High Incidence of Persistent Primitive Arteries in Moyamoya and Quasi-Moyamoya Diseases

Masaki KOMIYAMA, Hideki NAKAJIMA, Misao NISHIKAWA, Toshihiro YASUI, Shouhei KITANO*, Hiroaki SAKAMOTO*, and Yoshihiko FU**

Departments of Neurosurgery and *Pediatric Neurosurgery, Osaka City General Hospital, Osaka; **Department of Neurosurgery, Tsukazaki Hospital, Hyogo

Abstract

This study investigated the incidences of persistent primitive arteries in patients with moyamoya disease, unilateral moyamoya disease, and quasi-moyamoya disease. Cerebral angiograms of 50 patients (39 moyamoya disease patients, 6 unilateral moyamoya disease patients, and 5 quasi-moyamoya disease patients) were retrospectively reviewed. There were 35 females and 15 males, aged from 3 to 63 years (mean 27.4 years). Persistent primitive carotid-basilar artery anastomoses were observed in three patients: primitive hypoglossal artery in one moyamoya disease patient, primitive trigeminal artery variant in one unilateral moyamoya disease patient, and an anastomosis between the accessory meningeal artery and the anterosuperior cerebellar artery in one quasi-moyamoya disease patient. The ophthalmic artery originated from the middle meningeal artery in three moyamoya and two quasi-moyamoya disease patients. The incidence of the persistent primitive arteries is significantly higher in patients with moyamoya disease (10.7%) and quasi-moyamoya disease (60%) than in patients with other disease (0.67%) (p < 0.001), so congenital factors may be important in the pathogenesis of moyamoya disease.

Key words: moyamoya disease, ophthalmic artery, primitive carotid-basilar artery anastomosis, primitive trigeminal artery

Introduction

Moyamoya disease has been known more than 30 years, but the etiology remains unclear. Acquired origin is more favored than congenital origin because serial angiographic observation of moyamoya disease patients shows progressive occlusive changes at the distal internal carotid arteries as well as development of basal moyamoya vessels. However, symmetry of the abnormal vasculature, familial occurrence, infantile occurrence, high prevalence among Japanese, associated persistent primitive arteries, and associated hereditary diseases suggest that the etiology cannot be simply considered as acquired.

Persistent primitive arteries have been found in association with moyamoya disease. Whether the underlying mechanisms that cause steno-occlusive changes at the distal internal carotid artery are the same or different is unknown. However, investigation of patients with persistent primitive arteries may provide some clues to the pathogenesis of moyamoya disease, unilateral moyamoya disease, and quasi-moyamoya disease. This retrospective study reviewed the cerebral angiograms of patients with and without moyamoya disease to investigate the incidence of persistent primitive arteries.

Materials and Methods

Diagnosis of moyamoya disease is based upon the clinical symptoms and angiographic features caused by bilateral steno-occlusive changes at the distal internal carotid arteries and/or at the proximal portion of the anterior cerebral and middle cerebral arteries, and development of moyamoya vessels at the base of the brain. Associated systemic diseases are exclusion criteria for moyamoya disease. There is no clear definition of "unilateral" moyamoya disease or "quasi-moyamoya disease." We defined
unilateral moyamoya disease as unilateral steno-occlusive state of the internal carotid artery, and/or anterior cerebral and middle cerebral arteries without atherosclerotic changes, and development of moyamoya vessels on the same side, whereas the contralateral intracranial vessels are normal or do not have typical vascular changes of moyamoya disease. Quasi-moyamoya disease has the same bilateral angiographic features as moyamoya disease and is associated with systemic diseases.

In the last 15 years, we treated 50 patients (35 females and 15 males) aged from 3 to 63 years old (mean 27.4 years). Thirty-nine patients had moyamoya disease, six had unilateral moyamoya disease, and five had quasi-moyamoya disease. The associated systemic diseases in quasi-moyamoya disease were congenital hydrocephalus in two, phacomatosis pigmentovascularis type IIIb in one, Down's syndrome in one, and congenital anastomosis between the portal vein and the inferior vena cava in one.

Film screen magnification angiography was used in the early 18 patients and digital subtraction angiography in the later 32 patients. Bilateral carotid and vertebral angiography were performed in all patients, and selective external and internal carotid artery injections with stereoscopic imaging technique were frequently performed. Cerebral angiograms were retrospectively reviewed with special reference to the persistent primitive arteries.

The incidence of persistent primitive arteries was calculated using the data base of 925 patients who underwent diagnostic cerebral angiography in the last 5 years for whom detailed information was available.

