



BILATERAL AGENESIS OF THE HUMAN INTERNAL CAROTID ARTERY

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ABSTRACT

Anomalies of the internal carotid artery associated with a violation of its embryonic development are classified as follows: agenesis, aplasia and hypoplasia. Agenesis is a rare vascular abnormality. The search and analyze the scientific articles data concerning the ICA embryogenesis and agenesis, absence of the internal carotid artery, to make comparative analysis of the adult skull with and without ICA. 104 human skulls served us as the research material.

Key words: internal carotid artery, embryonic development, carotid canal

INTRODUCTION

In recent years a growing interest in the development of blood vessels of the brain is connected with requests of vascular surgery, neurosurgery and functional diagnostics. Congenital cerebrovascular pathology, including aplasia or hypoplasia of blood vessels, atypical vessel morphology, etc., is the result of the developmental disorders in the embryonic period. Some of them are compensated and become clinically asymptomatic. Others cause diseases and lead to death due to hemorrhage or ischemia (1). The need for accurate knowledge concerning the development of cerebrovascular pathology is determined by the introduction of new surgical technologies - minimally invasive and endoscopic methods, which pose new challenges for researchers. Aplasia and severe hypoplasia of the internal carotid artery (ICA) are relatively rare congenital vascular disorders detected in less than 0.01% of the population (2-4).

An important role in the formation of vascular disorders, along with acquired factors, plays congenital anomalies associated with the impaired ICA embryogenesis. These include:

agenesis, aplasia and hypoplasia of the ICA. Congenital absence of the ICA can be bilateral but more often unilateral. In many patients, the above pathology remains asymptomatic due to the development of reliable collateral blood supply routes. However, problems arise later in connection with the development of intracranial aneurysms in 25-43% of patients (5-7). After studying the ICA congenital anomalies scientists define agenesis as the complete ICA absence due to complete absence of the carotid canal. In aplasia, some of the ICA segments are preserved, and the carotid canal is underdeveloped. In hypoplasia, the ICA diameter is less than 1.5 mm; the carotid canal is present, but significantly narrowed. The real incidence of carotid artery agenesis is unclear; in most cases, such a congenital pathology is detected occasionally by means of ultrasound, magnetic resonance imaging (MRI) or computed tomography (CT) (8, 9). In 1787 Tode described and documented the case of the ICA absence at autopsy. For the first time, the diagnosis of ICA aplasia was angiographically verified by H. Verbiest. ICA aplasia is most often unilateral, but there are also reports of its being bilateral (10-12). During embryonic development, the arterial system of the brain goes through a complex multi-stage pathway of formation. Artery embryogenesis pathology at any stage determines preservation of cerebrovascular blood supply features inherent in the

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intrauterine period after birth. The development of the cerebrovascular system corresponds to the stages of the central nervous system (CNS) structural maturation. The carotid and vertebral systems in the first months of embryonic development are formed separately of each other. Fusion of the two systems and the formation of the Willis circle occur during the 3rd month of fetal life.

The role of the Willis circle in providing compensatory blood circulation is undeniable however, multiple anastomoses of small branches of the cortical and deep branches of the anterior, middle and posterior cerebral arteries are of much greater importance. The development of a wide network of anastomoses begins in the embryonic period. Connection of arterial reservoirs during embryogenesis is carried out by means of carotid-basilar anastomoses, including the proatlantis intersegmental artery, sublingual, auricular and trigeminal primitive arteries. According to the views of some scientists, the segmental agenesis of the ICA leads to involution of all proximally located segments of the artery and persistence of embryonic anastomoses via which passes the collateral blood flow (13). In 1996 Butillier offered the currently used classification of ICA segments (14). A cervical segment, (C1), - ICA starts from the common carotid artery bifurcation and extends to the external opening of the temporal bone carotid canal, anteriorly it passes to the jugular aperture. A petrosal segment, (C2), - ICA is located inside the petrosal part of the temporal bone in the carotid canal. This segment extends right up to the ragged opening and is divided into three sections: ascending (vertical); knee (bend); horizontal. The segment of the ragged opening, (C3), is short and is located at the place where the artery passes through the upper part of the ragged opening; the lower part of the ragged hole is filled with fibro-cartilaginous tissue. Segments C2 and C3 are combined into a petrosa part. Cavernous segment (C4) – the ICA passes through the cavernous sinus. The wedge-shaped ICA segment, (C5) is short, passes the cavernous sinus through the proximal dura mater and enters the subarachnoid space. Ophthalmic segment, (C6) - is located horizontally passing until the end of posterior connective artery. The communicative segment (C7), the final ICA segment, passes between the optic and

