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A1 Segment Hypoplasia/aplasia Detected by Magnetic Resonance Angiography in Neuropediatric Patients

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= Abstract =

Purpose : A variation in the circle of Willis is not so common, but the most frequent type is hypoplasia/aplasia of the precommunicating anterior cerebral arteries (A1 segment). We aimed to examine the incidence and the clinical significance of A1 segment hypoplasia/aplasia in neuropediatric patients.

Methods : We retrospectively studied children with A1 segment hypoplasia/aplasia in brain magnetic resonance angiography (MRA) and compared the clinical and radiological aspects between children with A1 segment hypoplasia/aplasia alone and with other variations in the circle of Willis.

Results : Among 301 patients, 34 patients (11.3%) had A1 segment hypoplasia/aplasia. They presented neurological symptoms such as chronic headache, dizziness and visual disturbance. Seven (20.6%) had family history of neurological illness. Twenty seven (79.4%) had A1 segment hypoplasia/aplasia only, and seven (20.6%) had another vascular abnormality. Seven (20.6%) showed abnormal brain magnetic resonance angiography (MRI) results, cerebral atrophy being the most frequent (n=5, 14.7%). The incidence of abnormal brain MRI was 11.1% (n=3) in single vascular abnormality and 57.1% (n=4), significantly higher (p-value 0.02) in combined abnormality group.

Conclusion : Structural alterations in the cerebral vasculature in children have important pathophysiological and clinical implications. Evaluation of variations in the circle of Willis, especially of A1 segment hypoplasia/aplasia using MRA is recommended.

Key Words : Circle of Willis, A1 segment, Hypoplasia, Aplasia, Magnetic resonance angiography

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Introduction

Several types of anatomical variation in the circle of Willis are already known, and only 42

% of adults possess complete anterior and posterior parts of the circle[1]. Collateral flow via the circle of Willis can be provided anteriorly via the right and left precommunicating anterior cerebral arteries (A1 segment) and the anterior communicating artery (AcomA) and posteriorly through the ipsilateral posterior communicating artery (PcomA) and precommunicating posterior cerebral artery (P1 segment). The continuity of the anterior and posterolateral parts of the circle of Willis directly affects the extent of anterior and posterior collateral pathways, respectively. Impaired collateral blood flow through the circle of Willis is accepted as a risk factor for ischemic stroke[2-5].

The most frequent type of anatomical variations in the circle of Willis is unilateral hypoplasia/aplasia of the A1 segment[6]. The incidence of this fetal variation ranges from 1 to 16% according to angiogram and autopsy reports[1, 2, 7-9]. However, all reports were based on data of adult patients, and no precise incidence in the pediatric population has been reported yet[10]. Besides, no consensus has been reached over clinical implications of A1 segment hypoplasia/aplasia either.

In this study, we examined the incidence of A1 segment hypoplasia/aplasia in neuropediatric patients and evaluated the difference in clinical characteristics and radiological findings between children with A1 segment hypoplasia/aplasia only and with combined vascular variation in the circle of Willis.

Materials and Methods

1. Patient group

We retrospectively studied 34 children who presented A1 segment hypoplasia/aplasia among 301 who received brain magnetic resonance angiography (MRA) at Gangnam Severance Hospital, Yonsei University between March 2006 and February 2010. All patients underwent brain magnetic resonance imaging (MRI) as well. This study was approved by the Institutional Review Board of Gangnam Severance Hospital.

2. Neuroimaging

Brain MRA was performed using a 3.0-T MR system with a gradient capability of 40 mT/m (Signa VH/i, GE Healthcare). A 3D-TOF technique was used with a repetition time/echo time of 23/3.6 milliseconds, ramped pulses from 15° to 25° with a center flip angle of 20°, a 220-mm field of view, and a 224×384 matrix size. The whole volume was divided into 3 slabs with a 38% overlap, and each slab consisted of 48 partitions, which resulted in a total of 172 slices of 1.0 mm.

Brain MRI and MRA results were reviewed by a board certified neuroradiologist, unaware of the patients' clinical conditions. The diagnosis of A1 segment hypoplasia was made when A1 segments were <1 mm in diameter or were absent on the MRA[2]. Every pair of A1 segments was evaluated as symmetric or asymmetric, grading the diameter of the smallest A1 segment as invisible, hypoplastic or less than half in diameter compared to the contralateral side[11].

3. Statistical analysis

Fisher's exact test was used to compare clinical conditions and radiological findings between children with A1 segment hypoplasia/aplasia alone and those with additional vascular variations in the circle of Willis.

