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W.-J. Moon
L. Porto
H. Lanfermann
R. Weis
F.E. Zanella

Agenesis of internal carotid artery associated with congenital anterior hypopituitarism

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W.-J. Moon (✉)
Department of Diagnostic Radiology,
Samsung Medical Center, 50 Ilwon-dong,
Kangnam-ku, Seoul 135-230, Korea
E-mail: rhiemoon@hananet.net
Tel.: +899-2-34102524
Fax: +899-2-34102559

W.-J. Moon · L. Porto
H. Lanfermann · F.E. Zanella
Institute of Neuroradiology, University
of Frankfurt, Schleusenweg 6,
60528 Frankfurt, Germany

R. Weis
Department of Pediatric Neurology,
University of Frankfurt, Schleusenweg 6,
60528 Frankfurt, Germany

Abstract We report a rare case of unilateral agenesis of the internal carotid artery in association with congenital anterior hypopituitarism. The collateral circulation is supplied by a transsellar intercavernous anastomotic vessel connecting the internal carotid arteries. These abnormalities are well depicted on MRI and MRA. The agenesis of the internal carotid artery may explain the pathogenesis of some of congenital anterior hypopituitarism.

Keywords Arteries · Abnormalities and anomalies · Internal carotid Artery · Pituitary · Congenital hypopituitarism

Introduction

Congenital anterior hypopituitarism has become detectable with the development of magnetic resonance (MR) imaging. MR imaging studies in patients with congenital anterior hypopituitarism reveal hypoplasia of the anterior pituitary and absence or hypoplasia of the pituitary stalk, with or without an ectopic posterior pituitary. Associated midline brain, cranial, and facial anomalies are found in about 10% of anterior hypopituitarism cases [1].

Congenital absence of the internal carotid artery (ICA) is a very rare vascular anomaly. Agenesis, aplasia, or hypoplasia are the three conditions responsible for an absent ICA and reflect different developmental failures. This anomaly may be completely asymptomatic, detected occasionally by skull base CT scan, MR imaging, angiography, or at autopsy or surgical procedures. The symptoms are related to cerebrovascular insufficiency, compression by enlarged intracranial vessels, and associated cerebral aneurysms. Diagnosis is important to explain the clinical and surgical problems related to this condition [2].

To our knowledge, only five previous cases of congenital absence of ICA with hypopituitarism have been reported [1, 3, 4, 5]. In this paper we report a case of agenesis of the left ICA with anterior gland aplasia and an ectopic posterior pituitary. We also discuss the imaging findings and pathogenesis of this condition.

Case report

A 5-year-old male patient presented with known anterior hypopituitarism and cryptorchidism. The patient was born vaginally to

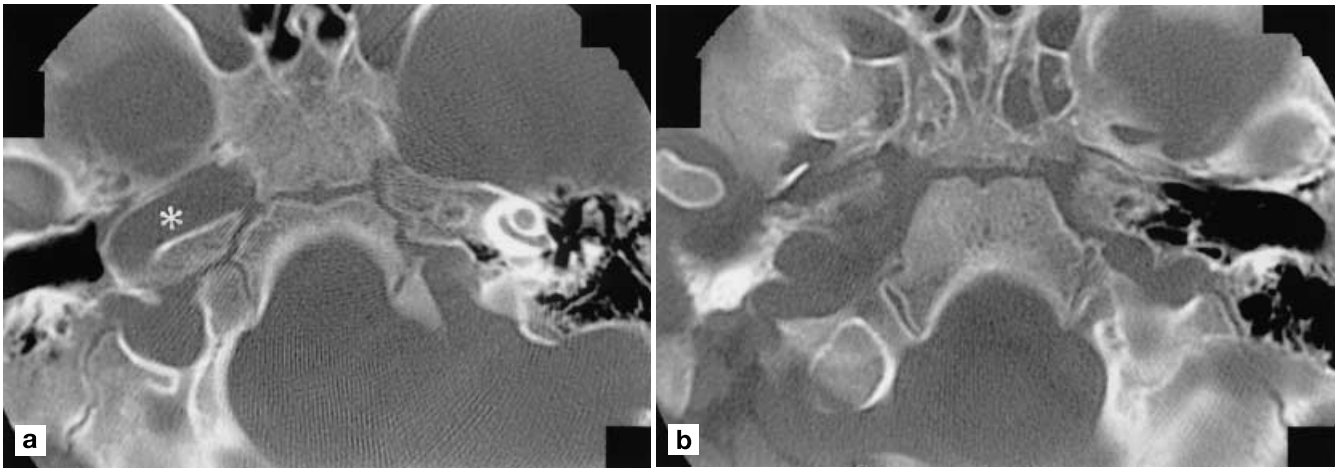

Fig. 1. High-resolution CT scan (3-mm thickness). The left carotid canal is completely absent. The right carotid canal can be clearly seen (*asterisk*)

a 26-year-old mother after a 42-week uncomplicated pregnancy; birth weight was 3,400 g. In the 2nd trimester of her pregnancy the mother was treated with penicillin for upper airway infection and dental abscess. The child had retrognathia and microphallus when born.