oculomotor nerves to the anterior perforated substance.

C6 and C7 segments together constitute the cerebral or supraclavicular part. Each of the described segments has a specific pathway and position. The following embryonic arteries start its route from these segments: ventral pharyngeal, mandibular, primitive maxillary, primitive trigeminal, dorsal and ventral ophthalmic. Each segment is independent and can cause agenesis. In such cases, the internal carotid blood flow is redirected to the above embryonic arteries to provide blood supply distal to the agenetic segment. All congenital anomalies of the ICA can be described on the basis of embryological data. The ICA develops from the 3rd branchial artery and dorsal aorta.

D.P. Padget studied the development of cerebral arteries by means of graphic reconstruction of 22 embryo sections from 4 to 43 mm parietal-coccygeal length (PCL) at the age of 24-52 days. Seven stages in the development of cerebral arteries were identified. The anterior and middle embryo brain of 4-5 mm PCL is supplied with blood by the ICA, and the rhomboid brain receives blood via transit carotid-basilar anastomoses i.e. trigeminal, auricular, sublingual and proatlantic embryonic arteries (15). In an embryo of 12-14 mm PCL basilar and vertebral arteries only start their differentiation, forming branches to the rhomboid brain. In the absence of the ICA, the pattern of collateral blood flow to the distal ICA depends on the stage at which the pathology developed. Kali et al suggested that the primitive pathways of collateral circulation (i.e. intercavernous anastomoses) would prevail if the pathology developed prior to the completion of the Willis circle formation. Most often, intercavernous anastomoses form as collaterals during ICA agenesis. It should be noted that in such a case, despite the aberrant type of ipsilateral ICA, the artery is preserved. An important part of the research, based on published data, is the description of the intrauterine stages of the cerebrovascular system development. Knowledge concerning the cerebral artery embryogenesis provides understanding of the possible anatomical options found both in clinically healthy and diseased individuals (16, 17). Agenesis of the internal carotid artery (AICA) and carotid artery hypoplasia are rare developmental anomalies. It is known that in embryogenesis there are 6-7 pairs of branchial arches. The

first, second, fifth and seventh branchial arches are completely reduced, the carotid arteries are formed from the third arch, the fourth aortic arch, and the pulmonary arteries develop from the sixth arch. The internal carotid artery is one of the terminal branches of the common carotid artery. According to the Butillier classification it includes the above seven segments. Formation of the internal carotid artery occurs on the 4th week of embryonic development, while the bones of the skull base start to be formed only on the 5th week. The medial edge of the groove is in the form of a roller, the lateral one being high and sharp, wraps at the 6th month forming the lower wall of the carotid canal. Normally, by the end of the 7th month, the medial and lateral edges of the groove are closed and at the 8–9th month the formation of the carotid canal is completed. As a result, absence of a vessel as such determines absence of a supporting bone channel formation. The intermediate parts of the internal carotid artery develop from the dorsal aorta between the first and third arches of the aorta. The distal part of the internal carotid artery develops from the dorsal ends of the first aortic arch. Formation of the internal carotid artery begins when the embryo size reaches 3 mm, and the final formation of the Willis circle ends with the completion of the anterior connecting artery development when it reaches 24 mm in length. The temporal bone begins to form at the 5-6th month of fetal development after emerging of the ossification centers in the cartilaginous auditory capsule (the future petrosa part). From the connective tissue, only the scaly part of the temporal bone develops, at the 9th week the center of ossification appears. In the tympanic part the center of ossification emerge at the 10th week of prenatal ontogenesis. The styloid process develops from the cartilage of the II visceral arch out of the two centers of ossification – the first one appears prior to the birth, and the second - during the 2nd year of the child's life. Fusion of the temporal bone parts begins even earlier, before the birth of the child and lasts up to 13 y.o. The styloid process grows into the temporal bone at the 2nd-12th year of the child's life. In the process of skull base bones development 3 stages are distinguished: 1) the membranous stage - from 2 weeks of intrauterine development; 2) cartilage stage - from 2 months of fetal development; 3) the bone stage, i.e. the appearance of ossification points, starts by the end of the 2nd and the beginning of the 3d month of fetal development. AICA occurs due to an abnormal regression of the first and third arches of the aorta with unclear etiology. Often, such anomalies are associated with the formation of aneurysms. Development of associated

