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RESEARCH ARTICLE

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Clinical features and endovascular treatment of ruptured peripheral cerebral aneurysms associated with moyamoya disease: an 8-year single-center experience

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ABSTRACT

Objective: Ruptured peripheral cerebral aneurysm (PPCA) associated with moyamoya disease (MMD) is rarely reported, and its optimal treatment remains controversial. This study aims to present the clinical characteristics, treatment strategies, and outcome predictors of this rare clinical entity.

Methods: A retrospective review of patients with hemorrhagic MMD from January 2013 to December 2020 was performed. All medical records were independently compiled and reviewed.

Results: Twenty-three patients were identified, 56.5% of whom were female. The mean age was 45.9 years with a peak age of onset of 51-60 years. Most patients (65.2%) developed intraventricular hemorrhage with or without intracerebral hemorrhage. These aneurysms were frequently located on the anterior (26.1%) and posterior (43.5%) choroidal arteries. Sixteen (69.6%) aneurysms were embolized and the remaining 7 (30.4%) were managed conservatively due to approach inaccessibility. Good outcomes were achieved in 82.6% of all cases, with 81.3% for embolization and 85.7% for observation. Complete occlusion was observed in all 16 aneurysms embolized. Of the conservatively treated aneurysms, 1 (14.3%) re-ruptured, 1 (14.3%) decreased in size, 2 (28.6%) disappeared, and 3 (42.8%) remained stable in size. Aneurysm rebleeding was associated with an unfavorable outcome (P = 0.026).

Conclusions: PPCA should be considered in the differential diagnosis of hemorrhagic MMD. Aneurysm rebleeding appears to be a potential predictor of poor outcome and therefore aggressive intervention should be advocated. Endovascular embolization may be safe and feasible, and conservative observation should be carefully chosen given the high risk of aneurysm re-rupture.

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KEYWORDS
Moyamoya disease; hemorrhage; aneurysm; treatment; outcome

Introduction

The prevalence of intracranial aneurysms in patients with moyamoya disease (MMD) has been reported to be 3%-18%, which is higher than the 2%-3% prevalence in the general population [1–3]. According to the anatomic location, such aneurysms are conventionally categorized as major trunk aneurysms originated from large arteries of the circle of Willis and peripheral cerebral aneurysms (PPCAs) located on the choroidal, lenticulostriate, thalamoperforator, meningeal, or moyamoya vessels [3–5]. MMD patients with cerebral aneurysms are at a potential hemorrhagic risk because such aneurysms are vulnerable to rupture due to the fragile vascular wall and increased hemodynamic stress [4–7]. Given this, prompt and appropriate intervention to prevent this aneurysm from rebleeding seems plausible.

However, the optimal treatment for MMD-related ruptured PPCAs remains controversial. Several authors have directly treated these aneurysms by endovascular embolization or surgical obliteration, while others have opted for revascularization surgery or conservative observation on the grounds that they may spontaneously regress [5,6,8–13].

To date, studies of ruptured PPCAs in MMD are relatively limited, and most of the literature consists of

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case reports only. Here, we retrospectively review the clinical characteristics and thereafter discuss the treatment and prognostic factors of ruptured PPCAs in MMD patients to improve the understanding of this rare but significant clinical entity. To the best of our knowledge, this is the largest study in the literature to date on ruptured PPCAs in MMD patients.

Methods

Patient selection

Consecutive patients with hemorrhagic MMD at our single institution from January 2013 to December 2020 were retrospectively reviewed, and their medical records were collected. This study adhered to the Declaration of Helsinki and was approved by the Ethics Committee of The Third Bethune Hospital of Jilin University (China-Japan Union Hospital of Jilin University), and written informed consent was obtained from all participants or their legal guardians. Written informed consent to publish has been obtained from all individuals or their legal guardian.

Intracranial hemorrhage was confirmed by non-contrast computed tomography, and the diagnosis of MMD was made by digital subtraction angiography according to the Japanese guideline [14]. The inclusion criteria were as follows: (1) patient definitively diagnosed with MMD; and (2) the presence of intracranial hemorrhage. Patients were excluded based on the following criteria: (1) hemorrhage not attributable to ruptured aneurysm; (2) patient with moyamoya syndrome; (3) patient with main trunk aneurysm; (4) lost to follow-up; and (5) inadequate clinical data.

We collected the following information from each patient: demographics, medical history, MMD characteristics (definitive or probable, Suzuki stage), admission presentation, type of hemorrhage, acute hydrocephalus, aneurysm location, treatment, and follow-up outcome.