**Results**

The persistent primitive hypoglossal artery as well as basilar tip aneurysm (ruptured and clipped) was noted in a 54-year-old female moyamoya disease patient as reported previously (Fig. 1). Anomalous origin of the left anterosuperior cerebellar artery from the ipsilateral internal carotid artery, known as the primitive trigeminal artery (PTA) variant, and an unruptured aneurysm of the distal anterior cerebral artery was observed in a 36-year-old female unilateral moyamoya disease patient. The right middle cerebral artery was occluded and moyamoya vessels developed on the right side (Fig. 2). An anomalous anastomosis between the accessory meningeal artery and the anterosuperior cerebellar artery was observed in a 3-year-old boy with quasi-moyamoya disease (phacomatosis pigmentovascularis type IIIb) (Fig. 3). This vascular anomaly was considered to be another variant of PTA and was reported elsewhere in detail.

Ophthalmic artery originating from the ipsilateral...
middle meningeal artery was observed in three patients with moyamoya disease and two patients with quasi-moyamoya disease (Fig. 4). There was no ophthalmic artery originating from the ipsilateral internal carotid artery, and ethmoidal moyamoya vessels were demonstrated through the ophthalmic artery anastomoses with the middle meningeal arteries in these five patients.

In the last 5 years, 1063 diagnostic angiograms were performed in 925 patients. There were 28 moyamoya and five quasi-moyamoya disease patients, and 892 non-moyamoya disease patients. Among the 28 moyamoya disease patients, one patient had primitive hypoglossal artery (3.6%) and two patients had the ophthalmic artery originating from the middle meningeal artery (7.1%). Among the five quasi-moyamoya disease patients, one patient had the PTA variant (20%) and two patients had the ophthalmic artery originating from the middle meningeal artery (40%). Among the 892 non-moyamoya disease patients, two patients had the PTA (0.22%), three had the PTA variant (0.34%), and one had the ophthalmic artery originating from the middle meningeal artery (0.11%).

Discussion

Several primitive carotid-basilar artery anastomoses, the primitive trigeminal, otic (acoustic), hypoglossal, and proatlantic intersegmental arteries, are present in the early embryological stage. Some may remain without involution as persistent primitive carotid-basilar artery anastomoses. Only 10 patients with these anastomoses in association with moyamoya disease have been reported.1,4,7,8,12,13,19,21) (Table 1). Including our two new patients, seven patients had the PTA, four patients had the PTA variant, and one patient had the primitive hypoglossal artery.7) No patients had either the primitive otic or proatlantic intersegmental artery. Among 11 patients with either the PTA or the variant, cases of the vascular anomaly on each side were equal except for a patient with bilateral PTAs.1) In these 11 patients, initial symptoms were caused by hemorrhage in five patients and by ischemia in five patients, and their causes were related to the moyamoya disease and not to the primitive arteries.

The PTA runs along the trigeminal nerve and anastomoses with the internal carotid artery at the C4-5 segments and the basilar artery between the anterosuperior cerebellar arteries and the anterior inferior cerebellar arteries. The PTA is first observed in the 3-mm embryo.14) This artery communicates with the primitive internal carotid artery at the 4-mm stage. The PTA also communicates with a fragment of the longitudinal neural artery. The basilar artery is formed by the union of the paired longitudinal neural arteries at 7- to 12-mm stage. The
PTA begins to involute and then disappears at the 14-mm stage. The incidence of the PTA is estimated at 0.1–0.2%.10

The PTA variant (trigeminocerebellar artery variant) is postulated to be the result of a persistent PTA associated with an incomplete fusion of the longitudinal neural arteries.2 Some patients with this anomaly have a communication between the cerebellar artery and the basilar artery. The incidence of this anomaly is 0.18%.17 The anastomosis between accessory meningeal artery and the anterosuperior cerebellar artery in our series is explained by the persistent anastomosis between the primitive stapedial artery and the PTA variant (stapedo-trigemino-cerebellar artery variant).5

The ophthalmic artery originated from the middle meningeal artery reaching the orbit through the superior orbital fissure in five patients. This anomaly is caused by the anastomosis between the primitive ophthalmic artery and the orbital branch of the primitive stapedial artery. Regression of the proximal segment of the primitive ophthalmic artery causes the ophthalmic artery to originate from the middle meningeal artery (ophthalmostapedial artery anastomosis).13 The incidence of this anomaly is 0.1%.15

The incidence of the persistent PTA, PTA variant, and the ophthalmic artery originating from the middle meningeal artery is 0.1–0.2%.10,15,17 In our series, persistent primitive arteries were observed in six of 892 non-moyamoya disease patients (0.67%), in three of 28 moyamoya disease patients (10.7%), and three of five quasi-moyamoya disease patients (60%) in the last 5 years. Thus, the incidence of the persistent primitive arteries was significantly higher in patients with moyamoya and quasi-moyamoya diseases (p < 0.001).

