INTRODUCTION

First described by Gould in 1941 (O’Leary 1991), glomus tumors of the temporal bone are a rare occurrence overall, estimated to affect approximately 0.012% in 600,000 (Bertrand 1976, Balatsouras 1992), but happen to be the most common true neoplasm of the middle ear. In particular, it is the most common pathologic condition of the jugular foramen and second most commonly diagnosed neoplasm of the temporal bone behind vestibular schwannomas.

PHYSIOLOGY

In actuality, the nomenclature “glomus” is a misnomer because these bodies derive from neural crest elements that are felt to migrate with sympathetic autonomic ganglion cells to form paraganglia (Gulya 1993). As a whole, the paraganglia constitute part of the neuroendocrine system found within the adrenal and extraneous systems. Glomus bodies in general are comprised of clusters of chief cells intertwined with arterioles and venules in a “zellballen” network, often serving as neurosecretory modulators of the vascular activity via the release of dopamine and norepinephrine.

In the temporal bone, paraganglia are felt to derive from the third branchial arch (Zak 1982) and perform as oxygen baroreceptors. One anatomical distinction from the adrenal neuroendocrine system is their non-chromaffin nature, lacking an affinity for chromium salts on histological analysis. Temporal bone paraganglia are composed of clusters of type I and type II cells. Chief cells constitute type I cells are have been divided into light and dark cell types, while type II cells are composed of supportive, sustentacular or modified Schwann cells.

On average, people possess two or three paraganglia in the temporal bone typically located in either the anterolateral jugular fossa or within the middle ear, although some have noted more paraganglia present when individuals reach the fifth decade of life. Temporal bone paraganglia are usually associated with the jugular bulb adventitia and the Jacobson and Arnold nerves. Paragangliomas originating from the glomus bodies affiliated with the jugular bulb are
designated as glomus jugulare while those arising from the middle ear are referred to as glomus tympanicum.

**TEMPORAL BONE PARAGANGLIOMA**

Temporal bone paragangliomas tend to affect Caucasians in the fifth decade of life. There is a higher female preponderance at a ratio of 6:1, and many tumors occur on the left side. Those that manifest in younger individuals tend to exhibit more aggressive behavior by either presenting with multifocal disease or actively secreting vasoactive substances. Multicentricity is generally present in only 5-10% of cases, but the incidence can increase to 50% in those affected by a familial autosomal dominant disorder. This disorder is associated with defects on chromosome 11 (Petropoulous 2000) but occurs in less than 10% of all paraganglioma cases. Metastasis occurs rarely at a rate of 3-4% but tends to involve regional lymph nodes, the lung, liver, spleen, and bone (Pluta 1994, Motegi 2008).

Histologically, paragangliomas have a cellular architecture similar to native paraganglia with clusters of chief cells arranged in the zellballen fashion. Most cells will demonstrate some degree of nuclear pleomorphism and hyperchromatism. Approximately 1-3% of tumors will actively store and secrete catecholamines, which is more common with glomus jugulare.

**PRESENTATION**

Hearing loss is the most common symptom individuals complain of, and it is usually conductive in nature, although some will exhibit sensorineural or mixed hearing loss if there is some invasion of the labyrinth. Others will experience pulsatile tinnitus, which typically manifests sooner with glomus tympanicum as compared to glomus jugulare. Other symptoms include aural fullness, vertigo, and headaches. Given its high propensity to bleed with even the slightest manipulation, otorrhagia may result if the tumor protrudes through the membrane.

In more locally advanced cases, there may be some accompanying neurological deficits depending on what anatomical structures are involved. Intrusion into the fallopian canal will result in a facial nerve palsy, while ataxia may arise with extension into the cerebellum at the posterior fossa. Some patients may complain of facial hypesthesia when there is tumor present at the petrous apex. Vernet syndrome arises with compression of cranial nerves IX, X, and XI at the jugular foramen, which can manifest with dysarthria, dysphagia, or shoulder weakness. The addition of Horner syndromic findings such as miosis, ptosis, and anhydrosis would suggest compression of the cervical sympathetic chain that constitutes Villaret syndrome.

