

## Pediatric moyamoya disease associated with ipsilateral internal carotid artery agenesis: illustrative case

Kokoro Kamisaka, MS, Shusuke Yamamoto, MD, Taisuke Shiro, MD, Emiko Hori, MD, PhD, Daina Kashiwazaki, MD, PhD, Naoki Akioka, MD, and Satoshi Kuroda, MD, PhD

Department of Neurosurgery, Graduate School of Medicine and Pharmaceutical Science, University of Toyama, Toyama, Japan

**BACKGROUND** Although most cases of internal carotid artery (ICA) agenesis are clinically silent due to a well-developed collateral pathway, some cases may develop ischemic symptoms when they are associated with other occlusive cerebrovascular disorders. The authors describe herein the first case with ICA agenesis that developed ischemic attack because of coincidence with moyamoya disease.

**OBSERVATIONS** A 3-year-old girl was admitted to the authors' hospital due to sudden onset of right arm weakness followed by clonic convulsion. Skull computed tomography could not identify the carotid canal on the left side. Simultaneously, magnetic resonance (MR) imaging and MR angiography demonstrated the luminal stenosis and outer diameter reduction of the carotid fork and posterior cerebral artery on the left side. She was diagnosed with unilateral moyamoya disease associated with ipsilateral ICA agenesis. She successfully underwent combined bypass surgery on the left side and has been free from any cerebrovascular events during a follow-up period of 6 months.

**LESSONS** When patients with ICA agenesis develop ischemic symptoms, careful investigation of the cause and appropriate care, including surgical treatment, are required.

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**KEYWORDS** internal carotid artery agenesis; moyamoya disease; combined bypass surgery

Moyamoya disease is a unique cerebrovascular disorder characterized by progressive occlusion in the terminal portion of the internal carotid artery (ICA) and its main branches, the anterior and middle cerebral arteries (ACA and MCA, respectively).<sup>1,2</sup> ICA agenesis is a rare malformation disorder that is estimated to occur in less than 0.01% of the population.<sup>3</sup> However, no case with ICA agenesis that developed moyamoya disease had been reported previously. In this report, we described the first case of pediatric moyamoya disease associated with ipsilateral ICA agenesis that emerged with ischemic stroke.

### Illustrative Case

A 3-year-old girl with intellectual disability was referred to our hospital because she suddenly developed right arm weakness followed by clonic convulsion in her right extremities. Physical examination showed

