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Persistent Trigeminal Artery Review: Classic and Variant Pattern - Embriology, Anatomic and Radiological Characteristics

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Abstract

Purpose: Persistent Primitive Trigeminal Artery (PPTA) is one of the four transient carotid-basilar anastomoses in embryologic development. It was first angiographically demonstrated by Sutton around 1950. PPTA variant patterns exist, and it is important to be recognized in the medical practical routine. Review the embryology, anatomic, and radiological characteristics of Persistent Trigeminal Artery, including the classic pattern and its variants according to the literature.

Methods: We conducted online bibliographic research on websites such as PubMed using the keywords "persistent trigeminal artery," "carotid-basilar anastomosis," and "MR persistent trigeminal artery." The articles used for this paper were those written in English, Spanish, or Portuguese that included the previously described words. We also collected the information from the Beneficência Portuguesa Hospital Radiology Service in Sao Paulo, Brazil, for comparison.

Results: In the series from the Radiology Service of the Beneficência Portuguesa Hospital in Sao Paulo, Brazil, we identified four PTA variants, which had an incidence of 0.13, consistent with the incidence reported in the literature.

Conclusions: We discovered a very low incidence of this important anastomotic variant. However, despite the low incidence of this pathology, the clinical relevance in some surgeries when we encounter a PPTA is essential to avoid complications, like bleeding or infarction.

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Keywords: Anatomy; Embryology; Persistent primitive trigeminal artery; Persistent trigeminal artery; Radiology

Introduction

Persistent Primitive Trigeminal Artery (PPTA) is one of the four transient carotid-basilar anastomoses in embryologic development. The earliest description of the artery dates to 1844 in the original work and drawings by Quain. [1] However, it was first angiographically demonstrated by Sutton around 1950. The reported incidence is between 0.1-0.6% on adult cerebral angiograms. The very low incidence reported for this embryologic anastomosis makes it an exciting target for studying and reviewing. These variants, if not recognized in the angiography or MRI, and if damaged during brain surgery or endovascular approach, can have catastrophic consequences for the patient, including death. This paper aims to conduct a bibliographic review of online articles to acquire knowledge and understand the concept of embryologic anastomosis to prevent potential harm. In order to accomplish this, we need to comprehend the development of the intracranial vascular system, specifically the Trigeminal Artery, as well as certain related disorders involving the Persistent Trigeminal Artery (PTA). Finally, we present images of some cases of the senior author with a Persistent Trigeminal Artery and some variants.

Material and Methods

We conducted online bibliographic research on websites such as PubMed using the keywords “persistent trigeminal artery,” “carotid-basilar anastomosis,” and “MR persistent trigeminal artery.” The articles used for this paper were those written in English, Spanish, or Portuguese that included the previously described words. Choose the articles within a 10-year time frame. Reviewing the articles was supervised by two authors, who selected the information related to the objectives established in the introduction. We also collected information from the Beneficência Portuguesa Hospital Radiology Service in Sao Paulo, Brazil, for comparison with the results reported in the existing literature. Performed the Magnetic Resonance and Angio-Resonance Magnetic exams (3D Time of Flight- TOF) using a 3T high-field machine (Siemens Erlangen, Germany and General Electric, Milwaukee, USA), as well as conventional angiography (Philips, Netherlands). A radiology technician conducted the exams, and one of the principal authors of this article performed the interpretation.

Results

The data obtained from the Radiology Service of the Beneficência Portuguesa comprises only the cases that one of the authors reviewed and identified throughout 30 years of service. Approximately 3,000 intracranial MRA procedures were evaluated annually. In this series, we identified four PTA variants with an incidence of 0.13%, consistent with the incidence reported in the literature. This paper highlights the indispensable comprehension and knowledge about this anatomy variation to prevent eventual complications followed by considerable morbi-mortality. The rapid and continuous evolution of the technology of MRI machines allows a higher diagnostic rate of these vascular anatomic variations, considering the broad range of populations studied for neurovascular investigation. The study included four female patients with a median age of 49 years. Only one patient presented with an aneurysm in the left paraclinoid (ophthalmic) segment. The posterior communicating artery (PComA) exhibited contralateral involvement in this case. The primary manifestation observed principal was a persistent headache, unaccompanied by any cranial nerve abnormalities. We did not encounter more variants, and as previously described, the classic presentation of PTA remains the most prevalent type. This also matches the literature review.

