Subtotal Resection for Management of Large Jugular Paragangliomas with Functional Lower Cranial Nerves

George B. Wanna, MD¹, Alex D. Sweeney, MD¹, Matthew L. Carlson, MD¹, Richard F. Latuska¹, Alejandro Rivas, MD¹, Marc L. Bennett, MD¹, James L. Netterville, MD¹, and David S. Haynes, MD¹

Abstract

Objectives. To evaluate tumor control following subtotal resection of advanced jugular paragangliomas in patients with functional lower cranial nerves and to investigate the utility of salvage radiotherapy for residual progressive disease.

Study Design. Case series with planned chart review.

Setting. Tertiary academic referral center.

Subjects and Methods. Patients who presented with advanced jugular paragangliomas and functional lower cranial nerves were analyzed. Primary outcome measures included extent of resection, long-term tumor control, need for additional treatment, and postoperative lower cranial nerve function.

Results. Twelve patients (mean age, 46.2 years; 7 women, 58.3%) who met inclusion criteria were evaluated between 1999 and 2013. The mean postoperative residual tumor volume was 27.7% (range, 3.5%-75.0%) of the preoperative volume. When the residual tumor volume was less than 20% of the preoperative volume, no tumor growth occurred over an average of 44.6 months of follow-up (P < .01). Four tumors (33.3%) demonstrated serial growth at a mean of 23.5 months following resection, 2 of which were treated with salvage stereotactic radiotherapy providing control through the last recorded follow-up. No patient experienced permanent postoperative lower cranial neuropathy as a result of surgery.

Conclusion. Subtotal resection of jugular paragangliomas with preservation of the lower cranial nerves is a viable management strategy. If more than 80% of the preoperative tumor volume is resected, the residual tumor seems less likely to grow.

Keywords
jugular paraganglioma, glomus jugulare, subtotal resection, pulsatile tinnitus

Introduction

Jugular paragangliomas (JPs) are the most common tumors of the jugular foramen.¹ Though histologically benign, they can be locally aggressive by invading adjacent structures, including the lower cranial nerves, carotid artery, and posterior fossa dura.² Open surgical approaches and radiotherapy are both discussed as primary treatment modalities for JPs. The emergence of stereotactic radiotherapy (SRT) and radiosurgery (SRS) has allowed for the delivery of therapeutic radiation doses with a less extensive side effect profile than that seen following conventional external beam therapy.³,⁴ However, in most centers, surgical resection remains the preferred treatment strategy for larger JPs, secreting tumors, and JPs in young patients and for patients who initially present with lower cranial nerve paralysis.⁵,⁶

To date, there is not a clear consensus on the management of JPs, especially in the setting of a large tumor and functional lower cranial nerves. Over the last decade, our center has adopted a less aggressive surgical approach for patients with functional lower cranial nerves who are candidates for surgical management owing to their age or the size of their tumors. This study seeks to evaluate planned subtotal resection as a primary management strategy in this unique patient population.

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Subjects and Methods

After institutional review board approval, a prospective clinical database was queried to identify all patients who were evaluated for JPs between 1999 and 2013. Patients with advanced JPs (Glasscock-Jackson grade 3 or 4) and functional lower cranial nerves (IX, X, XI, or XII) were selected. All patients were informed of the risks and benefits of all available treatment modalities, including resection, observation, and radiation. In the group of patients who elected to undergo microsurgical resection, data analysis included only those cases in which a planned subtotal resection was performed to avoid lower cranial nerve injury. Patients were excluded if they had malignant tumors or complete preoperative paralysis of 1 or more lower cranial nerves or if they were without at least 12 months of clinical or radiographic follow-up.

