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Surgical Management of Carotid Body Tumors: A Triple Center Retrospective Study in Sana'a City, Yemen

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ABSTRACT

Context and Objective: Carotid body tumors (CBTs) are the most common paragangliomas of the head, and neck, accounting for 80% of cases. Although their symptoms are minor, these tumors deserve special attention in order to reach an accurate diagnosis, and appropriate treatment. In the past decades, interest in studying these tumors has increased; however, apparently no published research has been conducted in Yemen. Therefore, we included the largest three hospitals in Sana'a City, Yemen discussing the sociodemographic features of patients, diagnosis challenges, surgical intervention, and complications of surgical procedures. **Patients and Methods:** Over a period of 4.5 years from January 2018 to June 2022, a retrospective study was conducted to identify cases of CBTs in patients who underwent surgical treatment of pathologically confirmed CBTs at the vascular surgery unit, department of general surgery in the three largest hospitals in Sana'a City, Yemen. We relied on the hospital charts to review the data on sociodemographic, perioperative, and surgical complications. CBT measurements were determined from preoperative magnetic resonance angiography, computed tomography, and ultrasound examinations of the neck. Shamblin's classification system was used to categorize CBTs based on their size and the challenge of the surgical removal. **Results:** Fifty-three CBTs were resected from 48 cases (42 women and 6 men; female:male ratio of 7:1). The age of the cases at presentation varied from 28 to 61 years (the mean age was 45 ± 11.6 years). The majority of cases (77%) were from mountainous areas with an altitude of more than 2000 meters above sea level. The recurrence rate was 4.2% (2 cases). All cases were benign and presented with a neck lump (100%), whereas 27 (56.7%) cases presented with disfigurement. Right-side tumors were in 19 (39.6%) cases, left-side tumors were in 24 (50%) cases, and bilateral tumors were in 5 (10.6%) cases. The distribution of cases in Champlin classes (I), (II), and (III) was 7 (14.7%), 27 (56.7%), and 14 (29.4%),

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respectively. The incidence of postoperative cranial nerve deficit (POCND) was about 17% in 8 cases. No strokes or mortality were recorded. **Conclusion:** Despite the inclusion of the three largest hospitals in Sana'a City along with the relatively long study period, CBTs are still rare neoplasms. In our experience, CBTs are predominantly tumors of middle age and more common in women, suggesting that we could be dealing with a different disease in Yemeni population, especially among those who dwell in the highlands. The experience of this casuistry shows that the surgical resection is relatively low-risk and the incidence of POCND was small.

Keywords: Carotid Body Tumors, Carotid Chemodectoma, Paragangliomas, Neoplasms, Head and neck surgery, Sana'a City, Yemen

INTRODUCTION

Carotid body tumors (CBTs), also called chemodectomas, paragangliomas, or carotid glomus tumors, grow along the sympathetic and parasympathetic chains of the human body. The most common site of these tumors is the head and neck region, and the majority of these cases are related to the carotid body [1,2]. The exact etiology of CBTs is unknown, but they are thought to be related to genetic mutations [3].

Symptoms of CBTs may include a painless mass in the neck, difficulty swallowing, hoarseness, and changes in voice. In some cases, the tumor may cause compression of nearby structures, leading to symptoms such as dizziness, fainting, or difficulty breathing [4].

With a reported prevalence of 1-2/100000, CBTs are uncommon neuroendocrine neoplasms that make up 0.5% of head and neck tumors and 0.012% of all body tumors [5-8].

CBTs are made of chromaffin-negative glomus cells that originate from the neural crest and are found in paraganglionic tissue [6].

Chronic hypoxemia from chronic obstructive pulmonary disease and high elevations have been associated with an increased prevalence of CBTs. The sporadic variety of carotid body paraganglioma is more frequent than the inherited form, and it tends to be slightly more common in women than men [9-11].

Even though CBTs are usually benign (noncancerous), they may have a malignant behave and spread locally or distantly, as well as cause mass-effect symptoms [12]. Previous research has shown that malignancy represents approximately 3% of CBTs [13-15]. A recent study concluded that although chemodectomas are often benign, they can present with metastases and compressive symptoms, making it crucial to comprehend their physiology and therapy [12].

