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Neoplastic Ruptured Cerebral Aneurysm Caused by Intimal Sarcoma: A Case Report

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Abstract

Intimal sarcomas (ISAs) are extremely rare malignant tumors that histologically occur in the tunica intima of large blood vessels of the systemic and pulmonary circulation. Herein, we describe a case of an ISA-based neoplastic aneurysm in the middle cerebral artery (MCA) that resulted in a subarachnoid hemorrhage (SAH). The patient presented to our hospital with severe consciousness disturbance (Glasgow Coma Scale E1V1M2) and anisocoria. On admission, computed tomography (CT) showed a diffuse SAH. At 8 months prior, he presented to a previous hospital with hoarseness. Thoracic CT revealed a threatened rupture of the aorta of the arch. After total arch replacement, he had been diagnosed with ISA from the pathological findings of the resected aorta. Thereafter, he had been treated with adjuvant chemotherapy and radiotherapy without any cerebral vascular imaging studies, before admission at our hospital. Angiogram revealed a multilobar fusiform aneurysm on the right MCA. We performed a superficial temporal artery-MCA anastomosis, trapping, and resection of the affected MCA (including the aneurysm), followed by external decompression. Microscopic hematoxylin-eosin staining showed proliferation of atypical spindle-shaped cells with enlarged nuclei in the lumen of the affected MCA. Immunostaining showed CD31 (±), ERG (+), MDM2 (+), CDK4 (+, slightly), SMA (±), MIB-1 index 13.9%, factor VIII (±), and desmin (–). These pathological findings indicated metastasis of the ISA, which formed the neoplastic aneurysm. An ISA can cause a neoplastic cerebral aneurysm. Therefore, once a patient is diagnosed with an ISA, it is necessary to check periodically the cerebral arteries.

Keywords: neoplastic cerebral aneurysm, subarachnoid hemorrhage, intimal sarcoma, clipping, metastasis

Introduction

An intimal sarcoma (ISA) is an extremely rare malignant tumor that histologically arises in the tunica intima of large blood vessels of the systemic and pulmonary circulation.[1,2] ISA at autopsy was first described in 1923.[3] Currently, although a number of case reports and small case series have been reported, diagnosis and treatment of ISA remains difficult.[1,4-9] ISA is highly invasive, and the mean overall survival time ranges from 5 to 18 months.[2] At the time of diagnosis, metastasis is found in approximately 75% of patients, with common locations including the bone, lung, liver, spleen, kidney, skin, and brain.[7-10] Herein, we describe a case of an ISA-metastasized middle cerebral artery (MCA) that formed a neoplastic aneurysm, resulting in a subarachnoid hemorrhage (SAH). To the best of our knowledge, no comparable cases have been reported to date.

