Aplastic or Twig-Like Middle Cerebral Artery Presenting with Intracerebral Hemorrhage During Pregnancy: Report of Two Cases

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INTRODUCTION

Anomalies of the middle cerebral artery (MCA) occur less frequently than that in the other major intracranial arteries.1 There are several MCA anomalies:1,2 accessory MCA, duplicated MCA, fenestrated MCA, and aplastic or twig-like MCA (Ap/T-MCA). In an Ap/T-MCA, the MCA trunk has either a stenosis or occlusion accompanied by collateral plexiform networks.1,3-11 Although there have been only a few reports describing Ap/T-MCA with the clinical features and pathogenesis being not well defined, an Ap/T-MCA can cause both ischemic and hemorrhagic strokes and frequently harbors aneurysms.3

Pregnancy induces various molecular and physiological changes, including a hyperdynamic state, impaired cerebral blood flow autoregulation, and increased blood-brain barrier permeability. These changes can lead to pregnancy-associated intracranial hemorrhage.12-15

CASE DESCRIPTION

In both patients, cerebral angiography revealed a stenocclusive lesion and an abnormal arterial network on the unilateral middle cerebral artery. One patient was treated conservatively for a putaminal hemorrhage, and a cesarean section was performed uneventfully 6 months after onset of the ICH. The other patient underwent a craniotomy for evacuation of the lobar hemorrhage. Subsequently, a cesarean section was performed uneventfully. Both patients gradually recovered without significant disabilities.

CONCLUSIONS: An Ap/T-MCA is a rare congenital anomaly and is a potential cause of ICH for pregnant patients. A cesarean section is a useful option for pregnant patients with this condition.
At 38 weeks of gestation, she underwent a planned cesarean section under epidural anesthesia, and delivered a baby girl with Apgar scores of 5, 7, and 9 at 1, 5, and 10 minutes, respectively. At her 6-month follow up, the patient was living her daily life with improved neurologic symptoms (modified Rankin scale of 1).

**Case 2**

A 27-year-old woman who was pregnant for 38 weeks was brought to our hospital with a sudden onset of headache and vomiting. On admission, she presented with impaired consciousness with a GCS score of 6 (E1V1M4). Her past medical history was not remarkable. A head CT showed an ICH in the left temporo-parietal lobe and intraventricular hemorrhage (Figure 2A). CTA demonstrated severe stenosis of the left MCA (Figure 2B).

A left-sided temporal craniotomy for hematoma evacuation was performed under general anesthesia. Postoperatively, her consciousness was slightly improved. However, at postoperative day 3, her conscious level decreased with a GCS score of 6 (E1V1M4). A head CT revealed enlarged ventricles, implying hydrocephalus, without additional intracranial hemorrhage. She underwent external ventricular drainage and had a cesarean section under general anesthesia simultaneously. She delivered a baby girl with Apgar scores of 8 and 9 at 1 and 5 minutes, respectively. The next day, endoscopic removal of the intraventricular hemorrhage was performed because head CT demonstrated expansion of the plexiform arterial networks (arrow heads). The enlarged LSAs have abnormal connections with medullary arteries in the periventricular area. Anomalous arteries from the A1 segment of the anterior cerebral artery and a branch of the anterior choroidal artery are continuous to the plexiform arterial networks. The distal MCA beyond the plexiform arterial networks has a normal vessel caliber with anterograde flow. An unruptured saccular aneurysm was found at the A1-A2 junction of the anterior cerebral artery (white arrow). A 3-dimensional rotation angiography showed the detailed angioarchitectures of the lesion.