After birth, he exhibited recurrent hypoglycemia and cerebral ketoacidosis. Despite intravenous glucose therapy, he continued to have intermittent hypoglycemia. Endocrinological evaluation showed central hypothyroidism, adrenocortical deficiency, and growth hormone deficiency, but no evidence of diabetes insipidus. The child was started on growth hormone, hydrocortisone, and thyroxine replacement. At age 5 years, his height was at the 3–10 percentile, his weight was at the 50–75 percentile, and he had infantile external male genitalia and cryptorchidism.

CT of the head (Fig. 1) revealed smaller than normal sella turcica and total absence of the left internal carotid canal. MR imaging (Fig. 2) showed no identifiable anterior pituitary and no normal posterior pituitary with an ectopic posterior pituitary. The left ICA was absent and the right ICA was mildly dilated. All other brain structures were normal. MR angiography (Fig. 3) revealed absence of the left ICA, the A1 segment of the left anterior cerebral artery, and the anterior communicating artery. A transsellar intercavernous anastomotic vessel was seen originating from the anterior cavernous segment of the right ICA, crossing the midline, pointing upwards to the left and connecting with the supraclinoid segment of the left ICA. The left A2 segment originated from the right A2 segment. Both posterior communicating arteries appeared normal. No other vascular abnormalities were apparent.

Discussion

Patients with congenital anterior hypopituitarism show highly characteristic features on MRI. The MR findings consist of one or more of the following: small sella turcica, small anterior pituitary, absence of the usual high signal intensity from the posterior pituitary, absence or hypoplasia of the distal pituitary stalk, and abnormal high-signal area in the median eminence. Many of these patients have a history of breech presentation at birth, some have other intracranial anomalies, and some have both midline anomalies and history of breech presentation.

Two hypotheses have been suggested to explain these findings [1]. One theory presumes that head trauma associated with breech delivery causes mechanical transection of the pituitary stalk. This theory does not adequately explain the associated midline anomalies, because these develop long before birth. The alternative theory suggests early fetal maldevelopment of midline structures including the fetal hypothalamic-pituitary axis with failure of fusion of the pituitary lobes. Anterior lobe dysfunction results because the anterior lobe is deprived of parts of its blood supply (via portal veins) and also deprived of hypothalamic stimulating hormones (also normally transmitted via the portal veins).

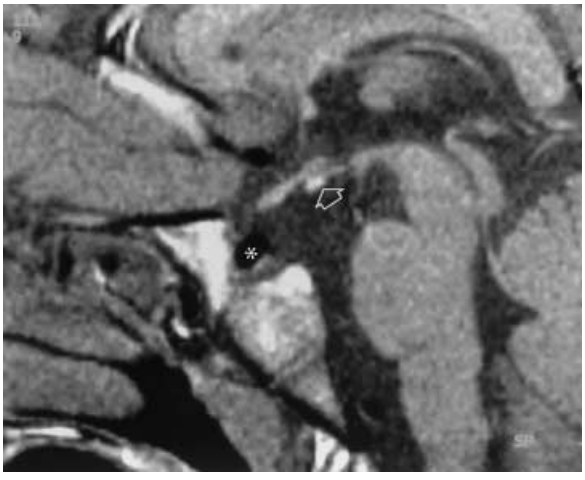

Fig. 2. MRI. A sagittal spin-echo T1-weighted image (450/20/90) shows the absence of the anterior and posterior pituitary gland in the small sella turcica. The ectopic posterior pituitary is seen as a small hyperintense nodule in the median eminence (*open arrow*). The flow void in the sella turcica is the right internal carotid artery (*asterisk*)