Discussion

Embryology and Development of the Intracranial Vascular System

The primary goal of developing the cerebral vascular system is to ensure a continuous and adequate supply of oxygen essential to support the growth and functioning of the developing, evolving brain. [2] This study aims to elucidate the sequential changes in the central nervous system, leading to the development of the vascular system as currently understood. Cerebral neurovascular development can be conceptually divided into two distinct phases: vasculogenesis, which is the formation of blood vessels from precursor cells, and angiogenesis, which is the subsequent process of blood vessel growth and maturation.

Vasculogenesis

Vasculogenesis is a crucial process that leads to the development of the vascular organ system and the initial blood cells. This process extends to the meninx primitiva and is responsible for forming the first arteriovenous loops.

The development of the vascular system originates from the specialization of mesodermal cells laterally and posteriorly, resulting in the formation of blood islands or hemangioblastic aggregates. These aggregates will differentiate into endothelial cells, subsequently forming vascular cords. These cords then canalize and interconnect, forming a plexular network that constructs the cardiovascular system. Vasculogenesis progresses in a cranial direction. The formation of the vascular lumen occurs through vacuolization of the endothelial cords. At the initial stage, it is challenging to distinguish between arteries and veins. [3] The endothelial channel proliferation occurs between the cranial ectoderm and the neural surface, initially in the forebrain and midbrain regions and later in the hindbrain. This proliferation progresses from the ventral to the dorsal regions. Later on, the vascular endothelium that lines the neural tube wall undergoes flattening, forming a capillary network. The superficial vascular layer establishes distinct connections with the paired dorsal aorta and cardinal veins, ultimately developing into the principal arteries and veins of the brain [4].

One of the seminal contributions in this particular area of research is the work conducted by Paget, [5] wherein he presented a comprehensive 7-stage investigation on the evolution of cerebral arteries. Next, we proceed to provide a concise overview of these stages.

Stage 1: During the early development of the embryo, the primitive carotid artery supplies the forebrain and hindbrain through transient carotid-vertebrobasilar connections. This occurs at a size of approximately 4-5 mm in a 28-29-day embryo. The Internal Carotid Artery (ICA) supplies blood to the three vesicles: forebrain, midbrain, and hindbrain. Upon reaching the forebrain, the artery divides into two branches: an anterior olfactory branch, which will develop into the Anterior Cerebral Artery (ACA), and a posterior branch surrounding the midbrain. The ICA also establishes a connection with the contralateral ICA posterior to the Rathke pouch, thereby forming the posterior segment of the prospective circle of Willis. The hindbrain receives blood supply from three presegmental and one intersegmental artery channel. Two arteries arise from the proximal ICA: the Trigeminal Artery at the level of the trigeminal ganglion and the Otic Artery at the level of the otic vesicle. Two arteries arise from the paired dorsal aorta: the Hypoglossal Artery, which runs alongside the hypoglossal nerve, and the Proatlantal Artery (also known as the first intersegmental cervical C1 artery), which runs alongside the first cervical nerve. These trunks provide the paired ventral bilateral longitudinal neural arteries that supply the hindbrain. When the bilateral longitudinal neural arteries have fused along the midline, regression of these arteries occurs. This communication exists for a brief duration of 4 to 8 days, at most, before disappearing, particularly in the case of the trigeminal and proatlantal arteries.

Stage 2: The Posterior Communicating Artery (PComA) formation occurs at 5-6 mm in a 29-day embryo. The formation of the PComA occurs through the convergence of the caudal segment of the ICA and bilateral longitudinal neural arteries. The subsequent components combine at the midline to create the Basilar Artery (BA).

Stage 3: The development of the forebrain arteries becomes evident, with the basilar and vertebral arteries completing at 7-12 mm within 32 days. The development of the trunk of the ACA occurs in a rostral direction. The Anterior Choroidal Artery (ACHA) follows a course towards the diencephalon. From the dorsal aspect of the PComA, two branches arise, namely the Posterior Choroidal Artery (PCHA) directed towards the diencephalon and the mesencephalic artery supplying the midbrain. The Vertebral Artery (VA) formation occurs as a longitudinal paravertebral anastomosis between the intersegmental cervical arteries, spanning from C7 to C1.

