Introduction

Paragangliomas are generally benign slow growing tumors with unique tissues of origin, location, genetics, potential for biochemical activity, and multi-centricity. Von Haller in 1743 was the first to describe paragangliomtic tissue— the carotid body, however the function remained unclear for decades. Von Luschka in 1862 and Marchand in 1891 from Europe first described carotid body tumors. Scudder in the United States described removal of a carotid body tumor in 1903. Anatomists described ganglions along the course of Jacobson's nerve as early as 1840, however no association with paragangliomas was made until 1941. Then Guild in 1953 described vascularized tissue of the convexity of the jugular bulb and promontory of the middle ear which he called glomic tissue.\(^1\)

The nomenclature regarding paragangliomas has been confusing. Various authors have referred to these tumors as glomus tumors, chemodectomas, non-chromaffin tumors, and carotid body tumors. Glenner and Grimely in 1974 clarified this confusion by separating the tumors into adrenal paragangliomas or pheochromocytomas and extra-adrenal tumors which are then subclassified as branchiomeric, intravagal, aortosympathetic or viseroautonomic. The branchiomeric and intravagal tumors are found in the head and neck and the correct terminology is paraganglioma based on location, ie. carotid paraganglioma and jugulotympanic paragangliomas. Although the terms carotid body tumor, glomus tympanicum and glomus jugulare persist in common use.\(^1\)

Approximately 90% of tumors arising from the paraganglion system are in the adrenal gland and these tumors are termed pheochromocytoma. The remaining 10% arise from extra-adrenal sites with 85% arising in the abdomen, 12% in the thorax, and the remaining 3% in the head and neck area.\(^2\) The most common paraganglioma of the head and neck is the carotid body, followed by jugulotympanic paragangliomas, and vagal paragangliomas. Other sites include the
larynx, nasal cavity, orbit, trachea, aortic body, lung, and mediastinum. Approximately 1 in 30,000 head and neck tumors is a paraganglioma. Malignancy has been reported in all locations of paragangliomas. Cellular criteria for malignancy, however, have not been established. Malignancy is determined by metastasis, which must be proven with biopsy, because paragangliomas may exhibit multicentricity. Local invasion or aggressive behavior do not indicate malignancy of the tumor. Malignant paragangliomas have been reported in 6% of carotid body paragangliomas, 5% of jugulotympanic paragangliomas, 10 to 19% of vagal paragangliomas, 3% of laryngeal paragangliomas, and in 17% of sinonasal paragangliomas. Accurate 5-year survival rates are not available because of the low malignancy rate of an uncommon tumor. Data from the National Cancer Data Base suggest a 60% 5-year survival rate based on 59 reported cases in which regional metastases were found. Distant metastases had a worse prognosis.

**Classification, Pathology, Biology and Differential Diagnosis**

The paraganglion system was the name coined by Mascorro and Yates to denote collection of neuroectoderm-derived chromaffin cells in extra-adrenal sites. The system is vital in fetal development until the formation of the adrenal medulla, as a source of catecholamines. The function of chromaffin cells is similar to those in the adrenal medulla. They secrete and store catecholamines, and release them on neuronal or chemical signals acting as endocholamines. Paraganglia contain two types of cells: type I, chief cells or granular cells; and type II, the supporting or sustentacular cells. Type I cells, in addition to the rich constellation of intracytoplasmic organelles, also contain dense-core granules seen on electron microscopy. These granules are filled with catecholamines and tryptophan-containing protein, a property that places them in the amine precursor and uptake decarboxylase system (APUD), currently called diffuse neuroendocrine system. Type II cells are support cells resembling Schwann cells in their phenotype and function. Microscopically and irrespective of the site of origin, paragangliomas have a common appearance and resemble adrenal pheochromocytomas. The tumor contains type I and II cells as well as numerous capillaries. Type I cells predominate and are arranged in an organoid-nested pattern, known as Zellballen and the architecture is enhanced by reticulin stain. The cells are polygonal or spindle-shaped with abundant granular eosinophilic or basophilic cytoplasm. Nuclear atypia is variable, and as in other endocrine neoplasms, does not correlate with the behavior. These tumor cells exhibit cuffing by sustentacular cells. Immunohistochemistry aids the diagnosis and differential diagnosis of this neoplasm. Type I cells stain positively with neuron-specific enolase, chromogranin A, synaptophysin, and serotonin. Type II cells stain with S-100 and focally with glial fibrillary acidic protein, a pattern paralleling that of normal paraganglia. Other neuroendocrine tumors may mimic paragangliomas. The World Health Organization has separated these tumors into epithelial and neural with the epithelial tumors including classical and atypical carcinoid tumors and small cell neuroendocrine carcinomas including oat cell, intermediate cell and combined. The neuronal tumor is the paraganglioma. Other tumors that are in the differential diagnosis include melanoma, renal cell carcinoma, medullary thyroid carcinoma and hemangiopericytoma.

