Moyamoya Disease with Concurrent von Recklinghausen's Disease and Cerebral Arteriovenous Malformation

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Summary

We present a rare autopsy case of von Recklinghausen's disease with Moyamoya vessels and arteriovenous malformation. A 58-year-old female patient suffered from dysarthria and dysphagia. On examination, Parkinson's signs, pseudobulbar palsy, and muscular weakness of the left extremity and pyramidal tract signs were observed. An enhanced brain computed tomography revealed abnormal high-density network vessels at the thalamus and midbrain. By cerebral angiography, the following changes were observed; occlusion of the right internal carotid artery at the bifurcation, and abrupt narrowing and occlusion of the left internal carotid artery at the bifurcation and siphon. A lateral vertebral arteriography revealed telangiectasia at the basilar tip. The patient died of pulmonary thromboembolism at age 61. The vessels of the circle of Willis were hypoplastic. The optic nerves, infundibulum and mammillary body were covered with a large number of ectatic vessels. Arteriovenous malformations were observed in the bilateral occipital lobes. Histopathologically, the elastic lamina of Moyamoya vessel was conspicuously wavy and often duplicated or triplicated, and discontinued occasionally. Discontinuity of the elastic lamina of the perforating arteries and circumferential arteries supplied by the middle cerebral artery (MCA), anterior CA (ACA) and posterior CA (PCA), was also occasionally observed. It is likely that the Moyamoya vessels in this patient were compensatorily formed by congenital hypoplasia of the internal artery, MCA, ACA and PCA.

Key words: Moyamoya disease – von Recklinghausen's disease – Arteriovenous malformation – Brain atrophy – Watershed infarction

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Introduction

Since the first documentation of so-called Moyamoya disease in 1957 [16], clinical and angiographic descriptions of this condition have accumulated in the literature [6]. The etiology and pathology of Moyamoya disease are still obscure [6]. Cases of Moyamoya disease associated with von Recklinghausen's disease have been reported [2, 3, 7, 9, 14, 15, 18, 20], as have a few cases of Moyamoya disease with arteriovenous malformation (AVM) [4, 10–12].

We recently encountered an autopsy case of Moyamoya disease, with both the rare conditions of von Recklinghausen's disease and AVM. To the best of our knowledge, this is the first case of Moyamoya disease associated with both complications, and in which one possible aspect of the etiological problems of Moyamoya disease is implied. We describe the histopathologic findings of this unique case and discuss the histomorphogenesis of Moyamoya disease in consideration with concurrent occurrences of these particular conditions.

Case Report

A 58-year-old female who had been diagnosed as having von Recklinghausen's disease since the age of 10 was admitted to the Omori Red Cross Hospital with the complaints of dysarthria and dysphagia. On exami-

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nation, numerous café au lait spots, and sessile and pedunculated yellowish-brown tumors were found on the skin of the whole body. Her blood pressure was 128/90 mm Hg. Her consciousness level was mild somnolence. Masked face, speech sluggishness, gait disturbance and muscle rigidity of the extremities were observed. Uvular elevation was not elicited. The tongue did not move laterally. Muscle weakness of the left extremities and hyperreflexia of all extremities were evident. Bilateral Babinski's signs were elicited. The sensory examination revealed truncal hypalgesia, and vibration sense was deteriorated in the upper extremities. Cerebellar signs were not recognized. Laboratory findings on admission were within normal limits regarding urinalysis, complete blood count and blood chemistry. Plain brain computed tomography (CT) showed severe cerebral atrophy, and an enhanced CT revealed numerous abnormal and tortuous high-density network vessels at the thalamus and midbrain. A cerebral arteriography revealed the following changes: the right internal carotid artery was obstructed at the bifurcation; AVM was demonstrated at the occipital lobe, and it was perfused

with an abnormal occipital branch of the right external carotid artery (Fig. 1A); the left internal carotid artery narrowed abruptly at the bifurcation and was occluded at the supraclinoid region after the branching of the ophthalmic artery (Fig. 1B); in contrast, the external carotid artery was clearly shown, and contrast medium reached the ipsilateral internal carotid artery area by anastomosis of the ophthalmic artery. A lateral vertebral arteriography revealed conspicuous telangiectasia at the basilar tip. The patient was thus diagnosed as having Moyamoya disease associated with von Recklinghausen's disease. After rehabilitation, the patient was discharged. Her general conditions gradually worsened, and she died of a pulmonary thromboembolism at age 61.

