» **Original Article** «

Carotid Body Tumors: A Review of 25 Years Experience in Diagnosis and Management of 56 Tumors

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Objective: To report our experience in the management of CBTs and review the literature.

Materials and Methods: 56 CBTs were operated upon over a period of 25 years. Surgical intervention was planned according to the Shamblin classification. Thirty-nine of the tumors were in males (69.64%), and 17 of the tumors were in females (30.36%). The average age was 42 (ages ranging between 32 and 47). Twenty-two tumors were diagnosed and treated with Shamblin type I, twenty-eight with type II and eight tumors with type III. All patients were unilateral except two had bilateral carotid tumors. Thirty-five lumps were de novo (group A), while 21 lumps were treated after a prior trial of removal (group B).

Results: The incidence of carotid reconstruction was lower among group A (1/35) compared to group B (9/21). Complications were less in group A than group B (23% vs. 30%). There were 4 cases with suspected malignancy and no recurrences during the follow-up period.

Conclusion: There is an increased incidence of major vascular reconstruction in cases not properly investigated or diagnosed and in cases with prior attempts of removal in Primary Hospitals. Proper diagnosis of suspicious lumps is mandatory. Resection of CBTs by surgeons with experience in vascular reconstruction is recommended. Vascular reconstructions have to be performed safely without serious complications. Also today, prior attempts of removal are not so common, with preoperative evaluation using the latest diagnostic tools. Cranial nerves injury (especially the Hypoglossal Nv) continues to be the most common complication.

Keywords: carotid body, paraganglioma, carotid resection

Introduction

The carotid body tumors were first described by von Haller in 1743. The incidence of carotid body tumors (CBTs) is less than 1 in 30000. CBTs represent more than half of neck paragangliomas (PGLs), yet still a very rare cause of neck lumps. Like other paragangliomas, CBTs originate from the neural crest.¹⁾ The most

common site is the carotid body. These lesions are rare before the age of 20.²⁾ Recent studies have reported that CBTs are more common in females rather than males (1.9:1) but, there are some Asian centers reporting their data vice versa.³⁾

The mechanisms of carotid body tumor formation remain unknown, but since 1930 it has been accepted that the carotid body is a chemoreceptor which monitors the oxygen tension of systemic arterial blood.⁴⁾ Thus carotid body tumors are associated with conditions producing chronic hypoxia, such as high altitude.

CBT is one of the most commonly seen jugular paraganglioma involving the carotid body chemoreceptors, but rarely seen clinically, so the corresponding diagnosis and management remain difficult.⁵⁾ They present a surgical challenge because of the frequent

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complications and difficulties caused by their high vascularity, proximity and possible infiltration of the carotid bifurcation, compression of cranial nerves in the neck, and extension to the skull base.⁵⁾ CBTs are so rare that management recommendations based on the usual prospective trials or by meta-analysis are not practical.⁶⁾ Because of the infrequent performance of CBT surgical procedures, individual surgeons or single institutions cannot accumulate a sufficient number of cases to report or evaluate their outcomes with statistical confidence.⁷⁾ An attempt to predict the difficulties encountered during resection and the outcome of treatment at our institution was made by reviewing our experience of this rare disease.

Patients and Methods

This is a retrospective study of patients with CBT, who were treated at our institution over a period of 25 years. There were 39 tumors in males (69.64%) and 17 tumors in females (30.36%). Age of the patients ranged between 32 and 47 years old. As mentioned by Lim, et al. in 2010,⁸⁾ Shamblin, et al. in 1971⁹⁾ classified carotid body tumors in relation to the carotid vessels. In this classification Group I was described as localized tumors not involving the carotid vessels. Group II tumors partially surrounded the vessels or adherent to them. Group III were described as larger tumors encasing the carotid vessels. As CBTs become larger in size they get more adherent to the vessels.⁸⁾

In this study, there were 22 tumors (39.28%) Shamblin type I, 26 tumors (46.42%) with Shamblin type II, 8 tumors (14.28%) with Shamblin type III and 2 patients (3.57%) with bilateral tumors. There were 2 groups all presenting with a lump in the neck, Group (A) 35 patients who were properly diagnosed as CBT and surgery was planned before operation And group (B) 21 patients who were not diagnosed as CBT and discovered intraoperatively while being operated upon as a neck swelling, and being referred to our Tertiary Hospital. Proper diagnosis was made by clinical presentation and imaging modalities; carotid arterial duplex, digital subtraction angiography (DSA), computed tomography (CT) and magnetic resonance imaging (MRI) of the neck. Pre-operatively diagnosed group (A) patients were classified according to Shamblin classification into three types, these included 12 Shamblin type I, 18 Shamblin type II and 5 Shamblin type III, and the group (B) patients were re-evaluated

and classified according to Shamblin classification before the definitive excision, these included 10 cases with Shamblin type I, 8 Shamblin type II and 3 Shamblin type III.