Due to their location and vascularization, these tumors present quite technical challenge for surgeons. Additionally, the impairment in the function of the nerve before surgery can exacerbate the complications resulting from the surgery, leading to a deficit in the VII, VIII, IX, X, XI, and XII cranial nerves.

The carotid body is responsible for sensing changes in blood oxygen levels and regulating breathing accordingly. Sana'a is the capital and largest city of Yemen and is located at an altitude of approximately 2,200 meters above sea level. It is known that in high-altitude environments, such as Sana'a City, the oxygen level in the air is lower than at sea level. This can lead to chronic hypoxia, which in turn can stimulate the carotid body to grow larger, which can increase the risk of developing CBTs. To our knowledge, no previous research has studied CBTs in Yemen. As a part of sharing our experience with CBTs, we aimed to evaluate sociodemographic characteristics, diagnosis challenges, surgical intervention, and complications of surgical procedures among patients who were treated at the three largest hospitals in Sana'a City, Yemen.

PATIENTS AND METHODS

Study Design and Patients

This is a retrospective study that included all patients who were diagnosed with CBTs between January 2018 and June 2022 at the vascular units of surgical departments in three hospitals in Sana'a City, Yemen. We included all patients who underwent surgical treatment for pathologically confirmed CBTs. On the other hand, patients who were managed nonoperatively, had severe organic diseases, and had incomplete sociodemographic, imaging, or operative records were excluded from our analysis.

Selection of Hospitals for Data Collection

To minimize a selection bias, we relied on selecting the hospitals from which data were collected based on the size of the hospital as well as the presence of vascular surgery units, including the three largest hospitals in Sana'a City, provided that two of them were public (Al-Thawra Modern General Hospital (TMGH) and republican hospital) and the third remaining was a private hospital, the University of Science and Technology Hospital (USTH).

Data Collection

Data were collected retrospectively using a computerized database, hospital charts, and medical records to identify all patients who underwent surgical treatment for pathologically confirmed CBTs. Patients were identified by their admission code and diagnosis. Each patient record was reviewed to collect their sociodemographic, preoperative,

perioperative, and postoperative data. From the patient's file, the patient's residence area was known. Patients with incomplete data on their residence had their phone numbers taken, and they were contacted and asked in which area they live permanently. Then, the Google Earth application was used to calculate the altitude of the patient's residence above sea level.

Diagnosis and Surgical Procedure

CBTs are challenging to diagnose, because they are uncommon and have few manifested symptoms. At first, neurological function was assessed; if necessary, neurologists were consulted. Then preoperative imaging studies such as a CT scan, ultrasound, or MRI were performed to diagnosis of CBTs as well as detect distant metastasis and local recurrence. Additionally, the diagnosis of CBTs was confirmed by biopsy. The preoperative embolization technique was not used in all three hospitals. Under general anesthesia, surgical procedures for CBTs are routinely performed. According to their size and the degree of contact the tumor has with the internal carotid artery (< 180°, between 180° and 270°, and >270°), CBTs were categorized using Shamblin's classification system. If CBTs were graded as Shamblin I, surgical resection was directly performed without interfering with the carotid artery. The external carotid artery was ligated in the resection of CBTs, which were graded as Shamblin II or III, and revealed a huge CBT with a partial or complete encasement of the carotid vessels. If a patient had bilateral CBTs, the less severe side was operated on first after recording the patient's Shamblin grade. Intraoperative nerve injuries were repaired if possible and recorded in operative documents. Histological examination of the specimen, paying particular attention to the tumor margin, was used to confirm complete excision.

Statistical Analysis

The questionnaires were pre-coded before being administered, and the same codes were used in data entry. Open-ended questions were post-coded, and the master coding sheets were securely stored. Data were analyzed using South Texas Art Therapy Association 17.0 software (Stata®17.0). Quantitative data were expressed as mean ± standard deviation (SD), and median (minimum-maximum). Qualitative data were expressed as frequency and percentage.

