Clinical Survey of Ischemic Cerebrovascular Disease in Children in a District of Japan

Shinya Satoh, MD; Reizo Shirane, MD; and Takashi Yoshimoto, MD

Ischemic cerebrovascular disease in children is relatively rare. To clarify the clinical features of ischemic stroke occurring in infants and children, we evaluated 54 cases of cerebral infarction, excluding cases of moyamoya disease, in patients < 16 years old at 24 clinics in the Tohoku (northeast) district of Japan. We observed two incidence peaks, one in little children and the other in junior high school students. Infection and minor head trauma were more frequently seen prior to ischemic strokes than was heart disease. The middle cerebral artery region, including the basal ganglia, was most commonly affected (49 patients, 91%) on computed tomograms. Angiography was performed in 48 patients (89%) and showed various types of occlusive lesions, mostly affecting the middle cerebral artery. Hemiparesis was the most common form of disability following ischemic strokes (48 patients, 89%). Surgical treatment was carried out in seven patients (13%). The clinical course of these cases showed that the recovery of children after a stroke tends to be better than that of adults, but that permanent disabilities, such as hemiparesis or mental retardation, occur commonly. Further investigation of juvenile cerebrovascular disease is important to prevent ischemic strokes in children. (Stroke 1991;22:586-589)

Cerebral infarction, a relatively rare disease in children, was often diagnosed as acute infantile hemiplegia before the widespread use of computed tomography (CT) and other imaging techniques. Although cases of cerebral infarction in children are no longer uncommon, little research has been done on this subject and many uncertainties remain concerning its incidence and etiology. We undertook this cooperative study to clarify the clinical features of childhood ischemic cerebral disorders.

Subjects and Methods

We studied 54 patients < 16 years of age who had ischemic cerebrovascular disease identified by CT scans carried out at the institutes participating in the Tohoku Cerebrovascular Disease Cooperative Study between January 1974 and July 1989. The age at onset, sex, clinical course, symptoms, prior medical history, radiologic findings, treatment, and prognosis of these cases were recorded. Although moyamoya disease also causes cerebral infarction, it is relatively common in Japan and is dealt with as a special entity of cerebrovascular disease. Therefore, cases of moyamoya disease were excluded from this study.

Results

The increased incidence of cerebral infarction in children during the 1980s over that during the 1970s may reflect the increased availability and use of CT, which did not come into wide use in Japan until 1979. Since 1979, there has been an incidence of 2–7 (mean 4.7, 95% confidence interval 3.7–5.7) cases/yr. The total population of the regions participating in the study is approximately 9.7 million people, with 2.4 million estimated to be < 16 years of age. Thus, it is calculated that the incidence of childhood cerebral infarction over the past 10 years in the Tohoku district was 0.05/100,000/yr for the entire population and 0.2/100,000/yr for those < 16 years of age, assuming a normal distribution of cases of childhood cerebral infarction in the survey region.

Figure 1 shows the age distribution of the subjects in our study. Two peaks of incidence were observed, the first during early childhood and the second during junior high school. Half of the patients were male and the other half were female.

Table 1 shows the clinical course. The majority of children (38) sustained a minor completed stroke. Unlike in juvenile moyamoya disease, only three patients presented with transient ischemic attacks (TIAs). Moreover, repeated TIAs and aggravation of symptoms were uncommon.

Motor paresis was the sign most frequently observed at onset (48 cases, 89%), followed by disturbances of consciousness (21 cases, 39%) and distur-
bances of language (19 cases, 35%). The symptoms in the majority of patients with disturbances of language or consciousness were mild and transient. Headache was common in school-age children, while convulsions were more frequent in children <3 years of age.

