Complex Glomus Jugulare Tumor: Management Issues

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Abstract Glomus tumors are rare and locally aggressive, vascular paragangliomas of the skull base. Tumors may progress to cause lower cranial nerve palsies and involve the major vascular structure in the skull base, and thus pose very difficult surgical challenges. One such case is presented, the management problems in such “complex glomus jugulare” tumors are discussed, and the literature reviewed.

Keywords Complex glomus jugulare · Skull base tumor · Paraganglioma

Introduction

Paragangliomas are unusual lesions accounting for 0.012% of all tumors, and 0.5% of all head and neck tumors [1]. They are slow growing, vascular tumors with a long natural history. Carotid body tumors account for 60% of head and neck paragangliomas and the rest include glomus jugulare, vagale and tympanicum. There exist 2 classification systems for glomus tumors as described by Fisch, and by Glasscock and Jackson. Both these systems classify tumors by their size and anatomical extent, but lay little stress on involvement of the vital neurovascular structures at the skull base. It is the involvement of the lower cranial nerves (IX, X, XI, XII) and involvement of the internal carotid artery (ICA) and vertebral artery (VA) that ultimately determines the prognosis and outcome in long term. Brainstem compression and poor contra-lateral venous

circulation are also major risk factors in the short term. Taking all these factors into account Al-Mefty and Teixeira [2] have coined the term “complex glomus jugulare tumors.” The following criteria have been listed for such lesions: giant size, multiple paragangliomas (bilateral or ipsilateral), malignancy, catecholamine secretion, association with other lesions such as a dural arteriovenous malformation or an adrenal tumor, or previous treatment with adverse outcome that makes surgical intervention a much higher risk, such as sacrifice of the carotid artery, radiation therapy, and postoperative deficits or adverse effects from embolization.

All glomus jugulare tumors pose therapeutic and surgical challenges with regard to therapeutic decision making and also the execution of the surgical excision. These challenges are further compounded in cases with complex glomus jugulare tumors. A representative case is presented and the special problems posed by catecholamine secretion, large tumor size, and the potential for undetected malignancy are discussed.

Case Report

A 32 years old female presented with complaints of left hemifacial pain, hoarseness and dizziness of 2 years duration. The patient also reported occasional high blood pressure with dizziness. The general physical examination revealed high blood pressure (180/100 mmHg). Local examination of the head-neck revealed a pulsatile mass in the left upper cervical region that was ill defined, non-tender, and slightly mobile side to side but not mobile vertically. The upper limit was not clearly definable and merging with the skull base; the lower limit was at the level of carotid bifurcation. There was left palatal palsy,

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fasciculations in the left half of tongue, and left vocal fold palsy. Otoscopy indicated an intact left tympanic membrane behind which a reddish mass was seen to be arising from the hypotympanum. The right ear demonstrated early attic retraction with normal hearing. No cerebellar signs were elicited on the clinical examination.

A glomus jugulare tumor was diagnosed as per the initial clinical features. Radiological evaluation by MRI and by CT showed a large expansile mass involving the left mastoid, jugular foramen, extending up to the left ICA and indenting the left cerebellar hemisphere (Fig. 1). The lesion was found to be invading the sigmoid sinus and the internal jugular vein (Fig. 2). CT angiography indicated an enhancing expansile soft tissue mass with similar extent and feeders from left ascending pharyngeal, internal maxillary and posterior auricular arteries.

24 h urinary catecholamine excretion levels were elevated (58 $\mu\text{g}/24\text{ h}$ —normal <30 μg). A screening ultrasound of the abdomen indicated no supra-renal masses, and an octreotide scintigraphy radionuclide scan confirmed a functional tumor in the left base of skull and further indicated of no other uptake site, thus excluding multicentricity (Fig. 3). The high catecholamine levels necessitated administration of sequential blockers and calcium channel blockers to control the hypertension.

The patient was taken up for surgical excision after adequate α and β blockade. A left infratemporal Fisch Type A approach was planned. Following the standard extended post aural infratemporal incision, the skin and pinna were elevated off the temporalis fascia, and the ear canal transected and closed in a cul-de-sac manner (Fig. 4a). Control

Fig. 1 Post gadolinium T1-weighted image showing enhancing tumor in the region of left jugular foramen involving the posterior fossa with compression of ipsilateral cerebellar hemisphere reaching anteriorly up to the carotid canal

Fig. 2 CT angiogram reconstructed sagittal image showing the anterior displacement of the ICA by an enhancing mass involving the jugular foramen, posterior fossa and extending up to C2 level

Fig. 3 PET-CT (DOTANOC) octreotide scintigraphy image showing uptake in a large area overlying the left jugular foramen and adjoining area

of the great vessels was obtained in the neck; the lower three cranial nerves were identified and dissected free from the IJV and the feeding vessels to the tumor ligated (Fig. 4b, c). The IJV was noted to be firm on palpation and filled with tumor. A complete canal wall down mastoidectomy was completed and the facial nerve delineated and transposed off its canal. The mastoid tip was removed to expose the digastric ridge and muscle which was transected (Fig. 4c). The styloid process and styloid complex muscles excised so as to enable access to the skull base and expose

