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Cerebral Arteriovenous Malformations Associated with Moyamoya Phenomenon

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Cerebral arteriovenous malformations (AVMs) are associated with a variety of alterations in the angioarchitecture of the feeding arteries and draining veins [1–3]. Between January 1985 and December 1988 we examined the angiograms of 97 patients with cerebral AVMs to assess their potential for endovascular treatment. Two patients showed occlusion of major vessels and an associated moyamoya phenomenon at the base of the brain. Vessel occlusion and moyamoya associated with AVMs are reviewed and hypotheses as to their development are discussed.

Case Reports

Case 1

A 54-year-old right-handed woman presented approximately 10 years earlier with transient episodes of numbness in the right hand and word-finding difficulty. She had noticed pulsatile tinnitus in the left ear 2 to 3 years earlier. The tinnitus had recently disappeared. Her neurologic examination was completely normal; she did not have a bruit or cutaneous lesions.

Cerebral angiography revealed bilateral frontal arteriovenous malformations (AVMs), an occluded right supraclinoid internal carotid artery, and a "fine reticular" collection of blood vessels in the basal region on the right (Figs. 1A and 1B).

The lesions were considered inoperable by several consulting neurosurgeons. The patient was placed on anticonvulsant therapy to control her transient neurologic events, which were thought to be seizures.

Despite adequate anticonvulsant therapy, the patient continued to suffer seizures as well as increasing headaches. There was no evidence that she had ever bled intracranially. She was referred to our institution for consideration of endovascular treatment.

MR imaging showed the bifrontal AVMs and a network of small vessels penetrating the basal ganglia and thalami bilaterally (Figs. 1C and 1D).

Repeat angiography showed two cortical AVMs involving the right frontal opercular cortex and the frontal pole of the left frontal lobe cortex as in the angiogram from 10 years earlier. Flow through these lesions was slow. Now, both internal carotid arteries showed evidence of complete occlusion at the supraclinoid levels (Figs. 1E–1J). A more extensive, rich, abnormal vascular network was seen arising from several sources, which mainly involved the thalamic and basal ganglia regions of both cerebral hemispheres (i.e., moyamoya phenomenon). Several of these small vessels showed microaneurysm formation (Fig. 1K). A prominent leptomeningeal anastomotic network was noted to supply the cortex of the right hemisphere and to a lesser extent the left hemisphere. The vascular malformations were supplied mainly by external carotid branches, which in turn also supplied healthy cortex. Venous drainage was through superficial cortical veins to the sagittal sinus as well as through the vein of Labbe to the transverse sinuses. Deep venous drainage of the AVMs was not seen.

The approach to these lesions by the endovascular route was not possible because of the occlusive disease in the carotids. The surgical approach had already been rejected on several occasions. Radiotherapy was not possible in this particular case because of the size and extent of the lesion. The patient was continued on medical therapy and will be followed closely to assess the natural history of this disease.

Case 2

A 44-year-old right-handed man presented 10 years earlier with a history of transient sensory ischemic attacks of the left body. These had been occurring for approximately 6 months. He was found to be neurologically intact. A right-sided parietal lobe AVM noted on CT scan was confirmed by angiography. There was no evidence of stenosis or occlusion of the right middle cerebral artery at this time. Surgical intervention was not recommended because of the risk of causing neurologic deficit in a patient with "benign" symptoms. There was no history to suggest the patient had ever bled. He was placed on anticonvulsant therapy. Despite various manipulations of the patient's medical therapy, the transient sensory attacks persisted. Subsequently, frequent and uncontrollable left-sided focal motor seizures became incapacitating for the patient. He was referred to our center for consideration of endovascular treatment.

MR imaging showed an AVM in the right parietal region and basal ganglia moyamoya vessels (Fig. 2A). Repeat angiography showed development of an occluded proximal right middle cerebral artery (Figs. 2B and 2C). An extensive vascular network of perforating lenticulostriate arteries bypassed the occlusion to supply the AVM through the distal right middle cerebral artery and the callosal marginal branch of the right anterior cerebral artery (Fig. 2D). The flow through the lesion was slow. In addition, the left vertebral arteriogram revealed multiple thalamic moyamoya vessels and leptomeningeal collateral vessels supplying the AVM (Figs. 2E and 2F). Venous drainage was through superficial cortical veins to the superior sagittal sinus. No deep venous drainage was identified.

