Persistent Trigeminal Artery in Endonasal Resection of Skull Base Tumors: A Systematic Review

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Abstract

Background Primitive persistent trigeminal artery (PTA) is an uncommon embryologic vascular communication between the carotid and basilar arteries, which can be intimately involved by skull base tumors (SBT). Owing to its rarity, skull base surgeons should familiarize themselves with the anatomical variations of PTA to avoid catastrophic complications.

Objective To appraise and summarize the available evidence of PTA involved by SBTs while advocating a standardized algorithm for the surgical planning of these patients.

Methods MEDLINE and PubMed databases were searched using keywords pertaining to PTA and SBTs. Demographics, clinical presentation, radiographic findings, outcomes, and adverse events were extracted and analyzed.

Results A total of 13 cases between 1973 and 2015 were identified. The mean patient age at presentation was 43 years with predilections toward females and pituitary adenomas. Headaches and endocrine abnormalities were the most common symptoms. The tumors were more frequently associated with Salas medial-type PTA (70%) and Saltzman type-I PTA (31%) than seen in the general population in angiographic studies. We also present a new case of atypical meningioma with Saltzman type-1 PTA.

Conclusion With endoscopic approaches to SBTs becoming more commonplace, surgeons may encounter this anatomical abnormality more frequently. It is important for both otolaryngologists and neurosurgeons to gain a complete understanding of the anatomical variations and neurointerventional capabilities for the successful endoscopic management of these situations.

Level of Evidence: 4.

Keywords

- ▶ persistent trigeminal artery
- ▶ arterial variants
- ▶ skull base surgery
- ▶ skull base tumor
- ▶ meningioma
- ▶ arteriovenous malformation

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Introduction

Primitive persistent trigeminal artery (PTA) is the most common and most cephalic of the persistent embryonic carotid-vertebrobasilar anastomosis to persist into adulthood, accounting for nearly 85% of all cases of such vessels.¹ Classically, PTA originates from the cavernous/C4 segment of the internal carotid artery (ICA) and communicates with the basilar artery (BA) in the posterior circulation. It was first described by Quain² in a cadaveric study in 1844 and Sutton³ in angiographic study in 1950. Since then, the incidence of the anomalous has been estimated to be 0.1 to 0.76% in the general population by angiographic studies.^{4–6}

As such, PTA is sometimes reported as an incidental finding in magnetic resonance angiography (MRA), computed tomography angiography, or digital subtraction angiography. Classification schemes such as Salas and Saltzman have been developed to describe PTA and its anatomic variants.^{7,8} PTA has been associated with an increased risk of vascular abnormalities, including concomitant cerebral arterial anomalies, aneurysms, and trigeminal-cavernous fistula. It has also been described as a rare cause of trigeminal nerve compression and thromboembolic ischemia.⁹ Its association with skull base tumors is rarer still, but cases of concurrent pituitary adenomas, meningiomas, chordomas, acoustic neuroma, and hemangioblastomas have been reported.^{1,10–18} To date, only 13 such cases have been documented in the literature, including the current study. We additionally report a case of recurrent skull base meningioma and discuss its unique surgical considerations in the context of a coexisting PTA.

Methods

A review of the published literature on skull base tumor and concurrent PTA was performed. The MEDLINE and PubMed databases were searched for all studies published from 1973 through September 1, 2015, using the following keywords: “persistent trigeminal artery,” “skull base tumor,” “meningioma,” and “pituitary adenoma.” All articles with insufficient data or radiologic studies, and cases of PTA with intracranial or non-skull base tumors were excluded. The full-text versions of the included studies were obtained and the bibliographies of these articles were searched for any additional relevant articles. We also include one new case of recurrent, atypical meningioma associated with primitive trigeminal artery treated at Cedars-Sinai Medical Center. The following data were extracted: patient demographics, presentation, associated pathology, imaging, treatment if any, and outcome. Data analysis was performed using Microsoft Excel (Microsoft Corp., Redmond, Washington, United States).

