CASE OF THE WEEK

PROFESSOR YASSER METWALLY

CLINICAL PICTURE

CLINICAL PICTURE:

A 43 years old male patient presented clinically with tinnitus in the right ear with bulbar, facial and trigeminal nerve dysfunction. Systemic examination revealed elevated blood pressure, with headache and tachycardia.

RADIOLOGICAL FINDINGS

RADIOLOGICAL FINDINGS:



Figure 1. Plain x ray skull base showing dilatation of the jugular foramen with irregular margins.

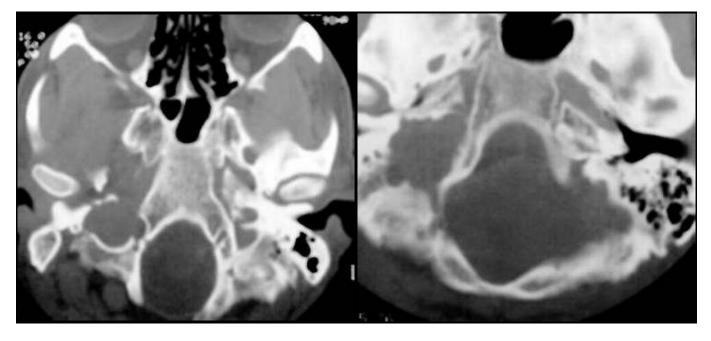


Figure 2. CT scan (bone window) showing dilatation of the jugular foramen with irregular margins.

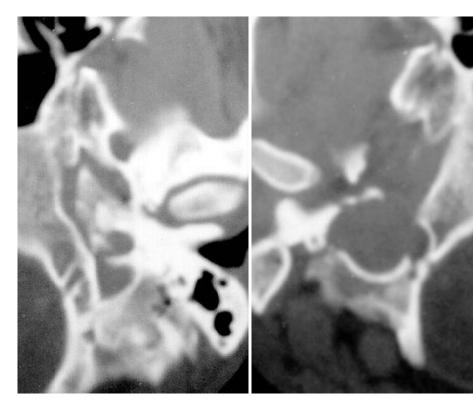


Figure 3. CT scan of the skull base showing wide destruction of the petrous bone with dilatation of the jugular foramen with irregular margins, compare A, (normal) with B image (abnormal).

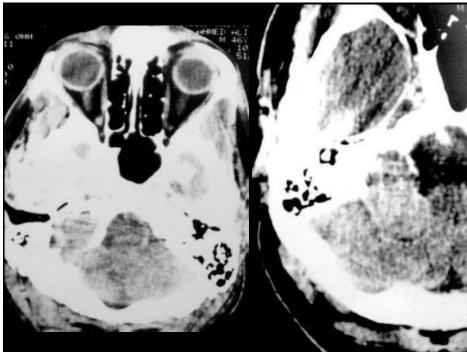
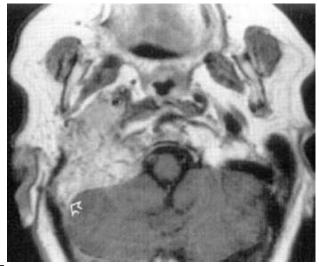


Figure 4. Glomus tumor extending into the cerebellopontine angle.





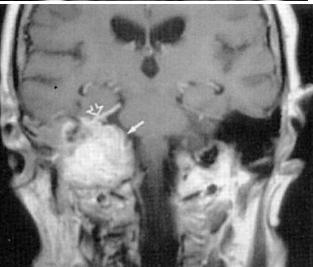


Figure 5. MRI T1 precontrast, and postcontrast, notice the marked enhancement of the glomus tumour.

DIAGNOSIS:

DIAGNOSIS: GLOMUS JUGULARE TUMOR (PARAGANGLIOMA).

DISCUSSION

DISCUSSION:

Although they may be located in diverse anatomic regions, the glomus organs of the human body are homologous organ systems with anatomic and functional similarity. Paraganglioma, glomerocytoma, and chemodectoma are terms used synonymously for tumors of these organ systems.

