Child's Nerv Syst (1996) 12:404–408

CASE REPORT

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Arteriovenous malformation associated with moyamoya disease

Received: 5 April 1995

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Abstract The first case of a child with an arteriovenous malformation (AVM) associated with moyamoya disease is reported. The patient presented ischemic symptoms and underwent indirect bypass surgery on both sides when she was 5 years old. Four years later she suffered from headache, and a small AVM of the left frontal lobe associated with the moyamoya vessels was detected. Single photon emission computed tomography (SPECT) was performed at age 11 and demonstrated low local cerebral blood flow (CBF) in the left frontal lobe and right temporal lobe, although the revascularization after the bypass surgery seemed to be effective, as judged on pancerebral angiography. We feel that brain ischemia due to the moyamoya disease may have played a causative role in the development of the AVM.

Key words Moyamoya disease · Arteriovenous malformation · Childhood

Introduction

Moyamoya disease is a nonatherosclerotic vasculopathy mainly affecting the end-arterial vascular bed, and has a characteristic "puff-of-smoke" angiographic appearance [6]. Although an association of moyamoya disease with cerebral aneurysms has been reported frequently [1], there have been only eight reported cases of moyamoya disease accompanied by an arteriovenous malformation (AVM) [2–5].

In this paper we present a childhood case of a cerebral arteriovenous malformation (AVM) associated with moyamoya disease, and discuss the pathogenesis of this case, with a review of the literature.

Case report

The patient, a right-handed Japanese girl, was admitted to a local hospital when she was 5 years old. Approximately 1 year earlier she had experienced transient episodes of motor weakness of the left arm and leg; otherwise she had been healthy. Pancerebral angiography revealed bilateral occlusion of the proximal middle cerebral arteries with abnormal clusters of vessels in the region of both basal ganglia. The findings were typical of moyamoya disease and were categorized as stage 3 moyamoya disease according to the classification system of Suzuki (Fig. 1). The patient underwent an indirect bypass procedure, encephaloduroarteriosynangiosis (EDAS), bilaterally. Her postoperative recovery was uneventful, with gradual resolution of the transient motor weakness over several weeks.

The clinical course was uneventful until 4 years following the operation, when the patient developed recurrent severe headaches and was admitted to our clinic at the Nagoya City General Hospital.