Tumor volume was calculated according to radiographic measurements based on the formula \((4/3)\pi r_1r_2r_3\), where \(r_1\), \(r_2\), and \(r_3\) correspond to the radii in 3 orthogonal planes.\(^7\) Tumor resection was limited to, at most, that which could be removed without purposefully compromising lower cranial nerve function or risking carotid injury. In some cases, tumor debulking was limited to the middle ear component per patient wishes. Residual tumor volume was calculated by comparing the first postoperative magnetic resonance imaging (MRI) with the preoperative MRI. Every patient was followed in the postoperative period with serial MRI and clinical examinations. Tumor progression over time was assessed in terms of radiologic growth of \(\geq 2\) mm in any dimension or new cranial neuropathy on physical examination. All postoperative MRI scans were interpreted by a staff neuroradiologist and surgeon. Tumors that grew following resection were treated with radiation, observation, or re-resection, and these patients were subsequently followed with serial imaging and clinical examination.

Results

Twelve patients met inclusion criteria and were analyzed. The average age at the time of surgery was 46.2 years (range, 26-64 years; median, 45 years), and 7 patients (58.3%) were women. All tumors were Glasscock-Jackson grade 3 or 4 (Table 1) based on preoperative imaging characteristics.\(^8\) Two of 12 tumors presented with recurrent disease after undergoing primary surgery and primary radiotherapy a mean of 80 months earlier. No patient reported a family history of paragangliomas, and no tumor was found to be functional. The most common symptoms at presentation were pulsatile tinnitus (83.3%) and hearing loss (75.0%), followed by aural fullness (58.3%), vertigo (41.7%), and otalgia (33.3%) (Figure 1). The most common finding on clinical examination was a retrotympanic middle ear mass (100%). One patient had evidence of complete ipsilateral cranial nerve VI paralysis at presentation. No patient had facial nerve palsy, nor did any patient have paralysis of cranial nerves IX, X, XI, or XII. The average preoperative tumor volume was 9.6 cm\(^3\).

Planned subtotal resection was selected as the initial treatment modality for all 12 patients. Tumor resection was achieved through an infratemporal fossa approach with ear canal overclosure in the majority of cases (66.7%). In these cases, the medial wall of the jugular bulb was used as a limit of dissection to prevent cranial nerve injuries. Other surgical approaches included postauricular tympanomastoidectomy with or without an extended facial recess and retrosigmoid craniotomy. All cranial nerves were left anatomically intact at the conclusion of tumor dissection. Mobilization of the vertical segment of the facial nerve was utilized in 1 patient. Average intraoperative blood loss was 485 mL. In no case were intraoperative vital signs noted to be labile during tumor resection. Following resection, average length of inpatient stay was 3.6 days. No patient experienced permanent cranial nerve injury following surgery. Eleven patients (92.3%) had House-Brackmann 1 facial function in the immediate postoperative period. One patient experienced House-Brackmann 3 facial function immediately following a surgery that involved facial nerve rerouting, and function returned to a House-Brackmann 1 within 4 months after surgery.

<table>
<thead>
<tr>
<th>Grade</th>
<th>Definition</th>
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<tr>
<td>I</td>
<td>A small tumor involving the jugular bulb, middle ear, and mastoid.</td>
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<tr>
<td>II</td>
<td>A tumor extending under the internal auditory canal; intracranial extension may be present.</td>
</tr>
<tr>
<td>III</td>
<td>A tumor extending into the petrous apex; intracranial extension may be present.</td>
</tr>
<tr>
<td>IV</td>
<td>A tumor extending beyond the petrous apex into the clivus or infratemporal fossa; intracranial extension may be present.</td>
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Figure 1. Patient symptoms at presentation.
All patients received postoperative MRI and were followed with serial imaging and clinical examination (Figure 2). The average residual tumor volume was 27.7% (range, 3.5%-75.0%) of the preoperative size. No subsequent tumor growth was identified in 8 tumors (66.7%) after an average follow-up of 44.6 months (range, 12-148 months; median, 30 months). In the 4 tumors (33.3%) that grew following subtotal resection, growth occurred at an average of 23.5 months (range, 8-37 months; median, 24.5 months). Tumor growth was asymptomatic in 2 of the 4 cases. In 1 patient, growth was associated with cranial nerve VII and X weakness, while another patient experienced recurrent pulsatile tinnitus. In patients with growing tumors, 2 elected for SRT, 1 chose observation, and 1 elected for a salvage resection, which is pending. In the patients receiving SRT, 2500 cGy was delivered in 5 sessions via Novalis Linear Accelerator. No subsequent tumor growth has been observed in either of these patients at an average of 12 months following SRT (8 and 16 months). Comparative patient data are listed in Table 2.

