A unique variant of a right persistent hypoglossal artery arising from the common carotid artery with complex cardiovascular anomalies in a female neonatal patient

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ABSTRACT

Persistent primitive hypoglossal artery is a carotid-vertebrobasilar anastomosis, which commonly arises from the internal carotid artery at the level of the C (cervical) 1-3 vertebrae. We describe a unique case of a female infant patient with this anomaly that has an unusually low origin from the distal common carotid artery just below the bifurcation at the level of roughly C5 and supplies the entire vertebrobasilar system. Additional cardiovascular anatomical variations were present: Tetralogy of Fallot and a right-sided aortic arch with mirror image branching. These singular variations are rare in the general population, but even rarer when combined. Awareness of these unusual vascular variants is clinically significant, as they may predispose the patients to early ischemic injury, hemorrhage, aneurysm formation, and can be essential in surgical planning. Therefore, radiographic imaging is of importance in proper diagnosis of such variants.

CASE REPORT

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A full work-up was conducted on a neonatal female patient who was suspected of having multiple congenital anomalies including, but not limited to, Tetralogy of Fallot (TOF) with pulmonary atresia. After an uneventful term 38-week, 5-day vaginal delivery, the baby underwent cardiac echogram on day one, which confirmed the TOF with pulmonary atresia and aortopulmonary collaterals. A head echogram on the same day revealed no abnormalities. Patient underwent brain magnetic resonance imaging (MRI) on day 3 in order to investigate for possible congenital brain anomalies. The MRI was remarkable for an incidental acute infarct in the left caudate head (Figure 1), which prompted a time-of-flight non-contrast magnetic resonance angiogram (TOF MRA) of the brain and neck on day 9.

The MRA found an unusual prominent vessel arising from the right common carotid artery (CCA) below the carotid bifurcation at roughly the 5th cervical level, coursing through the right hypoglossal canal and supplying the basilar artery (Figure 2). The right vertebral artery was not identified and a tiny, hypoplastic cervical left vertebral artery was seen, which was not identified intracranially and may terminate in the posterior-inferior cerebellar artery. The right internal carotid artery (ICA) was small in caliber and originated distal to the origin of the hypoglossal artery. The MRA neck again demonstrated a right-sided aortic arch with mirror branching, which was detailed in a previous chest computed tomography angiogram (CTA) (Figure 3). Further work-up came back negative for other abnormalities, and the patient was stabilized with discharge plans of pending cardiac surgery for the TOF at our medical center at a later time.

DISCUSSION

Etiology & Demographics:

Unilateral persistent primitive hypoglossal artery (PPHA) is a rare anomaly that occurs in the general population at a rate of roughly 0.1 - 0.2%, more commonly seen on the left, with currently assumed rates of bilateral PPHA being much rarer [1]. PPHA is a congenital vascular variation that occurs from failure of the primitive hypoglossal artery to regress. During early vascular development of the hindbrain, four paired branches from the developing internal carotid artery (cranial remodeling of the dorsal aortae) supply the midline vascular plexus of the longitudinal neural arteries (LNAs) that will form the basilar artery (Figure 4) [2,3]. From cranial to caudal, these paired branches are: the trigeminal artery (TA) the otic artery (OA), the hypoglossal artery (HA), and the proatlantal artery (ProA). The incidence of the persistent trigeminal artery has been estimated between 0.1 - 0.7%, depending on the modality being used [4]. The incidence of the otic artery and proatlantal artery is much more rare, with only a few case reports having been reported. The posterior vertebrobasilar supply becomes progressively independent as the ICAs shift to supply the developing anterior brain. The posterior communicating arteries develop from the ICAs and maintain contact with the basilar artery cranially. As the vertebral arteries and basilar artery coalesce, they incorporate a segment of the ProA, while the other 3 typically regress (Figure 4C).

