

arterial and aortic beds, do not appear related to accumulation of apoproteins or their respective lipoproteins.

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Fibromuscular Dysplasia and Multiple Dissecting Aneurysms of Intracranial Arteries

A Further Cause of Moyamoya Syndrome

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SUMMARY A 16-year-old boy, who had sudden left-sided hemiplegia, died two weeks following onset of symptoms. A right carotid angiogram showed stenosis at the termination of the internal carotid artery. The middle cerebral artery had a beaded appearance and some of its branches were occluded. A basal "moyamoya" syndrome

and transdural anastomoses were present. At autopsy, multiple intracranial dissecting aneurysms were found. Arteries of the body displayed fibromuscular dysplasia (FMD). The relevance of dysplastic changes of intracranial arteries and the relationship to moyamoya syndrome are discussed.

MANY REPORTS have been published in recent years on fibromuscular dysplasia (FMD) and moyamoya syndrome and they have been reviewed in the *Journal de Neuro-radiologie*, volume 1, numbers 1 and 2, 1974. We present a case which shows features of both these conditions and, in addition, dissecting aneurysms of the intracranial arteries.

Case Report

RM, a 16-year-old boy, had had repeated attacks of middle ear infection and frontal sinusitis in recent years. The family history was unremarkable. On March 10, 1974, after throwing a snowball he suddenly had a severe headache and lost consciousness. After admission to the hospital he regained consciousness but was unable to move the left side of his body and he still had a headache. On physical examination he was alert and correctly orientated but a little euphoric. He laid on his left side and had no neck stiffness. He had a left hemiparesis affecting more severely the left

arm and hemianesthesia of the left side. The left plantar response was extensor and the right was flexor. He had slight miosis and ptosis on the right side, no visual disturbances, and normal fundi. No bruit was heard in the neck. The blood pressure was 110/70 mm Hg, the blood cell count was normal, and the ESR was 6 mm in the first hour. The cerebrospinal fluid was clear and the pressure was 250 mm H₂O. The cell count was 1 cell per cubic millimeter, and Pandy's test was negative. The EEG showed a marked delta focus in the right frontoparietal region. X-rays of the skull were normal. On March 19, 1974, the right common carotid artery was punctured during general anesthesia. The cervical part of the internal carotid artery showed regular corrugation (stationary waves). Stenosis was present in the supraclinoidal portion of this artery. The terminal part of the internal carotid artery and its main intracranial branches showed multiple, repeated stenoses (beaded appearance) and some branches were occluded. The frontopolar artery was extremely thin.

The lenticulostriate arteries and the anterior choroidal artery were very prominent. A flush was present in the striate and the contour of the head of the caudate was out-

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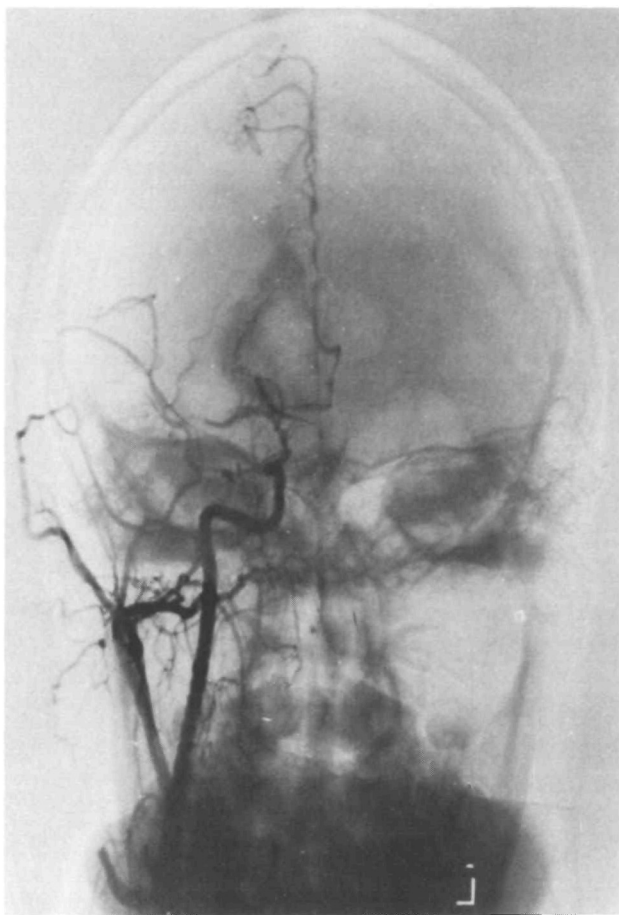