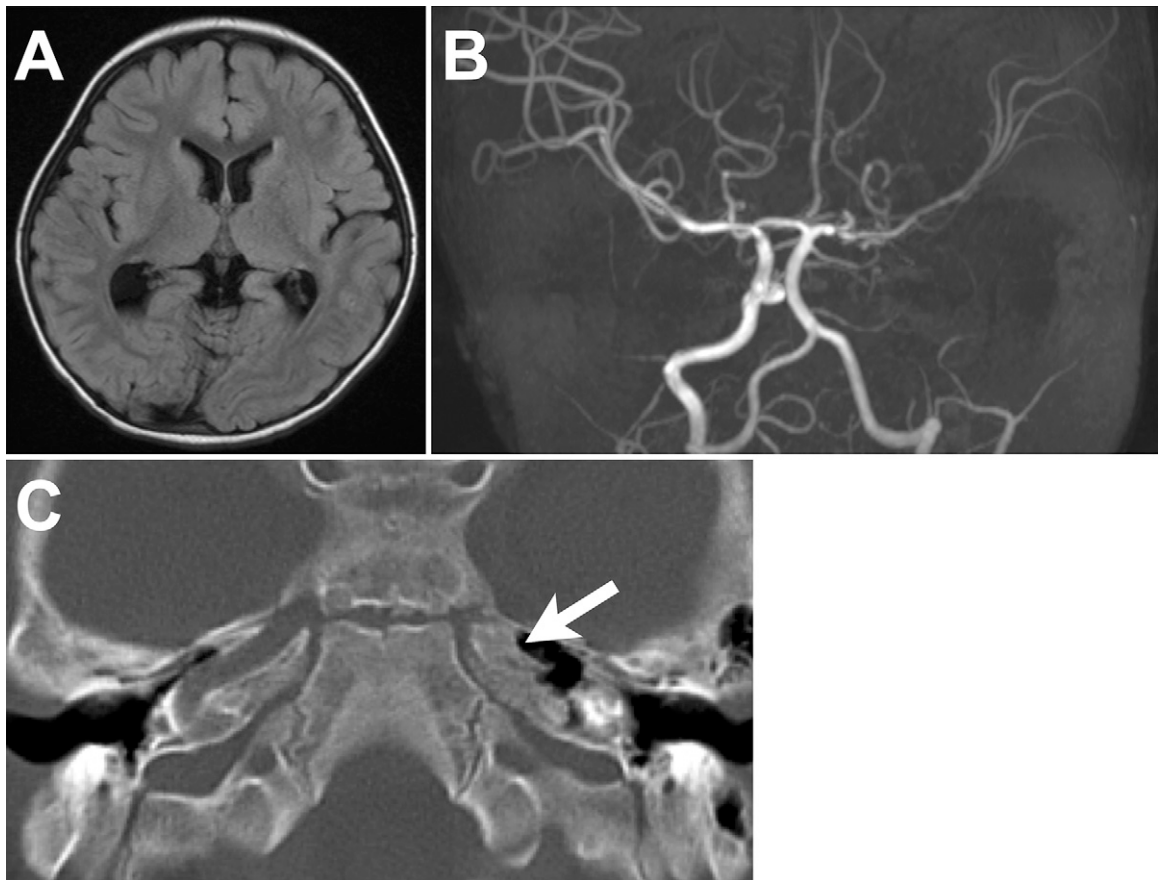
no other abnormal findings. Magnetic resonance (MR) imaging (MRI) showed no abnormalities in the brain parenchyma (Fig. 1A). MR angiography demonstrated the defect of the proximal portion of the left ICA. The left posterior communicating artery (PcomA) directly provided collateral blood flow to the horizontal portion of MCA (M1), and the left ACA originated from the M1 portion, making the horizontal portion of the ACA (A1) longer than usual. In addition, MR angiography showed severe stenosis of the horizontal portion of the MCA and the posterior cerebral artery (PCA) on the left side (Fig. 1B and C). Skull computed tomography (CT) demonstrated no development of the carotid canal on the left side (Fig. 1C). On three-dimensional constructive interference in steady state (3D-CISS), the outer diameter of the M1 and the peduncular portion of the PCA (P2) were smaller on the left side than on the right side. The values of each portion were 1.4 mm versus

**ABBREVIATIONS** 3D-CISS = three-dimensional constructive interference in steady state; ACA = anterior cerebral artery; CT = computed tomography; ICA = internal carotid artery; MCA = middle cerebral artery; MR = magnetic resonance; MRI = magnetic resonance imaging; PCA = posterior cerebral artery; PcomA = posterior communicating artery; STA = superficial temporal artery; TIA = transient ischemic attack.

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**FIG. 1.** No parenchymal lesions were observed on fluid-attenuated inversion recovery MRI at initial presentation (A). MR angiography showed that the left ICA was absent. The horizontal portion of the left MCA (M1) was directly provided collateral blood flow from the left PcomA. The left ACA originated from M1 portion (B). Skull CT scan showed the defect of the left carotid canal (C, arrow).