Traditionally, a PPHA includes the following: arises from the ICA (less commonly the external carotid) at the level of C1 to C3, passes through the hypoglossal canal on its way to the basilar artery, and if persistent, has a hypoplastic or absent posterior vertebral-basilar circulation [5]. Since patency of an artery is determined by persistent flow, if the hypoglossal artery remains patent, the associated vertebral artery usually regresses. In our case the PPHA did not arise from the ICA or the external carotid, but rather the common carotid suggesting that this variant incorporated a segment of the right LNA (Figure 5). The vertebral arteries (VAs) form from the consolidation of the LNAs and generally arise from the 7th thoracic intersegmental or subclavian arteries; however, they infrequently can arise from the aorta via the 6th thoracic intersegmental artery (Figure 5B) [6]. As in our case, an origin from the common carotid, which usually arises from the 3rd aortic arch, is rare. Early in vertebral artery development, numerous cervical and thoracic intersegmental branches transiently communicate with the dorsal aortae and developing ICA. Based on the anatomy in this newborn, we suspect that one of the cervical intersegmental branches adjacent to the developing common carotid (3rd aortic arch) remained patent joining the common carotid to the right LNA/VA (Figure 5C).

The aortic arch usually ascends from the aortic valve of the left ventricle of the heart as the mesodermal in origin brachial arches develop, and then, it loops overtop the pulmonary vasculature and bends to the left to descend down the posterior aspect of the thoracic cavity [7]. In our patient and roughly 0.05% of the population, the aortic arch develops with a mirror aspect where the arch bends to the right and the corresponding vessels are reversely flipped [8]. As seen in this patient, this change in normal development could be the root issue causing further developmental errors and variations with apparent clinical manifestations. From these variants and others, the medical community is quickly recording and identifying many different anomalies in order to better understand the developmental linkage and integration between them and the clinical setting. Below, a discussion of the implications of anatomical variants and clinical syndromes is presented with regards to how they can better be identified and managed clinically.

Clinical & Imaging findings:

A few cases have also been reported on patients with a right PPHA and associated clinical sequelae: a 2-year-old male with contralateral hemiplegia, a 50-year-old male with syncope and dysarthria, and a 46-year-old female with seizure activity [9,10,11]. For our patient, no specific clinical manifestations were apparent, but most likely, will manifest later in life due to the neurologic insult identified on the brain MRI. The particular variant of a low-origin PPHA arising from the common carotid artery has not yet been reported, as to our knowledge. PPHA has previously been associated with TOF, however, this combination of cardiac and vascular anomalies may be unique for this patient. In the instance of the patient presented above, there were no clinical signs of ischemic stroke at the time of imaging; however, if left undiagnosed, the patient could have easily developed additional infarcts and clinical symptoms in the future [12]. An increased risk of intracranial hemorrhage or ischemia stroke in patients with vascular variants, as well as intracranial aneurysms at the junction with the basilar artery, has been previously reported, with rates ranging between 26 - 33% of cases. In some of these reported cases of PPHA, there were signs and symptoms of dysarthria, hemiplegia, and seizure, or glossopharyngeal neuralgia and hypoglossal palsy related to mass effect within the hypoglossal canal [13]. If these variants were not diagnosed in a timely manner, the current interventions, root causes, and future medical care surely could have been more complicated, with potential serious medical consequences for the patients. Identifying these variants early with screening could potentially decrease possible neurovascular complications and hopefully increase

the quality of life with proper preventative measures, including blood pressure and diabetes control.

On angiographic imaging studies, the PPHA typically arises from the distal cervical ICA between C1 and C3, courses posterior to the ICA, enters the base of the skull through the hypoglossal canal and joins or continues into the basilar artery. It is common for the ipsilateral vertebral artery to be hypoplastic or absent and therefore, when present, the PPHA becomes the main blood supplier for the posterior circulation. More infrequently, it can also arise from the external carotid artery. As previously discussed above, the MRA shows this persistent anastomotic connection between the anterior (carotid) and posterior (basilar) circulation, which we presume to be the remnant of the embryological hypoglossal artery coming from the common carotid at the level of C5 (Figure 2).

Treatment & Prognosis:

For a PPHA, there is no definitive guidance for treatment. Symptomatic management is the mainstay of treatment, with emphasis on maintaining appropriate blood pressure control, while monitoring clinically for development of neurologic symptoms. Due to the preferential blood flow to the high oxygen-demanding brain areas and the potential decrease in posterior circulation flow, an ischemic insult is probably the greatest concern for these patients. In the presence of an intracranial aneurysm, there is a high risk of developing intracranial hemorrhage. Preventive treatment of an aneurysm related to the PPHA can be considered, if deemed clinically necessary to avert acute rupture.