Case Report

A 38-year-old man presented to our hospital with severe

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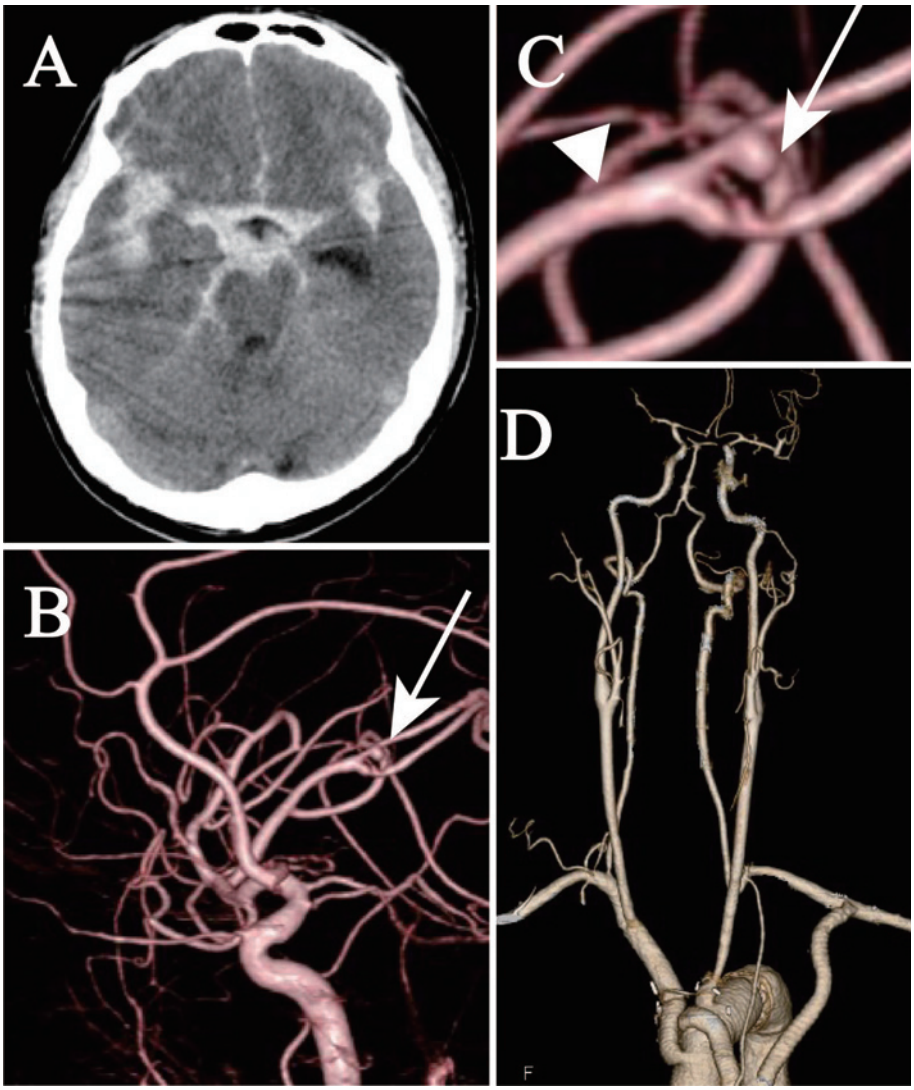

Fig. 1 Preoperative imaging. (A) Head plain computed tomography showed a diffuse subarachnoid hemorrhage. (B) Lateral 3D reconstruction of right ICA angiogram showed a multilobar fusiform aneurysm on the right M2-3 junction (arrow). (C) Magnification of lateral 3D reconstruction of right ICA angiogram clearly indicates multifocal fusiform aneurysm at the M2-3 junction (arrow). Arrow head shows the right M2. (D) Computed tomography angiogram showed no obvious dissecting changes (e.g., aneurysm formation) from the common carotid artery to the intracranial internal carotid artery.

consciousness disturbance (Glasgow Coma Scale (GCS) E1 V1M2) and anisocoria. Computed tomography (CT) imaging showed a diffuse SAH (right > left) (Fig. 1A). Angiogram revealed a multilobar fusiform aneurysm on the right MCA (at the M2 and M3 bifurcation) (Fig. 1B, C) and an irregular small aneurysm on the top of the basilar artery. No obvious dissecting changes such as aneurysm formation were observed from the common carotid artery (CCA) to the internal carotid artery on CT angiogram (Fig. 1D). On the basis of the hemorrhage distribution, we determined that the right M2-3 fusiform aneurysm caused the SAH.