As mentioned, paragangliomas have the capacity to produce neuropeptides. This production begins with tyrosine, which is obtained from the diet or synthesized from phenylalanine in the liver. Tyrosine is converted to L-dopa by tyrosine hydroxylase which is the
rate limiting step and inhibited by catechols such as dopa, norepinephrine, and dopamine. The next step in the pathway converts L-dopa to dopamine with the enzyme amino acid decarboxylase. Dopamine B-hydroxylase then converts dopamine to norepinephrine. The final conversion of norepinephrine to epinephrine is catalyzed by phenylethanolamine-N-methyltransferase. This enzyme exists only in the adrenal medulla and in small numbers of neurons in the CNS. Because this enzyme does not occur in head and neck paragangliomas, these tumors to not accumulate or secrete epinephrine. Instead paragangliomas tend to accumulate norepinephrine. Other neurotransmitters also may be produced, including serotonin, vasoactive intestinal peptide, and neuron specific enolase. The capacity for neuropeptide synthesis in head and neck paragangliomas does not translate immediately to clinical findings. Although all paragangliomas have neurosecretory granules, only 1% to 3% are considered functional. Norepinephrine levels must be four to five times above normal to elevate blood pressure. Patients should be asked about signs and symptoms indicating elevated catecholamines. Complaints of headaches, palpitations, flushing, and perspiration should be evaluated. In these patients a 24-hour urine collection is examined for norepinephrine and metabolites, including vanillylmandelic acid and normetanephrine. Excess epinephrine or metanephrine should prompt suspicion of an adrenal pheochromocytoma, because head and neck paraganglioma lack the enzyme to convert norepinephrine to epinephrine. Alpha and Beta-adrenergic blocking is undertaken if a tumor is found to be functional preoperatively. This decreases the risk from sudden catecholamine release that may occur with tumor manipulation in surgery.4

Most paragangliomas are solitary. Multiple pheochromocytomas and paragangliomas are seen in familial syndromes, mainly multiple endocrine neoplasia types IIA and IIB. Multiple endocrine neoplasia type IIA (Sipple's syndrome) is characterized by germline mutation of the RET proto-oncogene on chromosome 10 and is characterized by the triad of medullary thyroid carcinoma, pheochromocytoma, and parathyroid hyperplasia. MEN IIB also presents with mucosal neuromas. The inheritance of MEN IIB also involves the RET proto-oncogene, but at a different site that type IIA. Other syndromes associated with paragangliomas are neurofibromatosis and von Hippel-Lindau disease, which is characterized by retinal angiomas, and cerebellar hemoangioblastomas. Carney described a triad of gastric leiomyosarcoma, pulmonary chondroma, and extra-adrenal functional paragangliomas as Carney's complex. In addition to these associations, a syndrome of familial paragangliomas characterized by multiple paragangliomas, especially in the head and neck region, has been described and occurs in approximately 10% of cases, most commonly as bilateral carotid body tumors. Genetic mapping reveals this syndrome to be linked to chromosomes 11q13.1 and 11q22-q23. The syndrome is autosomal dominant but phenotypically is expressed only if the father transmits the abnormal gene, an excellent example of genomic imprinting.2,8 Additionally, an increased incidence of carotid body tumors has been suggested in individuals living at altitudes greater than 2000 m, atmospheric hypoxia, or with conditions causing chronic arterial hypoxemia such as cyanotic heart conditions and chronic lung disorders.3

