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Segmental vulnerability and vascular neurocristopathy of the internal carotid artery

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I have read the article of "Dolichoectasia of the internal carotid artery terminus, posterior communicating artery, and posterior cerebral artery: the embryonic caudal ramus internal carotid segmental vulnerability legacy" by Kobkitsuksakul et al.[1] with great interest. The authors introduced the segmental concept of the cerebral arteries to explain the vascular pathology of dolichoectasia in their clinical cases. I would like to comment on this article.

Segmental concept of the internal carotid artery

The segmental concept of the cerebral arteries was proposed by Pierre Lasjaunias in 2000.[2] This explains the conceptual segments of the cerebral arteries with each segment being accompanied by the different developmental and phylogenetic characteristics even if the artery looks like a simple pipe. Embryological steps in the first few weeks of life are memorized in the arterial anatomy, which reflects the evolutional events of the vertebrate developments in the past several hundred million years.[2] This segmental concept is more readily applied to the internal carotid artery (ICA). The memories of the evolution are imprinted into the wall of the ICA, in the same way as the genetic mutations are engraved in the genomes during the vertebrate evolution. Each segment of the ICA has its own vulnerability and susceptibility. Most of the segmental identities are established during development and are preserved throughout life.

Lasjaunias proposed seven segments of the ICA between the cervical carotid bifurcation and the posterior communicating artery.[2] Each border between segments has the primitive arteries or their remnants, such as (1) the distal end of the carotid duct (a distal part of the dorsal aorta between the 3rd and 4th aortic arches), (2) primitive hyoid artery (carotico-tympanic artery or the dorsal end of the second aortic arch), (3) primitive mandibular artery (the dorsal end of the first aortic arch), (4) primitive trigeminal artery or primitive maxillary artery (inferior posterior hypophyseal artery), (5) primitive dorsal ophthalmic artery (inferolateral trunk: ILT), and (6) primitive ventral ophthalmic artery, arranged in the order from the cervical carotid bifurcation to the posterior communicating artery (Figure 1(a)).

Modified segmental concept with updated embryology of the ophthalmic artery

Because both dorsal and ventral ophthalmic arteries are intradural arteries throughout embryogenesis,[3] it is denied that the ILT being the remnant of the primitive dorsal ophthalmic artery. In consideration of the updated embryology of the ophthalmic artery, the ophthalmic artery at C3 portion origin must be the final form of the primitive ophthalmic artery composed of the primitive ventral and dorsal ophthalmic arteries.[4,5] Thus, Figure 1(a) can be redrawn as Figure 1(b). Phylogenetically, the origin of the ophthalmic artery is variable, i.e., it can originate from C3 portion (human, *Tupaia*, *Aotus*, and *Saguinus*), C2 to IC terminal origin (lemur and loris), and A1 of the anterior cerebral artery (most mammals, for example, dog).[6] This means that the ophthalmic artery of the A1 origin is not the remnant of the primitive ventral ophthalmic artery. Wherever the origin of the artery is located, the artery courses through the optic canal is the definitive ophthalmic artery. The size of the ophthalmic artery is also variable and depends on the amount of the tissue that supplied by this artery. It is believed that the inferior posterior hypophyseal artery is the remnant artery of the medial branch of the primitive maxillary artery and the ILT is the remnant of the lateral branch of the primitive maxillary artery.[7] However, the embryology of the ILT is not well elucidated. Two branches of the identical artery (the primitive maxillary artery) cannot be branched off from the ICA at the different points because this is contrary to the segmental concept. The embryological precursor of the ILT can be called as "the premandibular artery" for descriptive purpose because of the area that supplies.