The patient had been diagnosed with ISA of the aortic arch at 8 months prior to admission at our hospital. At 8 months prior to admission, he presented to a previous hospital with hoarseness. According to the data from the previous hospital, D-dimer was slightly elevated at 3.5 μg/mL on blood examination, and no tumor markers were measured. Thoracic CT revealed a rupture of the aorta of the arch. However, head CT and CT angiogram were not performed. Then, he received total arch replacement (including the right brachiocephalic artery, left CCA, and left subclavian artery) for threatened rupture of the aortic arch aneurysm. The pathological findings obtained from the resected aorta and those arteries were as follows. Spindle-shaped atypical cells with enlarged nuclei were also found (hematoxylin-eosin staining) in the primary lesion of the thoracic aorta. Tumor cells of primary lesion had invaded

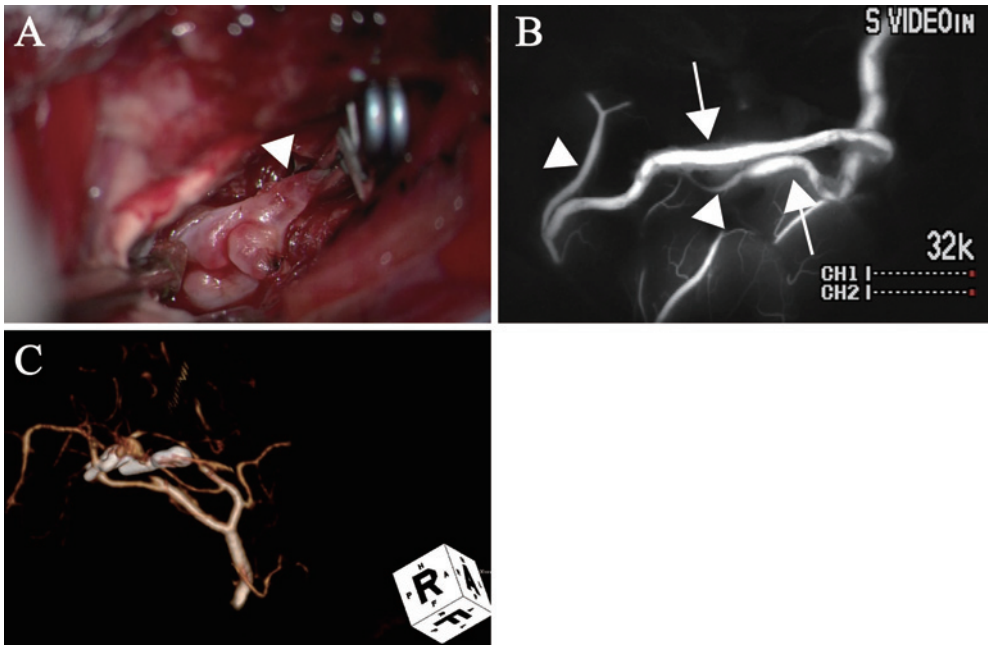

Fig. 2 Microscopic operative view and postoperative imaging. (A) A multifocal fusiform aneurysm was observed at the bifurcation of the M2-3 junction. Trapping of the M2 segment was performed (arrowhead). (B) Intravenous indocyanine green injection revealed excellent patency of the STA-MCA bypass. Arrows and arrowheads indicate the STAs and MCAs, respectively. (C) Computed tomography angiogram showed disappearance of the aneurysm.

the tunica adventitia, with disruption of the lamina elastica interna. Immunostaining showed cytokeratin (–), CD3 (–), CD20 (–), S-100 (–), desmin (–), myogenin (–), CD31 (–), CD34 (–), CD99 (–), calcitonin (–), CDK4 (+, slightly), MDM2 (+), ERG (+), and MIB-1 index 15%. These pathological findings indicated an ISA. All resected vessel margins were positive for tumor cells of primary lesion.

At 7 months prior to admission, he received intramedullary nail insertion for pathological fractures due to bone metastases of ISA and tumor curettage for disease-related intertrochanteric femoral fracture caused by metastasis. Intensity-modulated radiation therapy (60 Gy in 30 fractions) was also performed on his aorta and right femoral metastasis, followed by chemotherapy (pazopanib, 800 mg/day) at the previous hospital. Conversely, the patient had not previously undergone any head imaging studies, such as CT angiogram, before admission at our hospital.