General pathologic findings

The lungs showed marked congestive edema, and recent thromboembolic conditions were recognized from the proximal to the peripheral pulmonary arteries in both lungs. Generalized congestion was noted in other

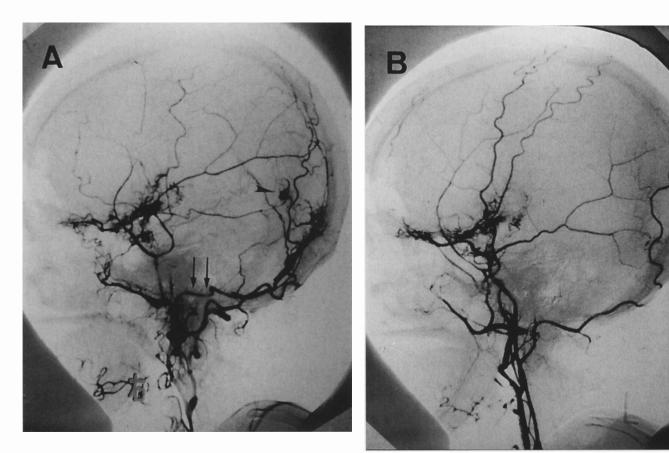


Fig. 1A. The right internal carotid artery, obstructed at the bifurcation. The AVM at the occipital region (arrowhead), supplied with an abnormal occipital branch of the external carotid artery (arrow) is shown. Right common carotid arteriogram, lateral projection.

Fig. 1B. The left internal carotid artery narrowed abruptly at the bifurcation, and was occluded after the branching of the ophthalmic artery at the supraclinoid region. Left common carotid arteriogram, lateral projection.

organs, including the liver and kidney. Systemic atherosclerosis of varying degrees was revealed, however, no stenotic or occlusive condition was recognized.

Neuropathological findings

The brain weighed 990 g. Macroscopically, the bilateral frontal and parietal lobes showed remarkable atrophy. The vertebrobasilar arteries showed extensive atherosclerotic conditions; however, the vessels of the circle of Willis were completely free from any atherosclerotic change (Fig. 2). The walls of these vessels were very thin and looked rather hypoplastic, and numerous dilated small arteries were sprouting from them. Three tumorous lesions ranging from 5 to 7 mm in diameter were recognized at the bilateral accessory nerves (2 in the left side, 1 in the right side). The optic nerves, infundibulum and mammillary body were covered with a large number of ectatic vessels, a finding which is consistent with Moyamoya vessels. Coronal sections of the cerebrum demonstrated remarkable atro-

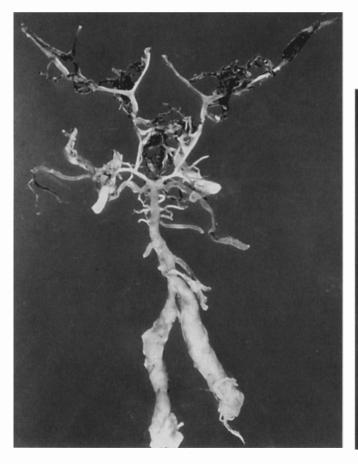


Fig. 2. Hypoplasia of the internal carotid artery, ACA, MCA, posterior cerebral artery (PCA) and posterior communicating artery is shown. There were no atheromatous change in these arteries. In contrast, the vertebral arteries showed severe atheromatous change.

phy, extending from the frontal to parietal lobe at the watershed area between the middle cerebral artery (MCA) and anterior cerebral artery (ACA). Mild cerebral atrophy at the borderzone region between the MCA and posterior cerebral artery (PCA) was also observed (Fig. 3). Large numbers of dilated vascular channels were seen in the bilateral occipital lobes. Numerous ectatic vessels were present around the tegmentum and in the pedunculum of the midbrain. The cerebellum had a normal appearance.