aneurysms is connected with hemodynamic features of the blood supply to the brain in the ICA absence.

According to A.Servo, in 25% of patients with the ICA pathology, SAH from aneurysm develops, while the incidence of cerebral aneurysms in the general population is 2-4% (7).

In addition, according to various literature sources, ICA agenesis can be combined with type II neurofibromatosis, aortic coarctation, polycystic kidney disease, Klippel – Trenone syndrome and corpus callosum. It is extremely rare for such patients to have ipsilateral Horner syndrome associated with impaired sympathetic innervation of the pupil dilator. However, in most cases, AICA is asymptomatic, but signs of blood supply ischemic insufficiency (transient ischemic attacks, headaches, etc.) may be noted. The purpose of this research is to study the anatomical and morphological characteristics of the adult skull with and without the carotid canal.

METHODS

The study material was 104 human skulls from the collection of Human Anatomy Department, Vitebsk State Medical University and the Department of Normal Anatomy, Belarusian State Medical University. The longitudinal and transverse dimensions of the carotid canal apertures and oval openings of the sphenoid bone were measured. Morphometric and statistical research methods (the Wilcoxon test) were used. Descriptive statistics are represented by the mode and interquartile range. *Me* is the median; the lower and upper quartiles: *Q25* - *Q75*, *N* - quantity. Differences were recognized as statistically significant at $p < 0.05$.

The data analysis was carried out using STATISTICA 10.0 package and Microsoft Excel. The study analyzed the data on ICA embryogenesis, ICA agenesis, absence of a carotid canal, types of collateral brain blood supply. It is necessary to distinguish between the concepts of "agenesis", "aplasia" and "hypoplasia". Often they are united under one word "dysgenesis". The definitions were first formulated in 1968 by T. Lie in the work "Congenital Malformations of the Carotid Arteries" (4). Agenesis is the lack of a carotid artery in case of complete absence of the carotid canal as there was no artery necessary

for its formation. The access of blood flow to the brain can be compensated through collateral circulation. In his work T. Lie described six types of collateral circulation. Type A has unilateral absence of the internal carotid artery with collateral circulation to the anterior cerebral artery through the anterior connecting artery (a. communicans anterior) and to the middle cerebral artery through the posterior connecting arteries (aa. communicantes posteriores). In type B, contralaterally to the middle and anterior cerebral arteries on the side with no ICA, the blood supply is compensated by the anterior connecting artery. Type C has bilateral agenesis of the carotid arteries with blood supply to the anterior and middle cerebral arteries through the posterior circulation by means of the posterior connecting artery. In type D agenesis of the cervical and cavernous parts of the internal carotid artery appears. In such a case blood circulation is restored by an anastomotic siphon from the contralateral cavernous part of the internal carotid artery. Type E or better called hypoplasia of the carotid artery with the preserved carotid canal and vessel remains. In this case, the diameter of the anterior cerebral arteries is shortened, however, the diameter of the posterior connecting artery, as well as the middle and posterior cerebral arteries are compensated.

