Recurrent Intracranial Hemorrhage in an Adult with Moyamoya Disease: Case Report, Radiographic Studies and Pathology

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ABSTRACT: Moyamoya disease is an unusual vascular disorder highlighted by progressive bilateral internal carotid artery occlusion and collateralization of intracranial blood flow. Recurrent multifocal cerebral ischemic events and isolated intracerebral hemorrhage are known to occur in this disorder. We report a 52 year old man who over a nine year period had four apparent intracranial hemorrhages. Serial angiograms demonstrated the evolution of moyamoya disease. Pathologic examination confirmed multiple vascular lesions, including two that were clinically silent.

RÉSUMÉ: Hémorragies intracrâniennes récurrentes chez un adulte atteint de la maladie de moyamoya: observation clinique, études radiologiques et anatomo-pathologiques La maladie de moyamoya est une affection vasculaire rare caractérisée par une occlusion progressive bilatérale des carotides internes et une collatéralisation du flot sanguin intracrânien. Des manifestations ischémiques cérébrales multifocales récurrentes et des hémorragies intracérébrales isolées se rencontrent dans cette maladie. Nous rapportons le cas d'un homme âgé de 52 ans qui aurait présenté quatre hémorragies intracrâniennes sur une période de neuf ans. Des angiogrammes sériés ont démontré l'évolution de la maladie de moyamoya. L'examen anatomo-pathologique a confirmé la présence de multiples lésions vasculaires incluant deux lésions cliniquement silencieuses.

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Moyamoya disease is a non-atherosclerotic occlusive disorder of intracranial arteries. We recently reviewed the natural history of an unusual case of adult variety moyamoya disease in which clinicoradiologic correlations were made over a nine year period. A post mortem examination was obtained. The case is remarkable for the number of hemorrhages, duration of the patient's symptomatic phase, and angiographic demonstration of the progression of the disease.

Case Report

The patient, a non-hypertensive, right-handed white male, had been in excellent health until age 43 when he was admitted with a severe headache and lumbar puncture revealed bloody cerebrospinal fluid. Cerebral angiography at that time showed marked narrowing of the supraclinoid segments of both internal carotid arteries. In addition, there was occlusion of most branches of the anterior and middle cerebral arteries bilaterally. Marked collateral circulation via penetrating arterioles was present (Figure 1). CT scan was not available at the time. There were no neurologic deficits at the time of discharge from the hospital.

During the next seven years the patient was hospitalized on two occasions because of acute headache with focal neurologic abnormalities. Left hemiparesis was present on the first of these admissions and a CT scan showed a right posterior frontal hematoma as well as an area of low density in the left posterior parietal region consistent with an earlier infarct (Figure 2). An acute global aphasia and right homonymous hemianopsia were found on the second admission along with minimal old left hemiparesis. CT scan demonstrated a left temporal lobe hematoma with blood in the left sylvian fissure as well as the old left-sided infarct previously detected (Figure 3). Hematologic and radiologic investigations for vasculitides, coagulopathies, and embolic disease were negative. Cerebral arteriography revealed that the anterior and middle cerebral arteries were now totally occluded proximally as were the supraclinoid internal carotid arteries bilaterally. There was also a marked reduction in the collateral circulation seen on the earlier study (Figure 4).

Aphasia improved significantly, but eighteen months later, nine years after his initial presentation, he was admitted following a brief period of unconsciousness. CT scan revealed a right basal ganglionic hemorrhage. Despite showing clinical improvement, he died following a cardiopulmonary arrest twenty days later.

General post mortem examination revealed moderate to severe coronary atherosclerosis. Vascular abnormalities were

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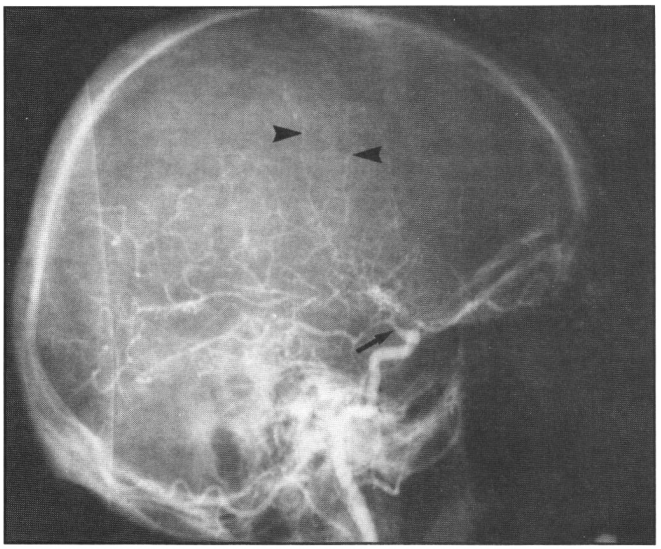

Figure 1 — Left carotid angiogram, lateral view, showing narrowing of the supraclinoid segment of the internal carotid artery (arrow) with a cluster of basal collaterals above. Occlusion of most branches of the anterior and middle cerebral arteries has occurred. Distal vessels appear irregular representing diminished flow (arrowheads).

