

Case Report

Clinical analysis of complications following surgical clipping of unilateral moyamoya disease associated with aneurysms

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Received January 27, 2016; Accepted April 21, 2016; Epub June 15, 2016; Published June 30, 2016

Abstract: Currently, there is insufficient research and experience concerning complications following surgical clipping treatment for unilateral moyamoya disease (MMD) associated with aneurysms. This study reports the experiences and lessons learned from the treatment of 13 such cases. The 13 cases included 10 men and 3 women aged 34-69 years old. Twelve cases were caused by subarachnoid hemorrhage (SAH), and one case was caused by combined intracerebral hematoma and SAH. Patients underwent computed tomographic angiography (CTA) and digital subtraction angiography (DSA) and were diagnosed with unilateral MMD associated with aneurysms. Among the 13 cases, there were 14 aneurysms. Eight of the aneurysms were located in the anterior communicating artery, 3 lesions were located in the middle cerebral artery, and 3 lesions were located in other positions. Following diagnosis, the patients received surgical clipping treatment. Six out of the 13 cases experienced ischemic complications, 2 cases included bleeding complications, 1 case involved preoperative bleeding, 3 cases involved infectious complications, and 1 case suffered seizures. After treatment, 7 patients received a Glasgow Outcome Scale (GOS) score of 5, 4 a score of 4, and 2 a score of 1. This study retrospectively analyzed the causes of these complications and prognostic factors and determined that some ischemic complications had a hemodynamic aspect and that satisfactory results were achievable after active treatment. Some ischemic complications represented a loss of equilibrium and denoted a very poor prognosis. Unilateral MMD may exhibit bleeding complications; these complications can be very serious and should receive attention. Due to the fragility and weak compensatory ability of blood vessels as well as the poor brain tissue compliance in MMD patients, these patients are prone to symptomatic vasospasm and bleeding at the surgical site.

Keywords: Unilateral moyamoya disease, aneurysm, clipping, complication

Introduction

Unilateral moyamoya disease (MMD) is rare in the clinic and has been inadequately studied [1]. Unilateral MMD associated with intracranial aneurysms is even less well reported [2, 3]. Similar to MMD associated with aneurysms, unilateral MMD associated with aneurysms is a high-risk disease and is difficult to treat. This difficulty is primarily due to the high hemodynamic pressure borne by the normal vasculature when MMD is present. In MMD patients, on the side of the lesion, brain tissue compliance and cerebrovascular compensatory function are both very poor. Patients are prone to complications [4, 5]. This study reports 13 cases of patients who experienced complications after diagnosis with unilateral MMD asso-

ciated with aneurysms in the past 6 years and summarizes the treatment experiences and lessons learned. This study demonstrates that complications primarily include ischemic and hemorrhagic complications. The complications typically occur on the MMD side and in cases in which the aneurysms are located in the anterior communicating artery. Because there are relatively few reports of complications following surgical clipping treatment for unilateral MMD associated with aneurysms, we summarize and report this group of cases.

Materials and methods

General information

This study summarizes 13 cases of complications following surgical clipping treatment for

unilateral MMD associated with aneurysms that were admitted and treated at the Department of Neurosurgery of the First Hospital of Jilin University between January 2008 and December 2013. These cases include 10 men and 3 women between 34 and 69 years of age (mean 51.2 years old). Six cases had a history of hypertension, 3 cases had a history of cerebral infarction, and 1 case had a history of cerebral hemorrhage. Patients underwent CT examination. Among the 13 cases, 12 were caused by subarachnoid hemorrhage (SAH), and 1 was caused by SAH combined with intracerebral hematoma. Hunt-Hess grades were as follows: 8 cases of grade II and 5 cases of grade III. Fisher grades were as follows: 10 cases of grade 2, 2 cases of grade 3, and 1 case of grade 1. Details are presented in **Table 1**.

Imaging examination

After disease onset, the patients received further computed tomographic angiography (CTA) and digital subtraction angiography (DSA) examinations to clarify the diagnosis of arterial aneurysm. These examinations also reveal the interaction between the aneurysm site and the neighboring vessels and can determine whether there is branching intracranial collateral circulation on the MMD side. Among the 13 cases, there were 14 aneurysms, including 1 case of multiple aneurysms lesions. Eight cases had aneurysms located in the anterior communicating artery, 3 cases had aneurysms located in the middle cerebral artery, 1 case had an aneurysm located at the A1 segment of the anterior cerebral artery, 1 case had an aneurysm located at the distal anterior cerebral artery, and 1 case had an aneurysm located in the eye artery. The sizes of the aneurysm lesions were 1.5 mm to 6.9 mm (average 3.6 mm). CTA or DSA did not find branching intracranial collateral circulation on the MMD side.

Surgical treatment

For aneurysms located in the anterior communicating artery and the A1 segment of the anterior cerebral artery, surgery was performed on the non-MMD side (i.e., the aneurysm side). Surgery was performed using the pterional approach to dissect the lateral fissure, expose the aneurysm, and clip it. For aneurysms in the anterior cerebral artery, surgery was performed using the interhemispheric approach to clean

up the hematoma. Alternatively, surgery was performed to clip the aneurysm from the lesion side, and Encephalo Duro Arterio Synangiosis (EDAS) was simultaneously performed.