Characteristic of this group of tumors is their high grade of vascularization; the entire organ is interlaced with an arterial vessel labyrinth that drains into wide venous vessels, situated predominantly on the surface of the tumor. The different locations of tumors of the paraganglion tissue result in the extraordinary variability in presenting clinical findings. Nonspecific otologic symptoms, including tinnitus and conductive hearing loss, must be further evaluated with audiometry and a neuro-otologic examination.

Background: Haller first logged glomus tumors of the head and neck into the medical record in 1762 when he described a mass at the carotid bifurcation that had a glomus bodylike structure. In 1950, Mulligan renamed this type of neoplasm as a chemodectoma to reflect its origins from chemoreceptor cells. In 1974, Glenner and Grimley renamed the tumor paraganglioma based on its anatomic and physiologic characteristics. They also created a classification method based on location, innervation, and microscopic appearance.

Pathophysiology: Glomus tumors of the head and neck paraganglia are part of the extraadrenal neuroendocrine

system. At birth, small patches of paraganglionic cells can be found widely dispersed throughout the body, mostly in association with autonomic nervous tissue. In the head and neck, such areas include the chemoreceptive areas (glomus tissue) of the carotid bifurcations, aortic arch, and the temporal bone. Mafee has noted that paraganglionic cells also can be found, although less frequently, in areas of the orbit (in association with the ciliary ganglion), pterygopalatine fossa (in association with the pterygopalatine ganglion), buccal mucosa, nasopharynx, larynx, and dermis. However, progressive involution, which lasts until puberty, normally obliterates the paraganglionic cells of these and other extraadrenal locations.

Histologically, all paraganglia are composed of chief cells (type I cells, ie, chemoreceptive cells) and sustentacular cells (type II cells, ie, supporting cells). The specific ratio of the two types of cells determines the function of that particular paraganglion.

Developmentally, both types of cells are of neuroectodermal origin, specifically arising from neural crest cells.

The major paraganglia that do not undergo involution are the carotid bodies. They line the medial wall of the bifurcation of the common carotid artery. These paraganglia are a functionally important chemoreceptive organ for homeostasis. Specifically, they detect changes in arterial partial pressures of oxygen and carbon dioxide and changes in pH and other blood-borne factors. Accordingly, the paraganglia can increase or decrease stimulation to the brainstem respiratory centers, which affects various cardiopulmonary functions, including respiratory rate and cardiac output.

Glomus tumors of the head and neck are associated with 4 primary locations as follow:

- Jugular bulb: Tumors here commonly are termed glomus jugulare tumors. These arise in the adventitia of the dome of the jugular bulb. This is the most common type of glomus tumor of the head and neck.
- Middle ear cavity: Tumors here commonly are termed glomus tympanicum tumors. They arise from the glomus bodies that run with the tympanic branch of the glossopharyngeal nerve. Glomus tympanicum tumors are the most common primary neoplasms of the middle ear.
- Vagus nerve: Tumors in this area commonly are termed glomus vagale tumors because of their usual close association with the vagus nerve. Specifically, they arise infratemporally along the course of the cervical vagus nerve.
- Carotid body: Carotid body glomus tumors (also termed carotid body tumors) occur at the bifurcation of the common carotid artery, arising from the tissue of the normal carotid body.

While glomus tumors usually appear as solitary lesions at one site, multiple lesions at multiple sites are not uncommon. As part of the neuroendocrine system, these tumors are highly vascularized. Clusters of tumor cells (type I cells interspersed with type II cells), termed zellballen, are surrounded by a dense network of capillary caliber blood vessels, which are characteristic of glomus tumors pathologically.

Frequency:

• Internationally: Glomus tumors represent 0.6% of neoplasms of the head and neck and 0.03% of all neoplasms. Glomus jugulare tumors are the most common head and neck glomus tumors, while the rarest are the glomus tympanicum tumors. Glomus tumors are the most common tumors of the inner ear, and they are the second most common tumors affecting the temporal bone, second only to schwannomas.

Mortality/Morbidity: The vast majority of glomus tumors is slow to grow and benign. Mortality ranges from 9-15% depending on location and the study; however, they can cause several clinically significant problems. Glomus tumors are soft tissue masses and can cause bulges that are displeasing aesthetically. Glomus jugulare and tympanicum tumors both can cause pulsatile tinnitus and conductive hearing loss. Cranial nerve (CN) deficits are also fairly common. CN VII and CN VIII can be compressed in the middle ear by glomus tympanicum tumors, and CN IX, CN X, and CN XI can be compressed by glomus jugulare tumors as a result of their course through the jugular foramen.