FIGURE 1A. *Right carotid angiogram: The cervical part of the internal carotid shows regular corrugation (stationary waves). The termination of the internal carotid and the proximal part of the middle and anterior cerebral artery have a beaded appearance. Branches of the middle cerebral artery are occluded. A moyamoya-like flush of the basal ganglia is present. The lenticulostriate arteries are prominent.*

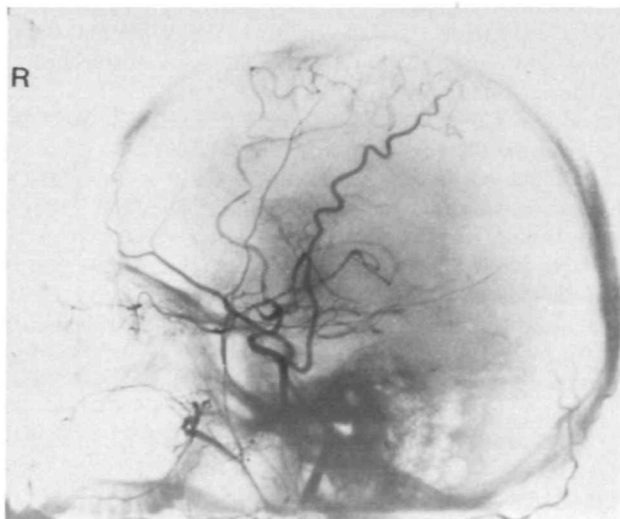


FIGURE 1B. *Right carotid angiogram: Stenosis of the supraclinoid part of the internal carotid (C2) and occlusion of a main branch of the middle cerebral artery. A basal moyamoya syndrome and early filling of the internal cerebral veins are present.*

lined very well. There was early filling of the internal cerebral veins (figs. 1A and B).

Transdural anastomoses were present in two regions. The parietal branch of the superficial temporal artery seemed to communicate with the peripheral part of the callosomarginal artery, which filled in a retrograde fashion. Another anastomosis was present between the middle meningeal and fronto-opercular arteries (fig. 1C).

The isotope brain scan did not show any significant uptake. Immunoelectrophoresis and direct Coombs test were normal. The Wassermann reaction of the blood serum was negative. The patient was treated with rheomacrodex and dexamethasone but his condition did not change. He died suddenly two weeks after the onset of hemiparesis.

The postmortem examination was performed 30 hours following death. The organs in the trunk were normal. When the internal carotid arteries in the neck were opened, there was slight undulation of the intimal surface. The renal arteries were not stenosed. The brain weighed 1,470 gm. The right cerebral hemisphere was soft in consistency and was much larger than the left. The right cerebral convolutions were flattened. The arteries at the base of the brain were thinner than normal. The right anterior, middle and



FIGURE 1C. *Right carotid angiogram: Transdural anastomoses are present. The middle cerebral artery shows multiple stenoses. The lenticulostriate arteries are very prominent.*

posterior cerebral arteries had the appearance of a string of beads, and seemed to be occluded by a thrombus. The wall of the supraclinoidal part of the internal carotid arteries was thickened and had a cartilaginous consistency, more marked on the right side which was thought to be occluded. No berry aneurysm of the intracranial arteries was found. The right uncus herniated through the tentorium cerebelli. The brain was cut coronally. There were swelling and softening of the right cerebral hemisphere: the frontal, temporal and parietal regions were affected. The midline structures were displaced 2 cm to the left. The head of the caudate nucleus, parts of the internal capsule, the medial part of the lentiform body, and the lateral part of the thalamus showed an older infarct and shrinkage, and the vessels in these regions were prominent.