Postoperative treatment and follow-up

After surgery, patients received symptomatic treatments. Head CT was regularly reviewed to observe signs of postoperative complications, such as bleeding and infarction, and to closely observe changes. If a patient had new onset or exacerbations of symptoms, CT was reviewed on an ongoing basis. After the onset of complications, the patients received symptomatic treatment. After treatment, if the patient survived, long-term prognosis was evaluated using Glasgow Outcome Scale (GOS) scores.

Results

Surgical approach

Among the 13 cases, 12 underwent clipping of the aneurysm from the normal vascular side (MMD contralateral), and 1 case underwent clipping from the MMD side as well as EDAS.

Detailed information and treatment of postoperative complications

Details of the complications: Of the 13 cases with complications, the time of complication onset varied from 10 hours to 6 months after surgery. The GCS scores at the time of complication onset were as follows: 2 cases with a score of 3-8, 3 cases with a score of 9-12, and 8 cases with a score of 13-15. The complications include ischemic complications, bleeding complications, bleeding at the surgery site and edema, infectious complications and seizures.

Classification of the complications: ① Three cases of ischemic limb paralysis on the MMD side without infarction manifestations on CT; 1 case of ischemic symptoms on the MMD side with partial frontal lobe infarction; and 1 case of ischemic symptoms on the MMD side with massive cerebral infarction. ② One case of intraventricular hemorrhage occurred on the MMD side; 1 case of MMD at the top of frontotemporal subdural hematoma. ③ One case of whole-brain blood vessels spasms, with symptoms of ischemia manifesting on the MMD side. ④ One case of bleeding at the surgery site associated with severe edema formation. ⑤

Complications following surgical clipping of unilateral MMD associated with aneurysms

Table 1. Summary of clinical information

No	Age/ gender	History of hyper- tension	Previous stroke	Hem- or- rhage	HH grading	Fisher grading	Location of aneurysm	Size of aneu- rysm	MMD side collateral anastomosis	Treatment of aneu- rysm	Types of com- plications	CT	Time of occu- rence	GCS	Treatment	Long- term GOS
1	69/M	Y	Cerebral hemor- rhage	SAH	2	2	Middle cerebral artery	1.9 mm	N	Clipping from the normal side	Ischemia on the MMD side	No new disease	12 h	13	Conservative treatment	5
2	34/M	N	Infarction	SAH	3	2	Anterior communi- cating artery	2.7 mm	N	Clipping from the normal side	Large area bleeding on the MMD side	Large infarc- tion	2 days	8	Conservative treatment	1
3	58/M	Y	N	SAH	2	2	Anterior communi- cating artery and Anterior cerebral artery	6.9 mm, 4.0 mm	N	Clipping from the MMD side	Ischemia on the MMD side	Frontal lobe infarction	5 days	13	Conservative treatment	4
4	49/M	N	N	SAH	2	1	Anterior communi- cating artery	2.5 mm	N	Clipping from the normal side	Ischemia on the MMD side	No new disease	2 days	12	Conservative treatment	5
5	32/F	N	N	SAH	2	2	Anterior communi- cating artery	1.5 mm	N	Clipping from the normal side	Ischemia on the MMD side	No new disease	14 days	12	Conservative treatment	4
6	54/M	N	N	SAH	2	2	Anterior communi- cating artery	4.5 mm	N	Clipping from the normal side	Intraventricular hemorrhage on the MMD side	Ventricle hemorrhage	1 days	15	Conservative treatment	4
7	45/M	N	N	SAH	2	2	Anterior communi- cating artery	2.1 mm	N	Clipping from the normal side	Subdural he- matoma on the MMD side	frontotem- poparietal subdural hematoma	7 days	15	Conservative treatment	5
8	59/M	Y	Infarction	SAH	3	3	Anterior communi- cating artery	5.3 mm	N	Clipping from the normal side	Vasospasm and ischemia on the MMD side	Whole-brain multiple low density lesions	4 days	12	Symptomatic treatment	4
9	54/M	Y	Infarction	SAH and hema- toma	3	3	distal middle cerebral artery	3.2 mm	N	Clipping from the normal side	Bleeding at the surgical side	Hematoma with edema at the surgery site	10 h	8	Symptomatic treatment	1
10	46/M	Y	N	SAH	2	2	Middle cerebral artery	2.3 mm	N	Clipping from the normal side	Intracranial infection	No new disease	3 days	15	Anti-infection treatment	5
11	59/F	Y	N	SAH	2	2	Middle cerebral artery	4.1 mmm	N	Clipping from the normal side	Intracranial infection	No new disease	7 days	13	Anti-infection treatment	5
12	54/F	N	N	SAH	3	2	Anterior com- municating artery aneurysm	3.2 mm	N	Clipping from the MMD side and EDAS	Scalp infection	No new disease	6 months	15	Removal of bone flap	5
13	52/M	N	N	SAH	3	2	Ophthalmic artery	6.6 mm	N	Clipping from the normal side	Seizures	No new disease	6 days	15	Anti-epileptic therapy	5