RESULTS

Based on the inclusion and exclusion criteria, a total of 53 CBTs from 48 patients between January 2018 and June 2022 were included in our final data analysis. We observed that duplex scanning was the best investigation for diagnosis, though CT-angiography and MRI-angiography scans were important for preoperative assessment. Sociodemographic characteristics, tumor features, and surgical outcomes are presented in the attached Table. Three-quarters (75%) of our cases were from TMGH, 7 (14.6%) were from USTH, and 5 (10.4%) were from Republican Hospital. The age of patients at presentation varied from 28 to 61 years (mean age was 45±11.6 years). Our patients were predominantly female (n = 42, 87.5%), with a female: male ratio of 7:1. More than three-quarters of cases involved residents of areas above 2,000 meters above sea level (N = 37, 77%). The recurrence rate was 4.2% (2 cases). All cases were malignant and presented with a neck lump (100%), whereas 27 (56.7%) cases had disfigurement, and one (2.1%) case had neck pain. Right-side tumors were in 19 (39.6%) cases, left-side tumors were in 24 (50%) cases, and bilateral tumors were in 5 (10.6%) cases. One case (2.1%) was associated with a functioning tumor. A familial type of CBT was presented in 2 (4.2%) cases. Multiple paragangliomas were presented in one case (2.1%). The distribution of cases in Champlin grades I, II, and III was 7 (14.7%), 27 (56.7%), and 14 (29.2%), respectively. The incidence of POCND was 16.8% in 8 cases. No strokes or mortality were recorded in our cohort of cases.

Table: Sociodemographic characteristics, tumor features and surgical outcome of 48 cases with carotid body tumors.

Variables	Frequency (%), Mean (SD) or Median (Minimum- maximum)
Hospital	
TMGH	36 (75)
Republican Hospital	5 (10.4)
USTH	7 (14.6)
Gender	
Female	42 (87.4)
Male	6 (12.6)
Age, (years)	
Mean (SD)	45 (11.6)
Median (Minimum- maximum)	46 (28-61)
An altitude of the patient's residence above sea level (meters)	
≥ 2000	37 (77)
< 2000	11 (23)
Tumor features	
Recurrent	2 (4.2)
Functioning	1 (2.1)
Right side	19 (39.6)
Left side	24 (50)
Bilateral or paired	5 (10.6)
Familial type of CBT	2 (4.2)
Multiple Paraganglioma	1 (2.1)
Symptoms	
Neck lump	48 (100)
Neck Pain	1 (2.1)
Disfigurement	27 (56.7)
Champlin grade	
I	7 (14.7)
II	27 (56.7)
III	14 (29.2)
POCND	8 (16.8)

DISCUSSION

Even with the inclusion of the three largest hospitals in Sana'a City, CBTs are still rare neoplasms. They represent the most common head and neck paraganglionomas; however, their diagnosis and management pose a challenge for surgeons [16]. In 1915, Mathews remarked that "this rare tumor presents unusual difficulties to the surgeon, and one should encounter it without suspecting the diagnosis; the experience will not be forgotten" [17]. Von Haller published the first description of the carotid body in 1743 [18]. It is a highly specialized organ situated at the bifurcation of the common carotid artery. This body's paraganglionic cells sense pH, pCO_2, and pO_2 fluctuations in the blood. The average carotid body size is 5 mm by 3 mm by 1.5 mm, though it can vary. Its mean weight in adults is 12.1 mg and ranges from 1 mg to 47 mg. The external carotid artery is where the majority of its feeder veins originate. The function of the carotid body is to involuntarily control the respiratory

and cardiovascular systems, as well as the temperature of the blood [19].

In our cohort of cases, duplex scanning was the best investigation for diagnosis, though CT-angiography and MRI-angiography scans were important for preoperative assessment as they can be highly helpful and may reveal enlargement of hypervascularized and bifurcation tumors. According to some authors, ultrasonography with Doppler flowmetry can help surgeons in the early stages of diagnosis [20]. However, CT scans or MRI are more effective at determining the anatomical correlations and dimensions of the tumor [21]. The main diagnostic tool is arterial imaging such as magnetic resonance angiography, contrast angiography, or computed angiotomography, thereby confirming or not confirming the suspected diagnosis. Magnetic resonance angiography seems to be preferable nowadays [22].