Stage 4: The mature pattern becomes evident at 12-14 mm, which occurs over 35 days. The branches originating from the anterior division of the ICA include the ACA, the Anterior Communicating Artery (AComA), the early Middle Cerebral Artery (MCA), the dorsal and ventral primitive ophthalmic branches, the prominent ACHA, the PCHA, and the mesencephalic arteries.

Stage 5: is known as the choroid stage. The adult pattern becomes evident in the 40-day embryo, with a 16-18 mm size. During weeks 5 to 7, the meninx primitive develops, forming the fourth, third, and lateral ventricles. The arterial feeders consist of the ACA in the anterior region, the ACHA in the inferior region, and the PCHA in the posterior region. The adult ACA is anatomically distinct from the tela choroidea due to the callosal and hippocampal commissures. However, it originates as a choroidal artery. The subfornical branch of the mentioned structure extends to Monro's foramen during the human fetus's development stage. The presence of choroidal and mesencephalic arteries aligns with the anatomical characteristics of the arterial feeders associated with the vein of Galen arteriovenous malformations.

During Stage 6 (20-40 mm, 44 days) and 7 (40 mm, 52 days), the development of the circle of Willis and the vertebrobasilar blood supply marks the completion of the mature pattern. The presence of the recurrent artery of Heubner is evident, indicating a fully developed MCA. The cortical territory supplied by the Posterior Cerebral Artery (PCA) derives from the dorsal branches of the mesencephalic arteries. This newly formed mesencephalic-PCA territory receives its blood supply from the VA and BA. The anterior inferior cerebellar artery (AICA) and posterior inferior cerebellar artery (PICA) exhibit increased visibility. In summary, the development of the arterial system in the brain occurs within an initially undifferentiated vascular meshwork, and it continuously adapts in response to the changing metabolic demands of the growing neural tissue [6].

Angiogenesis

This discussion will focus on two primary phenomena, cellular proliferation and migration, which occur before the 20th week of development. The development of the brain vasculature occurs in two distinct stages. In the periventricular germinal zone, the first stage primarily takes place and is mostly completed before the 20th week of gestation. The second stage occurs in the cortical plate after the 27th week of gestation. [7] The process of angiogenesis originates from the surface network, specifically

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from the capillary layer of the leptomeningeal vascular meshwork. [8] From a genetic perspective, VEGF-A (vascular endothelial growth factor) plays a pivotal role in the process of angiogenesis, primarily through its interaction with the VEGFR-2 receptor and the coreceptor Neuropilin-1. However, the determination of vascular fate is primarily dependent on flow.

Anatomic Variants and Malformations of the Arterial Vascular System

Persistent vestigial arteries can be observed during the arterial vascular system development. Persistent trigeminal, otic, hypoglossal, and pro-atlantal arteries characterize the blood supply of the hindbrain during embryonic development. (Figure 1) Since this stage consists of minute capillaries, it only lasts a few days. Vascular disorders frequently accompany observing these arteries, particularly aneurysms. [9,10] Either a malfunction in the inhibition processes can be attributed to the persistence of embryonal vessels or a malfunction in the induction of the vascular changes that typically occur later.

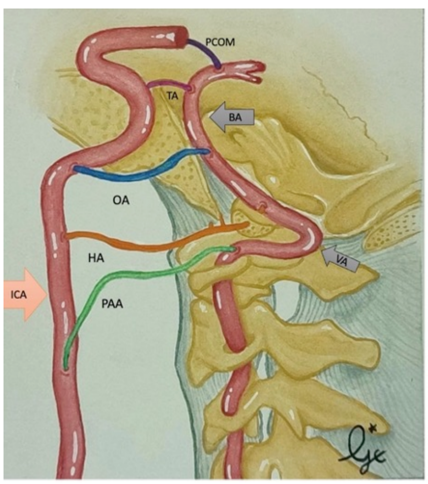


Figure 1: Persistent vestigial arteries: Trigeminal artery (TA) between the proximal carotid siphon and mid-BA; Otic Artery (OA) between proximal intrapetrous segment and the inferior third of the BA via the IAM; Hypoglossal Artery (HA) between extracranial IAC at the origin of the PICA; Proatlantal (PAA) between the extracranial ICA and the occipitovertebral segment of the VA.