Results

The average age of the 13 patients in this review was 43.15 years, ranging from 19 to 73 years. Nine patients were female (69%) and four patients were male (31%). There was an observed gender preference of female:male (2.5) and laterality of left:right (1.6) in cases of PTA that are associated with

skull base tumors. The most common presenting symptom was headache in five patients, followed by endocrine abnormalities including galactorrhea, amenorrhea, and obesity. Four cases had cranial nerve (CN) involvement, of which CN VI was the most frequently affected.

The most commonly associated skull base pathology is the pituitary adenoma (seven cases, 54%), followed by meningioma and chordoma (two cases each, 15%), and hemangioblastoma and acoustic neuroma (one case each). Surgical resection was the most common treatment modality. The transsphenoid endoscopic approach was employed in eight cases, or 61% of patients. Other treatments included tricyclic antidepressants, β -blockers, and dopamine agonist. Six patients showed disease-free outcome following surgery, while three were noted to be subtotal resections.

The use of classification schemes of the PTA was not consistent. We noted that the Salas medial-type PTA was more common than the lateral type (70%; 7:3). The occurrence of Saltzman type-I PTA also doubled that of type II (4:2). Only one case of skull base tumor was reported to be associated with a Saltzman type-III PTA, known as a PTA variant (►Table 1).

Report of a Case

A 73-year-old woman with a history of right sphenoid wing meningioma, which was treated previously 3 years prior with an open-approach orbital zygomatic craniotomy followed by external beam radiation, presented to the neurosurgical clinic for routine surveillance after yearly magnetic resonance imaging (MRI). The patient denied any changes in her status, including any changes in visual acuity, and her neurologic exam was normal. Unexpectedly, the patient had a 4 to 5 cm new mass filling her sphenoid sinus, which was absent from the scan 1 year prior. Given the drastic onset and location, the patient was scheduled for transnasal transsphenoidal resection of this tumor.

On the patient's preoperative MRI with contrast, the surgeons noticed that there was a persistent primitive trigeminal artery on the left (►Fig. 1). Given the rapid growth and concern for possible sarcomatous change, the decision was made to proceed with the surgery with special caution of the artery. Preoperative angiography was performed, and unfortunately no collateral flow was identified in the left posterior circulation (►Fig. 2). Therefore, the surgeons were aware that the artery could not be sacrificed. Review of previous imaging also demonstrated the PTA, but given the original lateral location of the tumor at the sphenoid wing, the finding was not relevant surgically.

During intraoperative dissection, the tumor was found to be rubbery in consistency and adherent to surrounding structures. The tumor was debulked meticulously using Doppler ultrasound and image-guided navigation without violation of the artery. Given its texture, the meningioma could not be completely freed from the PTA, which allowed for residual tumor. Final pathology revealed WHO grade II atypical meningioma (►Fig. 3). Despite postoperative chemoradiation including bevacizumab (vascular endothelial