Patients with tumors that did not grow were noted to be significantly older (50.8 vs 37.0 years, \( P < .01 \)). There was no significant difference in preoperative tumor volume between the 2 groups (\( P = .36 \)). Patients with progressive residual disease had significantly greater residual tumor burden following surgery compared to subjects with stable postoperative disease (59.2% vs 11.9%; \( P < .01 \)) (Table 3).
multiple cranial nerves can be devastating, especially in a detrimental effect on speech and swallowing. Injury to Loss of function in any one of these cranial nerves can have high incidence of injury during tumor growth and resection. of cranial nerves IX to XI to the tumor epicenter portends a cannot be marginalized. JPs arise from within the adventitia cranial nerve function. technically possible, it often occurs at the expense of lower cranial nerves is unclear. There is strong evidence to support either surgical resection or SRT/SRS as a primary treatment modality. Surgical management has historically sought to achieve complete resection, when possible.8 While total resection is the only way to completely eradicate disease, it can be associated with a high risk of new cranial nerve injuries, especially in large tumors. Our early experience with JPs identified 156 patients in whom complete tumor removal was achieved.9 It was noted that the tumor was inseparable from the lower cranial nerves in 69% of these cases. Sanna et al reported their experience with the surgical management of 53 JPs classified as Fisch C or D (Table 4).10,11 Total tumor removal was achieved in 83%, and the recurrence rate was 10%. The incidence of new lower cranial nerve injuries in the postoperative period varied from 18% to 39% depending on the presence of intracranial extension. In the experience of Moe et al, gross total resection was achieved in 74% of cases, and new cranial nerve injury occurred in 50% of subjects.12 Fayad et al reported on the operative outcomes of 48 patients.2 Total tumor resection was achieved in 81%, and when tumors that were Fisch class C or worse were evaluated, new lower cranial nerve injury could be as high as 81.8%.2 Although complete surgical excision of JPs is technically possible, it often occurs at the expense of lower cranial nerve function.

The morbidity of unilateral lower cranial nerve paralysis cannot be marginalized. JPs arise from within the adventitia of the jugular bulb, and the intimate anatomic relationship of cranial nerves IX to XI to the tumor epicenter portends a high incidence of injury during tumor growth and resection. Loss of function in any one of these cranial nerves can have a detrimental effect on speech and swallowing. Injury to multiple cranial nerves can be devastating, especially in elderly patients.13 In many cases of lower cranial nerve injury, additional surgical intervention may be required to improve upper aerodigestive function.14,15 Additionally, meaningful return of function may not be achievable even despite these measures.

The concept of subtotal resection of JPs has been described in the setting of advanced patient age or intact neurologic function. Jackson and colleagues reported modifications in surgical technique that can be used for hearing preservation.16 In their series, the likelihood of successful preservation was inversely correlated with tumor size. Cosetti et al encouraged the consideration of subtotal resection, radiation therapy, or observation of both glomus jugulare and tympanicum in patients greater than 60 years of age.17 Through this approach, 1 of 3 patients undergoing subtotal resection of glomus jugulare experienced radiologic tumor growth 6 years following surgery and was treated with salvage radiation therapy. Willen et al described their experience with 5 patients greater than 60 years of age who underwent a planned subtotal resection and salvage radiotherapy for glomus jugulare tumors that were Fisch class C3 or larger.18 They reported that no patient experienced clinical progression of disease following this treatment strategy at a mean of 19 months of follow-up. Determining the relative efficacy of subtotal resection versus gross total resection and radiotherapy has thus far proven elusive. A meta-analysis by Ivan et al appraised these management strategies in terms of tumor control and treatment-associated cranial neuropathy, but a lack of available data in patients undergoing a subtotal resection limited the comparison.19

