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Radioguided Surgical Resection of Carotid Body Tumors

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Abstract

Aim: We present our experience about surgical resection of carotid body tumor (CBT) and to define the role of colour coded ultrasound (CCU) and of somatostatin receptor scintigraphy (SRS) with Indium-111-DTPA-pentreotide (Octreoscan®) using both planar and single photon emission tomography (SPECT) technique.
Methods: Twenty-three patients suffering from 27 CBTs were treated from 1997 to 2014. Preoperative investigations included CCU and SRS-SPECT. All tumours were grouped according to Shamblin's classification. Intraoperative radiocaptation by Octreoscan was also carried out in all cases to evaluate the radicality of surgery.
Results: Preoperatively CCU showed CBTs with sensitivity 100%. Radioisotope imaging identified the CBTs as carotid body tumors in 25 cases while no radio isotopic uptake was detected in 2 cervical vagal schwannoma. Combined data from CCU and SPECT allowed determining tumour size in order to select 12 larger tumours.
Intraoperative Octreoscan demonstrated microscopic tumour leftovers promptly removed in 2 cases and an unrespectable remnant at the base of skull in another case.
During follow-up (6 months-10 years, mean 3.9 years) CCU and radioisotope scans showed no recurrence in 25 cases, a slightly enlargement of that intracranial residual as detected during surgery in 1 patients and a little recurrence in another one case.
Conclusion: CCU may allow an early and noninvasive detection of CBTs and hence safer operations. The combined use of CCU and SPECT provide useful data to identify that tumour and to evaluate their extent and carotid arteries infiltration. Radioisotope imaging is a sensitive modality to detect metastases and lymph node involvement that are markers of CBT malignancy. Mid and long terms results in terms of recurrence and carotid repairs patency seems very encouraging with this approach. After surgery CCU and SPECT seem to be accurate modalities for surveillance for an early detection of CBTs recurrence.

Keywords: Carotid body tumours; Colour-coded ultrasound; SRS-SPECT

Introduction

Carotid body tumors (CBTs) represent more than half of neck paragangliomas but rarely seen clinically so the corresponding diagnosis and management remain difficult.

As regards the diagnostic approach, proper diagnosis of CBT can be made by clinical presentation and several imaging modalities. Notwithstanding, since it contains somatostatin receptor sites, the somatostatin receptor scintigraphy (SRS) with Indium-111-DTPA-pentreotide (Octreoscan®) with single photon emission tomography (SPECT) technique may be used to identify either the primary tumour or metastases in distant locations and recurrence which is reported in about 6% of cases [1] after surgery.

Although CBTs are malignant in only 5-15% of cases [2-15], their early excision is always advisable since they can encase the vessels and the nerves, compress and dislocate pharynx and even erode the base of the skull. This makes these tumors a surgical challenge according to Shamblin's clinicopathologic analysis [3]. In Shamblin's, 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.

The incidence rate of surgical complications may be higher in Shamblin II and III. In these cases neural and vascular injures are possible during the surgical exposure of the mass. Approximately 20% of patients develop a permanent cranial nerve dysfunction, but this varies depending on the size of the tumor [4]. Stroke is another potential complication of CBT resection though occurs in less than 5% of patients [5].

Since the larger tumors have adhesions with neighboring structures and are often highly vascularized, many Authors suggest a preoperative endovascular embolization in order to reduce the tumor mass e the bleeding during surgery [6]. However, also preoperative embolization of tumor may have an inherent risk of cerebral ischemia.

In this report, we assess difficulties and outcomes in the surgical management of CBT, patients treated with and without preoperative embolization with an emphasis on perioperative use of SRS-SPECT for an exhaustive diagnosis and follow-up.

Materials and methods

Twenty-three patients were operated upon for 27 carotid body tumours (bilateral in 4 cases) from 1997 to September 2014. All the patients were submitted to perioperative somatostatin receptor scintigraphy; before surgery and during follow-up the tracer used was indium-111-DTPA-pentetreotide (Octreoscan®) and the technique employed in that investigation was both planar and single photon emission tomography (SPECT); during surgery a gamma-probe was

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use. Average age was 50 years (range, 23-75 years) and 40% of patients were males.

Imaging modalities performed included CCU (Ultramark 9 ATL Philips in the first part of experience and then Toshiba Aplio XP) which was the first diagnostic approach in all patients (Figure 1A and 1B). Typical ultrasound features included the presence of a solid hypoechoic vascular mass that has low–resistance flow pattern on Doppler frequency analysis, hyper vascularization was shown by colour and power Doppler imaging; CCU also showed wall carotid involvement if present.

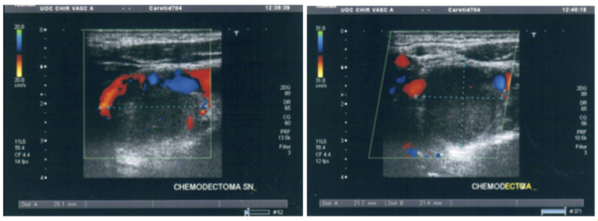

Figure1A-1B: Colour Coded Ultrasound that shows a big CBT of carotid bifurcation.

CTA and MRA were associated to ultrasounds to define tumor feeding vessels, their relationship with adjacent structures and their superior level in the neck for a better planning of the best surgical approach. Total body CTA scan or MR were not performed to minimize the risks related to high dose of contrast media and radiation.