Treatment strategy

Endovascular embolization as a first-line treatment for MMD-associated PPCAs was performed under general anesthesia. Briefly, the microcatheter was navigated to or as close as possible to the aneurysm, and then the liquid adhesive agents were used to embolize the aneurysm, sacrificing the proximal and distal segment of the parent artery. Direct open surgery, revascularization bypass, or conservative observation were alternatives when selective catheterization was inaccessible. External ventricular drainage was performed in cases of acute hydrocephalus and neurological deterioration.

Follow-up outcome

All patients were discharged after the acute phase of intracranial hemorrhage. Routine clinical follow-up was initiated at 1 and 6 months after discharge and annually thereafter. Neurological outcome, as assessed by the modified Rankin Scale (mRS), was dichotomized categorized as good (mRS 0-3) or poor (mRS 4-6).

Statistical analysis

Continuous data were expressed as mean ± standard deviation. Pearson's chi-squared test or Fisher's exact test was used to assess categorical and continuous variables, respectively. Statistics were calculated with SPSS version 19.0 (IBM Corp, Armonk, New York, USA). A 2-sided $p < 0.05$ was considered significant.

Results

A total of 178 patients with hemorrhagic MMD were screened, of whom 23 (12.9%) were finally eligible for inclusion in the study (Figure 1, Table 1). We present a comprehensive mapping of aneurysm types, treatment, and outcome using a Sankey diagram (Figure 2). General demographic and aneurysm characteristics are summarized in Table 2.

Of these, 13 (56.5%) were female and 10 (43.5%) were male, with a female to male ratio of 1.3:1. The mean age was 45.9 years (range 24–73 years), and the age distribution was as follows: 21–30 years ($n = 4$; 17.4%), 31–40 years ($n = 1$; 4.3%), 41–50 years ($n = 7$; 30.4%), 51–60 years ($n = 10$; 43.5%), ≥61 years ($n = 1$; 4.3%). Twelve patients (52.2%) had hypertension, 3 (13.0%) had diabetes mellitus, and 2 (8.7%) had hyperlipidemia.

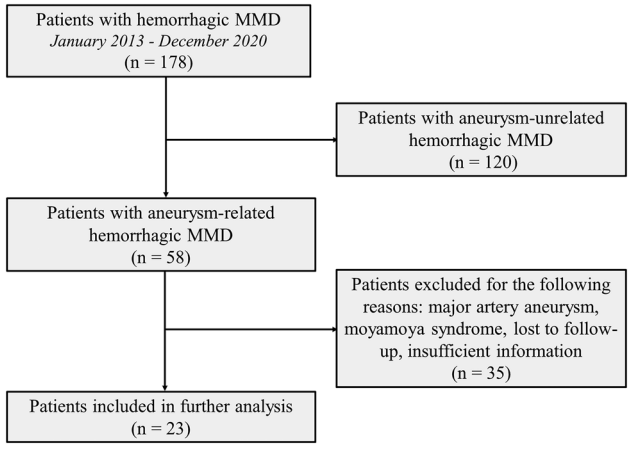

Figure 1. Patient flow diagram. MMD, moyamoya disease.

Table 1. Patient summary.