Although the incidence of actively secreting temporal bone paragangliomas is significantly low, the presence of one can present similarly as an individual with a pheochromocytoma. Patients with this clinical picture typically present with flushing and diaphoresis, palpitations, labile hypertension, orthostatic changes, headaches, and diarrhea. A clinical suspicion for this warrants further investigation with measuring serum catecholamines and a 24-hour urinary collection of vanillylmandelic acid and metanephrine.

On physical examination, a glomus tumor classically presents as a reddish-blue or violaceous mass medial to the tympanic membrane. Smaller ones tend to be visualized in the inferior quadrants of the tympanic membrane, while a magnified view with either binocular microscopy or endoscopic otoscopy may reveal some pulsations to the tumors. Blanching of the mass with application of positive pressure with pneumatic otoscopy is known as the Brown sign,
and the Aquino sign is the observation of decreased pulsations with carotid compression. Auscultation over the mastoid or infra-auricular region may appreciate a bruit, otherwise referred to as objective tinnitus.

**RADIOLOGY**

Radiographical imaging with at least computed tomography (CT) constitutes the mainstay of working up a glomus tumor. The primary focus with CT is assessing the bony partition between the jugular fossa and hypotympanum as that typically helps distinguish between a glomus jugulare from a glomus tympanicum. Specifically, a glomus jugulare often erodes through the jugular fossa while a glomus tympanicum occupies the middle ear with general preservation of the bony partition. In a similar fashion, CT imaging is able to evaluate for any erosion to the caroticojugular spine which separates the jugular bulb from the petrous carotid artery. As with the jugular fossa, a glomus jugulare can erode through this bony landmark to raise clinical suspicion for possible carotid involvement by the neoplasm.

Given its superiority in assessing the bony anatomy compared to magnetic resonance imaging (MRI), CT is useful to determine if there is any intracranial extension or invasion of the fallopian canal housing the facial nerve. Furthermore, other vascular abnormalities such as a high jugular bulb or an aberrant carotid artery can be ruled out with a CT, which is important as these two conditions can masquerade in a similar presentation as a glomus tumor. A dehiscent jugular bulb is typically darker blue in color and located more posteriorly than a glomus tumor on otoscopy, while an aberrant carotid lies more anteriorly and is paler in appearance.

Glomus tumors classically present with characteristic flow voids on MRI that resemble a mixture of “salt and pepper.” Similarly, MRI is better suited than CT at evaluating for intraluminal involvement of the petrous carotid artery and for occlusion of either the jugular vein or sigmoid sinus by the neoplasm. Although not as well-suited to evaluate bony structures, the advantage of MRI over CT lies in its ability to better delineate soft tissues so as to ascertain between paraganglioma and native tissue. Consequently, the utility of MRI in evaluating intracranial involvement is demonstrated by determining either intradural or extradural extension.

Other tumors that can manifest in the jugular fossa and should be ruled out include schwannomas and meningiomas, which are the second and third most frequently occurring neoplasms at that site behind glomus jugulare, respectively. Schwannomas can enlarge and erode the jugular foramen on CT similar to a glomus tumor, but the erosion typically presents with smooth borders as opposed to the irregular margins associated with a glomus jugulare. They tend to be isointense on T1-weighted imaging and hyperintense in T2-weighted imaging with significant gadolinium enhancement on MRI. Meningiomas are often difficult to distinguish from schwannomas on CT with its propensity to infiltrate the bone around the jugular foramen. They are isointense on both T1-weighted and T2-weighted MRI imaging, but they exhibit characteristic “dural tails” not found with schwannomas.