Functioning tumors, which are quite rare, can increase risk of mortality. These active tumors secrete catecholamines, which can produce clinical manifestations of hypertension, headaches, palpitations, and tachycardia.

Sex: Carotid body tumors show no sex predilection; however, some studies have shown evidence of sex predilection for vagale and jugulare tumors in female-to-male ratios of 2.7:1 and 5:1, respectively.

Age: Studies have indicated the peak age of incidence in patients with carotid body tumors is 45-50 years, while the peak age of incidence in patients with vagal and jugular origin is 50-60 years. Glomus tumors of the head and neck are extremely rare in pediatric patients.

Anatomy: Glomus jugulare tumors typically are located just under the skull base, at the bulb of the external jugular vein. The tumors may spread superiorly into the jugular foramen causing CN IX, CN X, and CN XI deficits. The primary blood supply to jugulare tumors is via the ascending pharyngeal artery. In addition, the occipital and posterior auricular arteries can contribute to vascularization.

Glomus tympanicum tumors arise in the middle ear cavity along the tympanic membrane, and they typically receive the same blood supply as jugulare tumors.

Glomus vagale tumors typically present as a cervical mass. The tumors receive their vascularization primarily through the occipital and ascending pharyngeal arteries. Less commonly, the maxillary artery and the muscular branches of the vertebral arteries can contribute vascularization as well.

Carotid body tumors lie in, and can cause splaying of, the carotid bifurcation. The blood supply for the tumors is typically from the external carotid artery. Vascularization also can arise from the internal carotid artery and vertebral arteries.

Clinical Details:

History

- Glomus vagale tumors: Typical presentation is of a slow-growing mass in the parapharyngeal space. Patients with these tumors may present with CN palsies of either one or a combination of the vagus, hypoglossal, accessory, and glossopharyngeal nerves late in the course of the tumor. Vagal nerve deficits are most common late, since the individual fibers are splayed across the surface of the tumor approximately 2 years after onset.
- Carotid body tumors: Patients are largely asymptomatic, presenting with a mobile, nontender, growing, lateral neck mass. Some patients may complain of hoarseness and dysphagia associated with compression of the trachea and esophagus and/or vertigo and paresis resulting from CN compression.
- Glomus jugulare tumors and glomus tympanicum tumors: Patients with either of these types of tumors often present with the same set of clinical features. The most common clinical presentation is pulsatile tinnitus. Other early symptoms include conduction hearing loss, aural pain, vertigo, and hoarseness. At later stages, deficits of the glossopharyngeal, vagus, and accessory CNs are common. In addition, deficits of the facial and vestibulocochlear nerves can be seen.

Since both glomus jugulare and tympanicum tumors present with identical clinical findings, clinical differentiation between the 2 types usually is impossible. However, preoperative diagnosis of the tumor type is important, since this determines the surgical approach; therefore, radiologic imaging is required in these patients.

Patients with functioning tumors may present with hypertension, headaches, palpitations, and tachycardia resulting from increased levels of circulating catecholamines.

A familial component may exist, which predisposes some patients to developing carotid body tumors. These patients also have a higher risk of developing multiple tumors.

Physical

All 3 lesion locations are characterized by the aggressive local growth of the affected paraganglia. Upon gross inspection of resected lesions, carotid body and vagale tumors generally are ovoid in shape with well-circumscribed borders. Conversely, jugulare lesions appear almost malignant, but the shape is a result of the torturous environment through which the tumor navigates during growth. Histologically, all 3 neoplasm locations usually are benign. Malignancies and distal metastatic deposits, while reported, are rare and extremely uncommon in these lesions.

Causes

Glomus tumors are believed to be an overresponse to a change in the body's homeostasis. An insidious link appears to

exist between oxygen deprivation and glomus tumor incidence. Compensatory hypertrophy of the carotid body has been known to occur only in patients with prolonged hypoxia and hypercapnia. Some studies have shown that long exposure to high altitudes appears to correlate with a 10-fold higher incidence of carotid body tumors but no increase of paragangliomas at other sites. Other studies are underway to explore the effects of smoking and other sources of longterm anoxia.