Case no.	Age/ sex	Past history	Suzuki stage	Admission symptom	Initial mRS	Hemorrhagic type	Acute hydrocephalus	Aneurysm location	Treatment	Follow-up(month)	Outcome (mRS)
1	45/F	HTN	Bilateral, III	Impaired consciousness	5	IVH	Yes	PChA	Embolization	85	Good (2)
2	38/F		Bilateral, III	Impaired consciousness	5	IVH	Yes	PChA	Embolization	85	Good (2)
3	56/F	HTN, DM	Bilateral, III	Headache	2	IVH		LSA	Embolization	83	Good (0)
4	45/F	HTN	Bilateral, III	Impaired consciousness	5	ICH + IVH	Yes	PChA	Embolization	83	Poor (4)
5	24/F	DM	Left, III	Headache	2	IVH		PChA	Observation	67	Good (0)
6	46/M		Bilateral, IV	Impaired consciousness	5	ICH + IVH	Yes	AChA	Embolization	61	Good (3)
7	44/F		Bilateral, III	Headache	2	SAH		PChA	Embolization	56	Good (0)
8	57/F	HTN	Right, III	Headache	2	SAH		AChA	Observation	53	Good (0)
9	55/M	HTN	Bilateral, IV	Hemiplegia	4	ICH + IVH		AChA	Embolization	53	Good (2)
10	69/M	DM, HL	Left, IV	Headache	2	ICH		RAH	Observation → rebleeding → death	1	Poor (6)
11	51/M	HTN	Bilateral, II	Headache	2	SAH		AChA	Observation	46	Good (0)
12	52/M	HTN	Right, II	Headache	2	IVH		PChA	Embolization	35	Good (0)
13	41/F		Bilateral, III	Hemiplegia	4	ICH + IVH		PChA	Observation	20	Good (2)
14	26/F		Bilateral, III	Headache	2	IVH		PChA	Embolization	74	Good (0)
15	58/M	HTN	Left, III	Headache	2	SAH		AChA	Observation	6	Good (1)
16	38/M		Bilateral, IV	Headache	2	IVH		PChA	Embolization	48	Good (1)
17	46/F	HTN	Bilateral, III	Impaired consciousness	5	ICH+IVH	Yes	Distal MCA	Embolization	8	Poor (4)
18	28/M		Bilateral, III	Impaired consciousness	5	IVH	Yes	PChA	Embolization	23	Good (2)
19	44/M	HTN	Left, II	Headache	2	SAH		Distal ACA	Embolization	17	Good (0)
20	55/F	HL	Right, II	Headache	2	SAH		Distal PCA	Embolization	6	Good (0)
21	30/M		Bilateral, III	Headache	2	IVH	Yes	AChA	Embolization	34	Poor (4)
22	53/F	HTN	Bilateral, II	Headache	2	SAH		Distal PCA	Embolization	9	Good (1)
23	51/F	HTN	Bilateral, IV	Impaired consciousness	5	ICH+IVH	Yes	Moyamoya vessel	Observation	6	Good (3)

ACA: anterior cerebral artery; AChA: anterior choroidal artery; DM: diabetes mellitus; F: female; HL: hyperlipemia; HTN: hypertension; ICH: intracerebral hemorrhage; IVH: intraventricular hemorrhage; LSA: lenticulostriate artery; M: male; MCA: middle cerebral artery; MMD: moyamoya disease; mRS: modified Rankin Scale; PCA: posterior cerebral artery; PChA: posterior choroidal artery; RAH: recurrent artery of Heubner; SAH: subarachnoid hemorrhage.

Regarding the characteristics of MMD, 16 patients (69.6%) had definite (bilateral) MMD and 7 (30.4%) had probable (unilateral) MMD; the distribution of the initial Suzuki stage of MMD was as follows: stage II, $n=5$ (21.7%); stage III, $n=13$ (56.5%); and stage IV, $n=5$ (21.8%).

These aneurysms were most frequently located on the posterior choroidal artery (PChA, 10/23, 43.5%), followed by the anterior choroidal artery (AChA, 6/23, 26.1%). Seven patients (30.4%) had subarachnoid hemorrhage (SAH), 9 (39.1%) had intraventricular hemorrhage (IVH), 1 (4.3%) had intracerebral hemorrhage (ICH), and 6 (26.1%) had IVH+ICH. Admission symptoms included headache (14/23, 60.9%), disturbance of consciousness (7/23, 30.4%), and hemiplegia (2/23, 8.7%).

All aneurysms were initially treated by endovascular embolization with a technical success rate of 69.6% (16/23). The adjacent segment of the parent artery and the aneurysm were occluded together without any related neurological deterioration (Figure 3). The remaining 7 aneurysms (7/23, 30.4%) failed not be embolized due to inaccessibility of the approach, and these patients declined surgical intervention of the aneurysms due to the potential risks and were subsequently managed conservatively. Acute hydrocephalus occurred in 4 cases (17.4%) and a ventricular drainage was subsequently performed.

Mean follow-up was 41.7 months (range, 1-85 months). Of the 23 patients, 19 (82.6%) had a favorable outcome and the remaining 4 (17.4%) had an unfavorable outcome. The rates of good outcome were 81.3% (13/16) and 85.7% (6/7) in the endovascular and conservative groups, respectively. Follow-up angiograms showed that complete occlusion was achieved in all 16 aneurysms