CT is often sufficient in imaging many glomus tumors since the main preoperative consideration is the status of the jugular bulb, and consequently, CT has supplanted venography to evaluate the jugular bulb. MRI is generally employed whenever the diagnosis or extent of the mass is in question. Given its ability to delineate native and neoplastic tissue, MRI is particularly useful when assessing intradural tumors. Caution is warranted when acquiring MRI
as it can overestimate tumor extent on T1-weighted imaging (Brackmann 2010), especially at the petrous apex as the marrow in that bone is hyperintense and indistinguishable from enhanced neoplasm in that same area. As such, evaluating the petrous apex radiographically is best achieved with both CT and MRI.

Magnetic resonance angiography is generally felt to be inadequate for assessing glomus tumors, and the utility of CT angiography is still under debate. The role of positron emission tomography (Hoegerle 2003) and octreotide scintigraphy (Bustillo 2004) is currently being investigated.

ANGIOGRAPHY

Angiography plays an important role in both the diagnostic workup of glomus tumors and in treating them with preoperative embolization via polyvinyl alcohol or intravascular coils. Occluding the blood supply to a glomus tumor approximately 1-2 days prior to surgical excision will improve intraoperative blood loss and even shrink the mass to assist with removal. Angiography is capable of assessing large tumors and identifying multicentric disease, but it also provides an opportunity to perform a balloon occlusion test to evaluate for adequate collateral intracranial blood flow if carotid sacrifice is anticipated. This possibility is important to consider and plan for in light of the significant morbidity associated with such an intraoperative decision including cerebral infarction and fatality (Linskey 1994).

The primary blood supply for most glomus tumors arises from either the inferior tympanic branch from the ascending pharyngeal artery or from the stylomastoid artery. The stylomastoid artery typically originates from either the occipital or posterior auricular arteries. Other arterial contributors include the middle meningeal artery and carotid arteries. Together, they form four major hemodynamically independent vascular compartments by which glomus tumors can derive from. The inferior tympanic branch of the ascending pharyngeal artery constitutes an inferomedial compartment, while the stylomastoid artery is the source of a posterolateral one. An anterior compartment may be formed from either the anterior tympanic branch of the internal maxillary artery or caroticotympanic branch of the internal carotid artery, and a branch from the middle meningeal artery creates a superior compartment. While individual and separate from one another, multiple compartments can contribute to a glomus tumor in up to 85% of cases.

PATTERN OF SPREAD

Glomus tumors, particularly glomus jugulare, tend to spread around the venous sinuses surrounding the jugular bulb. Sometimes collectively referred to as the “danger zone,” the venous sinuses most commonly involved include the inferior petrosal sinus, internal jugular vein, and the sigmoid sinus (Minor 1994). From here, these tumors can extend toward and beyond the protympanum, hypotympanum, mesotympanum, or intracranial cavity. Of note, while intracranial extension is suspected radiographically in approximately 14-20% of cases (Rigby 1996), up to 50% are pertinent for intraoperative findings of some degree of dural involvement (Spector 1976, Andrews 1989, Jackson 1990).

Neoplastic spread from the protympanum is often facilitated with involvement of the peritubal cell tracts toward the petrous apex, the carotid canal toward the middle cranial fossa, or the Eustachian tube toward the nasopharynx. Extension from the hypotympanum often results in luminal invasion of either the sigmoid sinus or internal jugular vein or spread toward the inferior
petrosal sinus or neural foramina at the skull base. A glomus tumor at the mesotympanum has a similar spread pattern as that of a cholesteatoma. It may reach toward the antrum and epitympanum or more posteriorly toward the facial recess, sinus tympani, or mastoid air cells. While it may extend laterally through the tympanic membrane toward the external auditory canal, a glomus tumor could proceed more medially through the round window and erode the cochlea and internal auditory canal.

**CLASSIFICATION**

There have been a number of schema proposed to describe the size and associated anatomical involvement of glomus tumors, with the first being the one described by Alford and Guilford in the early 1960’s that based their classification on the surgical approach employed to remove the tumor. The more commonly cited ones currently include those developed by Glasscock and Jackson and by Fisch (Brackmann 2010).