Then, because the MCA bifurcation itself was aneurysmal, we decided to perform a superficial temporal artery-MCA (STA-MCA) anastomosis, trapping, resection of the affected MCA (including the aneurysm), and external decompression, rather than conventional clipping. After ensuring the frontal and parietal branches of the STA, a unilateral craniotomy was attempted. The STA-MCA anastomosis was performed, and the sylvian fissure was spread apart while the subarachnoid hematoma was flushed. A multifocal fusiform aneurysm was observed at the M2-3 junction (Fig. 2A). After trapping an M2 segment and two M3 segments of the MCA, the affected M2-M3 junction (including the aneurysm) was resected. We confirmed excellent patency of the STA-MCA bypass by intravenous indocyanine green injection (Fig. 2B).

On postoperative day 1, CT angiogram showed aneurysm disappearance (Fig. 2C). Then on postoperative day 2, the patient's consciousness improved to GCS E3VTM6. Finally on postoperative day 39, he was then transferred to another hospital with a modified Rankin Scale of 5.

Microscopic hematoxylin-eosin staining showed proliferation of atypical spindle-shaped cells with enlarged nuclei in the lumen of the affected MCA (Fig. 3A, B). Additionally, some of the atypical spindle cells had invaded beyond the smooth muscle of the tunica media into the tunica adventitia. Elastica van Gieson staining showed disappearance of the lamina elastica interna (Fig. 3C, D). At the rupture site, the lamina elastica interna had disappeared, forming an aneurysm (Fig. 3E). Immunostaining showed CD34 (–), CD31 (±), ERG (+), MDM2 (+), CDK4 (+), SMA (±), MIB-1 index 13.9%, factor VIII (±), and desmin (–) (Fig. 4). These pathological findings indicated that the ISA metastasis had formed a neoplastic aneurysm. These pathological results also showed total resection of the tumor.

Written informed consent for publication of the patient's information and images was provided by his family.

Discussion

Herein, we describe a case of an ISA metastasizing to the MCA, which formed an aneurysm that ruptured and