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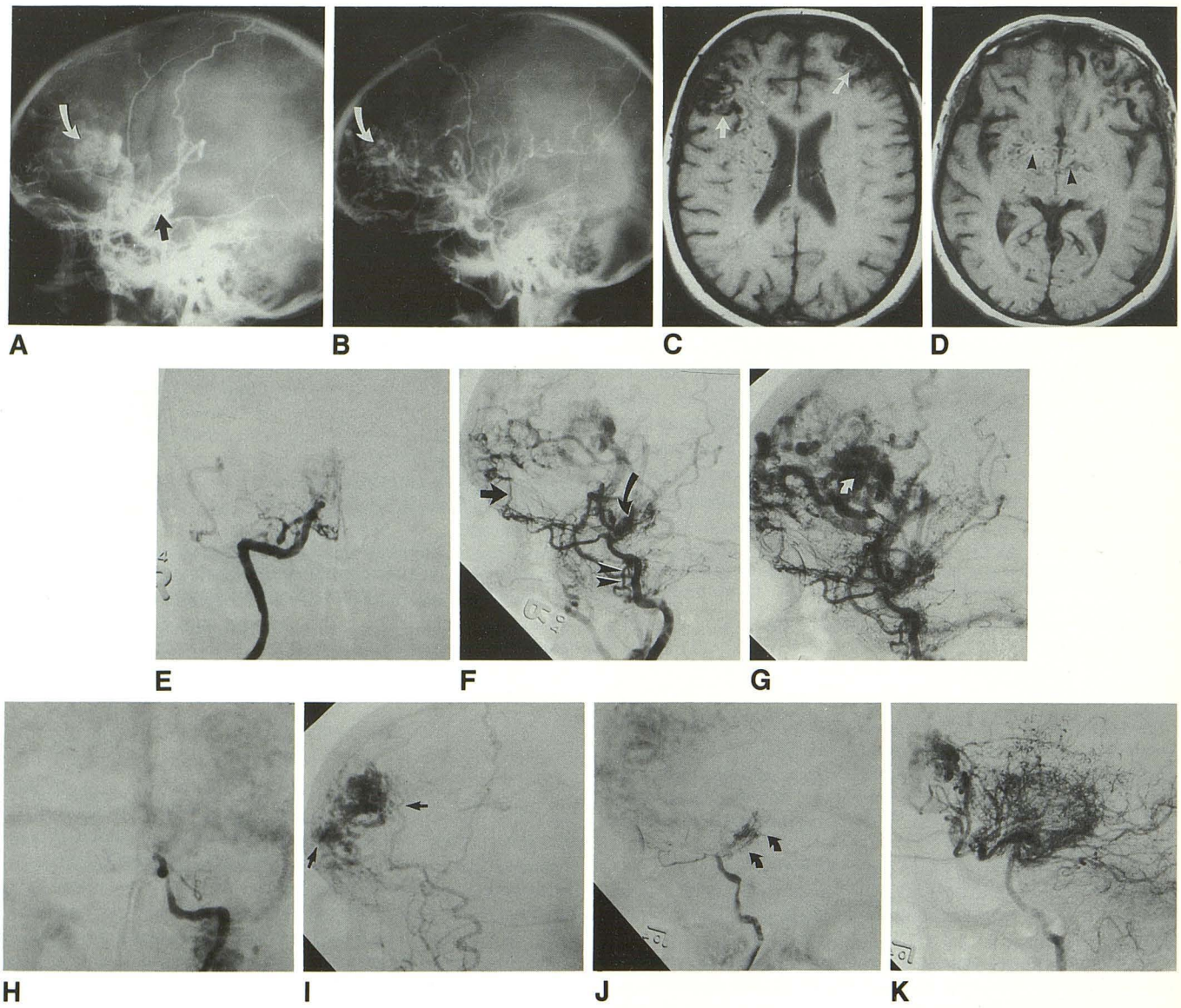

Fig. 1.—54-year-old right-handed woman with history of transient episodes of numbness in right hand and word-finding difficulty.