From complicated vascular surgeries to the field of imaging, these variants have caused challenges and questioning among physicians treating anatomically variant patients. Being able to identify these variants via imaging modalities before surgery would greatly change the process and prognosis of the intervention and treatment planning. For children and infants, MRI would be the imaging modality of choice due to lack of radiation, even though it is more difficult to obtain on a routine basis, due to the cost, time, and potential need for sedation/anesthesia [13,14]. In adult patients, either MRA or CTA can be obtained to evaluate the vascular anatomy, as they have been shown to have similar sensitivity. Right PPHA is an under-reported variant that demands more investigation into its potential genetic causes and clinical implications, including potential risk factors. It is important for the clinicians to be aware of these variants and follow up on patients for potential clinical symptoms, so they can better identify patients earlier in the disease process and manage appropriately to decrease both morbidity and mortality.

Differential Diagnosis:

Although the above information supports a PPHA as the diagnosis, there are a few other potential anatomical variations that this artery could represent (Table 2), including:

·**Proatlantal artery type I**– Due to its incorporation into the LNAs and the posterior circulation.

·**Vertebral artery variant**– Due to the near complete absence of traditional vertebral blood vessels on MRA.

In conclusion, we presented a unique anatomical variant in regard to the cardiovascular system, specifically a right PPHA originating from the common carotid artery in a patient with a TOF, right aortic arch, and mirror-image branching. We covered the epidemiology, embryology, and developmental trajectory of these complex anomalies and conducted a literature review of past reported similar cases. Lastly, we stated the implications in the clinical setting and imaging required for proper identification and management, along with potential differential diagnoses of this anatomical anomaly.

TEACHING POINT

The persistent primitive hypoglossal artery is a carotid-vertebrobasilar anastomosis, which commonly arises from the internal carotid artery at the level of the C1-3 vertebrae, enters the skull base through the hypoglossal canal and supplies the basilar artery. Knowledge of this rare but important variant can have significant implications for medical management and surgical planning.