The following arteries are considered to be persistent vestigial arteries:

1) The Persistent Trigeminal Artery is the most frequently observed vestigial artery, which typically undergoes regression by the fifth week of development. The reported incidence of this condition ranges from 0.1% to 0.6% on cerebral angiograms in adult populations. The extension of the ICA occurs from its entry into the cavernous sinus to the middle portion of the BA. Several authors have described the factors contributing to the elimination of trigeminal anastomosis. These factors include a shifting in the relative position of the carotid and basilar ends of the anastomosis, as well as the interposition of the basal sphenoid cartilage between the carotid and basilar ends during the 12- to 20-mm stages. The failure of regression of the trigeminal artery is believed to be caused by the occlusion of the proximal portion of the internal carotid artery in the fetus, in addition to other previously described factors. The trigeminal arteries are situated hemodynamically at the junction between the two anastomoses of the developing basilar artery [11].

2) The PTA can be anatomically divided into two parts. The medial part of the PTA courses into the sella and perforates the dura mater within a groove located laterally to the clivus. On the other hand, the PTA's lateral part runs alongside the trigeminal nerve's sensory roots and exits at Meckel's cave, situated below the petroclinoid ligament. The classification proposed by Saltzman is contingent upon the territories that the PTA supplies. Three types have been described, and we will thoroughly examine them in terms of angiographic anatomy and imaging findings. [12] Reported variations of the precavernous portion of the ICA, known as precavernous terminal arteries (PTAv). These arteries originate directly from the ICA and terminate as cerebellar arteries [1,2,13,14].

3) The otic artery is an artery that originates from the ICA within the carotid canal. The structure emerges from the internal acoustic meatus and subsequently converges with the BA. Considerable controversy has surrounded the existence of the anastomotic artery, with only a limited number of cases thus far demonstrating all of its defining characteristics.

4) The hypoglossal artery originates from the ICA at the C1-C3 level. It enters the cranium through the hypoglossal canal and forms the terminal VA. From the terminal VA, it gives rise to the ipsilateral PICA and BA. The Vertebral Arteries (VAs) exhibit hypoplasia or absence, with the contralateral VA terminating in the PICA [15].

5) The proatlantal artery connects the ipsilateral proximal ICA or, less commonly, the External Carotid Artery (ECA) to the interoccipito-atlantal horizontal VA segment. Hypoplasia or aplasia of the VAs typically characterizes this artery. Changes in flow dynamics associated with Persistent Vestigial Arteries may contribute to the susceptibility of developing brain vascular malformations, including aneurysms, Arteriovenous Malformations (AVMs), Moya-Moya disease, pial fistulas, and cranial nerve conflicts [16,17].

Angiographic Anatomy and Imaging Findings

Angiography: Cerebral angiography with Digital Subtraction (DSA) remains the gold standard for diagnosing and identifying Persistent Trigeminal Artery (PTA) conditions (Figure 2). Angiographic studies widely utilize Saltzman's classification. Researchers initially documented this phenomenon in 1959 and classified it into three distinct types. [18,19] Saltzman type I refers to a condition where the Superior Cerebellar Artery (SCA) and PCA supply the upper BA. At the same time, the proximal BA is usually underdeveloped, and the ipsilateral posterior communicating artery (PCom) is absent. Saltzman type II refers to a condition where the BA supplies the SCAs exclusively, while the ICAs supply the PCAs through the PComs. In this type, the initial segment of the PCAs, known as the basilar segment, is absent. Saltzman type III refers to a condition where the trigeminal artery connects with a residual portion of the primitive paired longitudinal neural artery. In this type, the trigeminal artery supplies only one cerebellar artery on the same side without joining the BA. The final type can be further classified into three subtypes: 3a, which anastomoses with the Superior Cerebellar Artery (SCA); 3b, which anastomoses with the AICA; and 3c, which anastomoses with the PICA. In the paper mentioned above by Weon, [20] They are attempting to reclassify the various types of PTA. Type 3 refers to the Persistent Primitive Trigeminal Artery (PPTA), which supplies the contralateral side by the contralateral PCA. In contrast, type 4 refers to the scenario where the PPTA supplies the ipsilateral PCA. The classification system includes a type 5, corresponding to Saltzman's type III variants. Specifically, type 5a is characterized by anastomosis with the SCA, type 5b with the AICA, and type 5c with the PICA (Figures 3,4). Siqueira et al. [21] reported an incidence of PTA variants (PTAVs) of 0.18% in a sizeable angiographic study.