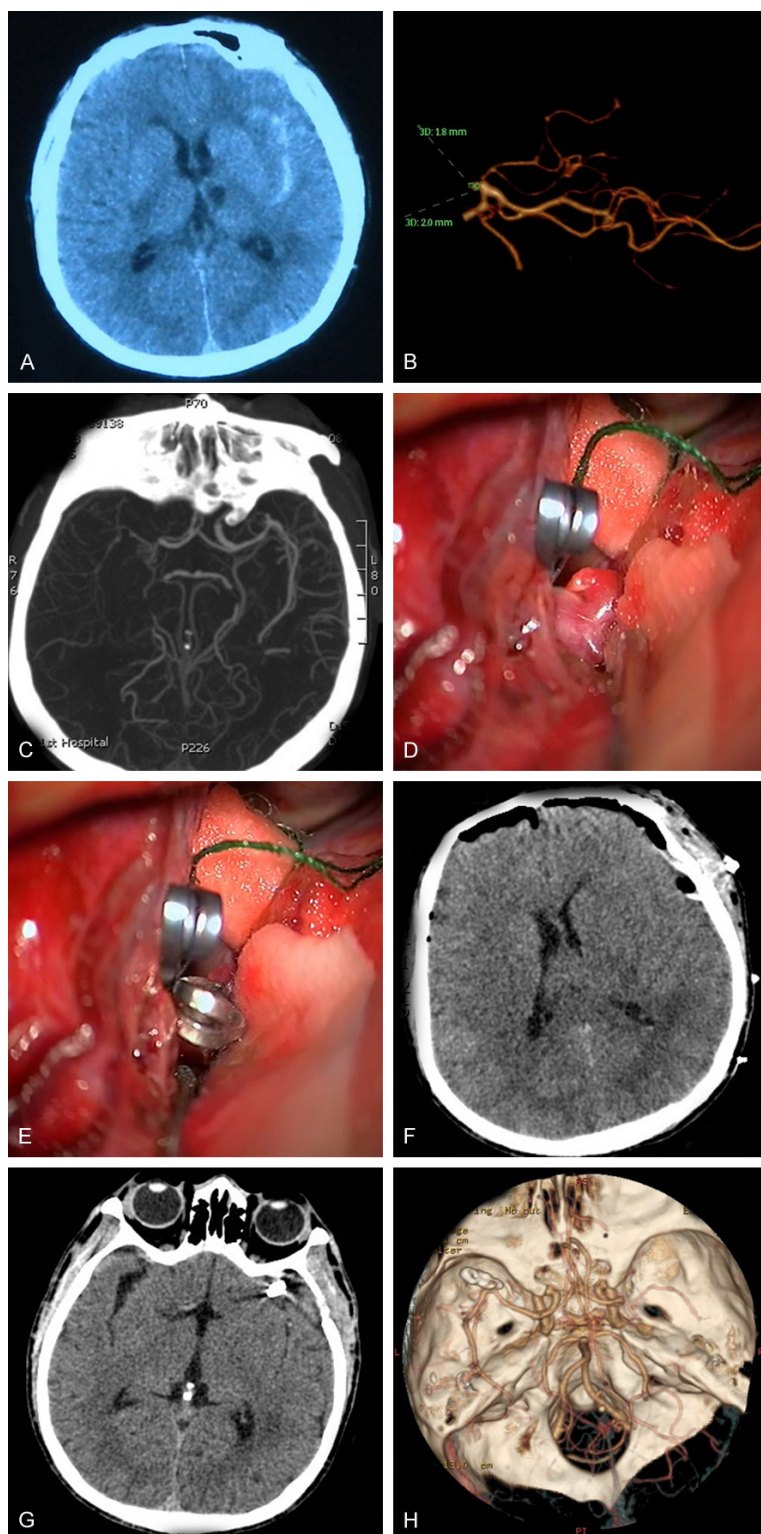


Figure 1. Case 1. A: Head CT revealed bleeding on the left lateral cistern and a visible low density shadow in the left thalamus. B, C: Head CTA revealed disappearance of normal vasculature in the artery distribution region of the right cerebral. The normal vasculature was replaced by abnormally proliferative blood vessels. D, E: Intraoperative image revealed an aneurysm, which was then clipped. F: Twelve-hour postoperative CT scan revealed no infarction or hemorrhage. G, H: Postoperative follow-up CT and CTA revealed complete clipping of the aneurysm, without new brain lesions.

Two cases of intracranial infection; 1 case of scalp infection; and 1 case of seizure.

