Clinical Science

Surgical resection of carotid body paragangliomas: 10 years of experience

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KEYWORDS:
Carotid body tumor; Paraganglioma; Head and neck surgery

Abstract

BACKGROUND: Carotid body tumors (CBTs) are relatively rare neoplasms, and even if they are considered predominantly benign, there is an indication for early surgical removal. The objective of this study was to conduct a review of the surgical management of CBTs.

METHODS: A retrospective study identified 34 cases (12 men and 19 women) of tumors in patients who had undergone surgical resection of pathologically confirmed CBTs over a period of 10 years from 2001 to 2011 in 2 academic departments of general surgery in Italy.

RESULTS: In our series, 10 CBTs (31%) were Shamblin class I, 13 (41%) were class II, and 9 tumors (27%) were class III. Two patients (6%) had transient cerebral ischemia immediately after operation. One patient (3%) died of postoperative cerebral ischemia after surgery for internal carotid artery thrombosis.

CONCLUSIONS: The experience of this casuistry shows that the procedure is relatively low risk for Shamblin I and II classes, whereas there is an increasing risk of neurovascular complications for Shamblin III class.

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Carotid body tumors (CBTs) belong to the classification of paragangliomas because they originate from paraganglia in chromaffin-negative glomus cells derived from the embryonic neural crest, functioning as part of the sympathetic nervous system (a branch of the autonomic nervous system). These cells normally act as special chemoreceptors located along blood vessels, particularly in the carotid bodies (at the bifurcation of the common carotid artery in the neck) and in aortic bodies (near the aortic arch).

Accordingly, CBT and other paragangliomas are categorized as originating from a neural cell line in the World Health Organization classification of neuroendocrine tumors. In the categorization proposed by Wick,1 paragangliomas belong to group II. Given the fact that they originate from cells of the orthosympathetic system, paragangliomas
Methods

Women.2–9 The incidence of bilateral carotid body lesions caroticum is the CBT.

Pharyngeal artery, which is the most common feeding vessel, and other feeding vessels were ligated. The tumors were then circumscribed and were carefully dissected in a periadventitial plane using bipolar cautery and a radiofrequency scalpel, avoiding injury to the vessel wall (Fig. 1). The tumors were then released from their attachment to the surrounding tissues. The carotid was covered by temporalis fascia in all cases.

We performed a review of the medical records focused on the preoperative assessment, including a complete history and physical examination with a cranial nerve examination, and intraoperative and postoperative assessment, which focused on arterial bleedings and cranial nerve deficits. Outcome data were collected at 1 month and 1 year postoperatively. A review of surgical reports focused on cranial nerve sacrifice and carotid involvement defined as sacrifice or bypass. Pathology reports were analyzed for the presence of metastatic disease and locally infiltrative characteristics defined as the involvement of surrounding bone, connective tissue, blood vessels, or nerves.

The primary end point was functional outcome as defined by the incidence of cerebral vascular accidents. Secondary end points included the incidence of postoperative cranial neuropathies, pathological findings such as potential prognostic factors for morbidity, and the impact of preoperative cranial neuropathies on long-term functional outcome.

Neurologic assessment and functional outcome were evaluated using the National Institutes of Health Stroke Scale26 for all patients in the first week of the postoperative period even if they did not have a detectable neurologic deficit. In this study, health-related quality of life was determined with the Sickness Impact Profile.27 Descriptive statistics are reported as numbers and percentages.

Results

Twelve tumors (35%) were located on the right side and 21 (64%) on the left side. A multicentric paraganglioma not from the head and neck was discovered in 2 patients (7%) who had a thoracic and a paravesical paraganglioma. No patient had a family history of paragangliomas. The most common symptom was a pulsatile neck mass without cranial nerve deficit. No patient had a functioning CBT who presented with palpitations, tachycardia, and hypertension accompanying an elevated catecholamine level. Preoperative cranial nerve X dysfunction was observed in 1 patient (3%).

<table>
<thead>
<tr>
<th>Shamblin class</th>
<th>No. of patients</th>
<th>Side (right:left)</th>
<th>Sex (female:male)</th>
<th>Median age (y)</th>
<th>Preoperative cranial nerve deficit</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>10 (1 bilateral) (31%)</td>
<td>6:5</td>
<td>6:4</td>
<td>44 (39–58)</td>
<td>None</td>
</tr>
<tr>
<td>II</td>
<td>12 (2 bilateral) (41%)</td>
<td>4:10</td>
<td>7:5</td>
<td>51 (44–59)</td>
<td>None</td>
</tr>
<tr>
<td>III</td>
<td>9 (27%)</td>
<td>2:7</td>
<td>6:3</td>
<td>59 (39–67)</td>
<td>1:9 (12%)</td>
</tr>
<tr>
<td>Total</td>
<td>31 (3 bilateral)</td>
<td>12:22</td>
<td>19:12</td>
<td>48 (36–67)</td>
<td>1:34 (3%)</td>
</tr>
</tbody>
</table>
Computed tomographic (CT) imaging and magnetic resonance imaging (MRI) revealed an enhancing mass splaying the ICA and the external carotid artery (ECA) of the carotid bifurcation, and the median tumor size of 34 CBTs was 3.8 cm (range 2.2 to 6.8 cm). Ten (29%) tumors were Shamblin class I, 13 (38%) were class II, and 9 (26%) were class III. The ascending pharyngeal artery was a major feeding artery for all tumors.