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Figure 1. (A) Computed tomography on admission showed an intracerebral hemorrhage in the putamen with moderate perihematomal edema. (B and C) Computed tomographic angiography (B) and magnetic resonance angiography (C) demonstrated a steno-occlusion of the left middle cerebral artery (MCA) (black and white arrow) with enlarged lenticulostriate arteries (LSA). (D) Right internal cerebral angiography demonstrated no evidence of a steno-occlusive lesion. (E) Left internal cerebral angiography revealed a focal occlusion of the M1 segment of the left MCA, plexiform arterial networks at the MCA trunk (black arrow), and enlarged LSAs arising from the plexiform arterial networks (arrow heads). The enlarged LSAs have abnormal connections with medullary arteries in the periventricular area. Anomalous arteries from the A1 segment of the anterior cerebral artery and a branch of the anterior choroidal artery are continuous to the plexiform arterial networks. The distal MCA beyond the plexiform arterial networks has a normal vessel caliber with anterograde flow. An unruptured saccular aneurysm was found at the A1-A2 junction of the anterior cerebral artery (white arrow). (F) A 3-dimensional rotation angiography showed the detailed angioarchitectures of the lesion.
intraventricular hemorrhage. Her postoperative course was uneventful.

Digital subtraction angiography and 3-dimensional rotation angiography were performed postoperatively, and revealed a focal occlusion of the M1 segment of the left MCA and plexiform arterial network at the ipsilateral MCA trunk (Figure 2D). LSAs arose from the plexiform arterial network. The LSAs had an abnormal connection with the medullary arteries. Her intracranial large vessels had no evidence of arteriosclerotic degeneration, and a transdural anastomosis was not detected. MRA demonstrated an occlusion of the M1 segment of the left MCA (Figure 2C).

She was transferred to another hospital for rehabilitation. One year after onset, her symptoms were improved with a modified Rankin scale of 1. Three years and 8 months after onset, she delivered a second girl by a planned cesarean section under epidural anesthesia to avoid blood pressure fluctuations. There were no complications during the second pregnancy and peripartum period.

**DISCUSSION**

Anomalies of the MCA are relatively rare, although accessory, duplicated, duplicated origin, early branching, fenestrated, and Ap/T-MCA have been reported. There have been only a few reports describing Ap/T-MCA with their clinical features and pathogenesis being not well known. Some authors have called this entity “unfused MCA,” “aplastic MCA,” “twig-like MCA,” “unfused/twig-like MCA,” and “Ap/T-MCA.” The term of this entity in this report was unified as “Ap/T-MCA.”
Pathogenesis
An Ap/T-MCA exhibits an angioarchitecture in which a plexiform arterial network exists with a steno-occlusive MCA in place of the normal MCA trunk. At the 12–14 mm embryologic stage (34–36 days), the MCA is still a plexiform arterial twig (Figure 3A). At the 16–18 mm stage (39–41 days), the MCA becomes a prominent stem with plexiform arteries by both fusion and regression. Finally, the MCA develops into the adult configuration at the 40 mm stage (Figure 3B). The Ap/T-MCA refers to congenital anomalies resulting from interference in the process of fusion and regression during the development of the embryonic MCA (Figure 3C).1,2,11

Prevalence and Epidemiology
Previous studies of cerebral angiography demonstrated an incidence ranging from 0.11%–1.17% for the Ap/T-MCA.3,6,9 Ap/T-MCA has a high prevalence in Asia, particularly in East Asia such as Taiwan, Korea, and Japan. The previously published cases of Ap/T-MCA are summarized in Table 1.

Angiographic Features
Although there have been no distinct diagnostic criteria, according to the previous reports, angiographic features of Ap/T-MCA are as follow:1,3-11 1) mixed patterns of plexiform arterial network and a steno-occlusive lesion exist on the unilateral MCA; 2) the LSAs arise from the plexiform arterial network instead of a normal MCA; 3) cortical branches of the MCA beyond the plexiform arterial network maintain a normal vessel caliber with anterograde flow; and 4) transdural collaterals were not found. A leptomeningeal collateral from either the anterior cerebral artery or posterior cerebral artery is observed in some cases.3 We made the diagnoses of Ap/T-MCA with our 2 cases because the radiologic features mentioned earlier were observed.

The diagnosis of the Ap/T-MCA based on CTA and MRA is difficult, and misdiagnosis as unilateral moyamoya disease (MMD), atherosclerotic steno-occlusive disease, or arteriovenous malformation occurs.3,9,10 Cerebral angiography is the gold standard for diagnosis of the Ap/T-MCA.3 In our 2 cases, the CTA and MRA were also unable to reveal the detailed angioarchitectures of the lesion. Taken together, cerebral angiography is recommended if a unilateral steno-occlusive MCA is found on either MRA or CTA.

