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APPROACH AND OUTCOME OF CAROTID BODY TUMOR AT A TERTIARY UNIVERSITY HOSPITAL: RETROSPECTIVE COHORT

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ABSTRACT

Introduction: Management of Carotid Body Tumor (CBT) has not been standardized and presents a challenge to treating physician. This study conducted at a tertiary hospital of a developing nation, analysed outcomes like nerve injury, hospital stay, recurrence, mortality following surgical excision of this highly vascular tumor. **Methods:** A retrospective review of all cases operated for CBT over five years between January 2015 to December 2019, at the institute were consecutively evaluated. Initially there were 18 patients, but on reviewing the HPE two were reported as Schwannomas, therefore total 16 patients were serially studied (n=16). Symptom duration evaluated as mean, median with its interquartile range (IQR). Categorization of tumors as per Shamblin classification was done, incidence of malignancy, nerve injury analyzed in percentage. **Results and conclusion:** All CBT were completely excised. Prevalence was higher amongst females (69%). Mean was 42.7 years ± 10.56 (SD) with median duration of symptoms being 14 months, interquartile range (IQR) of 13 months (Q1=11.5, Q3=24.5 months). 50% of tumors were Shamblin type II, remaining tumors equally distributed in type I and III. One tumor reported as malignant. Overall complication rate was 18.75%, incidence of cranial nerve injury - 12.5%. CBT is a locally aggressive, slow growing lesion hence has a delayed presentation. Early excision is best chance for cure, hence prompt referral to specialist centre with a multidisciplinary team provides best chance for treatment reducing the inadvertent injury to surrounding neurovascular structures.

Keywords: Carotid Body Tumor, paraganglioma, high altitude, succinate dehydrogenase, Shamblin classification, nerve injury.

INTRODUCTION

The carotid body was first described by Albrecht vonHaller in 1743.[1] It is a specialized organ around 2-6 mm in size located in adventitia of carotid bifurcation, supplied by the ascending pharyngeal artery and innervated through Glossopharyngeal and Vagus nerve.[2]It is a chemoreceptor stimulated by hypoxia, acidosis and hypercapnia.[3] CBT also known as Chemodectomas or paragangliomas are rare, highly vascular lesions with a reported incidence of about 1-2 / 100,000.[4],[5]These slow growing tumors have a higher incidence in females and are rare before the age of 20 years.[6]Majority of the patients are asymptomatic therefore present at an advanced stage, once the tumor has reached a considerable size to cause compressive symptoms. Presenting symptoms are usually pain, dysphagia and autonomic dysfunction.[7]Although most of tumors are benign, delayed presentation can lead to local invasion, malignancy (10%)[2] resulting in incomplete removal, cranial nerve dysfunction or significant surgical morbidity. First excision of CBT was performed in 1880 by Reigner but the patient didn't survive, Maydl in 1886 removed the tumor but the patient survived with hemiplegia and aphasia.[8] First successful surgical excision was performed by Albert in 1889,[9] but the current practice of a sub adventitial dissection was advocated by Gordon-Taylor in 1940.[10]The hyperplastic variant of CBT is more commonly associated with chronic hypoxemia like in high altitudes. Most of our patients belong to such regions and they have a presentation different from those of familial variant.