Assuming that Shamblin I and II represent the minor complex categories, they were compared in a single category with the more complex category (only in this comparison was there a significant $P$ value). According to the Shamblin classification, the median tumor size was 2.4 cm (range 2.2 to 3.4 cm) in Shamblin I and II tumors and 4.7 cm (range 3.2 to 6.8 cm) in Shamblin III tumors ($P = .005$). The median intraoperative blood loss was 140 mL (range 80 to 250 mL) in Shamblin I and II tumors and 450 mL (range 300 to 750 mL) in Shamblin III tumors ($P = .003$); the median operation time, including ICA reconstruction time, was 180 minutes (range 150 to 320 minutes) and 250 minutes (range 220 to 440 minutes), respectively ($P = .019$). The hospital length of stay was 7 days in all groups (Table 2).

There was only 1 case of hemorrhage in which a mass of $34 \times 65$ mm at the bifurcation of the carotid artery, as seen on MRI, was attached to the ICA with multiple areas of hemorrhage and cystic degeneration. The superior laryngeal nerve and its branches (the external laryngeal nerve, which is the smaller and external branch, and internal laryngeal nerve, which is the bigger and internal branch), vagus, sympathetic chain, and hypoglossal nerves were preserved in all but 1 case in which the tumor was found to be adherent to the hypoglossal nerve, and, hence, it had to be sacrificed. In 1 case of a Shamblin III tumor in which the tumor was found invading the inner walls of the ECA, the artery was ligated and resected with the tumor. One large Shamblin III tumor was found extending superiorly into the infratemporal fossa. This was approached using a transmandibular infratemporal fossa approach.

The ECA was ligated in 4 patients (4:31, 12%) during operation: 1 patient belonged to Shamblin II and 3 to Shamblin III. After tumor resection, small tears in the ICA in 2 patients (2:31, 6%) who belonged to Shamblin II and III, respectively, were repaired primarily. A portion of the ICA had to be resected in 1 patient belonging to Shamblin III (1:9, 11%). In the case with ICA resection, polytetrafluoroethylene (PTFE)–prosthetic vascular graft interposition was performed (Table 3).

Two patients (2:31, 6%) (1 with ICA direct repair and 1 with ICA graft repair) had transient cerebral ischemia immediately after the operation, which was likely associated with the manipulation of the ICA during vascular reconstruction. In fact, in these 2 cases, the use of a vascular shunt with resection and reconstruction of the ICA was necessary because of the larger size of the tumor and the narrow operative space indicating difficulty when excising the tumor. In fact, by using the shunt, the direction of the ICA was clearer, and the cranial nerve structures were more evident.

In these 2 patients, transient cerebral ischemia manifested in both patients with contralateral paralysis and dysarthria, which resolved within 24 hours. No further alterations in neurologic assessment and Sickness Impact Profile scales were noted at the follow-up. One further patient (1:31, 3%) died of postoperative cerebral ischemia after undergoing surgery for ICA thrombosis. In this case, posterior transverse plication was performed during ICA reconstruction. These complications were all observed in Shamblin III.

Postoperative cranial nerve deficits developed in 8 patients (8:31, 26%) immediately after surgery, and they all belonged to Shamblin II (3:12, 25%) and III (5:9, 55%) ($P = .03$). They included 6 cranial nerve X, 1 cranial nerve XII, and 1 superior laryngeal nerve deficits. Three of them who had cranial nerve X deficits recovered within 12 months, and postoperative permanent cranial nerve X deficit occurred in 3 patients (9%). One patient (3%) who

<table>
<thead>
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<th>Table 2</th>
<th>Surgical records of tumors according to Shamblin class</th>
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<tr>
<td>Characteristics</td>
<td>Shamblin I–II (n = 23)</td>
</tr>
<tr>
<td>Tumor size (mm)</td>
<td>24 (22–34)</td>
</tr>
<tr>
<td>Estimated blood loss (mL)</td>
<td>140 (80–250)</td>
</tr>
<tr>
<td>Operation time (min)</td>
<td>180 (150–320)</td>
</tr>
<tr>
<td>Hospital stay (d)</td>
<td>7 (6–11)</td>
</tr>
</tbody>
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presented with preoperative cranial nerve X dysfunction showed postoperative permanent vocal fold paralysis and underwent medialization laryngoplasty.