Treatment of complications:

① Three cases of ischemic limb paralysis on the MMD side without infarction manifestations on CT; 1 case of ischemic symptoms on the MMD side with partial frontal lobe infarction. These 4 patients received treatment to improve circulation and experienced good recovery. ② One case of ischemic symptoms on the MMD side with massive cerebral infarction. This patient did not receive surgical intervention due to the patient's critical condition; the patient subsequently died. ③ One case of intraventricular hemorrhage on the MMD side; one case of MMD at the frontotemporoparietalsubduralhematoma. These 2 patients received conservative treatment, and recoveries were satisfactory. ④ One case of whole-brain blood vessels spasms, with symptoms of ischemia manifesting on the MMD side. The patient received symptomatic treatment and exhibited good recovery. ⑤ One case of bleeding at the surgery site associated with severe edema formation. This patient did not receive surgical intervention due to critical conditions and subsequently died. ⑥ Two cases of intracranial infection; 1 case of scalp infection; and 1 case of seizure. These 4 patients received symptomatic treatment and exhibited good recovery.

Follow-up results

The GCS scores at the six-month to one-year follow-up included 7 cases with a score of 5, 4 cases with a score of 4, and 2 cases with a score of 1.

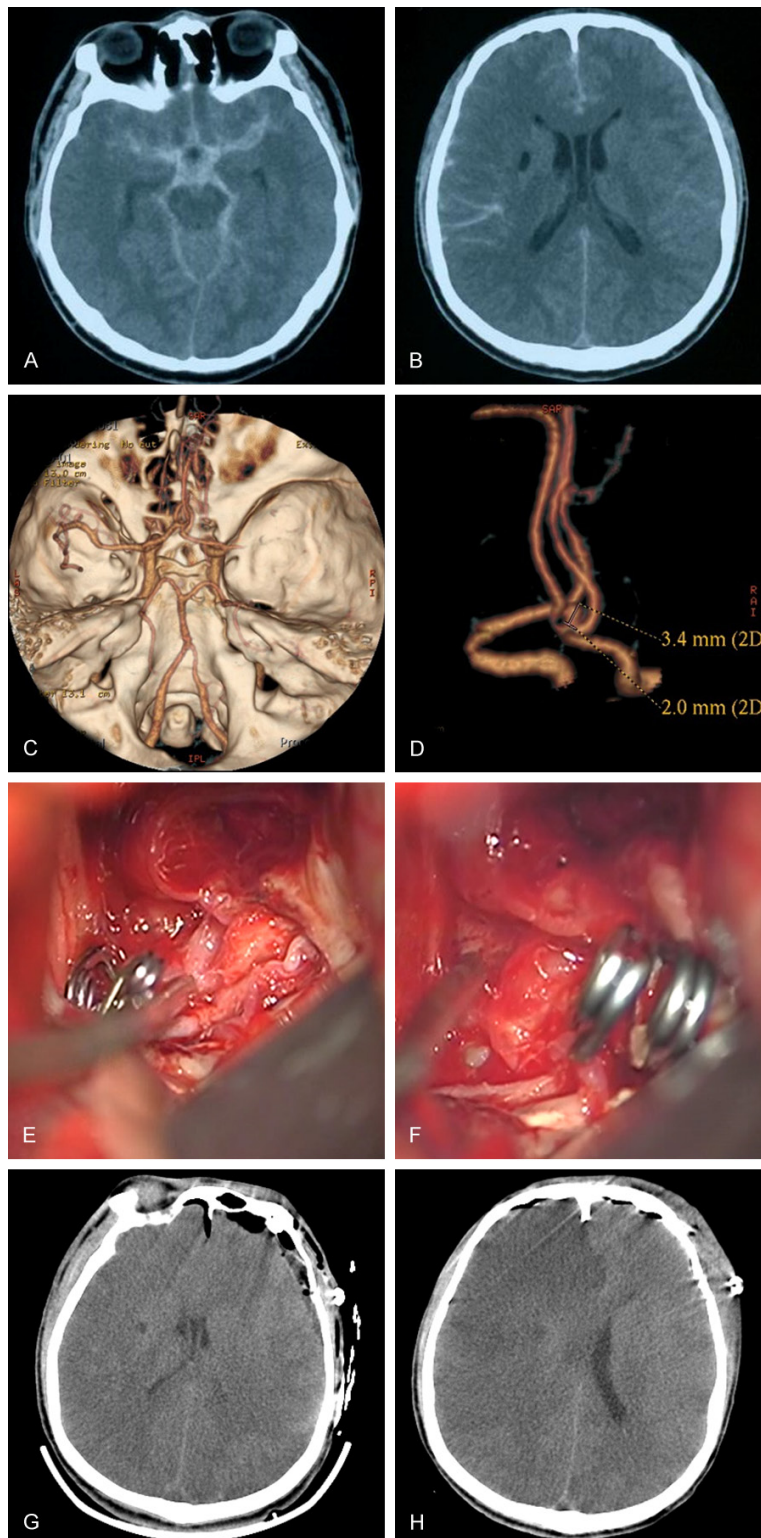


Figure 2. Case 2. A, B: Head CT revealed bleeding in the bilateral lateral fissure cistern, suprasellar cistern, ambient cistern and interhemispheric fissure and old low density infarcts above the right side of the putamen. C, D: Head CTA revealed aneurysms in the anterior communicating artery; normal blood vessels in the right middle artery had disappeared and were replaced by abnormally proliferative blood vessels. E, F: Intraoperative imaging revealed an aneurysm in the anterior communicating artery, which was then

clipped. G, H: After 2 and 3 days, respectively, head CT revealed gradually increasing aneurysms in the right hemisphere.