***A* and *B*, Right (*A*) and left (*B*) common carotid angiograms from 1978. Note bilateral frontal arteriovenous malformations (AVMs) (*curved arrows*), occluded right supraclinoid internal carotid artery, and a fine reticular collection of blood vessels in the basal region on the right (*straight arrow* in *A*).**

***C* and *D*, Axial T1-weighted spin-echo MR images (700/20) show flow void of bifrontal cerebral AVMs (*arrows* in *C*). Small vessels are also demonstrated in the deep basal ganglia regions (*arrowheads* in *D*) and represent the moyamoya vessels.**

***E–G*, Right internal carotid arteriograms from 1988 show occlusion of right internal carotid artery distal to ophthalmic artery. Dilated lenticulostriate arteries (moyamoya vessels) are seen at carotid termination (*curved arrow* in *F*). Collateral vessels from the ophthalmic artery (ethmoidal moyamoya) (*straight arrow* in *F*) and transdural collaterals from inferior-lateral trunk (*arrowheads* in *F*) are also visualized. These form an abnormal vascular network supplying the right frontal AVM nidus (*curved arrow* in *G*).**

***H–J*, Left common carotid arteriograms from 1988 show a left frontal lobe AVM supplied by transosseous/transdural collateral branches of external carotid artery (*arrows* in *I*). Decreased flow is demonstrated in the occluded internal carotid artery, which gives off basal moyamoya vessels (*curved arrows* in *J*).**

***K*, Left vertebral arteriogram shows a network of multiple small collateral channels at base of brain. Microaneurysms are also demonstrated.**

Because of the occlusive disease of the middle cerebral artery and the supply to this AVM by multiple small collateral vessels (i.e., moyamoya), effective endovascular therapy for this lesion was not possible. To separate the vascular malformation from the adjacent feeding anastomotic vessels would be difficult surgically and was considered too risky. Continued medical treatment was considered the most appropriate and safest approach for this patient.

Discussion

Cerebral AVMs are developmental lesions of the cerebral circulation. Although congenital, the network of feeding arteries and draining veins of an AVM is not a static entity [1–3]; morphologic changes may occur during the evolution of these lesions.

