
CAROTID BODY TUMORS IN INHABITANTS OF ALTITUDES HIGHER THAN 2000 METERS ABOVE SEA LEVEL

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Abstract: *Background.* Carotid body tumors (CBTs) are rare. Diagnosis is usually delayed until the tumors reach a critical volume and a mass appears in the neck, which is often asymptomatic.

Methods. We reviewed retrospectively the cases with CBT diagnosed from 1965 to 1995 in the Hospital de Oncología in México City with inhabitants at an altitude higher than 2200 m above sea level to see whether these tumors have the same characteristics as those of inhabitants of countries of lower altitudes. We reviewed the clinical features, diagnostic procedures, therapy, results, and complications.

Results. There were 120 CBT cases, which represent 79% of the parapharyngeal space tumors diagnosed at our hospital; 116 (96%) were benign and 4 (3.3%) were malignant. Women predominated (89%), and the female-male ratio was 8.3:1. Five patients had multiple paragangliomas, and one had a family history of CBT. Eighty patients (66%) underwent surgery. This was done by cervical approach in 78 cases (97%), and 2 (2.5%) required additional mandibulotomy. There were three deaths due to brain ischemia after carotid ligation. Forty-one patients were followed without treatment, due to advanced age, concomitant diseases, or great volume of the tumor. Median follow-up of these patients was 47 months, during which time no patient reported additional symptoms, accelerated enlargement of the tumor, or metastasis. With a median follow-up of 54 months, only one patient devel-

oped local recurrence and three patients developed distant metastasis.

Conclusions. We conclude that cases of CBT in our high-altitude population differ significantly from those cases in inhabitants of cities in the U.S. or Europe of less than 1500 m above sea level. Those of high altitudes have an evident female predominance (8.3:1), low rate of bilaterality (5%), and a family history of 1% versus a discrete female predominance (2:1), bilaterality from 10% to 20%, and family history from 7% to 25% in low altitudes. When adequate criteria are used to determine surgical resectability, a complete resection is achieved in 85% of cases, with low or null mortality and high local control. © 1998 John Wiley & Sons, Inc. *Head Neck* 20: 374–378, 1998.

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Carotid body tumors (CBTs) are slow-growing tumors, and their diagnosis is usually not possible until they have reached a considerable volume and a mass appears in the neck. The complexity of anatomic structures that are present in the region presents challenges to the surgeon. Some authors^{1–3} classify all CBTs as parapharyngeal space tumors (PSTs), whereas others^{4–7} postulate that only those CBTs extended above the posterior belly of the digastric muscle can be considered PST.

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Carotid body tumors most frequently develop in inhabitants of altitudes higher than 2000 m above sea level. The incidence increases in direct relation to altitude (1×1000 at sea level, 9×1000 between 2000 and 3000 m, and 12×1000 between 3000 and 4500 m).⁸⁻¹⁰ It has already been corroborated that at altitudes higher than 2000 m, the atmospheric oxygen pressure is diminished and produces a chronic hypoxia, which induces a hyperplasia of the carotid body, a possible reason that inhabitants of cities such as Quito, Mexico City, and the Peruvian and Bolivian Andes have a higher risk of developing CBT.¹¹⁻¹⁴

Different studies from Europe and the U.S. report that CBTs represent between 7% and 28% of parapharyngeal space tumors (PSTs).^{1,5,15,16} We analyzed our experience in the diagnosis and treatment of CBT developing in inhabitants of the Valley of Mexico at altitudes higher than 2000 m above sea level, to determine whether CBTs in our patients have the same characteristics as those of studies of inhabitants of Europe or the U.S.

MATERIALS AND METHODS

During the period between January 1965 and October 1995, 120 CBTs were diagnosed at the Hospital de Oncología del Centro Médico Nacional of the Mexican Institute of Social Security in Mexico City. The clinical features, diagnostic procedures, the therapy and its results, complications of treatment, and the final status of the patients were reviewed.

RESULTS

One hundred twenty CBTs were diagnosed and determined to have a female predominance (89%), with a female-male ratio of 8.3:1. Mean age was 49 years (range, 21–82 years). There were 56% on the left side and 44% on the right side. Six cases had multiple paragangliomas of the head and neck (5%). One hundred sixteen CBTs were benign (95%) and 4 were malignant (3.3%). Tumor size ranged from 2 to 12 cm (mean, 5.4 cm). The most common symptom was the presence of the tumor. One patient developed transient brain ischemia, and three had paralysis of the X nerve.