Therefore, cerebral blood circulation mainly proceeds through them. Type F demonstrates compensation of the absent ICA blood flow through anastomosis with distal branches of the external carotid artery (ECA).

Also, there is a special case when in embryogenesis with complete AICA on the same side there is no reduction of the trigeminal artery (a. trigeminalis). During embryonic development it is an additional source of blood supply and is reduced later. However, in case of AICA, reduction may not occur, and the trigeminal artery, originating from a rather large basilar artery (a. basilaris), can serve as one of the main sources of cerebral blood supply. In a simplified form it is possible to say that collateral blood supply can be carried out in three ways: through the cerebral arterial circle (intracranial collaterals), through the embryonic arteries (extracranial - intracranial collaterals) and through anastomoses from the external carotid artery (extracranial collaterals). Extracranial collaterals - is the connecting link between the ICA and the ECA. These are anastomoses between the facial, maxillary, superficial temporal arteries and the orbital artery. Anastomosis between the ECA and the ICA is also provided by the embryonic vessels a.

primitive otica and a. primitive olfactoria and others. Extracranial - intracranial collaterals – anastomoses, are located inside the skull and are formed by rudimentary embryonic vessels (extracranial branches of the ICA) with the basilar artery (inside the skull).

The following embryonic arteries are distinguished: the anterior connecting artery (a. Communicans anterior), the trigeminal artery (a. Trigeminalis), the auricular artery (a. Otica), the hyoid artery (a. Hypoglossalis), the proatlantic artery (a. Proatlantis).

Intracranial collaterals provide cerebral blood supply and form anastomoses between the individual arteries of the brain: the arterial circle of the brain base (Willis circle); anastomoses on the surface of the brain between the cerebral arteries, branches of the vertebral artery, etc.

RESULTS

While examining the structure of 104 skulls the outer and inner bases, the following findings were revealed: only in one adult skull (**Figure 1**) the left and right carotid channels are completely absent and, therefore, its external and internal apertures are also absent. According to the literature data, development of the carotid canal is directly related to the development of the ICA (1).



Figure 1 a. Skull with agenesis outside view



Figure 1b. Skull with agenesis inside view

Absence of a vessel leads to absence of a supporting bone channel formation. In the remaining 103 skulls, the aperture of the carotid canal averages 21.99 mm² (**Table 1**). When viewed from the outside and compared with a conventional skull in the occipital bone, the front edge of the large occipital foramen is not pointed but rather flattened. Thus, two short grooves can be distinguished here. The petrosa-occipital fissure is almost entirely made of bone tissue. The jugular and mastoid processes are clearly distinguishable. When examining the external apertures of the carotid canal, it was found that more than half of all openings (54%) are oval, 30% round, 12% pear-shaped. The complete absence of the carotid canal on the left and right sides was noted on only one skull (**Figure 1 a**). The left spinous and oval openings are significantly enlarged on both sides. The right spinous opening is extended anteriorly. On the inner base of the skull, a number of Turkish saddle signs are clearly visible (**Figure 1 b**). The back of the saddle has the form of a pointed ridge with characteristic elevations on both sides, representing the posterior inclined processes. The tubercle of the saddle is poorly expressed, the precross groove facing posteriorly. The pituitary fossa and the wedge-shaped eminence are well defined. The carotid groove is divided into anterior and posterior parts by a crest, poorly visible on the right and significantly expressed on the left and located in the region of the absent middle bent process. The front part of the carotid groove approaches the oval opening while the back part approaches the ragged one. The optic canal, the superior orbital fissure and the round opening on both sides are normally expressed. The internal and external apertures of the temporal bone carotid canal are absent from both sides, which proves the complete absence of the carotid canal on both sides. Other temporal bone formations have classic form. In the abnormally changed skull, a groove is well defined on the left and on the right, passing from the oval opening to the carotid groove of the sphenoid bone body. The groove which approaches the ragged opening is less noticeable. It is necessary to take into account that on the left, the grooves are better expressed. The average area of oval openings was 21-23 mm², while the average area of the external apertures of the carotid canal was 32 mm². Calculation of the areas was carried out as follows: The longitudinal