The details are presented in **Table 1**; **Figures 1-5** depict typical cases.

Discussion

MMD refers to the progressive occlusion of the intracranial carotid artery terminus and is associated with the formation of extensive collateral vessels (moyamoya vessels) at the base of the brain. The diagnostic criteria of the Research Committee on Moyamoya Disease consider only cases with bilateral lesions to be cases of definitive MMD. However, some cases with unilateral involvement also exhibit angiographic findings on the affected side similar to those of definitive cases and are therefore classified as probable MMD or unilateral MMD [6, 7]. The prevalence of unilateral MMD has been reported to be in the range of 9.5% to 17.8% among patients with MMD. Therefore, cases of unilateral MMDs are rare in the clinic [8]. When MMD occurs, the pressure of the posterior circulation is increased, and the probability of artery aneurysms at the top of the basilar artery greatly increases [9]. This situation is similar to the incidence of artery aneurysms at the top of the basilar artery following bilateral carotid artery occlusion. Thus, increased hemodynamic pressure in the normal region within MMD tends to promote aneurysms [10]. When unilateral MMD occurs, intracranial hemodynamic changes that are similar to those of MMD also occur; however, the changes

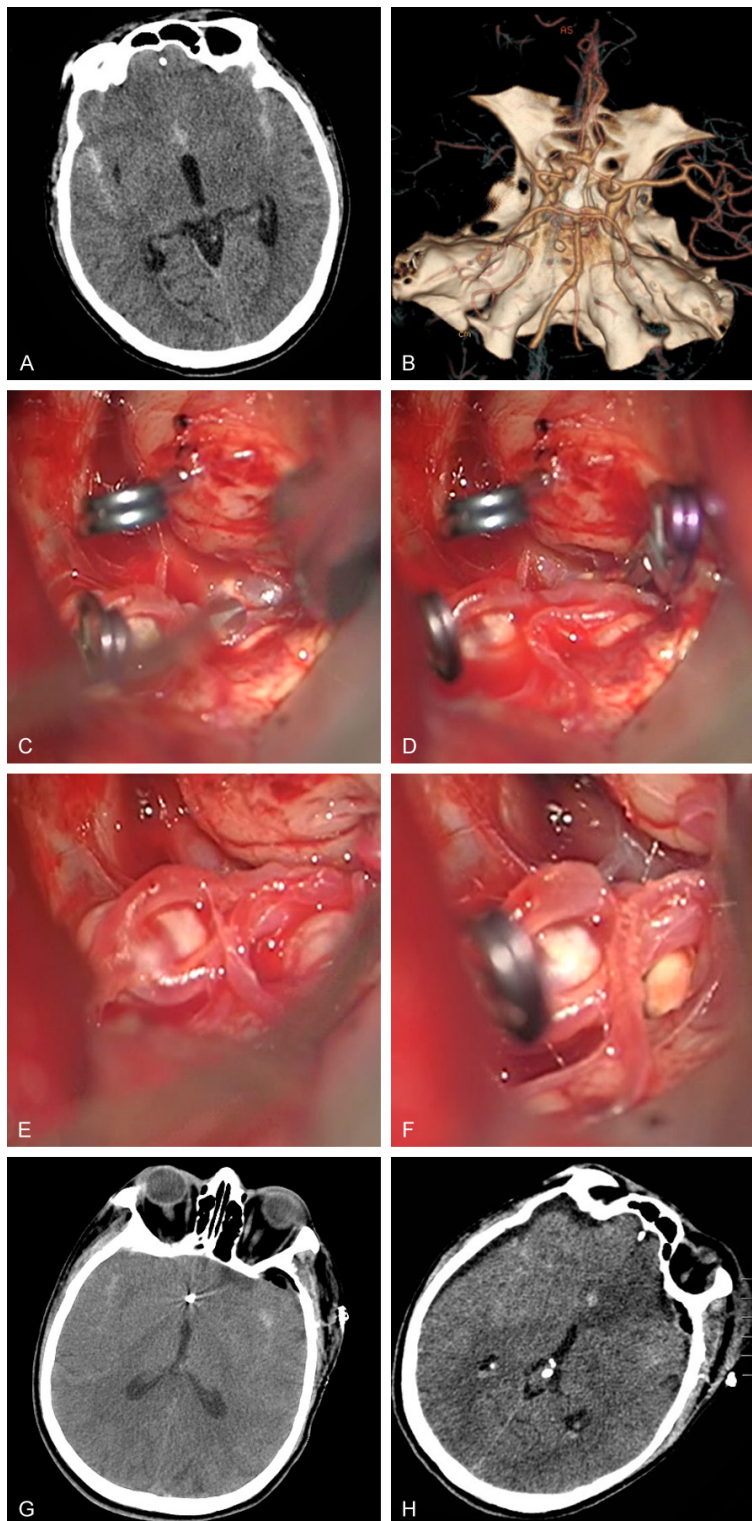


Figure 3. Case 3. A: Head CT revealed bleeding in the bilateral lateral fissure cistern and interhemispheric fissure. B: Head CTA revealed 2 aneurysm lesions in the left anterior cerebral artery and the anterior communicating artery; normal blood vessels in the left middle artery had disappeared and were replaced by abnormally proliferative blood vessels. C-F: Intraoperative imaging revealed 2 aneurysms, which were clipped. G: Days after surgery, head CT revealed complete absorption of the hematoma in the bilateral

lateral fissure. H: Five days after surgery, head CT revealed low-density infarct lesions in the left frontal lobe.