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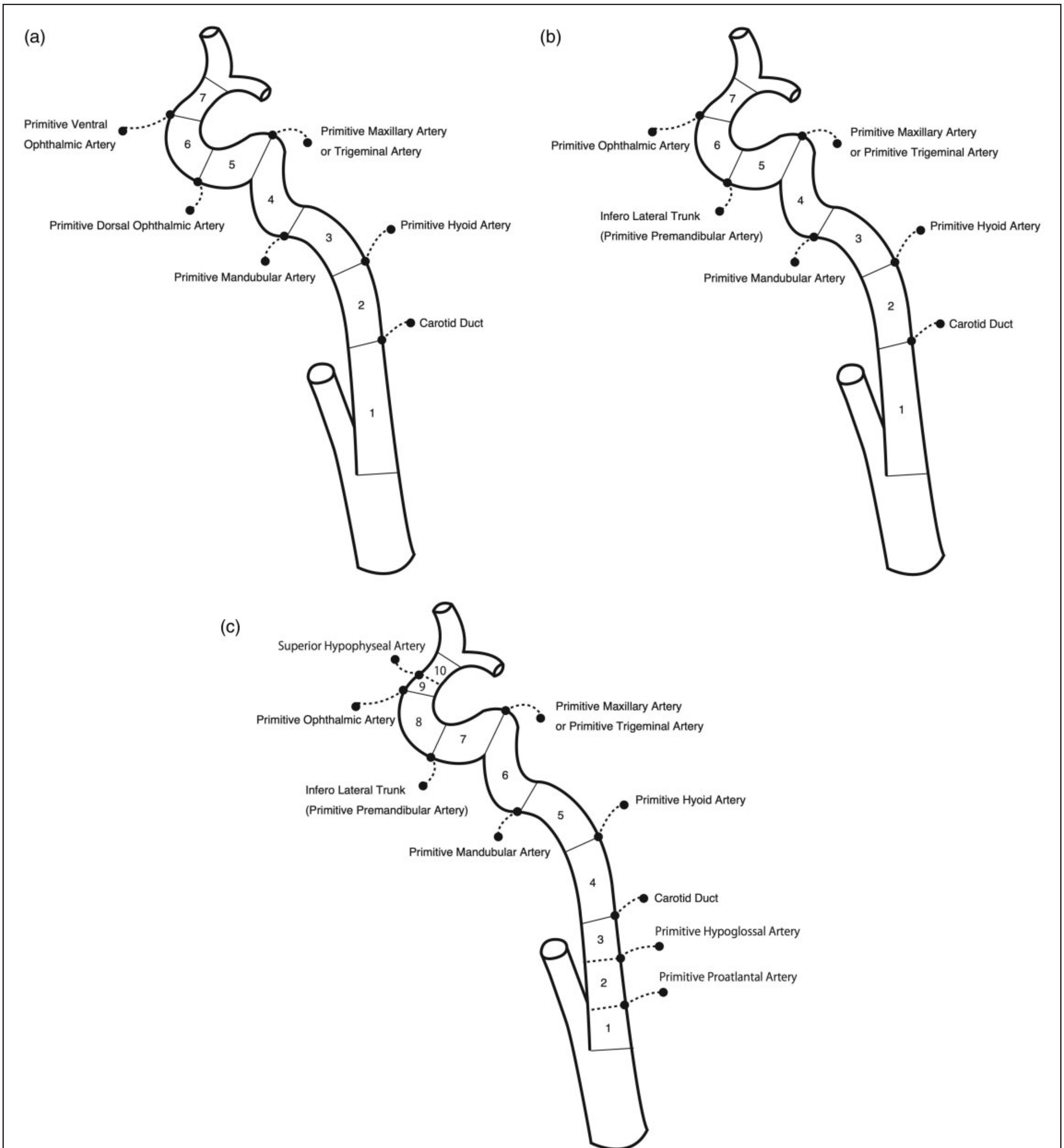

Figure 1. (a) Segmental concept of the internal carotid artery (ICA) by Lasjaunias P. There are seven segments between the cervical bifurcation and the origin of the posterior communicating artery. Namely, they are (1) cervical, (2) ascending intrapetrous, (3) horizontal intrapetrous, (4) ascending foramen lacerum, (5) horizontal intra-cavernous, (6) clinoid, and (7) termination. Between the segments, there are primitive arteries or their remnants. (b) Segmental concept of the ICA with updated embryology of the ophthalmic artery. ILT is not the remnant of the primitive dorsal ophthalmic artery. The primitive ophthalmic artery is composed of the ventral and dorsal ophthalmic arteries which runs through the optic canal. (c) Updated segmental concept of the ICA. Possible embryological border between the segments are added, namely, primitive proatlantal artery, primitive hypoglossal artery, and superior hypophyseal artery. In the concept, 10 conceptual segments are noted.

Additional conceptual segments of the internal carotid artery

As the origins of the ophthalmic arteries are variable, those of the primitive proatlantal artery (the future occipital artery) and the primitive hypoglossal artery (the future hypoglossal branch of the ascending pharyngeal artery) can also be variable. They originate from the external carotid artery, but they can also originate from the proximal ICA segment between the cervical carotid bifurcation and the possible carotid duct. Occasionally, the superior hypophyseal artery acts as the primitive artery in various anomalies including fenestration and anastomosis with the contralateral ICA. Thus, the number of carotid segments should not be rigidly fixed to 7 as proposed by Lasjaunias. Important thing proposed by him is that the ICA is embryologically segmented and each segment has different embryological backgrounds. Phenotypes of the segmental lesions include agenesis, regression, dysplasia, duplication, fenestration, rete formation, stenosis, enlargement, looping, dolichoectasia, arteritis (angiitis) due to bacterial or viral infection, and so forth.[2] Their extents of the lesions are usually distinct from one embryonic artery or its remnant to the other one. Figure 1(c) includes possible 10 embryological segments for the modified segmental concept.

Anterior and posterior circulations and neural crest cells

In the clinical practice, we often use the terminologies of anterior and posterior circulations, for example, acute ischemic stroke in the anterior circulation and giant aneurysms in the posterior circulation. There is no clear definition of the anterior or posterior circulation, but in general, it is supposed that the anterior circulation is the territory that the ICA supplies while the posterior circulation is the territory that the vertebral artery supplies. It is not clearly defined whether the cortical territory of the posterior cerebral artery (PCA: P2-P4) belongs to the anterior or posterior circulation.