Results

1. Patient characteristics and MRA findings

The incidence of A1 segment hypoplasia/aplasia was 34 (11.3%) of a total of 301 patients. Twenty seven of them (79.4%) had only A1 segment hypoplasia/aplasia. Thirteen patients (38.2%) had right A1 segment hypoplasia, and 12 (35.3 %) had left A1 segment hypoplasia (Fig. 1). One child (2.9%) was found with right A1 segment aplasia, and another one with left A1 segment aplasia (Fig. 2). Combined vascular abnormalities in addition to A1 segment hypoplasia/aplasia were also detected in 7 (20.6%) children: right A1 segment hypoplasia combined with left P1 segment aplasia in one (2.9%), left P1 segment hypoplasia in one (2.9%), and right PcomA hyperplasia in one (2.9%); left A1 segment hypoplasia combined with left P1 segment hypoplasia in one (2.9%), right P1 segment hypoplasia in one (2.9%), and right vertebral hypoplasia in one (2.9%); and bilateral A1 segment hypoplasia

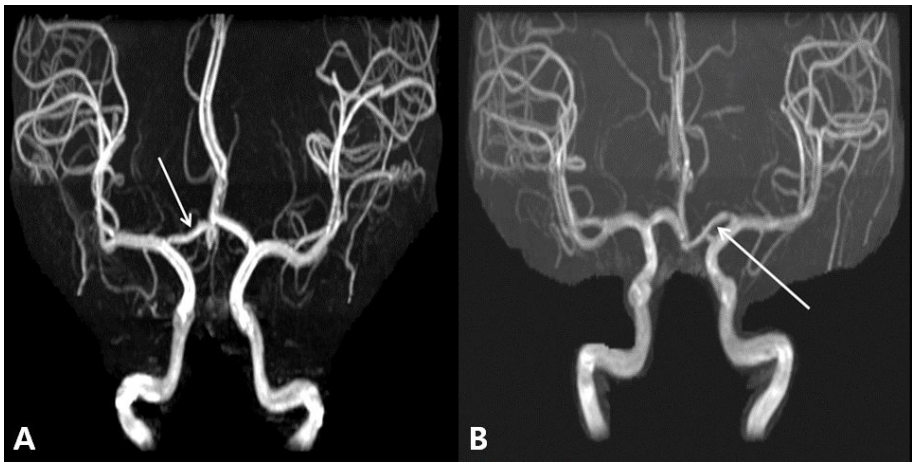

Fig. 1. Right A1 segment hypoplasia (A) and left A1 segment hypoplasia (B).

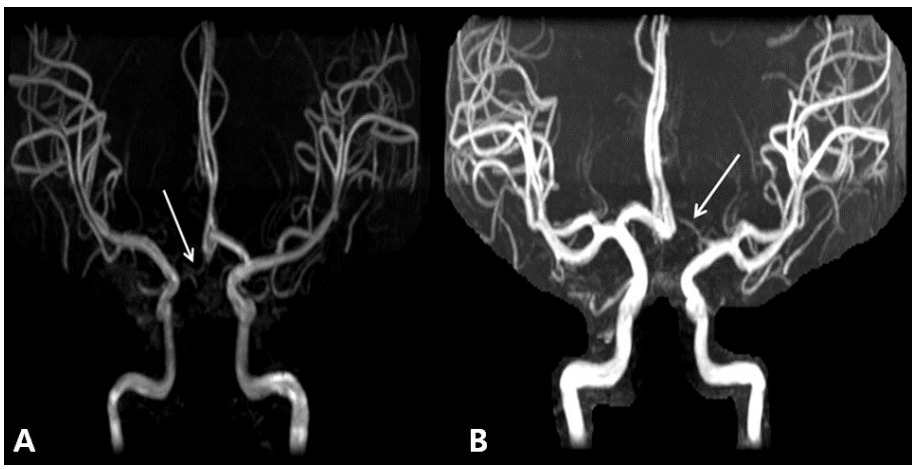

Fig. 2. Right A1 segment aplasia (A) and left A1 segment aplasia (B).