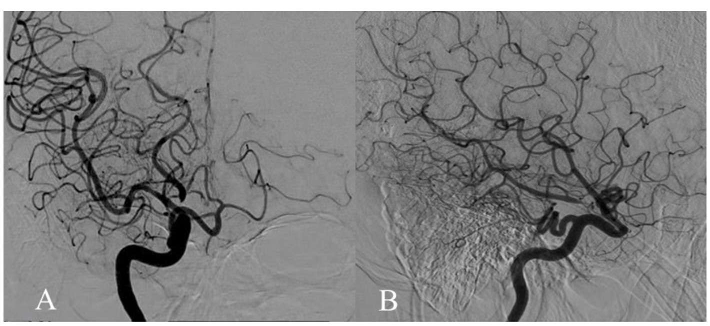
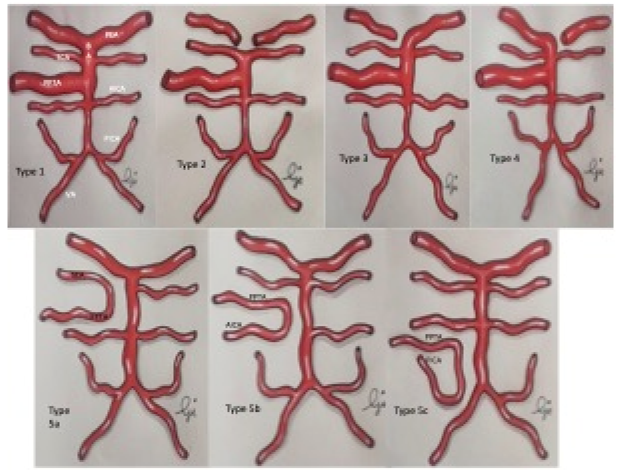


Figure 2: A) DSA showing classic PTA from ICA to BA. B) Lateral view showing classic PTA (yellow arrow). (Saltzman type 1).



Figures 3: Representation of the modified Saltzaman Classification of PTA. We can appreciate the five types and subtypes of these modifications, including Type 1: PPTA is the main supply of the Basilar Artery (BA), Posterior Cerebral Artery (PCA), and Superior Cerebellar Artery (SCA) territories with the adult type of both PCA's. Type 2: PPTA is the main supply of the SCA territories, and PCAs receive the supply predominantly through a patent Posterior Communicant Artery (PComA). Type 3: The contralateral PCA is supplied by the PPTA, and the ipsilateral PCA receives the supply from anterior circulation via PComA. Type 4: The ipsilateral PCA is supplied by the PPTA, and the contralateral PCA receives the blood supply by the anterior circulation via PComA. Type 5: PPTA with no interposition of the BA. These types are subclassified as 5a, 5b, and 5c according to the terminate pattern of the PPTA with the SCA, Anterior Cerebellar Artery (AICA), and Posterior Inferior Cerebellar Artery (PICA).

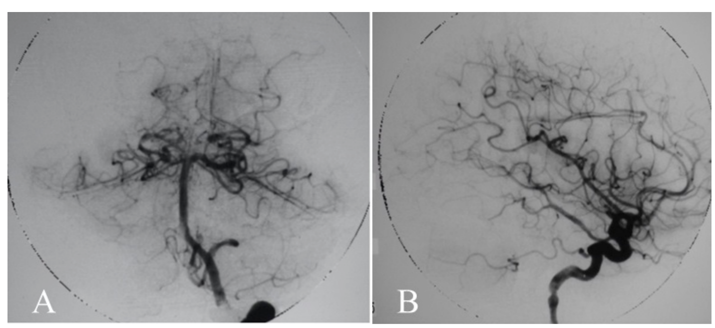


Figure 4: A) Left vertebral angiogram: Absence of right PICA blush parenchimography phase (blue circle). B) Lateral angiogram of Internal Carotid angiogram showing right PICA trigeminal variant arising from right intracavernous Carotid Artery (red arrow). (modified Saltzman type 5c).