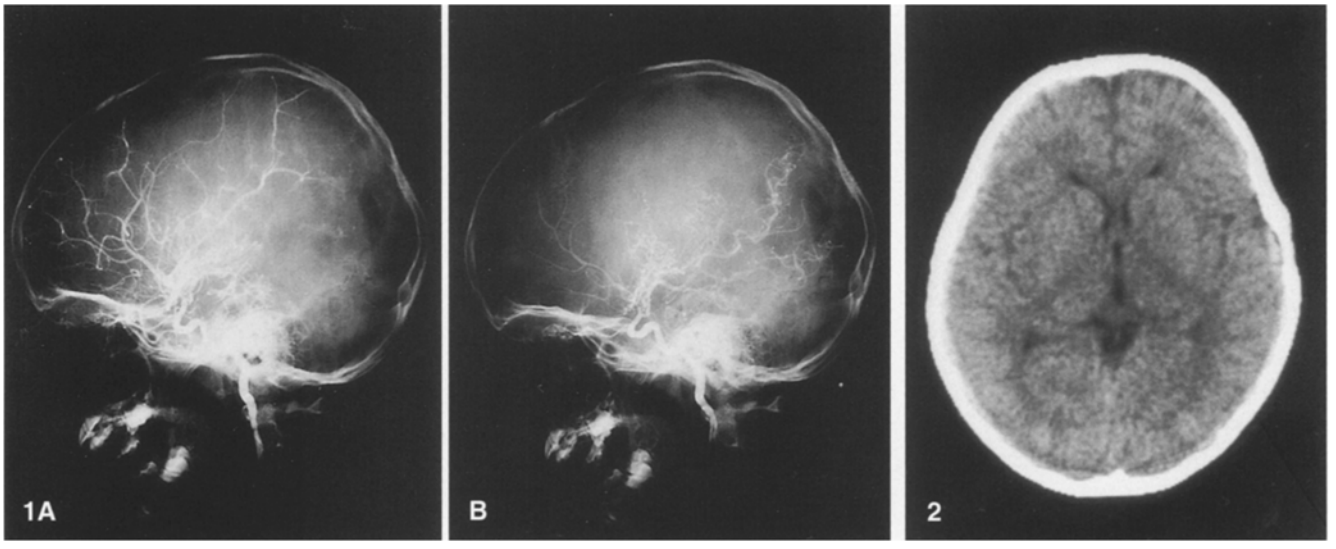

Fig. 1A,B Cerebral angiography at age 5: **A** lateral right carotid, **B** lateral left carotid. Occlusion of the internal carotid arteries is shown just distal to the origin of the posterior communicating arteries, with reconstruction of the middle cerebral arteries and extensive telangiectatic-type revascularization on both sides

Fig. 2 A computed tomogram at age 9, showing no abnormality

A computed tomography (CT) scan revealed no abnormality (Fig. 2). Pancerebral angiography was performed and demonstrated not only good revascularization through the bilateral indirect bypasses, but also a small cerebral AVM in the left frontal lobe. A multitude of anastomotic connections had been established between the superficial temporal arteries (STAs) and the underlying brain. The moyamoya vessels in the region of both basal ganglia had reduced slightly. The small AVM of the left frontal lobe was fed by the moyamoya vessels and drained into the cortical veins (Fig. 3). At this time, she was placed on a regime of anticonvulsants and symptomatic therapy, and her headaches resolved over a few days. Her clinical course was subsequently uneventful. However, she was readmitted to our hospital at age 11, after mild hemiparesis developed on the right side. A CT scan revealed no abnormal lesion. A cerebral angiogram was almost identical to the angiogram performed at age 9. There was good bilateral revascularization following the bilateral EDAS. Single photon emission computed tomography (SPECT) was also performed and demonstrated low local cerebral blood flow (CBF) in the left frontal and right temporal lobes (Fig. 4). The patient was treated with conservative medical therapy, and her hemiparesis improved substantially, with the return of spontaneous use of the left extremities over 1 week.

The clinical course was uneventful until 4 years later, when she again suffered from repeated headaches and was readmitted to our hospital. A magnetic resonance (MR) imaging study showed an AVM with an aneurysmal vessel in the left frontal lobe (Fig. 5). Cerebral angiography demonstrated an increase in the anastomotic connections between the STAs and the underlying brain, with a further decrease in the moyamoya vessels in the basal ganglia compared to the angiogram performed at age 9. Furthermore, there was marked dilation of the draining veins of the AVM in the left frontal lobe (Fig. 6). Positron emission tomography (PET) was performed with $^{15}O_2$ at this time and showed no region of low CBF (Fig. 7). She was continued on a regime of medical therapy. We plan to follow her progress closely and assess the natural history of this disease.

Discussion

To our knowledge, moyamoya disease in association with a cerebral AVM has been reported in only eight cases including ours (Table 1) [2–5]. Patient ages have ranged

Table 1 Accumulated reported cases of arteriovenous malformation (AVM) associated with moyamoya disease

References	Age/sex	Symptom	Stage of moyamoya disease	Site of AVM
Nagayama et al. 1986 [4]	33/M	Ischemia	L3, R3	Right frontal lobe
Lichtor and Mullan 1987 [2]	34/M	Ischemia	L3, R3	Corpus callosum
	50/F	Ischemia	L1, R3	Right MCA distribution
	43/M	Hemorrhage	L1, R3	Right frontal lobe
Okada et al. 1990 [5]	38/F	Ischemia	L1, R3	Left frontal lobe
Montanera et al. 1990 [3]	54/F	Ischemia	L3, R3	Bilateral frontal lobe
	44/F	Ischemia	L3, R3	Right parietal lobe
Present case	15/F	Ischemia	L3, R3	Left frontal lobe

