ORIGINAL ARTICLE

Cervical Paragangliomas—Tumor Control and Long-Term Functional Results after Surgery

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ABSTRACT

Objective: To report long-term functional results of the surgical treatment of cervical paragangliomas. Patients and Methods: A retrospective review of 22 patients with 34 head and neck paragangliomas of which 27 were resected between 1981 and 2004. Of these, 16 were carotid body tumors and 11 were vagal paragangliomas. There were 13 women and 9 men with an average age of 48.6 years (range, 26 to 75 years; median, 49 years) and the mean follow-up period was 82 months (range, 3 to 184 months; median, 61 months). Results: There were 13 solitary tumors of which 5 were carotid body tumors and 8 vagal paragangliomas. Multiple head and neck paragangliomas were seen in 9 patients (41%). The incidence of associated multiple tumors was 64.3% for carotid body tumors and 38.5% for vagal paragangliomas. Complete tumor resection was achieved in all but 1 patient in whom a small intradural residual vagal paraganglioma had to be left. The internal carotid artery was preserved in all carotid body tumor resections. Lower cranial nerve deficits were sustained in 1 carotid body tumor resection only, but in all cases with multiple tumors. All patients with vagal paragangliomas had or developed a vagal nerve paralysis. In 4 cases minor complications developed postoperatively. No recurrent tumors were seen during the follow-up period. Conclusions: Even in large head and neck paragangliomas surgical treatment provides excellent tumor control with low postoperative morbidity. A wait-and-scan policy may be more appropriate for those patients with multiple tumors, advanced age, or

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high operative risk and for those whose tumors have recurred following radiotherapy.

KEYWORDS: Paraganglioma, carotid body, glomus vagale, surgery, treatment outcome

Paragangliomas are rare, vascular, neuroendocrine tumors that develop in the extra-adrenal paraganglion tissue. They represent fewer than 0.5% of all head and neck tumors.[1] In the head and neck, paragangliomas most commonly develop in the carotid body, the tympanic plexus (glomus tympanicum), the jugular bulb (glomus jugulare), and the vagal nerve ganglia (glomus vagale). Paragangliomas have also been reported in the nose, the paranasal sinuses, the sympathetic ganglia, the larynx, and the eye, but tumors at these sites are most unusual.[2] These tumors grow slowly and are said to have a median doubling time of 4.2 years.[3] Without therapy they may grow to a considerable size and become life-threatening.[3] They tend to show a locally aggressive and infiltrative growth pattern, destroying surrounding structures. Though paragangliomas are mainly benign, some cases of malignant tumors have been described. Malignant transformation has been reported in 16 to 19% of glomus vagale tumors, in 6% of carotid body tumors, and in 2 to 4% of glomus tympanicum tumors.[1] Paragangliomas may be solitary but sometimes patients with multiple tumors are encountered. Multiple tumors are most commonly associated with a carotid body tumor and least commonly with a glomus tympanicum tumor.[3] It is now recognized that several of these tumors are inherited through mutations of the genes that encode for the succinyl dehydrogenase enzymes, SDHD and SDHB. Both genes are inherited in an autosomal dominant fashion but the SDHD gene is subject to maternal imprinting while the SDHB gene has incomplete penetrance.[4] Patients with the inherited gene almost invariably have multiple tumors.[4] Currently, three treatment options are recognized: surgical resection, radiation therapy, and a wait-and-scan policy. Of these, surgery is the only curative treatment. However, because surgery may be complicated by significant morbidity, especially in larger tumors, it is considered by some to be controversial.

The purpose of this study was to present our long-term results after surgery of cervical paragangliomas with special emphasis on tumor control and lower cranial nerve deficits.

MATERIALS AND METHODS

A retrospective analysis was performed on 22 patients with 34 cervical paragangliomas of which 27 were treated at the Department of Otorhinolaryngology, Head and Neck and Facial Plastic Surgery of the Hospital Fulda gAG between 1981 and 2004. The study group consisted of 13 female and 9 male patients with a mean age of 48.6 years (range, 26 to 75 years; median, 49 years). Five patients had a solitary carotid body tumor and 8 patients a solitary glomus vagale tumor. Nine patients had multiple paragangliomas, all of which included a carotid body tumor (64.3% of all carotid body tumors) and in 5 patients a glomus vagale was present (38.5% of glomus vagale tumors). Table 1 shows the combinations of different paragangliomas in the 9 patients. None of them had a positive family history of paragangliomas.