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FIGURES

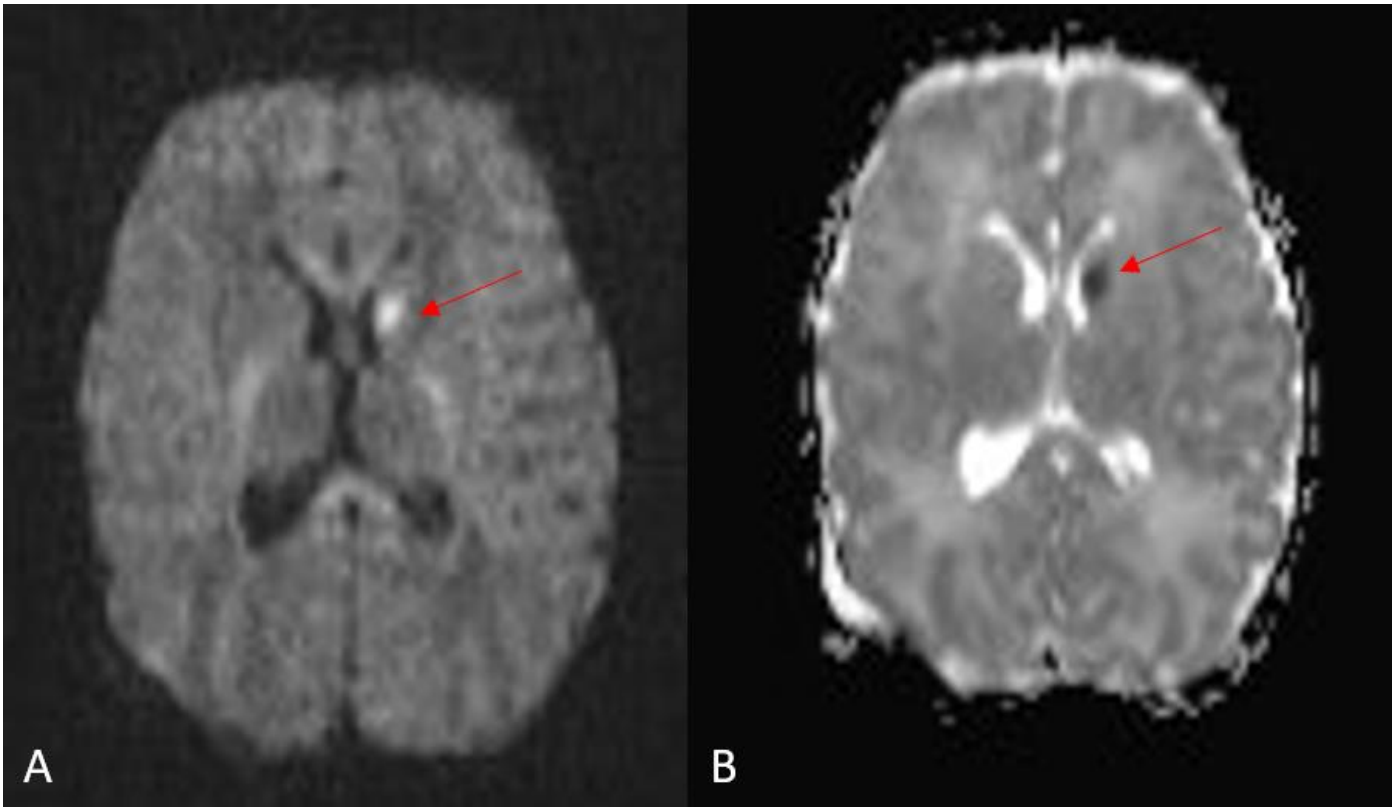

Figure 1: 3-day-old female patient with persistent primitive hypoglossal artery.

Findings: A) Axial diffusion weighted and B) axial apparent diffusion coefficient images of the brain showing a small acute infarct in the left caudate head (arrows).

Technique: 3T Siemens Trio Tim MRI scanner. A) Axial diffusion weighted imaging (DWI), TR: 5400, TE: 99, 3 mm slice thickness. B) Axial apparent diffusion coefficient (ADC), TR: 5400, TE: 99, 3 mm slice thickness.