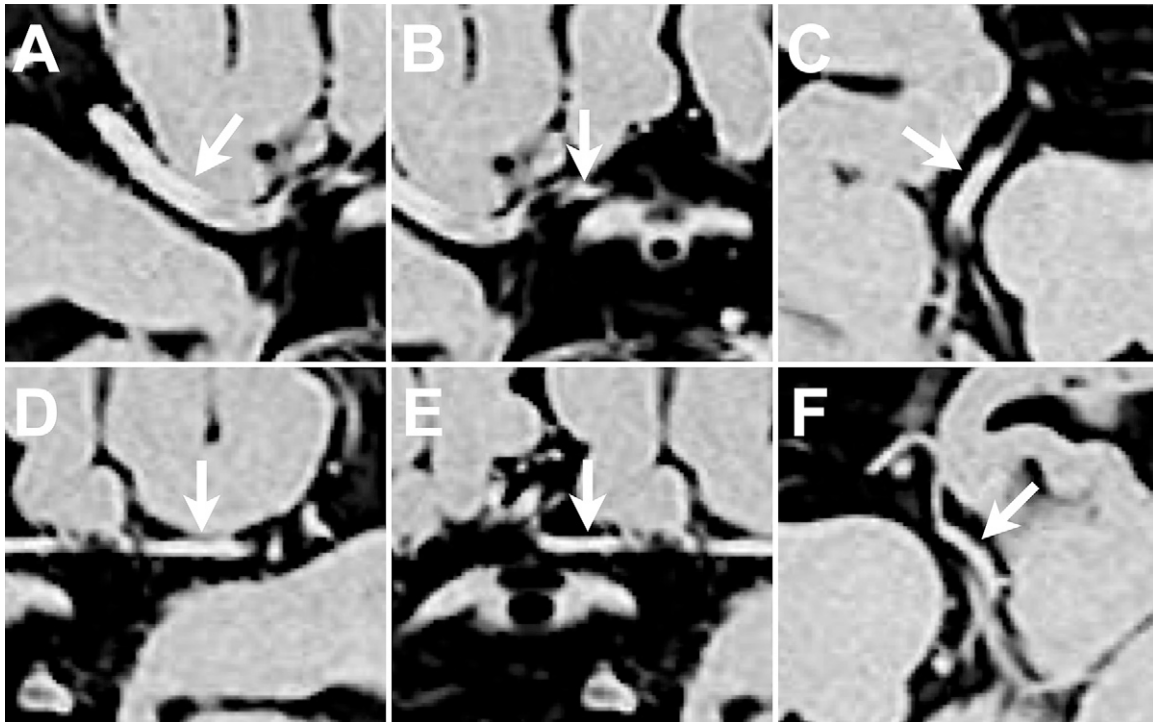
2.2 mm and 0.8 mm versus 1.6 mm, respectively. The outer diameter of the A1 portion was 1.2 mm on both sides (Fig. 2). Given the results, she was considered to have congenital left ICA agenesis and acquired unilateral moyamoya disease on the same side. *N*-isopropyl-*p*-[<sup>123</sup>I]-iodoamphetamine single-photon emission computed tomography showed a marked decrease of cerebral blood flow in the left cerebral hemisphere, including the ACA, MCA, and PCA territories (Fig. 3A, arrows). She underwent superficial temporal artery to middle cerebral artery (STA-MCA) double anastomosis combined with encephalo-duro-my-arterio-pericranial synangiosis on the left side.<sup>4-6</sup> To eliminate cerebral ischemia in the ICA and PCA territories, we applied the one-stage method that we developed previously.<sup>7</sup> During surgery, the frontal and parietal branches of the STA were anastomosed to the central artery and the posterior temporal artery in an end-to-side fashion with 10-0 nylon threads, respectively. The patency was confirmed using indocyanine green video angiography. The dural flaps were turned into the epirachnoid space. Then, the brain surface was covered using the temporal muscle and frontal pericranium. The patient's postoperative course was uneventful. Her cerebral blood flow markedly recovered in the left whole hemisphere, including the ACA, MCA, and PCA territories, 5 days after surgery (Fig. 3B). On the follow-up MR angiography performed 4 months after surgery, the STA-MCA bypasses were patent. On the one hand, the middle meningeal artery and deep

temporal artery markedly dilated their caliber, indicating the sufficient development of indirect bypass.<sup>8</sup> On the other hand, the flow signal of the left ACA and MCA disappeared, which suggested the progression of disease stage during 4 months after surgery (Fig. 3C). She has been free from any cerebrovascular events for 6 months after surgery.

## Discussion

ICA agenesis occurs at an early stage during embryonic development, and the diagnosis is based on proving the absence of a carotid canal on a CT scan. The pattern of collateral circulation in ICA agenesis varies from case to case and has been classified into six patterns by Lie.<sup>9</sup> Among them, the collateral pattern in this case was "unilateral absence of the ICA with collateral circulation to the ipsilateral ACA through the anterior communicating artery (AcomA) and to the ipsilateral MCA through the PcomA," which was considered type A of Lie.<sup>9</sup>

Recent studies using heavy T2-weighted MRI, including the 3D-CISS technique, have shown that the involved arteries specifically decrease their outer diameter as well as their internal caliber in moyamoya disease.<sup>10,11</sup> Furthermore, involved PCAs also decrease their outer diameters.<sup>12</sup> These phenomena may be related to specific pathological changes, including fibrocellular thickening of the intima, an irregular undulation (waving) of the internal elastic lamina, and



**FIG. 2.** With the use of 3D-CISS, the outer diameters of the horizontal portion of MCA (M1), the outer diameters of the horizontal portion of ACA (A1), and the peduncular portion of PCA (P2) on the right side (A–C) and the left side (D–F) were quantified. The values of right M1 and P2 segments were smaller in the right side than the left side (1.4 mm vs. 2.2 mm, and 0.8 mm vs. 1.6 mm, respectively). The values of A1 segments were 1.2 mm in both sides. Arrows show the sites of quantification.

