The so-called 'Moyamoya disease'

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SYNOPSIS In addition to occlusion of the distal part and branches of the internal carotid artery in two adult patients, angiography revealed a fine vascular network on the convex surface and at the base of the brain, identical with the angiographic picture of 'Moyamoya disease'. On the basis of the pathological examinations, the occlusion of the cerebral blood vessels was caused by arteriosclerosis in both cases. The causes and conditions of development of the 'Moyamoya' picture are discussed. In the authors' opinion, this is not an independent disease: under the conditions described the characteristic pattern may develop in any type of vascular occlusion as a special form of accessory circulation in the cerebral areas the blood supply of which has been impaired.

In 1956 Kudo observed in a boy's angiogram an irregular cerebrovascular network which did not conform to the normal anatomical configuration of the cerebral blood vessels (Kudo, 1968). As a result of further clinical observation he arrived at the conclusion that the unusual vascular network corresponded with collateral vessels and might have resulted from an insufficiency of the circle of Willis. In the 1960s, similar cases were reported by several Japanese authors. By 1964, 21 cases had been published in the Japanese literature. In their first report Takeuchi (1961) and Nomura and Suzuki (1962) described this condition as a special type of occlusion of the internal carotid artery. Fukuyama and his co-workers (1965) and Sano (1965) spoke of telangiectasia. Nishio (1964) and Nishimoto *et al.* (1965, 1966) regarded it as a vascular malformation. They considered it an entity peculiar to Japan. In 1968 Nishimoto and Takeuchi collected 96, and Kudo 12 cases; in 1969 Suzuki and Takaku reported 20 cases of 'cerebrovascular Moyamoya disease'. The first cases outside Japan were published by Leeds and Abbot (1965). Their two patients—a 12 year old boy and a 9 year old girl—were, however, of Japanese descent. Cases of white children with Moyamoya disease were reported by Simon *et al.* (1968), Busch (1969), and by Prenskey and Davis (1970). Urbánek *et al.* (1970) referred to their case as 'Nishimoto-Takeuchi-Kudo disease'.

In occlusive cerebrovascular disease similar angiographic vascular patterns, regarded by them as collateral channels, had previously been reported by several authors (Krayenbühl and Yasargil, 1965; Weidner *et al.* 1965; Taveras, 1969; Jones and Wetzell, 1970; Terracciano *et al.*, 1970; de Gutiérrez-Mahoney and Schechter, 1971). In connection with their cases of non-Japanese children, Hilal *et al.* (1971) assume that the angiographic alteration in question is not a process with a special aetiology but the result of occlusion of the circle of Willis from various causes. Their findings were, however, not checked by necropsy.

Two of our cases that came to necropsy seem to lend themselves to a study of the causes of 'Moyamoya disease'.

CASE 1

I.K., a 43 year old male, was first admitted to this department on 17 March 1962. The family history was non-contributory. When he was 27 years of age, the right upper extremity suddenly became paralysed, the condition disappearing after a short time. At the age of 39 years, paralysis of the right upper extremity reappeared, but this time it also involved the lower extremity, and his speech became difficult. His symptoms disappeared within a few months. Four years later, three months after a newer sudden onset of palsy of the right extremities and speech disorder, he was admitted to this department.

FIG. 1. Case 1. I.K., 46 year old male. Left carotid angiogram. The contrast medium has reached the branches of both anterior cerebral arteries. The lateral view shows a tapering pericallosal artery occluded distal to the coronal suture. Only the frontal branches of the middle cerebral artery are filled. In the area of the perforating arteries there is an unusual net-like vascular pattern. A similar vascular picture, occasionally resembling a shaving-brush, may also be seen adjacent to the frontal superficial vessels.

Physical examination of the internal organs disclosed no pathological signs. Blood pressure was 155/90 mmHg. Neurological examination showed anisocoria (left pupil wider than right), right facial paresis of central type, muscle tone in the right upper extremity somewhat exaggerated, especially in the flexors. There was no paresis in the extremities. The abdominal reflexes were sluggish. Mild dysphasia of motor type was present. Consciousness was clear.