Carotid Body Tumors

The carotid body tumor is the most common paraganglioma in the head and neck, and the
most frequent combination of multiple tumors is bilateral carotid body tumors. The overall incidence of multiple tumors is about 10%; some of these may be unrecognized familial genetic mutations. If a familial pattern is recognized the incidence of multiple tumors is between 30 and 50%. Every patient with a carotid body tumor, regardless of family history, should undergo MR imaging of the entire head and neck region to detect multiple tumors. Because multiple tumors may develop metachronously, long-term follow-up is indicated for all patients. If an isolated carotid body tumor is present and the family history is negative other available family members may be assessed by physical exam only. If no other evidence of other tumors is seen, the family of the unilateral patient is given educational information and observed without medical imaging. In patients with multiple paragangliomas it is recommended that the entire extended family of these patients be examined and undergo an MRI screening.6

The average age of diagnosis of carotid body tumors is approximately 45 years and there seems to be a slight predilection for women. The characteristic feature of carotid body tumors is slow growth rate, which is reflected clinically by the delay between the first symptoms and the diagnosis, which averages between four and seven years. A carotid body tumor usually presents as a lateral cervical mass, which is often less mobile in the cranio-caudal direction because of its adherence to the carotid arteries. Many carotid body tumors are pulsatile by transmission from the carotid vessels or less commonly expand themselves, reflecting their extreme intrinsic vascularity. Sometimes, a bruit may be heard by auscultation, but can disappear with carotid compression. The consistency varies from soft and elastic to firm and they are generally non-tender. Approximately 10% of cases present with cranial nerve palsy, most frequently involving the vagal nerve.5

The preferred imaging choice for carotid body tumors is MRI and MRA. They provide good insight into the vascularization of the tumor and the origin and contribution of the several branches of the external carotid arteries. Additionally, MR is the best modality to assess for occult, multifocal tumors and is sensitive for tumors as small as 0.8 cm. The recommended study includes T1, T1 post-gadolinium, T2 Axial FLAIR, and FSE T2 with fat saturation in various planes from the skull base to the thoracic inlet. Angiography, though no longer the first-line imaging method, remains valuable for preoperative evaluation, and the possibility of preoperative embolization. The use of pre-operative embolization is controversial. Some authors recommend its use for large tumors to decrease blood loss, and most do not use for small tumors. In any instance, if used, surgery should be planned 24-48 hours following in order to avoid revascularization, edema, or local inflammation.9 Additionally, angiography with temporary balloon occlusion using clinical and EEG monitoring combined with technetium 99m single-photon emission CT scanning provides greater than 90% specificity as to the tolerance of collateral cerebral circulation in select cases.5

Shamblin in 1971 produced a three-stage classification system used to grade the difficulty of resection in carotid body tumors. Type I tumors were defined as localized and easily resected. Type II covered tumors adherent to or partially surrounding the vessels. Type III carotid body tumors completely encased the carotids. Approximately 70% of tumors are type II or III and increase the risk for injury to the carotid vessels and cranial nerves during resection. Unfortunately, most reports do not mention a specific tumor classification and a more uniform system is needed for analysis of results and consistency of communication in the literature.5
The therapeutic options for carotid body tumors include observation, surgery, and radiation therapy. The preferred treatment of carotid body tumors by the majority of authors is surgical resection. However, this is not without controversy. The incidence of post-operative complication is related to tumor size with tumors less than 5 cm in diameter having a neurologic injury rate of 14%, but in tumors larger than 5 cm vagal nerve paralysis or other complications are common (67%). Overall the incidence of cerebrovascular complication is less than 5%, and permanent cranial nerve impairment as a complication of surgery overall occurs in approximately 20% of cases, and once again is highly variable based on size of tumor. Minimizing surgical complications requires a multi-disciplinary approach utilizing head and neck surgeons familiar with cervical neurovascular anatomy for approaching the tumor and the vascular surgeon for assistance in resection and vascular repair if necessary. The keys to successful surgery are careful preoperative planning, proximal and distal control of the vasculature with vessel loops, careful identification and preservation of neural structures if possible, dissection in the periventricial, white line or plane of Gordon, and preparation for vascular reconstruction if necessary with suture repair, patch grafting, or interposition saphenous vein graft. Routine intraoperative shunting in not recommended and should be used only as necessary in patients who do not tolerated pre-operative balloon occlusion testing. Shunts cause vascular complications, including hemorrhage and thrombosis and are associated with a 6.4% incidence of CNS complications and 1.6% mortality rate.