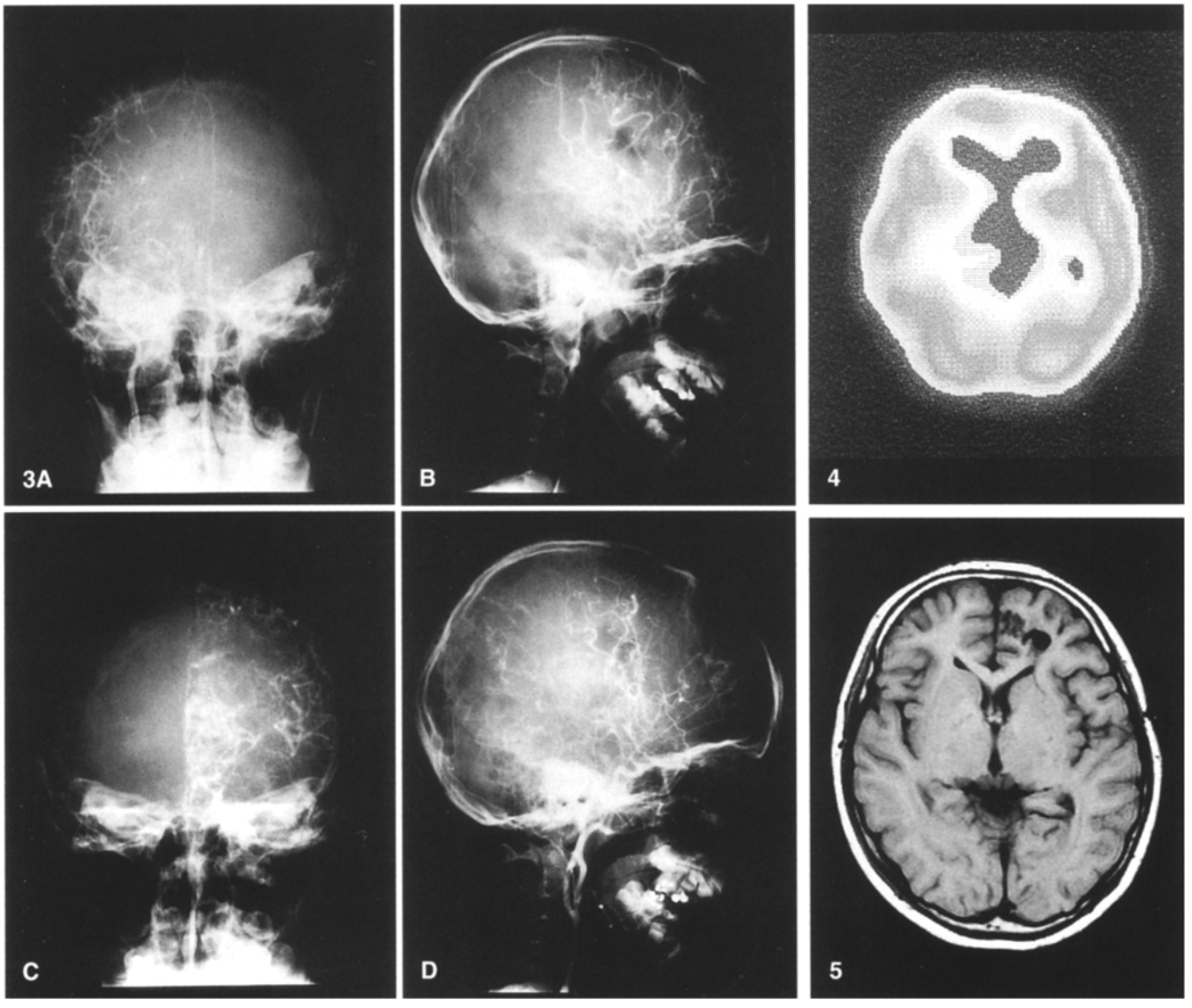

Fig. 3A–D Cerebral angiography at age 9: **A** Anteroposterior right carotid, **B** lateral right carotid, **C** anteroposterior left carotid, **D** lateral left carotid. Occlusion of the internal carotid arteries is revealed on both sides, with abnormal clusters of vessels in the region of the basal ganglia bilaterally, typical of moyamoya disease. In addition, the angiogram shows an arteriovenous malformation (AVM) involving the left frontal lobe, fed by the moyamoya vessels and draining into the cortical veins

Fig. 4 *N*-Isopropyl-*p*-[^{123}I]iodoamphetamine (IMP) was injected intravenously and 20 min later single photon emission computed tomography (SPECT) was performed. SPECT demonstrated low local cerebral blood flow (CBF) in the left frontal lobe and right temporal lobe

Fig. 5 Axial T1-weighted magnetic resonance image showing the flowvoid of a frontal cerebral AVM with an aneurysmal dilated vessel

from 15 to 54 years; the mean is 39 years, which is indicative of the frequent occurrence in older individuals. The present case is the first detected in childhood. There were five men and three women. The initial symptoms were ischemic (muscle weakness, sensory disturbance, etc.) in seven cases and headache due to intracranial hemorrhage in the eighth. All reported patients were categorized as having stage 1–3 moyamoya disease according to the classification system of Suzuki [6] at the time that the AVM and the moyamoya vessels were detected.