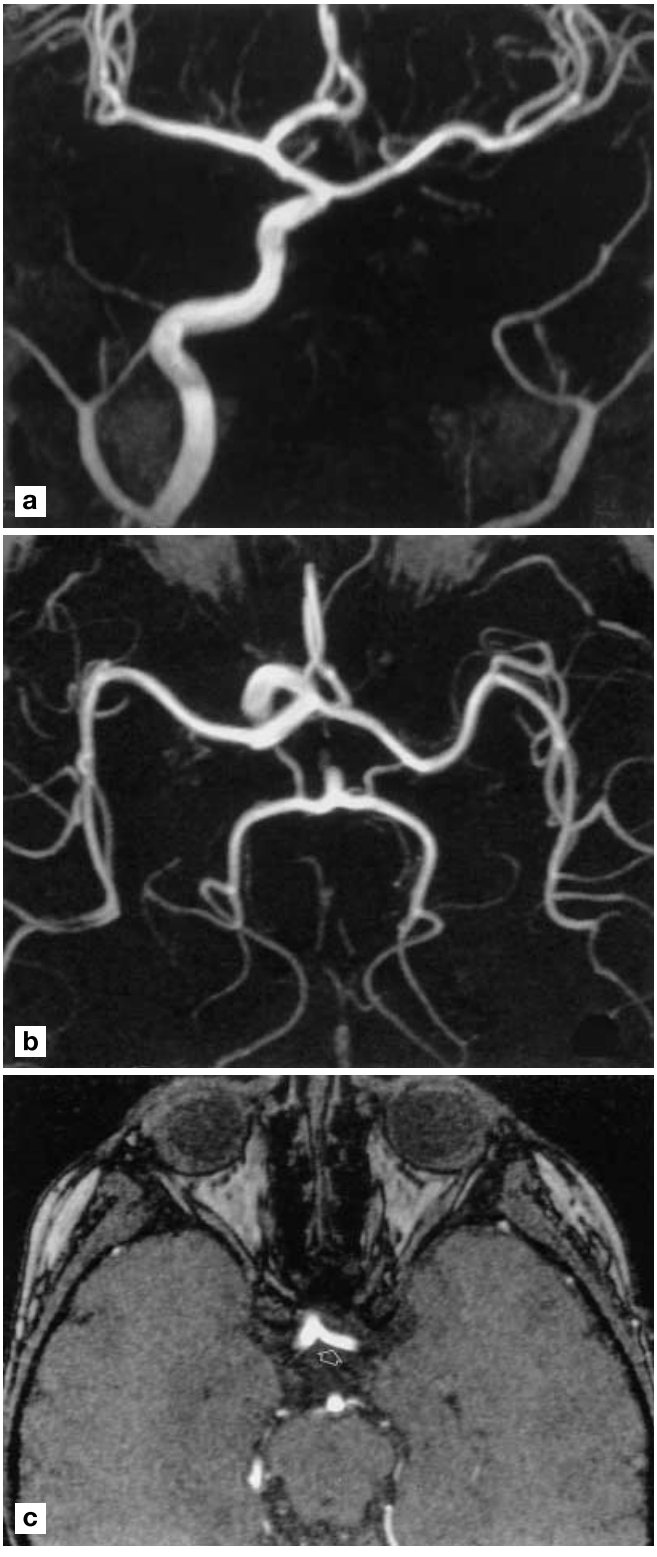

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Fig. 3a–c. MRA. **a** MR angiograms obtained using the 3D time-of-flight technique with 35.0/7.0, flip angle of 20 degrees, and 0.8-mm section thickness. Maximum-intensity projection reconstruction in the anteroposterior view shows absence of the left ICA. **b** Maximum-intensity projection reconstruction in the superoinferior view shows normal posterior communicating arteries and basilar arterial system. **c** Axial source image shows abnormal transsellar intercavernous collateral vessel anastomosing from the right ICA to the left supraclinoid ICA (*open arrow*)

Proponents of this latter theory suggest that fetal position and the normal progress of labor require a normally functioning fetal pituitary. If the fetal gland is dysfunctional, breech presentation and delivery may result. Thus this theory can explain the associations with both breech presentations and midline anomalies [1].

Agenesis of the ICA is a rare finding, with fewer than 80 reports in the literature [2]. It is often clinically silent due to the development of adequate collateral circulation from the contralateral ICA and basilar artery systems. Carotid agenesis is essentially discovered in adult patients, pediatric cases being exceptional. Cases have been associated with hemiplegia, seizures, transient ischemic episodes, intracranial hemorrhage, and a 20%–30% incidence of aneurysm formation. Previously, only five cases of ICA dysgenesis had been reported in association with congenital hypopituitarism, of which two cases were agenesis of ICA, the other three cases being hypoplasia. The mechanism involved in agenesis of the ICA remains controversial. It may result from either regression at a later stage after an initial period of normal development or, more probably, from an early interruption of development.