Histopathological findings of the cerebral tissue

The elastic laminas of the ectatic vessels at the optic nerve, infundibulum, mammillary body and midbrain were conspicuously wavy and often duplicated or triplicated, and disrupted occasionally with attenuated media (Fig. 4A, B). Inflammatory cell infiltration was absent in these vessels. Disruption of the elastic lamina of the perforating and circumferential arteries supplied by the MCA, ACA and PCA was occasionally observed (Fig. 4C). Marked gliosis and cystic formation by liquefaction degeneration were revealed in the severely atrophic cerebral cortex at the watershed area between the MCA and ACA, as well as between the MCA and PCA. The deep white matter of the cerebrum showed

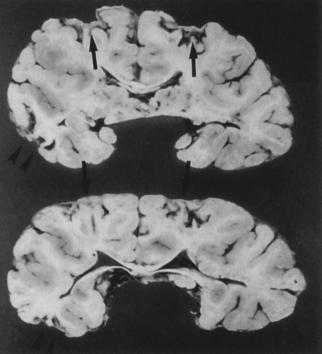
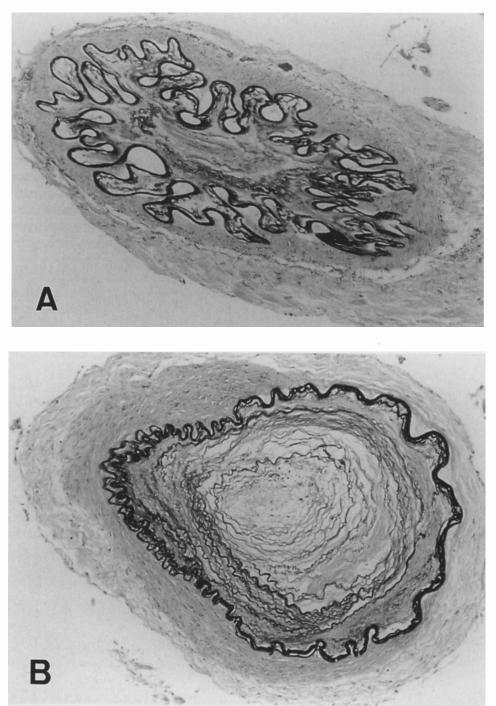


Fig. 3. Conspicuous brain atrophy is shown at the precentral gyrus (arrow) and right inferior temporal gyrus (arrowhead), which are watershed areas between the MCA and ACA, and the MCA and PCA, respectively.



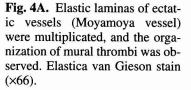


Fig. 4B. Multiplicated elastic lamina of ectatic vessels (Moyamoya vessel) was observed. The vascular lumen was occluded. Elastica van Gieson stain (×66).

gliosis, nerve fiber rarefaction and incomplete infarction with macrophages. Distinct AVM lesions were observed; they were microscopically dilated arteries and veins with thin walls, and they were occasionally associated with chronic organized thrombi, gliosis and cystic degeneration in the medial side of the bilateral occipital lobes (Fig. 5). Many dilated abnormal vessels were observed adjacent to the optic nerve and at the optic chiasm. Similar abnormal vessels were also shown around the tegmentum and at the pedunculum of the midbrain. The pons, medulla and cerebellum were in normal condition. In the accessory nerve, micronodular tumorous lesions of neurofibroma and meningioma were found.

Discussion

Since the first report by Hilal et al. [3] in 1971 of three cases of Moyamoya disease in patients affected by neurofibromatosis, several similar cases have been reported [2, 7, 9, 14, 15, 18, 20]. These patients all had

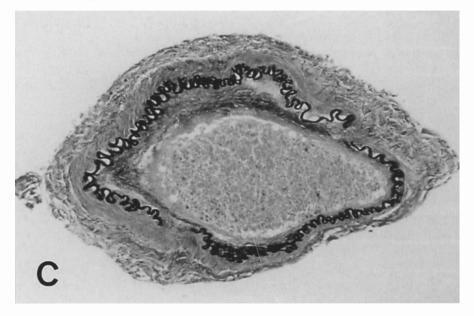


Fig. 4C. Segmental disruption of elastic lamina of the circumferential artery supplied by the MCA was observed at the frontal lobe. Elastica van Gieson stain (\times 66).

