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Persistent primitive hypoglossal artery: a case study with a dissertation on its embryo-pathological rationale

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Abstract. Persistent Primitive Hypoglossal Artery (PPHA) is a developmental anomaly of the brain superficial arterial circulation and is classified as a condition of carotid-vertebrobasilar anastomosis persistence caused by lack of reabsorption of the vascular network running on the hindbrain surface between the 4th and 5th embryonic week. It has an incidence between 0.03 and 0.9%, it is the second most frequent seen persistence of carotid-vertebrobasilar anastomoses after the trigeminal artery (TA), representing 85% of all persistent vestigial arteries (0.1–0.6%). Here a case of Persistent Primitive Hypoglossal Artery (PPHA) is reported being detailed in its morphological and clinical aspects. The patient, a 55-year-old female patient with high cardiovascular risk without specific symptoms presents at radiological morphological examination with an anomalous bifurcation of the ICA which gives rise to the ICA itself, which ascends without collateral branches up to the carotid foramen in the cranial base, and to an accessory artery, which enters the hypoglossal canal on the contour of the great occipital foramen, as a PPHA. A comprehensive embryologic analysis of this anatomical variant is offered and clinical awareness on it raised in view of a more informed an effective realization of it in daily clinical practice.

Keywords: anatomical variant, angiography, congenital, cardiovascular, persistent primitive hypoglossal artery.

INTRODUCTION AND AIM

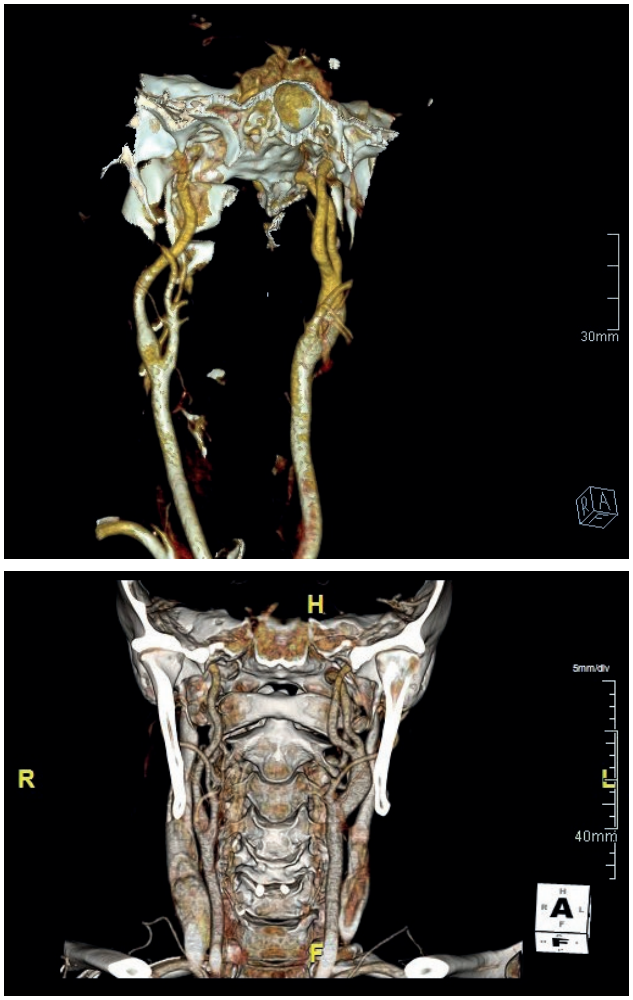
Persistent Primitive Hypoglossal Artery (PPHA) is a condition of carotid-vertebrobasilar anastomosis persistence due to lack of reabsorption of the vascular network running on the hindbrain surface between the 4th and 5th

embryonic week; it is included among the developmental anomalies of the brain superficial arterial circulation, which in turn are frequently associated with anomalies in the development of the internal carotid arteries (ICAs). With an angiographic incidence of 0.027 to 0.26% (Zhang et al. 2021), having also been reported up to 0.9% (See et al. 2017), and with a greater frequency in females and a predilection for the left side (Srinivas et al. 2016), it mostly represents an incidental finding detected during radiology carried out for other reasons, as it is associated with a limited symptomatology and presents few significant signs. First described during an anatomical dissection in 1889 (Batujeff 1889), with its first angiographic description dating back to 1961 (Begg 1961), PPHA may occur in association with aneurysms (Nakamura et al. 2000) and its well-known association with the ipsilateral vertebral artery agenesia (VA) seems to play an ischemic role in the event of inflow reduction in ICA, which alone supplies vascularisation on its own side (Zhang et al. 2016).

