Cerebral dissecting aneurysms in patients with moyamoya disease

Report of two cases

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Dissecting intracranial arterial aneurysms were identified in a 16-year-old girl and a 48-year-old man with moyamoya disease. Hemiplegia or tetraplegia rapidly developed. Angiography revealed bilateral stenoses or occlusion of the bifurcation of the internal carotid arteries (ICAs) and an unusual vascular network at the base of the brain. Autopsy confirmed massive hemorrhage from the thalamus and putamen, with intraventricular extension. The intracranial segments of both ICA's were markedly stenotic in both patients, due to eccentric fibroelastic intimal thickening. In one patient, a dissecting aneurysm was identified microscopically, involving the proximal segment of the left anterior cerebral artery. In the other patient, the right middle cerebral artery (MCA) was dissected beneath the internal elastic lamina along the entire length of the horizontal segment of the MCA. Thus, cerebral dissecting aneurysms may be present in patients with moyamoya disease.

KEY WORDS • cerebral aneurysm • dissecting aneurysm • moyamoya disease

MOYAMOYA disease is a rare but well known clinical entity characterized by an unusual vascular network at the base of the brain.\textsuperscript{25,34} Typical pathology includes localized stenoses or occlusion at the distal ends of both internal carotid arteries (ICAs) and proximal segments of the anterior cerebral arteries (ACA's) and middle cerebral arteries (MCA's), due to eccentric intimal fibrous thickening with laminated elastic fibers. This picture is associated with medium- or small-sized dilated arteries (moyamoya vessels) that function as a collateral pathway.\textsuperscript{13,24} The morphogenesis of these intracranial vascular lesions remains obscure.

Dissecting aneurysms of intracranial arteries are also rare, but they are recognized as one cause of acute hemiplegia in young previously healthy individuals.\textsuperscript{6,10,17,20,29,36,37} We report two patients with moyamoya disease and cerebral dissecting aneurysms, verified histopathologically.

Case Reports

Case 1

This previously healthy 16-year-old Japanese girl was admitted to Awaji Hospital with tetraplegia and unresponsiveness. On the previous day, she had slipped and fallen from a bicycle, striking the back of her head, but had suffered no apparent sequelae. Four hours before admission, she complained of severe headache and rapidly became semicomatose.

Examination. Physical examination on admission revealed a well developed girl in a semicomatose state. Blood pressure was 130/80 mm Hg, and pulse was 96 beats/min. The extremities were flaccid and responded little to painful stimuli. Stiff neck and conjugate roving eye movement were noted. The plantar responses were bilaterally extensor. Laboratory data revealed a normal blood chemistry, platelet count, and coagulation time. Liver and renal functions ap-
peared to be normal. Platelet aggregation activity induced by adenosine diphosphate was moderately exaggerated. The cerebrospinal fluid was bloody and under high pressure.

Cerebral angiography revealed complete occlusion of both ICA's just distal to the origin of the posterior communicating artery; a prominent basal vascular network (moyamoya vessels) was also visible. Both posterior cerebral arteries (PCA's) were fairly well opacified through the posterior communicating arteries by contrast medium.

Course. The patient was treated with dexamethasone (24 mg/day) and tranexamic acid (6 gm/day). She gradually regained consciousness for a few days, but remained confused. Left hemiparesis and left homonymous hemianopsia became apparent. The general condition was stable for 2 weeks, but thereafter her consciousness gradually deteriorated and she died on the 20th hospital day.

Postmortem Examination. The brain was swollen and the surface was bloody due to subarachnoid hemorrhage (SAH). There was falcial herniation of the right cingulate gyrus. Coronal section of the brain showed a massive hemorrhage in the right thalamus which extended into the ventricles. The anterior part of the circle of Willis and the main branches were narrow and firm. Numerous small vessels were noted at the base of the brain. The vertebral, basilar, and posterior cerebral arteries appeared normal.

Microscopically, both ICA's were stenosed by eccentric fibroelastic intimal thickening at the distal ends (Fig. 1a). Both ACA's and MCA's were also stenotic due to concentric fibrous intimal thickening. The narrowed lumen of the left MCA was completely occluded with fresh thrombus (Fig. 1b). The proximal segment of the right ACA was dissected, mainly beneath the internal elastic lamina. This space was filled with unclotted blood (Fig. 1c). Microscopic examination of the extracranial arteries revealed no specific vascular lesion.