In 20 cases, diagnosis was made exclusively by clinical features, after which the patients underwent surgery and diagnosis was confirmed. The most common diagnostic procedure was arteriography (radiologic in 51 cases [67%] and scintigraphic in 20 cases [25%]). Computed tomography (CT) was done preoperatively in 17 cases (21%)

and magnetic resonance imaging (MRI) in one patient. Eighty patients (67%) underwent surgery, 68 with a complete resection (85%), 2 with complete resection plus postoperative radiotherapy (2.5%), 3 with partial resection (4%), and 7 with partial resection plus external radiotherapy (9%). Radiotherapy was given with Cobalt or electrons with a dose of 4500–5640 cGy over 5–6 weeks. Indication of radiotherapy was histopathologic evidence of malignancy in three patients with neck node metastases and large, irresectable benign tumors in 6 patients aged 32, 33, 38, 44, 51, and 59 years. Surgery was done by cervical approach in 78 cases (97%), and 2 patients required additional mandibulotomy (2.5%).

Twenty-six patients developed the following postoperative complications: hematoma in 7 (9%), seroma in 1, upper airway obstruction in 3 (tracheostomy), and 3 deaths due to ischemia after carotid ligation. As a result of surgery, 10 patients (12%) had lesions of the X and XII cranial nerves, 2 (2.5%) of the IX cranial nerve, and 4 paresis of the mandibular branch of the facial nerve. One patient (1%) developed local recurrence and 3 distant metastasis (4%).

Forty-one patients (27%) have been followed without treatment after diagnosis was corroborated by CT, ultrasound, or scintigraphy. The mean size of these tumors was 5.3 cm, and the mean age of the patients was 60 years. Median follow-up of the 41 patients without treatment was 47 months, during which time no patient reported additional symptoms, accelerated enlargement of the tumor, or metastasis.

DISCUSSION

Carotid body tumors are rare and mostly benign tumors. These tumors reach a considerable volume due to the low frequency of symptoms. That is why in the patients in this study, the mean time of evolution was 43 months. This is partly due to the low socio-cultural level of our population. In this series, the mean tumor size was 5.4 cm. Carotid body tumors comprise 7% to 28% of the PSTs of the series reported in the U.S. or Europe, whereas in Mexico City, CBTs represent 79%. The rate of malignancy is low (3.3%), similar to that of other series.

There is an evident predominance of females in this study, with female-male ratio of 8.3:1. We cannot explain this difference. We think that it may be due to the greater pulmonary capacity and the higher affinity to sports in men, thus allowing them to avoid chronic hypoxia. Also,

women have a periodic loss of erythrocytes during their monthly menstruation. Carrau² reports a ratio of 1:1 in 23 cases in the U.S. Parry,¹⁷ in 222 cases of CBT collected from different studies, reported a female predominance of 2:1, and a similar ratio was found by Dickinson in England.¹⁸ Nevertheless, in inhabitants in the Peruvian Andes at more than 2000 m of altitude, the female predominance was 6.33:1,¹⁹ and there is a study of patients in the Valley of Mexico where the female predominance reached a ratio of 19:1.²⁰ We conclude that women inhabitants of altitudes more than 2000 m above sea level have a greater risk of developing CBT than do men and that this predominance diminishes in direct relationship to the altitude (Table 1).

Multicentricity of CBT in this study was 5%, whereas in studies from the U.S. and Europe, it varied from 10% to 20%.²¹⁻²³ In our cases, we found a family history of CBT in 1%, whereas in the U.S., it has been reported to be from 7% to 10%, and in Italy, 25%.^{2,4,24,25} In patients with a family history, the presence of multiple tumors has been reported as high as 42%. The suspected gene is transmitted with an autosomal-dominant mode of inheritance, with incomplete penetration and less frequent phenotypic expression that appears to exhibit a genomic imprinting originating in the paternal gene. It has been postulated that the affected gene is located in the long arm of chromosome 11. By cytogenetic analysis, there have also been abnormalities found in chromosomes 5 and 7.^{26,27}

In nine CBTs of our patients, other synchronous or metachronous tumors were diagnosed. It is important to note that two cases were another type of neuroendocrine tumor (pulmonary carcinoids). Apparently, this association has not been previously reported, and there is only one report of pulmonary carcinoid associated with a pheochromocytoma in a patient whose sister had a bilateral CBT, suggesting a genetic syndrome.²⁸

Cervical cancer was associated in three cases. This reflects the fact that this tumor has the high-

est incidence in our country, and that CBT develops predominantly in women within the ages at which they are at high risk for cervical cancer. The association of CBT and thyroid carcinoma was reported by Albores-Saavedra²⁹ and appears to be incidental.

