Successful Management of a Catecholamine-Secreting Glomus Jugulare Tumor with Radiosurgery Alone

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Abstract

Secretory glomus jugulare tumors are often resected surgically to control the systemic effects of the catecholamines they produce. This involves complex skull base surgery, which carries significant risks and frequent morbidity. Stereotactic radiosurgery (SRS) is a recently recognized treatment for glomus jugulare tumors, though little is known about its use in secretory tumors.

Case Report A young fit patient with a catecholamine-secreting glomus jugulare tumor was treated with SRS alone and over the following 37 months her urinary catecholamine excretion fell to near normal levels, and serial magnetic resonance imaging (MRI) confirmed a reduction in tumor volume.

Discussion Radiosurgery is an accepted treatment for glomus jugulare tumors and is now readily available to skull base surgeons. In this case a catecholamine-secreting tumor was successfully controlled with radiosurgery alone. Further research and long-term follow-up will determine the role of this treatment in the nonsurgical management of secreting glomus jugulare tumors.

Keywords

- glomus jugulare
- radiosurgery
- catecholamines
- gamma knife

Introduction

Glomus jugulare tumor (GJT) is a rare neuroendocrine neoplasm derived from the paraganglia around the jugular foramen of the temporal bone. Although slow-growing, it can cause significant morbidity through compression and erosion of local structures. In 1 to 3% of cases, the GJT secretes catecholamines, which in high enough levels may result in systemic effects and pheochromocytoma-like symptoms.¹ Historically, the treatment of this tumor has consisted of surgical resection, external beam radiotherapy (EBRT), or a combination of both. Each of these treatment options carries a significant risk of morbidity, which is why stereotactic radiosurgery (SRS) has become an increasingly popular treat-

ment. There is now good evidence for the effectiveness and safety of this relatively new approach to the management of non-secreting GJT, but there is very little in the literature on its use in secreting GJT.

Case Report

A 37-year-old fit and well woman attended the otolaryngology (ENT) outpatient department with a short history of new-onset left-sided pulsatile tinnitus and mild hearing loss. Otoloscopic examination revealed a red mass medial to the inferior tympanic membrane on the left side, a normal right ear, and no cranial nerve deficit. There were no other neurological or otological findings. Blood pressure was 140/87,

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Fig. 1 Gadolinium-enhanced magnetic resonance scan of the left-sided glomus jugulare tumor.

pulse was 90 beats per minute, and there were no symptoms or signs of catecholamine excess.

Initial investigation consisted of pure tone audiometry, which showed a left-sided conductive hearing loss with a mean bone conduction threshold of -6.25dB and a mean air conduction threshold of 26.25dB. Imaging investigations included computed tomography (CT) and gadolinium-enhanced magnetic resonance imaging (MRI), which revealed a 32 × 19 mm enhancing mass at the left jugular foramen with intracranial extension, middle ear extension, and sigmoid sinus and internal jugular vein extension (► **Fig. 1**). An octreotide scan with single photon emission CT was also performed, which showed marked uptake around the left jugular fossa, strongly suggestive of a GJT. Urinary noradren-

aline excretion was 3,370 nmol in 24 hours (normal range < 601) and plasma normetanephrine was 4,380 pmol/L (normal range < 1,180), but other urinary and plasma catecholamines were within normal limits. A gut hormone assay showed an elevated chromogranin B level of 161 pmol/L (normal < 151), but all other hormones including calcitonin were within normal limits.

The patient was discussed at the skull base multidisciplinary team meeting and, after a discussion with her during which she expressed a desire to explore all nonsurgical avenues of treatment, she was referred to a SRS unit for consideration for radiosurgery. She also received input from the clinical endocrinology team, who monitored her blood pressure and hormonal status and started phenoxybenzamine 10 mg at night prior to radiosurgery. However, she could only tolerate this for a week and refused alternative weaker α -blockers. Genetic analysis revealed a pathogenic deletion of exon 6 of the *SDHC* gene. This finding is consistent with familial paraganglioma and is associated with increased rates of synchronous paragangliomas elsewhere in the body.² In the light of this finding, the patient was referred for further genetic counseling and advised to have three yearly MRI scans of her thorax and abdomen to identify any new paragangliomas.

