procedure to differentiate medium arteritis of MPA from PAN. In our case, medium arteritis was diagnosed as MPA-derived vasculitis with NET staining.

Conclusion

Aneurysmal rupture is one of the life-threatening complications in MPA. MPA with ruptured aneurysms tends to present initially as renal-limited vasculitis, which requires close monitoring especially if the C-reactive protein level is high. Most aneurysms in MPA are small, asymptomatic and sometimes rapidly enlarging, making them difficult to detect before rupture. Endovascular intervention has a high survival rate and should be prepared for emergencies. Immunosuppressive agents have the potential to regress aneurysms and prevent rupture, suggesting the need for early induction of treatment.

Declarations

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Conflict of interest The authors have declared no conflicts of interest.
Ethics approval Written informed consent was obtained from the patient’s family.
Data availability Data are available upon reasonable request.
Author contributions Keita Imanishi and Kazuhiro Yasuo contributed to the study's conception and design. Keita Imanishi drafted the initial manuscript. Kazuhiro Yasuo supervised the process critically. All authors approved the final manuscript and take full responsibility for the integrity and accuracy of all aspects of the work.

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Figure and Table

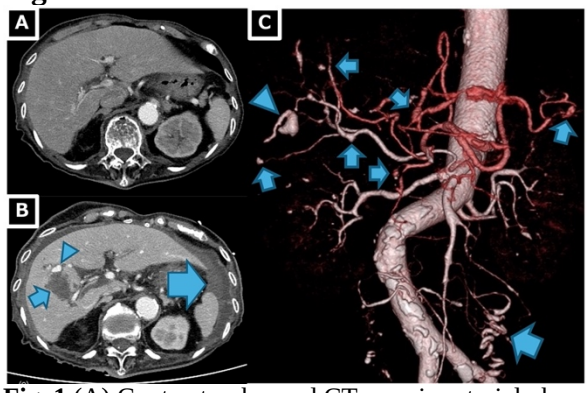

Fig. 1 (A) Contrast-enhanced CT scan in arterial phase: No abnormality of visceral arteries on admission. (B) Contrast-enhanced CT scan in arterial phase: an aneurysm (60 × 25 × 70 mm, arrowhead) and a hematoma (small arrow) in the right liver lobe and hemorrhagic ascites (large arrow) on the 11th day. (C) 3D-CT angiography (reconstruction of CT on the 11th day): Multiple microaneurysms (arrows) in the hepatic, splenic, superior pancreaticoduodenal and ovarian arteries, notably a ruptured aneurysm (arrowhead) in the right hepatic artery.

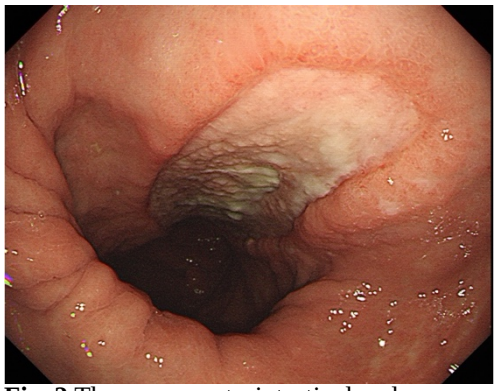

Fig. 2 The upper gastrointestinal endoscopy on the 9th day revealed the gastric ulcer (70 × 30 mm) with regenerative epithelium at the margins in healing stage.