The tissue was fixed in neutral 10% formalin saline and embedded in paraffin. The brain, myocardium, liver, spleen and kidneys were examined and particular attention was given to the following arteries: aorta, renal, femoral, carotid, middle meningeal, basilar, vertebral and anterior, middle and posterior cerebral. Sections were stained by hematoxylin-eosin, cresyl violet, Cluver Barrera, Weigert's elastic, Azan and Berlin Blue.

Some proliferation of vasa vasorum in the aorta was noted. Longitudinal sections of the right internal carotid artery in the neck showed corrugation of the wall (figs. 2A-D). In these regions either fibroelastic intimal cushions or attenuation of the medial coat were present. There were multiple interruptions and calcification in the internal elastic lamina. There was marked loss in elastic fibers of the media. Increase of metachromatic ground substance and fibro-

blasts were found between smooth muscle cells. The ground substance contained many vacuoles. Some muscle cells showed large, dark, distorted nuclei. Similar changes occurred in the renal and femoral arteries. In addition, the right carotid siphon showed a stenosis which was due to muscular hyperplasia of the medial coat (fig. 3A). In the left carotid siphon large intimal cushions were found (fig. 3B). A dissecting aneurysm was present in the terminal part of the right internal carotid artery (fig. 4). Serial sections of this part of the artery showed multiple folds of internal elastic lamina which were separated from the medial coat; endothelial cells lined both aspects of the elastic lamina, but no rupture was found in the intima in the numerous sections examined from this region.

Recent dissections were present in branches of the right anterior, middle and posterior cerebral arteries, and the original lumen was compressed (fig. 5A). In addition, main branches of the right anterior and middle cerebral arteries presented older dissections which showed organization and endothelialization of the false lumen (fig. 5B). Dissection was discontinuous and resulted in repeated attenuations of the lumen in longitudinal sections (fig. 6). Proliferation of mesenchymal cells and abundant metachromatic ground substance occurred adjacent to the external surface of the internal elastic lamina. Cellular bridges permeated the blood in the dissecting aneurysm and sometimes these cells formed sinusoidal channels (fig. 6). A rupture was found in the internal elastica of a main branch of the middle cerebral artery and endothelial cells had proliferated and covered the edges of the ruptured elastica (fig. 7A). Two lumina were present in some of the small perforating basal arteries (fig. 7B). A

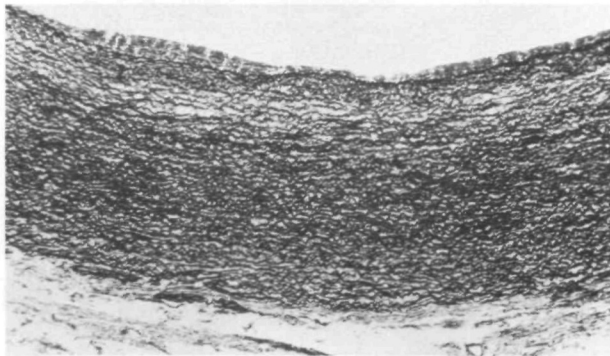


FIGURE 2A. Normal internal carotid artery. Weigert's elastic, $\times 90$.

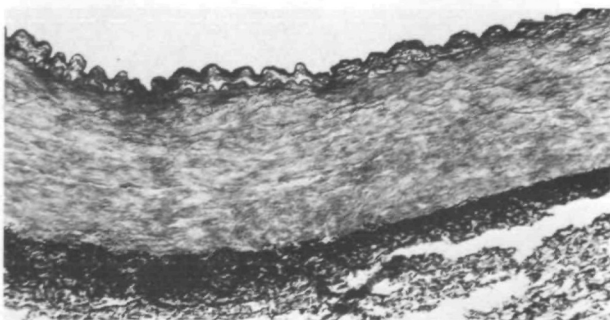


FIGURE 2B. The media of the internal carotid artery of this patient shows loss of elastic fibers. Weigert's elastic, $\times 54$.

