Management of Carotid Bifurcation Tumors: 30-Year Experience

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Background: The carotid bifurcation can host a variety of tumors requiring complex surgical management. Treatment requires resection and, in some cases, vascular reconstruction that may compromise the cerebral circulation. The most frequent lesion at this location is the carotid body tumor (CBT). CBT are classified according to Shamblin in 3 types depending on the degree of carotid vessels encasement. Our main objective was to report our clinical experience managing carotid bifurcation tumors throughout the last 30 years.

Methods: Between 1984 and 2014, we treated 30 patients with 32 carotid bifurcation tumors. There were 21 women and 9 men (2.3:1), with a mean age of 45.5 years (18–75). The most frequent presentation was an asymptomatic neck swelling or palpable mass localized at the carotid triangle (86.7%).

Results: Thirty of 32 tumors were resected. Since 1994, computed tomography scan has been the most frequently used diagnostic imaging tool (80%), followed by magnetic resonance imaging. Angiography was used mainly during the first 10 years of the study period. Mean size of the tumor was 44.6 mm (20–73 mm). Nineteen (63%) were classified as Shamblin II and 6 (20%) as Shamblin’s III. All specimens were analyzed by a pathologist; 28 tumors (93%) were confirmed as paragangliomas, 2 (7%) were diagnosed as schwannomas. Two patients underwent preoperative embolization of the CBT; 5 patients (17%) required simultaneous carotid revascularization, all of them Shamblin III. Mean hospitalization time was 4.5 days (1–35 days). Transient extracranial nerve deficit was observed in 7 patients (23.3%). Three patients (Shamblin III) required red blood cells transfusion. One patient (Shamblin III) underwent a planned en bloc excision of the vagus nerve. There was no perioperative mortality or procedure-related stroke. No malignancy or tumor recurrence were observed during follow-up.

Conclusions: CBTs can be diagnosed on clinical grounds requiring vascular imaging confirmation. These infrequent lesions are generally benign. Early surgical removal by surgeons with vascular expertise avoids permanent neurologic and/or vascular complications.

INTRODUCTION

The carotid triangle is an anatomic landmark where different types of tumors may grow. Among others tumors: carotid body tumor (CBT), schwannoma, lymphomas, metastases, and other paragangliomas, most requiring surgical removal.

The most frequent lesion in this location is the CBT, also known as carotid glomus tumor, carotid paraganglioma, or chemodectoma, with an incidence of 1:30,000. According to Georgiadis et al., CBT account for 60% of head and neck paragangliomas. Other parangliomas are jugulotympanic, vagale, and larynx paragangliomas.

One of 10 cases are familial in origin and about 10% are bilateral. CBT is believed to be more frequent in populations residing at high altitudes.

Embryologically CBT is derived from the neuroectoderm and has the potential of secreting amino...
active substances (reported in up to 5% of the cases).\textsuperscript{1,10}

Clinically, CBT most frequently present as an asymptomatic slow growing mass at the carotid triangle.\textsuperscript{1,10} Surgery is the primary treatment, with the first reports made in the 17th century.\textsuperscript{11} In 1903, Scudder published the first successful CBT resection,\textsuperscript{11} preserving the carotid artery. In 1940, Gordon-Taylor\textsuperscript{12} described the technique of periadventitial dissection, which has remained as the standard surgical technique.

According to Shamblin,\textsuperscript{13} CBT are classified in types I, II, or III, depending on the grade of carotid attachment and encasement (Fig. 1).

Large tumors can get attached to, deform, and completely surround the carotid bifurcation and nearby cranial nerves, becoming a surgical challenge, that may require carotid revascularization and consequently could have neurologic morbidity derived from cranial nerve injury and/or ischemic stroke.

Our first surgical experience with this tumor dates back to the mid 1980s. Our first 10 cases were reported previously.\textsuperscript{14} The aim of this study is to retrospectively review our experience with 30 consecutive patients treated since 1984.

**METHODS**

All patients with carotid bifurcation tumors who underwent surgery by members of our Vascular and Endovascular Surgery Department between 1984 and 2014 were included in this analysis.