There was a little defect in recent as well as in remote memory. He was otherwise coordinated intellectually. The cerebrospinal fluid obtained by the lumbar route was normal in every respect. An electroencephalogram (EEG) contained slow waves of frontotemporal distribution on the left side. Radiographs of the skull showed no abnormality. Lumbar pneumoencephalography demonstrated that the ventricular system was greatly dilated but sym-

metrical subarachnoid filling with air was diffuse and dense.

He was admitted to our department for a second time three years later on 16 April 1965. He had fallen ill six months earlier when pronounced psychomotor restlessness of some hours' duration appeared. Then he gradually became inattentive.

No abnormality of the internal organs was detected other than emphysema. Blood pressure was 135/100 mmHg. There was a right facial palsy of

central origin, exaggeration of tone of Wernicke-Mann type in the muscles of the right extremities, hemiparesis of moderate degree especially in the right upper extremity, and spastic signs on the right. Mild dysphasia of motor type was present. A sucking reflex and bilateral grasp reflexes were found. The patient was alert, partially disorientated, with reduced psychomotility. Cerebrospinal fluid obtained by lumbar puncture was normal. An EEG showed a frontal slow wave focus on the right.

FIG. 2. Case 1. The basal cerebral vessels. The difference in thickness between the basilar and internal carotid arteries is striking.

(a)

(b)

FIG. 3. Case 1. Hypervascularization of the surface of the brain: (a) left, (b) right frontocentral region.

CAROTID ANGIOGRAPHY The thin right internal carotid artery was occluded proximal to the origin of the ophthalmic artery. The internal carotid artery was unusually thin on the left side, too; the vessel wall of the siphon appeared uneven and irregularly constricted. The branches of both anterior cerebral arteries were filled and a vascular pattern was present similar to a shaving brush and connected with the superficial vessels scattered in the frontal region. Unusual, net-like vascularization in the territory of the perforating arteries was seen. Only the frontal branches of the middle cerebral artery were outlined (Fig. 1).

His general state and consciousness deteriorated gradually and he died on 3 May 1965.

NECROPSY Bilateral confluent bronchopneumonia was found. The heart, with scars in its musculature, weighed 310 g. The aortic wall was moderately atheromatous with small thrombotic deposits in its abdominal portion. Both carotid arteries were sclerotic. In the left internal carotid artery there was an old organized thrombus which had spread as far as the bifurcation. The wall of the right internal carotid artery was rigid, its lumen less than 2 mm, and the left middle cerebral artery was similarly filiform. The posterior branches of both middle cerebral arteries were unevenly thick and their lumina obstructed at several points. The left posterior communicating artery was a vascular bundle with no lumen; the right was also extremely thin. The basilar artery, forming a direct continuation of the left vertebral artery, was thick and had an atheromatous plaque at its origin on the left. The right vertebral artery was hypoplastic. Otherwise, the lumina of the posterior cerebral, basilar, and vertebral arteries were patent, as were those of the last mentioned arteries in the cervical region (Fig. 2). The entire brain, which weighed 1,200 g, was atrophic. The atrophy was more accentuated in the frontal regions. The leptomeninges were thick and milky. On the convex surface, territories highly vascularized by tiny vessels could be seen on both sides, the vascularization being more accentuated on the right (Fig. 3). The lateral ventricles were greatly dilated, otherwise no pathological changes were seen on the slices cut in a frontal plane; the slices of the brainstem showed no abnormality. Histological examination disclosed a pseudolaminar cortical softening in the hemisphere sections. The carotid arteries were markedly sclerotic and the intracranial arteries showed a similar change. There were no signs of thromboangiitis or angiitis more distally.