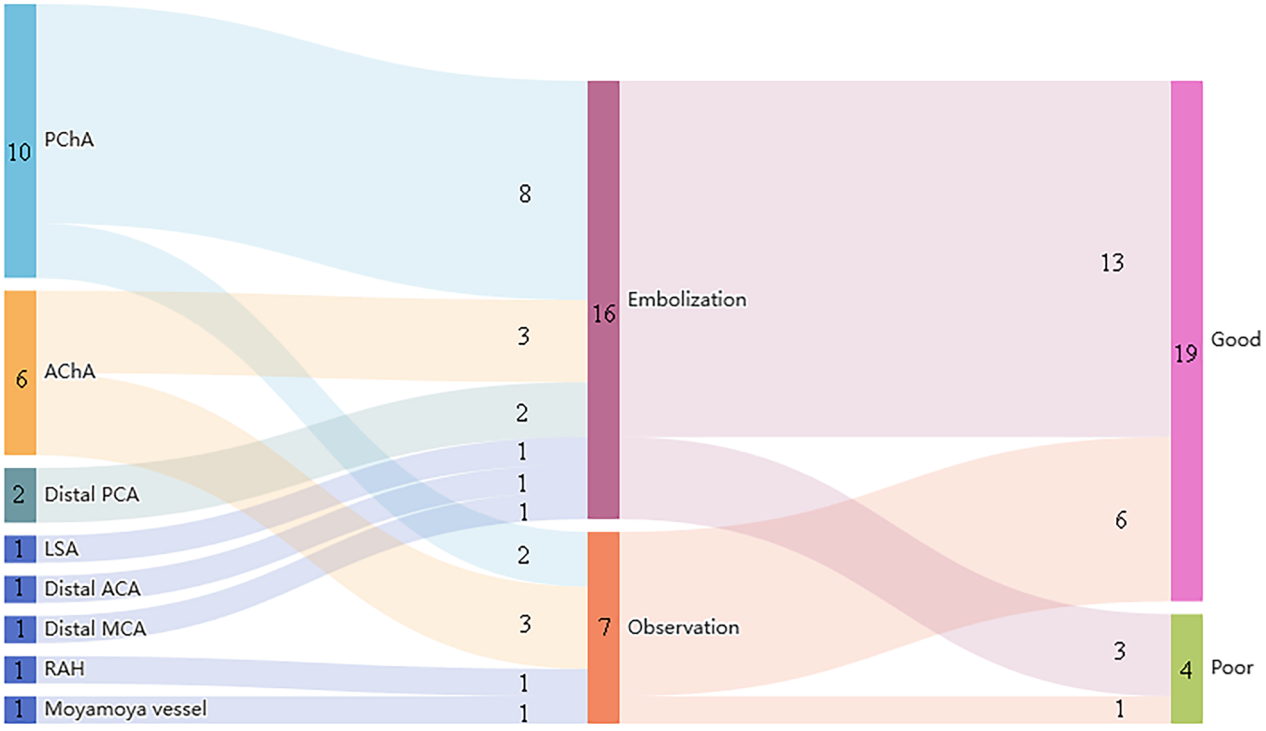

Figure 2. Sankey diagram of aneurysm types, treatment, and outcome. ACA: anterior cerebral artery; AChA: anterior choroidal artery; LSA: lenticulostriate artery; MCA: Middle cerebral artery; PCA: posterior cerebral artery; PChA: posterior choroidal artery; RAH: recurrent artery of heubner.

treated with endovascular embolization. Of the 7 aneurysms under conservative observation, 1 (14.3%) experienced aneurysm rebleeding leading to the patient's death at the 1-month follow-up, 2 (28.6%) disappeared, 1 (14.3%) decreased in size, and 3 (42.8%) remained stable in size during the follow-up period (Figure 4). There was a significant difference between aneurysm rebleeding and outcome ($p = 0.026$) (Table 3).

Discussion

Compared to main branch aneurysms in the MMD population, the number of reports on MMD-associated PPCAs is relatively few, suggesting that such aneurysms may be underestimated in clinical practice because they are typically small, deep and easily missed on routine brain imaging. Moreover, most PPCAs may remain undiagnosed unless they rupture and cause intracranial hemorrhage. Although the exact mechanism of the formation, growth, and rupture of this lesion remains to be elucidated, previous studies have shown that prolonged hemodynamic stress and arterial wall attenuation are involved [3,4,6,15].

In terms of clinical characteristics, our study showed that MMD-associated PPCAs seemed to: (1) have a slight female predominance (56.5%), (2) have a peak age of onset of 51–60 years (43.5%), (3) frequently present with headache (60.9%), (4) are commonly accompanied by IVH with or without ICH (65.2%), and (5) often originate from the PChA and AChA (69.6%). Therefore, PAA should be considered as a potential source of bleeding in the setting of hemorrhagic MMD, especially when correlated with the aforementioned features, and conventional cerebral angiography is necessary to identify such a lesion to avoid missed diagnosis and misdiagnosis [12].

