Moyamoya Disease — A Review

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SUMMARY One hundred cases of Moyamoya disease were encountered between 1961 and 1980. This report describes the clinical characteristics and emphasizes the angiographic findings and clinical correlation in this disease. Reasons for the differences in clinical and radiological presentation in children versus adults are proposed and a possible pathophysiological mechanism is outlined. Treatment with perivascular sympathectomy and superior cervical ganglionectomy may be useful but more investigation needs to be carried out into the pathogenesis of the disease before more definitive therapy is realized.

MOYAMOYA, a Japanese word meaning "something hazy like a puff of cigarette smoke drifting in the air," is the descriptive term we apply to a peculiar angiographic picture consisting of abnormal net-like vessels at the base of the brain (fig. 1). In addition to this abnormality, angiography usually reveals stenosis or occlusion of the internal carotid artery at the level of its terminal bifurcation together with abnormalities of the anterior and middle cerebral arteries. These changes are usually bilateral.

In 1963, we suggested that this pattern constituted a new disease entity and since then, many similar cases have been reported not only in Japan, but from all over the world. The purpose of this paper is to review our personal experience based on 100 cases encountered between 1961 and 1980, and to make some suggestions as to pathophysiology and possible treatment.

Clinical Characteristics

Of the 100 cases seen between 1961 and 1980, 46 were children under 15 years of age and 54 were adults. The age distribution was bimodal with one peak occurring in the first decade and the second in the fourth decade. There were 40 males and 60 females. In this group, a past history of inflammation in the head or neck region was frequently observed and these are detailed in table 1. Routine hematology, biochemistry, and serological investigations have not been rewarding.

In most cases, the symptomatic presentation of Moyamoya disease depends on the age of the patients as seen in table 2. Children present typically with recurrent episodes of sudden hemiplegia that might alternate sides. Fine involuntary movements of the extremities and slowly progressive mental impairment have also been observed. Adults, on the other hand, more commonly present with evidence of intracranial hemorrhage, and this can be either on the basis of intracerebral hemorrhage with a rupture into the ventricles or subarachnoid hemorrhage.

Laboratory Findings and Their Clinical Correlation

EEG

The EEG in Moyamoya disease can be quite distinctive. Twenty to sixty seconds following the termination of hyperventilation, there is the return of high voltage slow waves and we have termed this the "rebuild-up" phenomenon (fig. 2). Although the mechanism is unknown, this pattern has not been reported in any other condition, and it may serve as a useful screening test.

CT Scan

The most consistent abnormality on CT scanning has been a low density area in the white matter of the temporal lobe. There was no relationship between the extent of low density and the stage of basal Moyamoya. The basal ganglia have looked surprisingly normal in all of our cases, and we have not observed

Table 1 Past History in 100 Patients with Moyamoya Disease

<table>
<thead>
<tr>
<th>Condition</th>
<th>Children 46 cases</th>
<th>Adults 54 cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tonsillitis</td>
<td>25</td>
<td>20</td>
</tr>
<tr>
<td>Otitis media</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td>Sinuitis maxillaris</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>High fever (at onset)</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Lung tuberculosis</td>
<td>2</td>
<td>5</td>
</tr>
<tr>
<td>Lymphadenitis</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Other infections</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Intolerance to infection</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Head trauma</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Renal disease</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0</td>
<td>8</td>
</tr>
</tbody>
</table>

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Moyamoya Disease/Suzuki et al.

TABLE 2  Signs and Symptoms of Moyamoya Disease

<table>
<thead>
<tr>
<th>Signs and Symptoms</th>
<th>Children</th>
<th>Adults</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motor disturbance</td>
<td>44</td>
<td>16</td>
</tr>
<tr>
<td>Involuntary movements</td>
<td>8</td>
<td>2</td>
</tr>
<tr>
<td>Sensory disturbances</td>
<td>8</td>
<td>10</td>
</tr>
<tr>
<td>Speech disturbance</td>
<td>15</td>
<td>8</td>
</tr>
<tr>
<td>Intracranial hemorrhage</td>
<td>2</td>
<td>23</td>
</tr>
<tr>
<td>Visual disturbance</td>
<td>6</td>
<td>6</td>
</tr>
<tr>
<td>Headache</td>
<td>8</td>
<td>11</td>
</tr>
<tr>
<td>Disturbance of consciousness</td>
<td>3</td>
<td>12</td>
</tr>
<tr>
<td>Convulsion</td>
<td>14</td>
<td>3</td>
</tr>
<tr>
<td>Mental deficit</td>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>Psychic disturbance</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Vertigo</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Apraxia</td>
<td>1</td>
<td>1</td>
</tr>
</tbody>
</table>

We have observed two kinds of collateral pathways from the extracranial to the intracranial arteries, and these have been termed ethmoidal and vault Moyamoya. Ethmoidal Moyamoya is seen as net-like vessels in the orbit that are perfused from the ophthalmic artery, the posterior and anterior ethmoidal arteries and the external carotid arteries. These vessels usually communicate with basal Moyamoya. In children, ethmoidal Moyamoya tends to grow in direct proportion to the severity of the staging of the disease; while in adults there is poor correlation in this respect. This difference may reflect the fact that some adults acquire the disease in later life, at which time they may have lost the capacity to form this collateral circulation.

Vault Moyamoya develops from transdural anastomoses derived from the middle meningeal and superficial temporal arteries. The location of the anastomotic...
Stage 1. Narrowing of carotid fork. Only the carotid fork stenosis is observed.

Stage 2. Initiation of basal moyamoya. All the main cerebral arteries are dilated.