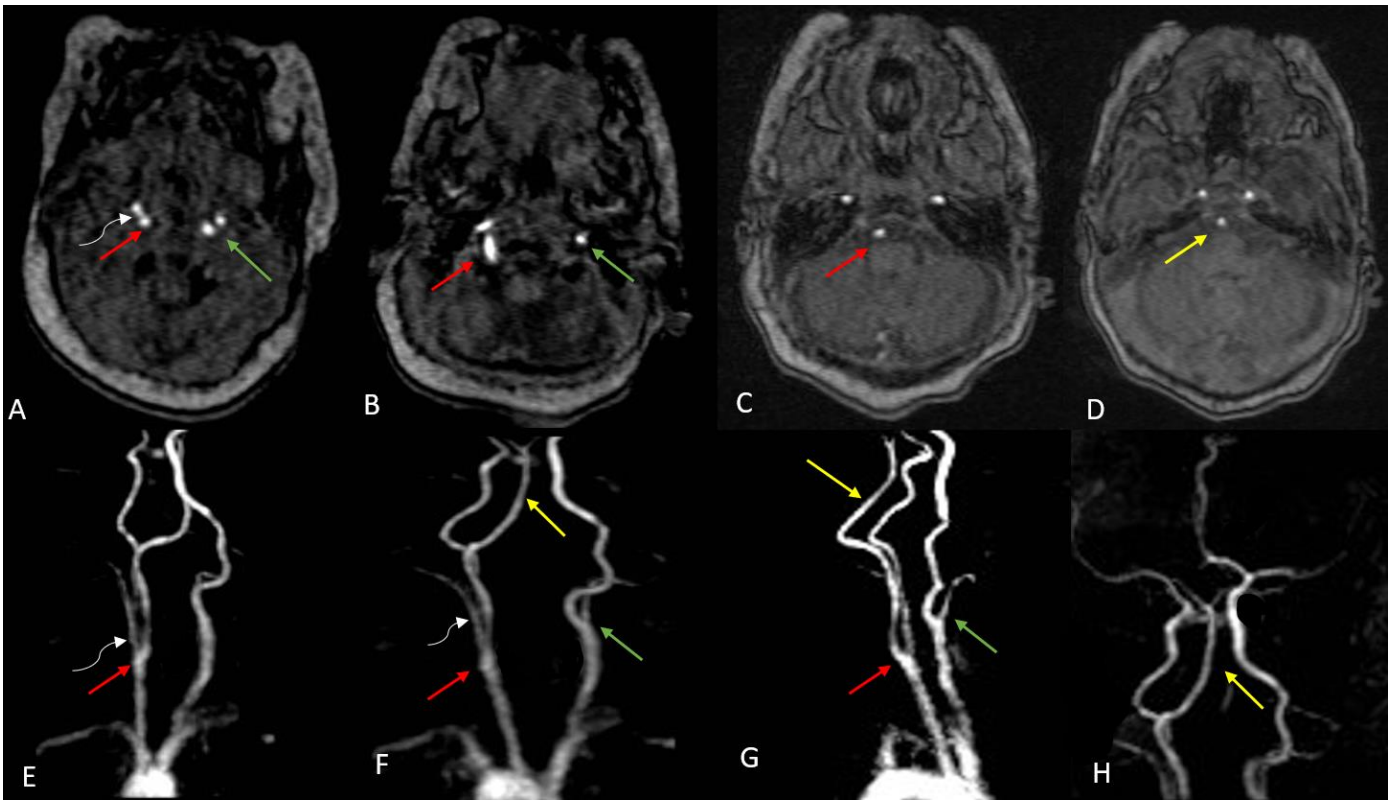

Figure 2: 9-day-old female patient with persistent primitive hypoglossal artery.

Findings: A, B) Axial Time-of-flight (TOF) axial MRA images: A) A large right PPHA arising posteriorly from the CCA (red arrow) and origin of the small right ICA at the level of C2 (white curves arrow); green arrow: left carotid bifurcation. B) Persistent right PPHA (red arrow) coursing through the hypoglossal canal at the level of the skull base; green arrow: left ICA. C, D) Axial TOF MRA images at the level of the cerebellopontine angles showing the continuation of the right PPHA as the intradural right vertebral artery (red arrow), giving rise to the basilar artery (yellow arrow); the left vertebral artery is not visualized. E, F, G) 3D TOF MRA images of the neck: low origin of the right PPHA (red arrows) arising posteriorly from the right CCA at the level of C5, and supplying the basilar artery (yellow arrows) and origin of the right ICA from the CCA distal to the PPHA (curved white arrows); green arrows: left carotid bifurcation. H) 3D TOF MRA image of the Circle of Willis shows normal location and morphology of the basilar artery arising from the right PPHA and non-visualized intracranial left vertebral artery.

Technique: 3T Siemens Trio Tim MRI scanner. A, B, C, D) Axial 2D Time-of-flight (TOF) MR angiographic images of the neck, TR: 20, TE: 3.41, 0.5 mm slice thickness. E, F, G) 3D TOF MR angiographic images of the neck at different obliquities, TR: 20, TE: 3.41. H) 3D TOF MR angiographic images of the Circle of Willis, TR: 20, TE: 3.41.