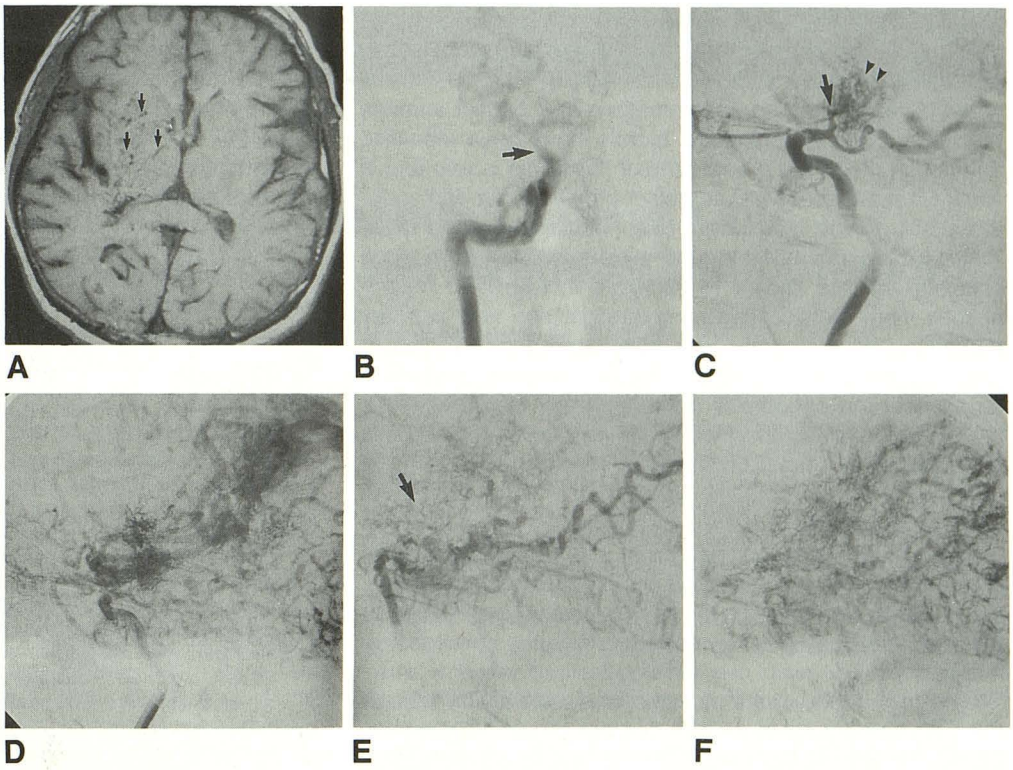

Fig. 2.—44-year-old right-handed man with history of transient sensory ischemic attacks of left side of body.

A, Axial T1-weighted spin-echo MR image (700/20) at level of basal ganglia demonstrates moyamoya collateral vessels (*arrows*).

***B–D*, Right internal carotid arteriograms show occlusion of proximal right middle cerebral artery (*arrows* in *B* and *C*) with multiple associated basal moyamoya vessels (*arrowheads* in *C*). The right parietal AVM is supplied by these basal moyamoya vessels as well as transdural and leptomeningeal collaterals.**

***E* and *F*, Left vertebral arteriograms show multiple basal moyamoya vessels (*arrow* in *E*) and an extensive leptomeningeal collateral vascular pattern.**

A cerebral AVM may be accompanied by a normal congenital variant such as a persistent carotid-vertebral anastomosis [2] or by a variety of dysplastic phenomena affecting feeding arteries or draining veins [1–10]. Dysplastic changes affecting the feeding arteries include aneurysms proximal to the cerebral AVM nidus [1–3, 5–8], arterial stenoses [1, 2, 4], and arterial occlusions [1, 2, 4, 9, 10]. Draining veins may develop venous stenoses, venous ectasias, and venous occlusions [1–3]. Flow-related arterial aneurysms, as well as venous occlusions or stenoses in association with AVMs, have been shown to have an increased risk of hemorrhage [2, 3].

The dysplastic morphology observed in the feeding arteries and draining veins of a cerebral AVM nidus is likely related to high-flow angiography [2–8]. Dysplastic changes may be induced in the feeding arteries and draining veins of experimentally produced arteriovenous fistulae [5, 11, 12]. These dysplastic changes include irregular enlargement and aneurysmal dilatation of the feeding arteries. The draining veins become elongated, tortuous, and dilated with thickened walls [11, 12]. Histology in these experimentally produced fistulae show exaggerated, irregular intimal thickening and destructive changes in the internal elastic membrane and media [11]. The endothelium may desquamate and promote adherence of platelets to the vessel wall [10]. A high-flow state may be induced clinically in a carotid artery by ligating the opposite side. The increased flow in this situation can result in aneurysm development in the carotid artery [3]. Decreasing flow by surgical removal or embolotherapy of a cerebral AVM nidus has resulted in regression of aneurysms associated with the feeding arteries [3, 5, 8]. This implies that some of this dysplasia that is associated with high flow may be reversible. Analysis of aneurysms associated with cerebral AVMs shows a statistical preference for those arteries directly supplying the AVM nidus [7].

Arterial stenosis and arterial occlusion are less common manifestations of high-flow dysplasia than is aneurysm formation [1, 4]. Mawad et al. [4] collected 13 cases of arterial stenosis or occlusion associated with the feeding arteries to a cerebral AVM nidus. They hypothesized that high flow through these vessels leads to intimal proliferation and stenosis. Other similar case reports have also appeared in the literature [1, 9, 10].