Magnetic Resonance: Three-Dimensional (3D) time of flight (TOF) magnetic resonance angiography (MRA) of the supra-aortic arteries has been widely employed as a non-invasive, safe, accurate, and efficient technique for assessing the vascular structures of the head and neck (Figure 5). [22] The 3D TOF-MRA technique is a multichunk 3D inflow MRA method that enables the visualization of the arterial lumen. This visualization is achieved by inflowing unsaturated blood through an image section containing pre-saturated static tissue. 3D TOF-MRA provides a more precise visualization of the intracranial arteries than 3D Contrast-Enhanced Magnetic Resonance Angiography (CE-MRA). 3D CE-MRA images can visualize the (PTA), (PTAVs) (Figures 6 and 7). 3D TOF-MRA axial source images provide a more precise visualization of the medial-type PTA trunk. The trunk originates from the ICA, passes through the cavernous sinus, and connects to the BA. In comparison, CE-MRA images offer a different level of clarity in visualizing this anatomical structure [23].

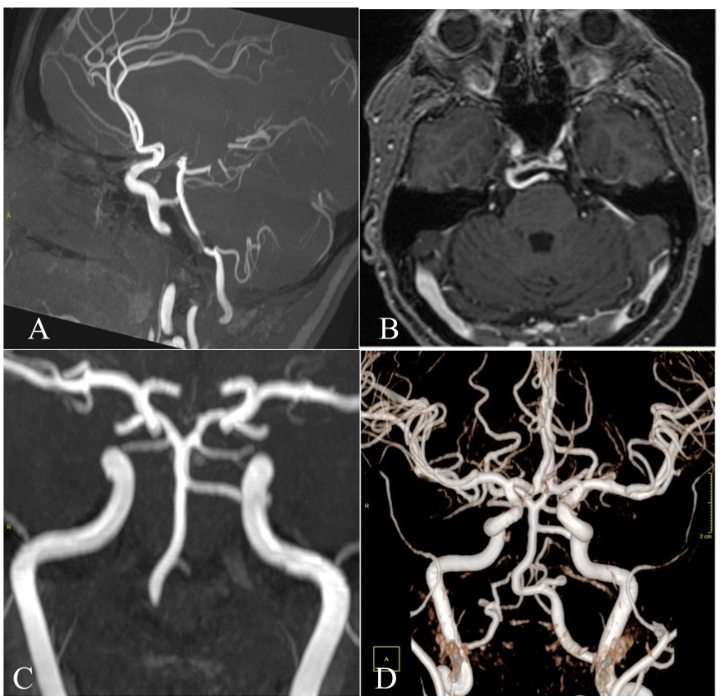


Figure 5: A) Sagittal MRA showing classic PTA from ICA to BA. B) Axial MRA showing classic PTA. C and D) Coronal MRA showing classic PTA from ICA to BA (yellow arrow) (Saltzman type 1).

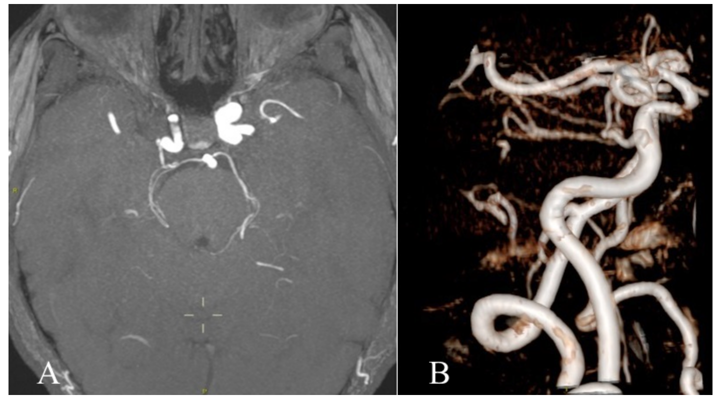


Figure 6: A) Right ACS trigeminal variant arising from right intracavernous Carotid Artery in an axial MR. B) Lateral view of an MRA showing right ACS trigeminal (yellow arrow). (modified Saltzman type 5a).