CASE 2

J.K., a 41 year old male, was admitted to our

service on 16 February 1968. He had been working in a uranium mine for 12 years. He drinks half a litre of wine daily and smokes 20 cigarettes a day. Family and personal history were non-contributory. For the last six months he had had spells of malaise with dizziness, during which the contours of objects became blurred and the right extremities numb and weak. Physical examination detected no pathological alteration in the internal organs. Blood pressure was 140/90 mmHg. He showed no abnormal neurological signs on admission. Consciousness was clear and personal and temporal orientation unimpaired. The lumbar and cisternal CSF was normal in every respect. An EEG showed a slight excess of slow activity in the frontocentral and centroparietal areas. Cisternal pneumoencephalography revealed abundant subarachnoid filling and bilateral diffuse cortical atrophy with frontal accentuation.

LEFT CAROTID ANGIOGRAPHY The internal carotid artery was thinner than usual and its lumen at the distal part of the siphon below the origin of the ophthalmic artery was narrowed to one-fourth of its original size. There was a circumscribed stenosis in the proximal portion of the posterior cerebral artery which originated from the internal carotid artery. The outlines of the anterior cerebral artery were faint and occasionally broken. The main trunk of the middle cerebral artery was narrower, with the exception of one thick frontal branch. The vessels of the Sylvian group were filled only at their origins, while at their endings a thick vascular network could be seen, consisting of tiny vessels, which occasionally gave a pattern like a shaving-brush. A similar network was seen next to the branches of the posterior cerebral arteries, and another in the territory of the perforating arteries. The sharply delineated filling defect representing the parietal region was striking (Fig. 4).

During his hospitalization several fits lasting 30 minutes to one hour were observed, associated with paresis of the right extremities and speech disturbances. Such a fit also appeared after pneumoencephalography and in response to the least effort made by the patient. On 5 April 1969 exploratory craniotomy was performed in the left parietal region, revealing atrophic gyri, wide sulci, and unusually compact cerebral white matter corresponding to the avascular region seen in the angiograms. In the operative field greyish-white seemingly obliterated arteries were found. After the operation hemiplegia on the right and total aphasia developed. A carotid angiography performed then showed that the left internal carotid artery was occluded proximal to the origin of the ophthalmic artery. The patient died on 10 April 1968.

FIG. 4. Case 2. J.K., 41 year old male. Left carotid angiogram. In continuation of the superficial branches of the middle cerebral artery occluded at different levels and continuous with the branches of the posterior cerebral arteries and at the base of the brain a fine, net-like pattern of unusual vascularization resembling a shaving-brush may be seen.

FIG. 5. Case 2. Left frontal side of the base of the brain.

Necropsy revealed incipient pneumonia. There were sclerotic plaques in the thoracic and abdominal segments of the aorta. Both internal carotid arteries were thinner than usual; the left was occluded in the cervical region. The left cerebral hemisphere as a whole was swollen, brittle, soft to the touch, and showed signs of herniation. The cerebral surface was

hyperaemic, especially on the left side. Some territories were hypervascularized, most markedly at the poles (Fig. 5). Thrombosis extended from the left internal carotid artery to the middle cerebral artery. The left anterior cerebral artery was thin. The posterior cerebral artery took its origin from the internal carotid artery and was connected only by a

FIG. 6. Case 2. Left frontal part of the cortex stained with Gallyas's silver method to visualize the vessels and connective tissue. At top, surface of the brain. $\times 80$.

thin branch with the long basilar artery reaching to the lower end of the medulla. On the right side, the anterior and middle cerebral arteries were unusually thick. The posterior cerebral artery was connected with the internal carotid artery only by a thin posterior communicating artery. Figure 6 shows the vascular connective tissue picture of a 150 μm section of the left frontal lobe with a distinctly vascularized surface, stained with the silver method of Gallyas (1969). Otherwise, histological examination revealed minute old foci within a widespread fresh softening of the left hemisphere. The cerebral vessels were moderately arteriosclerotic. No signs of obliterating thromboangiitis were seen at histological examination of the heart, kidney, lung, liver, spleen, or peripheral vessels.