Radiation local control for paragangliomas is defined as of no evidence of tumor progression following therapy with long term follow-up. Most tumors will show some regression of disease while others will remain stable, but not enlarge. Several studies have reported local control rates of 90-100% for carotid body tumors both for primary radiation patients as well as post-surgical patients with residual disease. Only one patient in three studies was noted to have any severe complications which was a delayed transient CNS syndrome. The most common dose fractions used to treat benign lesions in a recent study were 45 Gy in 25 fractions over 5 weeks. Two patients with malignant tumors received between 65 and 70 Gy. Another evolving area of therapy is stereotactic radiotherapy, which theoretically delivers focused dosing to the affected area. Despite these reports of success, most authors continue to advocate surgical therapy for most carotid body tumors especially if less than 5 cm due to the relatively low rate of complications from surgery. The arguments against radiation therapy include the fact that the tumor is ever present and that viable chief cells have been shown histologically and therefore the patient is not truly "cured", the risk of paraganglioma malignancy, complications of radiation including microvascular, carotid artery disease, temporal bone osteoradionecrosis, and radiation induced malignancy.

Special consideration should be given to the management of multicentric paragangliomas because of the significant morbidity of bilateral cranial nerve deficits on speech and swallowing. Given the slow growth rate of paragangliomas a wait and scan policy, including annual MR imaging, must be considered for each carotid body tumor, especially in the elderly or deconditioned patients. However keep in mind that the complication rate for surgery correlates strongly with tumor size. In the patient with bilateral paraganglioma every effort must be made to save at least one vagal nerve and its laryngeal branches. Before surgery of a large carotid body tumor or paraganglioma invading the skull-base, a contralateral (type I) carotid body tumor
must be removed. In the case of pre-existing palsy (whether caused by surgery or the natural course of the tumor), the contralateral side should be extirpated only if growth has been observed clinically or radiologically. In these cases, further bilateral cranial nerve damage must be prevented. In the case of enlarging tumor, radiation therapy may be an option and some authors are advocating this therapy.

Another recently described and rarely recognized, but probably more common than reported problem following bilateral carotid body excision is baroreflex failure syndrome. The clinical manifestations are caused by the loss of buffering of blood pressure with consequent volatility of arterial pressure and heart rate on both sides of the spectrum. After the excision of the second tumor, patients have sudden hypertension for 24-72 hours, followed by sharp fluctuations of arterial pressure and episodic hypertension with sometimes systolic and diastolic pressure values of 280 and 160 mm Hg, respectively. Headache, dizziness, tachycardia, diaphoresis, and flushing are generally present only when the blood pressure rises. Marked hypotension and reduced heart rate may also occur when the patient is drowsy or under sedation. Most patients also have high emotional lability, even between arterial pressure surges. Therapy consists of sodium nitroprusside in the early recovery phase to prevent excessive hypertension. Clonidine which is a peripheral and central alpha-2 agonist or phenoxybenzamine which is an alpha-1 and alpha-2 antagonist may be used orally for long term control.

Vagal Paragangliomas

Vagal paragangliomas are rare, highly vascular lesions of neural crest origin that arise from paraganglionic tissue associated with one of the three ganglia of the vagus nerve. They account for less than 5% of all head and neck paragangliomas, and only approximately 200 cases have been reported in the medical literature.

Vagal paraganglioma usually originate from the first 2 cm of the extracranial course of the vagus nerve, and most commonly are associated with the inferior vagal, or nodose ganglion. They may be limited to the cervical region, be firmly attached to the skull base, or extend intracranially.