The Glasscock-Jackson classification scheme divides into two separate systems, one for glomus tympanicum and another one for glomus jugulare, which are detailed in Tables 1 and 2, respectively. A superscript connotes the extent of intracranial extension if present.

Table 1. Glasscock-Jackson Glomus Tympanicum Classification

<table>
<thead>
<tr>
<th>TYPE</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Limited to the promontory</td>
</tr>
<tr>
<td>II</td>
<td>Completely fills the middle ear space</td>
</tr>
<tr>
<td>III</td>
<td>Fills the middle ear and extends to mastoid</td>
</tr>
<tr>
<td>IV</td>
<td>Extend into external auditory canal</td>
</tr>
<tr>
<td></td>
<td>May extend anterior to internal carotid artery</td>
</tr>
</tbody>
</table>
Table 2. Glasscock-Jackson Glomus Jugulare Classification

<table>
<thead>
<tr>
<th>TYPE</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Involves jugular bulb, middle ear, and mastoid</td>
</tr>
<tr>
<td>II</td>
<td>Extends underneath internal auditory canal</td>
</tr>
<tr>
<td></td>
<td>May have intracranial extension</td>
</tr>
<tr>
<td>III</td>
<td>Extends into petrous apex</td>
</tr>
<tr>
<td></td>
<td>May have intracranial extension</td>
</tr>
<tr>
<td>IV</td>
<td>Extends into clivus and infratemporal fossa</td>
</tr>
<tr>
<td></td>
<td>May have intracranial extension</td>
</tr>
</tbody>
</table>

In contrast, Fisch’s system utilizes a single system that is applicable to both types of glomus tumors which is presented in Table 3. It has been associated closely with related mortality and morbidity.

Table 3. Fisch Classification

<table>
<thead>
<tr>
<th>TYPE</th>
<th>CHARACTERISTICS</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Limited to middle ear cleft</td>
</tr>
<tr>
<td>B</td>
<td>Limited to tympanomastoid complex</td>
</tr>
<tr>
<td></td>
<td>No infralabyrinthine involvement</td>
</tr>
<tr>
<td>C</td>
<td>Involves labyrinthine compartment</td>
</tr>
<tr>
<td></td>
<td>Extends to petrous apex</td>
</tr>
<tr>
<td>D</td>
<td>Intracranial involvement</td>
</tr>
</tbody>
</table>

For type C tumors, it is further divided into three possibilities depending on the degree of invasion of the carotid canal. There is limited involvement of the vertical portion of the carotid canal with C1 tumors but frank invasion of that segment in C2 tumors. Extension into the horizontal portion of the carotid canal constitutes C3 tumors. In a similar fashion, type D tumors are subdivided into D1 and D2 tumors, depending on whether or not the degree of intracranial extension exceeds two centimeters, respectively.

**SURGERY**

Classically, surgical excision is regarded as the definitive treatment modality for glomus tumors although there has been a growing role for radiotherapy, especially in poor surgical candidates or cases of incomplete resection. For the rare occurrence of a vasoactively secreting tumor, it is important to include alpha- and beta-blockade as part of the treatment plan.

In general, a transcanal approach is sufficient for small glomus tympanicum tumors on the promontory whose borders are all clearly visible through the tympanic membrane. A portion
of the external auditory canal may be drilled as needed to access the hypotympanum. Exposing the facial recess is often necessary for glomus tympanicum tumors that extend from the middle ear toward the mastoid region. In contrast, a combined transmastoid-transcervical approach is required to adequately access and remove a glomus jugulare. Larger tumors are better addressed with a modified infratemporal approach. Neoplastic invasion of the foramen magnum and cavernous sinus are typically regarded as unresectable cases (Jackson 1982, Rufini 2006).