Resection was performed through a longitudinal cervical incision made along the anterior border of the sternomastoid muscle. The internal jugular vein was identified and the common facial vein ligated. The common carotid artery was dissected to obtain proximal control. The technique used involved sub-adventitial or sometimes periadventitial resection. Cutting into the tumor was sometimes reserved to in the advanced Shamblin classes to free the carotid vessels of the encircling tumor and finally securing the feeders. The decision for vascular repair was usually made intra-operatively at this point. Intraoperative assessment revealed that there were a total of 22 small, 26 medium, and eight large sized masses (in both groups). When resection only was possible, dissection continued from the side of tumor less encasing the vessels (whether medial or lateral) and continued usually till the nearby vessel is freed. This was followed by freeing the carotid bifurcation and progression in a caudo-cranial direction (**Fig. 1**). When difficulties were encountered on one side of the tumor, dissection was continued from the other side. The shift from side to side was continued to ensure the safest resection of the tumor. The hypoglossal nerve, the vagus nerve and sometimes the glossopharyngeal nerve, were identified away from the tumor and if infiltrated, gradually and meticulously dissected and freed if possible. Resection of the tumour occasionally entailed some form of carotid resection and reconstruction (n = 10): ICA resection and reconstruction by an autologous saphenous vein (n = 7), ICA resection and reconstruction by an end-to-end anastomosis (n = 1), or repair of an ICA tear by lateral sutures (n = 2). The choice of the vascular techniques employed was individually decided by the operating surgeons.

Postoperative complications were recorded and included nerve injuries, cerebrovascular accidents and wound complications. Histopathological diagnosis was reviewed to make sure of the diagnosis and screen for malignancy. The main criteria of malignancy were obtained from operative notes, e.g., lymph node metastases and aggressive local infiltration of adjacent tissues. Patients were followed up for recurrences, progression of complications and appearance of new tumors.

Fig. 1 Stages of tumour dissection: (A) proximal control of CCA, (B) dissection started at the bifurcation and progressed to ECA, (C) ECA is skeletonized and dissection is continued in a caudo-cranial direction, (D) ICA is skeletonized and the tumour is removed. CCA: common carotid artery; ECA: external carotid artery; ICA: internal carotid artery.

Results

This study included 54 patients with 56 tumors as 2 patients who presented with a lump on one side had a contralateral tumor discovered during investigations. The mean age was 42 years ranging between 32 and 47 years. All patients presented with a neck lump just below the angle of the mandible. However, only 35 lumps were diagnosed correctly as CBT prior to surgery (62.5%). These 35 patients were classified as group A. The remaining 21 lumps (37.5%) were misdiagnosed as a cervical lymph node. In these patients there was no obvious cause for lymphadenopathy, and they were scheduled for an excisional biopsy. These 21 patients were classified as group B. These patients (37.5%) were operated upon in other primary hospitals, and when the operators faced excessive bleeding and/or discovered the close proximity to the carotid vessels, they decided to abort the procedure after hemostasis, wound closure, and transferred the

patient to our hospital. The misdiagnosed lumps were re-operated upon at our hospital, where proper evaluation of the tumor was done before definitive surgery; including Radiologic imaging that was done either to establish or confirm the diagnosis, or to assess the anatomic extent of the mass in the neck. Imaging modalities used included arterial duplex (Fig. 2), CT, magnetic resonance angiography (MRA), DSA, and multi-detector CT (Fig. 3).

Shamblin's class did not show any significant influence on the presentation, or the complications. However, there was an increase in vascular reconstruction among Shamblin's III tumors (almost 50% of Shamblin III cases in both groups A and B).

There was an increase of vascular reconstructions among group B patients compared to group A (9/21 in group B vs. 1/35 in group A). The external carotid artery was resected en-block with the tumour in eight cases (Shamblin type III). Temporary carotid shunts

Fig. 2 Arterial duplex scan showing the characteristic image of a mass splaying the carotid bifurcation.

were used during internal carotid artery clamping in five cases, all in group B cases, whenever stump pressure was below 40 mmHg.