MATERIAL AND METHODS

This study has been approved by The Institutional Review Committee (IRC) of Institute of Medicine, Tribhuvan University, Kathmandu. The ethics approval reference no. is – 377 (6-11) E2 / 076/077. Medical records of all the patients operated for CBT at Manmohan Cardiothoracic Vascular & Transplant Center, between January 2015 to December 2019 were traced and analyzed. Patient demographics, tumor classification (Shamblin) and operative outcome were studied for each patient. Initially eighteen records were studied, but on reviewing their histopathological examination (HPE), two of them were reported as schwannomas, hence they were excluded from this study. So, a total of sixteen patients were evaluated for the five-year period. Most common presenting symptom was a slow growing, painless neck mass. None of the patients in this study had a family history of paragangliomas or cranial nerve deficit at presentation. Physical examination revealed firm rubbery pulsatile mass, palpable along the carotid arterial trace, mobile in horizontal plane, situated below the mandibular angle. With the provisional diagnosis of a vascular tumor, they were first evaluated by doppler ultrasonography, followed by CT angiogram for all patients to assess tumor features, proximity to vessels and gauge operative difficulty (Fig. 1). Patients were operated under general anesthesia (GA). Resection was performed through a longitudinal cervical incision along the anterior border of sternocleidomastoid muscle. Patients were heparinized with 5000 IU of unfractionated heparin (UFH) intravenously prior handling of artery. Dissection directed to gain control of common carotid artery (CCA), internal and external carotid arteries (ICA, ECA) before attempting mobilization. Nerves were identified away from the tumor and excision was by sub-adventitial dissection technique. Cerebral oximetry was used during surgery in all patients and cell scavenging system used with tumors of Shamblin III or larger type II tumors. All tumors excised (Fig 2) were sent for HPE (Fig 3) and were reviewed in follow up visit. In the post-operative period, progress was observed and complications noted. Patient follow up was bi annual for first year, annual for second year and then *si opus sit* (SOS). The overall mean length of follow up was 12 months (range being six – 48 months).During follow up, they were evaluated by physical examination and duplex ultrasonography. The patient with malignant

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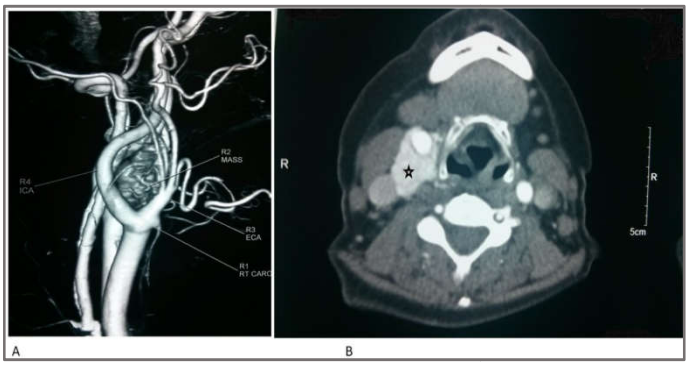
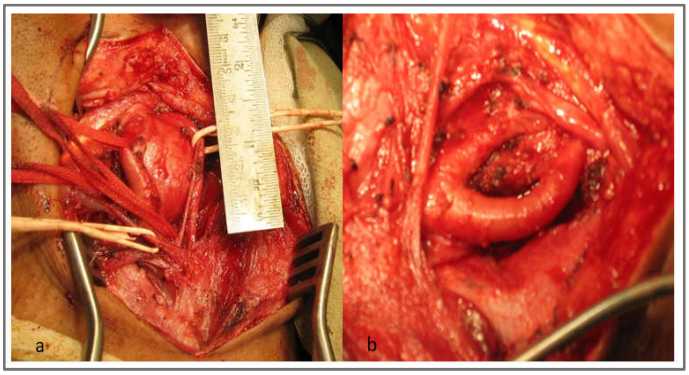
CBT was on continuous bi annual follow up, he was disease free till the last visit. Data was entered in MS excel sheet, mean and standard deviation (SD) analyzed for age at presentation and duration of hospital stay. Median and interquartile range (IQR) for duration of symptoms. Various operative interventions during excision used were assessed. Overall complication and cranial nerve injury calculated in percentage.

Fig. 1 Carotid CT angiogram



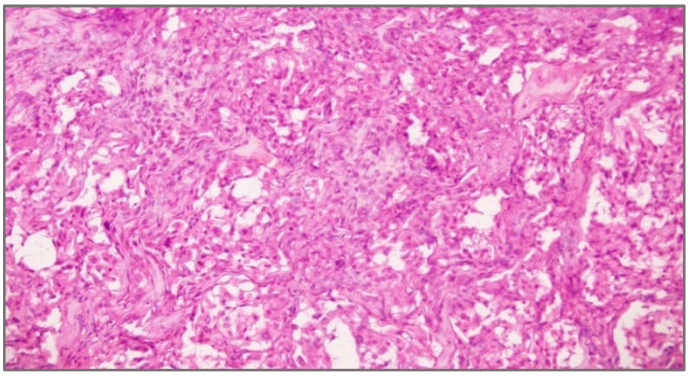
- 3D reconstruction of carotid vessels with CBT, shows splaying of carotid bifurcation. R1 common carotid artery; R2 CBT; R3 external carotid artery; R4 internal carotid artery
- right carotid body tumor (*) encasing the external & internal carotid arteries. (Shamblin 3)