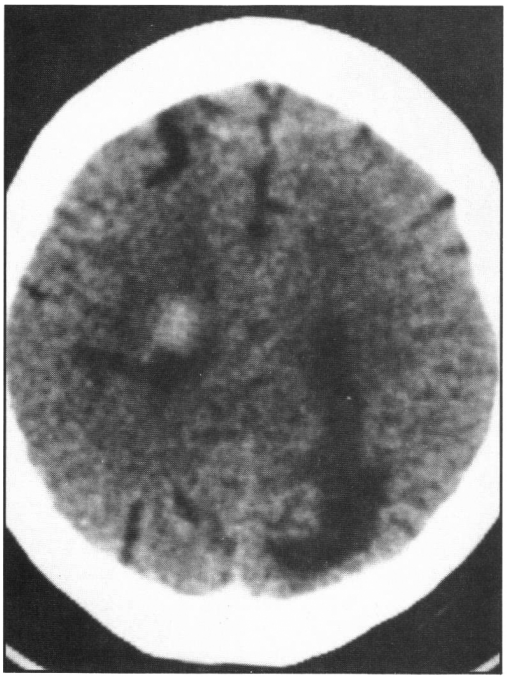

Figure 2 — Computed tomogram without contrast showing a hematoma in the right posterior frontal region as well as an area of low density in the left posterior parietal lobe.

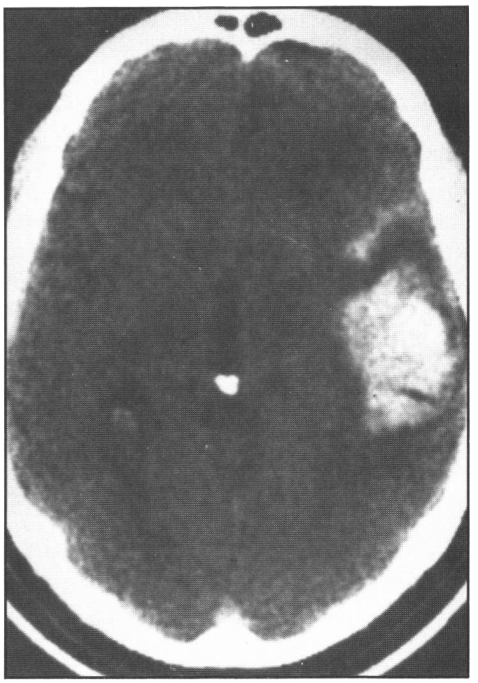

Figure 3 — Computed tomogram without contrast shows large left temporal lobe hematoma, blood in left sylvian fissure, and calcified pineal.

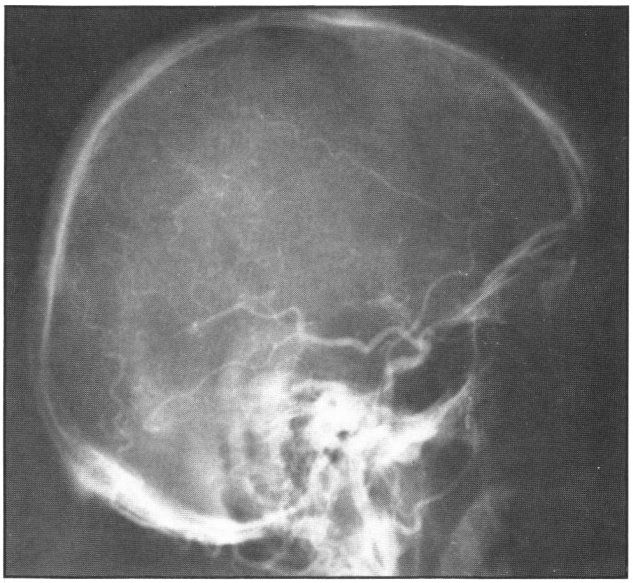

Figure 4 — Left carotid angiogram, seven years later, lateral view, a marked decrease in the degree of collateral circulation is seen. Similar serial changes were seen angiographically on the right side.