There exists a divergence of opinion as to the etiological relationship between the formation of the AVM and the moyamoya vessels. The AVMs in the reported cases either caused the moyamoya disease, were caused by the moyamoya disease, or were coincidental. According to Montanera et al. [3], a combination of arterial stenosis induced by the stress of high flow feeding the AVM and angiogenesis

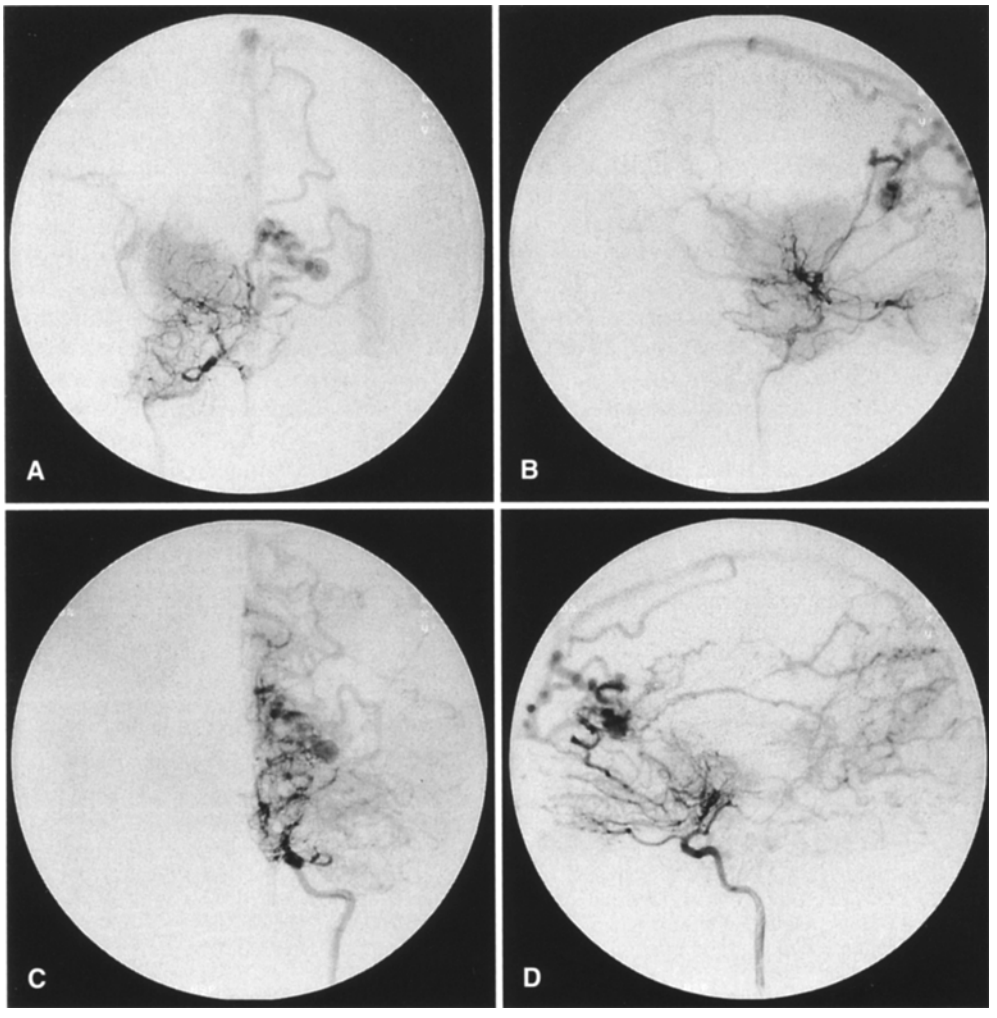

Fig. 6A–D Cerebral angiography at age 15: **A** anteroposterior right carotid, **B** lateral right carotid, **C** anteroposterior left carotid, **D** lateral left carotid. Increased anastomotic connections are shown between the bilateral STAs and the underlying brain, with bilaterally decreased moyamoya vessels in the basal ganglia compared with the angiogram obtained at age 9. Dilation of the draining veins of the AVM in the left frontal lobe is also seen