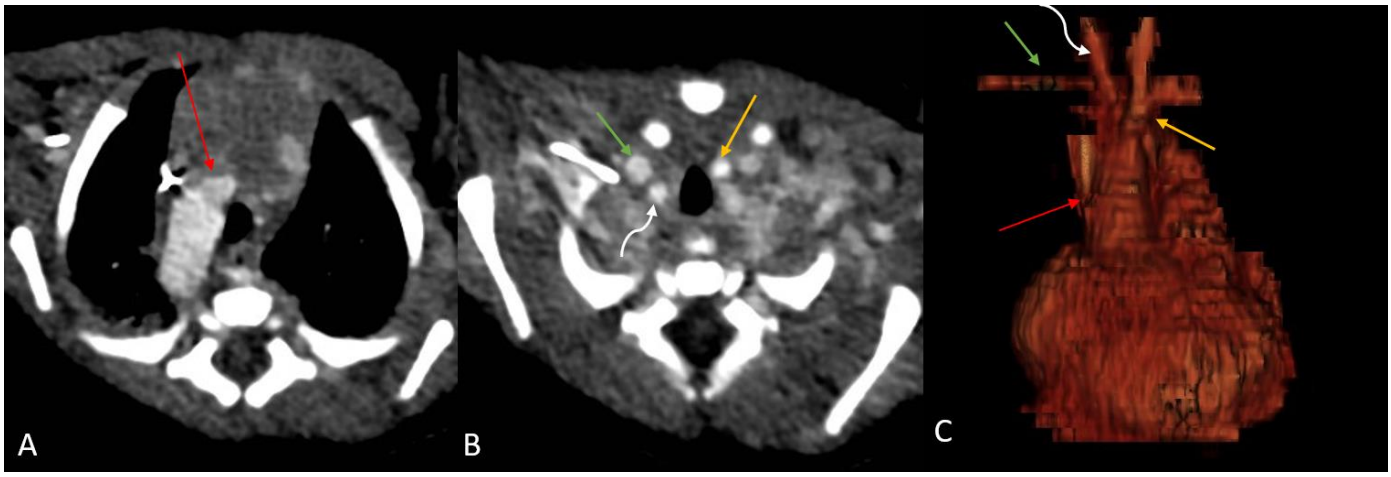

Figure 3: 9-day-old female patient with persistent primitive hypoglossal artery, Tetralogy of Fallot, right aortic arch and mirror-image branching.

Findings: A) Axial CT angiogram image through the aortic arch showing a right aortic arch (red arrow). B) Axial CT angiogram image at the thoracic inlet. C) 3D reconstructed image showing mirror image branching, with a left brachiocephalic artery (yellow arrows), right subclavian artery (green arrows), and right common carotid artery (curved white arrows) originating from the right aortic arch (red arrow).

Technique: Discovery CT750 HD (128-slice) CT scanner, GE Medical Systems. A, B) Axial CT angiographic images of the chest (199 mA, 80 kV, 2.5 mm slice thickness) acquired immediately after intravenous contrast injection (6 mL Isovue 300). C) 3D reconstruction using TeraRecon processing software (Foster City, CA, USA).