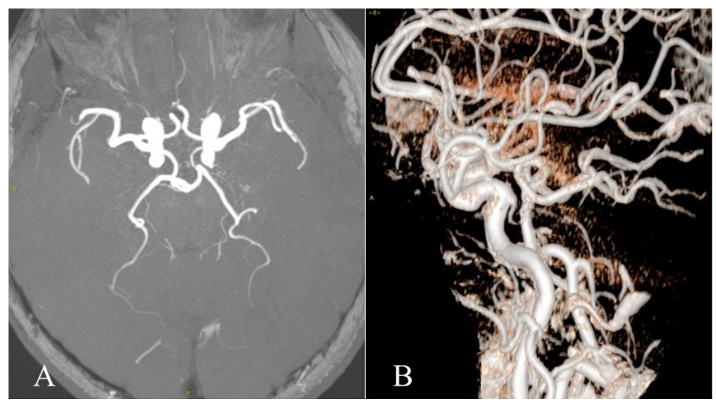


Figure 7: A) Left AICA trigeminal variant arising from the left intracavernous carotid artery in an axial MRA (yellow arrow). B) Lateral view of a MRA left AICA trigeminal (red arrow). (modified Saltzman type 5b).

Surgical Anatomy and Clinical Relevance: A PTA may originate from the left or right ICA. The most common sites of origin for a PTA are the intracavernous carotid artery's posterior bend or lateral wall. [24] About the dorsum sellae, approximately 50 to 59% of all cases of PTA penetrate the sella, perforate the dura near the clivus, and then join the BA with thinning of the sellar floor; in the remaining 41 to 50% of cases, the PTA runs laterals to the sella turcica. Ohshiro et al. [25] classified PTA into two types: a medial type in which the artery runs through the dorsum sellae and perforates the dura mater near the clivus, and a lateral type in which the artery runs between the sensory root of the trigeminal nerve and the lateral side of the sella to penetrate the dura mater medial to Meckel's cave [26].

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Salas Classification: Salas et al. classified the PTA by its relationship to the abducens nerve, distinguishing two variations: [27,28]

1) Lateral O Petrosal Variation: Refers to the anatomical condition in which the trigeminal artery takes a lateral course to the IVth cranial nerve. The arterial branch originates from the posterolateral region of the C4 segment of the cavernous carotid artery. It passes beneath the nerve and penetrates the dura mater just medial to the sensory root of the trigeminal nerve. This variant may be associated with brainstem ischemia, ophthalmoplegia, and trigeminal neuralgia.

2) Medial O Sphenoid Variation: In cases where the PTA takes a medial course relative to the abducens nerve, it originates from the posteromedial aspect of the C4 segment of the cavernous carotid artery and penetrates the dura of the dorsum sellae. The medial variant can be associated with posterior fossa symptoms secondary to a steal phenomenon. These variants are also significant to identify since they may be the origin of a hemorrhage in an endoscopic approach in the pathologies of the seller.

The PTA joins the BA between the SCA, AICA, and PICA. Researchers have described some branches from the PTA, such as pontine perforators and branches to the trigeminal ganglion, the meningohypophyseal trunk, and its branches and cerebellar arteries. Identifying these branches is essential because they function as brain stem vessels. The occlusion of these vessels can result in infarction or ischemic lesions [29,30].

Associated Clinical Conditions

Certain clinical conditions allow the identification of PTA, such as:

a) Cerebrovascular anomalies: fenestrations and ectasias of the ACA, hypoplasia of the BA and VA, absence of the common carotid artery (CCA) or both ICAs, occlusion of VA, and PHACE Syndrom [31].

b) The prevalence of aneurysms in the PTA is comparable to that in the general population. Aneurysms originating from the PTA itself are relatively uncommon and can occur either from the main trunk of the PTA or from a variant of the PTA. Clinically, patients may exhibit symptoms such as sixth nerve palsy, subarachnoid hemorrhage, or carotid cavernous fistula [32].

c) Vertebrobasilar insufficiency and brain stem ischemia: T Microemboli originating from an atherosclerotic carotid artery may contribute to a decreased blood flow in the BA.

d) Carotid-cavernous Fistulas: may develop spontaneously or after a traumatic event and are best treated with endovascular occlusion techniques.

e) Other conditions: Moyamoya disease, NF-1, Klippel-Fiel Syndrome, and AVMs [33].

Conclusions

Our findings at a specialized third-level private Hospital in Vascular Neurosurgery align with the universal literature, showing a very low incidence of this important anastomotic variant. Neurosurgeons and interventional neuroradiologists must be vigilant in recognizing this anatomical variant due to its potential catastrophic consequences for patients during conventional or endovascular treatments of associated pathologies, as well as its implications for clinical neurological conditions.

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