While individual cases may warrant specific intraoperative alterations, a transmastoid-transcervical approach to a glomus jugulare involves performing a complete mastoidectomy and opening the facial recess. The dissection is extended more inferiorly toward the upper cervical neck to identify vasculature and lower cranial nerves. The facial nerve is carefully dissected out as it courses through the temporal bone and toward the parotid, and the mastoid tip is amputated. For most glomus jugulare tumors, the facial nerve is often transposed anteriorly to facilitate full exposure of the neoplasm prior to removal with subsequent ligation of the internal jugular vein and packing the sigmoid sinus.

Fisch developed three general approaches for tumors that involve the infratemporal fossa. A Type A approach is similar in methodology to a transmastoid-transcervical approach and provides access to the jugular bulb, vertical petrous carotid artery, and posterior aspect of the infratemporal fossa. There is more exposure anteriorly with a Type B approach that facilitates exploration of the petrous apex and allows access to the mid-clivus, horizontal internal carotid artery, and the superior infratemporal fossa. A Type C approach essentially provides the most exposure with its extent to the anterosuperior infratemporal fossa with the potential to reach the nasopharynx, rostral clivus, cavernous sinus and parasellar area, pterygopalatine fossa, and foramen rotundum.

Although the exact surgical plan will need to be tailored to the individual patient, the initial steps to conducting a modified infratemporal fossa approach share a resemblance to those taken with a transmastoid-transcervical procedure. A similar postauricular incision with extension toward the upper neck is created, and the facial nerve is dissected and transposed. One significant difference is that the external auditory canal is transected and oversewn, and the canal itself along with the tympanic membrane and middle ear contents lateral to the stapes are mobilized. To reach the anterosuperior infratemporal fossa, the zygoma and temporomandibular joint would typically need to be resected and the temporalis reflected inferiorly to dislocate the mandible anteroinferiorly.

Intracranial tumors near the foramen magnum may require a transcondylar, suboccipital approach to fully expose and subsequently remove them. The first major step involves identifying the vertebral artery posterior and inferior to the mastoid tip and along the transverse process of the first cervical vertebra. The bony occiput is removed to expose the occipital condyle and jugular tubercle, which allows access to the hypoglossal nerve and cranial-cervical junction. It is important to consider performing a cervical stabilization procedure if more than half of the condyle is resected.

In general, it is typically advised that any tumor adherent to the internal carotid be left alone to avoid potentially devastating hemorrhage. Especially for glomus jugulare, preservation of cranial nerves is enhanced if the medial wall of the jugular bulb is left intact. Intradural involvement is observed most commonly at the jugular bulb, and proceeding forth with en-bloc resection is usually pursued if intraoperative blood loss by that point is less than 2000mL. Most
surgeons will opt to perform staged procedures to remove intracranial tumors if the blood loss is higher or for profoundly large neoplasms.

Patients need to be counseled extensively on potential complications related to surgical excision. In addition to bleeding-related problems, the close proximity with lower cranial nerves prompts discussion of the possibility of facial nerve injury, hoarseness, dysphagia, or dysarthria. Cerebrospinal fluid leak may arise from removing tumors with intracranial extension. Some late-onset sequelae include tympanic membrane perforations and cholesteatoma (O’Leary 1989, Forest 2001).

**RADIOTHERAPY**

Stereotactic, external beam radiotherapy is an increasingly attractive alternative for individuals who are poor surgical candidates or reluctant to undergo surgery. Furthermore, radiotherapy has been found to be effective in an adjuvant role for multimodality treatment often rendered for incompletely resected or multicentric tumors.

Radiotherapy appears to be comparable to surgery in regards to tumor control, recurrence rates, and morbidity. An important distinction is that radiotherapy is not an ablative treatment; rather, it induces obliterative endarteritis in tumor vessels to halt neoplastic growth but with the aspiration that it results in less cranial neuropathies with the avoidance of potential injury during surgery. Tumor control rates with this method has been estimated at over 90% (Maarouf 2003, Krych 2006), although regrowth has been reported 10-15 years after treatment (Brackmann 2010).