Only three patients had a prior medical history showing them to be at risk for cerebral infarction; two had heart disease (valvular disorder, left atrial myxoma) and one had renal hypertension (Table 2). None of the remaining 51 patients had medical histories with risk factors for cerebrovascular disease, but 20 had disorders somewhat related to the onset of cerebral infarction, if not direct danger signals. These included 10 children with inflammatory diseases due to infection of the upper respiratory tract or with fever of unknown origin and 10 with mild head trauma occurring several hours prior to onset of the cerebrovascular disorder. The remaining 31 patients had no abnormalities preceding the cerebral ischemia, but about half of them had red blood cell counts greater than the age- and sex-specific 90th percentile at the time of admission to the hospital. In addition, four of the children with cerebral ischemia of unknown etiology (one with a previous respiratory infection and three with unspecified systemic disorders) had hyperlipidemia. This lipid abnormality is characterized by high levels of triglyceride and/or low density lipoprotein cholesterol. These three patients had no family history of lipid disorders or cerebral infarction. In this study, no patients had either hemoglobinopathy or a congenital metabolic disease.

Study of the low-density areas observed in CT scans (Table 3) showed that the majority (31, 57%) were in the basal ganglia and that 18 (33%) were in the territory of cortical branches of the middle cerebral artery (MCA). Therefore, in 91% (49) of these patients, the infarct lay in the territory of the MCA (including the basal ganglia). In only five children were there findings of hemorrhagic infarction during the course of the disease; four of the five later showed atrophy of the cerebral hemispheres.

Angiography was performed in 48 patients (Table 4). Similar to the CT findings, lesions of the MCA were most frequent; some 30% of the 48 children had multiple lesions of the carotid fork, C1, A1 and M1 or C1, M1, and M2. These multiple lesions were generally close to one another, and no patient had distant or contralateral vascular lesions. Most lesions were abnormalities of the vascular wall and stenoses or occlusions, but three patients had the so-called string of beads lesion, one with a fusiform aneurysm and two with elongation of the cervical internal carotid artery. Twenty-two children underwent angiography more than once during the course of the disease, and 11 (50%) showed notable improvement.

Of the 54 patients, seven (13%) underwent surgical therapy, including superficial temporal artery—MCA anastomosis, encephaloduroarteriosynangiosis, encephalomyoarteriosynangiosis, cervical sympathectomy, repair of a coiled cervical internal carotid artery, and external decompression. The remaining 47 patients (87%) received conservative medical therapy.

The paresis was classified according to the six-level scheme of De Jong.10 There was a tendency for paresis of the upper limbs to be more severe than that of the lower limbs at the time of onset, but recovery of the lower limbs was somewhat more favorable.

Study of the so-called activities of daily living (ADL) 6 months following onset showed that almost all patients improved from their condition at onset, with the majority being capable of normal ADLs. Of the 14 patients with ADL scores of 4 at onset, 12 improved to scores of 0 or 1. On the other hand, 6 months after onset almost half (44%, 24) of the 54 patients still had neurologic deficits of some kind. The majority of these deficits were, as noted above, of the upper limbs, particularly fine motor control. Due to

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**TABLE 1. Clinical Course of 54 Children With Ischemic Cerebrovascular Disease**

<table>
<thead>
<tr>
<th>Clinical course</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transient ischemic attack</td>
<td>3</td>
</tr>
<tr>
<td>Reversible ischemic neurologic deficits</td>
<td>12</td>
</tr>
<tr>
<td>Completed stroke</td>
<td></td>
</tr>
<tr>
<td>Minor (mild deficits)</td>
<td>38</td>
</tr>
<tr>
<td>Major (severe deficits)</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
</tr>
</tbody>
</table>

**TABLE 2. Risk Factors and Primary Disease in 54 Children With Ischemic Cerebrovascular Disease**

<table>
<thead>
<tr>
<th>Risk factors and primary disease</th>
<th>No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Valvular heart disease</td>
<td>1</td>
</tr>
<tr>
<td>Left atrial myxoma</td>
<td>1</td>
</tr>
<tr>
<td>Renal hypertension</td>
<td>1</td>
</tr>
<tr>
<td>Without risk factor</td>
<td>51</td>
</tr>
<tr>
<td>With infection or fever of unknown origin</td>
<td>10</td>
</tr>
<tr>
<td>With head trauma</td>
<td>10</td>
</tr>
<tr>
<td>Without primary disease</td>
<td>31</td>
</tr>
<tr>
<td>Total</td>
<td>54</td>
</tr>
</tbody>
</table>
convulsions and developmental disorders, the prognosis was poor in four patients (all little children).