Sixteen carotid body tumors and 11 glomus vagale tumors were resected. In patients with multiple tumors all paragangliomas on the same side were resected simultaneously. Solitary paragangliomas were resected through a cervical approach and there was never any need to split the

Table 1 Multiple Tumor Distribution and Treatment

Patient	Site	Multiple Tumors	Treatment
Number 1	Left	JTT + CBT	Surgery
	Right	GV + CBT	Surgery
Number 2	Left	CBT	Surgery
	Right	GV	Treated previously
Number 3	Left	GV + CBT	Surgery
	Right	—	—
Number 4	Left	CBT	Surgery
	Right	CBT	Surgery
Number 5	Left	GV + CBT	Surgery refused
	Right	GV + CBT	Surgery
Number 6	Left	JTT + CBT	Surgery
	Right	CBT	Surgery
Number 7	Left	JTT + CBT	Surgery
	Right	CBT	Surgery refused
Number 8	Left	JTT + CBT	Surgery
	Right	JTT + GV + CBT	Treated previously
Number 9	Left	CBT	Surgery refused
	Right	JTT	Surgery

JTT, jugulotympanic tumor; CBT, carotid body tumor; GV, glomus vagale.

mandible. An infratemporal fossa approach was employed in patients with multiple paragangliomas that included a glomus jugulare tumor. All tumors were subjected to histopathological examination to confirm the diagnosis and intraoperative frozen sections were undertaken to ensure complete removal.

All patients had CT and MR scans as well as bilateral carotid angiography before surgery. In this way, multiple tumors were excluded. All carotid body tumors were categorized according to the Shamblin classification.[5] The volume of glomus vagale tumors was calculated from their MR scans as there was no generally accepted staging system. Preoperative embolization was undertaken in 16 patients and a balloon occlusion test was performed in 3 patients.

All patients were followed as outpatients for a mean period of 82 months (range, 3 to 184 months; median, 61 months). Follow-up included clinical examination as well as serial MR scans. One patient had a postoperative carotid angiogram.

RESULTS

Carotid Body Tumors

There were 14 patients with 20 carotid body tumors (5 solitary tumors and 15 multiple tumors). Of them, we resected 16 completely, 3 patients refused surgery, and 1 tumor had been resected at another hospital. There were 4 carotid body tumors that were staged as Shamblin I, 11 as Shamblin II, and 1 as Shamblin III.

A carotid body tumor only was removed in 9 patients. In 7 patients a glomus vagale tumor and glomus tympanicum tumor were removed simultaneously. None of the patients received radiotherapy either before or after surgery. Preoperative embolization of the tumor was undertaken in 10 patients. None of the patients had cranial nerve deficits before surgery. The internal carotid artery had to be repaired in just 1 patient and ligation was never necessary.

In the group of patients with solitary carotid body tumors only 1 patient acquired deficits of the glossopharyngeal, vagus, and hypoglossal nerves as a result of surgery and this did not lead to aspiration. This corresponds to an incidence of 11.1% lower cranial nerve deficits. In contrast, whenever multiple tumors on the same side were resected simultaneously the patients acquired lower cranial nerve deficits. Table 2 itemizes these results. No recurrence of carotid body tumors has been found over a mean follow-up period of 79.3 months.

One patient with postoperative complications is worth mentioning individually. He had four paragangliomas. In the first operation a left-sided carotid body tumor and a glomus jugulare tumor were removed. This was complicated by ninth, tenth, and eleventh cranial nerve deficits and temporary aspiration. Eight months later, the contralateral carotid body tumor and glomus vagale were removed and this caused ninth and tenth cranial nerve deficits. Because of aspiration the patient developed pneumonia and epileptic seizures. A cricopharyngeal myotomy was performed and a feeding tube was inserted as a temporary measure.