ICA resection and reconstruction by an autologous saphenous vein ($n = 7$), was used in 1 case with Shamblin type III in group A, 3 cases with Shamblin type III in group B and three cases with Shamblin type II in group B. ICA resection and reconstruction by an end-to-end anastomosis ($n = 1$ case with Shamblin type II in group B) or repair of an ICA tear by lateral sutures ($n = 2$ cases with Shamblin II in group B).

Dissection and resection of the upper part of the tumor, which is usually in close contact with ICA and the last four cranial nerves before they diverge in different directions, was the most difficult and problematic part after the ICA dissection. Most cranial nerve injuries were encountered at this point, especially the Hypoglossal nerve which represented the higher incidence of post operative cranial nerve injury and residual deficit 6 months after surgery. This injury occurred in six cases with Shamblin type III tumors (four in group A and two in group B). Four cases with neuropraxia recovered completely within 6 months and two cases had permanent deficit (Table 1).

Only one case with Shamblin type II tumor in group A had superior laryngeal nerve injury, that was not incapacitating to the patient (Table 1).

Cerebro-vascular insults (Stroke and TIAs) occurred in cases where there was excessive dissection and manipulations around the ICA, and all resolved within 6 months after surgery. TIAs were experienced by the 2 cases who had lateral suturing of the ICA, Duplex ultrasonography (US) revealed 30%–40% stenosis and was treated with antiplatelets. As for stroke, two cases with ICA resection and grafting had post-operative CVStroke that recovered within 6 months with very minimal residual deficit (Table 1).

According to Shamblin classification,⁹⁾ there were 22 (Shamblin type I), 26 (Shamblin type II), and 8 (Shamblin type III). All tumors were managed by resection only, except four. Three large tumors (>8 cm diameter) were managed by pre-operative radiotherapy which succeeded to lower the size of the mass and became amenable to resection. One tumor was found intra-operatively to be infiltrating the tissues and difficult to remove totally. Subtotal resection was done after sacrificing the external carotid artery and the patient received post-operative radiotherapy after the histopathological exam proved to be malignant.

All 56 tumors were sent to histopathological examination and proved to be benign except the one with subtotal resection.

Postoperative complications occurred in 12 cases (17.85%) of operated cases (Table 1). All complications resolved within 6 months of follow-up after surgery apart from two hypoglossal injuries (3.57%), which were permanent.

Apart from the 2 patients with bilateral CBTs no patients had any other paragangliomas, and no family members of our patients had similar lumps. No recurrences occurred during the follow-up period (2 to 56 months, mean: 37 months).

There were no mortalities in the perioperative period or during follow-up.

Discussion

CBTs are technically challenging neck tumors because of their location. The rarity of CBTs made it difficult to interpret the results and outcomes of their treatment. Publications arise usually from single centers recording the experience of a group of surgeons, each of them

Fig. 3 Multi-detector computed tomography (MD-CT) demonstrating the highly vascular mass splaying the carotid bifurcation. Relation to skull base is also shown.

Table 1 Postoperative complications

Complication	Number (%)
TIA	2 (3.57%)
Stroke	2 (3.57%)
Hypoglossal nerve injury	6 (10.71%)
Superior laryngeal nerve injury	1 (1.78%)
Hematoma	1 (1.78%)
Total	12 (17.85%)

TIA: transient ischemic attack

encountering only few cases during their career. Because of unpredictable malignant potential, early and complete surgical resection is often recommended.¹⁰⁾

Carotid body tumors can be bilateral in 5% of sporadic cases, and in 33% of familial cases. Sporadic PGLs are multifocal in only 10% to 20%; however, in familial cases, up to 80% are multifocal. Familial cases of PGL have been shown to be caused by germline mutations in three of the four succinate dehydrogenase (SDH) subunit genes—SDHB, SDHC, and SDHD.¹¹⁾

Our patients' demographics showed characteristics similar to Latin American series as the low incidence of malignancy, and bilaterality when compared to non-Latin series.¹²⁾ This could reflect a potential genetic pattern.