As stated by Padget [6], such an anomaly occurs before 24 days (3-mm stage) of embryogenesis, where the ICA is formed from the terminal segments of the dorsal aorta and the 3rd aortic arch arteries. If no ICA is present during the development of the skull, beginning at the 5th to 6th week of gestation, no carotid canal develops. ICA branches to the adenohypophyseal pocket develop on the 28th day of gestation. The human pituitary primordia develop at the 4th-week stage. In the 5 weeks of gestation, Rathke's pouch fuses with the infundibulum and gives rise to diverticula formation on the floor of the diencephalon. During the 6th week, the two connected primordia descend to the sphenoid cartilage and reach their final place, and the fetal pituitary is embryologically intact by 11–12 weeks. The hypophyseal portal vascular system develops at 14–15 weeks and is completed by 20 weeks [7]. The blood supply of the anterior and posterior pituitary gland is from the superior and inferior hypophyseal arteries respectively, which arise from the ICAs. The anterior pituitary receives the vast majority of its blood supply indirectly by the hypophyseal portal system.

In our case, agenesis of the left ICA must have occurred before 5 to 6 weeks' gestation as no carotid canal was seen

on CT. The presence of a small sella turcica on CT suggests that an anatomical pituitary in some form was present at the time of skull formation. Therefore, the absence of an anterior pituitary on MR images may be due to transient interruption in the blood flow from the right ICA, which resulted in an inadequate blood supply to sustain both anterior and posterior pituitary growth. However, the normal structure of the brain on MR images in our case suggests good collateral supply. The second possible hypothesis is that maldevelopment of the hypophyseal portal system during weeks 14–20 causes hypopituitary dysfunction. As the anterior pituitary receives most of its blood supply from the hypophyseal portal system, complete disruption of the portal vessels can result in anterior pituitary infarction. The third possible hypothesis is that as an anomalous collateral is prominently dilated crossing the anterior part of the sella; it is also plausible that the dilated collateral vessel compresses the anterior pituitary continuously, which results in anterior pituitary hypoplasia.

Depending on the location of the ICA agenesis, either embryonic arteries or the circle of Willis vessels such as the posterior communicating arteries are used as collateral pathways [8]. Our patient shows the anomalous intercavernous collateral arising from the right ICA and reconstituting most of the supraclinoid portion of the left ICA. It appears almost identical to one described by Lie [9], except that the posterior communicating artery on the affected side appears normal in our case. In the case of unilateral absence of the ICA it is usual that an enlarged posterior communicating artery or anterior communicating artery provides the circulation of the affected hemisphere [9]. In our case, the posterior communicating artery on the affected side was clearly seen but was not enlarged enough to supply the affected hemisphere.

There are two hypotheses to explain the anomalous intercavernous vessels. One is that it is an abnormal anastomosis of the two fetal trigeminal arteries [9]. The other suggests the hypertrophy of normally developing vessels, which include the primitive maxillary [10, 11], the inferior hypophyseal or capsular [12], and preexisting rami from the cavernous carotid artery [13]. In our case, hypertrophy of the normally developing vessel is more plausible. The presence of the normal posterior communicating artery suggests that inadequate collateral supply from the posterior communicating artery may stimulate the occurrence of a hypertrophic intercavernous vessel. In our case, the hypertrophic anterior capsular artery is most likely, because of the anterior location of this vessel inside the sella [12].

Several authors [1, 3, 4, 5] have suggested that the association of ICA dysgenesis and hypopituitarism is another expression of a neural-crest differentiation and/or migration disorder. Among five previously reported cases of the absence of the ICA and hypopituitarism, three cases showed associated midline anomaly such as single central maxillary tooth, transsphenoidal encephalocele, and optic nerve coloboma. Noden [14] cited several studies demonstrating that the smooth muscle cells and connective tissue forming the walls of the aortic arches and most of the craniofacial arteries are of cephalic neural-crest origin. Reinvestigation of the early embryogenesis of the rostromedial part of the brain also shows that the hormone-secreting part of the anterior pituitary derives from the neuroectoderm of the most rostral neural fold rather than from the ectoderm of the stomodeum [10, 11]. Therefore, a defect in early embryogenesis of neural crest might result in poor development of both the ICA and pituitary gland or both the ICA and hypophyseal portal system.

Patients with agenesis of the ICA should be followed clinically and radiologically because of the documented increased frequency of intracranial aneurysm, although they show no clinical symptoms related to vascular anomaly on initial study.

In summary, agenesis of the ICA is a rare associated anomaly in congenital anterior hypopituitarism, can explain pathogenesis in some cases of congenital hypopituitarism, and is also clinically important by itself by reason of the possibility of future development of cerebral aneurysms.

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