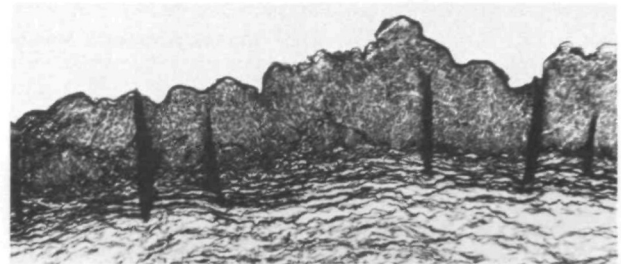


FIGURE 2C. Longitudinal section of the internal carotid artery shows corrugation of the internal surface. Weigert's elastic, $\times 54$.

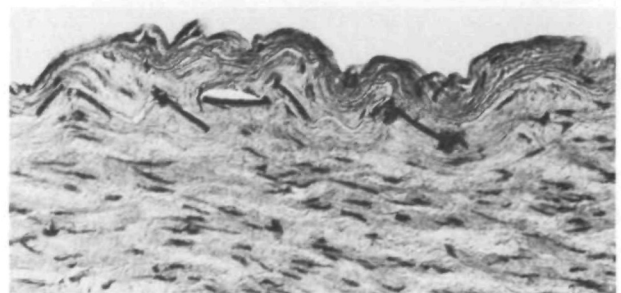


FIGURE 2D. Internal carotid artery shows calcification of fragments of the internal elastic lamina. Hematoxylin and eosin, $\times 390$.

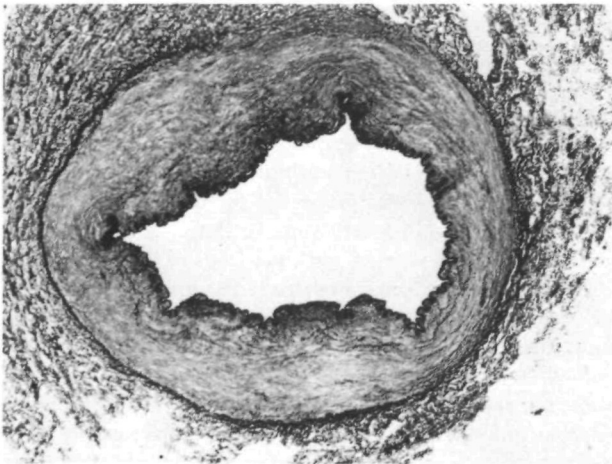


FIGURE 3A. Right carotid siphon (C2) shows stenosis of the lumen due to hyperplasia of the media. Weigert's elastic, $\times 33$.

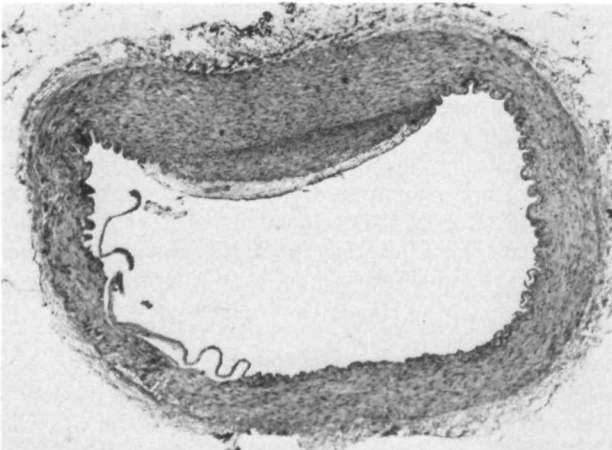


FIGURE 3B. Left carotid siphon (C2) shows a fibroelastic intimal cushion. Hematoxylin and eosin, $\times 33$.