PATHOLOGY OF GLOMUS TUMOURS

- Highly vascular tumours derived from the chemoreceptors situated in the region of jugular fossa, around the superior ganglion of the vagus nerve and the tympanic branch of the glossopharyngeal nerve.
- Pathology Pathology

Pathology

- The tumours consist of polygonal cells with hyperchromatic nuclei. the intralesional blood vessels have a sinusoidal pattern.
- The tumours are supplied by the the ascending pharyngeal artery (branch from the external carotid artery) the tumours may partially fill the internal jugular vein.

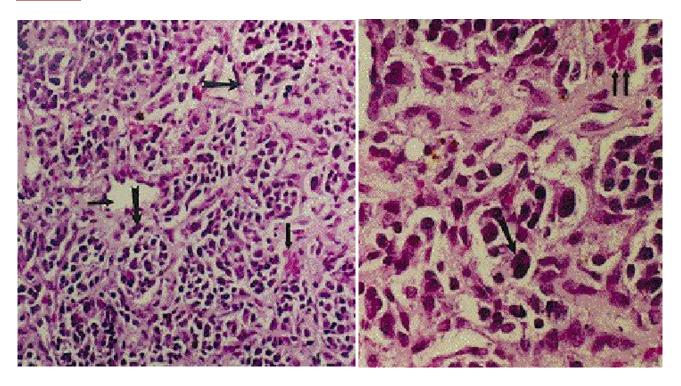


Figure 6. A, Glomus jugulare tumor showing "Zellballen" (large arrows), cell nests of 5 to 30 cells with eosinophilic granular cytoplasm sometimes with considerable nuclear pleomorphism as seen here. Small arrows indicate blood vessels. B, High power photo of tumor to show pleomorphic nuclei (large arrow), not an uncommon feature of these tumors. Mitoses are rare. The double arrows point to a small vessel.

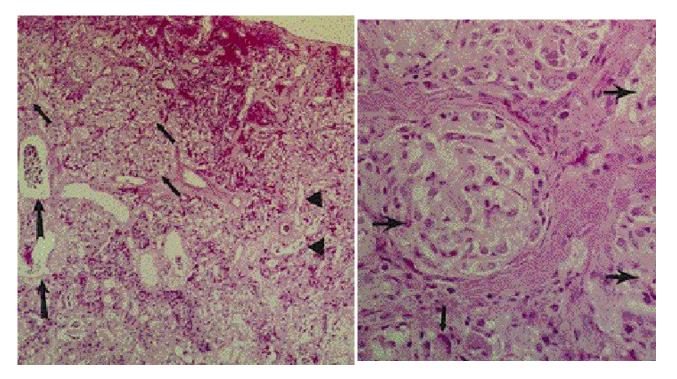


Figure 7. A, Recurrent glomus jugulare shows blood spaces (large arrows) with endothelial lining. Small sinusoids indicated by triangles. Cell nests are present (small arrows) but they are not as well seen as in other examples. B, Glomus tumor, carotid, high power to show "Zellballen" (large arrows). These cells are of neural crest origin. Thick bands of collagen separate the nests. Some nuclear pleomorphism is seen (small arrows).

- Paragangliomas or glomus tumors are generally benign but some metastasize. They are more common in women than in men and generally appear in the latter half of life.
- The glomus tympanicum arises from the promontory of the middle ear and can be seen (6 or 10 power magnification) as a small red or pink mass that pulsates. Symptoms are a loud tinnitus and, depending on the size of the tumor, a conductive hearing loss.
- The glomus jugulare tumor arises from the dome of the jugular bulb or walls of the jugular fossa and grows much larger than the glomus tympanicus tumor. There are no early symptoms but eventually neural deficits appear as cranial nerves VII, VIII, IX, X, and XII become involved. The tumor grows upward through the floor of the middle ear and may be seen as a mass filling the middle ear or even growing into the floor of the ear canal. Sometimes the tumor presents as an aural polyp filling the ear canal. Then bleeding is common and may be profuse.
- The carotid body paraganglioma presents in the neck at the carotid bifurcation and can be moved sidewise but not vertically. Bilateral carotid body tumors are known, especially in the familial form. This tumor, too, can be locally invasive with involvement of the vagus nerve and obliteration of the internal jugular vein. It may metastasize.
- Diagnosis of any of these tumors is made by an arteriogram or CAT scan with contrast.
- Treatment of all of these tumors is preferably by surgery, but irradiation therapy is effective in limiting further growth and may even shrink some tumors.