Rhim at al. reported 19 patients with aneurysm-related hemorrhagic MMD and found that 73.7% of them had bilateral MMD, and all of them were Suzuki stage III or IV at the time of hemorrhage [6]. These results were somewhat consistent with those of our study (bilateral MMD, 69.6%; Suzuki stage III or IV, 78.3%). Patients with unilateral MMD are prone to the formation of anterior circulation aneurysms on the unaffected side due to increased hemodynamic stress, whereas patients with bilateral MMD are susceptible to the formation of posterior circulation aneurysms [1,2]. Under these circumstances, the late Suzuki stages are often accompanied by uncoordinated distribution of the cerebral circulation and development of collateral compensation in the posterior circulation, thereby predisposing to the formation of PPCAs due to sufficient long-term hemodynamic burden on the fragile collateral vessels [1,3,16]. In short, aneurysmal formation

Table 2. General demographics of study population.

Number of patients	23
Age(years, mean ± SD)	45.9 ± 11.7
Sex	
Male	10(43.5%)
Female	13(56.5%)
Past history	
HTN	12(52.2%)
DM	3 (13.0%)
HL	2(8.7%)
MMD	
Unilateral	7(30.4%)
Bilateral	16(69.6%)
Suzuki stage	
II	5(21.7%)
III	13(56.5%)
IV	5(21.7%)
Admission symptom	
Headache	14(60.9%)
Impaired consciousness	7(30.4%)
Hemiplegia	2(8.7%)
Hemorrhagic type	
IVH	9(39.1%)
SAH	7(30.4%)
IVH+ICH	6(26.1%)
ICH	1(4.3%)
Acute hydrocephalus	8(34.8%)
Aneurysm location	
PChA	10(43.5%)
AChA	6(26.1%)
Distal PCA	2(8.7%)
Distal ACA	1(4.3%)
Distal MCA	1(4.3%)
LSA	1(4.3%)
Moyamoya vessel	1(4.3%)
RAH	1(4.3%)
Treatment	
Embolization	16(69.6%)
Observation	7(30.4%)
Aneurysm re-rupture	1(4.3%)
Time of follow-up (months, mean ± SD)	41.7 ± 29.4
Outcome	
Good	19(82.6%)
Poor	4(17.4%)

ACA: anterior cerebral artery; AChA: anterior choroidal artery; DM: diabetes mellitus; HL: hyperlipemia; HTN: hypertension; ICH: intracerebral hemorrhage; IVH: intraventricular hemorrhage; LSA: lenticulostriate artery; MCA: middle cerebral artery; MMD: moyamoya disease; PCA: posterior cerebral artery; PChA: posterior choroidal artery; RAH: recurrent artery of Heubner; SAH: subarachnoid hemorrhage.

and rupture depend on several factors, including size, location, morphometry, vascular architecture, and hemodynamic stress. Theoretically, MMD-associated PPCAs are considered to be at high risk for hemorrhagic stroke due to the pathologic vascular structure, such as fragmented internal elastic lamina and attenuated tunica media, and increased hemodynamic stress [1–3]. In light of this, timely intervention of these aneurysms appears essential to prevent potentially life-threatening hemorrhage. However, optimal management remains controversial.

On the one hand, such aneurysms have been treated directly (endovascular embolization/direct obliteration) or indirectly (cerebral revascularization), of which endovascular therapy has become the current first-line option, typically by distal parent vessel occlusion [4,11,17,18]. We chose liquid adhesive embolization rather than coiling, with or without stenting assistance, because the aneurysm and its parent vessel are usually small and fragile, and delivery of the coil or stent may cause them to rupture. In our cases, the aneurysm was usually obliterated together with the adjacent parent artery and there were no related complications. It should be noted that super-selective catheterization is challenging because the parent artery of PPCAs tends to be thin and tortuous. Ni et al. reported 17 cases of PPCAs associated with MMD, and in 13 (76.5%) of these cases, technical difficulties were encountered in the arterial approach to the aneurysms [5]. Rhim et al. reported that endovascular embolization was attempted in 8 patients and failed in 3 (37.5%) [6]. In this study, 7 (30.4%) of 23 patients were not successfully treated with this approach due to inaccessibility. These differences may be explained to some extent by patient selection bias.