not found in the systemic arteries, including the aorta and its major branches. Gross and microscopic examination of the brain revealed the following lesions: a mild, diffuse subarachnoid hemorrhage; a remote bland infarct measuring 5.5 x 3.0 x 1.5 cm involving the left posterior parietal lobe; an area of old hemorrhage measuring 1.1 x 0.8 x 0.9 cm involving the left temporal lobe; an unsuspected subacute hemorrhage measuring 1.3 x 1.1 x 1.0 cm involving the left caudate; and a 6.5 x 4.0 x 2.0 cm recent hemorrhage involving the right basal ganglia, anterior centrum semiovale, internal capsule and anterior-superior thalamus. No herniations were noted. At the trifurcation, the middle and anterior cerebral arteries were markedly thinned. The middle cerebral artery was never more than 3 mm in external diameter and the anterior cerebral artery never more than 2 mm. The available internal carotid arteries were 5 to 7 mm in external diameter and showed mild atherosclerotic

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change. Microscopic examination of the anterior and middle cerebral arteries demonstrated marked thinning or absence of the muscular media, thickening of the elastica with a prominent undulating pattern and thickening of the intima with loose connective tissue (Figure 5). Often the lumen was completely obliterated. Inflammation was absent. Atherosclerosis was minimal and no aneurysms were detected macroscopically or microscopically. No amyloid was detected using Congo red stain. Similar appearing but smaller vessels were occasionally detected in the basal ganglia parenchyma. The posterior circulation, including the posterior cerebral arteries were minimally affected.

Discussion

Moyamoya is a Japanese description of the hazy appearance of smoke drifting in the air. The term applies to the appearance of collateral vessels in this disease which become the major source of blood flow to the territory of the anterior and middle cerebral arteries.[1] Collateral blood flow in this disorder is provided in part by penetrating arteries originating from the proximal intracranial arteries of the circle of Willis.[2] Other sources of collateral blood flow include leptomeningeal artery anastomoses on the surface of the brain as well as transdural connections between the external and internal carotid arteries. These vessels serve as compensation for the progressive bilateral occlusion of the distal internal carotid and proximal anterior and middle cerebral arteries. The telangiectatic vessels in the basal ganglia provide the angiographic pattern for which the disease is named. In children the condition is manifested primarily as repeated ischemic events. Adults, on the other hand, are usually subject to a monophasic intracranial hemorrhage.[1,3-5] Although first described by the Japanese, the disease is known to occur worldwide.

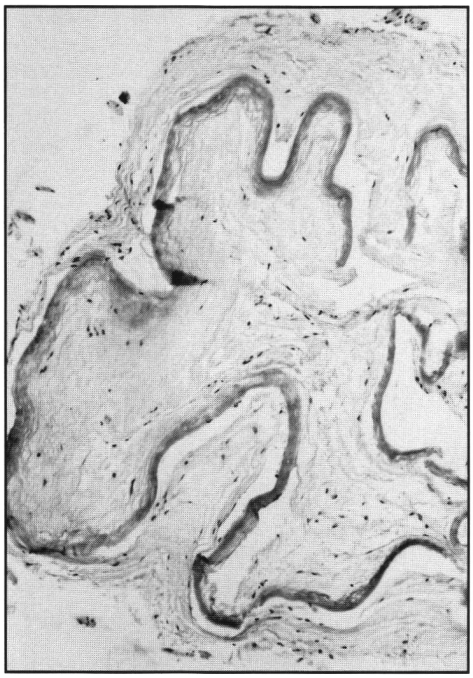

Figure 5 — Hematoxylin and eosin stained section of the left anterior cerebral artery 1 cm above the origin of the anterior communicating artery. Note the complete loss of muscular media, the thickened elastic lamina and the complete occlusion of the lumen by loose connective tissue. There is no inflammation. (Magnification 95x).

Our case demonstrates an unusual natural history of the disorder in that the patient presented with four separate documented intracranial hemorrhages over a nine year period. In addition, necropsy revealed a fifth clinically undetected hemorrhage in the area of the left caudate nucleus. It is probable that bleeding resulted from the rupture of primary penetrating arterioles making up the collateral circulation. The CT scans in our case also demonstrated an area of low density in the left posterior parietal region for which no clinical event could be identified. Pathology confirmed this to have been an ischemic infarct.

At one time intraparenchymal hemorrhage was rarely reported in moyamoya disease.[6] The nature of hemorrhage in this disorder was often misinterpreted in the pre-CT scan era when only the subarachnoid component was detectable by lumbar puncture.[1,5] Characteristically, hemorrhage was regarded as subarachnoid at the time of our patient's first documented bleed. It is now clear that hemorrhages occurring in moyamoya disease are usually intraparenchymal with extension to the subarachnoid space. Unlike the patients of Yamashita et al[7] who reported frequent ventricular extension and fatal bleeds in 17 of 22 histologically verified cases of this disease, our patient survived at least five episodes of intracranial hemorrhage.