While awaiting radiosurgery, the patient developed a hoarse voice. Examination revealed left-sided vocal cord palsy, left sternocleidomastoid weakness, and mild tongue fasciculation, suggesting lower cranial nerve involvement. Repeat imaging demonstrated growth of the tumor to 42 × 36 mm. Despite this, she continued to express a preference for nonsurgical management, and underwent radiosurgery using a Model C Gamma Knife (Elekta, Sweden). Gross tumor volume (GTV) was 13.3 cm³, prescription isodose volume (PIV) was 12.7 cm³, and prescription dose was 14 Gy to 50% isodose (► **Fig. 2**). The treatment quality measures showed the conformity (NCI) 1.2, selectivity 0.92, and

Fig. 2 Gamma knife treatment plan on fat saturation magnetic resonance images. The yellow line represents the 50% isodose line, corresponding to the prescription dose of 14Gy.

gradient index 3.1. There were no immediate or late complications and no deterioration in cranial nerve function.

Follow-up consisted of regular clinical assessment, MRI, and serum and urine catecholamine measurements. The patient experienced an improvement in her tinnitus and hearing and a slight improvement in her vocal cord palsy, and her blood pressure remained stable. She developed no facial weakness, vestibular disturbance, or cranial nerve deficit after radiosurgery. At 37 months follow-up, the tumor size had reduced by approximately 40% to 35 × 26 mm and urinary noradrenaline had fallen to 647 nmol/24 hours, only slightly above the normal upper limit of 601 nmol/24 hours (→Fig. 3). Serum normetanephrine also fell from 4,380 pmol/L to 936 pmol/L, well below the normal upper limit of 1,180 nmol/L (→Fig. 4), and chromogranin B fell from 160 pmol/L to 81 pmol/L (normal < 151).

Discussion

GJT is a slow-growing but locally destructive neoplasm within the jugular foramen of the temporal bone. It is usually benign and belongs to a group of neuroendocrine tumors derived from the neural crest and found around autonomic ganglia, known as paragangliomas.¹ Other examples are pheochromocytoma arising from the adrenal medulla, glomus vagale, and carotid body tumors. Although rare, GJT is the commonest tumor of the middle ear and occurs most frequently in female patients in the fifth and sixth decades of life.³ Presenting features include conductive deafness and pulsatile tinnitus and, less commonly, neurological deficit in the lower cranial nerves. Left untreated, GJTs may expand intracranially or extracranially and invade local structures. In 1 to 3% of patients the GJT is found to secrete catecholamines (usually noradrenaline),¹ which may cause pheochromocytomalike features such as headache, palpitations, perspiration, pallor, and orthostasis.⁴ Around one third of head and neck paragangliomas are genetically determined, and several susceptibility genes have been identified, namely *SDHB*, *SDHC*, *SDHD*, *SDHAF2* and *VHL*.²

The intimate relationship between these tumors and the lower cranial nerves, jugular bulb, inner ear, and dural sinuses provides a significant challenge for surgical treatment. Historically, treatment of GJT has consisted of surgical resection

either alone or in combination with EBRT.⁵ Early evidence that radiotherapy does not destroy the catecholamine-secreting chief cells in GJT led to a preference for surgical resection of secreting tumors.⁶ Although microsurgical techniques have advanced considerably in recent years, there is still significant morbidity associated with operating in such a complex anatomical area. One review of 374 patients treated with surgical resection found that although the rate of total resection was 88.2%, new postoperative cranial nerve deficits occurred in up to 59%, cerebrospinal fluid (CSF) leak in 8.3%, and death in 1.3%.⁷