Table 2 Lower Cranial Nerve Deficits and Aspiration before and after Surgery of 16 Patients with Carotid Body Tumors, Subdivided into Solitary and Multiple Tumor Status

Cranial Nerves	CBT ($n=9$)		CBT and JTT/GV ($n=7$)	
	Dysfunction		Dysfunction	
	Preop	Postop	Preop	Postop
Seventh	—	—	—	3
Ninth	—	1	—	7
Tenth	—	1	—	7
Eleventh	—	—	—	2
Twelfth	—	1	—	2
Aspiration	—	—	1	5
Deafness*	—	—	—	4

*Deafness was due to removal of the jugulotympanic tumor caused by blind sac closure.
CBT, carotid body tumor; JTT, jugulotympanic tumor; GV, glomus vagale.

Currently, he does not have any aspiration and there has been no recurrence of his tumors over the 12-year follow-up period.

Glomus Vagale Tumors

There were 14 glomus vagale tumors and of these 11 were resected. One patient refused surgery and 2 tumors had been resected elsewhere before. The mean tumor volume was 55.7 cm^3 (range, 9.5 to 130 cm^3). Three of these tumors were in patients with multiple tumors. Preoperatively, 3 patients had lower cranial nerve deficits, of whom 2 had been operated elsewhere before and presented to us with recurrent tumors. Preoperative embolization of 10 tumors was undertaken.

All patients had vagal nerve palsies after surgery although the nerve was sectioned in five cases only. Regardless of whether the vagus was sectioned or not, five patients suffered from aspiration postoperatively. Table 3 summarizes the cranial nerve deficits both pre- and postoperatively.

In three cases there were postoperative complications. One patient suffered from hemorrhage which required a return to the surgical theater. Two patients had postoperative pneumonia which was caused by aspiration. One of these patients was managed satisfactorily by a period of nasogastric feeding and swallowing therapy. The other patient required a tracheostomy, cricopharyngeal myotomy, and a feeding tube. He continues to aspirate and has refused surgery to remove tumors on the contralateral side of his neck.

Table 3 Lower Cranial Nerve Deficits before and after Surgery of 11 Glomus Vagale Tumors

Cranial Nerves	Preoperative Dysfunction	Intraoperative Section	Postoperative Dysfunction
Seventh	—	—	2
Ninth	1	2	8
Tenth	3	5	12
Eleventh	1	—	3
Twelfth	2	3	5
Aspiration	—		5

During the mean follow-up period of 64 months no tumor recurrence has developed. In one patient angiography performed 3 months after surgery demonstrated a small intradural tumor remnant within the jugular foramen. It was decided to observe this residual disease but the patient has defaulted from further follow-up.

DISCUSSION

Carotid body tumors are reported to be the most common head and neck paraganglioma, accounting for 60 to 78% of tumors. Glomus vagale tumors are much less common and account for 2.5 to 4.5% of tumors.[6,7] In our series, the incidence of carotid body tumors was 21.1%, and that of glomus vagale tumors was 14.7%. Thus, glomus vagale tumors are over-represented in this series[8] and carotid body tumors correspondingly under-represented.[9] In fact, at our institution, 64.2% of head and neck paragangliomas are jugulotympanic lesions and these have not been

included in this report. Familial head and neck paragangliomas accounted for just 10% of our cases.[7] Multiple, often bilateral, carotid body tumors represent ~10% of sporadic and 25 to 33% of familial cases.[5] The incidence of glomus vagale tumors in patients with familial multiple tumors was 89%, whereas it was only 23% for patients without a family history of paragangliomas.[10,11] The incidence of multiple tumors in our series was 64.3% for patients with carotid body tumors and 38.5% for those with glomus vagale tumors. Bilateral tumors were present in 42.8% of those with carotid body tumors and 7.1% of patients with glomus vagale tumors. The latter percentage is similar to previous reports on glomus vagale tumors, but the percentage of bilateral carotid body tumors is much higher than previously reported in the literature.[5,12] Metastasizing carotid body tumors have been reported to develop in fewer than 5% of cases. Metastatic disease from cervical paragangliomas is usually confined to the neck[1,5] and is said to be more common with glomus vagale tumors than with carotid body tumors.[9] None of our patients had malignant tumors or developed metastatic disease.