Case 2

This previously healthy 48-year-old Japanese man was admitted to a local hospital because of left hemiplegia. A few hours before admission, he had been found in a semicomatose state. Cerebral angiography
revealed marked stenoses at the ends of both ICA’s and an unusual basal vascular network (Fig. 2). The patient was transferred to Wakayama Medical College Hospital for emergency surgery.

**Examination.** On admission, blood pressure was 150/70 mm Hg, and laboratory examination revealed a white blood cell count of 16,900/cu mm, a red blood cell count of 328 x 10^4/cu mm, and a platelet count of 128,000/cu mm. Other laboratory data were unremarkable. Cerebral computerized tomography revealed a massive high-density mass in the right basal ganglia extending into the ventricles.

**Operation.** Craniotomy was performed on the day of admission, and the hematoma was subtotally removed. During the 2nd postoperative day, the patient’s consciousness gradually improved. On the 3rd hospital day, there was an acute drop in blood pressure, and he became semicomatose. He died on the 10th hospital day.

**Postmortem Examination.** The brain, weighing 1780 gm, was markedly swollen. The surface was covered with blood as the result of SAH. The cerebellar tonsils were herniated into the foramen magnum. Horizontal section of the brain revealed a massive hematoma of the right basal ganglia and the temporal lobe, extending to the lateral ventricles and to the base of the brain. The brain parenchyma surrounding the hematoma was markedly edematous. The circle of Willis and the major branches appeared normal in diameter, but were firm. Numerous small vessels, arising from the ICA, ACA, posterior communicating, and anterior choroidal arteries, anastomosed with the distal segments of the ACA and MCA. A large number of small vessels from these vascular channels entered the base of the brain.

Microscopic examination revealed marked stenoses of both ICA’s at their distal ends, due to focal eccentric fibroelastic intimal thickening (Fig. 3a). The right MCA was completely occluded at its origin by fresh thrombus, and was dissected beneath the thickened intima along the entire length of the horizontal segment of the MCA. A cross section at the proximal one-third of the MCA showed narrowing of the lumen due to a subintimal hematoma. The dissected space was filled with a fresh thrombus extending to the true lumen through a tear in the internal elastic lamina (Fig. 3b). At the distal segment of the MCA, which had a fibrous intimal thickening, the dissected space was noted both above and beneath the internal elastic lamina, and communicated with the true lumen (Fig. 3c). A dilated artery, derived from the MCA, was also dissected and was markedly expanded (Fig. 3d).

In addition, the left ICA also presented separation of the thickened intima from the attenuated media at the distal end (Fig. 3a).

Microscopic examination of the extracranial arteries showed no specific vascular change, except for a mild to moderate atherosclerosis in the coronary arteries.

**Discussion**

Many investigators have emphasized that cerebral dissecting aneurysms should be considered in the differential diagnosis in cases of acute cerebrovascular accidents, especially when they occur in young individuals.6,10,17,19,20,29,30,37 This condition is characterized angiographically by the so-called “string sign”7,12,16,23 or “double lumen” appearance8,17 in the affected arteries. However, such evidence is not always clinically apparent.1,12,16,30,37,38 Histopathological findings all show a characteristic dissection of the wall.2,3,12,18,19,21,25,36 Many pathogenic and etiological factors have been considered as the possible cause of the cerebral dissecting aneurysms. These include syphilis,25 fibromuscular dysplasia,1,26 atherosclerosis,1 mucoid degeneration of the media,14 a congenital medial defect, fibrous or fibroelastic intimal thickening,19 fraying and splitting of the internal elastic lamina,3 trauma,5,6,16,26 surgery,2,27,30 homocystinuria,9,15 migraine,1,32 and strenuous physical exertion,7,19,31,37

We have previously studied 22 autopsy cases with moyamoya disease, and reported the pathological findings in 19.22 We concluded that in all except a 7-year-old girl, who presented with systemic vascular lesions due to fibromuscular dysplasia, the lesions were always present bilaterally at the distal ends of the ICA, and consisted of eccentric fibroelastic intimal thickening with laminated elastic fibers. We believed that these lesions could be considered as an excessive and unusual proliferation of “intimal pads” seen in
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Individuals without specific vascular lesions. Histologically, we identified cerebral dissecting aneurysms in two of the 22 patients. We considered that these cerebral dissecting aneurysms were not incidental findings in moyamoya disease but might be attributed to the intimal lesions in this disorder.