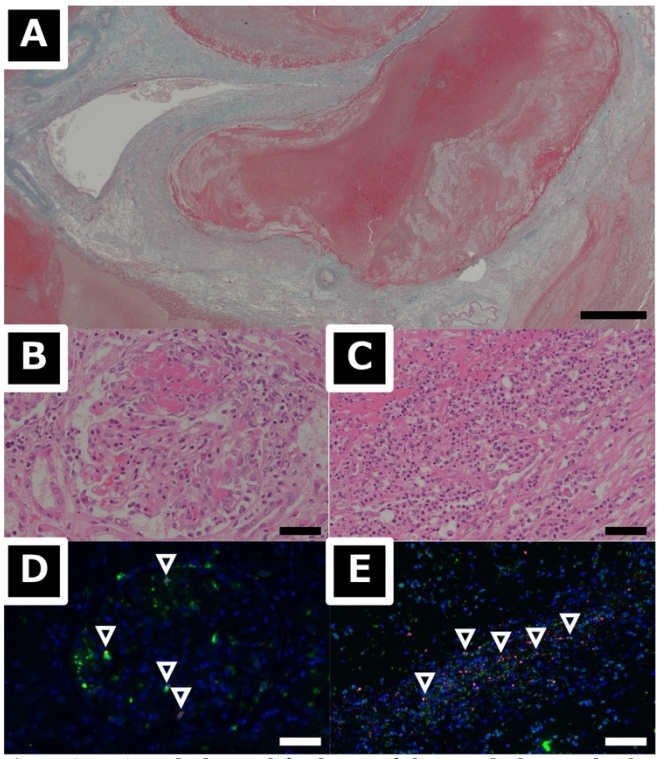

Fig. 3 (B, D) Pathological findings of the renal glomerular lesion of our case: (B) Hematoxylin and Eosin staining. Bar, 50 μm. (D) Merge of Citrullinated histone H3 (Cit-H3), DNA and myeloperoxidase (MPO) staining. Bar, 50 μm: Numerous neutrophils showing co-localization (arrowheads) with Cit-H3 (red), extracellular DNA (blue) and MPO (green). (A, C, E) Pathological findings of the ruptured hepatic aneurysm: (A) Masson-Goldner staining. Bar, 1 mm. (C) Hematoxylin and Eosin staining. Bar, 50 μm : Fibrinoid necrosis and marked neutrophil-based inflammatory cell infiltration in all layers of the arterial wall. (E) Merge of Cit-H3, DNA and MPO staining. Bar, 50 μm: Co-localization of NETs markers (arrowheads) proving that the origin of the hepatic aneurysm lesion was MPA.

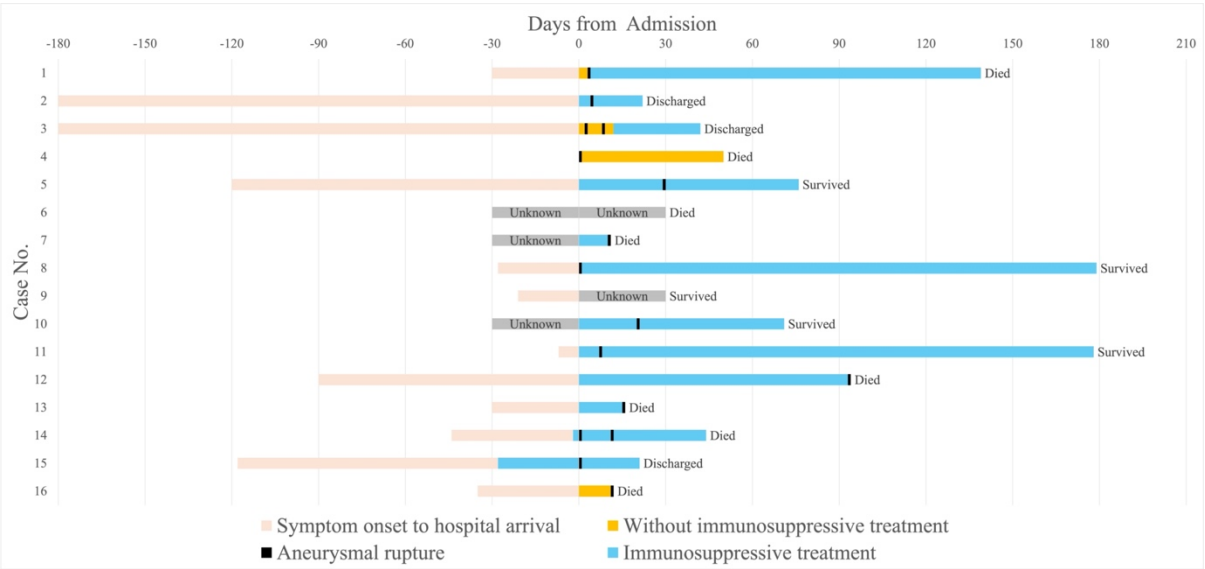

Fig. 4 Clinical courses and outcomes of individual patients included in this review: Cases 1-15 in the figure correspond to patients [5-19] in order. Case 16 is our patient.