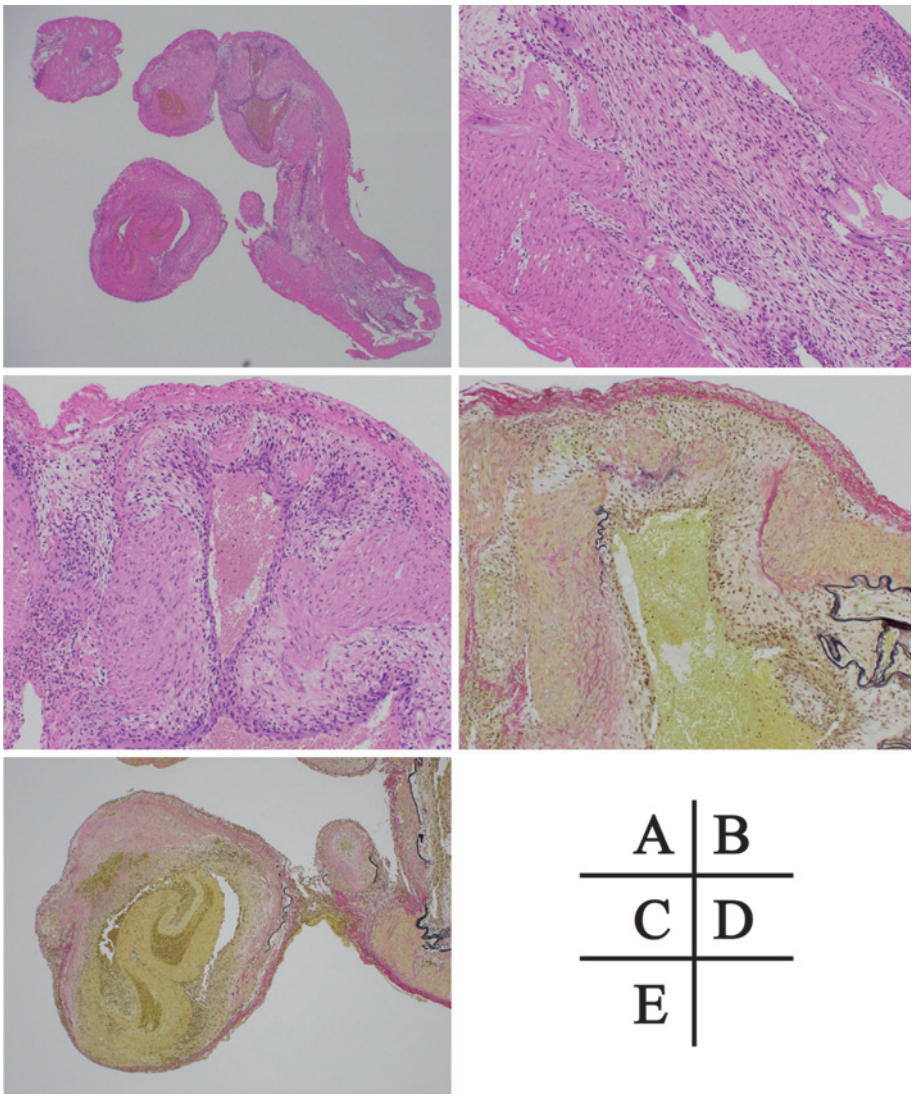

Fig. 3 Pathological findings. (A) Hematoxylin-eosin staining showing an overall view of the collected specimen (20× magnification). (B) Hematoxylin-eosin staining (100× magnification) showed proliferation of atypical spindle-shaped cells with enlarged nuclei in the lumen of the affected middle cerebral artery. (C, D) Infiltration of atypical spindle-shaped cells beyond the smooth muscle of the tunica media to the tunica adventitia. (D) Elastica van Gieson staining (100× magnification) showing disappearance of the lamina elastica interna in the same area. (E) At the ruptured site, the lamina elastica interna had disappeared, creating an aneurysm with thrombus formation in the lumen.

caused an SAH. ISA is categorized as a malignant mesenchymal tumor in the World Health Organization classification.[2] Histologically, ISAs arise in the tunica intima of large blood vessels of the systemic and pulmonary circulation.[1,2] ISAs develop extensively in the lumen of blood vessels and present with symptoms of embolization, ischemia, and stenosis. In rare cases, this can cause cerebral infarction, deep vein thrombosis, gastrointestinal bleeding, and ulcerative colitis.[10-12] In the present case, the tunica intima of the resected MCA intima was thickened irregularly, and a large part of the tunica intima was replaced by a sarcoma composed of spindle-shaped cells. The tumor had stenosed the lumen of the MCA and was accompanied by thrombi formation. The tumor cells had also destroyed the lamina elastica interna and invaded the tunica media and the tunica adventitia, forming an aneurysm. The tumor cells consisted of large spindle-shaped cells, and immunostaining was partially positive for CD31 and SMA; positive for ERG, MDM2, and CDK4; and negative for desmin (Fig. 4). Although the tumor cells were negative for desmin and partially positive for SMA, they did not differentiate into smooth muscle cells or myofibroblasts. The tumor was also partially positive for CD31 and positive for ERG, indicating differentiation from an angiosarcoma. However, as the tumor was poorly differentiated, it was not considered to be an angiosarcoma. As described above, the tumor was