Duplex US, CT, MRI, MRA and DSA are requested for patients with suspected CBT for diagnosis. DSA is the gold standard in CBTs¹³⁾ to diagnose and plan the treatment. In addition to showing the site, size, and

feeding vessels of the tumor, confirming the patency of the Circle of Willis, identifying the presence of other head and neck paragangliomas, DSA can identify the dominant feeding vessel, thereby allowing for preoperative embolization.^{12,14,15)} Color coded ultrasonography (CCU) allows early and non-invasive accurate detection of tumors with 100% sensitivity even when not palpable.¹⁶⁾ The combined use of CCU and somatostatin receptor scintigraphy with planar and single photon emission tomography was found beneficial in identifying the extent of tumors, and degree of arterial infiltration.¹⁴⁾ CT and MRI show the infiltration in the neck and in between the vessels. MRA is more preferable than MRI as it gives both images of the tumor and data on the vascular involvement.^{12,15,17)}

DSA is now being replaced by the emerging MDCT, which provides an accurate angiogram and adds the advantage of detecting the extent and the relation to the skull base and surrounding structures in case of large CBTs.¹⁴⁾

Octreotide scanning, a nuclear medicine imaging procedure, could also be useful for detecting the presence of multicentric or metastatic paragangliomas, and for distinguishing scar from residual tumor after surgery.¹²⁾

Although it was described that the carotid body is located in the adventitia of the carotid bifurcation,^{6,12)} others,^{7,17,18)} including the authors believe that it lies in the peri-adventitial plane. Thus, it is possible to

resect the tumour through the existing space between the vessels and the tumor. This anatomic distinction is critical for safe surgical procedures, as dissection in the deeper plane may lead to carotid injury (and repair or resection), and lack of appreciation of this anatomic detail may account for complications.⁷⁾ Farr agrees with early resection of CBTs as this might avoid carotid artery resection, since the tumor grows somewhat loosely attached to the arterial wall and would thus be easier to detach at an early stage.¹⁹⁾

In this study, the need for vascular reconstruction was considered as continuation of the procedure of excising the tumour and was not considered as a complication. Vascular resection and reconstruction was inevitable in 10 tumors (15.38%) in this study. The rate of vascular repair in the literature ranged between 20% (Ma, et al., 2009)¹⁷⁾ and 24% (Kotelis, et al., 2009).¹⁸⁾ So there is a need for the presence of vascular experience among the operating team.^{10,15,20)} Makeieff, et al.,²⁰⁾ adopted a dissection technique starting from the periphery of the tumor and ending at the bifurcation. They considered the posterior surface of the bifurcation the most difficult part of dissection and finished dissection at this point. We consider the most problematic point the upper part of the tumor, which is usually in close contact with ICA and the last four cranial nerves before they diverge in different directions. Most cranial nerve injuries were encountered at this point. Thus, we begun dissection at the carotid bifurcation and continued in a caudal-cranial fashion. This approach was associated with decreased mortality and stroke rates since the late 1980s.²¹⁾

A modified Shamblin's classification was proposed by Luna-Ortiz, et al. in 2006 to improve the prediction of difficulties and complications.²²⁾ They proposed a class IIIa which represents the old class III, and a class IIIb which includes tumors of any class (I, II, or III) where there is infiltration of the vessel wall and not just circumferential encasement. According to the modified classification the need for vascular resection and reconstruction was significantly higher among class IIIb tumors. Since most of the Shamblin's III cases included in this study could be considered as class IIIa, it was expected to have some of them successfully excised without vascular resection. The distinction between vascular encasement and vascular infiltration should be clear when interpreting the outcomes of resection of Shamblin III

tumors. Van der Bogt, et al.²¹⁾ used another subdivision of the Shamblin's classification (A, B and C) to define the degree of adherence to the carotid.

The rate of complications varies greatly from one study to the other. In this study the overall rate of complications was 17.85%. The incidence of cranial nerve injury was 10.71% but only 3.57% were permanent. Makaieff, et al.²⁰⁾ reported that the incidence of cranial nerve injury and stroke was 14.03%. Tumors more than 4 cm incurred a higher risk during removal. Early detection of smaller tumors should reduce the morbidity of the procedure.²⁰⁾