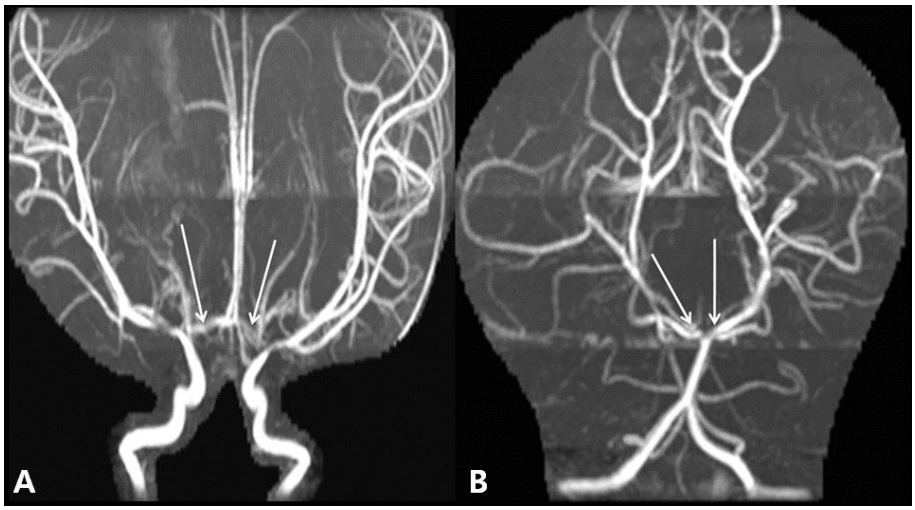

Fig. 3. Both A1 segment hypoplasia (A) with both P1 segment hypoplasia (B).

Table 1. Brain MRA Findings (n=34)

Brain MRA findings	No. of patients (%)
Single vascular abnormality	27 (79.4)
Rt. A1 segment hypoplasia	13 (38.2)
Lt. A1 segment hypoplasia	12 (35.3)
Rt. A1 segment aplasia	1 (2.9)
Lt. A1 segment aplasia	1 (2.9)
Concurrent vascular abnormality	7 (20.6)
Rt. A1 segment hypoplasia with Lt. P1 segment aplasia	1 (2.9)
Rt. A1 segment hypoplasia with Lt. P1 segment hypoplasia	1 (2.9)
Rt. A1 segment hypoplasia with Rt. PcomA hyperplasia	1 (2.9)
Lt. A1 segment hypoplasia with Lt. P1 segment hypoplasia	1 (2.9)
Lt. A1 segment hypoplasia with Rt. P1 segment hypoplasia	1 (2.9)
Lt. A1 segment hypoplasia with Rt. vertebral hypoplasia	1 (2.9)
Both A1 segment hypoplasia with both P1 segment hypoplasia	1 (2.9)

Abbreviations : Rt, right; Lt, left; MRA, magnetic resonance angiography; A1 segment, precommunicating anterior cerebral arteries; P1 segment, precommunicating posterior cerebral artery; PcomA, posterior communicating artery

combined with bilateral P1 segment hypoplasia in one (2.9%) (Fig. 3).

The male to female ratio of the patients was 1:1.12. Their mean age at the onset of neurological symptom was 10.2 years (±4.1 years) and underwent brain MRA at 11.3 years (±4.4 years) (Table 1).

2. Clinical symptoms

The most common initial neurological symptom was chronic headache (n=21, 61.8%) followed by dizziness (n=10, 9.4%), visual disturbance (n=6, 17.6%), recurrent nausea/vomiting (n=6, 17.6%), syncope (n=4, 11.8%), seizure and weakness of extremities (n=3, 8.8%). There

was each one case (2.9%) of dysarthria, ataxia, tremor, hemiplegia, and developmental delay as his or her initial symptom, respectively (Table 2).

3. MRI findings

Among 34 patients with A1 segment hypoplasia/aplasia, only 7 (20.6%) showed abnormal MRI results. The most frequent abnormal finding was cerebral atrophy which occurred in 5 pati-

Table 2. Characteristics of A1 Segment Hypoplasia and Combined Vascular Abnormality

Value	Patients with single vascular abnormality (n=27)	Patients with combined vascular abnormality (n=7)	*P*-value
Age of neurological symptom onset (years) (Mean±SD)	10.8±3.6	7.9±5.4	
Age at brain MRA (years) (Mean±SD)	11.6±3.8	9.9±6.4	
Neurological symptom			
Chronic headache	17 (63.0)	4 (57.1)	1.00
Dizziness	8 (29.6)	2 (28.6)	1.00
Visual disturbance	5 (18.5)	1 (14.3)	1.00
Recurrent nausea/vomiting	6 (22.2)	0 (0)	0.31
Syncope	4 (14.8)	0 (0)	0.56
Seizure	2 (7.4)	1 (14.3)	0.51
Weakness of extremity	3 (11.1)	0 (0)	1.00
Dysarthria	1 (3.7)	0 (0)	1.00
Ataxia	1 (3.7)	0 (0)	1.00
Tremor	1 (3.7)	0 (0)	1.00
Hemiplegia	0 (0)	1 (14.3)	0.21
Delayed development	1 (3.7)	0 (0)	1.00
Brain MRI finding			
Abnormal	3 (11.1)	4 (57.1)	0.02*
Cerebral atrophy	2 (7.4)	3 (42.9)	0.10
Cerebellar atrophy	1 (3.7)	0 (0)	1.00
Neuroglial cyst	0 (0)	1 (14.3)	0.21
Cerebral infarction	0 (0)	1 (14.3)	0.21
Leukodystrophy	1 (3.7)	0 (0)	1.00
Normal	24 (88.9)	3 (42.9)	0.02*
Family history			
Transient ischemic attack	4 (14.8)	0 (0)	0.56
Migraine	2 (7.4)	0 (0)	1.00
Hypertension	2 (7.4)	0 (0)	1.00
Brain Tumor	1 (3.7)	0 (0)	1.00
Depression	1 (3.7)	0 (0)	1.00
Moyamoya disease	1 (3.7)	0 (0)	1.00
None	20 (74.1)	7 (100)	0.30