DISCUSSION

The occlusion of the distal portion of the internal carotid artery and the vascular pattern of unusually fine, thin vessels on the convex and basal surfaces of the cerebral hemispheres in the

angiograms of our patients do not differ from the 'Moyamoya' picture as described in the Japanese literature. The question arises whether this is an independent disease, as assumed by the Japanese authors, or simply an angiographic phenomenon accompanying vascular occlusion of various origins.

Nishimoto and Takeuchi (1968) knew only of three Japanese cases verified by necropsy. On the cerebral vessels of two young girls, one of whom died of intracerebral and the other of subdural haemorrhage, they saw no pathological signs except for thickening of the intimal layer and emphasized that there were no inflammatory signs. In the third case, a 12 year old girl with signs of juvenile arteriosclerosis, the vessels of the circle of Willis were thrombosed. At the necropsy of a 44 year old male, Vuia *et al.* (1970) found haemorrhage in the frontal white matter, arteriosclerosis and hypoplasia of the anterior part of the circle of Willis. In our cases we also saw arteriosclerosis of different degrees of severity in the major vessels, and it was atheromatosis that resulted in occlusion of the distal part of the internal carotid artery and of the cerebral vessels. We found no signs of other vascular disease either at the necropsy or the histological examination. In our patients, therefore, the characteristic angiographic 'Moyamoya' pattern was associated with arteriosclerotic vascular occlusion—that is, it was observed in the absence of any other specific vascular lesion. On the basis of the pathological findings, this phenomenon may be supposed to occur when there is occlusion of the basal cerebral vessels of any pathogenesis and some factors have promoted the development of the 'Moyamoya' pattern. In our opinion the 'Moyamoya' picture is produced by an accessory vascularization of the cerebral territories the blood supply of which has been impaired.

Theoretically, two conditions are necessary to the development of the 'Moyamoya' picture. One of them is the absence of any compensating circulation via the circle of Willis. This is the case if one of the internal carotid arteries is occluded in its terminal part, including its branches or, as in the case of Vuia *et al.* (1970), where, besides the occlusion at the level of the siphon, the circle of Willis was primarily hypoplastic. The Japanese authors considered also

an occlusion extending to the basal cerebral vascular circle as one of the characteristic features of 'Moyamoya' disease. Of course, the frequency of occlusions at this site and that of 'Moyamoya' cases do not coincide, these occlusions representing the most severe forms of carotid occlusion frequently and rapidly leading to death. The other condition for the formation of a 'Moyamoya' pattern in the presence of earlier vascular occlusions is that there should be a possibility of developing a collateral circulation of this type.

As to the genesis of the vessels which make up this network, there is no uniform opinion. Some authors speak of the persistence of early, embryonic blood vessels which resume function later but they may also be newly-formed vessels. Either possibility may be reckoned with, mostly at a young age. This can be one of the causes of the high incidence in children. In addition, the rate of development of the occlusion cannot be disregarded. Irrespective of whether it is a case of embryonic vessels resuming function or one of new vessels being formed, a slow rate of occlusion favours hypervascularization.

Japanese authors have reported a relatively large number of 'Moyamoya' patients, a considerable proportion of whom are children. The cases outside Japan were of Japanese origin too, so it is not surprising that 'Moyamoya disease' is regarded as peculiar to the Japanese. But the apparent small number of non-Japanese cases could also be due to the fact that angiography is less frequently done in children. In their larger material consisting of 87 children without tumour or head injury who had unilateral symptoms Hilal *et al.* (1971) found the 'Moyamoya' phenomenon in five of 17 arterial occlusions.

Nevertheless, it is not our aim to deny the existence of a hitherto unknown vascular disease affecting the Japanese and often causing bilateral distal carotid occlusion. From the analysis of our two adult cases that came to necropsy we believe that there can be no doubt that the 'Moyamoya' phenomenon revealed by angiography is a compensatory vascularization which may develop after occlusion, of any origin, of the arteries at the base of the brain.

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