Hemorrhagic Stroke Due to Ap/T-MCA
An Ap/T-MCA may present with hemorrhagic or ischemic stroke, or without symptoms.3 More than half of the reported cases presented with hemorrhagic stroke, including subarachnoid hemorrhage, ICH, and intraventricular hemorrhage (Table 1). The mechanisms of hemorrhagic stroke in Ap/T-MCA are responsible for rupture of either collateral vessels, including plexiform arterial network, or flow-related aneurysms. In previous reports, Ap/T-MCAs frequently harbored aneurysms at the arterial twigs or anomalous arteries (Table 1).3,6,9,11 The arterial twigs were fragile because of their immature arterial wall with less developed muscular layer.3,5,8,11 Therefore, hemodynamic stress on the arterial twigs may easily form flow-related aneurysms.3,9,10 In case 1, a small unruptured aneurysm existed at the left A1-A2 junction of the anterior cerebral artery, suggesting a flow-related aneurysm. In case 2, there was no evidence of any aneurysms at the intracranial arteries. A periventricular anastomosis has been reported as an indicator of hemorrhagic risk in the patients with hemorrhagic MMD, and is defined as an anastomosis between the perforating or choroidal artery and medullary artery in the periventricular area.16,17 This anastomosis is considered to be fragile because of the histologically abnormal connection.16,17 In the 2 cases, the LSAs were connected with...
medullary arteries in the periventricular area, which is considered to be vulnerable to rupture.

### Differences Between Ap/T-MCA and MMD

The major different diagnosis of this entity is MMD. MMD is a cerebrovascular disease characterized by spontaneous progressive steno-occlusion at the terminal portion of both the ICA and their

| Author, Year | Case Number | Age (Year), Sex | Nationality | Clinical Presentation | Side of Ap/T-MCA | Site of Aneurysm |
|--------------|-------------|----------------|-------------|-----------------------|-----------------|-----------------|
| Liu et al., 2005 | 1 | 67, F | Taiwan | ICH, SAH | Lt | Lt M1 |
| 2 | 44, M | Taiwan | ICH, SAH | Lt | Lt M1 |
| Cekirge et al., 2005 | 3 | 32, M | Turkey | SAH, IVH | Lt | Lt A1 |
| Rodriguez-Hernández et al., 2011 | 4 | 52, M | USA | ICH | Rt | Rt M1 |
| Seo et al., 2012 | 5 | 49, F | Korea | ICH | Lt | Rt ICA |
| 6 | 10, F | Korea | Infarction | Lt | - |
| 7 | 72, F | Korea | ICH | Rt | - |
| 8 | 58, M | Korea | Incidental | Lt | Bil ICA |
| 9 | 58, M | Korea | Incidental | Lt | - |
| 10 | 45, F | Korea | ICH | Lt | - |
| 11 | 56, F | Korea | Infarction | Rt | - |
| 12 | 73, M | Korea | SAH | Rt | Rt MCA |
| 13 | 51, F | Korea | Incidental | Lt | - |
| 14 | 58, F | Korea | Incidental | Rt | Lt ICA |
| 15 | 73, M | Korea | SAH | Lt | Rt ICA |
| 16 | 61, M | Korea | Incidental | Lt | - |
| 17 | 38, M | Korea | Incidental | Lt | - |
| 18 | 74, M | Korea | ICH | Lt | - |
| 19 | 56, F | Korea | Infarction | Rt | - |
| Shin et al., 2014 | 20 | 42, M | Korea | SAH, ICH, IVH | Lt | Lt M1 |
| 21 | 49, F | Korea | SAH, ICH, IVH | Lt | Lt M1 |
| 22 | 46, F | Korea | SAH, ICH, IVH | Lt | Lt M1, Lt A1 |
| 23 | 26, M | Korea | SAH, IVH | Rt | Rt PLCho |
| Akkan et al., 2015 | 24 | 54, M | Turkey | Incidental | Rt | Lt ICA |
| 25 | 43, M | Turkey | Incidental | Rt | - |
| 26 | 53, F | Turkey | Incidental | Rt | - |
| 27 | 37, F | Turkey | Incidental | Rt | - |
| 28 | 44, M | Turkey | ICH | Lt | - |
| 29 | 40, F | Turkey | Incidental | Lt | - |
| Tashiro et al., 2016 | 30 | 76, F | Japan | SAH | Lt | - |
| 31 | 81, F | Japan | SAH | Lt | - |
| Lutz et al., 2018 | 32 | 40, F | Germany | TIA | Lt | - |
| Matsunaga et al., 2018 | 33 | 19, F | Japan | TIA | Rt | - |
| Present study | 34 | 36, F | Japan | ICH | Lt | Lt A1 |
| 35 | 27, F | Japan | ICH, IVH | Lt | - |