Discussion

Cerebral infarction in children is relatively rare. The one report by Schoenberg et al.\textsuperscript{11} indicates an incidence of 0.63/100,000/yr in the vicinity of Rochester, Minn. Therefore, estimation of its actual incidence with any certainty is difficult. Although the number of reported cases is small, a number of articles have clarified the clinical features of juvenile cerebral infarction.\textsuperscript{2-8}

From previous reports and the previously common diagnosis of acute infantile hemiplegia, the onset of cerebral infarction in children is often accompanied by motor paresis,\textsuperscript{6} most frequent in little children and junior high school–age children, and is equally common in girls and boys.\textsuperscript{4,6} Our survey confirms these features.

Although our rate is an estimation, we calculated the incidence of juvenile cerebral infarction in the Tohoku district to be 0.2/100,000/yr for children <16 years of age, which is considerably lower than that reported by Schoenberg et al.\textsuperscript{11} This difference in incidence (as will be explained further below) may reflect the relatively low incidence of heart disease in Japan. With regard to the site of the cerebrovascular lesions, our survey is consistent with previous reports of a high incidence in the vicinity of the MCA. The angiographic features of this study are similar to those of the report of Hilal et al.\textsuperscript{12} Stenosis or occlusion frequently involved the supraclinoid segment of the internal carotid artery and/or the proximal segment of the MCA, the anterior cerebral artery, and the central perforating arteries.

One motivation for undertaking the present survey was to determine the principal causes of cerebral infarction in children. Except for infarction due to thrombosis originating in heart disorders, clearly the etiology of cerebral infarction in children should differ from the arteriosclerosis that causes adult cases. As mentioned earlier, only two patients had cardiac disease and in the vast majority of the cases no clear-cut factor was responsible for the infarction. Among these unexplained cases, however, many had infections or mild head trauma, which often precede attacks of cerebral ischemia.\textsuperscript{4,6,12-14} Our angiographic results suggest that, rather than a single discrete lesion, a somewhat diffuse vascular abnormality was common. Follow-up angiography showed relatively good recovery from such lesions. As Raybaud et al.\textsuperscript{15} have indicated, the cerebral ischemia in such cases may have been caused by vasculitis or vasospasm. Infections preceding cerebral infarction need not be confined to the head and neck region and are generally systemic disorders, so the possibility of vasculitis cannot be excluded. Moreover, dehydration during a fever may be a factor inducing cerebral ischemia, and it is noteworthy that approximately half of the patients without clearly causal preceding disorders had increased red blood cell counts. Among the patients with preceding mild head trauma, none in this survey had broken bones or required sutures. Thus, a direct insult to the cerebral blood vessels was unlikely, but stenosis or an occlusive response to mechanical stimulation of the vessels should be considered. With regard to the relation between hyperlipidemia and cerebral infarction, too little data are available to make conclusive statements, but it is of interest that there has been at least one previous study on the etiology of brain infarction and lipid metabolism.\textsuperscript{15}

Finally, the majority of patients were treated conservatively. No significant difference in prognosis was observed between the surgically managed group and the conservatively treated group in this study. However, debate remains as to whether surgical therapy is preferable in patients in whom symptoms continue to progress.\textsuperscript{2,8,14}

Some have argued that the prognosis in cases of childhood cerebral infarction is good\textsuperscript{4,7} while others have maintained that it is poor.\textsuperscript{2,3,5,10} From our survey, it is clear that this difference of opinion is more apparent than real. We found improvements in the ADL score of almost all patients, suggesting a better prognosis in children than in adults. On the other hand, about half of the children retained some kind of neurologic deficit that would accompany them through critical developmental periods. In this respect, we cannot say that the prognosis is favorable in childhood cases.
In conclusion, cerebral infarction is rarer in children than in adults, with functional recovery in children being relatively good. Unfortunately, because the disorder arises during a time of critical development, the importance of prevention may be even greater in children than it is in adults. Many uncertainties remain concerning the nature of such infarction in childhood, but angiographic findings indicate that in some cases the vascular changes are reversible. The possibility of preventing the onset and arresting the progression of such disease should be considered and underlines the importance of further research.

Acknowledgments

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References


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