Table 1 Studies meeting criteria for review

Year	Authors	Age (y)	Sex	Pathology	Site	Clinical symptoms and endocrine dysfunction	Surgical approach	Laterality of PTA	Follow-up	Other remarks
1973	Szdzuy et al ¹⁸	19	F	Acoustic neuroma	CPA	Headache, tinnitus, vertigo	NR	Left	NR	Saltzman type-I PTA
1981	Cahill et al ¹⁹	27	F	Pituitary adenoma (prolactinoma)	IS	Headache, amenorrhea, galactorrhea	Transsphenoid	Left	NED (18 mo)	Saltzman type-I PTA. Patient developed a unilateral internuclear ophthalmoplegia secondary to an embolic event during preoperative angiography, which nearly resolved over the course of 9 d
1989	Lee and Kelly ¹	19	M	Pituitary adenoma (Cushing disease)	IS	Obesity, diabetes mellitus, hypertensive, acne	Transsphenoid	Left	NED	Salas medial-type PTA. In axial and coronal CT, PTA was visualized to penetrate and create a groove over the left dorsum sellae
1989	Minokura et al ¹⁷	52	F	Meningioma	Petroclival	Gait disturbance, cerebellar ataxia, CN V/VIII impairment	Transpetrosal-trans tentorial and transzygomatic	Left	NED	Saltzman type-III PTA. Variant PTA was confirmed to course along CN V, replacing AICA
1991	Szeifert et al ¹⁶	24	F	Pituitary adenoma	Sellar	ASX	Transsphenoid	Left	NED	Salas medial-type PTA
1996	Piotin et al ²⁰	52	F	Pituitary adenoma (nonsecreting)	IS	ASX	Transsphenoid	Right	NR	Salas lateral-type PTA
2000	Abe et al ¹⁵	44	M	Pituitary adenoma (nonsecreting)	IS + SS	Headache, bite temporal hemianopsia, panhypopituitarism	Transsphenoid	Left	AWD (subtotal resection)	Salas lateral-type PTA. Saltzman type-I PTA. Preoperative MRI demonstrated tumoral apoplexy
2006	Murai et al ¹⁴	72	M	Hemangioblastoma	Cerebellar vermis	Headaches, vertigo	Occipital transtentorial	Right	NED	Salas lateral-type PTA. Associated with large aneurysm at bifurcation of right cavernous internal carotid artery and the PTA. Declined further intervention for aneurysm
2010	Baltsavias and Valavanis ³	64	F	Chordoma	Clivus + IS + sphenoid sinus	CN VI palsy	Transsphenoid	Left	NED	Salas medial-type PTA. Saltzman type-II PTA. Intraoperative laceration of PTA required endovascular occlusion prior to completion of tumor resection
2014	Machado et al ¹¹	41	F	Pituitary adenoma (nonsecreting)	IS	Headache	None	Right	AWD	Salas medial-type PTA. Medically treated with amitriptyline 25 mg/d and propranolol 40 mg twice daily for headache prophylaxis with partial response. Stable 2-y surveillance MRI
		42	F	Pituitary adenoma (prolactinoma)	IS	Amenorrhea, galactorrhea, obesity	None	Left	AWD	Salas medial-type PTA. Medically treated with cabergoline 0.5 mg/2 wk with resolution of amenorrhea/galactorrhea
2015	Navas et al ¹⁰	32	M	Chordoma	IS + SS + PS + sphenoid sinus	Right hemifacial paresthesia, CN VI palsy	Transsphenoid	Right	AWD (subtotal resection)	Salas medial-type PTA. Saltzman type II. PTA was preoperatively treated with endovascular occlusion by coiling
2015	Present study	73	F	Meningioma	IS + sphenoid sinus	ASX	Transsphenoid	Left	DOD (subtotal resection)	Salas medial-type PTA. Saltzman type I. Atypical, recurrent meningioma. PTA was unable to be dissected free of lesion

Abbreviations: ASX, asymptomatic; AWD, alive with disease; CN, cranial nerve; CPA, cerebellopontine angle; DOD, dead of disease; F, female; IS, intrasellar; M, male; NED, no evidence of disease; NR, none reported; PS, parasellar; PTA, primitive trigeminal artery; SS, suprasellar.

Fig. 1 Skull base meningioma and persistent trigeminal artery. (A) Axial, T1-weighted, gadolinium-enhanced MRI. Preoperative MRI of persistent trigeminal artery (arrows) with an intrasellar course through the recurrent meningioma. Intracavernous internal carotid artery (arrowhead). (B) Axial T2-weighted fluid attenuated inversion recovery (FLAIR) MRI.