Direct open surgery of this aneurysm poses a significant challenge given its deep location, small size, and fragility, with a high complication rate of 21% to 70% [11,18]. Nevertheless, this option has its unique advantages, such as surgical hematoma evacuation and harvesting of the lesion for histopathological analysis. To date, the development and application of intraoperative assistive technologies, including stereotaxy, neuronavigation, and neuroendoscopy, have made direct open surgery safer and less invasive [8].

Some authors have proposed cerebral revascularization as an alternative treatment for MMD-associated PPCAs, arguing that these aneurysms may regress spontaneously after bypass surgery [5,19,20]. The reduction of the hemodynamic burden on the aneurysm and its parent artery after revascularization may be responsible for the spontaneous resolution of such lesions [20]. This phenomenon reflects to some extent that hemodynamic stress may be involved in the mechanism of this aneurysm formation. It should be noted that complications, such as cerebral infarction, may occur postoperatively. Sun et al. reviewed 108 MMD patients who underwent 174 hemispherical revascularizations, and found that 13 (7.47%) procedures resulted in new or expanded infarcts [21]. They concluded that higher Suzuki stage on the non-operative side, posterior cerebral artery involvement, and intraoperative hypotension might be independent risk factors for the occurrence of postoperative infarction. In addition, intracerebral hemorrhage due to rupture of a *de novo* aneurysm originating at the anastomotic site has been reported, and long-term monitoring after bypass surgery appears to be necessary [22,23].