Although CBTs have been observed in children, they are predominantly a disease of middle age, with the average age of onset at 45 years [19]. Except that there were no children in our cases, this is consistent with our findings, as the mean age of our cases was 45 years too. The mean age of Chinese patients with CBTs was 43 years [23]. A recent study was conducted by Kim et al. who studied 332 American patients, who were predominantly women (72%). The mean age at diagnosis was 51 years [24]. Khan et al. described 18 Pakistani patients of CBTs, of whom 11 women and 7 men, with a median age of 40 years, ranged from 23 to 60 years [25]. Generally, the incidence of CBTs tends to increase with advancing age. However, the exact reasons for the age-related increase in CBT incidence are not fully understood. It is believed that cumulative exposure to risk factors such as chronic hypoxia, smoking, and genetic predisposition may contribute to the development of CBTs over time.

This is not surprising as CBTs were more common in our cases of females, as this result was reported by several previous studies from different geographical regions in the world [2,19,24,25]. Our finding ranks second in terms of gender differences after the study that was conducted in Mexico, where the female:male ratio was 31.2:1 (96.9% were women) [26]. The reasons for the gender difference are not fully understood, but hormonal factors may play a significant role. Estrogen receptors have been found in CBTs, suggesting a potential influence of hormones on their development and growth [27,28]. Additionally, there may be differences in the clinical presentation and behavior of CBTs between both genders, as women are more likely to be symptomatic compared to men. The possible explanation of the higher ratios in both our study and the Mexican study is that both studies were conducted at altitudes of > 2000 meters and > 5000 meters from sea level, respectively. This explanation is supported by the high proportion of cases (77%) in our study who live at an altitude higher than 2000 meters above sea level. The impact of altitude on CBTs has inspired many endeavors to explain this phenomenon. The amount of atmospheric oxygen decreases above 2000 meters, resulting in chronic hypoxia. As a result, carotid type 1 cells become stressed as they compensate for lower oxygen levels. Over time, functioning glomic tissue and capillary blood vessels grow in size, causing hypertrophy. Eventually, neoplasia and hyperplasia of type 1 cells occur. At high altitudes, CBTs seem to be the most dramatic manifestation of this mechanism [9,29,30]. This concept is also backed by their benign clinical course and slow rate of growth, which could help to explain why CBTs are more common in people who live at high altitudes, as observed in our study population.

Although we did not observe any malignant cases, it is important to mention that the literature has estimated the incidence of malignancy in CBTs to be between 0 and 10% [31,32].

Due to its unique location close to carotid vessels and lower cranial nerves (X–XII), tumor enlargement results in progressive symptoms such as odynophagia, hoarseness of voice, dysphagia, or other cranial nerve deficits. The patients may provide a medical history that points to symptoms related to catecholamine production, such as palpitations, obstructive sleep apnea, blushing, and fluctuating hypertension. A slow-growing mass near the carotid bifurcation, with or without peripheral cervical neuropathy brought on by large tumors, is one of the main signs and symptoms of CBTs [33]. All our cases presented with a complaint of neck lump, whereas only one (2.1%) case complained of neck pain. In the study by Yonghui, et al. 20.43% of their cases complained of pain [32]. CBTs can grow to be quite large, and in some cases, they can cause disfigurement. In our study, disfigurement was an associated feature in 56.7% of cases. The degree of disfigurement that can occur with CBTs varies depending on the size and location of the tumor. CBTs are typically located at the carotid bifurcation, which is a critical anatomical region in the neck. As they grow, they can cause visible swelling or a mass in the neck, leading to a noticeable asymmetry. In some cases, the tumor may be palpable or visible as a lump. Smaller tumors may not cause any noticeable disfigurement, while larger tumors can cause a bulge in the neck, asymmetry of the face, and difficulty swallowing. CBTs can even cause the eyes to bulge in some cases. It is important to note that not all CBTs cause significant disfigurement, and the impact can vary from person to person. The management of CBTs, whether through observation, surgical resection, or other treatment modalities, is typically aimed at minimizing disfigurement

and preserving function while ensuring the best possible outcome for the patient.