Fig. 2 Intraoperative image



- Intraoperative image showing CBT, ICA and ECA. Arteries are taken under control
- post excision

Fig. 3 HPE of CBT



Finely granular cytoplasm, round to oval nuclei with stippled chromatin
(Hematoxylin and Eosin stain, light microscopy, x400 magnification)

RESULTS

We evaluated a total of sixteen patients over five-year period, with an incidence of about 3.2 cases per year and 69% were females. Mean age of presentation was 42.7 years, oldest patient being of 67 years, youngest patient was 22 years old. Median duration of symptoms was 14 months. In this study majority had a CBT of Shamblin type II variant (eight). Remaining had tumor variants equally distributed in Shamblin type I and III respectively. CCA and ICA were clamped to facilitate dissection in six (37.5%) patients after confirming an adequate ICA systolic stump pressure (greater than 50mmHg). The Pruitt-Inahara outlying carotid shunt was used in seven (43.8%) cases. Excision of ICA for complete tumor removal was done in one patient (6.2%) and it was replaced by Polytetrafluoroethylene (PTFE) conduit of six-millimeter size. One patient underwent ECA ligation for a Shamblin type III tumor. She developed acute thrombosis of CCA and underwent immediate re-exploration with thrombectomy. She sustained left ischemic stroke with right sided hemiparesis. One of the tumors was reported as malignant CBT in HPE, with lymphovascular and perineural invasion. The tumor was classified as a Shamblin type III. Patient received adjuvant radiotherapy and remained tumor free in subsequent follow up. He sustained permanent right hemi glossal paresthesia. Mean gross volumes of CBT was 4.2 cm^3, 11 cm^3, 26 cm^3, for Shamblin type I, II, III respectively. This study had an overall complication rate of 18.75% and cranial nerve injury of 12.5% which included ischemic stroke in one patient, cranial nerve injury amongst two. There was no mortality in this series and no recurrences. Summary of patient profile, operative and clinical data of cases is presented in Table 1

DISCUSSION

It is well known that climate can influence development of neoplasm's, for example people living in regions which receive ample sunshine are more prone to develop skin cancers like Basal Cell Carcinoma, Malignant Melanoma. Similarly high altitudes may predispose to tumorigenesis by subtle means and a Peruvian pathologist Arias Stella was the first to draw attention to enlarged carotid bodies in the normal high-altitude dweller in 1969.[11] Stella et al, also reported the high incidence of chemodectomas of the head and neck in adults living in the Andes in which 23 of their 25 subjects with CBT had lived in altitudes between 2105 to 4350 meters.[12]Rodriguez et al,[13] evaluated 120 CBT in inhabitants of high altitudes and concluded higher female preponderance of 89%, low rate of bilaterality (5%) and family history of 1% which is similar to this study with a prevalence of 69% amongst females, none with family history or bilateral tumors. Paridaans MP et al,[14]in a retrospective study - spanning over six years - of 41 consecutive patients operated for CBT have concluded that their technique of craniocaudal dissection is reproducible and yields superior outcomes. The technique encompassed early identification of Vagus, Hypoglossal and Accessory nerves while taking control of ICA, ligating the feeding vessel of the tumor - Ascending Pharyngeal Artery - at the cranial end of CBT, then proceeding with dissection in cranial to caudal direction. The complication of temporary cranial nerve deficit was reported at 26.7% in their study. Although a similar technique of dissection was employed in this study, in which the important nerves were first dissected safe from the tumor, taking control of ICA, CCA and then proceeding with dissection, permanent nerve damage was reported amongst two patients. This could be attributed to a larger average size of tumors, especially in Shamblin III type. Bilateral tumors are frequently associated with the familial variant of CBT. This observation was also made by Ferrante AM et al,[15] in their 2015 article where they had nine patients with positive family history and six with bilateral lesions amongst the 33 patients they studied.