Here we report a case of PPHA, which we detail in its morphological and clinical aspects. This single case study will then prompt a discussion on the embryologic rationale of this anatomical variant.

CASE REPORT

A 55-year-old female patient referred to our Cardiology Outpatient Service with a high cardiovascular risk (i.e. smoking, high cholesterol levels) without specific symptoms: since atherosclerosis, as is currently known, is multi-district disease, there is a tendency shared between radiologists and cardiologists to perform a single exam to study both the coronaries and epiaortic vessels, thus benefiting from a single administration of contrast medium. In our specific case, the extension of the study up to the supra-aortic vessels incidentally led to an angio-CT diagnosis of PPHA. The multi-slice CardioSync CT Scan (*Siemens Somatom Volume Zoom*) for the study of coronary arteries and epiaortic vessels after riodine non-ionic contrast medium administration was used: the volume rendering reconstruction (Fig. 1) of the epiaortic vessels shows an anomalous bifurcation of the ICA, which gives rise to the ICA itself, which ascends without collateral branches up to the carotid foramen in the cranial base, and to an accessory artery, which enters the hypoglossal canal on the contour of the great occipital foramen, as a PPHA. The anomalous ICA bifurcation was confirmed by MIP (maximum intensity projection) reconstruction (Fig. 2), while Multiplanar Reformation (MPR) describes the supra-aortic trunks' courses (Fig. 3).



Figures 1. Volume rendering reconstruction of the epiaortic vessels with evidence of an anomalous bifurcation of the ICA (top and bottom images).

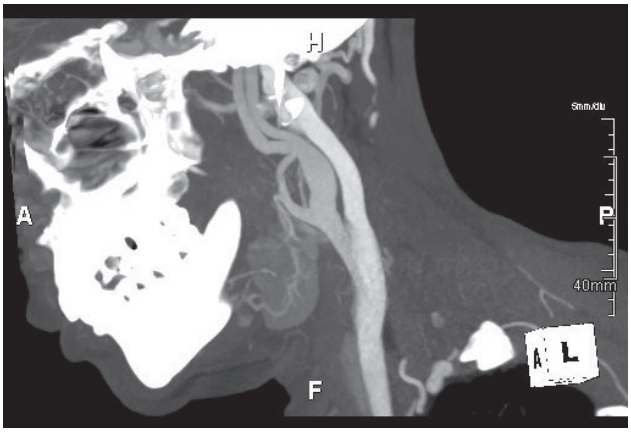


Figure 2. MIP (maximum intensity projection) reconstruction confirming an anomalous ICA bifurcation.