Disruption of the intima is common in atherosclerotic cerebral vessels. It is well recognized that intramural hemorrhage or rupture of atheroma commonly occurs in atherosclerotic arteries and leads to cerebral thrombosis secondary to thrombus formation in the vicinity of the tear of the thickened intima. These intimal tears, however, only rarely develop into a cerebral dissecting aneurysm. Therefore, the oc-

Fig. 3. Photomicrographs in Case 2. a: One of the tangential serial sections of the bifurcation of the left internal carotid artery. Fibroelastic intimal thickening is noted at the distal end, along with complete occlusion of the middle cerebral artery (MCA). Note separation of the thickened intima from the attenuated media (arrowheads). Elastica van Gieson, × 16. b: Right MCA at a proximal third of the horizontal segment. A fresh thrombus fills the dissected space and extends to the true lumen through the tear of the internal elastic lamina. Elastica van Gieson, × 38. c: Right MCA at a distal third of the horizontal segment. The false lumen communicates with the markedly stenosed true lumen through a tear of the thickened intima. H & E, × 38. d: A dilated perforating artery branched off from the right MCA showing marked expansion and dissection of the wall. Elastica van Gieson, × 14.
currence and development of the cerebral dissecting aneurysm might relate to two different factors: tears of the intima and segmental separation of the intima from the media. In the juvenile or young adult, the intima would rarely tear; however, should this occur, the dissection would readily extend and develop. The degree of intimal thickening and fraying, splitting, or reduplication of the internal elastic lamina could be responsible for disruption of the intima in young individuals. Intimal thickening of the cerebral arteries in moyamoya disease may also be implicated in this dissection.

Pilz and Hartjes reported a 16-year-old boy with luminal narrowing of the right ICA, “string of beads” configuration of the ipsilateral MCA, and an abnormal basal vascular network. Autopsy revealed that the stenosis in the ICA did not result from intimal thickening but rather from a dissecting aneurysm complicated by a medial type of fibromuscular dysplasia. The unusual ipsilateral vascular network may be the result of an acute obstruction of the ICA. Histologically, their findings differ from those seen in our patients, except for the dissecting aneurysm.

When the dissecting aneurysms actually developed in our patients is unknown. However, it was speculated that massive cerebral hemorrhage occurred first, followed by dissecting aneurysms as the cerebral lesions were not the infarcts usually seen as a result of dissecting aneurysms. The massive hemorrhage was detected very early in the clinical course by computerized tomography or by lumbar puncture. The histological findings that the dissected space was filled with either uncotted blood or fresh thrombi showing no apparent organization also support this speculation.

There was no direct evidence of trauma during the procedure of removal of the hematoma or at autopsy in our Case 2. In Case 1, there was an episode of head trauma on the day before admission, but without any apparent sequelae. Therefore, the significance of the head trauma and surgery could be minimized as additional causative factors in our patients.

Cerebral hemorrhage was the most common and fatal accident in patients with moyamoya disease in our investigation. When dissecting aneurysms occurred in the ICA or main branches of the circle of Willis following massive cerebral hemorrhage, cerebral blood flow through perforating arteries, as a collateral pathway from these branches, is decreased, and the patients’ neurological condition further deteriorates, in addition to the effect of the massive hemorrhage. It may be difficult, sometimes impossible, to detect clinically cerebral dissecting aneurysms in patients with moyamoya disease: the main branches of the circle of Willis are almost always poorly demonstrated angiographically due to bilateral ICA stenosis or occlusions. Even if the ACA or MCA could be identified via transdural or leptomeningeal anastomoses, they will usually appear too narrow and too obscure to make a diagnosis. It should be emphasized that cerebral dissecting aneurysms may occur in patients with moyamoya disease.

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