Etiologies to cause steno-occlusive changes at the distal portion of the internal carotid artery and development of moyamoya vessels in moyamoya disease and quasi-moyamoya disease are unknown. It is also unknown that these unknown etiologies in moyamoya disease and quasi-moyamoya disease are identical or different. However, it can be concluded from our study that congenital factors may be important in the pathogenesis of moyamoya disease and quasi-moyamoya disease due to the high incidence of persistent primitive arteries.

Table 1 Summary of cases of persistent primitive carotid-basilar artery anastomoses associated with moyamoya disease

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Author (Year)</th>
<th>Age</th>
<th>Sex</th>
<th>Vascular anomaly</th>
<th>Laterality of anomaly</th>
<th>Onset</th>
<th>Side of symptoms</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Otsuki et al. (1982)8</td>
<td>51</td>
<td>M</td>
<td>PTA</td>
<td>lt</td>
<td>hemorrhage</td>
<td>lt</td>
<td>quasi-moyamoya disease?</td>
</tr>
<tr>
<td>2</td>
<td>Kwak and Kadoya (1983)8</td>
<td>44</td>
<td>M</td>
<td>PTA</td>
<td>rt</td>
<td>hemorrhage</td>
<td>lt</td>
<td>falx artery aneurysm</td>
</tr>
<tr>
<td>3</td>
<td>Nakao and Fukumitsu (1985)12</td>
<td>56</td>
<td>F</td>
<td>PTA</td>
<td>lt</td>
<td>hemorrhage</td>
<td>rt</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Kinjo et al. (1988)10</td>
<td>16</td>
<td>F</td>
<td>PTA</td>
<td>rt</td>
<td>ischemia</td>
<td>lt</td>
<td>onset at the age of 6</td>
</tr>
<tr>
<td>5</td>
<td>Kurose et al. (1989)17</td>
<td>44</td>
<td>F</td>
<td>PHA</td>
<td>lt</td>
<td>infarction</td>
<td>lt</td>
<td>basilar tip aneurysm</td>
</tr>
<tr>
<td>6</td>
<td>Tan et al. (1991)20</td>
<td>35</td>
<td>F</td>
<td>PTA</td>
<td>rt</td>
<td>loss of consciousness</td>
<td>not specified</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Chen and Liu (1993)13</td>
<td>64</td>
<td>F</td>
<td>PTA</td>
<td>bil</td>
<td>hemorrhage</td>
<td>lt</td>
<td>rt PTA aneurysm</td>
</tr>
<tr>
<td>8</td>
<td>Suzuki et al. (1990)19</td>
<td>2</td>
<td>F</td>
<td>PTA variant</td>
<td>lt</td>
<td>infarction</td>
<td>bil</td>
<td>identical twin</td>
</tr>
<tr>
<td>9</td>
<td>6</td>
<td>F</td>
<td>PTA variant</td>
<td>lt</td>
<td>infarction</td>
<td>bil</td>
<td>identical twin</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Present series</td>
<td>36</td>
<td>F</td>
<td>PTA variant</td>
<td>lt</td>
<td>hemorrhage</td>
<td>rt</td>
<td>unilateral moyamoya disease</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td>M</td>
<td>PTA variant*</td>
<td>rt</td>
<td>infarction</td>
<td>rt</td>
<td>quasi-moyamoya disease</td>
<td></td>
</tr>
</tbody>
</table>


References


Neurol Med Chir (Tokyo) 39, June, 1999
This retrospective review of a large series of angiograms by Komiyama et al. has demonstrated a higher incidence of persistent primitive arteries in patients with moyamoya disease and moyamoya syndrome than in the general population undergoing angiography for other conditions. Epidemiological studies such as this often lend insight into the etiology and pathogenesis of disorders. The higher incidence of persistent primitive arteries in patients with moyamoya disease and syndrome suggest there may be congenital factors that influence the development of progressive occlusive changes in the intracranial arteries. Such epidemiologic studies often raise more questions than answers.

In the present series, ten percent of the patients with moyamoya disease had persistent primitive arteries. This observation does not shed light into the etiology of the condition in the other ninety percent. Additionally, in this series and other reports of persistent primitive arteries in moyamoya disease, there is no clear relationship between the side of the persistent artery and the side of the patient's symptoms. These observations are not criticisms of this retrospective review. Careful evaluation of epidemiologic factors often provides important pieces to an evolving puzzle. Possibly, the condition we term "moyamoya disease," in fact, is related to a variety of etiologies. The final angiographic picture may illustrate the limited repertoire of manifestations of the cerebral vasculature to a variety of insults.

Daniel L. Barrow, M.D.
Department of Neurosurgery
Emory University School of Medicine
Georgia, U.S.A.