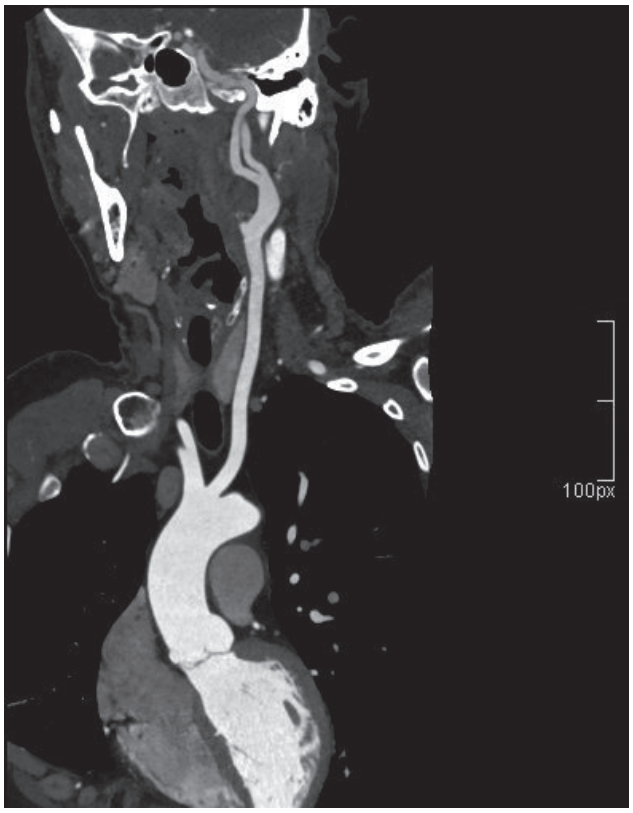


Figure 3. Multiplanar Reformation (MPR) describing the courses of the supra-aortic trunks.

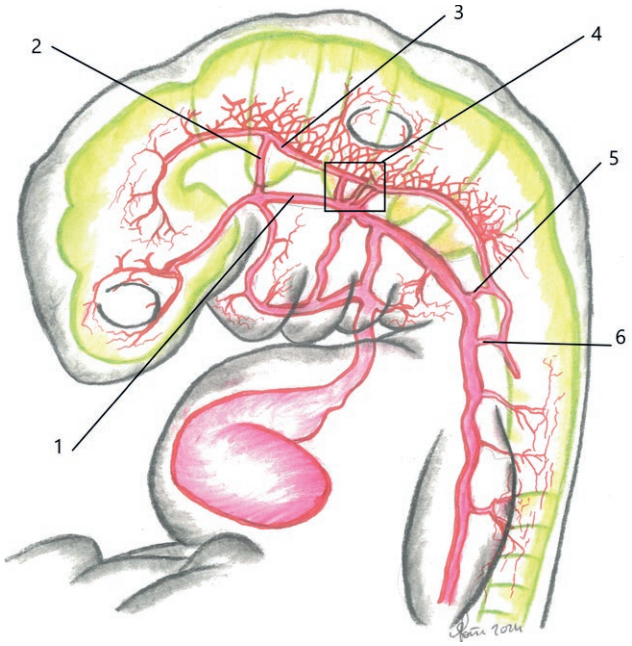


Figure 4. 1. dorsal aorta; 2. trigeminal artery; 3. longitudinal neural artery; 4. otic branches; 5. primitive hypoglossal artery; 6. proatlantal intersegmental artery.

DISCUSSION

a. Embryology

The heart begins to form in the second week of embryonic development (Fig. 4) by the migration to the edges of the trilaminar embryo of pre-cardiac mesodermal cells, which differentiate into cardiomyocytes; by the end of the second week the neural tissue rapid growth causes the flat embryo to fold and tubularise, hence causing the heart to acquire the inverted-Y shape and then (week IV) the S-shaped loop, which will form the cardiac cavities of later life (Buijtendijk et al. 2020). At the beginning located in a cephalic position, the heart then descends into the thorax where its connection with the paired dorsal aorta undergoes changes which will give rise to the adult aortic configuration, via the production and remodeling of six pairs of arteries of the branchial arches. The artery of the first branchial arch first forms the primitive mandibular artery which later becomes the Vidian artery, the dorsal portion of the II branchial arch artery becomes Internal Carotid Artery (ICA) passing through the stages of hyoid and stapedial, while the ventral portion becomes first the ventral pharyngeal artery and then the External Carotid Artery (ECA). The carotid-tympanic artery is the adult remnant of the II branchial arch artery: the artery of the third branchial arch merges with the distal portion of the double dorsal paired aorta to form the proximal portions of the ICAs, while the artery of the IV branchial arch forms the aortic arch on the left side and the subclavian arch on the right side. The arteries of the sixth branchial arch contribute to the formation of the two primitive pulmonary arteries with their proximate portion, while there is no scientific agreement on the role of the artery of the fifth branchial arch (Klostranee & Krings 2022).