A 63% incidence of cranial nerve injury was noted in patients who had major vascular reconstruction versus a 27% incidence in patients who had CBT resection only.¹⁰⁾ Having said that it should also be mentioned that carotid artery reconstruction at the time of tumor resection can be performed safely and that additional morbidity or mortality may reflect advanced tumor pathology rather than operative technique.¹⁰⁾ According to the review published in 2007 by the JVRG (Joint Vascular Research Group),¹⁵⁾ CBT resection was associated with overall morbidity rate of 33% and 1% mortality rate. Main complications after surgery were reported to be; cranial nerve injuries in 19% of cases with recovery in most cases within 6 months to reach 3%. Only one case (1%) with a malignant 20 cm tumor resulted in permanent vagus nerve injury. Wound hematoma was also recorded as a common complication together with cutaneous nerve injuries and Horner's syndrome. TIAs and stroke were also common post operative complications as compared to the international studies ranging between 0% and 8%.¹³⁾ This variation may be attributable to the experience of the operating surgeon.¹⁵⁾ In our study the incidence was 3.57% for TIA and 3.57% for stroke. There is a low but constant risk of malignancy ranging between 4%–10% in various reports.^{10,15,19)} This series showed four large tumors (>8 cm) with suspected malignancy due to their size and pattern of infiltration in the neck. We used pre-operative radiotherapy for three of them, which reduced the size and vascularity and made them amenable to resection. The fourth was incompletely resected and received post-operative radiotherapy for the remaining tumor tissue in the neck. Histopathological examination showed evidence of malignancy so and the follow-up never showed lymph node metastasis.

Mendenhall, et al. in 2011 emphasized that paragangliomas are histologically benign tumors resembling the parent tissue and consist of nests of epithelioid cells within stroma-containing, thin-walled blood vessels and non-myelinated nerve fibers. Although the tumor is well circumscribed, a true capsule is not seen. The criterion of malignancy is based on the development of metastases rather than the histologic appearance.²⁾ Wieneke and Smith in 2009 proposed that less than 10% of paragangliomas are malignant, and it is not always possible to predict malignant behavior based on histologic features alone.¹⁾ Follow up of the regional lymph nodes in patients after resection is of ultimate importance as lymphatic metastases occur in about 5% of carotid body tumor patients after resection.²⁾ Carotid body tumors have a low risk for distant metastases, and no metastatic disease was reported.³⁾

The management of head and neck paragangliomas include surgical resection, external beam radiotherapy, and stereotactic radiotherapy.^{23,24)} Small lesions may be successfully removed with little risk to the patient. However, if resection of the carotid vessels is anticipated or if a large lesion is fixed or unresectable because of size, radiotherapy is the preferred initial treatment. Irradiation is used frequently to treat glomus tumors, particularly those in the tympanicum and jugulare bulb, or carotid body tumors.²⁵⁾

Local control after radiotherapy is defined as stable disease or partial regression with no evidence of growth.

Farr used radiotherapy for minimal residual tumor after incomplete resection¹⁹⁾ and Sajid, et al. showed that it was used only in one case for tumor destaging.¹⁵⁾ In the present study four cases received radiotherapy; three preoperatively to reduce the size of a large tumour and one postoperatively after it turned out to be malignant with residual tumour left.

Large CBTs can be resected safely with or without preoperative embolization. Preoperative embolization may simplify the conduct of the operation and reduce blood loss but does not decrease rates of cranial nerve injury, although most are temporary.²⁶⁾ In this study we did not use pre-operative embolization.

Qin, et al.²⁷⁾ and Makeieff, et al.²⁰⁾ demonstrated that routine preoperative embolization is not required and should be limited to unresectable tumors to prevent disease progression rather than cure. The reason for that is that embolization has its own risks in the form of an associated inflammatory response that

makes precise periadventitial dissection more difficult²⁸⁾ and the risk of intracranial embolization.²⁰⁾ Also it did not affect the probability of need for vascular repair.²⁹⁾ Currently embolization is recommended only for: tumors more than 5 cm in size, Shamblin's class III and those that extend significantly cranially.³⁰⁾

An alternative to embolization is the insertion of a covered stent in the external carotid artery.³¹⁾

Conclusion

This study confirms that the need for vascular reconstruction is high in large sized tumors and in cases with prior attempts of removal without proper diagnosis. Vascular reconstructions can be performed safely without serious complications. The accurate and prompt diagnosis of CBTs from the start is essential to avoid unsuccessful removal attempts. The latest diagnostic tools made the situation of misdiagnosis rare nowadays.

It is also hoped that a more optimal cooperation could be shaped in future between vascular surgery and radiation oncology academic centers for the treatment of the intriguing tumors of carotid body and other paragangliomas.

Disclosure Statement

The authors have nothing to disclose.

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