Neural crest (NC) is called the fourth germ layer and is characteristic to the vertebrates phylogenetically. NC cells are pluripotent and give rise to a variety of derivatives after migration in early embryogenesis, such as neurons, glias, cartilage, connective tissue, pigment cells, and adrenal cells. Although the endothelium of the vessels is composed of the cells of the mesodermal origin throughout the body, the media of the cerebral artery is different. NC contributes to the media of the ICA while the media of the vertebra-basilar (VB) system is composed of the cells of mesodermal origin.[8] NC is classified by location along the neural axis into cephalic, vagal, trunk, and sacral NCs. Only cephalic NC contributes to the arteries of the circle of Willis and their branches.[8]

Rostral and caudal divisions of the internal carotid artery

Embryologically, the ICA bifurcates into rostral and caudal divisions at the origin of the posterior communicating artery. The rostral division is the ICA per se and its branches distal to the posterior communicating artery. The caudal division includes the posterior communicating artery and P1 segment of the PCA. The P2-4 segments of the PCA are transferred from the telencephalic branches of the anterior choroidal artery to P1 of the PCA. This is called "distal annexation." In the original description by Lasjaunias, the basilar artery distal to the primitive trigeminal artery is regarded as a part of the caudal division of the ICA. However, the distal basilar artery and superior cerebellar artery (SCA) are not the ICA origin embryologically. This is because the cerebellum is an outgrowth of the dorsalmost alar plate of the caudal isthmus and the first rhombomere (rhombomere 1),[9] and the artery supplying the cerebellum must be belonged to the VB system. In fact, NC characteristic to the ICA system is not found in the media of the SCA, because it is of mesodermal origin. Consequently, embryological border between the anterior and posterior circulations is located between the PCA and SCA as shown in Figure 2. Eventually, the caudal division of the ICA comprises the posterior communicating artery and the entire PCA (P1-4).

Neurocristopathy: The neural crest related disease

The pathological processes of NC origin are called "neurocristopathy," which is classified into neoplastic and dysgenetic.[10] The former includes neuroblastoma, paraganglioma, and neurofibromatosis type 1 while the latter includes Hirschsprung disease, DiGeorge syndrome, coarctation of the aorta, agenesis/hypogenesis of the ICA, PHACE syndrome, and moyamoya disease.[11]

Kobkitsuksakul et al.[1] presented four patients with figures. Patient in their Figure 2 had aneurysmal changes at the right posterior communicating artery

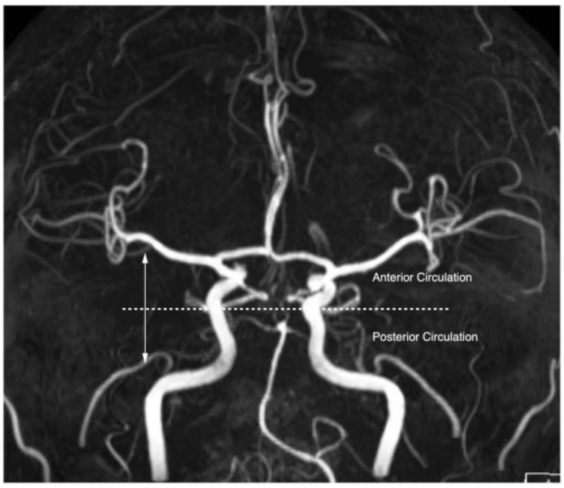

Figure 2. Magnetic resonance angiography (antero-posterior view). The border between the anterior and posterior circulations is clearly shown in this case because cortical branches (P2-P4) of bilateral posterior cerebral arteries are solely supplied by the embryonic-type (exact expression of the fetal-type[12]) posterior communicating arteries. The dotted line separates two circulations. The media of the cerebral arteries in the anterior circulation is of the neural crest origin while that in the posterior circulation is of the mesodermal origin.

and P1 of the PCA as well as right ICA occlusion. Patient in Figure 3 had dolichoectasia of the right supraclinoid ICA, right P1, and distal basilar artery. Patient in Figure 4 had dolichoectasia of the left distal ICA, P1, and basilar tip with hyostapedial artery, and the right aplastic ICA. Patient in Figure 5 had dolichoectasia of the left ICA and P1. Of note, the SCA was normal in all these four patients. They discussed their cases in view of the embryological segmental involvement of the terminal (rostral) ICA and the caudal division of the ICA, but their pathologies (dolichoectasia, ICA occlusion, and ICA aplasia) are located both in the rostral and caudal divisions of the ICA as well as in the cervical ICA. In other words, these lesions are involved solely in the ICA system without distinct segmentations. Thus, the pathological processes are confined to the anterior circulation. I believe that the presented pathologies in these cases can be better discussed in the context of "the vascular neurocristopathy" rather than the segmental involvement of the terminal ICA and the caudal division of the ICA.

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