Dokkyo Journal of Medical Sciences
34(2) : 115～118, 2007

Case Report

MRA Diagnosis of Down Syndrome Associated with Moyamoya Syndrome Presenting Multiple Cerebral Infarctions in a 1-year-old Girl

George Imataka[1], Masahiko Mitsui[1], Naoto Shimura[1], Teisuke Hashimoto[2], Hideo Yamanouchi[1], and Osamu Arisaka[1]

[1] *Department of Pediatrics, Dokkyo Medical University, Japan*
[2] *Department of Radiology, Dokkyo Medical University, Japan*

SUMMARY

It is known that various complications are observed in patients with Down syndrome. We report a 1-year-old girl with Down syndrome who developed moyamoya syndrome presenting multiple cerebral infarction. Her chief complaints were recurrent convulsion and weakness on the left side of the body. Brain CT and MRI demonstrated multiple abnormal signals, and the lesion was diagnosed as multiple cerebral infarction. Since obstruction of the right anterior and middle cerebral arteries was observed by MRA, the patient was diagnosed with moyamoya syndrome. Moyamoya syndrome accompanied by Down syndrome advances in the early stage, and since it often occurs with cerebral infarction, the timing of its early diagnosis by MRA and caution of cerebral infarction are important. However, no guidelines for the control of moyamoya syndrome have been established in Down syndrome. Therefore, MRA should be performed in patients in whom moyamoya disease is suspected, because no useful method for the prevention of this complication disease has established.

Key Words : Down syndrome, moyamoya disease, cerebral infarction, MRA

INTRODUCTION

Moyamoya disease (spontaneous occlusion of the circle of Willis) is a cerebrovascular disorder of unknown etiology. The internal carotid artery is gradually constricted and occluded in the distal end region, and moyamoya blood vessels are developed from the cerebral arterial perforator branches and choroid artery[1]. According to the diagnostic criteria of the Ministry of Health and Welfare in Japan, lesions definitely diagnosed by cerebrovascular imaging and MRA are defined as moyamoya disease. On the other hand, lesions with Down syndrome, arteriosclerosis, autoimmune diseases, meningitis, cerebral tumor, von Recklinghausen's disease, head injury, and radiation to the head, and similar cerebrovascular lesions are defined as moyamoya syndrome[2]. The incidence of moyamoya syndrome peaks in children and adults, but it is low in infants. Clinically, the initial symptoms are headache, involuntary movements, and convulsion by respiratory loading. Since patients with psychomotor retardation and babies do not complain, detection of initial symptoms and early diagnosis are difficult[3]. We encountered a 1-year-old girl with moyamoya syndrome accompanied by Down syndrome, in whom the initial symptoms were convulsion and multiple cerebral in-

Received November 10, 2006 ; accepted January 31, 2007
Reprint requests to : George Imataka MD, PhD
Department of Pediatrics, Dokkyo Medical University, 880 Kitakobayashi, Mibu, Shimotsuga, Tochigi 321-0293, Japan
e-mail : geo@dokkyomed.ac.jp

farction. In this study, we report the clinical course of this patient with a discussion.

CASE REPORT

The patient was a 1-year-old girl who consulted the emergency outpatient department with the chief complaint of hemi-convulsion. Her father was 39 years old, and her mother was 34 years old. No consanguious marriage existed and her family had no history of convulsion. This girl was born with a body weight of 3052 g at 38 weeks of *in vitro* fertilization-embryo transfer (IVF-ET) gestation. The Apgar score was 8 points 1 min after birth without asphyxia. Previously, the mother terminated the pregnancy of a boy with anencephaly. The girl's face was similar to patients with Down syndrome, and complete 21 trisomy was confirmed by the G-band chromosomal test. Transient abnormal myelopoiesis and transient thrombocytopenia were observed, but neither congenital cardiac diseases nor combined malformation in the digestive tract was detected. With regard to motor development, laughing caused by cradling was observed 6 months after birth, holding-up of the head 10 months after birth, and rolling over 1 year and 1 month after birth. However, the mother was worried about poor movement of the girl's left hand from 6 months after birth.