Reports on the angiographic features moyamoya disease have demonstrated the occurrence of serial changes.[1,8] The natural progression has been divided into stages, beginning with distal internal carotid artery narrowing at the region of the terminal bifurcation. Following this, the moyamoya appears in the area of the basal ganglia while some branches of the anterior and middle cerebral arteries can still be identified. With time there is obliteration of the larger intracerebral arteries and an increase in the moyamoya. The late stages of the disease are characterized by a loss of the moyamoya as penetrating arterioles occlude due to the spreading disease process.[1,8]

The development of collateral vessels in the area of the basal ganglia is an adaptation found in several types of arterial disease. This angiographic appearance has been described with severe atherosclerosis,[10] tuberculous meningitis,[11] sickle cell disease,[12] following radiation therapy,[13] or associated with neurofibromatosis.[14] Moyamoya disease is, however, a primary disorder of intracranial arteries characterized by bilateral extension of vascular occlusion both proximally and distally from the terminal internal carotid artery. Obliteration of the collateral vessels eventually occurs as well. Progression from early to late stages of moyamoya disease does not occur over a precise time course. Reports of serial angiography in patients with moyamoya disease have in general included younger patients, studied for ischemic symptomatology. Follow-up angiograms demonstrating progressive disease were performed 9 months to 5 years later in reported cases.[1,15]

The adult variety of moyamoya disease is described as frequently being non-progressive both angiographically and clinically.[1,8] This has been attributed to a diminished capacity of the penetrating arterioles to develop the extensive anastamotic channels seen in children.[8] In view of the fact that intracranial hemorrhage caused the initial symptoms in 42% of the adults

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with moyamoya disease reported in a large series,[8] it is possible that the clinical course in these patients excluded the possibility of serial angiography. This would be expected if the mortality rate was high or significant disability resulted from the initial bleed.

Intracerebral hemorrhage with angiographic absence of branches of the anterior and middle cerebral artery circulation is a feature of adult moyamoya disease. However, these patients do not often suffer ischemic symptomatology. Reduction of cerebral flood flow requirements in adults as compared to children has been proposed as a possible explanation.[16] The occurrence of intracerebral hemorrhage may be explained by the findings of histopathologic studies on intracranial arteries from patients with moyamoya disease. These have shown intimal thickening with loose connective tissue, elastic lamina thickening with apparent vessel contraction leading to a peculiar undulating pattern, and the formation of microaneurysms. These dilated arteries and microaneurysms have been implicated as predisposing to arterial rupture.[7] The media of cerebral arteries of patients with moyamoya disease have a characteristic microscopic appearance. This has been described as "moth-eaten change"[16] because of an irregular atrophy of smooth muscle cells and fibrosis. These changes are similar to those in the arteries of hypertensive patients who died of intracerebral hemorrhage.[17] There is no explanation to date for the presence of similar histologic findings in these two distinct diseases. It is suggested that some of the findings follow rather than precede hemorrhage.

Reports on the pathology of moyamoya disease shed light on the frequency of recurrent hemorrhage in this disorder. Two large pathologic series totalling 48 patients note the presence of multiple cerebral infarcts along with a single primary acute or remote intracranial hemorrhage.[7,9] Recurrent intracerebral hemorrhage may be a feature of numerous conditions. Hypertensive cerebrovascular disease is the most common among these. Vascular malformations, vasculitis, metastatic disease or bleeding diathesis are also etiologic possibilities. When intracerebral hemorrhage and infarction occur in the same patient, the differential diagnosis also includes embolic disease, vasculitides, clotting disorders or amyloid angiopathy. In the absence of associated laboratory abnormalities, systemic signs, or characteristic angiographic features, we did not consider any of the vasculitides responsible for the patient's symptoms. Normal echocardiogram, unremarkable angiography of the aortic arch and its proximal branches, as well as repeatedly negative blood cultures, excluded recurrent emboli in our patient. Coagulopathies were not considered because of the normal laboratory tests pertinent to these conditions.

Amyloid angiopathy shares many features with moyamoya disease. In both conditions large and small intracranial arteries are affected, resulting in both intracerebral hemorrhage and infarction. Unfortunately, there are no readily available tests to differentiate these two conditions. However, amyloid angiopathy tends to affect an older population than moyamoya disease. The patients with amyloid angiopathy often also have features of dementia. Cerebral infarctions due to amyloid angiopathy tend to be multiple, and small in size. Intracerebral hemorrhages in this condition are multifocal and usually petechial.[18] However, large intracerebral hemorrhage can occur in amyloid angiopathy as well as in moyamoya disease. Intracerebral hemorrhage associated with amyloid angiopathy is generally located more superficially in white matter adjacent to the cerebral cortex, particularly in the occipital and temporoparietal regions.[18,1-9] The intracerebral hemorrhage in moyamoya disease is typically found in deeper subcortical areas, often rupturing into the lateral ventricles.[7]

The diagnosis of moyamoya disease in our patient could only have been made by performing bilateral cerebral angiography. CT scanning has supplemented angiography at many institutions but elsewhere is often utilized as a substitution. This may result in the prevalence of this disease being understated.

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