b. Vascular anomalies

The most common vascular anomalies of the vessels of the neck (Fig. 5) include the common origin of the brachiocephalic trunk and left Common Carotid Artery (CCA), the aberrant right subclavian artery, also called *arteria lusoria*, the ICA aplasia or hypoplasia; ICA is embryologically divided into 7 segments (I - cervical, II - ascending petrosus, III - horizontal petrosus, IV - ascending cavernous, V - horizontal cavernous, VI - clinoid and VII - terminal): ICA hypoplasia is frequently seen close to the bifurcation (segment I) (Kathuria et

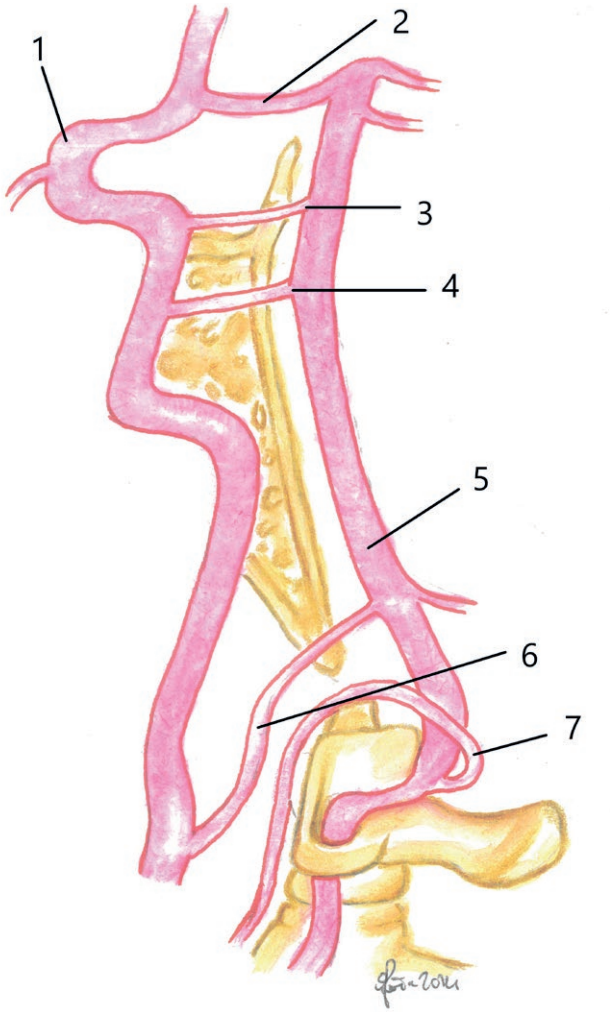


Figure 5. 1. internal carotid artery; 2. posterior communicating artery; 3. trigeminal artery; 4. otic artery; 5. vertebro-basilar trunk; 6. hypoglossal artery; 7. proatlantal artery.

al. 2011), while the aplasia is observed at carotid foramen (segment II, with canal of reduced caliber or even absent) (Given et al. 2001). Two other known anomalies are the aberrant ICA (more common in female), and the persistent stapedial artery (in 3% associated with the absence of the spinous foramen). As regard to the superficial cerebral arteries we recognize 7 chronological and morphological stages of development: stages I and II are observed in the 4th week (development of the vertebro-basilar trunk – VBT - and the posterior communicating artery - PCA), stages III and IV up to the 35th day (formation of basal nuclei vessels, of the ophthalmic arteries, the choroid plexus and the completion of the circle of Willis) and stages V, VI and VII, between 40 and 52 days (vascularization of the remaining superficial cerebral and cerebellar territories) (Klostranee & Krings 2022). In stage I (28-29 days) the ICA bifurcates into an olfactory cranial branch that will become the anterior cerebral artery (ACA) and in a caudal branch that will give rise to the PCA: 4 anastomotic bridges exist between the two ICAs and two parallel neural arteries running on the hindbrain surface. This network is basically formed by transient anastomoses between ICAs and VBT and is represented by the trigeminal artery (TA), the hypoglossal artery (HA), by an otic branch (OB) and a distal proatlantoid artery (PAA) (Lie 1968). During stage IV (5-6 mm length) the PCA is completed and the OB, followed by the HA, TA and the distal PAA regress (Coulier 2018). In stage VII the intersegmental PAA continues to vascularize the hindbrain until the complete development of the vertebral arteries (VAs) (32 days, 7-12 mm), which are made up of transverse anastomoses between adjacent cervical intersegmental arteries: later they become sub-occipital intersegmental arteries to move towards the intersegmental artery of C6, to form the origin of the adult vertebral and subclavian arteries.