The mother consulted the emergency outpatient department with the chief complaint of convulsion on the left side of the body. No fever was observed. The heart rate was high (130/min), and respiration was spontaneous and stable. The girl had had a cold for 4 days. On the day of consultation, the girl woke up at 8 o'clock, and cried intensely. Immediately after crying, a 1-min convulsion on the left side of the body occurred twice, and the girl consulted our department. At the first examination, no responses to calling but those to pain stimulation were obtained, and the consciousness level was estimated to be 3 according to the Japan coma scale. The left upper and lower limbs were relaxed without movement. The deep tendon reflex of the 4 limbs was dominant in the left upper and lower limbs. Babinski's reflex was positive on the left side and negative on the right. No meningeal irritation sign was detected. There was no bilateral difference in the pupils, but nystagmus was observed. Since convulsion on the left side of the body occurred twice during the examination period, the girl was admitted. Biochemical examination indicated no blood gas acidosis, and demonstrated that the hematological values, hepatic and renal functions, electrolytes, inflammatory reactions, sugar, and the blood coagulation system were all within their normal ranges. Anti-nuclear antibody, anti-Sm antibody, anti-cardiolipin IgM antibody, IgG antibody, anti-platelet antibody, and anti-neutrophil antibody were all negative. Cardiac ultrasonography was normal. Brain CT (Fig. 1) demonstrated multiple low density areas in the frontal, parietal, and occipital regions on the right side, and the girl was diagnosed with multiple cerebral infarction. Drip injection of a plasma extender with low-molecular dextran-L and an osmotic diuretic with Glyceol were performed. Furthermore, the anticonvulsant Phenobarbital was administered. On day 2, the girl made eye contact with others, and the consciousness level was Japan coma scale 2. No convulsion recurred. Brain T2-weighted MRI demonstrated multiple high signal intensity areas, which agreed with those detected by brain CT (Fig. 2). Brain MRA revealed that the right anterior and middle cerebral ar-

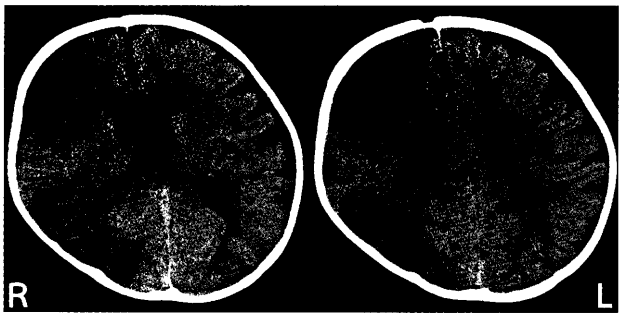

Fig. 1 Brain CT (day 1) showed multiple low density areas in the frontal, parietal, and occipital regions mainly in the left cerebral hemisphere.

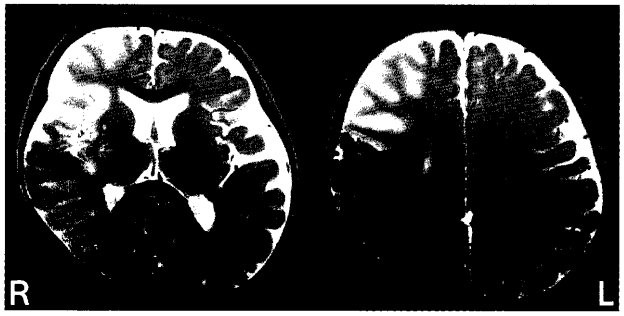

Fig. 2 Brain MRI (day 2) (Spin echo method of T2-weighted imaging ; TE = 4000 msec, TR = 100 msec) demonstrated multiple high intensity areas due to cerebral infarction.

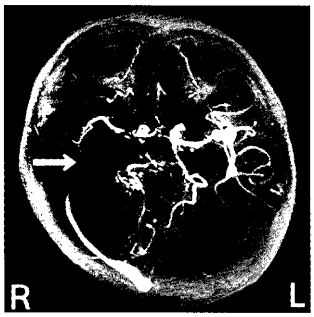

Fig. 3 Brain MRA (day 2) showed moyamoya vessels distal to the right anterior and middle cerebral arteries.