Fig. 4 Surgical steps of the operation demonstrating blind sac closure of the EAC (**a**); delineation of the vessels and nerves in the neck and ligation of the arteries feeding the tumor (**b**); mastoidectomy and facial nerve transposition; removal of the mastoid tip and the digastric muscle (**c, e**); and removal of the styloid complex (**d**) to gain

exposure to the skull base and foraminal openings of ICA and IJV (solid arrow). **e** Opening the sigmoid sinus and jugular bulb to demonstrate intra-luminal tumor prior to excision. The lumen of the IJV is demonstrated and the transposed facial nerve is noted superiorly

the IX nerve, the superior-most sections of the ICA and IJV and the lower end of the jugular foramen (Fig. 4d). The IJV was then ligated and cut (Fig. 4d).

The sigmoid sinus and adjacent retrosinus dura were exposed till the level of transverse sinus, the sigmoid sinus was then occluded extra-luminally, and then slit open below the level of occlusion. The lumen of the sigmoid sinus was filled with a firm pinkish tumor and no significant immediate bleeding was encountered. The sigmoid sinus slit was then extended inferiorly to open up the jugular foramen and IJV, and so expose the entire intra-luminal tumor (Fig. 4e). As per expectation for glomus jugulare tumors, the tumor was not adherent to the medial intimal surface of the jugular bulb and adjoining sinus. The tumor was however mechanically occluding the medially placed openings of the inferior petrosal sinus- and intense venous bleeding on tumor removal from these sinuses was therefore anticipated, and accordingly encountered. Such bleeding was promptly controlled by careful and minimal packing of the sinus openings with gelfoam and surgical patties.

Residual tumor adherent to the posterior fossa dura was cauterized by bipolar coagulation to shrink its size and decrease vascularity, and then dissected off. The posterior fossa dura was followed anteriorly onto the anterior petrous apex medial to the ICA and tumor removed similarly so as to achieve complete gross tumor excision. The tumor was noted to be in relation to the vertical petrous carotid artery (Stage C1), but not in relation to the horizontal petrous carotid (Fig. 1).

The facial nerve was seated in a groove in the anterior canal wall (Fig. 4e). The cavity was obliterated with abdominal fat. An ipsilateral type IV thyroplasty (cricothyroid approximation) was undertaken so as to tense and medialise the paralysed ipsilateral vocal fold, and so limit problems with post-operative aspiration [3].

Post operative histopathology confirmed a paraganglioma. The patient's voice improved post surgery as did the blood pressure, leading to discontinuation of the α and β blockers, though treatment with calcium channel blockers needed to continue. A Grade V facial palsy developed in the immediate post op period, but improved gradually over 6 months to Grade II. A repeat MR 6 months after surgery indicated a small 1.5 cm tumor remnant along the CP angle dura, and this residual tumor has since been treated with stereotactic radiotherapy (Gamma Knife). A year since she has remained stable without any further growth of the lesion or new lesions.

Discussion

Glomus tumors were first described by Rosenwasser in 1945 [4]. They account for 15% of all skull base lesions

[5]. They are generally slow growing, benign but locally destructive vascular tumors. The incidence of functional activity in skull base paragangliomas is 1–2% [6, 7]. Patients are usually middle aged and present with tinnitus (76%) and hearing loss (60%), lower cranial nerve palsies (10–12%) [8], earache, ear discharge, and ear bleeding. Clinical examination indicates to the presence of a vascular (pulsatile) lesion in the upper neck, hearing loss, cranial nerve deficits, bluish/reddish mass behind the TM or a fleshy granular mass in the ear, and a bruit over the mastoid. Elevated blood pressure is associated with functional tumors but normal blood pressure does not rule out secretory activity. Postural hypotension is a common finding in functional tumors and should be checked for. Urinary catecholamine excretion estimation to screen for functional tumors is routinely undertaken at our center for all paragangliomas as recommended by Schwaber et al. [9]. The clinical diagnosis is confirmed by appropriate radiology and biopsy is not advisable.

Investigations serve two purposes—first to assess the clinically overt symptomatic lesion for surgery or otherwise, and second to locate or exclude other paragangliomas. Currently both CT and MRI are used for preoperative imaging as they are complimentary. High resolution CT is useful for small early lesions—especially glomus tympanicum. Contrast enhanced CT scans show moderate to markedly enhancing tumors. Glomus jugulare tumors arise in the jugular foramen and result in irregular lytic lesions without any surrounding bony sclerosis. Early lesions cause subtle enlargement of the jugular foramen, bony erosions are first seen in the lateral margin of jugular foramen. There is typical involvement of the jugulo-carotid crest and the jugular spine, and extension towards the hypoglossal canal. Glomus tympanicum are separated from the jugular bulb by a bony plate which helps in the distinction between the two tumors. Further growth of glomus jugulare into the neck results in anterior displacement of the ICA. Routine screening of the neck especially the carotid bifurcation is advisable to detect any other synchronous paragangliomas. MRI pictures demonstrate isohypointense tumors in T1W images with intense post contrast enhancement; T2W images show hyperintense lesions. A typical “salt and pepper” appearance in T1W post contrast images can be seen in lesions larger than 2 cm where the vascular spaces are seen as flow voids. Separation of tumor from bone marrow and fat has been aided by STIR and fat suppression techniques.