Consequently, patients must be counseled that they essentially would “live in coexistence” with a glomus tumor addressed with radiotherapy. Regular surveillance includes serial radiographical imaging, which should reveal a residual mass that is either stable in appearance or even reduced in size. There should be decreased enhancement on CT and decreased T2-weighted enhancement with diminished flow voids on MRI (Swartz 2009). As alluded to earlier, regrowth of irradiated glomus tumors is possible, but other potential complications include damage to other cranial nerves, osteoradionecrosis, and even radiation-induced malignancies (Lustig 1997). The incidence of these long-term effects is still being investigated.

Ultimately, the main question is whether a glomus tumor is likely to result in significant morbidity or mortality in the natural course of the patient’s remaining life. It would be reasonable to opt for surgical excision in a younger, healthier individual as compared to an elderly one with medical co-morbidities who might be better addressed with nonsurgical endeavors (Glasscock 2003).

**CONCLUSION**

Glomus tumors are the most common neoplasm in the middle ear and second-most of the temporal bone, but they are still uncommonly encountered overall. There are certain symptoms and physical examination findings that are classically associated with these tumors, and they commonly exhibit characteristic radiographical features. Although surgery is considered the most definitive treatment option, radiotherapy has been found to be an acceptable alternative for nonsurgical candidates.
Discussant's comments by Dr. Dayton Young:

Thank you Dr. Pham. That was a good presentation, very extensive and well covered. The first thing to keep in mind is that they are rare tumors and they are benign tumors. They can be very slow growing but they can also be very destructive tumors. There is controversy about how to manage these tumors especially if they are very big. Typically they grow from three different locations, the jugular bulb, just below the jugular bulb in the neck, and in the middle ear, and they spread out, into the middle ear and down into the neck. If the tumor is starting in the ear it is usually detected early, and if it is small, it is taken out. If it is in the neck it is usually found out early and also taken out. It’s the ones that start in the jugular bulb that can go a long time without being noticed. These tumors spread via the routes of least resistance but they usually grow up into the ear and the mastoid. A common route is along the carotid artery which is why the resection techniques go along that artery, up into the petrous apex and toward the cavernous sinus, or along the jugular vein and into the middle ear or the posterior fossa.

When they are a small they are easy to take out. When they are big they involve taking something out of the neck, rerouting the facial nerve, cutting the ear canal. To get along the carotid artery you have to move the temporomandibular joint forward, drill down the anterior wall of the ear canal, drill through the back wall of the TMJ, find the Eustachian tube, drill through the Eustachian tube, find the carotid artery, and there’s the tumor on the other side of that. In cutting the Eustachian tube you are taking out the whole middle ear system. Then you start following the carotid artery up towards the carotid artery, and you have a big risk of stroke.

These things are technically feasible, as we have advanced considerably of the past twenty years but it’s also controversial as to how far to take that in a patient because the cure may be worse than the disease, and that’s where you have to tailor this to the patient. For example, the House group has a 20% risk of facial nerve sacrifice. About 20% are losing their vagus nerve, you have a decent percentage of stroke, and sometimes you have to sacrifice the carotid artery, and of course this is preceded by a balloon occlusion test.

Radiotherapy is, of course, an option, but it is the vascular tissue around the tumor that responds to it, not really the tumor tissue itself. We know that it will shrink the tumor, but we have learned that with external beam radiation we can expect the tumor to begin to grow again after about fifteen or twenty years. We’ve got good results with stereotactic radiation therapy but our followup is only out to thirteen or fifteen years, so we really don’t know what’s going to happen. It is, therefore, controversial whether to palliate these patients, use radiation, or operate on them, which, of course, is the definitive cure.
REFERENCES


Russel EJ. Functional angiography of the head and neck. AJNR 1986; 7:927-936.