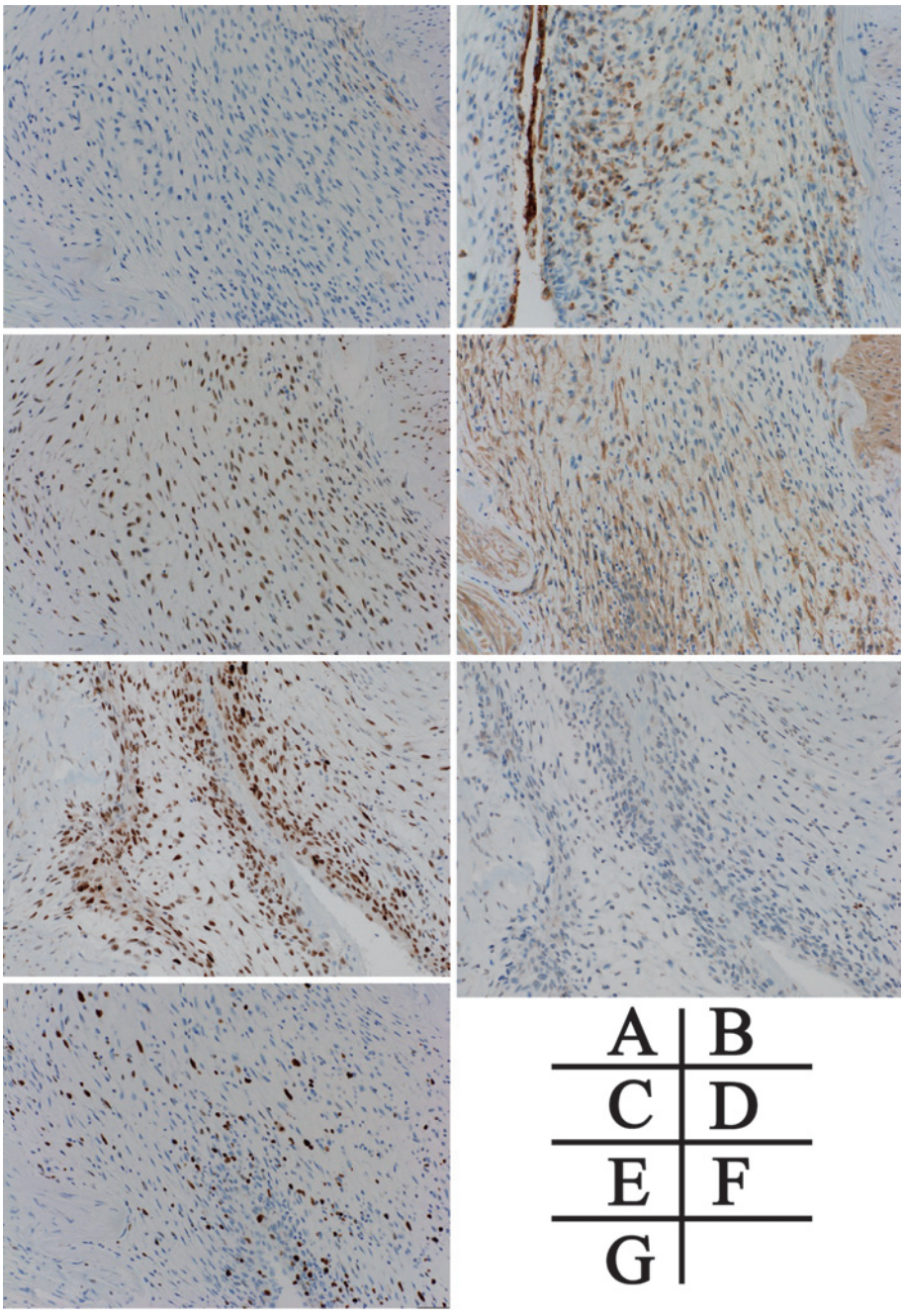

Fig. 4 Immunohistological findings. Immunostaining showed (A) CD34 (−), (B) CD31 (±), (C) ERG (+), (D) SMA (±), (E) MDM2 (+), (F) CDK4 (+, slightly), and (G) MIB-1 index 13.9% (A-E, G: 200× magnification, F: 400× magnification, respectively).

immunopositive for MDM2 and CDK4. Marked nuclear overexpression of MDM2 and amplification of the 12q12-15 region (including CDK4 and MDM2) were previously reported in ISAs.[2,13-15] Therefore, we diagnosed the tumor in the affected MCA as an ISA.