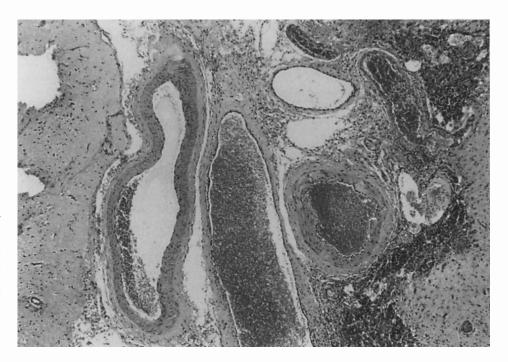


Fig. 5. Distinct AVM lesions were shown in the medial side of the bilateral occipital lobes. They were microscopically dilated arteries and veins with thin walls and they were occasionally associated with chronic organized thrombi, gliosis and cystic degeneration. Hematoxylin and eosin stain (×12.5).

stenotic vascular lesions to some degree in the internal carotid arteries. Yamada et al. [21] studied seventy-six patients with idiopathic Moyamoya disease by angiography. Sixty-six (43%) of the 152 PCAs examined had a stenotic or occluded lesion. The frequencies of cerebral infarctions, ventricular dilation and cerebral atrophy were correlated with steno-occlusive PCA lesions. As for the etiology of Moyamoya disease, congenital factors were originally considered to be important [13, 16]. The high incidence of Moyamoya disease among the Japanese, and occasional familial occurrences of

this disease strongly suggest a congenital origin [6]. The association of the other anomalies might also support a congenital cause of this disease [1, 5]. Postnatal arterial occlusion with a secondary development of collaterals has also been considered for the etiology of Moyamoya disease [17, 22]. Zulch et al. [22] reported a case in which typical Moyamoya arteries developed in an adult within only 23 months, suggesting an acquired disorder. In addition, Takeuchi et al. [17] described the rapid development of Moyamoya vessels after severe vasospasm, and they proposed that the development of

such vessels should be considered a Moyamoya phenomenon that is different from the prototype of Moyamoya disease of unknown etiology.

In the present case, the right internal carotid artery was obstructed at the bifurcation, and the left internal carotid artery was stenotic at the bifurcation and occlusive at the siphon. The terminal portion of the internal carotid artery and the initial portions of the MCA and ACA were hypoplastic. Histologically, the elastic lamina of the perforating and circumferential arteries that were supplied by the MCA, ACA and PCA were occasionally discontinuous. It is reasonable to conclude that the Moyamoya vessels in this patient were compensatorily formed by congenital hypoplasia of the internal carotid artery, MCA and ACA.

The occurrence of cerebral infarction, severe brain atrophy and marked ischemic changes at watershed areas were not described in the reported cases of Moyamoya disease associated with von Recklinghausen's disease. The mechanisms whereby watershed infarcts develop have been controversial for many years [19]. A study using positron emission tomography (PET) showed that the anterior borderzone region between the ACA and MCA may be selectively vulnerable to severe carotid stenosis, which produces diminished perfusion in this region through lowered hemodynamic reserve [8]. In the present case, it is possible that such cerebral ischemic and atrophic changes especially in the borderzone region between the ACA and MCA occurred from chronic ischemia through hypoperfusion due to hypoplasia of the cerebral arteries.

There have been a few case reports of Moyamoya disease accompanied by AVM [4, 10-12]. All of the AVMs of the reported cases communicated with Moyamoya vessels. Mawad et al. [11] hypothesized that once the supraclinoid stenosis takes place, Moyamoya collaterals of various types may develop and the ensuing hemodynamic shunt maintains the blood flow to the vascular malformation. Although the combination of occlusive vascular disease and cerebral AVM may be a rare congenital coincidence, it is more likely that the increased blood flow to the malformation and increased blood turbulence lead to intimal hyperplasia, endothelial thickening and progressive occlusion. Lichtor et al. [10] emphasized that AVM was most likely to be secondary to Moyamoya disease due to the following mechanism. In the presence of ischemia, the available anastomotic channels, which are the perforating vessels and their end capillaries, would probably open up and become distended, without a rich capillary linkage to the cortex. These capillaries could only discharge their increased flow into normal draining veins which in turn become distended, taking on the appearance of an AVM. The AVM of our case, in contrast, were situated at the bilateral occipital lobes supplied by an abnormal occipital branch of the right external carotid artery which did not communicate with Moyamoya vessels. The AVM in our case thus might not originate secondarily to Moyamoya vessels, but essentially: it is more likely that this association is a rare congenital coincidence induced by von Recklinghausen's disease.

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