Authors studied the incidence of persistent primitive arteries in moyamoya and quasi-moyamoya diseases,

Neurul Med Chir (Tokyo) 39, June, 1999
utilizing a retrospective analysis. They reviewed the reported cases of primitive arterial anastomoses in association with moyamoya disease, including their own cases. They found that the incidence of persistent primitive arteries is significantly higher in patients with moyamoya disease and quasi-moyamoya diseases than other diseases, and concluded that congenital factors may conduct an important role in the pathogenesis of moyamoya disease.

As pointed out by Pierre Lasjaunias, arterial territory evolves from a state of hemodynamic balance into an anatomic variant, which is fulfilled by anastomosis, annexation and disappearance of blood vessels during ontogenesis. Anatomic variant reflects the final result of the various orienting forces from outside sources exerted on the embryo during its development. Ischemia, which develops in patients with moyamoya and quasi-moyamoya diseases, appears when regional balance is destroyed, and eventually lead to variation of anastomotic vessels. Persistent primitive arteries such as hyoid, otic, or trigeminal arteries, and contralateral rete mirabile may be the point of entry of vascular rerouting in cases of segmental agenesis of certain parts of the internal carotid artery. In this sense, it seems intrinsic that the incidence of persistent primitive arteries is higher in patients with moyamoya disease and quasi-moyamoya disease. However, we would agree with the author's conclusion that congenital factors play an important role in the pathogenesis of moyamoya and quasi-moyamoya disease.

Kyu Sung Lee, M.D.
and Kyu Chang Lee, M.D.
Department of Neurosurgery
Yonsei University College of Medicine
Seoul, R.O.K.

The authors retrospectively investigated the angiographic characteristics of moyamoya disease and its related diseases and pointed out the high incidence of persistent primitive arteries and other variants of congenital angiographic architecture such as middle meningeal origin of the ophthalmic artery. They concluded that the persistent trigeminal artery is present significantly more often than in non-moyamoya disease patients and discussed congenital factors in the pathogenesis of moyamoya disease.

The authors should be congratulated for their novel findings. Persistent primitive arteries usually share the physiological blood supply to the brain and their role can be enhanced in moyamoya disease.

Yoshiaki Shikawa, M.D.
Department of Neurosurgery
Kyorin University School of Medicine
Tokyo, Japan

This is a retrospective study dealing with the congenital vascular anomalies associated with moyamoya and quasi-moyamoya diseases. The authors found persistent primitive carotid-basilar anastomosis in three cases, and the ophthalmic artery originating from the middle meningeal artery in 5 cases among 50 patients (39 cases of moyamoya, 6 cases of unilateral moyamoya and 5 cases of quasi-moyamoya disease). They suggested that these incidences of "congenital vascular anomaly" was significantly higher in these patients compared with patients with other diseases. They also suggested that this may indicate that congenital factors are involved in the pathogenesis of moyamoya disease. In this study, they showed consecutive statistical findings of angiography during last 15 years and showed the results of incidence of persistent primitive artery and ophthalmic artery originating from the middle meningeal artery. This is a valuable contribution to the investigation of moyamoya disease and these data should be taken in consideration carefully.

There is confusion concerning the definition of moyamoya disease. The authors defined quasi-moyamoya disease as cases showing the same bilateral angiographic features as moyamoya disease and associated with systemic diseases. According to reference no. 21 of this article, Watanabe and Suzuki defined quasi-moyamoya disease as moyamoya-like cases not fulfilling the strict criteria of "true" moyamoya disease. It is apparent that quasi-moyamoya disease includes unilateral moyamoya, moyamoya vessels with occlusion or stenosis not in the terminal portion of the internal carotid artery and typical angiographic appearance of moyamoya disease with known causal lesion. I think some cases of quasi-moyamoya disease in this article should be classified into "true" moyamoya disease. Furthermore, unilateral moyamoya in this article should be classified into quasi-moyamoya disease.

The authors included the ophthalmic artery originating from the middle meningeal artery (ophthalmomo-stapedial artery anastomosis) into the same "congenital" category with persistent primitive arteries. They cited the article by Picard et al. (ref. 15 of this article) and indicated the incidence of this anomaly as 0.1%. With the development of high quality digital angiographical method and improved angiographical techniques (i.e. super-selective angiography, etc.), the incidence of this "anomaly" is much higher than expected in my own experience.

It is still difficult to understand the pathogenesis of moyamoya disease. Genetic investigation concerning familial moyamoya disease suggests DNA abnormality is commonly found in these cases. However, scientific analysis of this rare disease needs more
cases and time to achieve any conclusion.

Reference


Akira TAKAHASHI, M.D.
Department of Neuroendovascular Therapy
Tohoku University School of Medicine
Sendai, Japan