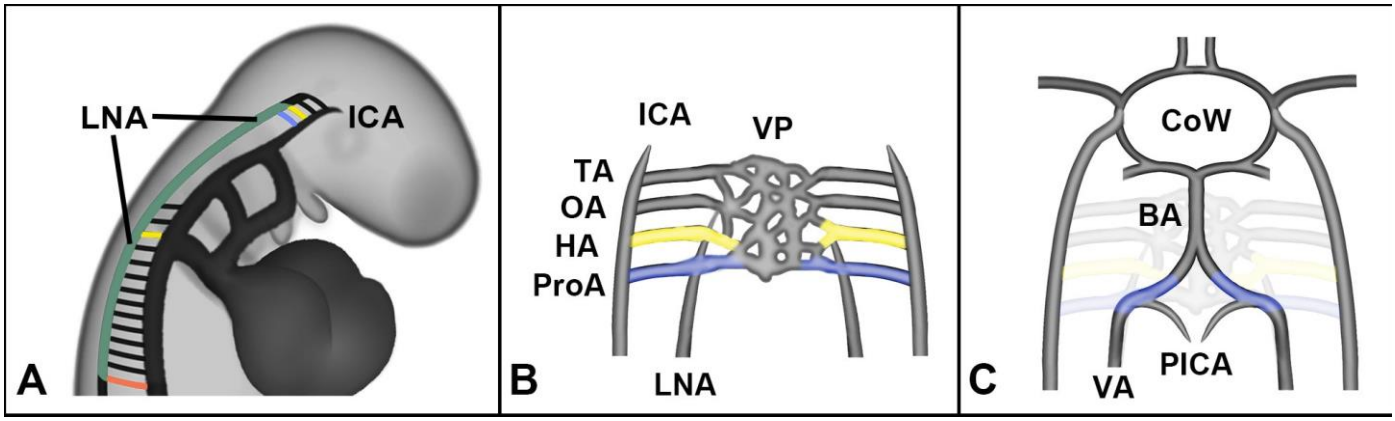

Figure 4: Cerebrovascular development of the hindbrain. A) Side view of an embryo showing the relationship between the developing internal carotid artery (ICA) and the longitudinal neural artery (LNA) (green). B) At the cranial end of the LNA a midline vascular plexus develops to supply the hindbrain supported by 4 branches from the ICA: Trigeminal artery (TA), otic artery (OA), hypoglossal artery (HA, yellow), and the proatlantal artery (ProA, blue). C) Following condensation of the VP and LNAs into the basilar artery (BA) and vertebral arteries (VA), respectively. Note that the VAs includes a portion of the ProAs as they fuse with the BA. PICA = posterior inferior cerebellar artery and CoW = Circle of Willis.