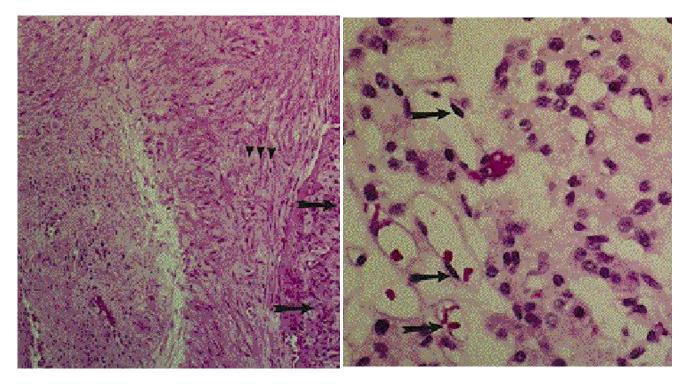


Figure 8. A, Glomus tumor (arrows), rests against adventitia (triangles) of carotid artery. B, Glomus tympanicus, with demonstration of sinusoids lined by endothelium (arrows).

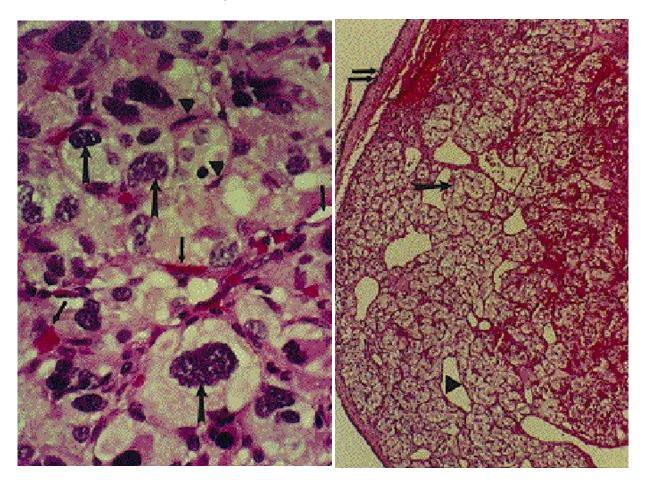


Figure 9. A, Glomus tumor, carotid, showing unusually large nuclei (large arrows) in large vacuolated cells. These rather spectacular hyperchromatic nuclei do not indicate malignancy but reflect the neuro-endocrine nature of the tumor. Note the blood-filled sinusoids (small arrows). Sustentacular cells (triangles) are modified Schwann cells, spindle-shaped and basophilic, and are seen at the margins of cell nests. B, Glomus tympanicus. Zellballen pattern

(arrow) is very definite and there are large vascular spaces (triangle). Also note the covering of the globular middle ear tumor with thin layer of epithelial cells over fibrous tissue (double arrows).

ANGIOGRAPHY OF GLOMUS TUMOURS

Prior to the advent of CT, selective angiography of the external carotid and vertebral arteries was used to establish the diagnosis, to assess the grade of vascularization, and to identify feeding vessels and associated vascular anomalies. In the early stages, glomus tumors receive their blood supply from branches of the external carotid artery. Advanced tumors gain supply from the vertebral and basilar arteries. Angiography used to be important for visualizing surgically important variants of vessels, such as the laterally displaced internal carotid artery in its petrous course, or a cranially localized jugular venous bulb.