are not as severe as those of MMD [11]. When unilateral MMD occurs, the normal side of the internal carotid artery will typically compensate the blood supply of the contralateral side and therefore experience greater blood pressure; this predisposes patients to aneurysms, such as aneurysms in the anterior communicating artery and cerebral aneurysm [12]. The high pressure in the parent artery of these types of aneurysms coupled with the existing unilateral MMD complicates the treatment and makes the patients difficult to treat. The risk of complication is also higher compared with the cases without unilateral MMD.

Currently, the treatments for intracranial aneurysms include surgical clipping and embolization, both of which are effective [13]. All patients included in this study were treated with surgical clipping. Surgery on unilateral MMD associated with aneurysms is usually a safe and effective method because the operation is typically performed on the side with normal blood vessels. However, because the arterial system of MMD is relatively fragile, the risk of surgery is quite high [14]. Unilateral MMD is rare, and research of unilateral MMD associated with aneurysms is also rare. In particular, research on complications of surgical clipping is minimal. This study summarizes the complications of 13 patients who received surgical clipping treatment of unilateral

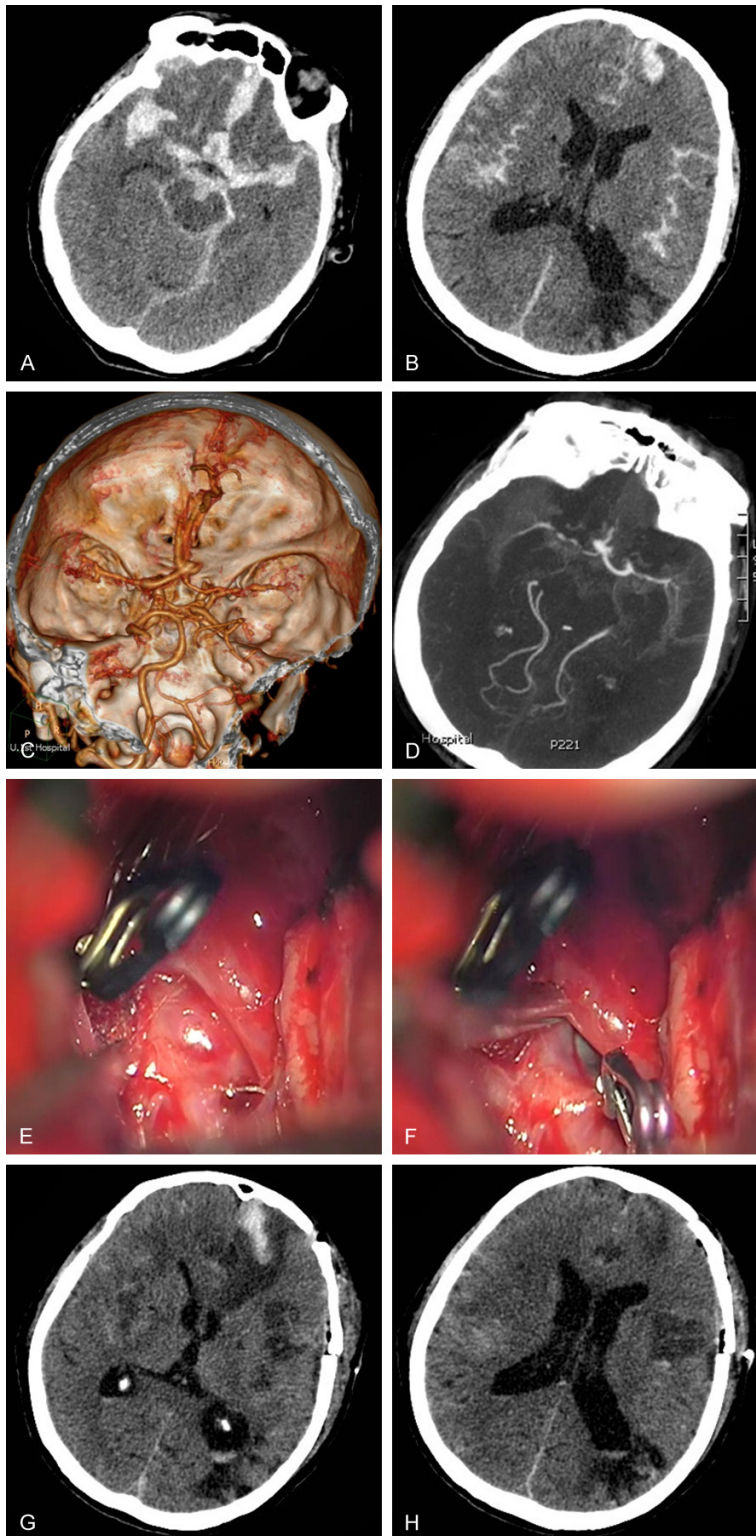


Figure 4. Case 8. A, B: Head CT revealed bleeding in the bilateral lateral fissure cistern, around the suprasellar cistern and in the interhemispheric fissure; there was a low density shadow in the left parietal lobe. C, D: Head CTA revealed an aneurysm in the anterior communicating artery. Normal blood vessels in the right cerebral middle artery area had disappeared and were replaced by abnormally proliferating blood vessels. E, F: An intraoperative image revealed an aneurysm, which was then clipped. G, H: Four