Boscarino G et al,[16]also shared parallel findings with 15% of patients with bilateral lesions. Current study presents contrast findings with no bilateral lesions or a positive family history, but all three studies have a higher prevalence of this tumor in females. The approximate incidence of familial paragangliomas is 10%,[17] genetic testing is proving to be an important additional investigation in these group of patients. Younger age at presentation with positive family history, or patients with multiple paragangliomas like bilateral CBT should be considered to be tested for mutation in Succinct Dehydrogenase (SDH) genes. Where available this test should be offered to select cohort of patients as this may aid in diagnosis of unsuspected synchronous lesions not only in patient by family members as well. Any patient with positive genetic testing should take ^{18}F-Dihydroxyphenylalanine (F-DOPA) positron emission tomography (PET) to scan other paragangliomas.[18] Surveillance screening should be done every five years if the PET is negative. Incidence of overall complication (18.75%) and cranial nerve injury (12.5%) was similar to study by Gad et al which reported complication and cranial nerve injury of 17.85%, 10.71% respectively.[19]Complications occurred in two patients of Shamblin type III, one of type I. Need for vascular reconstruction is reported variedly ranging from 20% (Ma et al) to 24% (Kotelis et al), but in this series all excisions were achieved by sub adventitial dissection, aided by ligation of ECA in one patient.[20]Also it was observed by Smith et al that there was a higher incidence of cranial nerve injury (67%) amongst those undergoing major vascular reconstruction versus those who did not (27%).[21]Amato et al did a comprehensive review of 625 cases from 19 studies and reported rates of transient cranial nerve dysfunction, vascular injury, permanent cranial nerve injury, stroke and mortality as 31%, 28%, 17%, 2.5% and 0.5% respectively[22]. This study had vascular injury and re exploration rate of 6.25%, with no perioperative mortality. The institution has seen a steady rise in managing patients with CBT. This can be compared with a previous study by Shrestha UK[23] of 2013 reviewing 15 CBT over ten year period, which is a more than 100% rise in number of cases. Table 2 presents a comprehensive comparison of some contemporary research articles.

Table 1 Summary of patient profile, operative and clinical data of cases

	n	%	Mean / Median	Morbidity
Total	16			
Patient demographics				
Females	11	69		
Males	5	31		
Age (years)			42.7 ± 10.56	
Clinical data				
Symptom duration (months)			14[a](IQR=13)	
Right sided CBT	7	43.75		
Left sided CBT	9	56.25		
Bi-lateral CBT	-			
Family history of CBT	-			
Preoperative CND [b]	-			
Hospital stay (days)			5.1 ± 2.6	
Imaging				
Duplex ultrasonography	16	100		
CT angiogram	16	100		
Surgical approach				
Complete resection	16	100		
ICA clamp	6	37.5		
Carotid shunt	7	43.8		
Ligation of ECA	1	6.2		
PTFE graft	1	6.2		
Shamblin classification				
I	4	25		
II	8	50		Hypoglossal n. injury
III	4	25		1. Glossopharyngeal + Vagus n. injury
				2. Re-exploration with CCA thrombectomy; CVA

- Median duration
- Cranial nerve dysfunction

Table 2 Comparison of contemporary studies

Study	Years	Patients (n)	CBT (n)	Male / Female	Mean age (y)	Shamblin I, II, III	Overall complication (%)	B/L CBT (%)	Malignant CBT (%)
Paridaans MP et al [14]	6	41	45	18 /23	38	7, 22, 16	26.7% [a]	41	2.4
Gad A et al[19]	25	-	56	39 / 17	42	22, 28, 8	25	3.5	7.1 [b]
Ferrante AM et al[15]	14	33	44	7 / 26	55	17, 19, 18 [c]	6.7	-	-
Shrestha UK[23]	10	14	15	6 / 8	41.9	0, 4, 11	20	7.1	-
Boscarino G et al[16]	12	20	26	6 / 20	-	-	7.6	15	-

- temporary cranial nerve damage
- reported as suspicious for malignancy by author
- divided into Group I, II, III as per size as <3cm, 3-5cm, > 5cm respectively

Conclusion

CBT although a benign lesion, where possible complete surgical excision with meticulous dissection from surrounding neurovascular structures remains the only cure for it. When carotid stump pressures are adequate, ligation with excision of tumor with the engulfed vessel can be performed when reconstruction not feasible. This is mostly employed for Shamblin type III tumors as a last resort.

CONFLICT OF INTEREST

Authors declare no conflict of interest

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