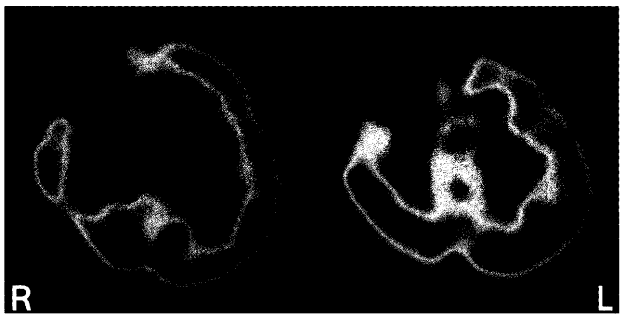

Fig. 4 ^{99m}Tc ECD-SPECT after Diamox administration (day 100) detected multiple decreases of cerebral blood flow in the frontal region of the left cerebral hemisphere.

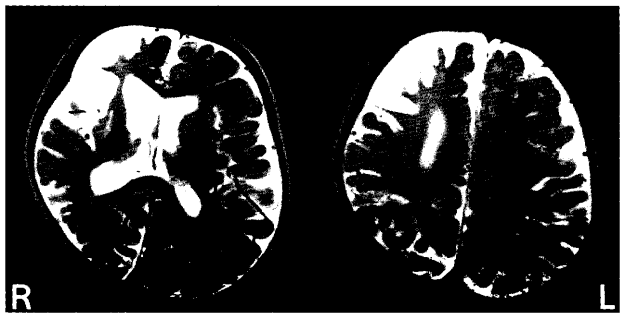

Fig. 5 Brain MRI T2W images showed both atrophic and post-infarction changes.

teries did not reach the peripheral regions. Moyamoya blood vessels were partially observed (Fig. 3), and the girl was diagnosed with cerebral infarction accompanied by moyamoya disease. Clinically, paralysis of the left upper and lower limbs was slightly improved by continuous rehabilitation. The girl was discharged from the hospital on day 15. On day 30, multiple decreases in the cerebral blood flow were observed mainly in the frontal region of the left cerebral hemisphere after Diamox administration (Fig. 4). Brain MRI performed on day 365 demonstrated that the infarction regions remained, and cerebral atrophy developed (Fig. 5).

Since then, the girl has had severe epileptic strokes over a few minutes several times per year. In the electroencephalogram (EEG) at the age of 9 years, spikes were observed in the left central area, but spindles rarely occurred. In the background, slow waves of 3–5 Hz were dominantly observed in the bilateral posterior occipital regions. The background activity was lower on the right side than on the left side hemisphere. Currently, the girl is 11 years old, and attends a school for the handicapped. The girl cannot walk because of paralysis in the left lower limb, but can maintain a sitting position. Language development is markedly delayed, and the girl speaks words singly. The parents do not consider that surgical treatment of moyamoya disease should be performed.

DISCUSSION

We reported moyamoya syndrome in a 1-year-old girl with Down syndrome. The chief complaint was convulsion on the left side of the body, and this patient was diagnosed with multiple cerebral infarction by radiographic imaging with CT and MRI. In addition, moyamoya syndrome was diagnosed with using MRA. The conventional hyperventilation test using EEG could not be applied to children, but MRA was useful for diagnosis of moyamoya syndrome. Since children with moyamoya disease have Down syndrome as a underlying disorder, it is classified into moyamoya syndrome. There have been several studies on Down syndrome and moyamoya syndromes. Fukushima et al.[4] observed moyamoya syndrome in 1 of 532 patients with Down syndrome, and speculated that its incidence is 0.19–0.25%. This percentage is about 3-fold higher than the incidence of moyamoya disease in the general population (0.07%) reported by Fukuyama et al.[5] On the other hand, it has been reported that there was neither a difference in the age of occurrence nor sexual difference between moyamoya syndrome in patients with Down syndrome and moyamoya disease in children[5,6]. The timing of MRA screening in patients with Down syndrome to achieve a good prognosis has not been clarified[7]. MRA screening of all patients with Down syndrome would cause medical economic prob-