The largest series reported by Netterville found that a neck mass was the most common presenting sign, followed closely by pulsatile tinnitus, pharyngeal mass, and hoarseness. In their series, 36% of previously untreated patients presented with cranial nerve deficits. The tenth cranial nerve was most commonly affected and was partially or totally paralyzed in 28% of patients. Other cranial nerve deficits included hypoglossal (17%), spinal accessory (11%), glossopharyngeal (11%), and facial (6%). Two patients presented with Horner's syndrome.

Magnetic resonance imaging has emerged as the most informative and valuable preoperative imaging technique for vagal paragangliomas. As with all paragangliomas they tend to have a classic salt and pepper appearance on T1 and T2 weighted MR images. Because of the anatomic site of origin of vagal paragangliomas in the poststyloid compartment of the parapharyngeal space, these lesions tend to displace the internal carotid artery anteriorly and medially, and do not tend to widen the carotid bifurcation. If skull base involvement is present a high resolution CT scan should also be obtained as it is superior in evaluating bony detail. The role for angiography is again primarily for embolization. Tumors smaller than 3 cm can be managed without embolization, while in tumors larger than 3 cm embolization is felt to be
beneficial decreasing vascularity for the purpose of dissection and decreasing blood loss.

Because vagal paragangliomas originate from the vagus nerve, often involve multiple cranial nerves, invade the skull base, and may extend intracranially, the excision of these lesions is challenging. Although many surgical approaches to the skull base have been described, the lateral approach allows for a single, continuous progression of exposure for vagal paragangliomas of any size or degree of skull base involvement. The approach is graduated for the size of tumor involved and the spectrum extends from limited cervical exposure to complete mastoidectomy, sigmoid sinus ligation, and mobilization of the facial nerve.

To excise vagal paragangliomas fully, sacrifice of the vagus nerve almost always is required. In the series by Netterville, 37 of 40 cases required a cranial nerve X sacrifice, and all 40 patients experienced permanent vocal cord paralysis. Additionally, Jackson reported new deficits for cranial nerves IX, X, XI, and XII occurring 39%, 25%, 26%, and 21% respectively for lateral skull base surgery for glomus vagale and jugulare. Because of this high rate of cranial nerve injury special consideration need to be given to elderly patients, who may have difficulty with postoperative recovery of swallow. Patients with preexisting paralyses of the contralateral vagus or hypoglossal nerves or those with bilateral vagal paragangliomas are not good surgical candidates. Patients for whom surgery probably would result in bilateral cranial nerve deficits are treated best initially by observation. If tumor growth is documented on imaging, external beam or stereotactic radiation is the best treatment option.13,14,15

Glomus Tympanicum and Glomus Jugulare Tumors

Management of tumors of the temporal bone produced a significant technical challenge, and it is only over the last 50 years that neurotologic techniques have emerged that have allowed removal of these tumors with "acceptable" morbidity, usually affecting cranial nerves. Resection was attempted as early as 1945 by Rosenwasser, however in most instances surgery was limited to exploration due to the extraordinary morbidity and mortality associated with resection. In the 1970's sporadic reports of complete successful tumor removal began to appear. In 1977 Fisch proposed the infratemporal fossa exposure for disease extending beyond the temporal bone confines. In 1980 and 1982, respectively Kinney and Fisch addressed the problem of intracranial extension. Jackson described a single-stage strategy for intracranial extension excision and guidelines for defect reconstruction and prevention of CSF leak. Tumor classification was proposed and two systems, the Fisch classification and the Glasscock-Jackson system are most widely used.

The most common physical sign in paraganglioma diagnosis is a vascular middle ear mass. The differential diagnosis of such a mass is globally small. A high jugular bulb is usually visually differentiable; it is posterior and more blue. A facial nerve neuroma can appear less vascular, and often is confined to the upper quadrants. Critically, an aberrant internal carotid artery must be differentiated from paraganglioma; it is often anterior in the mesotympanum. Primary neoplasms of the middle ear, meningioma, and acoustic neuroma are often not separable. Brown's sign is an uncommon physical finding (10-30%).