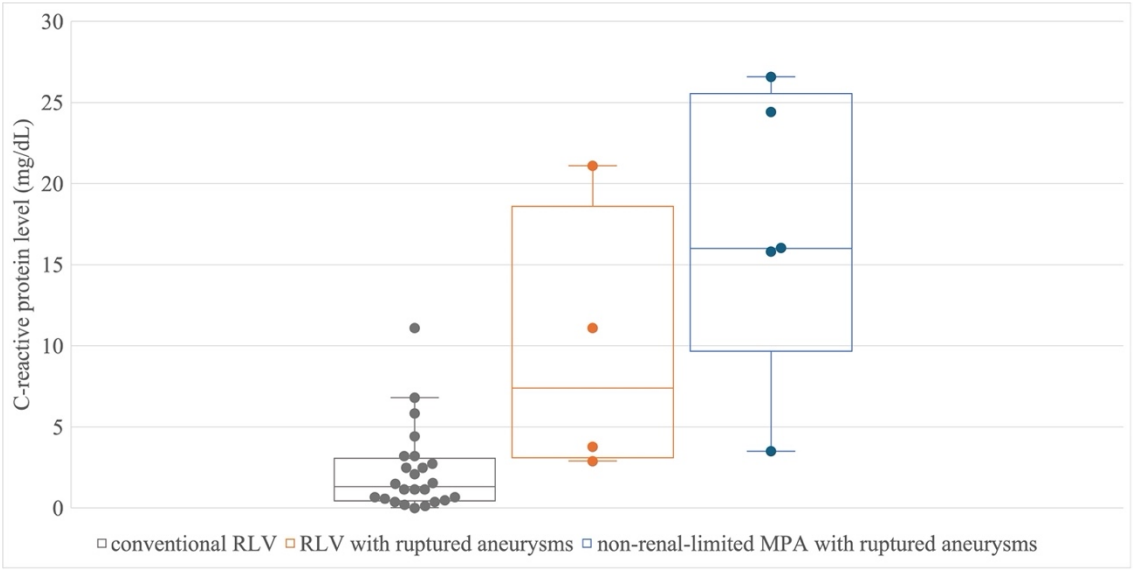

Fig. 5 Boxplots of C-reactive protein levels in the 3 groups: the conventional RLV group [26], the group initially diagnosed with RLV and complicated with ruptured aneurysms, the group diagnosed with non-renal-limited MPA and complicated with ruptured aneurysms. The box spans the interquartile range of the data. The middle line of the box indicates the median. The whiskers range from the upper extreme to the lower extreme of the data. The data are plotted as individual points. Compared to the conventional RLV group, the RLV with ruptured aneurysms group and the non-renal-limited MPA with ruptured aneurysms group tend to have higher C-reactive protein levels.

	Day 1	Day 2	Day 4	Day 7	Day 8	Day 9	Day 11	Reference
White blood cell count − $\times 10^3/\mu L$	19.44	20.18	25.79	20.53		19.06	16.76	33.0-86.0
Hemoglobin − g/dL	7.0	6.9	7.4	6.8		7.1	6.0	11.6-14.8
Platelet count − $\times 10^4/\mu L$	65.6	72.5	65.2	57.9		52.7	41.8	15.8-34.8
Total bilirubin − mg/dL	0.47	0.39	0.49	0.60	0.68	0.59	1.09	0.40-1.50
Direct bilirubin − mg/dL	0.13	0.12		0.19	0.20			0.10-0.30
Aspartate aminotransferase − U/L	18	16	85	839	154	73	303	13-30
Alanine aminotransferase − U/L	18	14	43	556	291	191	180	7-23
Lactate dehydrogenase − U/L	135	182	201	407	174		482	124-222
Alkaline phosphatase − U/L	114	101	111	407	330	332	427	38-113
γ-Glutamyl transpeptidase − U/L	36	33	38	178	135	128	196	9-32
Albumin − g/dL	1.8		1.6	1.4	1.4	1.3		4.1-5.1
Blood urea nitrogen − mg/dL	24.4	22.2	26.5	26.4	27.6	32.6	34.6	8.0-20.0
Creatinine − mg/dL	0.81	0.79	0.79	0.97	1.03	1.19	1.36	0.46-0.79
C-reactive protein − mg/dL	16.01	17.86	16.19	14.23	17.96	20.79	9.73	<0.14
Myeloperoxidase-ANCA − U/mL	114							<3.5
Proteinase 3-ANCA − U/mL	Negative							Negative
Urinalysis								
Protein	1+							Negative
Occult blood	3+							Negative
White blood cell count − /HPF	5-9							<5
Red blood cell count − /HPF	20-29*							<5

Table 1 Laboratory parameters of our case. Reference ranges are from laboratories of the authors' institutions.
*Isomorphic.

Symptoms before aneurysmal rupture − no. (%)	
Systemic symptoms	13 (81.25)
Respiratory symptoms	4 (25)
Neurological symptoms	4 (25)
Abdominal symptoms	1 (6.25)
Urinary symptoms	1 (6.25)
Organ Involvement − no. (%)	
Kidney	16 (100)
Lung	4 (25)
Peripheral nervous system	4 (25)
Skin	2 (12.5)
Gastrointestinal tract	2 (12.5)
Median laboratory values at diagnosis (range)	
White blood cell count − $\times 10^3/\mu L$	15.08 (10.4-32.71)
Hemoglobin − g/dL	8.75 (7-11.9)
Platelet count − $\times 10^4/\mu L$	39.6 (13.9-65.6)
Creatinine − mg/dL	3.8 (0.81-8.13)
C-reactive protein − mg/dL	15.85 (2.9-26.6)
ANCA subtype − no. (%)	
Myeloperoxidase	15 (93.75)
Proteinase 3	0 (0)
Median Birmingham Vasculitis Activity Score at diagnosis (range)	23.5 (14-37)
Initial diagnosis − no. (%)	
Non renal limited vasculitis	7 (43.75)
Renal limited vasculitis	7 (43.75)
Autopsy-proven systemic vasculitis	2 (12.75)

Table 2 Clinical features of MPA cases included in this review.