days after surgery, CT revealed multiple low-density areas in the bilateral cerebral hemispheres and no new ischemic lesion in the brain tissue.

MMD associated with aneurysms and includes a clinical analysis. A retrospective analysis of the 13 cases identified 3 cases with histories of cerebral infarction and 1 case with a history of cerebral hemorrhage. These results suggest that abnormalities of intracranial vasculature occur in cases of unilateral MMD, similar to cases of MMD. In cases of MMD, normal blood vessels are prone to ischemia and bleeding after withstanding high pressure. Similar developments affect moyamoya blood vessels [15]. Therefore, in cases of unilateral MMD, surgical treatment is more risky compared with that of cases without MMD.

Among the cases of complications after clipping included in this study, most cases (8 cases) involved unilateral MMD combined with aneurysms in the anterior communicating artery, followed by middle cerebral artery aneurysms (3 cases). There are two explanations for this phenomenon. One is that there is a higher incidence of intracranial aneurysm of the anterior communicating artery relative to the incidence of brain aneurysm. This is consistent with epidemiological characteristics of the sites of intracranial aneurysm [16]; The other possibility is that aneurysms in the anterior communicating artery are typically in a deep location, close to the MMD vessels on the opposite side and surrounded by rich collateral circulation. These characteris-

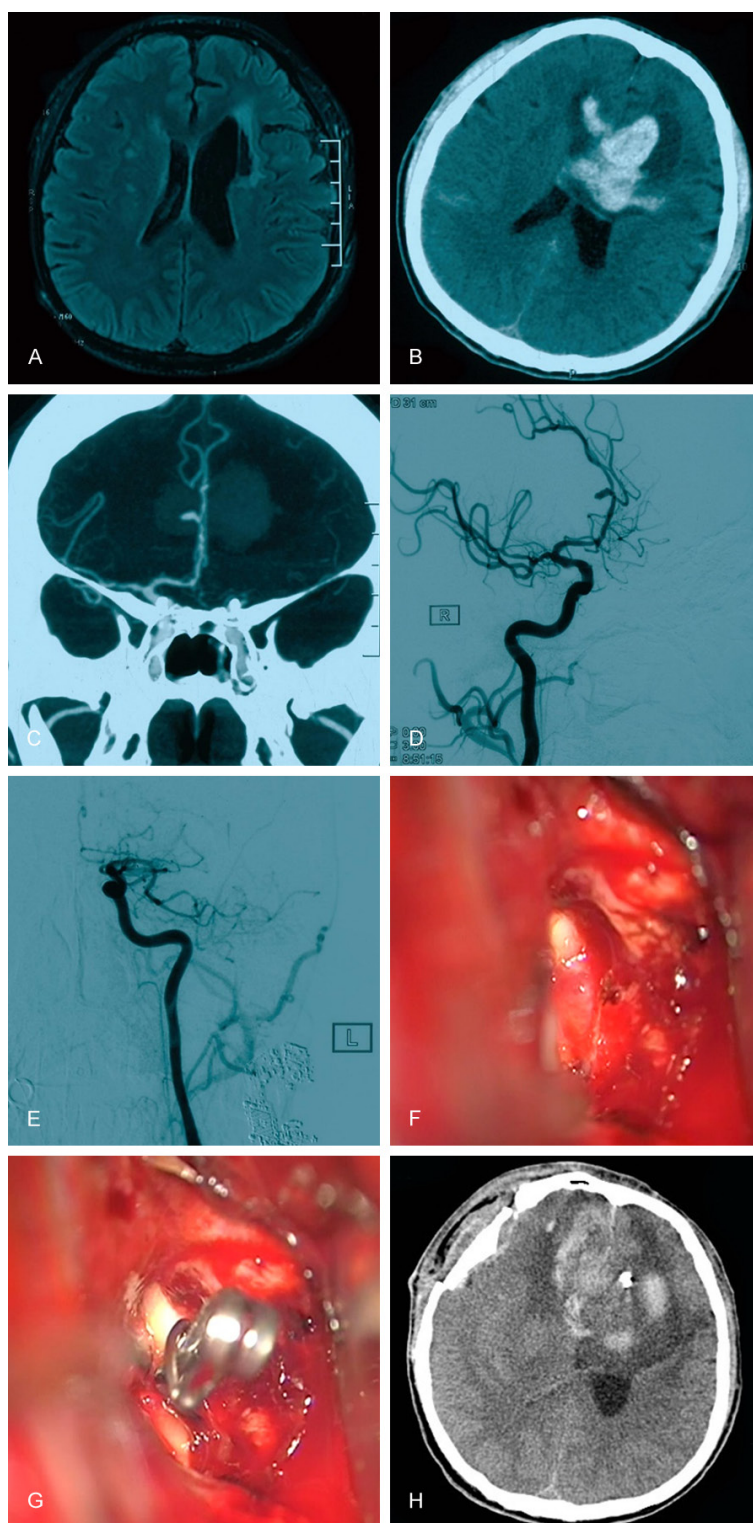


Figure 5. Case 9. A: Two months prior to surgery, MRI revealed infarction in and around the ventricular zone and the corona radiata. B, C: MIP of the CT and CTA revealed a hematoma above the corpus callosum inside the interhemispheric fissure, accompanied by SAH. D: Angiography of the right interior carotid artery revealed mild stenosis in the middle cerebral artery. E: Angiography of the left internal carotid artery revealed occlusion of the internal carotid artery terminus, and there were visible moyamoya vessels at the terminus. F, G: Intraoperative imaging revealed an aneurysm at

the distal anterior cerebral artery, which was then clipped. H: Ten hours after surgery, a CT scan revealed bleeding at the surgery site, with peripheral low density edema; the surrounding tissue had translocated due to pressure.

tics make clipping risky and prone to complications. Brain aneurysms are typically located in a shallow position and confer a relatively low risk of complication [17]. In cases of unilateral MMD associated with aneurysms, surgical clipping of the anterior communicating artery aneurysm involves a decision of the surgical side. Because moyamoya vessels on the MMD side are more vulnerable and have poor compensation in cases of unilateral MMD, when starting the surgery from the MMD side, even slight traction may lead to limb paralysis [18]. Therefore, among the 13 cases in this study, 12 patients were treated from the side with normal vasculature. For 1 case, because of the polarity of aneurysm, the patient received surgery from the MMD side and also received parallel EDAS.

The retrospective analysis of 13 cases of complications summarizes the complications into the following categories. ① MMD side ischemia coupled with paralyzed limb and without infarction on CT: In this study, there were 3 such cases. The complications primarily occurred within 12 hours after surgery, although some occurred after two weeks. These complications might be correlated with traction to the brain tissue, interference of cerebral blood flow regulation or cerebrospinal fluid loss during surgery [19]. They may also be related to vascular function on the MMD side due to anes-