We present two cases that demonstrate occlusions or stenoses of the arteries that would ordinarily supply the territory of the cerebral AVM. Arterial flow to the brain and AVM nidus distal to these occlusions was supplied by numerous small collateral vessels. Ectatic and tortuous lenticulostriate arteries originating from the occluded vessels formed an anastomotic network at the basis of the brain. These are termed basal moyamoya vessels. Collateral flow was also supplied by ophthalmic artery branches to the frontal lobes (ethmoidal moyamoya) and through transosseous/transdural anastomoses to the surface of the brain (vault moyamoya) [13–15].

To date, these moyamoya vessels have been considered as collateral channels that preexist and enlarge due to hemodynamic need. The hemodynamic need comes from the ischemic brain and the low-resistance AVM nidus distal to the site of arterial stenosis or occlusion. In other words, this represents angioectasia. Another factor to consider is the relationship of angiogenesis to both cerebral AVM and moyamoya phenomenon [16]. The microvascular system usually remains quiescent without capillary formation for prolonged periods of time. However, this microvascular system appears

capable of initiating new capillary growth (i.e., angiogenesis). This may be in response to various physiological stimuli, such as ovulation, or to pathologic conditions, such as tumor growth, wound healing, inflammation, and certain immune reactions. Several angiogenic factors have been identified that contribute to the proliferation of capillaries in vivo and in vitro. Among these, basic fibroblast growth factor and endothelial cell growth factor have been isolated from the brain. Transforming growth factors have been isolated from blood platelets and are known to stimulate increases in macrophages, fibroblasts, collagen production, and new capillary formation [16]. Cerebral AVMs have been demonstrated to sequester platelets in vivo and this is thought to be due to turbulence and endothelial damage within the AVM nidus [17]. It is possible, therefore, that in part the moyamoya phenomenon in these patients may represent formation of new capillaries (i.e., angiogenesis) in response to the release of these angiogenic factors. The angiogenic stimulus or angiogenic factors may originate from in situ sequestration of platelets and fibrin within the AVM nidus or its feeding arteries. Macrophages attracted to the site of platelet aggregation or the brain itself may also have a role in initiating new capillary formation [16].

Pathologic study of the moyamoya vessels at the base of the brain demonstrates various degrees of luminal stenosis, intimal thickening, discontinuity of the internal elastic lamina, and microaneurysm formation. There may be rupture of the vascular wall, with or without fibrin deposits [18]. In the adult, cerebral hemorrhage is the most common clinical presentation of moyamoya [13, 14]. This includes intracerebral hematoma [19], subarachnoid hemorrhage [13, 14, 20], and intraventricular hemorrhage [14, 21, 22]. The hemorrhage is presumably due to the presence of these small, fragile moyamoya vessels with their associated microaneurysms [21]. It would seem, therefore, that the presence of these moyamoya vessels could put this subgroup of cerebral AVM patients (AVM and moyamoya) at additional risk for cerebral hemorrhage. Alternatively, it was suggested by Mawad et al. [4] that the presence of arterial stenosis reduces the blood flow to the AVM nidus and consequently represents a built-in protective mechanism against cerebral hemorrhage. Only three of their 13 patients presented with cerebral hemorrhage versus nine presenting with seizures. This flow-related arterial stenosis and moyamoya phenomenon was further offered as a possible explanation for the rare occurrence of spontaneous occlusion of cerebral AVMs [4].

In conclusion, we present two patients with cerebral AVMs who have associated stenosis or occlusion of the feeding arteries as well as moyamoya phenomenon. Arterial stenosis is probably induced by the stress of high blood flow on vascular endothelium [4]. A combination of angioectasia and angiogenesis may then lead to the moyamoya phenomenon. To our knowledge, there has been no satisfactory explanation as to why this is such a rare phenomenon, nor why this subset of cerebral AVM patients appears to be particularly vulnerable to flow-induced vasculopathy.

Treatment options are limited for these patients. Surgical therapy may present higher risk in that many transosseous, transdural, and leptomeningeal anastomoses that supply healthy brain parenchyma could be disrupted during craniotomy. Stereotactic radiation, being most effective for smaller lesions (Steiner L, paper presented at annual meeting of International Congress of Neurological Surgery, Sao Paulo, June 1977), was not considered a viable option in our two patients. The vessel occlusions prevent treatment of these patients by an endovascular approach.

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