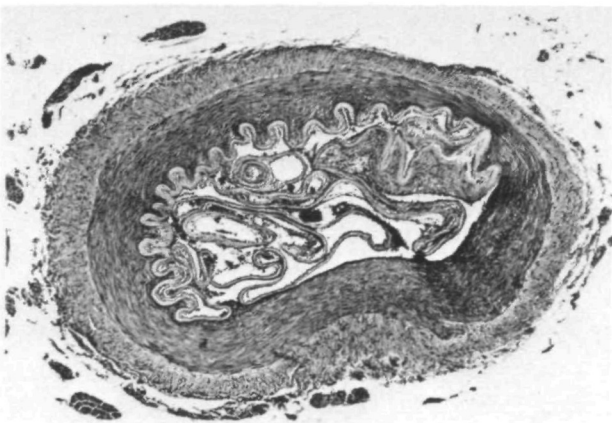


FIGURE 4. The supraclinoid part of the right internal carotid (C1) artery contains multiple folds of internal elastic lamina; endothelial cells line both sides of the folds of the elastic lamina. An intimal cushion is present on the dissected internal elastic lamina. The media is attenuated (right upper corner) and the adventitia is thickened. Hematoxylin and eosin, $\times 54$.

dissecting aneurysm was present in an intracerebral artery in the right lentiform nucleus. The following dysplastic changes were noted throughout all intracranial arteries (figs. 3B, 7A, and 7C): large fibroelastic intimal cushions sometimes containing smooth muscle cells, thickening and splitting of the internal elastic lamina, irregular arrangement of muscle fibers, attenuation and defects of the medial coat, fibroplasia between the internal elastic lamina and the media, and fibrous thickening of the adventitia. Both middle meningeal arteries showed fibroelastic thickening of the intima. Extensive infarction had occurred in the corpus striatum, globus pallidus, lateral thalamus and white matter on the right side.

The infarcted regions showed proliferation of the capillaries and were infiltrated by fat granule cells. Foci of disseminated infarcts of similar appearance occurred in the hypothalamus and the cortex of the frontal, temporal and parietal regions of the right hemisphere. Extensive recent in-

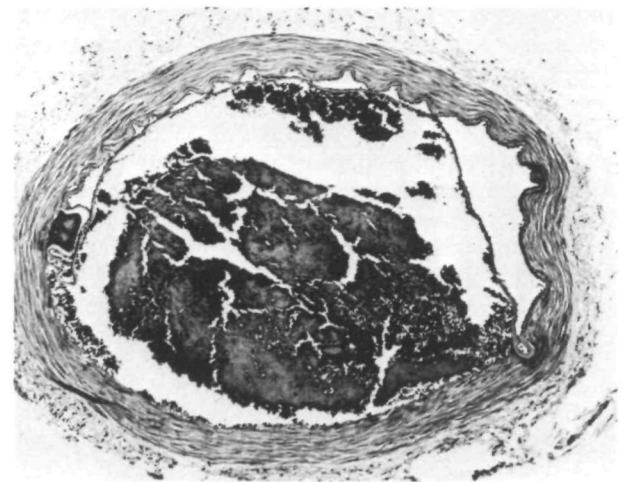


FIGURE 5A. A recent dissecting aneurysm is present in the right posterior cerebral artery. The original lumen is compressed. Hematoxylin and eosin, $\times 66$.

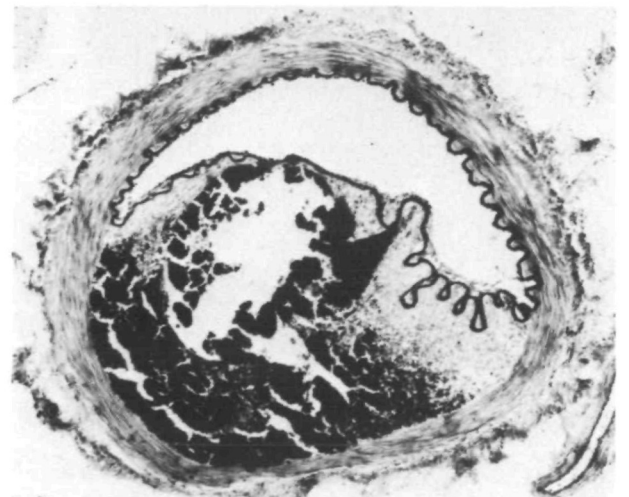


FIGURE 5B. Early organization of a dissecting aneurysm in the pericallosal artery, of which the original lumen is stenosed. Proliferation of mesenchymal cells is seen outside the internal elastic lamina. Cluver-Barrera, $\times 60$.