EBRT initially emerged as a treatment option for GJT in patients unsuitable for surgical resection or in cases where total resection was not achieved. Rather than reducing tumor volume, it aims to achieve cessation of tumor growth and is thought to work by producing perivascular fibrosis and small vessel injury, thus reducing the vascularity of the tumor.⁶ It avoids the risks of invasive skull base surgery, though there is some controversy surrounding its use in secreting GJT due to previously mentioned reports of chief cell radio-insensitivity and a lack of long-term follow up. EBRT also carries significant risk of acute complications such as radiation-induced otitis or mastoiditis, alopecia, and mucositis, as well as long-term complications such as hearing loss, temporal bone necrosis, brain necrosis, pituitary and hypothalamic insufficiency, and osteosarcoma.⁷

There are several reports in the literature of secreting GJTs treated with EBRT. In 1994, Pluta et al described a patient who had previously undergone extracranial debulking of a secreting GJT followed by EBRT to the intracranial component.⁸ After 22 years she presented with a CSF leak containing very high levels of norepinephrine. Urine and plasma levels were normal, there was no tumor growth, and she remained asymptomatic. This highlights the possible benefits of radiation in secreting GJTs but also supports reports of chief cell radioinsensitivity, as the tumor was continuing to secrete subclinical levels of catecholamines. Furthermore, the patient developed her CSF leak as a result of osteodural radiation necrosis and was also found to be amenorrheic due to hypogonadotropic hypogonadism, a further complication of her radiation. Schwaber et al reported a case of norepinephrine-secreting GJT in a patient who was not a candidate for surgery and was treated with EBRT alone in 1988. They were

Fig. 3 Graph showing serial 24-hour urinary noradrenaline excretion. (Dashed line represents upper limit of normal range).

Fig. 4 Graph showing serial measurements of plasma normetanephrine. (Dashed lines represent normal range).

not able to demonstrate an improvement in hypertension or norepinephrine levels 20 months posttreatment.⁹

SRS emerged in the middle of the 20th century as a method of delivering high-dose radiation to a very specific area and was initially used to treat intracerebral tumors. Gamma knife surgery uses cobalt-60 sources to achieve this highly accurate delivery of radiation and is the method of SRS most frequently used in GJT.⁵ SRS is a desirable treatment for GJT because it allows focused high-dose radiation to be delivered to the tumor with very little delivery to surrounding tissues. Furthermore, it is argued that it may be more cost effective than surgery and external beam radiotherapy, as it can usually be performed in one day and has lower complication rates.⁷ There is evidence in the literature relating to the efficacy of SRS in GJT.¹⁰ Several large reviews and meta-analyses have demonstrated comparable tumor control rates and reduced complication rates when compared with surgical resection.^{7,11,12} They do not, however, identify specific outcomes for catecholamine-secreting GJTs.

The case described here demonstrates effective tumor control in a catecholamine-secreting GJT using SRS alone. At 37 months follow-up there was approximately a 40% reduction in tumor volume and a reduction of urinary noradrenaline and plasma normetanephrine to near-normal levels. There is only one other case in the literature of a catecholamine-secreting GJT treated with SRS alone.¹³ Castrucci et al delivered a single-fraction 18 Gy dose using the Leksell gamma knife unit and at 32 months follow-up have reported good blood pressure control, resolution of symptoms, and reduction in tumor volume. They also noted posttreatment levels of urinary noradrenaline to around 1.5 times the upper reference limit and plasma normetanephrine to around 2.2 times the upper reference limit.

In conclusion, our findings, along with those of Castrucci et al and previous work on EBRT, indicate that SRS alone can be an efficacious treatment in cases of catecholamine-secreting GJT. Although previous work has shown resistance of secreting GJTs to standard radiation therapy, which is important when selecting a management plan for these patients, SRS allows delivery of much higher-dose radiation without risk-

ing damage to surrounding tissues. Longer-term follow-up of these patients may in time provide more evidence of the efficacy and safety of SRS in the treatment of GIT.

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