Figure 10. Angiography, arterial phase, showing the glomus pathological blood vessels

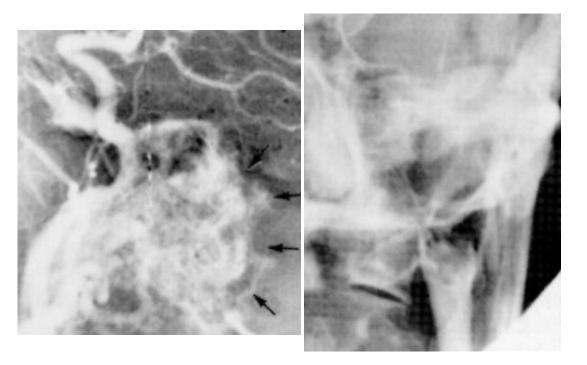


Figure 11. Angiography of a case of glomus tumour, notice the pathological tumour vessels, the tumour cloud, and the complete obstruction of the internal jugular vein

ANGIOGRAPHY OF GLOMUS TUMOURS

Angiography	Often have the characteristics of arteriovenous malformations
Angiography	• Enlarged afferent arteries
Angiography	• Early filling of large veins
Angiography	• The tumour appears as a fairly homogeneous cloud
Angiography	• Partial filling to complete obstruction of the internal jugular vein

NB. ALL THE ABOVE FEATURES ARE ONLY DEMONSTRATED BY SELECTIVE EXTERNAL CAROTID ANGIOGRAPHY

CT SCAN IMAGING OF GLOMUS TUMOURS

CT is currently performed to categorize glomus tumors and to depict foraminal expansion. High resolution CT can reveal the intratympanic and intracranial expansion of the tumor and clarify its relationship to the cervical soft tissues and to identify an aberrant carotid artery, or high jugular bulb. In most cases, glomus tumors can be differentiated from other skull base processes rising dynamic CT with a time- density profile.

However, CT produces a relatively high ratio of false-negative and false-positive results, especially when performed only after intravenous administration of contrast agent. Small tumors, especially those originating from the tympanic glomus, render diagnosis more difficult because they present only as hypointense areas without osseous destruction. MR imaging, dynamic MR, and MRA, with their superior soft-tissue contrast, have since become the diagnostic modalities of choice for evaluating these tumors.

CT SCAN PICTURE OF GLOMUS TUMOURS

CT scan

CT scan

• Often wide destruction of the jugular foramen, petrous bone, base of the middle fossa, and dorsum of the sella turcica

CT scan

- The tumour is often hyperdense on noncontrast ct scan, with dense and uniform contrast enhancement. The tumour might extent intracranially into the middle fossa in the parasellar region or the cerebellopontine angle. Infiltrations of the internal acoustic canal might occasionally occur
- Classification of Glomus Tumors.

For pretherapeutic planning, glomus tumors must be differentiated according to their origin and location. Several classification systems exist for staging these tumors.

Type A tumors represent the glomus tympanicum tumors at the cochlear promontory, whereas hypotympanic tumors are classified as type B tumors, which erode the hypotympanic osseous structures. Characteristically, the cortical border of the jugular bulb is not affected. Type C tumors are defined as jugular glomus tumors without intracranial expansion and are subclassified in types Cl to C4 according to the extent of osseous involvement. Type D glomus tumors are glomus jugulare tumors with intracranial expansion and either extradural or intradural tumor spread.

CLASSIFICATION OF GLOMUS TUMORS OF THE SKULL BASE

ТҮРЕ	DESCRIPTION
Type A	Glomus tympanicum tumor
	Glomus hypotympanicum tumor
Type B	Cortical margins of the jugular bulb unimpaired
	Erosion of the hypotympanic bone
Туре С	Glomus jugulare tumor without intracranial extension
	Cl: Minimal erosion of the vertical segment of the carotid canal
	C2: Complete erosion of the vertical segment of the carotid canal
	C3: Erosion of the horizontal segment of the carotid canal
	C4: Erosion of the foramen lacerum, cavernous sinus
Type D	Glomus jugulare tumor with intracranial extension
	De: Extradural
	Di: Intradural

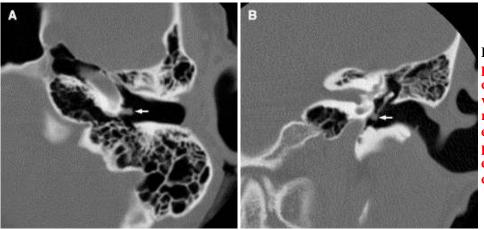


Figure 12. Glomus tympanicum paraganglioma. (A, B) Axial and coronal CT in a 36-year-old woman pulsatile tinnitus with and retrotympanic mass on otoscopic examination. A small soft-tissue mass is present at the medial wall of the middle ear overlying the lower portion of the cochlear promontory (arrows).