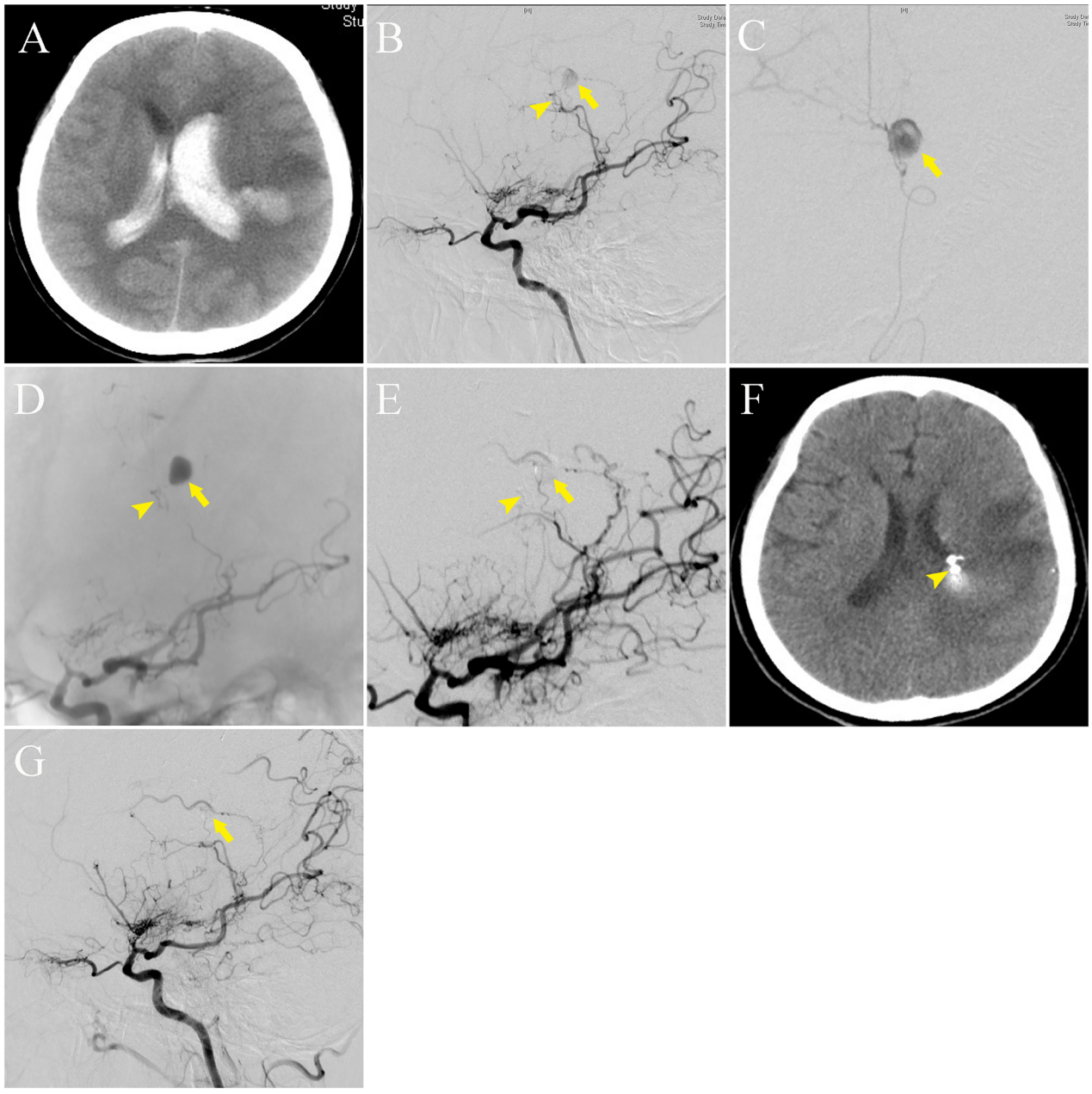

Figure 3. Patient 4. (A) Emergency brain computed tomography (CT) showing acute focal hemorrhage with ventricular extension. (B) Left internal carotid artery angiogram showing moyamoya collaterals, distal posterior choroidal artery (PChA) aneurysm (arrow), and its proximal parent artery (arrowhead). (C) Selective angiogram showing the PChA aneurysm (arrow). (D) Glubran occlusion of the aneurysm (arrow) and the target artery (arrowhead). (E) Postembolization angiogram showing complete obliteration of the aneurysm (arrow) and its proximal parent artery (arrowhead). (F) Postoperative brain CT showing the adjacent branch and aneurysm filled with liquid adhesive (arrowhead). (G) Follow-up angiogram of the left common carotid artery showing the disappearance of the aneurysmal lesion (arrow).

On the other hand, conservative treatment has been reported as a viable alternative for MMD-associated ruptured PPCAs that are technically inaccessible. Rhim et al. described that 14 ruptured PPCAs in adult MMD were managed conservatively, and 12 of them resolved during follow-up [6]. Cerebral vasospasm and secondary thrombosis have been proposed to explain the phenomenon of spontaneous aneurysm regression under conservative treatment [24,25]. Since such aneurysms usually arise from the small collateral vessels, vasospasm after hemorrhage may result in retention of blood flowing into the aneurysm sac, leading to thrombosis obliteration. In addition, this aneurysm is generally considered a pseudoaneurysm and has a natural history of spontaneous regression.

Figure 4. Patient 5. (A) Internal carotid artery angiogram showing an aneurysm (arrow) on the distal posterior choroidal artery. (B) The aneurysm (arrow) was under conservative management and resolved spontaneously on the 18-month follow-up angiogram.

Table 3. Risk factor for poor outcome (univariate analysis).

Parameter	Good ($n=19$)	Poor ($n=4$)	*P*
Age(years, mean ± SD)	45.1 ± 10.8	48.6 ± 16.2	0.518
Sex			1.000
Male	8	2	
Female	11	2	
Past history			0.534
HN	10	2	
DM	2	1	
HL	1	1	
MMD			0.589
Unilateral	6	2	
Bilateral	13	2	
Suzuki Stage			0.504
II	5	0	
III	10	3	
IV	4	1	
Admission presentation			0.509
Headache	12	2	
Impaired consciousness	5	2	
Hemiplegia	2	0	
Hemorrhagic type			0.057
ICH	0	1	
IVH	8	1	
SAH	7	0	
IVH+ICH	4	2	
Acute hydrocephalus	5	3	0.063
Aneurysm location			0.340
AChA	5	1	
PChA	9	1	
LSA	1	0	
RAH	1	1	
Moyamoya vessel	1	0	
Distal ACA	1	0	
Distal MCA	0	1	
Distal PCA	2	0	
Treatment			0.795
Embolization	13	3	
Observation	6	1	
Aneurysm rebleeding	0	1	0.026

ACA: anterior cerebral artery; AChA: anterior choroidal artery; DM: diabetes mellitus; HL: hyperlipemia; HTN: hypertension; ICH: intracerebral hemorrhage; IVH: intraventricular hemorrhage; LSA: lenticulostriate artery; MCA: middle cerebral artery; MMD: moyamoya disease; PCA: posterior cerebral artery; PChA: posterior choroidal artery; RAH: recurrent artery of Heubner; SAH: subarachnoid hemorrhage.

Table 4. Re-ruptured PPCAs managed conservatively in MMD patients with adequate individual information in the literature.