Patient information was retrieved from clinical databases, paper charts, electronic records, and our imaging databank. Tumors were graded according to Shamblin’s classification (Table I).

We treated 30 patients with 32 tumors. Four patients were referred to our service for definitive treatment after attempted resection at another institution.

A lateral neck approach anterior to the sternocleidomastoid muscle was used in all cases. Careful dissection of the vascular structures and nerves

**Table I. Clinical characteristics of 30 patients treated for CBT**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients, n</td>
<td>30</td>
</tr>
<tr>
<td>Age mean, (range)</td>
<td>45.5 (18–75)</td>
</tr>
<tr>
<td>Men, n (%)</td>
<td>9 (30)</td>
</tr>
<tr>
<td>Women, n (%)</td>
<td>21 (70)</td>
</tr>
<tr>
<td>Right side, n (%)</td>
<td>17 (56.7)</td>
</tr>
<tr>
<td>Left side, n (%)</td>
<td>13 (43.3)</td>
</tr>
<tr>
<td>Bilateral, n (%)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Median of evolution (range, months)</td>
<td>10 (3–120)</td>
</tr>
<tr>
<td>Tumor size (mean mm)</td>
<td>44.7</td>
</tr>
<tr>
<td>Asymptomatic growth, n (%)</td>
<td>26 (86.7)</td>
</tr>
<tr>
<td>Symptomatic growth, n (%)</td>
<td>4 (13.3)</td>
</tr>
<tr>
<td>Shamblin I, n (%)</td>
<td>5 (16.7)</td>
</tr>
<tr>
<td>Shamblin II, n (%)</td>
<td>19 (63.3)</td>
</tr>
<tr>
<td>Shamblin III, n (%)</td>
<td>6 (20)</td>
</tr>
</tbody>
</table>
was performed, detaching the lesion from the carotid artery, using electrocautery and ligation of many small anomalous feeding vessels arising, typically, from the external carotid artery (ECA). When required, internal carotid revascularization was performed.

Operative results are analyzed according to Shamblin’s category (Table II).

Neurologic complications were recorded as central (stroke and/or transient ischemic attack) or extracranial (transitory or permanent cranial nerve injury).

Histopathologic diagnosis was obtained in every case, using immunohistochemistry assays in cases deeming necessary, according to the pathologist’s criteria.

Statistical analysis was performed using analysis of variance.

RESULTS

Thirty of 32 carotid bifurcation tumors were resected: 21 in women and 9 in men (2.3:1). Two female patients presented with bilateral CBT; both deferred contralateral surgery and decided to undergo surveillance.

Mean age at surgery was 45.5 (18–75 years).

Right-sided tumors were slightly more frequent (17 patients, 56.7%).

The main complaint was a neck swelling localized in the carotid triangle, asymptomatic in 26 patients (86.7%) and sensitive in 4 (13.3%). One patient also complained of ipsilateral tinnitus.

CT scan was the most widely used diagnostic method (80%), and MRI was performed in 11 patients. Intra-arterial angiography was also performed in 11 patients, mostly during the first decade of this study.

Mean tumor size was 44.6 mm (20–73 mm), with significant differences in size between Shamblin’s group (Table II).

Two patients (6.7%) underwent preoperative selective embolization of the tumor (1 patient Shamblin II and the other Shamblin III), with no difference in blood loss or operative time.

Patients in Shamblin categories I and II underwent simple resection of the tumor.

Five patients with Shamblin III tumors (83.3%) required carotid artery reconstruction. Three patients underwent en bloc resection of the internal carotid artery (ICA) and required common carotid artery (CCA) to ICA saphenous vein bypass with ligation of the ECA. In 2 cases, sufficient ICA remained after tumor resection for direct reimplantation onto the CCA.

Operative results are summarized in Table II.

Mean operative time differed among Shamblin categories: 66 min in Shamblin type I cases, 134 min in Shamblin type II patients, and 240 min in Shamblin type III group patients. Shamblin type III group had a mean operative blood loss of 1,500 mL (1,000–2,500 mL).