MRI IMAGING OF GLOMUS TUMOURS

Several factors make primary evaluation of glomus jugulare tumors with MR imaging advantageous. MR imaging is

superior to CT because of its superior soft-tissue contrast in the absence of signal from surrounding bone tissue. Flow phenomena allow visualization of flowing blood, and are a further reason for the superiority of MR imaging. The topographic relationship of the carotid siphon and the jugular bulb can be reliably determined on unenhanced MR images. MR imaging also allows differentiation between glomus tumors and vascular anomalies, the most frequent of which are the aberrant internal carotid artery and the cranial jugular bulb.

The aberrant internal carotid artery is characterized by atresia from the carotid bifurcation to the petrous segment, with collateralization of the atretic segment over the ascending pharyngeal and the caroticotympanic arteries. The cranial jugular bulb is caused by a diverticular bulge of the superolateral part of the jugular bulb into the hypotympanic cavity. Such vessel variants can be clearly differentiated from glomus tumors extending into the jugular vein after administration of GD-DTPA, particularly in coronal slice orientation or when using MRA. Retrograde phlebography of the internal jugular vein has thus become largely obsolete.

In some patients with small glomus tumors, plain MR imaging reveals at best limited diagnostic information. In these cases, fast imaging techniques with GD-DTPA facilitate the diagnosis. Similar to the time-density profile obtained in dynamic CT, the signal intensity of glomus tumors can be plotted over time when analyzing fast gradient-echo sequences. In all untreated glomus tumors, a rapid and high increase in signal intensity can be observed during the first 60 seconds after administration of GD-DTPA, with an average enhancement factor of 2.5. Enhancement reaches its maximum after 120 to 160 seconds, decreasing approximately 300 to 350 seconds after administration of contrast.

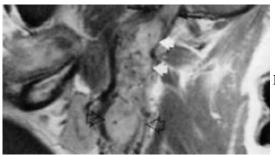


Figure 13. Glomus tumour, MRI T1 notice the salt and pepper appearance

This pattern of signal intensity after injection is due to the high degree of vascularization of these tumors and correlates with the findings of dynamic CT. In comparing the signal intensities of plain and enhanced sequences, an average GD-DTPA uptake of up to 205% is seen in tumors; enhancement is significantly lower in muscle (23%) and fatty tissue (51%). Analysis of mean enhancement and enhancement-time curves facilitates the diagnosis of glomus tumors and contributes to the differential diagnosis. Characteristically, the analysis of the dynamic series in glomus tumors demonstrates the dropout effect in form of a dip in the time-intensity curve with high dose contrast material injection. This characteristic dropout effect can be observed in all glomus tumors, independent of their location. size, or classification. In dynamic CT, scans with time-density profiles do not show this characteristic dropout effect and lesion differentiation renders difficult.

In most patients, optimal imaging with clear demarcation of the vascularized parts of the tumor is achieved by administration of GD-DTPA, although in some patients with large tumors no additional information is obtained with contrast enhancement. In several comparative analyses, MR imaging was found to be superior to CT in diagnostic accuracy, determination of topographic orientation, and demarcation of glomus tumors. Especially for processes infiltrating the middle cranial fossa (coherent mastoiditis, small glomus tumors), enhanced MR imaging shows its superior diagnostic potential. All patients with glomus tumors of the skull base or the temporal bone must undergo an angiographic study (digital subtraction angiography [DSA] or MRA). Evaluation of the vascular supply reveals important additional information regarding the vascularization of the tumor and the hemodynamic situation in the Circle of Willis. Other glomus tumors are seen to be supplied by the ascending pharyngeal artery.