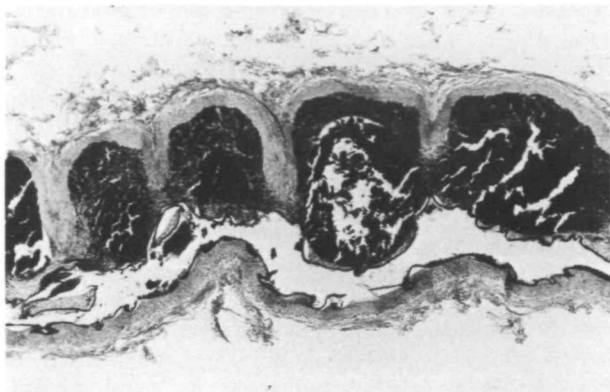


FIGURE 6. The right middle cerebral artery presents a dissecting aneurysm which periodically varies in its extension. Sinusoidal channels are present in the dissected area. Weigert's elastic, $\times 42$.

farcts and severe edema also occurred in the right hemisphere. An increase in the number of vascular channels was particularly marked in the basal ganglia on the right side. Many of the vessels showed cuffing by lymphocytes.

Significant changes were not found in the myocardium, lungs, spleen and kidney. The liver showed some fatty infiltration.

Discussion

The main morphological findings were dissecting aneurysms limited to the intracranial arteries and arterial dysplasia¹ which was generalized. The main arteries of the right cerebral hemisphere were occluded by recent dissecting aneurysms and the resulting massive infarction accounted for the sudden death of the patient. Most occlusions were not present at arteriography one week earlier. Other dissecting aneurysms at different stages of organization were present in branches of the middle and anterior cerebral arteries. It is assumed that some blood flow was present in the false lumen of the dissected arteries since the blood was not clotted; in addition, there was no breakdown of hemoglobin, and some arteries had two patent lumina. Dissection was not distributed equally over the arterial wall. The internal elastic lamina was still fixed to the medial coat in many



FIGURE 7A. The right middle cerebral artery exhibits a large intimal cushion which shows splitting of the intima (to the left). The internal elastic lamina is ruptured (arrow). Weigert's elastic, $\times 27$.



FIGURE 7B. A small perforating basal artery has two lumina. Hematoxylin and eosin, $\times 90$.