The most common presenting symptom is pulsatile tinnitus (80%), followed by hearing
loss (60%). Invasion of the labyrinth determines the degree of sensorineural hearing loss. TM erosion and bleeding are late symptoms. Lower cranial nerve dysfunction is common and includes dysphagia, hoarseness, aspiration, tongue paralysis, shoulder drop, and voice weakness. Facial nerve paralysis signals advanced disease, and is an indication of poor facial nerve prognosis. Myringotomy and biopsy are strictly avoided. Hemorrhage and the ensuing brisk bleeding can be controlled only by transcanal packing, which risks structural damage to the ear.

The CT scan with thin-section temporal bone detail is the best test to differentiate glomus tympanicum tumors from glomus jugulare tumors and to assess the extent of the tumor relative to vital anatomy of the temporal bone. An intact jugular bulb defines a glomus tympanicum tumor. If a jugular paraganglioma is present, intracranial extension and the relation of the tumor to the regional neurovascular anatomy are assessed best by MR imaging. MR imaging is also performed of the head and neck to assess multicentricity. Bilateral carotid angiography is performed to evaluate the relationship of the tumor to the internal carotid artery, and is done immediately preoperatively so that embolization can be accomplished simultaneously if desired.

As with other paragangliomas, treatment consists of observation, surgery, radiation, or a combination, and the treatment plan is individualized based on diagnostic survey outcome, patient age and health, and tumor type. Observation is selected when, in the natural course of the patient’s projected lifespan, the paraganglioma is not expected to cause excessive morbidity or mortality. The paraganglioma is imaged annually to assess its individual biologic behavior. For the symptomatic patient in which their medical condition allows surgery or radiation therapy may be considered an option. Once again bilateral tumors create therapeutic challenge. For glomus tympanicum and jugulare, Jackson recommends operation on the most life-threatening lesion first. The postsurgical neurological outcome then determines future management. After one is operated on and the patient emerges neurologically intact, the residual lesion is operated on no earlier than 6 months postoperatively. Neurological sequelae from the first operation may mandate palliation. Phonopharyngeal denervation and deafferentation bilaterally are to be avoided. Paraganglioma growth is multidirectional and occurs as the tumor spreads from its point of origin along tracts of least resistance, predominately the air cell system of the temporal bone. Vascular lumina, neurovascular foramina, and the eustachian tube provide routes of extratemporal extension intracranially, into the infratemporal fossa or along the skull base. Bone erosion is by ischemic necrosis. This variable tumor extent mandates a system of surgical, multidisciplinary approaches that can create an operation to match the patient’s disease. Two fundamentals of successful surgery are management of the facial nerve including mobilization if necessary and gaining proximal and distal control of the internal carotid artery, which at times is achieved in its intracranial segment.

Glomus tympanicum tumors for which the entire margins of the tumor can be seen circumferentially, can be exposed and removed by transcanal tympanotomy strategies. When any margin is indistinct on otoscopy (ie. II-IV), a postauricular, transmastoid approach, using the extended facial recess or the infratympanic extended facial recess approaches should be used. If the ossicular mechanism or TM is involved, resection deficits can be repaired by traditional tympanoplastic techniques. A canal wall down strategy rarely is indicated. Attachment or involvement of the jugular bulb necessitates abortion of the procedure and the patient's return for
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a larger procedure. In glomus jugulare types I and II, (those confined to the infralabyrinthine chamber, involving only the tympanic segment of the internal carotid artery), a hearing conservation approach can be used. The incision is the same as the one described for lateral temporal bone surgery of glomus vagale; the vessels and cranial nerves IX, X, XI, and XII are identified and controlled in the neck. The extratemporal facial nerve is identified and if needed may be mobilized. A complete mastoidectomy is performed with removal of the mastoid tip. An extended facial recess exposure is made through removal of the inferior temporal bone and skeletonization of the inferior-anterior external auditory canal, which is preserved. This step allows access to the mesotympanum and exposure of the tympanic internal carotid artery to the level of the eustachian tube. The internal jugular vein is ligated in the neck and proximal control of bleeding of intrajugular tumor is controlled with surgicel packing. For glomus jugulare types III and IV a modified or extended infratemporal fossa approach is necessary. In this procedure a complete conductive hearing loss is conceded and the external auditory canal, TM, and middle ear contents lateral to the stapes are resected. Maneuvers such as dislocation or resection of the mandible and/or zygoma, and minimal middle fossa exposure may be necessary. If intracranial extension is resected the problem if CSF leak combined with a large defect may require pedicled trapezius or rectus abdominal free-flap reconstruction. 