lems. Under the present circumstances, there are no guidelines for whether MRA screening should be performed in all patients with Down syndrome, in whom the incidence of moyamoya syndrome is estimated to be 1－3 per 1,000 patients[7,8]. However, differences between moyamoya syndrome in children with Down syndrome and moyamoya disease have been clinically studied, and the higher severity of the former has been reported. Cramer et al.[6] and Fukuyama et al.[5] have reported the following characteristics of moyamoya syndrome in Down syndrome : (1) Moyamoya syndrome occurs in younger patients than moyamoya disease. (2) The initial symptoms are not transient cerebral ischemic symptoms, but cerebral infarction is often observed. (3) Severe lesions developing up to the posterior cerebral artery region are often observed. Rapid advancement of lesions in the circle of Willis in Down syndrome is suggested, but the mechanism remains unclarified.

Evaluation of build up observed in EEG by the hyperventilation loading test is generally considered useful for the early diagnosis of moyamoya disease. However, since the induction of cerebral ischemia attacks by hyperventilation in patients in whom moyamoya disease is suspected is a risk, this method is not recommended by some researchers. Since hyperventilation-loading EEG do not occur in patients with Down syndrome and infants, this method is not applicable. As moyamoya syndrome in Down syndrome is severe, brain MRA rather than examination of EEG should be performed when initial symptoms, such as mild convulsion and paralysis, epilepsy, consciousness disorder, and headache are observed in Down syndrome. However, the diagnosis of initial symptoms is difficult in children with Down syndrome because psychomotor retardation is often observed, and moyamoya syndrome occurs in young children. It is necessary to study the timing and period of brain MRA examination for the prevention and screening of moyamoya syndrome in patients with Down syndrome. It is important to consider a complication of moyamoya disease in children with Down syndrome, who cannot sufficiently report changes in the body condition. Furthermore, less invasive MRA should be performed in patients in whom moyamoya disease is suspected, because no useful method for the prevention of this disease has been established.

Acknowledgements. This work was supported by the Dokkyo Medical University, Investigator-Initiated Research Grant (No. 2005-01-5) and the Ministry of Education, Culture, Sports, Science and Technology (MEXT) KAKENHI 18790733 Grant-in-Aid for Young Scientists (B).

REFERENCES

1) Seol HJ, Wang KC, Kim SK. et al : Headache in pediatric moyamoya disease : review of 204 consecutive cases. J Neurosurg, **103** : 439-442, 2005.
2) Fukui M. : Guidelines for the diagnosis and treatment of spontaneous occlusion of the circle of Willis ('moyamoya' disease). Research Committee on Spontaneous Occlusion of the Circle of Willis (Moyamoya Disease) of the Ministry of Health and Welfare, Japan. Clin Neurol Neurosurg 99 Suppl, **2** : S238-240, 1997.
3) Hsu ML, Chen CJ, Juan CJ, Yuh YS, Cheng SN, Chen SJ. : Moyamoya disease initially mimicking MELAS syndrome in a 14-month-old child. Acta Paedriatr Taiwan, **45** : 104-107, 2004.
4) Fukushima Y, Kondo Y, Kuroki Y et al : Are Down syndrome patients predisposed to moyamoya disease? Eur J Pediatr, **144** : 516-517, 1986.
5) Fukuyama Y, Osawa M, Kanai N. : Moyamoya syndrome and Down syndrome. Brain Dev, **14** : 254-256, 1992.
6) Cramer SC, Robertson RL, Dooling EC, Scott RM. : Moyamoya and Down syndrome clinical and radiological features. Stroke, **27** : 2131-2125, 1996.
7) Erguven M, Deveci M, Turgut T. : Moyamoya disease and Down syndrome. Indian J Pediatr., **72** : 697-699, 2005.
8) Sabde S, Tullu MS, Lahiri KR, Vaswani RK. : Moyamoya syndrome in a child with Down syndrome. Arch Med Res, **36** : 421-424, 2005.