There was no operative mortality.

Seven patients (23.3%) had transient postoperative extracranial nerve dysfunction; there was no significant difference among Shamblin groups (3 patients with X cranial nerve deficit, 2 patients with XI cranial nerve deficit, 1 patient with both X and XII cranial nerve deficit, and 1 patient with Horner’s syndrome).

One patient with a Shamblin III tumor measuring 73 mm of diameter required an en bloc resection of

Table II. Differences in surgical management according to Shamblin classification of tumor extension

<table>
<thead>
<tr>
<th>Surgical variables</th>
<th>Shamblin I</th>
<th>Shamblin II</th>
<th>Shamblin III</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
<td>5</td>
<td>19</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Mean size (mm)</td>
<td>27.7</td>
<td>43.4</td>
<td>66</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Simple resection</td>
<td>5 (100)</td>
<td>19 (100)</td>
<td>1 (16.7)</td>
<td></td>
</tr>
<tr>
<td>Revascularization</td>
<td>0</td>
<td>0</td>
<td>5 (83.3)</td>
<td></td>
</tr>
<tr>
<td>Preoperative embolization</td>
<td>0</td>
<td>1 (5.3)</td>
<td>1 (17)</td>
<td></td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>66</td>
<td>133.6</td>
<td>240</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Median hospitalization time</td>
<td>1.5 (1–3)</td>
<td>3 (2–7)</td>
<td>4.5 (2–35)</td>
<td>0.08</td>
</tr>
</tbody>
</table>

Table III. Surgical results: summary of operative complications in published series

<table>
<thead>
<tr>
<th>Complications of CBT excision</th>
<th>Patients (N)</th>
<th>Cranial nerve injury (%)</th>
<th>Surgery-related stroke (%)</th>
<th>Mortality (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sajid1</td>
<td>95</td>
<td>19</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Kruger10</td>
<td>39</td>
<td>22</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>S Wang17</td>
<td>29</td>
<td>41</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Makeieff23</td>
<td>52</td>
<td>42</td>
<td>1.78</td>
<td>0</td>
</tr>
<tr>
<td>Power31</td>
<td>131</td>
<td>33</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Luna-Ortiz35</td>
<td>46</td>
<td>49</td>
<td>0</td>
<td>1.5</td>
</tr>
<tr>
<td>Present series</td>
<td>30</td>
<td>23</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
the vagus nerve, which was completely encased by the tumor mass. At 1 year of follow-up, she has no clinical sequelae.

One patient (Shamblin II, no carotid reconstruction), with a patent foramen ovale presented with a transient minor central deficit on the second postoperative day, secondary to embolic occlusion of a posterior cerebral artery branch, originated from localized calf muscle deep vein thrombosis despite thromboprophylaxis. She fully recovered and was discharged the fifth postoperative day, treated with permanent oral anticoagulation.

Histopathology confirmed paraganglioma in 28 of 30 tumors (93.3%).

Two cases were diagnosed as schwannomas (both Shamblin II). No malignancy was observed.

Since 2005, immunohistochemical assays have been performed in 8 cases for the presence of chromogranin A and S-protein, with no difference in the final diagnosis.

Follow-up was obtained in 24 (80%) patients (1–156 months, mean 3.2 years) Recurrence has not occurred during follow-up.

One patient died of a pancreatic cancer 11 months after CBT treatment. Another patient presented with gallbladder cancer resected at an early stage at 3 years of follow-up.

**DISCUSSION**

CBT (also known as paraganglioma) is derived from the mesodermal cells of the carotid body. Histologically, the carotid body measures between 2 and 5 mm and is located in the adventitia of the carotid bifurcation. It is innervated by the glossopharyngeal nerve and its blood supply derives from the ECA.

It is composed of 3 types of cardiorespiratory regulator cells, which are sensitive to blood pH, pCO₂, and pO₂:

- Type I or chief cells are catecholamine producer cells, organized in cells nests known as Zellballen,
- Type II sustentacular or sheath cells (similar features as Schwann cells),
- Type III terminal sensitive nerve cells from the glossopharyngeal nerve.