Clinical diagnosis of a pulsatile tumor of the subdiaphragic region greater than 5 cm is relatively simple in our hospital; nevertheless, when the tumor does not pulse, it is necessary to carry out complementary procedures. In a suspected CBT, we determine whether the patient is a candidate for surgical procedure based on the patient's age, size of the tumor, and concomitant diseases, according to the criteria established by Javid³⁰ and Conley.³¹ If the patient is not able to have surgery, the diagnosis is confirmed by a dynamic scintiangiography. This is a non-invasive procedure with minimal risk to the patient. This method, described in 1972 by Serafini³² and corroborated by Peters³³ in 1979, was used in 26% of our patients. Another alternative is ultrasound, also a non-invasive procedure with high resolution and sensitivity.

Only cases with a clinical suspicion of CBT and candidates to surgical resection are submitted to a carotid angiography to confirm the diagnosis. The tumor is considered resectable if the internal carotid artery has at least 2 cm free of tumor before the cranial base. This procedure also allows us to see the brain circulation. To establish the relationship of the tumor with other structures, it is necessary to do a CT scan with axial and coronal views. We have minimal experience with CT and/or MRI, because only in 18 cases were these procedures done preoperatively. Magnetic resonance is a procedure that provides images of the same areas provided by the CT scan as well as the opportunity to assess the vascular circulation of the neck and brain with minimum risk to the patient, allowing selection of the surgical approach to achieve a complete resection with the least morbidity. In this study, we corroborated the proposal that 97% of the tumors submitted to surgery could be resected by a cervical-parotid approach, and only 2.5% required additional osteotomy. We achieved a complete resection in 85% of the cases, with a mortality rate of 2.7%, which has decreased to 0% during the last decade. Replacement of internal carotid artery with saphenous vein graft was considered in case of resectable CBT group III of Shamblin's classification³⁴ or

Table 1. Comparison between carotid body tumors (CBTs) of high and low altitudes.

	CBTs in Mexico	CBTs in U.S./Europe
Malignant	3.3%	4% to 15%
Female predominance	8.3:1	2:1
Multicentricity	5%	10% to 20%
Family history	1%	7% to 25%

in case of vessel injury during resection of the tumor.

Although mortality has been avoided in our patients during the last decade, there is still a 20% occurrence of cranial nerve postoperative paralysis (VII, IX, X, XI, and XII nerves), a rate similar to that (25%) reported by others.^{20,34,35} Local control is adequate when it is possible to achieve a complete resection, even in malignant CBT, when surgery is followed by external radiotherapy, with recurrence of 5.5%.³⁶

CONCLUSIONS

Carotid body tumors in inhabitants of higher altitudes differ significantly from those developed in inhabitants of cities in the U.S. or Europe at less than 1500 m above sea level. Those of high altitudes have an evident female predominance (8.3:1), low rate of bilaterality (5%), and a family history of 1% versus a discrete female predominance (2:1), bilaterality from 10% to 20%, and family history from 7% to 25% in low altitudes.

Carotid body tumors have a low malignancy rate (5%) and could be excised with low or nil mortality risk if the surgical decision is adequate. In our department, surgery is indicated in patients younger than 60 years of age, with acceptable anesthetic risk, and with a margin of 2 cm of internal carotid artery free of tumor from the cranial base. Otherwise, due to the slow growth and low malignancy rates of this tumor and, on the other hand, to the high rate of postoperative morbidity, we suggest a follow-up on patients and the use of radiotherapy in case of accelerated enlargement of the tumor, appearance of new symptoms, or evidence of malignancy. None of the 41 patients followed without treatment required radiotherapy in this study; we think this supports adequately our treatment policy. We selected 60 years of age as the borderline, because life expectancy of women in Mexico is 73.4 years; thus, the possibility that a slow-growth, benign tumor diagnosed at 60 years could produce symptoms that indicate surgery is very low.

A cervical-parotid approach is adequate in 97% of CBTs; however, the surgeon must be prepared to do a mandibulotomy, if required. In case of a complete resection, local control is adequate, and distant metastases develop in only 4%.

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