*statistically significant
Abbreviations : MRA, magnetic resonance angiography; MRI, magnetic resonance imaging; SD, standard deviation

ents (14.7%). Cerebellar atrophy, neuroglial cyst, cerebral infarction, and leukodystrophy were observed in 1 (2.9%) patient each. One patient who had cerebral infarction concomitantly had bilateral A1 segment hypoplasia and bilateral P1 segment hypoplasia (Table 2).

4. Family history of neurological disease

Among 34 patients with A1 segment hypoplasia/aplasia, 7 (20.6%) had a family history of neurological illness: transient ischemic attack (n=4, 11.8%), hypertension (n=2, 5.9%), migraine (n=2, 5.9%), brain tumor (n=1, 2.9%), depression (n=1, 2.9%), and Moyamoya disease (n=1, 2.9%) (Table 2).

5. Characteristics of A1 segment hypoplasia and combined vascular abnormality

In the present study, patients with single vascular abnormality and combined vascular abnormality among 34 children with A1 segment hypoplasia were compared on various aspects.

Patients with combined vascular abnormalities were younger when the first neurological symptom appeared and underwent brain MRA earlier than the children with a single vascular abnormality, but without significance. There was no significant difference in the percentage of neurological symptoms either. When comparing brain MRI of both groups, the incidence of abnormal lesion was 11.1% (n=3) in the group with a single vascular abnormality and 57.1% (n=4) in the group with combined abnormalities (P=0.02). There was no difference in family history between the two groups (Table 2).

Discussion

The incidence of A1 segment hypoplasia/aplasia in our patients was 11.3% which was similar to that of adults (1−16%)[1, 7−9]. However, the incidence in children is certainly high enough to be noticed[2, 12]. To our knowledge there has been no study on this topic with a large number of pediatric patients. The incidence of A1 segment hypoplasia/aplasia in children can be valuable information since it is regarded as a possible risk factor of various neurological illness in adulthood. Van Everdingen et al. have stated that a single hypoplastic A1 segment may be clinically irrelevant when one of the other primary collateral pathways is present[13]. However, other subsequent studies reported A1 segment hypoplasia combined with a carotid occlusive disease as a risk factor of low flow infarcts[14, 15]. Also, Yu et al. reported that A1 segment is not only an anatomically important collateral circulation pathway, but also a source of various penetrating striatal arteries supplying blood flow to the anterior hypothalamus, septum pellucidum, and the anterior and inferior portions of the corpus striatum; thus, any alteration in A1 segment is a considerable risk factor of stroke[2]. Recent studies reported that an abnormal arterial structure can disturb normal blood flow, causing turbulence and increasing arterial wall stress, which in turn contributes to the formation of aneurysm[6, 16]. However, in our study, only one patient had cerebral infarction, and no case of aneurysm was found. It might be due to the fact that incidence of cerebrovascular disease is originally lower in pediatric age group. While cerebral vascular variations could impair collateral blood flow through the circle of Willis, causing

ischemia, it might depend on the length of the period exposed to the circumstance. In short, pediatric patients with risks may not present any abnormal sign until full-blown disease is manifested.

The most frequent initial symptom in our patients was chronic headache. Some studies proposed a hypothesis that the circle of Willis anomalies may correlate with alterations in cerebral hemodynamics and contribute to migraine susceptibility along with ischemic complications of migraine[17]. Altered cerebral blood flow has been demonstrated in regions supplied by variant circle of Willis vessels. Dysregulation of cerebral blood flow may cause ischemia and increase metabolic demand related to neuronal hyperexcitability, leading to cortical spreading depression, and may predispose individuals with migraine to ischemic lesions and stroke. However, it was hard to determine the relationship between cerebral blood flow and specific symptoms since a variety of symptoms were observed in the present study. However, the fact that 20.6% of our patients had a family history of transient ischemic attack or migraine, which implies that A1 segment hypoplasia/aplasia is somehow related with neurological diseases and might play a role in the occurrence of neurological diseases in the long term. There has been no detailed longitudinal report on the change in brain vasculature in relation to growth and development. It is important to observe children with A1 segment hypoplasia/aplasia on a regular basis and to check their physical conditions when they reach adulthood.