The surgical results for glomus tympanicum are generally good. Of 80 patients followed by Jackson with Glasscock-Jackson classifications of 34% type I, 52% type II, 3% type III, and 11% type IV, a mastoid approach was performed in 89% with a canal wall down approach in 16% and transcanal approach in 11%. There were two recurrences at 3 and 14 years postoperatively and one may have been a 2nd tumor identified at the geniculate. There were four subtotal resections. Surgical control was 92.5%. There was one major complication: a cerebrovascular accident after internal carotid artery dissection which caused hemiparesis and resolved to cane mobility. There was one facial nerve paralysis that when decompressed completely recovered.

The results from lateral temporal bone surgery of the skull base including glomus jugulare, glomus vagale, and carotid body tumors with skull base extension have an increased likelihood of morbidity. A group of patients followed by Jackson included 152 patients with surgery for glomus jugulare, 27 for glomus vagale, and 3 for carotid body tumor with skull base extension. Glomus jugulare classification was class I 21.4%, class II 20.6%, class III 34.9%, class IV 23%. Twenty six tumors remained unclassified because they occurred prior to the classification system. Subtotal resection occurred in 18 patients (9.9%), mostly elderly patients who had internal carotid artery or cranial nerve preservation. Of those patients, 28% currently have no evidence of recurrent disease; 22% are alive with disease, whereas 50% have not been followed-up. There were nine recurrences (5.5%). Time to recurrence averaged 98 months and all were glomus jugulare tumors. Preoperative cranial nerve deficits were present in 46% (cranial nerve VII, 18%, VIII 13%, IX 21%, X 30%, XI 17%, XII 24%). Preoperative cranial nerve deficits were associated with a significantly higher(P<0.01) incidence of intracranial extension and deficits of cranial nerves XI, XII were associated with intracranial extension greater than 50% of the time. New cranial nerve deficits occurred for cranial nerve IX in 57%, X in 40%, XI in 62%, and XII in 54% of cases that involved the pars nervosa. New cranial nerve VII deficits occurred in 4.4%; all reanimated at operation. When preoperative cranial nerve deficits were present, pars nervosa was involved and the cranial nerve was resected
in 61%. Without preoperative cranial nerve deficit or intracranial nerve extension present, only 11% required cranial nerve section. Preoperative cranial nerve VII paralysis resulted in facial nerve resection segmentally in 100%. After 1987 when they revised their reconstruction scheme, CSF leak incidence was 4.5% (two rhinorrhea and one neck collection). The mortality rate was 2.7% (5/182). Three deaths related to ICA resection and two from pulmonary emboli which were related to preoperative alpha and beta blockades for tumor catecholamine secretion.

Surgical tumor control (cure; not coexistence with tumor) was achieved in 85%. Complete tumor elimination, when attempted, was achieved in 95%.\textsuperscript{16,17} Rehabilitation strategies outlined by Netterville have shortened in-patient care, time to first glutition, and recovery time dramatically. Speech and voice are improved, and oral intake is facilitated, and outcome horizons are elevated. The morbid aftermath of neurotologic skull base surgery is minimized by the following. In the first postoperative week, Gelfoam injection is used, then in approximately 3 months, vocal cord medialization is planned with or without arytenoid adduction. Primary phonosurgery is no longer performed due to the lack of feedback with the patient under general anesthesia. When velopharyngeal insufficiency is a problem the soft palate is sutured to the posterior pharyngeal wall unilaterally, therefore restoring nasal competency, speech, and deglutition. Facial nerve rehabilitation is accomplished via the usual surgical algorithms.\textsuperscript{16,19}