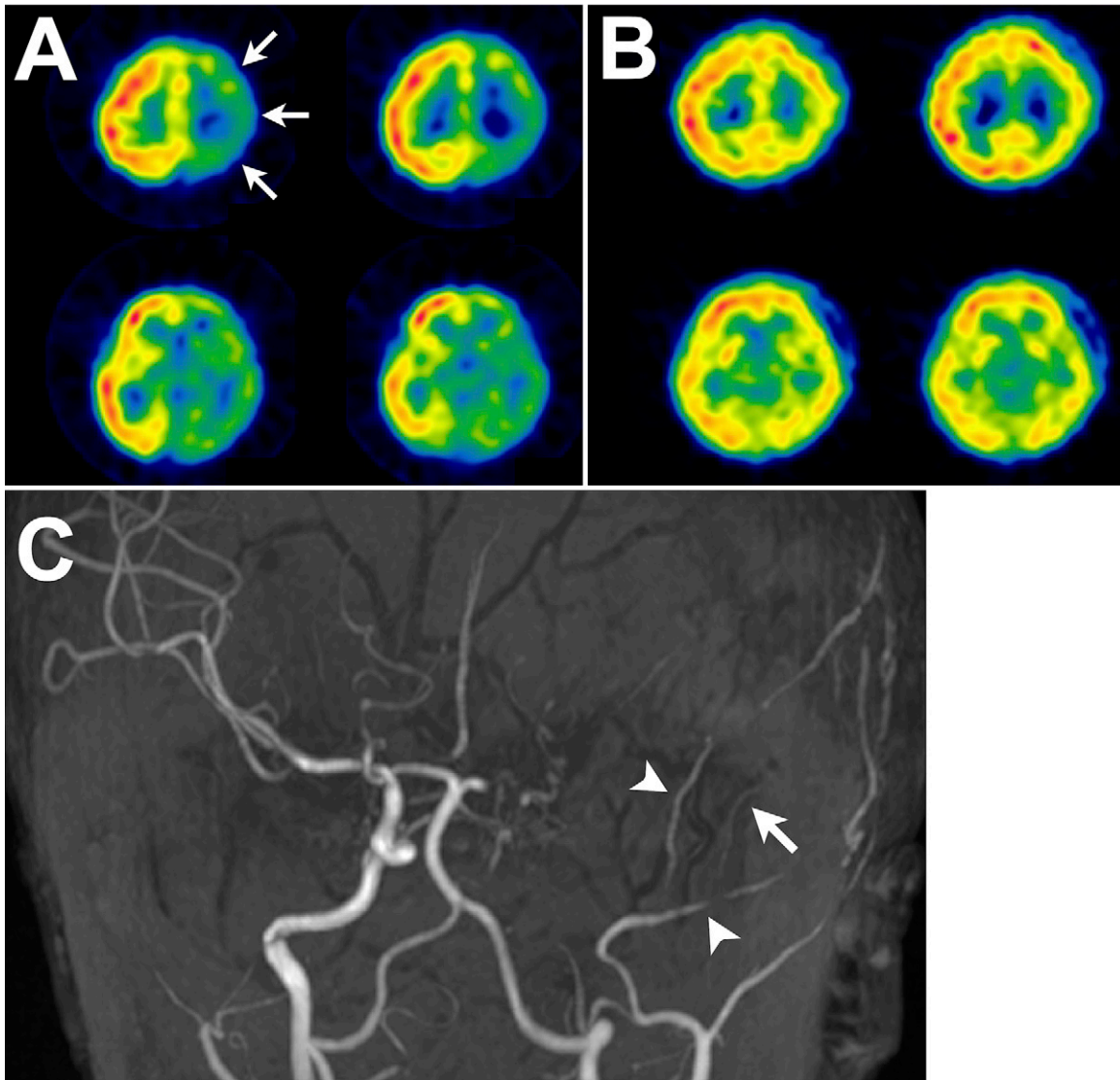
attenuation of the media in moyamoya disease.<sup>13,14</sup> Intimal thickening should lead directly to narrowing of the arterial lumen. In contrast, attenuation of the media and waving of internal elastic lamina could decrease the volume of the arterial wall, causing narrowing of the outer diameter. Because such shrinkage of involved arteries is not observed in intracranial arterial stenosis, this is quite helpful to distinguish moyamoya disease from other disorders such as atherosclerosis in elderly patient cases.<sup>10</sup> In this case, MR angiography showed a marked stenosis in the left M1 and P2 portions. There is a possibility that cerebral ischemia due to ICA agenesis resulted in the reduction of the flow signal on MR angiography, which appeared to be moyamoya disease. However, 3D-CISS images demonstrated that their outer diameters were smaller than those on the contralateral side, which is a pathognomonic finding of moyamoya disease.<sup>10–12</sup> Furthermore, MR angiography performed 4 months after combined bypass surgery clearly showed the disappearance of flow signal of the left ACA and MCA, which is a commonly observed disease progression after surgery in moyamoya disease.<sup>15</sup> In addition, postoperative dilatation of the middle meningeal artery and deep temporal artery in this case strongly suggests the development of surgical collaterals through indirect bypass, which also supports the diagnosis of moyamoya disease.<sup>8</sup> Indeed, there is no report denoting the effect of indirect bypass surgery in ICA agenesis. Moreover, this case was free from abnormal eye findings that indicated the incidence of other syndromes, such as PHACE syndrome (posterior fossa and other structural brain malformations; large hemangiomas of the face, neck, and/or scalp; anatomical anomalies of the cerebral or cervical arteries; cardiac anomalies/coarctation of the aorta; and eye abnormalities) and morning