Fig. 2 Cerebral angiogram of the left internal carotid artery (A) demonstrating persistent trigeminal artery (PTA). More proximal angiogram (B) fails to show vertebral artery and collateral flow to the posterior circulation.

growth factor A inhibitor) and sunitinib (tyrosine kinase A inhibitor) and repeat debulking, the tumor persisted. With declining functional status, the patient passed away approximately 1 year after her endoscopic surgery.

Discussion

Carotid-vertebrobasilar anastomoses include the hypoglossal, proatlantic intersegmental artery and otic artery, which are named according to their associated fetal anatomy in the 4- to 5-mm embryonic stage.¹² These anastomoses obliterate as bilateral longitudinal neural arteries (LNAs) fuse to form the

BA in the 5- to 9-mm embryo. Obliterating at the 7- to 14-mm embryo stage, the trigeminal artery is the last connection to disappear and therefore the most common to persist.^{9,21} The PTA supplies the LNAs/BA prior to the development of posterior communicating arteries (PCoAs) as the predominant collateral communications between anterior and posterior circulation and the vertebral arteries.

Since its first description by Quain² and Sutton,³ two classifications schemes have been accepted of the primitive trigeminal artery. In eight cases, Saltzman proposed the angiographic classification which divides PTA into three main types.⁷ Saltzman type-I PTA joins the BA between the superior cerebellar

Fig. 3 Atypical meningioma. Hematoxylin and eosin (H&E) sections show meningeal whorls. However, the presence of multiple foci of intrinsic tumor necrosis (asterisk), areas of hypercellularity, prominent nucleoli, and increased mitotic activity designate the tumor as an atypical meningioma. H&E stain, 100 × .

arteries (SCAs) and anterior inferior cerebellar arteries (AICAs) and supplies the entire vertebrobasilar system distal to the anastomosis. As such, the BA proximal to the insertion of the PTA is usually hypoplastic and the ipsilateral PCoA absent. As the predominant supply of the posterior circulation, Saltzman type-I PTA precludes endovascular occlusion and warrants extreme caution during dissection. Sacrifice of the Saltzman type-I PTA during intractable hemorrhage may lead to posterior circulation ischemia and stroke.

In Saltzman type II, PTA joins the BA in the same location. However, patent PCoA and proximal BA remain the dominant supply of posterior cerebral artery (PCA). Therefore, a skull base tumor associated with Saltzman type-II PTA as identified on angiography can undergo endovascular occlusion to decrease bleeding risk, increase surgical exposure, or treat inadvertent lacerations during surgery.

Direct anastomoses of the cerebellar arteries with the cavernous portion of the ICA without connection to the BA are known as Saltzman type-III PTA or PTA variants (PTAV). The AICA variant is the more common type but both variants of the SCAs or posterior inferior cerebellar arteries can arise from the ICA.⁴ A recent angiographic study using 3D time-of-flight MRA estimates the prevalence of PTAV to be 0.2%.²²

In another description, Salas et al classified the PTA by its relationship to the abducens nerve (CN VI) into a medial (sphenoidal) type and a lateral (petrosal) type.^{8,23} The lateral- or petrosal-type PTA originates from the posterolateral aspect of posterior genu segment of the cavernous ICA (C4) and courses lateral under the abducens nerve to penetrate the dura medial to the sensory root of the trigeminal nerve in Meckel cave. As it crosses CN VI, the PTA may displace the nerve superiorly and clinically cause diplopia from nerve palsy.⁹ This origin may be common with or separate from the meningohypophyseal trunk (MHT), as the lateral-type PTA may give rise to the same branching vessels normally arising from MHT (dorsal meningeal, tentorial, and inferior hypophyseal artery). The anomalous artery then joins the BA between the origins of AICA and SCA to supply bilateral PCA and SCA.