Radiation treatment for glomus tympanicum tumors is nearly universally not recommended due to the good surgical results discussed above. Radiation treatment for skull base paragangliomas is severely controversial despite reports of good results and low complications, primarily because the therapy does not rid the patient of tumor, but instead in most instances aborts any further growth. The University of Florida reported on 42 temporal bone paragangliomas treated with a mean dose of 42.9 Gy of external beam radiation therapy and median follow-up of approximately 10 years. Local control, once again defined as no evidence of tumor progression after radiotherapy was obtained in 39 of 42 (93%) tumors including nine patients that had been previously treated with surgery, radiation, or radiation and surgery. There was no relationship between the likelihood of local control and whether the lesion had been treated previously or the extent of tumor. One patient underwent salvage surgery after disease progression and is disease free at 2.5 years so that early ultimate local control was 95%. One of the 40 patients experienced severe radiation mucositis that necessitated hospitalization and an unplanned treatment break. There were no other severe complications, no fatal complications and no radiation-induced malignancies.\textsuperscript{10} Cummings reported on 45 patients treated with radiotherapy for temporal bone paragangliomas between 1958 and 1978. Treatment consisted of radiotherapy alone in 34 patients, following local recurrence after surgery in 2 patients, and after subtotal resection in 9 patients. Most patients received 35 Gy and they were followed for a median of 10 years. Local control was obtained in 93%; all 3 patients who experienced a local recurrence were salvaged successfully by an operation (1 patient) or a second course of radiotherapy (2 patients). Two of three recurrences were believed to be secondary to a geographic miss. Complete symptomatic relief of tinnitus occurred in 27/35, vertigo 5/5, discharge, bleeding 3/3, pain 7/7, however only 2/37 improved hearing and 8/21 had relief of sensation of mass effect. Complications included four patients complaining of chronic otitis externa, one external canal stenosis, and one who required surgical drainage for chronic otitis media. The only serious complications were in one patient who accidentally received 7,000 cGy in 26 days who died of brain necrosis, and one who received 5,800 cGy in 20 fractions who
required surgical debridement for soft tissue and bone necrosis 10 years later.\textsuperscript{18}

**Other paragangliomas of the head and neck**

Laryngeal paragangliomas may present in the supraglottic or infraglottic region. No reported cases of multicentricity or familial cases have been reported, and no cases of secreting tumors have been reported. Supraglottic tumors present with hoarseness, shortness of breath, and odynophagia. Vocal cord paralysis is not a common finding preoperatively. Diagnosis is usually made at the time of biopsy of a submucosal laryngeal mass, which may cause brisk bleeding and necessitate a tracheotomy and laryngeal packing; all submucosal laryngeal masses should be imaged before any attempt at biopsy. Open surgical procedures including hemisupraglottic laryngectomy and lateral laryngotomy or pharyngotomy. Infraglottic paragangliomas are rare. They may be situated on the inner surface of the cricoid cartilage, the outer surface of the cricoid cartilage, in the cricothyroid membrane, or in the capsule of the thyroid gland. Symptoms include hoarseness, obstruction, and hemoptysis. Treatment is some form of surgical resection via laryngofissure or lateral approach.

Nasal paragangliomas are rare. Clinical symptoms are similar to those of any obstructing nasal lesion: congestion and rhinorrhea. Occasionally epistaxis may be the presenting sign. On exam the tumors may appear as nasal polyps located on the middle or inferior turbinate, posterior choanae, septum, premaxilla, middle meatus, or ethmoid, and frontal sinuses. Excision can be accomplished by intranasal or external local excision.

**Summary**

Paraganglioma are slow growing, usually benign neoplasms which can be found in many different locations. In the past nomenclature has been confusing, but currently paraganglioma of a particular location is accurate with several unique terms surviving. A thoughtful workup of the patient is necessary regarding multicentricity and familial patterns as well as the possibility of neuropeptide activity. The carotid body tumor is the most common paraganglioma of the head and neck. Surgery is the most common treatment although radiation may be considered in certain circumstances. Temporal bone paragangliomas are more rare and tend to be much more difficult to treat surgically with the exception of glomus tympanicum tumors. While surgical excision is now possible, cranial nerve deficits are likely and radiation therapy is a consideration. Other paraganglioma are rare, but should be considered.

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