Year	Authors	Age /sex	Hemorrhage type	Aneurysm location	Time of rebleeding after the initial ictus	Treatment	Outcome
1985	Konishi et al. [26]	57/F	IVH	AChA	20 days	Conservative → rebleeding → died	Poor
1994	Hamada et al. [27]	41/F	IVH	PChA	14 days	Conservative → rebleeding → aneurysmectomy	Poor
		48/F	IVH	AChA	35 days	Conservative → rebleeding → surgical clipping	Good
1997	Kawai et al. [19]	19/M	IVH	AChA	18 months	Conservative → rebleeding → bilateral EDMAS → disappeared (2 years)	Good
2004	Ali et al. [8]	26/M	ICH + IVH	PChA	14 days	Conservative → rebleeding → aneurysmectomy	Poor
2010	Leung et al. [9]	31/M	ICH	Distal PCA	?	Conservative → rebleeding → embolization failed → aneurysmectomy	Good
2013	Hayashi et al. [28]	61/F	IVH	AChA	7 years	Conservative → rebleeding → surgical coagulation	Poor
2013	He et al. [10]	42/M	IVH	AChA	14 months	Conservative → rebleeding → conservative	Good
2017	Kim et al. [11]	22/F	ICH + IVH	AChA	7 days	Conservative → rebleeding → surgical clipping → died	Poor
2022	Fu et al. [12]	73/M	ICH + IVH	RAH	35 days	Embolization failed → conservative → rebleeding → died	Poor
2023	Ding et al. [13]	38/M	IVH	AChA	1 day	Conservative → rebleeding → aneurysmectomy	Good

AChA: anterior choroidal artery; EDMAS: encephalo-duro-myo-arterio-synangiosis; F: female; ICH: intracerebral hemorrhage; IVH: intraventricular hemorrhage; M: male; MMD: moyamoya disease; PAA: peripheral artery aneurysm; PCA: posterior cerebral artery; PChA: posterior choroidal artery; RAH: recurrent artery of Heubner.

The overall prognosis of our patients was favorable (82.6%), and good outcomes were achieved in 81.3% and 85.7% of cases treated with endovascular embolization and conservative observation, respectively. This result suggests that the therapeutic effects of the two treatment groups seem to be comparable. However, it should be noted that patients treated with observation may have a high risk of rebleeding, as high as 40%, resulting in a worse prognosis [18]. In the current study, aneurysm re-rupture was observed in 1 (14.3%) of the 7 patients who received conservative management, which unfortunately led to the patient's death. In addition, we conducted a thorough literature review of reported cases of MMD-associated ruptured PPCAs and identified 11 patients with adequate individual information who were managed conservatively and experienced aneurysm rebleeding (Table 4) [8–13, 19, 26–28]. Of these, only 5 patients attained a favorable outcome and the remaining 6 had an unfavorable outcome (disability, 3/11, 27.3%; death, 3/11, 27.3%). This result indicated that aneurysm rebleeding seemed to be associated with an adverse outcome, which was consistent with our study. Time from the initial diagnosis to aneurysm re-rupture was available for 10 patients and ranged from 1 day to 7 years (mean, 12 months). Notably, most rebleeding episodes (7/10, 70%) occurred within the first 35 days (early stage), indicating that prompt evaluation and aggressive intervention should be initiated to prevent future bleeding.

This study had several limitations. First, a potential selection bias does exist because of the single-center, retrospective, and observational nature of this study. Second, although to our knowledge this is the largest reported series of patients with ruptured PPCAs related to MMD, the number of cases was relatively small. Third, direct open surgery and cerebral revascularization were not performed. Fourth, the patients included were from a specific region, and the results of this study may not be representative of the entire population.

Conclusions

PPCA rupture should be considered when dealing with hemorrhagic MMD. Aggressive intervention for such aneurysms should be advocated, as their rebleeding may predict an unfavorable prognosis. Endovascular treatment may be a safe and feasible option, and conservative observation should be carefully chosen due to the risk of early aneurysm re-rupture. Further studies are warranted to determine the appropriate management of this underestimated clinical lesion.

Disclosure statement

The authors report no conflict of interest.

Funding

No funding was received.

Authors contributions

Zheng Feng and Chao Fu developed the study concept and design. Zheng Feng and Yongquan Chang completed the acquisition of data. Zheng Feng, Weidong Yu and Chao Fu made contributions to data analysis. Zheng Feng, Yongquan Chang, Xingyi Jin, Weidong Yu and Chao Fu made contributions to data interpretation. Zheng Feng and Chao Fu drafted the manuscript. All authors critically revised, read and approved the final version of the manuscript, and agreed to be accountable for the study.

Data availability statement

All data are available without restriction by contacting Chao Fu.

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