Pathologic examinations of all tumors revealed benign histology of paragangliomas without cases of malignant CBT. The CBTs described in our series had a similar histopathologic appearance. Under the microscope, 2 types of cells displaying typical nest-like or alveolar architectural patterns were observed. Type I cells, or chief cells, are epithelioid cells often with enlarged hyperchromatic nuclei and arranged in solid groups called “Zellballen.” These groups of chief cells were surrounded by a flattened layer of type II cells or sustentacular cells, which were visualized by immunohistochemical staining for S-100 protein type I and type II cells characteristically located within a dense network of capillaries.28 Chief cells were quite uniform or presented pronounced nuclear pleomorphism, such as bizarre and huge multinucleated cells. They were immunohistochemically positive for chromogranins. There was no recurrence or delayed complications at the median follow-up of 44 months.

**Comments**

CBTs are usually classified using the criteria described by Shamblin et al (Table 4).29 Shamblin class I CBTs are localized tumors with splaying of the carotid bifurcation but little attachment to the carotid vessels. Complete surgical resection is generally possible with only a minimal risk of vascular or cranial nerve complications.23 Shamblin class II CBTs partially surround the carotid vessels, and complete resection is more challenging. Shamblin class III CBTs intimately surround the carotid. Complete resection is very challenging and often requires temporary interruption of the cerebral circulation for vascular reconstruction. The risk of permanent vascular and neural defects is significantly higher than for class I and class II tumors.30

B-mode sonography and color duplex sonography are inexpensive, noninvasive diagnostic tools that are often used as the first imaging step for cervical CBTs.23,31 Carotid paragangliomas are easily detected using CT imaging and magnetic resonance angiography (MRA). CT angiography depicts the anatomy more accurately than MRA because of its better spatial resolution. However, contrast-enhanced MRA is better suited for screening and detecting multiple lesions. Both cross-sectional methods can be used for operative navigation. Moreover, MRI can identify glomus tumors when the characteristic flow voids are present.11–31 In fact, paragangliomas are observed by MRI in T1-weighted sequences with low signal intensity and in T2 with a hyperintense signal. After the intravenous administration of contrast material, these tumors exhibit a pattern of intense and homogenous enhancement similar to CT imaging. The use of intravenous contrast material is not essential in MRI. The classic “salt-and-pepper” appearance of paragangliomas greater than 1 cm in diameter corresponds to multiple

<table>
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<th>Table 3</th>
<th>Neurovascular complications according to Shamblin class</th>
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<tr>
<td>Characteristics</td>
<td>Shamblin I (n = 11 CBTs) (%)</td>
</tr>
<tr>
<td>Vascular repair</td>
<td></td>
</tr>
<tr>
<td>ICA direct repair</td>
<td>—</td>
</tr>
<tr>
<td>ICA graft</td>
<td>—</td>
</tr>
<tr>
<td>ECA closure</td>
<td>—</td>
</tr>
<tr>
<td>Stroke</td>
<td></td>
</tr>
<tr>
<td>Transient</td>
<td>—</td>
</tr>
<tr>
<td>Permanent</td>
<td>—</td>
</tr>
<tr>
<td>Postoperative CN deficit</td>
<td></td>
</tr>
<tr>
<td>IX</td>
<td></td>
</tr>
<tr>
<td>X</td>
<td>—</td>
</tr>
<tr>
<td>XI</td>
<td>—</td>
</tr>
<tr>
<td>XII</td>
<td>—</td>
</tr>
<tr>
<td>Sympathetic nerve</td>
<td>—</td>
</tr>
<tr>
<td>Superior laryngeal nerve</td>
<td>—</td>
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</table>

CBT = carotid body tumor; CN = cranial nerve; ICA = internal carotid artery.

<table>
<thead>
<tr>
<th>Table 4</th>
<th>The Shamblin classification of carotid body tumors</th>
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<tbody>
<tr>
<td>Class</td>
<td>Tumor characteristics</td>
</tr>
<tr>
<td>I</td>
<td>Splaying of the carotid bifurcation with little attachment to the carotid vessels; complete resection with very little morbidity</td>
</tr>
<tr>
<td>II</td>
<td>Partial surrounding of internal and external carotid artery; complete resection more challenging</td>
</tr>
<tr>
<td>III</td>
<td>Complete surrounding of the carotid vessels; complete resection often requires major vessel reconstruction</td>
</tr>
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areas of signal void (because of the slow flow of vessels or hemorrhage) interspersed with hyperintense foci. 