Figure 14. Glomus jugulare. (A) Axial contrast-enhanced MR image shows an enhancing mass in the right jugular foramen (arrows). (B) Axial T2-weighted MR image shows high signal intensity but no "salt and pepper" appearance. Note the high signal intensity inflammatory changes in the adjacent mastoid cells (arrow). (C) Coronal contrast-enhanced MR image shows enhanced mass within the right jugular foramen (arrows).

The high overall reliability of MR imaging is based on its capacity to reveal other tumors of the temporal bone and the cerebellopontine angle. Schwannomas and meningiomas can be readily identified by their typical topographic sites and the characteristic temporal characteristics of signal intensity after administration of GD-DTPA. In contrast to glomus tumors, these tumors show a slower increase in signal intensity during the early phase and a constant increase up to the seventh minute after injection.

MRI IMAGING OF GLOMUS TUMOURS

- MRI MRI MRI MRI
 - Glomus jugulare tumours often have a salt- and- pepper mixture of intensity on both T1,T2 images. This is because of the low signal intensity caused by the flow void of the tumour vessels
 - The tumours often show dense contrast enhancement on the T1 images

SUMMARY

SUMMARY

Paragangliomas of the head and neck are ubiquitous in their distribution, originating from the paraganglia or glomus cells within the carotid body, vagal nerve, middle ear, jugular foramen, and numerous other locations. The typical patient is middle-aged and presents late in the course of the disease, with a painless slow-growing mass. Clinical manifestations include hoarseness of voice, lower cranial nerve palsies, pulsatile tinnitus, and other neuro-otologic symptoms. The overall prognosis of patients with a cervical paraganglioma is favorable, whereas its temporal bone counterpart often results in recurrence, residual tumor, and neurovascular compromise when in the advanced stage.

Pathologic examination reveals a characteristic biphenotypic cell line, composed of chief cells and sustentacular cells with a peripheral fibrovascular stromal layer that are organized into a whorled pattern ("zellballen"). Imaging hallmarks of paragangliomas of the head and neck include an enhancing soft-tissue mass in the carotid space, jugular foramen, or tympanic cavity at computed tomography; a salt-and-pepper appearance at standard spin-echo magnetic resonance imaging; and an intense blush at angiography. Imaging studies depict the location and extent of tumor involvement, help determine the surgical approach, and help predict operative morbidity and mortality. Surgical treatment is definitive. Radiation treatment is included as a palliative adjunct for the exceptional paraganglioma not amenable to surgery.

The extraadrenal neuroendocrine system comprises an integrated and complex system of dispersed tissue throughout the body that possesses unique regulatory functions. A single collection of this tissue is called a paraganglion, and the entire chain of tissue constitutes the paraganglia. Paraganglia are frequently located near nerves and vessels, belying their special chemoreceptor function. They arise from neural crest progenitor cells and are therefore of neuroectodermal origin. Paraganglia in the head and neck migrate along a branchiomeric (of the branchial mesoderm) distribution, whereas those in the chest, abdomen, and pelvis follow the path of parasympathetic nerve fibers along the perivertebral-periaortic axis.

Paragangliomas, the tumors of the paraganglia, arise from this specialized tissue at any site along these specific locations within the body. Accordingly, the distribution of these lesions is widespread. Within the head and neck, the four most common sites are the carotid body at the common carotid artery (CCA) bifurcation, the jugular foramen, along the vagus nerve, and within the middle ear. These masses produce characteristic findings on radiologic images, particularly computed tomographic (CT), magnetic resonance (MR) imaging, and angiographic studies. In this article, using approximately 90 cases from the Thompson Archives of the Department of Radiologic Pathology at the Armed Forces Institute of Pathology, we correlate the imaging features of paragangliomas with the underlying pathologic findings and highlight the distinctive features that allow the radiologist to suggest the diagnosis.

• Addendum

- A new version of this PDF file (with a new case) is uploaded in my web site every week (every Saturday and remains available till Friday.)
- To download the current version follow the link "http://pdf.yassermetwally.com/case.pdf".
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- At the end of each year, all the publications are compiled on a single CD-ROM, please contact the author to know more details.
- Screen resolution is better set at 1024*768 pixel screen area for optimum display.
- For an archive of the previously reported cases go to <u>www.yassermetwally.net</u>, then under pages in the right panel, scroll down and click on the text entry "downloadable case records in PDF format"

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