In the event of a recurrence of CBTs, the treatment options are similar to those for the initial tumor. In our cohort of cases, the recurrence rate after complete excision was 4.2%. In the study by Nora et al., the recurrence rate was 6% [34]. Surgical excision is the preferred treatment, but it may be more challenging in the setting of recurrent tumors. A recent study found that male gender was associated with a higher risk of local recurrence of CBTs [35]. Larger tumor sizes and incomplete resection may also be associated with a higher risk of recurrence. It is important and necessary that more research be conducted to study and understand the associated risk factors for the recurrence of CBTs.

In our study, the incidence of bilateral CBTs was 10.5%. This is similar to what was reported in India (10%) [19]. Although malignancy was not observed in our cases, bilateral CBTs are usually malignant [19]. The cause of bilateral CBTs is not fully understood, but it is thought to be due to a genetic mutation. There is a strong relationship between bilateral CBTs and familial CBTs [36,37]. In fact, about one-third of people with bilateral CBTs have a family history of CBTs [38,39]. In our cohort of cases, familial cases were 2 (4.2%), which is slightly higher than a third of cases with bilateral CBTs. Given the possibility of vascular or cranial nerve damage, it is evident that in patients with bilateral CBTs, the procedures should not be performed simultaneously but should be spaced apart [2]. Patients who cannot undergo surgery, such as those who are clinically unstable, elderly, or who are definitely going to have a stroke, should only get conservative treatment. Despite the fact that most institutions do not advise it, certain authors have suggested using radiotherapy. Additionally, several previous studies have demonstrated that this therapeutic method is ineffective in treating these tumors [40-42].

The tumor's size affects not only how it behaves clinically but also how it must be treated. In 1971, Shamblin et al. innovated a classification system for CBTs based on the size of the tumor. Grade I (14.7% in our cases) is for the small tumors that are easily dissected away from the vessels. Paragangliomas of medium size that were closely associated with compressed carotid vessels but could be separated by careful and unintentional dissection were grade II in their classification (56.7% in our cases). Tumors that are large in size, envelop the carotid artery, and require resection and partial or complete vascular replacement was grade III (29.2% in our cases). Lone et al. found in their study that 23% of their cases were Shamblin Grade I, 66% were Shamblin Grade II, and 11% were Shamblin Grade III [19]. The carotid arteries and cranial nerves can be damaged, and excessive blood loss can occur during resection of a paraganglioma of the carotid body. The majority of researchers agree that the preferred treatment for the majority of carotid body paragangliomas (Shamblin I and II) is surgical excision with meticulous subadventitial dissection [4,5,13,26,43,44]. Resection of the external and/or internal carotid arteries is required for Shamblin III carotid body paragangliomas. The external carotid artery may occasionally need to be sacrificed, the internal and common carotid arteries anastomosed, or vascular reconstruction using grafts performed [2,10,22]. If the internal carotid is damaged or encased in a tumor during resection, immediate replacement or repair should be performed. Bleeding is another additional problem during the excision of the tumor that can occasionally be extremely severe. In cases presenting as Shamblin III with complete involvement of the internal carotid artery, some authors have reported using a stent placed within this artery [45]. Occurrences of technical complications in anastomoses between the common and internal carotid arteries after carotid body resection have also been documented in the literature. These cases evolved with several hematomas and, in some cases, strokes caused by deficits in cerebral irrigation [2,46]. Stroke did not occur in our cohort of cases.

Developments in modern surgical techniques have contributed to reducing the incidence of postoperative stroke in the resection of CBTs to less than 5%. However, the incidence of POCND is still startlingly high and ranges from 20% to 40% [19]. POCND in CBTs can occur due to the tumor's proximity to cranial nerves, particularly the glossopharyngeal nerve (cranial nerve IX), vagus nerve (cranial nerve X), and hypoglossal nerve (cranial nerve XII). The occurrence and severity of POCND can vary depending on several factors, such as tumor size, location, and the extent of surgical resection. In the literature, POCND was the most frequent major complication [47,48]. In our cases, the incidence of POCND was about 17% in 8 cases. This finding is very close to the study's finding by Sajid, et al. which was 19% [13]. Nevertheless, the incidence rate of POCND can be as high as 50% [13,34]. According to the largest meta-analysis study to date, which included more than 4,300 patients, the overall incidence rate of POCND was approximately 25% [49]. Introducing the craniocaudal dissection of the tumors by Bogt et al. reduced the risk of permanent POCND and carotid artery injury from 26% to 7% [50]. The lack of preoperative information to help determine an individual's risk of developing POCND inspired a group of 35 surgeons from 16 different institutions from different countries to study the relationship between tumor distance to the base of the skull and tumor size, with complications such as POCND. They found that the overall incidence rate of POCND was 24%. They also revealed that every 1 cm decrease in the