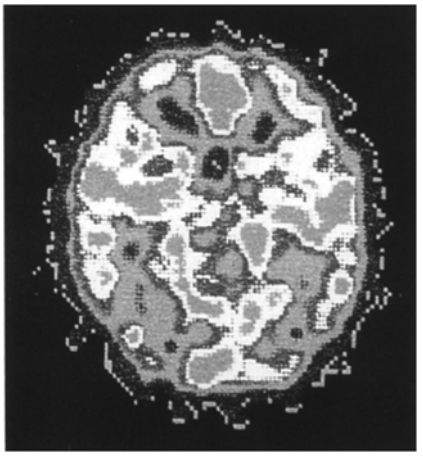

Fig. 7 $^{15}O_2$ positron emission tomography at age 15, demonstrating no region of low CBF

in response to the release of angiogenetic factors associated with the AVM may lead to moyamoya disease. In their case, moyamoya vessels associated with a parietal lobe AVM were detected 10 years after initial discovery of the AVM by cerebral angiography. At that time there was no evidence of stenosis or occlusion of the ipsilateral middle cerebral artery. On the other hand, Lichtor and Mullan [2] reported that in their case the AVM was probably secondary to the moyamoya disease [2]. They assumed that anastomotic channels opened up and became distended, causing increased flow into a normal draining vein in the presence of ischemia, and thus appeared to be an AVM. Another mechanism is related to the presence and recanalization of clots. Okada et al [5] stated that in their case the coexistence of the AVM and moyamoya disease was incidental because there were no moyamoya vessels around the AVM.

In the present case, we share the opinion of Lichtor and Mullan that the AVM is secondary to the moyamoya disease. Our patient's ischemic symptoms were repeatedly

present after the bypass procedure, and the SPECT performed at age 11 demonstrated low CBF in the region of AVM, indicating the presence of brain ischemia. Moreover, the AVM associated with the moyamoya vessels was initially detected 4 years after the moyamoya vessels were found at age 5. Thus, we feel that the ischemic phenomena caused by the moyamoya disease may have played a role in the development of the AVM.

Recently, Takahashi et al. [7] have reported that the level of basic fibroblast growth factor (bFGF) had a tendency to be elevated in the cerebrospinal fluid of patients with moyamoya disease who had effective indirect bypass procedures. Thus, bFGF may play an important role in the pathogenesis of moyamoya disease. Contrary to the idea of Montanera et al. [3], this factor may lead to opening and distension of anastomotic channels from the moyamoya vessels to the cortical veins, appearing as an AVM. For this reason, we speculate that the pathogenesis of coexisting AVM and moyamoya disease may be associated with the angiogenetic factor, bFGF.

Okada et al. [5] have reported the first surgical resection of an AVM accompanying moyamoya vessels. In this case, there were no moyamoya vessels around the AVM. On the other hand, in the present case, indirect bypass surgery was performed at age 5 and there were a multitude of anastomotic connections between the STAs and the underlying brain. The surgical approach was considered too risky because of the difficulty of separating the vascular malformation from the adjacent anastomotic feeding vessels. An endovascular approach to the AVM was not possible because of the occlusion of the middle cerebral artery and the supply of this AVM by the moyamoya vessels. For these reasons, we consider continued conservative medical therapy to be the most appropriate and safest treatment for our patient.

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EDITORIAL COMMENT

Aneurysms occurring in association with moyamoya disease have been well described. Arteriovenous malformations are less likely but also occur in patients with moyamoya disease. This particular case report points out the need for careful follow-up of patients with moyamoya disease, particularly those who have undergone bypass procedures. It is only with follow-up studies that we can become aware of the true incidence of arteriovenous malformations and aneurysms in these patients.

Harold J. Hoffman, Toronto