Stage 3. Intensification of moyamoya. Remarkable moyamoya vessels at the base of the brain. The defect of the middle and anterior cerebral arteries is observed.

Stage 4. Minimization of Moyamoya. The defect of the posterior cerebral artery is observed.

Channels' origin corresponds to the region of the sutures as shown in figure 5. Again the correlation between angiographic staging and degree of collateral flow was only apparent in children.

The angiographic findings in adults differ from those in children in other ways and this is largely reflected in the adult presentation with evidence of intracranial hemorrhage. Those individuals who present with intracerebral and intraventricular hemorrhage may harbor a small aneurysm near the wall of the lateral ventricle. We previously reported three patients with such aneurysms in the peripheral portion of the posterior choroidal circulation. On repeat angiography some months later, these aneurysms were no longer visible and they were therefore felt to be pseudo-aneurysms. There is some support for this in the Moyamoya report of Yuasa et al. where an aneurysm was delineated in the left temporal lobe associated with a hematoma. Pathological examination of the hematoma specimen showed the "aneurysm wall" to be composed of concentric layers of fibrin and red blood cells. It appears that in adults with Moyamoya disease, there is a tendency for small arteries near the ventricular wall to rupture.

The other presentation in adults which is less common is that due to rupture of a saccular aneurysm.
Stage 5. Reduction of moyamoya. All the main cerebral arteries missing.

Stage 6. Disappearance of moyamoya. Cerebral blood flow supplied only from external carotid artery.

Of the total of 12 cases reported, 5 have involved aneurysms of the basilar bifurcation. The unusual prominence of aneurysmal rupture at this site may relate to compromise of the anterior circulation and increased flow in the vertebro-basilar system.

The difference in presentation between children and adults with Moyamoya disease is striking. We have some evidence to suggest that adults are less able to form collateral vessels than children. The medial striate arteries in fetuses, children and adults were examined and it was found that with aging there was a reduction in the number of anastomoses and in the calibre of vessels. The disease process in children is dynamic and progressive, while in adults it appears static and arrested and this may be the basis for the clinical dichotomy that we have outlined.

Pathology

Until recently, there were only a handful of autopsy reports on Moyamoya disease. Although the pathological findings have not been uniform, the most prominent features have been intimal thickening and excessive infolding and thickening or deficiencies in the internal elastic lamina. An arteritis of the vessel wall has not been documented.

Yamashita et al. have recently reported on the histopathology of the intracerebral perforating arteries in 22 patients with Moyamoya disease. These vessels showed microaneurysm formation, focal fibrin deposits and marked attenuation of the wall with diminution of the elastic lamina. Although the pathogenesis is not clear, these vessels appear predisposed to rupture and they offer some insight into the occurrence of intracerebral hemorrhage commonly seen in adults.

Pathophysiology and Treatment

Moyamoya disease remains largely an angiographic diagnosis of diverse etiology. Congenital and acquired categories have been proposed. The congenital form has been related to an arterial dysplastic process where...
there are both cerebral and systemic vascular abnormalities.\textsuperscript{27-30} There is some evidence for a hereditary factor in that the disease occurs predominantly among the Japanese where a rate of familial cases of more than 7\% has been reported.\textsuperscript{31} Additional familial cases have been reported from Europe\textsuperscript{32, 33} and in a pair of identical twins.\textsuperscript{34} Moyamoya vessels have also been found in several acquired diseases including sickle cell anemia,\textsuperscript{35} neurofibromatosis,\textsuperscript{36} tuberculous meningitis,\textsuperscript{37} leptospirosis,\textsuperscript{38} atherosclerosis,\textsuperscript{39} disease associated with connective tissue abnormalities\textsuperscript{40} and following radiation therapy.\textsuperscript{41}

We have been impressed by the frequency of a past history of chronic inflammation in the cervical region in patients with Moyamoya disease. In pursuit of an inflammatory mechanism, mongrel dogs were injected with foreign protein and the arteries in the region of the internal carotid bifurcation showed many of the pathological changes seen in Moyamoya disease (fig. 6). The localized nature of these changes suggests to us that the extensive sympathetic innervation about the internal carotid arteries may be playing a role. We have been encouraged by our results following perivascular sympathectomy and superior cervical ganglionectomy on a number of patients.\textsuperscript{42} We have observed clinical improvement in many of these cases. (Tables 3-6)

There have been several reports of treatment with superficial temporal artery-middle cerebral artery bypass\textsuperscript{43-45} in order to improve cerebral blood flow, and good results in both children and adults have been reported. However, the efficacy of this procedure has not been firmly established and is currently under investigation.

\textbf{Conclusion}

We have reviewed 100 cases of Moyamoya disease seen between 1961 and 1980. There were striking differences in the clinical and radiological presentation between children and adults. Children typically presented with recurrent episodes of sudden hemiplegia based on ischemic events while adults often presented with evidence of intracranial hemorrhage. This difference may be based on the fact that the disease process in children appears progressive with ample collateral flow while in adults it is often arrested and, in the latter altered circulatory dynamics may be playing a role.
The etiology of Moyamoya disease is still unknown. However, our clinical and experimental studies suggest that the disease is an acquired one in which both an immunological vascular reaction and a subsequent inflammation play an important role. Perivascular sympathetic and superior cervical ganglionectomy may be useful but more definitive therapy will have to await further clarification of the underlying pathophysiological mechanism.

Acknowledgments

Figure 3 and sections of figure 4 in this STROKE article have previously appeared in an article by J. Suzuki in Arch. Neurol. 36, 1979.

References

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J Suzuki and N Kodama

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