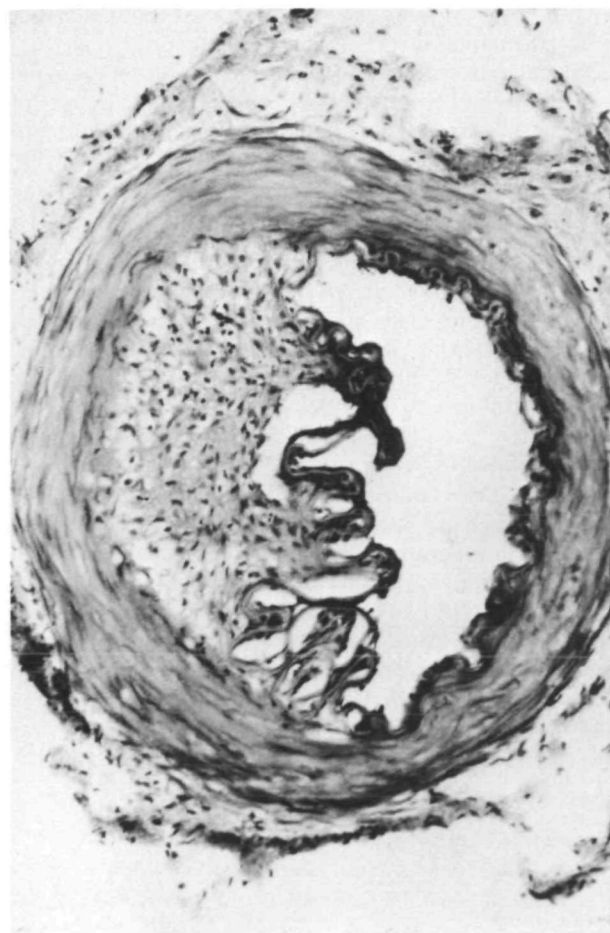


FIGURE 7C. Fibroplasia between the internal elastica and the media is seen in a small artery of the island of Reil. Cresyl violet, $\times 90$.

places, which is shown in figure 6. The dissection resulted in multiple stenoses of the lumen and showed the beaded radiological and macroscopic appearance.

Dissecting aneurysms of the intracranial arteries are rare but are well documented in the literature as a cause of sudden hemiplegia in young subjects,² with arteriography demonstrating occlusion or stenosis of the intracranial arteries in these cases. As in the present case, dissection occurs always between the internal elastic lamina and the media. Discontinuous dissection and early organization so far have not been reported.

The changes in large extracranial arteries are compatible with fibromuscular dysplasia³ and are most pronounced throughout the internal carotid artery. Dysplastic changes also were found in the intracranial arteries of the carotid and vertebrobasilar systems. But what do the dysplastic changes mean? Hassler⁴ described them as physiological changes in newborn and healthy young individuals, but other authors^{5,6} regard them as pathological and related to arteriosclerosis. The following arguments favor the view that the changes in intracranial arteries are part of a generalized arterial disorder.

- (1) The intracranial dissecting aneurysms showed rupture of the intima adjacent to an intimal cushion where the media was defective.⁷
- (2) Also, in cases of intracranial dissecting aneurysms the arteries of the body show foci of medial necrosis and of fragmentation of the elastica.⁸
- (3) In patients with berry aneurysms of the intracranial arteries the fibroelastic intimal cushions and defects of the media are larger and more frequent than normal.⁹
- (4) Intracranial berry aneurysms occur frequently in patients with fibromuscular dysplasia of the renal and carotid arteries.^{10,11}

We assume that berry aneurysms and dissecting aneurysms of intracranial arteries are different manifestations of the same underlying disorder. However, clear-cut criteria are lacking which would separate relevant dysplastic changes of intracranial arteries from incidental or even physiological findings. The relation of medial degeneration¹² and fibromuscular dysplasia also has not been elucidated.

There are three reports on *intracranial* fibromuscular dysplasia and they are based on the beaded appearance of the arteries in the angiograms in analogy to the observations in the renal and internal carotid arteries;¹³⁻¹⁵ they were not confirmed by autopsy. In another case there was histological "evidence" in intracranial arteries, but the authors emphasized that the changes were "infraradiological" and the angiogram appeared to be normal.¹¹ In our case the beaded appearance of the right middle cerebral artery was due to the peculiar form of a dissecting aneurysm. In addition

to the dissecting aneurysm, fibroplasia between the internal elastic lamina and the media was the only finding which was sufficient to account for stenosis of an intracranial artery (fig. 7C), but this finding was more likely due to organization of a dissecting aneurysm rather than to primary fibroplasia. The beaded angiographical appearance of the right internal carotid artery in the neck displayed stationary waves.¹⁶ At autopsy this artery showed definite pathological changes (fig. 2). These findings favor the suggestion of Bergquist et al.¹⁷ that stationary waves may be the precursor of fibromuscular dysplasia. The radiological and morphological findings in the right hemisphere are compatible with the changes found in the moyamoya syndrome except that in this case the changes were unilateral. A radiological appearance very similar to that seen in the moyamoya syndrome may occur in occlusion of the middle cerebral artery in children, due to hypertrophy of the striate branches.¹⁸ This might be the more likely explanation of the present case.

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