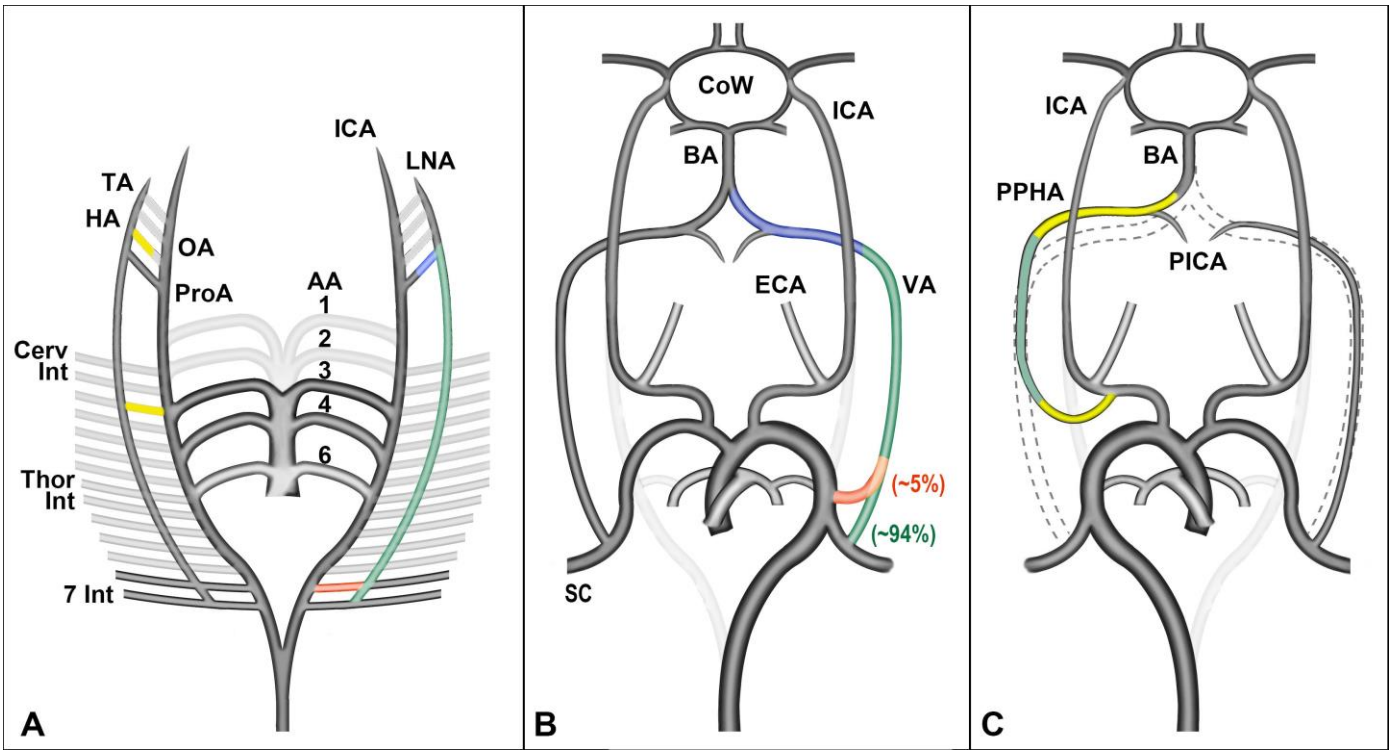

Figure 5: Aortic arch and vertebral artery development. A) Schematic diagram of the aortic arches, the internal carotid arteries that develop from the dorsal aortae, and their vascular connections to the longitudinal neural arteries (LNA) through intersegmental arteries. The lightly shaded vessels typically regress. B) Following further development of a left arching aorta, the interconnections are shown for the 7th intersegmental or subclavian artery (SC), the internal and external carotid arteries (ICA and ECA, respectively), the vertebral arteries (VA), and the basilar artery (BA) with its connection to the Circle of Willis (CoW). Some lightly shaded regressed vessels of the early double arch are shown for a frame of reference. C) Schematic diagram of our patients suspected development. TA = trigeminal artery, HA = hypoglossal artery (yellow), OA = otic artery, ProA = proatlantal artery (blue), AA = aortic arches, Cerv Int = cervical intersegmental arteries, Thor Int = thoracic intersegmental arteries, 7 Int = 7th Intersegmental artery (will become the subclavian (SC) artery), 6th Intersegmental artery (orange), PICA = posterior inferior cerebellar artery, and PPHA = persistent primitive hypoglossal artery (PPHA). Dashed lines indicate the expected vertebral artery pattern.

Etiology	Idiopathic failure of proper embryologic development in-utero with lack of regression.
Incidence	PPHA is very uncommon, roughly 0.1 - 0.2%. It is more commonly seen on the left and unilateral.
Gender ratio	More frequent in females, exact ratios unidentified to date.
Age predilection	Congenital anomaly presenting at birth.
Risk factors	Genetic, in-utero exposure, or idiopathic.
Treatment	Clinical management of blood pressure control and supportive of potential neurological associations, including ischemic stroke, treatment of intracranial aneurysms, surgical decompression for mass effect on cranial nerves, proper surgical planning prior to any neck or vascular surgery.
Prognosis	Ischemic infarct, hemorrhage, seizure activity, and neurologic sequelae, or no complications.
Findings on imaging	Vessel that typically arises from the distal cervical ICA between C1 and C3, enters the base of the skull through the hypoglossal canal and joins or continues into the basilar artery. Our particular variant arises from the common carotid artery around C5.

Table 1: Summary table for persistent primitive hypoglossal artery

	Magnetic Resonance Angiogram (MRA)/ Computed Tomography Angiogram (CTA)
Persistent primitive hypoglossal artery	Arises from the distal cervical ICA between C1 and C3, courses posterior to the ICA, enters the base of the skull through the hypoglossal canal and joins or continues into the basilar artery. It has an anterior course in the neck and does not pass through the transverse foramina or foramen magnum, like a typical vertebral artery.
Proatlantal artery type 1	Arises from the ICA at the C2-3 cervical levels and passes through the foramen magnum, where it joins the vertebral artery. It has an anterior course in the neck and does not pass through the transverse foramina, like a typical vertebral artery.
Vertebral artery variant [15]	Very rare variant of the vertebral artery, arises from the common carotid artery, ascends through its usual course through the transverse foramina of the cervical vertebrae and enters the skull through the foramen magnum. Typically, the vertebral artery arises from the subclavian artery or more rarely directly from the aortic arch.

Table 2: Differential diagnosis table for persistent primitive hypoglossal artery

ABBREVIATIONS

CCA = Common Carotid Artery
CTA = Computed Tomography Angiogram
HA = Hypoglossal Artery
ICA = Internal Carotid Artery
LNA = Longitudinal Neural Artery
MRI = Magnetic Resonance Imaging
OA = Otic Artery
PPHA = Persistent Primitive Hypoglossal Artery
ProaA = Proatlantal Artery
TA = Trigeminal Artery
TOF = Tetralogy of Fallot
TOF MRA = Time-Of-Fight Magnetic Resonance Angiogram
VA = Vertebral Artery

KEYWORDS

Persistent Primitive Hypoglossal Artery; Carotid-Vertebrobasilar anastomosis; Rare Vascular Anatomical Variant; Cardiovascular Anomaly; Magnetic Radiographic Image; MRI; Magnetic Radiographic Angiogram; MRA; Computed Tomography Angiogram; CTA

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