Cellular response to PaO₂ variations is wide: from atrophy with persistent hyperoxia and/or hyperplasia and hypertrophy with persistent hypoxia.¹⁵

Although the general incidence of CBT (1:30,000) is low,¹⁸ in high altitude living populations, as in some areas in South America, higher incidences have been reported.⁶⁻⁹

The main features to establish a diagnosis are clinical suspicion and a careful physical examination. Frequently, a CBT presents as a painless submandibular mass, with lateral but no cranio-caudal mobility (Fontaine’s sign). The slow growth rate of CBT makes early diagnosis challenging.¹¹ The average time between awareness of a neck swelling and diagnosis in our series was 18.8 months. Less often CBT may present with local symptoms including discomfort at the carotid triangle, tinnitus, or even carotid sinus syndrome.¹⁶⁻¹⁸

CBT may present at a wide range of age (18–75 in our study) being described as early as 13 years of age.²

CBT can present as sporadic or familial form, being more frequent the sporadic, unilateral cases associated with chronic hypoxia.¹⁷,¹⁹,²⁰

The familial form of CBT accounts for 10–30% of the cases, most commonly bilateral lesions, associated with NEM-2 syndrome and male inheritance.⁸,²¹,²² In this series, 1 female patient (3%) with bilateral tumors reported her father having undergone CBT resection in the past.

Malignant tumors may account for 5–7% of cases.¹,¹⁷,²³ They present at an early age, have a more locoregional invasive pattern and may present with hepatic or lung metastasis. Given the low incidence of a disseminated disease, further studies to rule out malignancy are not obtained unless malignancy is found in the pathologic study of the specimen.

There are some reports proposing fine-needle aspiration biopsy as a diagnostic alternative.²³,²⁴ In our opinion, it should not be performed given the high risk of a major hemorrhage in this highly vascularized tissue.

Our imaging protocol shifted from conventional angiography during the first decade, to CT scan or MRI, as in most of current reported series.

Differential diagnosis of CBT includes: carotid aneurysms, brachial cysts, parotid and other salivary tumors, cervical lymphadenopathy, neurofibroma, schwannoma, other paragangliomas (vagale or jugulare), or even accessories thyroid glands.⁴,⁵,²⁷,²⁸

Surgical resection is the gold standard of treatment for this lesion. It can be challenging in large tumors, given its highly vascularized stroma, the frequent involvement of cranial nerves and risk of cerebral ischemia.⁸,¹⁷,²⁶,²⁹

Preoperative embolization is controversial. In our experience, it did not make a difference in intraoperative blood loss or operative time.³⁰⁻³³

Resection of Shamblin type III lesions are associated to higher morbidity due to potential cranial...
nerve injury, stroke, significant blood loss, and prolonged both operative and hospitalization time, compared with smaller tumors.\textsuperscript{23,25,26,34,35}

In our experience, 50\% of Shamblin III tumors required en bloc resection and over 80\% underwent carotid revascularization.

The complication rate observed in the present series includes a 23.3\% incidence of transient extra-crural nerve dysfunction. We did not observe procedure-related stroke or operative mortality (Table III).

Histopathologic study of the specimens revealed 28 CBT and 2 schwannomas. The latter were clinically suspected and diagnosed as CBT by imaging. At operation, the involvement of neighboring structures in these 2 cases was similar compared with medium-sized CBT.

We believe schwannomas must be regarded in conjunction with CBT as carotid bifurcation tumors, and should be resected,\textsuperscript{36} as the only way to establish a definitive diagnosis and to prevent neurovascular damage caused by tumor growth.

CONCLUSIONS

CBT is an infrequent condition in Chile. Most cases are benign lesions. However, it has the propensity of growing, encasing the carotid vessels, and therefore potentially affecting brain circulation. Its resection can pose a significant challenge to the surgeon, who must be familiar with various revascularization techniques to ensure adequate brain perfusion. Our long-term follow-up has confirmed the benign nature of this tumor.

REFERENCES