Nuclear medicine evaluation may be used. CBTs typically show avid uptake with different functional imaging techniques, namely 18F-fluorodihydroxyphenylalanine positron emission tomography/computed tomography, 18F-fluorodeoxyglucose positron emission tomography/computed tomography, and 123I-metaiodobenzylguanidine scintigraphy; the latter is paraganglioma specific. Furthermore, somatostatin receptor imaging has a sensitivity of greater than 90% for head and neck paragangliomas (HNP) using 111In-octreotide scintigraphy. Positron-emitting somatostatin receptor imaging agents, such as 68Ga-1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-peptides, have shown promising sensitivities in small series.

The angiographic examinations do not provide additional diagnostic information compared with CT imaging and MRI but may allow a possible preoperative embolization or ICA stenting of Shamblin class III CBTs. The majority of cases of CBTs should undergo complete surgical resection because this a therapeutic option potentially offering a cure for the patient. Histologically, carotid body paragangliomas resemble the normal architecture of the carotid body.

Unfortunately, nuclear pleomorphism, mitotic activity, necrosis, or vascular or perineural invasion cannot predict the biological behavior because all these features may also be found in benign CBTs. Therefore, CBTs are mostly considered benign lesions; however, malignant behavior is often encountered. This diagnosis is reserved for the tumors with local, regional, and distant metastasis. The rate of malignancy is reported to be 6% to 12.5% of all cases, and 7% to 9% of the cases are hereditary.

The size of the tumor is important not only for its clinical manifestations but also for treatment. In 1971, Shamblin introduced a classification system based on tumor size. They classified small tumors that could be easily dissected away from the vessels as group I. Group II (10 of our cases) included paragangliomas of medium size that were intimately associated and compressed carotid vessels but could be separated with careful subadventitial dissection. Group III (9 of our cases) consisted of tumors that were large and typically encased the carotid artery requiring partial or complete vessel resection and replacement. In our casuistry, 3 tumors encased the ECA and 6 tumors the ICA.

Resection of carotid body paraganglioma carries inherent risks of injury to the cranial nerves, carotid arteries, and excessive blood loss. The surgical excision with careful subadventitial dissection is the treatment of choice for most carotid body paragangliomas (Shamblin I and II). Shamblin III carotid body paragangliomas require resection of the ECA and/or ICA. If the internal carotid is encased in a tumor or damaged during resection, immediate repair/replacement should be performed. The second problem during tumor excision is bleeding, which sometimes can be massive.

In such cases, clamping of all carotid arteries is useful along with the placement of an internal carotid shunt. An intraoperative shunt also can be used in the following circumstances to aid in CBT resection and shorten surgical time:

1. To avoid the injury of cranial nerves: when the large size of the tumor and the narrow operative space make it difficult to excise the tumor and easy to injure the cranial nerves, under the guidance of the shunt, the direction of the ICA is more distinct, and cranial nerves are more clear, which helps tumor dissection.

2. To decrease the size of the tumor: with the use of a shunt, blood supply to the tumor decreases, thereby decreasing the size of the tumor.

Considering our experience with our casuistry, we recommend a Pruitt-Inahara (Le Maitre Vascular, Milan, Italy) double balloon occlusive internal carotid shunt. The placement of this shunt through an incision on the common carotid artery contributes to adequate bleeding control from the common carotid artery and the ICA and protects the brain. This procedure provides a clean and dry operative field during tumor removal. Some other articles recommend angiographic embolization preoperatively. The preoperative embolization of a carotid body paraganglioma can be performed using ethanol or polyvinyl alcohol. The final result is complete devascularization. In the past, carotid body paragangliomas were considered radioresistant. However, more recent studies indicate good responses to radiation therapy. Most authors recommend radiotherapy for giant and recurrent carotid body paragangliomas and malignant carotid body paragangliomas metastatic to the regional lymph nodes.

Modern surgical techniques and recent proposals for preoperative embolization and reinforcement of the wall of the ICA with a stent may aid in the management of surgical carotid bifurcation, reducing the complications of lacerations, spasms, and thrombosis. Covered stents have been used as an alternative to embolization when it was believed to reduce the risk for distal embolization. This technique also results in reduced intraoperative blood loss and, theoretically, small nutrient branches that may not be apparent on angiograms are more likely to be excluded with a covered stent.

Conclusions

Despite the benign nature of CBTs, from a histopathological point of view and reports documenting their slow growth rate, surgical resection remains the treatment of choice for these diseases. The neurovascular operative and postoperative complications described are directly related to their dimensions according to the classification of Shamblin. For Shamblin type I and II CBTs, which represent the majority of this disease (with a reported frequency of more than 70%), the peri- and postoperative
risk of neurovascular complications is low. The complication rate increases strongly for Shamblin III type CBTs (accounting for nearly 30% of all cases).  

References