c. PPHA

The PPHA has an incidence between 0.03 and 0.9% (Kings et al. 2015) and is the second most frequent seen persistence of carotid-vertebrobasilar anastomoses after the TA, representing 85% of all persistent vestigial arteries (0.1 – 0.6%); Persistent TA has been described to cross the sella turcica in 50% of the cases observed, forming a bridge between the ICA, the PCA and the middle third of the VBT: persistent intersegmental PAA is rarer, with fewer than 50 cases described (Tsukamoto et al., 1981) and has a horizontal sub-occipital course that overlaps with that of the VAs, except that there is no transit through the transversal foramina of the vertebrae from C6 to C1 (Anderson & Sonheimer 1976). A persistent OB that establishes an angiographically visible anastomosis with the ICA is largely still debated (Lasjaunias et al. 2001). The HA usually rises from the cervical portion of the ICA (C1-C2) and enters the posterior cranial fossa joined with the hypoglossal nerve: A didactic description is provided by the so-called Lie criteria (Lie 1968) which identify the HA originating 1) from the ICA at C1-C3 level as a large branch, 2) passing through the hypoglossal canal after a twisted course, 3) anastomoses with the VBT and 4) it is associated with the radiological absence of the PCA. The VBT appears vascularised beyond the anastomosis with the PPHA and often the VAs are hypoplastic (Elhammady et al. 2007); Brismar (Brismar 1976) added two more criteria: 5) the PPHA can rise from the ICA as an extra-cranial branch 6) and it passes through the condyloid foramen before joining

the distal part of the VBT. Exception to these criteria is represented by the described connection with the inferior posterior cerebellar artery without anastomosis with the VBT (Uchino & Suzuki 2018). Originating more frequently by the ICA (Type I) (Coulier 2018), the PPHA can also have a rare origin from ECA (Type II), in which case an anastomosis with the VA through the hypoglossal canal (Meguro et al. 2007) and one between the ECA and VBT have been observed; more frequent in females and on the left side (Srinivas et al. 2016), it represents an incidental diagnostic finding due to its asymptomatic nature, although exist aneurysms at the PPHA and VBT junction level (26%) (Huynh-Le et al. 2004), and neuralgia, glossopharyngeal palsy and malformations of the craniocervical junction are reported. Abnormal bifurcation of the ICA due to the PPHA may increase the risk of carotid bulb atherosclerosis (Vlychou et al. 2003), while the absence or hypoplasia of the Vas and the PCAs oblige the ICA of the affected side to supply the brainstem, cerebellum and ipsilateral hemisphere alone, exposing to ischemic risk in case of reduction of carotid inflow (De Caro et al. 1995); brain aneurysms associated with PPHA (Nakamura et al. 2000), ICA (Fantini et al. 1994; McCartney et al. 1989) and ECA (Type II) (Welten et al. 1988) atherosclerosis involving the root of the PPHA, PPHA aneurysm within the hypoglossal canal associated with subarachnoid hemorrhage (Kimball et al. 2015), as well as stenosis Doppler signals without angiographic confirmation associated with PPHA (suggesting that this condition may increase arterial flows by simulating carotid stenosis) have been described (Widmann & Sumpio 1992). For this reason, due to a larger-than-normal hemispheric perfusion provided by the ICA, some authors have also suggested routine electroencephalographic monitoring during endoarterectomy (McCartney et al. 1989).

CONCLUSION

The present study and annexed commentary have highlighted the embryonic origin of the anatomical variant represented by the PPHA. It should be stressed that an enhanced knowledge of anatomical variants can allow better diagnoses and therapies by clinicians in their daily practice.

PATIENT CONSENT

The patient signed her written informed consent before the performance of the radiological exams.

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