We considered that the ISA may have metastasized hemodynamically, rather than directly invading from the CCA to the MCA, as follows. First, preoperative CTA revealed no vascular abnormalities (e.g., dissecting changes) from the CCA to the intracranial internal carotid artery. Second, the surgical margins of the removed MCA were negative. Finally, aneurysm formation was also observed at the tip of the basilar artery, as well as the MCA. Previous studies reported that released tumor masses can form aneurysms in other organs and vessels.[16,17] Thus, we concluded that the ISA, which originated in the aortic arch, had metastasized hemodynamically to form the MCA.

In a systematic review of neoplastic cerebral aneurysms, of 96 patients with oncotic cerebral aneurysms, cerebral aneurysms induced by cardiac myxoma accounted for

60.4%, and those caused by choriocarcinoma and other tumors accounted for 26.1% and 13.5%, respectively.[18] However, in that study, there were no cases of neoplastic cerebral aneurysms originating from the ISA. The incidence rates of intracranial hemorrhage were 19.6% in myxoma, 100% in choriocarcinoma, and 84.6% in other tumor aneurysms. Neoplastic cerebral aneurysms of myxoma were also treated conservatively in 75.9% of cases, those of choriocarcinoma were treated by surgery and/or chemotherapy in 92% of cases, and those of other tumors were treated by surgery with or without chemotherapy in 69.2% of cases. Finally, the mortality rates were 11.4% for neoplastic cerebral aneurysms from myxoma, 60.9% for those from choriocarcinoma, and 92.3% for those from other tumors.[18]

Effective treatments of ISA are under development. Although total resection is recommended, it is difficult because the lesion is often the pulmonary artery or the aorta.[6] Anthracycline, gemcitabine, and pazopanib have been used as chemotherapy, but effective regimens are still unclear.[19] Therefore, currently, there is no sufficient treatment to prevent metastasis. Although head CT angiogram had not been performed before onset of SAH in the present case, it is desirable to check periodically the brain and cerebral arteries using MRI/A or CT angiogram because hemodynamic metastasis of ISA to the brain[9] and cerebral vessels (as the present case) can occur.

Additionally, the optimal treatment strategy for neoplastic aneurysms remains unclear.[3,18] For example, early craniotomy and conservative treatment by periodically checking for aneurysm growth have both been recommended.[18] Roeltgen et al. classified oncotic aneurysms into three main categories: (1) those that continue to grow and rupture, (2) those that stop growing and regress spontaneously, and (3) those that disappear with chemotherapy.[20] If the aneurysm grows, we suggest that aggressive treatment, including trapping and removal of affected arteries, should be considered to avoid rupture such as the present case. Because the aneurysm was ruptured in the present case, we performed trapping of the MCA (M2-3), including the aneurysm, with an STA-MCA bypass. Additionally, there is evidence that multiple neoplastic aneurysms are relatively common.[18,21] Indeed, the present case also had a neoplastic aneurysm in the basilar artery. Although chemotherapy and radiotherapy were considered for postoperative therapy in our case, they were not performed because of his poor modified Rankin Scale resulting from the initial SAH. Further studies are required to determine the optimal treatment strategies for ISA and neoplastic aneurysms.

Conclusion

We reported a case of a neoplastic ruptured cerebral aneurysm caused by metastasis of an ISA. ISAs can form neoplastic cerebral aneurysms. Therefore, once a patient is diagnosed with an ISA, it is desirable to check periodically the cerebral arteries.

Acknowledgments

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Conflicts of Interest Disclosure

The authors declare that there are no conflicts of interest.

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