Surgical treatment has been the standard approach to cervical paragangliomas for many years. Cure rates of 89 to 100% have been reported.[8,13] Advances in preoperative and operative techniques together with better postoperative care have reduced complication rates. Preoperative cranial nerve deficits have been reported in up to 30% of patients with glomus vagale tumors and in 20% of those with carotid body tumors.[8,14] In our series just one patient with bilateral carotid body tumors suffered from aspiration as a result of a vagal palsy and three patients with glomus vagale tumors also presented with established lower cranial nerve deficits (ninth, tenth, eleventh, and twelfth), but did not have any aspiration. The risk of cranial nerve palsy as a complication of carotid body tumor surgery has been reported to range from 10 to 40%.[9,12,15] As would be expected, the rate of neural complications is greater in patients with Shamblin II and III tumors. In this series, postoperative cranial nerve palsies developed in 11.1% of patients with solitary carotid body tumors and 100% of patients with multiple tumors. This latter group comprise patients with glomus vagale and jugulotympanic tumors, the resection of which are recognized to be associated with higher morbidity. There was no correlation between the tumor size and incidence of cranial nerve palsies. The rate of major vascular complications has dropped from 30% in the 1960s to less than 1% in most recent reports.[12] We did not have any major vascular complication in any of our patients. After glomus vagale surgery, all our patients had vagal palsies as would be expected.[8] In addition, all these patients had additional nerve deficits as detailed in Table 3. Despite this, aspiration affected only five patients, of whom three needed further treatment, that is, tracheostomy, feeding tube, and cricipharyngeal myotomy. Fortunately, only one patient is still dependent on a feeding tube (gastrostomy).

During the follow-up period, there were no tumor recurrences. The one patient with subtotal tumor resection has had no progression of the disease process to date. Including residual disease, our crude local control rate after surgery for both carotid body and glomus vagale tumors was 96.4%. This result is better than that previously reported in the literature.[8,16]

Recent reports have been published about the use of radiotherapy as the first-choice treatment for paragangliomas.[16,17] The main arguments in favor of this are that it is less invasive than surgery, has fewer complications, and achieves high rates of local control.[16–18] Hinerman and colleagues[16] quoted a 96 to 100% tumor control rate after radiation therapy of cervical paragangliomas using 45 Gy. However, the cure criterion for radiotherapy is difficult to evaluate as it is not disappearance but cessation of growth that is evaluated.[13,16,17] Histological examination has shown that the chief cells are hardly affected by radiation but the distinctive vascular structure of the tumor becomes replaced by fibrous

connective tissue.[19] This would seem to be a concern in a potentially malignant tumor which has been reported in 3 to 5%.[20] Further complications of radiation therapy may include inflammation of the external auditory canal and middle ear, osteoradionecrosis, cranial nerve neuropathies, and direct injury to brain tissue. Furthermore, it must be remembered that if radiation therapy fails surgery will be more difficult.[8,15,17,21]

In summary, the management of cervical paragangliomas is difficult and remains a challenge. Treatment must be individualized, taking into account the patient's age, tumor site and size, multicentricity, and pre-existing cranial nerve deficits. The likelihood of tumor control is high whether treatment is by surgery or radiotherapy. However, there is no consensus regarding the choice between surgery and radiotherapy. In general, patients with solitary lesions that are potentially resectable with acceptable morbidity are better treated surgically. It may be reasonable to postpone surgery until cranial nerve impairment becomes evident or other vital structures are threatened.[8,9,12,15,19,22] For patients with multiple tumors, treatment options will be influenced by the location of the tumors, age of the patient, comorbidities, and whether past radiotherapy has been given. A watchful waiting policy with interval scans could be prudent. Most important, every patient should have lifetime follow-up with serial MR scans and angiography if necessary, as recurrence can develop even after many disease-free years.

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