Ap/T-MCA, aplastic or twig-like middle cerebral artery; F, female; ICH, intracerebral hemorrhage; SAH, subarachnoid hemorrhage; Lt, left; M, male; IVH, intraventricular hemorrhage; Rt, right; ICA, internal cerebral artery; Bil, bilateral; MCA, middle cerebral artery; PLCho, Posterior lateral choroidal artery; TIA, transient ischemic attack.
proximal branches, and is accompanied by moyamoya vessels in the basal ganglia. 12-15 Transdural collaterals are also evident in most cases. 16 Although previous diagnostic criteria for MMD required bilateral findings, the diagnostic criteria for definitive MMD were revised to include unilateral involvement as well (statement by the Research Committee on MMD Research on Intractable Diseases of the Ministry of Health, Labour and Welfare, Japan). However, in the revised diagnostic criteria, a definitive diagnosis of MMD requires cerebral angiography in unilateral cases. The presence of a mixed pattern of a focal steno-occlusive lesion and plexiform artery network at the MCA, and the lack of ICA involvement distinguish Ap/T-MCA from MMD.

**Influence of Pregnancy on Ap/T-MCA**

Pregnancy-associated intracranial hemorrhage is a rare and potentially devastating event. 20,21 Preexisting cerebrovascular diseases, such as arteriovenous malformation, aneurysm, and MMD, were detected in more than half of the pregnancy-associated intracranial hemorrhages. 22-24 The underlying mechanisms of pregnancy-associated intracranial hemorrhage are consequences of physiologic changes, such as hemodynamics, cerebral blood flow autoregulation, and blood-brain barrier permeability. 24-26 Additionally, various molecular changes that occur in pregnancy affect the function of endothelial cells, capillaries, and smooth muscle cells, and are responsible for pregnancy-associated intracranial hemorrhage. 25 In the patients with an Ap/T-MCA during pregnancy, these changes may have a significant impact on the fragile collateral vessels, including arterial twigs, or on flow-related aneurysms, contributing to intracranial hemorrhage.

To the best of our knowledge, there have been no reports of pregnancy and delivery in a patient with Ap/T-MCA. In the MMD that is in a similar underlying condition to Ap/T-MCA, there are no consistent guidelines for delivery, although a majority of pregnant women with MMD undergo cesarean section to avoid blood pressure fluctuations. 13,20,24,25 According to a previous report, cesarean section is recommended for pregnant women with MMD if 1) rapid control of blood pressure is required, 2) the patient’s condition is unstable (e.g., intracranial hemorrhage), and 3) fetal distress is detected. 25 In the 2 cases, cesarean sections were selected, which were successful without any strokes during the peripartum period. In case 2, there was also no complication during the second pregnancy and peripartum period.

**CONCLUSIONS**

An Ap/T-MCA is a rare congenital anomaly and is a potential cause of ICH for pregnant patients. Various physiological and molecular changes induced by pregnancy may be associated with a rupture of the fragile collateral vessels in the patients with Ap/T-MCA. Cesarean section under general or epidural anesthesia is a safe option for pregnant patients with ICH due to Ap/T-MCA.

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