glory syndrome, that may show malformation of intracranial arteries. Taken together, this case was considered to have had congenital left ICA agenesis and acquired unilateral moyamoya disease on the same side. ICA agenesis is known to be associated with other developmental abnormalities, such as congenital Horner syndrome, PHACE abnormalities, coarctation of aorta Goldenhar syndrome, and Klippel-Feil syndrome.<sup>16–21</sup> However, there are no reports on the coincidence of moyamoya disease with ICA agenesis. We should consider the possibility that a long-term, persistent cerebral ischemia due to ICA agenesis may trigger the occurrence of moyamoya disease.

Zhang et al.<sup>3</sup> reviewed 64 patients with ICA agenesis and divided them into three groups according to their age. Developmental delay was reported in 13 (54.2%) of 24 cases under 20 years of age, which is in good agreement with the clinical course of this case. Until the onset of moyamoya disease, cerebral ischemic symptoms did not occur as a result of extensive collateral blood flow through the PcomA, but later, transient ischemic attack (TIA) in the form of the right arm weakness may have developed due to severe stenosis of the M1 and P1 portions due to moyamoya disease. Convulsive seizures were also thought to have been triggered by cerebral ischemia. In fact, no epileptic seizures occurred after surgery, although no anti-epileptic drugs were administered.

### Observations

In this report, we first described a 3-year-old case of moyamoya disease associated with ipsilateral ICA agenesis that emerged with TIA and epilepsy. In addition to luminal stenosis of the involved arteries, 3D-CISS was quite useful to diagnose this



**FIG. 3.** *N*-isopropyl-*p*-[<sup>123</sup>I]-iodoamphetamine single-photon emission computed tomography on admission showed a marked decrease of cerebral blood flow in the left cerebral hemisphere, including the ACA, MCA, and PCA territories (**A**, arrows). Cerebral blood flow markedly improved in the left whole hemisphere, including the ACA, MCA, and PCA territories, 5 days after combined bypass surgery (**B**). The follow-up MR angiography at 4 months after surgery showed that STA-MCA bypasses were patent. The middle meningeal artery (arrowheads) and deep temporal artery (arrow) were markedly dilated compared with before surgery. The left ACA and MCA were occluded, which suggested the progression of disease stage during 4 months after surgery (**C**).

patient with moyamoya disease by identifying the outer diameter reduction. One-stage revascularization surgery for anterior and posterior circulation could successfully improve cerebral hemodynamics in the whole hemisphere, including the PCA territory.

### Lessons

Although most cases of ICA agenesis are clinically silent, some cases show ischemic symptoms because of coincidence of other occlusive cerebrovascular disorders. When patients with ICA agenesis develop ischemic symptoms, careful investigation of the cause and appropriate care, including surgical therapy, are mandatory.

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#### Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

#### Author Contributions

Conception and design: Kuroda. Acquisition of data: Yamamoto, Kamisaka, Shiro, Kashiwazaki, Akioka, Kuroda. Analysis and interpretation of data: Hori, Kuroda. Drafting the article: Yamamoto, Kamisaka. Critically revising the article: Kuroda. Reviewed submitted version of manuscript: Akioka, Kuroda. Approved the final version of the manuscript on behalf of all authors: Yamamoto. Study supervision: Kuroda.

#### Correspondence

Shusuke Yamamoto: Graduate School of Medicine and Pharmaceutical Science, University of Toyama, Toyama, Japan. shuyama@med.u-toyama.ac.jp.