Since the publication of our initial experience with JPs,9 our management algorithm has evolved. Currently, if patients are candidates for surgical management, the extent of the resection performed depends on preoperative cranial nerve function and the size of the tumor. In patients with extensive lower cranial nerve palsies or small tumors that are separated from the lower cranial nerves by an exploitable plane of dissection, we still favor gross total resection. However, for patients with large tumors that are inseparable from functional lower cranial nerves, we recommend partial resection with the intent of avoiding new cranial neuropa-thy. Our results suggest that resecting greater than 80% of the preoperative tumor volume is associated with a lower risk of postoperative progression in terms of radiologic growth and/or clinical symptoms. In cases where postoperative tumor growth occurs, SRT/SRS is offered. Our sample size of 12 patients is small, making a lack of statistical power an obvious weakness of this study. Additionally, given the slow growth pattern generally expected of these tumors, our follow-up data are limited, particularly in the subset of patients receiving salvage SRT/SRS. Further work will be directed toward the validation of our treatment algorithm with increasing patient numbers and time of follow-up.

### Table 4. Fisch Staging System for Jugular Paraganglioma Tumors.

<table>
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<tr>
<th>Class</th>
<th>Definition</th>
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<tr>
<td>A</td>
<td>Tumors limited to the middle ear space</td>
</tr>
<tr>
<td>B</td>
<td>Tumors limited to the middle ear or mastoid without involvement of the infralabyrinthine space of the temporal bone</td>
</tr>
<tr>
<td>C1</td>
<td>Tumors involving infralabyrinthine and apical spaces of the temporal bone, with extension into the apex</td>
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<tr>
<td>D1</td>
<td>Tumors with intracranial extension &lt; 2 cm in diameter</td>
</tr>
<tr>
<td>D2</td>
<td>Tumors with intracranial extension &gt; 2 cm in diameter</td>
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### Discussion

To date, the treatment algorithm for patients with large JPs and functional lower cranial nerves is unclear. There is strong evidence to support either surgical resection or SRT/SRS as a primary treatment modality. Surgical management has historically sought to achieve complete resection, when possible. While total resection is the only way to completely eradicate disease, it can be associated with a high risk of new cranial nerve injuries, especially in large tumors. Our early experience with JPs identified 156 patients in whom complete tumor removal was achieved. It was noted that the tumor was inseparable from the lower cranial nerves in 69% of these cases. Sanna et al reported their experience with the surgical management of 53 JPs classified as Fisch C or D (Table 4). Total tumor removal was achieved in 83%, and the recurrence rate was 10%. The incidence of new lower cranial nerve injuries in the postoperative period varied from 18% to 39% depending on the presence of intracranial extension. In the experience of Moe et al, gross total resection was achieved in 74% of cases, and new cranial nerve injury occurred in 50% of subjects. Fayad et al reported on the operative outcomes of 48 patients. Total tumor resection was achieved in 81%, and when tumors that were Fisch class C or worse were evaluated, new lower cranial nerve injury could be as high as 81.8%. Although complete surgical excision of JPs is technically possible, it often occurs at the expense of lower cranial nerve function.

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Conclusion

There remains no consensus regarding the best management of large JPs, particularly in the setting of a growing tumor and functional lower cranial nerves. Although treatment paradigms have historically encouraged complete resection, including cranial nerve sacrifice if necessary, we now consider subtotal resection in patients with large JPs and functional lower cranial nerves to prevent unnecessary neurologic morbidity. In this setting, our data suggest that removing a larger percentage of the tumor leads to a lower incidence of residual tumor growth.

Author Contributions

George B. Wanna, conception and design, IRB application and approval, data analysis, drafting and editing manuscript, final approval; Alex D. Sweeney, conception and design, data collection and analysis, drafting and editing manuscript, final approval; Matthew L. Carlson, conception and design, data analysis, drafting and editing manuscript, final approval; Richard F. Latuska, data collection and analysis, manuscript revision, final approval; Alejandro Rivas, data analysis, manuscript revision, final approval; Marc L. Bennett, data collection and analysis, manuscript revision, final approval; David S. Haynes, concept and design, data analysis, manuscript revision, final approval.

Disclosures

Competing interests: David S. Haynes is a consultant for Stryker/Synthes, Cochlear, Advanced Bionics, and MED-EL GmbH.

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References