On the other hand, the medial (sphenoid)-type PTA arises posteromedially from the posterior vertical segment of C4 and travels medial to the abducens nerve and pierces the dura of the dorsum sella. As such, the medial type has an intrasellar course and has been implicated as a potential vascular risk during transsphenoidal skull base surgery.^{1,10,13}

PTA is usually an incidental finding; however, studies have shown an association with wide-ranging cerebrovascular pathologies, including PHACE syndrome, arteriovenous malformation, trigeminal cavernous fistulas, intracranial aneurysms, carotid/vertebral/aortic arch anomalies, and trigeminal nerve compression.^{21,24} Even more rare is the association of PTA with skull base tumors such as meningioma, pituitary adenoma, chordoma, and hemangioblastoma.^{10,14}

Fig. 4 Management algorithm. Preoperative planning for skull base tumors associated with persistent trigeminal artery.

Only two cases of meningioma have involved the primitive trigeminal artery despite being the most common of all primary brain tumors (~36.1%; ▶ **Table 1**).²⁵ Surgical resection is the mainstay of treatment with adjuvant external beam radiotherapy utilized for recurrent, atypical, or inaccessible disease or in patients with significant comorbidities. Recent case series of 35 patients who had undergone endoscopic resection of skull base meningioma showed that the major factors influencing operative time were the encasement of major vessels and invasion of tumor into brain.²⁶ Intraoperative hemorrhage from vascular structures including persistent congenital vessels may be difficult to control and can be potentially fatal.

The incidence of the skull base tumors in patients with PTA is not significantly different than that of the general population. However, the relative frequency of the intrasellar, Salas medial-type PTA in patients with skull base tumors is 2.3 times more common than the lateral type (▶ **Table 1**). This contrasts large angiographic studies which showed the Salas lateral type to be 11 times as frequent as the medial type, but this difference may be a result of small sample size.⁴ Given that the medial-type PTA inherently carries higher risk of hemorrhage during surgical dissection, we propose a diagnostic algorithm for the work-up of these patients with skull base tumors. (▶ **Fig. 4**)

If a lateral-type PTA is confirmed on the preoperative MRI, no further imaging is necessary given that lateral-type PTA would not interfere with transsphenoidal and transclival exposure of the posterior fossa. This is fortunate given that lateral-type PTAs are likely to have significant branches to the CNs or brain parenchyma.¹³

Conversely, if a medial-type PTA is confirmed, a cerebral angiography is warranted to distinguish the Saltzman classification and to determine whether the PTA is the dominant supply to the PCA. A preoperative MRA would also delineate the course of the medial PTA for surgical navigation. If there is decreased or nonpatency of PCoA and proximal BA on angiography, the skull base team may choose to dissect carefully around the PTA, although inadvertent injury may require neurointerventional coil occlusion of the offended artery at a higher risk of posterior circulation stroke. However, if collateral circulation to the PCA is confirmed in Saltzman type-II PTA, the skull base team may consider preoperative endovascular occlusion of the PTA to minimize the risk of intraoperative hemorrhage or increase surgical exposure. This was recently performed successfully in the complete resection of an intrasellar chordoma.¹⁰ Unlike that of the lateral-type PTA, Salas medial-type PTA usually only gives rise to small dural branches and may be sacrificed without significant neurological sequelae.

The surgical management aiming at the complete and safe resection of a skull base tumor with such a rare association, PTA incorporated within the lesion, should include preoperative endovascular occlusion. Cerebral angiography may assist with the decision to occlude the PTA. In the presented case, there was no collateral circulation found on angiography (Salas medial type and Saltzman type I), and therefore the PTA could not be sacrificed. The presence of the

PTA inhibited the gross total resection of the tumor, which directly impacted the overall outcome. As such, thorough knowledge of the vascular variants is invaluable in the perioperative planning for the skull base surgeon.

Conclusion

The intimate relationship between skull base tumors and the surrounding neurovascular structures of the brain makes their surgical removal a challenge. PTA is an uncommon anatomic variation of the carotidobasilar circulation that must be considered during endoscopic endonasal skull base surgery. Preoperative recognition and careful surgical planning, as well as an experienced neurointerventional radiology team, is advocated in the successful management of these skull base lesions.

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