thetics [20]. These complications were mostly functional complications, as these patients did not exhibit infarction by CT scan; the symptoms disappeared after microcirculation treatment. ② Ischemic symptoms on the MMD side with serious ischemia: In this study, 1 case exhibited delayed frontal lobe infarction, and 1 case had a large area of cerebral infarction and tissue death. Both represented cases of unilateral MMD coupled with aneurysm in the anterior communicating artery. As such, for patients with unilateral MMD coupled with aneurysm in the anterior communicating artery, disastrous consequences may occur after clipping treatment. ③ Two cases of bleeding on the MMD side, including 1 case of intraventricular hemorrhage and 1 case of subdural hematoma. This type of bleeding is similar to contralateral intracerebral hemorrhage caused by ipsilateral surgery and is related to translocation of the brain tissue after loss of cerebrospinal fluid. Because vessels on the MMD side are vulnerable, this type of bleeding is more likely to occur [21]. Because of the small amount of bleeding, most patients can undergo conservative treatment. ④ Whole-brain blood vessels spasm and lack of hyperlipidemia on the MMD side: There was 1 case that experienced these symptoms. Cerebral vasospasm after SAH is common [22]. The case in our study was rather unique, as vasospasm occurred on both sides after SAH. Postoperative CT revealed multiple low-density regions, but only the MMD side exhibited ischemic symptoms. This suggests poor compensatory ability of the MMD vasculature because the symptoms appeared after spasm. ⑤ One case of bleeding at the surgical site accompanied by severe edema. This was a serious case. A retrospective analysis of the reasons for the bleeding suggested poor compliance of the brain tissue. This is a disastrous situation, and the patient died. ⑥ In addition, there are conventional complications of brain surgery. In the present study, there were 2 cases of intracranial infection, 1 case of scalp infection, and 1 case of seizure. Symptomatic treatment of these complications can have satisfactory results.

In summary, this study retrospectively analyzed 13 cases of complications following surgical clipping treatment for unilateral MMD associated with aneurysms. We believe that the surgical treatment of unilateral MMD associated

with aneurysms may result in ischemic and bleeding complications. Some ischemic complications are hemodynamic in nature. Symptomatic treatment can achieve satisfactory results. Some ischemic complications are more serious and can lead to large areas of cerebral infarction. The prognosis in such cases is poor. Similar to MMD, unilateral MMD can have bleeding complications. There were 2 such cases in this study, but neither was serious. However, in theory, severe bleeding complications may occur. Thus, such complications should receive attention. Because the vasculature on the MMD side is fragile and has poor compensatory ability, coupled with poor compliance of brain tissue, symptoms are prone to appear after vasospasm, and the surgical area tends to bleed.

Disclosure of conflict of interest

None.

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