tumor distance to the base of the skull increased the risk of at least one POCND. The risk of hypoglossal or vagus nerve involvement increased 2-fold when CBT was 1 cm closer to the base of the skull. Additionally, they demonstrated that larger CBTs and a higher Shamblin grade were associated with higher rates of nerve injuries [35]. The findings of their study are supported by similar findings from several studies around the world [8,51,52]. However, the findings are not consistent, and the current evidence is inconclusive, as other studies reported that there was no association between the rate of POCND and a higher Shamblin grade [53,54]. Overall, the specific risk of POCND occurrence can vary depending on the type of surgery, the location of the procedure, and individual patient factors.

Finally, there was no mortality in our cases; however, it is important to mention that the mortality rate is less than 2% in the literature [1].

LIMITATIONS

Our study, like any other study, has limitations that must be acknowledged. The retrospective design of the study gave us no control over the quality of CBT's records. Although our study was multicenter, it may have a procedural bias due to the variance in surgeon skills as well as different levels of treatment, which may differ from one surgeon to another and from one hospital to another. Another limitation was the lack of independent adjudication of surgical resection outcomes since we relied on hospital charts for the recording of these events. However, these are commonly used and accepted methods used in the studies. Over a period of 4.5 years, we have observed a small number of cases; however, given the rare nature of these tumors, the sample of 48 patients can be regarded as considerable. Regardless of the previously described limitations, our descriptive study ultimately adds input for other prospective studies that can be conducted in a larger population of CBTs, which in turn may contribute to identifying the independent predictors of POCND in Yemeni patients.

CONCLUSION

Despite the inclusion of the three largest hospitals in Sana'a City and the relatively long study period, CBTs are still rare neoplasms that we encounter in our experience, and they should be kept in mind as a differential diagnosis for painless lateral neck lumps. The use of current diagnostic tools is crucial for correctly diagnosing CBTs. Therefore, a thorough preoperative evaluation of CBTs is especially important. In our experience, CBTs are predominantly tumors of middle age and more common in women, suggesting that we could be dealing with a different disease in Yemeni population, especially among those who dwell in the highlands. CBTs may have malignant behavior; however, all of our cases were benign. The experience of this casuistry shows that the surgical resection is relatively low risk and the incidence of POCND was small. These highly vascular tumors, although uncommon, should be operated by an experienced and skilled vascular surgeon to reduce complications. Moreover, postoperative complications can be minimized through careful dissections and retractions. More collaborative and extensive studies are required to support our findings.

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INFORMATION DISCLOSURE

Since the data collection was based on a retrospective chart review, informed consent was not necessary. We conducted our study in accordance with the Declaration of Helsinki by including basic principles of ensuring the study participant's privacy, risk, and benefit and by having it conducted by trained professionals. Furthermore, the purpose of the study was explained to the medical director and staff of the hospital, and permission to access patient charts was obtained from all heads of surgery departments as well as clinical service directors in all three hospitals. For the purpose of confidentiality, patients' names were not used at the time of data collection; instead, a specific identification number was given for each patient. All other personal and health information were de-identified and kept separately, so every effort was made to maintain confidentiality throughout the study period and afterwards. Besides, information obtained in the course of the study was only handled by the research team. Moreover, the confidentiality of the data was assured by pre-coding the questionnaires and securely storing the master coding sheets.

DATA AVAILABILITY STATEMENT

All original data are available in the vascular surgery unit, department of general surgery, TMGH, Sana'a City, Yemen, represented by the head of vascular surgery unit, Professor Nabeel Almadwahi as well as Dr. Mohammed Saleh Najran.

CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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Nil.

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