Most pediatric patients with A1 segment hypoplasia/aplasia tend to have a single unilateral vascular abnormality. We also observed only 1 child with bilateral A1 segment hypoplasia/aplasia, and he was also the only one with cerebral infarction. However, patients with A1 segment hypoplasia combined with other variation in the circle of Willis showed significantly higher incidence (79.4%) of brain lesion on MRI. This might be due to the presence of less effective collateral pathway, which possibly creates a pathologic environment for the brain. Although A1 segment hypoplasia/aplasia is not directly associated with any specific neurological disease, we recommend more active evaluation and extended term follow up studies in pediatric patients, especially in those with combined vascular abnormalities.

Children with cerebral vascular variations have a higher possibility of developing alteration in the cerebral vasculature as they grow old; for example, atherosclerosis may act as a worsening factor. Bad diet or living habits can quicken the manifestation of diabetes, hypertension or other adult diseases and aggravate vascular changes as well[18-20]. For children with continuous neurological symptoms or with a family history of transient ischemic attack, it would be helpful to evaluate variations in the circle of Willis, especially focusing on A1 segment hypoplasia/aplasia. MRA could be very useful in such cases. Structural alterations in the cerebral vasculature in children have important pathophysiological and clinical implications. Identifying such alterations could help us better understand a developmental mechanism for cerebrovascular disease or infarction susceptibility, screen pediatric patients with a possible risk of progressive cerebral ischemia, and provide them with preventative therapies accordingly. Further studies on A1 segment hypoplasia in normal pediatric populations might help us better understand its implications, and a large-scale prospective study on the influence

of cerebral vascular variations in children with neurological diseases will help us even further.

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한 글 요 약

소아신경 환아에서 뇌혈관 자기공명 조영술에 의해 발견된 전대뇌동맥 첫번째 분지의 형성저하/무형성

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*연세대학교 의과대학 영상의학교실**

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목 적 : 대뇌동맥륜의 변이는 흔하지 않지만, 그 중 가장 많이 관찰되는 유형은 전대뇌동맥 첫번째 분지(A1 segment)의 형성저하/무형성이다. 저자들은 소아신경 환아에서 전대뇌동맥 첫번째 분지의 형성저하/무형성의 발생빈도와 임상적 의의에 대해 연구하였다.

방 법 : 뇌혈관 자기공명 조영술을 시행한 환아들 중 전대뇌동맥 첫번째 분지의 형성저하/무형성을 보인 환아들을 대상으로 후향적 연구를 하였으며 단독으로 전대뇌동맥 첫번째 분지의 형성저하/무형성의 변이를 보인 환아들과 다른 대뇌동맥륜의 변이를 동반한 환아들의 임상 및 영상의학적 양상을 비교 분석하였다.

결 과 : 뇌혈관 자기공명 조영술을 시행한 301명의 환아들 중 34명(11.3%)이 전대뇌동맥 첫번째 분지의 형성저하/무형성의 소견을 보였다. 환아들은 만성 두통, 어지러움, 시각장애 같은 신경학적 증상을 보였는데, 34명 중 7명(20.6%)은 신경학적 질환의 가족력을 가지고 있었다. 27명(79.4%)은 전대뇌동맥 첫번째 분지의 형성저하/무형성의 단독 변이를 보였고, 7명(20.6%)은 다른 혈관 이상을 동반하고 있었다. 또한 7명(20.6%)에서는 뇌 자기공명 영상에서 이상 소견을 보였고, 뇌위축 소견이 5명(14.7%)으로 가장 많았다. 단독 혈관 변이를 보인 환아 중 뇌 자기공명 영상의 이상 소견을 보인 빈도는 11.1% (3/27)이었고 다른 혈관 이상을 동반한 환아에서의 빈도는 57.1% (4/7)로 통계학적으로 유의하였다.

결 론 : 소아에서 뇌혈관의 구조적 변이는 병태생리학적으로 또한 임상적으로 중요한 영향을 미칠 수 있으므로 뇌혈관 자기공명 조영술을 이용하여 대뇌동맥륜의 변이들, 특히 전대뇌동맥 첫번째 분지의 형성저하/무형성에 대한 적극적인 평가가 필요할 것으로 판단된다.

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