The other modality for imaging these tumors is radio-nuclide scanning with MIBG (meta-iodo-benzyl-guanidine) and other octreotide analogues. MIBG is the traditional compound used for such imaging. It is incorporated into vesicles or neurosecretory granules, and is taken up by non-adreno-medullary neuroendocrine tumours, carcinoid

tumours and medullary thyroid carcinomas. It has been found to demonstrate an overall 90% sensitivity and very high specificity for the diagnosis of chromaffin tumours (phaeochromocytomas, paragangliomas and neuroblastomas) [10, 11].

Octreotide analogues (namely ^{111}I -pentoctreotide) also demonstrate uptake by neuroendocrine tumours, as they have a high affinity for the somatostatin type 2 receptor (SSRT2) present on these tumors [12]. Radiolabelled octreotide has been shown to have a detection rate of 67–91% for all neuroendocrine tumours but is of low specificity as uptake is also demonstrable in many other tumours, granulomas and autoimmune diseases [12]. An accuracy rate of 90%, a sensitivity rate of 94%, and specificity of 75% has been reported [13]. Newer somatostatin receptor agents such as Ga68-DOTANOC show promise of improved sensitivity because of its high affinity for subtypes 2 and 5 (SSTR2, SSTR5) [14].

Therapeutic decisions and the choice of treatment modality for particular patients can be difficult and need to be individualized for each patient. The tumor is usually benign, though locally invasive, and progresses slowly. Treatment may be essential for advanced tumors which may be bleeding through the ear. For smaller tumors with minimal symptoms, treatment aims however focus towards preventing the anticipated progression leading to lower cranial nerve paralysis (which may prove life threatening), or to intracranial extension. Surgical excision is conventionally considered standard, although radiation therapy and stereotactic radiation are also options. All therapies have the potential for complications, and surgery can also lead to the transient or permanent worsening of cranial nerve function. It may be appropriate to withhold treatment for some older patients with small asymptomatic tumors, and to adopt a policy of observation and interval MR scanning (“wait & scan policy”). Symptomatic patients and younger asymptomatic patients with progressive lesions merit treatment.

The choice of surgical approach is determined by the extent of the lesion and has well been described in the De la Cruz classification [15]. Centers with expertise and large long term experiences have reported of surgical excision leading to complete removal of the tumor in 82–90% [8, 16–18] and 98% disease free survival [16].

Workers have compared surgery, radiotherapy and radiosurgery (Table 1) [18, 19]. Radiosurgery however has primarily been used for small volume tumors/residual tumors. Gottfried et al. [18] concluded that the results of radio-surgery were promising, but noted concerns with regard to possible late recurrences. They also noted from previously published studies of conventional radiotherapy that such treatment was associated with frequent recurrences at lower radiation doses and with significant radiation-induced complications at higher doses. The possible

Table 1 Comparison results of surgery, radiation and radiosurgery

	Surgery (%)	Radiosurgery ^a /radiotherapy ^b (%)
Cure rate	92.1 ^a 94 ^b	88.2 ^a 89 ^b
Recurrence rate	3.1 ^a 7 ^b	2.1 ^a 8 ^b
Mortality	1.3 ^a 2.5 ^b	Nil ^a 6 ^b

^a Gottfried et al. [18]

^b Carrasco and Rosenman [19]

complications from radiation include radiation-induced otitis, mastoiditis, altered taste sensations, alopecia, mucositis and dermatitis, facial nerve palsy, hearing loss, temporal bone necrosis, brain necrosis, secondary malignancy including osteosarcoma, late metastasis to bone and lungs, CSF leakage from radiation-induced dural and temporal bone necrosis, and pituitary/hypothalamic insufficiency.

Malignant transformation (unrelated to radiotherapy) has been reported in 16–19% of glomus vagale tumors, in 6% of carotid body tumors, and in 2–4% of glomus tympanicum tumors [20]. Malignant tumors may show histological capsular invasion, but are often indistinguishable from benign tumors on histology [21]. Large tumor size (>5 cm in size and >80 g in weight), and recurrent tumors are clinical pointers towards possible malignancy, but often the first confirmation of malignancy is by the detection of metastatic spread to bone, lymph nodes or the lung [21]. Remine et al. [22] are of the opinion that catecholamine secreting paragangliomas (CSPG) may have increased malignant potential (38%) when compared to pheochromocytoma (10%), and nonsecreting glomus tumors (less than 10%). The malignant transformation of CSPG is particularly more for carotid and laryngeal tumors in the head and neck [23].

A newer method of treatment being currently explored is the use of radionuclide ablation by utilizing the high concentration of somatostatin hormone-binding sites on these tumors [24]. Treatment with radioactivity labeled somatostatin analogue octreotide has been noted to arrest tumor growth over 3–5 years [25, 26]. Such treatment has the potential to supplement or replace radiation therapy and stereotactic radiation in the future.

Conflict of interest None.

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