and transverse dimensions of the oval foramen and the external aperture of the carotid canal were measured in each skull. Since most openings had an oval shape, their area was defined according to the formula for ellipse area calculation (1): $S = a * b * \pi$. Where **S** is the area of the ellipse, **a** is the minor ellipse semiaxis (half the transverse dimension), **b** is the major ellipse semiaxis (half the longitudinal dimension). The value of π was equal to 3.1415.

According to a statistical analysis, since normally the left and right sides either differ slightly from each other, or do not differ at all, in the further study they were equated. In the abnormally changed skull, the oval and spinous openings of both sides are significantly enlarged and extended in the anteroposterior direction. The longitudinal dimension of the oval left opening was 9 mm, the transverse dimension was 7 mm, the transverse dimension is 6 mm on the right, and the longitudinal dimension is 8 mm, which is significantly higher than the average data. It is also worth noting that in the same skull oval openings were of a non-standard shape. The shape of the oval openings was most often oval (94%), much less often triangular (3%) and diamond (3%). In skull #1 with bilateral agenesis of the ICA, the shape and significant size of the openings was determined by the structures passing through these openings. According to T. Louzh's description, in the embryonic period of vascular development there are variants of the ICA and ECA branches. So, in the cervical region from the ICA there are primitive hyoid, primitive auditory, primitive trigeminal arteries. The branch of the maxillary artery (ECA branch) is the middle meningeal artery entering the cranial cavity through the spinous foramen.

The additional meningeal artery passes from the middle meningeal artery and then enters the cranial cavity through the oval opening. It further goes to the cavernous sinus, where it probably anastomoses with the arteries of the Willis circle. The main diagnostic method for AICA is cerebral angiography. It is necessary to differentiate AICA from acquired pathologies (thrombosis, atherosclerosis). The fundamental diagnostic factor is the size of the carotid canal in the temporal bone pyramid – in case of the ICA dysplasia the carotid canal is significantly narrowed or absent. Thus, the

formation of the carotid channel is directly related to the ICA formation during embryonic development. Computed tomography is also very effective since it may confirm the absence of carotid channels. The congenital nature of the revealed changes is proved by the fact that the bone channel of the internal carotid artery on the affected side is underdeveloped and slit-shaped. Presence of aneurysm from the anterior connecting artery is most likely due to the constant excessive hemodynamic effect on the vessel wall. The internal carotid artery supplies the anterior and middle brain through its anterior and posterior posterior branches. The process in which the initial vasculature consolidates into permanent arteries explains the majority of the cerebral arteries options and abnormalities. Obviously, anomalies and variants of the cerebral arteries are biologically less reliable and lead to the pathology development (18).

CONCLUSION

1. The research of literature data on the embryonic development of the ICA, the carotid canal, types of collateral cerebral blood supply proves that congenital ICA agenesis is a rare (usually asymptomatic) vascular anomaly.

Intracranial blood circulation is supported by collateral anastomoses mainly through the Willis circle, preserved embryonic vessels and numerous anastomoses with the ECA branches.

Knowledge of the ICA embryogenesis provides understanding of the possible anatomical options encountered in both clinically healthy and diseased individuals.

2. The research of our own anatomical material (104 skulls) revealed only one skull with agenesis of the carotid canal on the left and right sides, as well as a number of anatomical formations suggesting that full blood supply to the brain was carried out by rudimentary embryonic vessels, being probably the ECA branches. Based on the literature data, it becomes clear that most cases of ICA agenesis are not clinically manifested due to well-developed anastomoses. It is possible to make accurate diagnosis of such congenital pathology only by means of MRI and MR angiography in combination with CT as it confirms absence of bone carotid canals.

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