Digital subtraction angiography (DSA) was carried out in 7 cases in order to perform an endovascular preoperative embolization to reduce tumour vascularity and size; embolization was always followed by surgery within 1 or 2 days. During DSA, contemporary occlusion of internal carotid artery (Matas test) was performed to determine the patient's tolerance to carotid cross-clamping.

Preoperative total body SRS- SPECT was carried out by intravenous injection of approximation 150 MBq 111In-pentreotide (StarCam 2000 at first and then StarCam 4000i). Nuclear scans were performed from head, neck, chest, abdomen and pelvis at 4 and 24 hours after injection with the medium energy collimators and both 171 keV and 245 keV with a 15% window. The protocol included a 40-minute acquisition on 128 × 256 matrix. SPECT images were obtained by 30-minute acquisition on 64 × 64 matrix by using the same collimators (Figure 2). All perioperative scans were evaluated by the same nuclear medicine physician. If abnormal radioactivity would have been detected in other regions of the body than neck, nuclear scans would have been repeated for the same areas during the follow-up.

When the mass has extended above the angle of the jaw a multidisciplinary treatment involving vascular and maxillofacial teams was planned. All tumours were grouped according to Shamblin's classification in order to assess the difficulty and morbidity of surgical resection. Intraoperative radio-localization was carried out on all lesions by a hand-held gamma-detecting probe connected to a special counting unit (Octreoscan-Navigator-USSC) within 24 hours radiopharmaceutical administration. Radioactivity measurements were undertaken on the tumour in vivo compared with the background on the tumour bed to detect remnants or lymph nodes invasion.

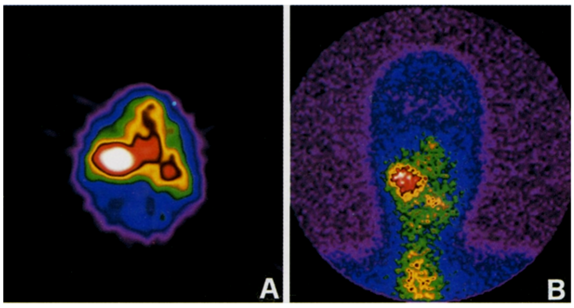

Figure 2: Markedly increased focal tracer uptake in the right cervical region in both planar (A) and SPECT (B) scans due to a massive chemodectomas at the right carotid bifurcation.

The carotid arteries were exposed through a longitudinal neck incision, hypoglossal and vagus nerves were always identified and the common, internal and external carotid arteries were dissected. Resection was always attempted from the inferior margin of the tumour at the carotid bifurcation and extended between the internal and external carotid arteries (Figures 3A, 3B and 4).

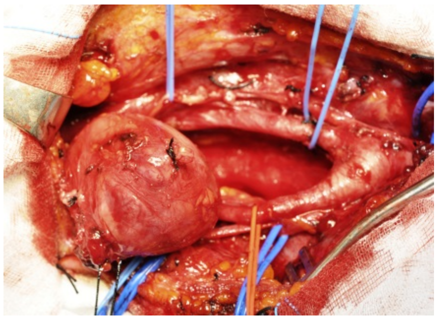

Figure 3A: Resection of a class III CBT

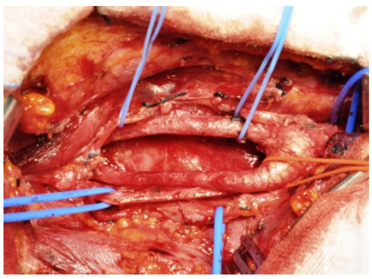

Figure 3B: Carotid bifurcation anatomy after complete tumor resection.

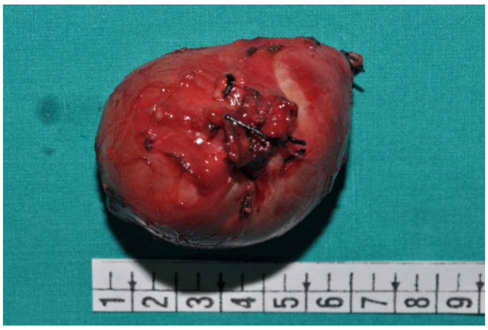

Figure 4: Shamblin III resected CBT

Preoperative CCU and radiosotopic scans suggested the need of a treatment involving vascular and maxillofacial teams in the 8 patients and intraoperative findings confirmed the need of that multidisciplinary approach.

9 CBT were classified as Shamblin I, 11 Shamblin II and 7 Shamblin III. None of the 9 Shamblin I tumours required an internal carotid artery resection although in 1 case external carotid artery was interrupted; they all were fairly easily removed without neurological complications. In 9 cases a vascular reconstruction of carotid axis was needed (Figure 5). Removal of the 11 CBTs in Shamblin II required: 4 external carotid artery resection, 1 carotid bifurcation PTFE patch angioplasty and 4 internal carotid artery replacements with an ASV graft. At surgery all tumours of Shamblin class III were extended above the angle of the mandible and required the digastric and pre-stilomastoid muscle resection plus vertical osteotomy of the mandibular ramus to get a wider space near the skull base. A forewarned maxillo-facial surgical team always resected and later reconstructed the mandibular bone in order to treat those CBTs.

The CBTs ablation with carotid arteries resection and internal carotid artery replacement (2 PTFE-TW and 2 ASV grafts) was carried out in 4 of these cases combined to external carotid artery resection.

The 2 patients suffering from vagus nerve neurinoma had the nerve resection; in another case vagus, hypoglossal and superior laryngeal nerves interruption was mandatory to allow complete removal of adhering tumours. The pathologic examination of the tumour and sampling of jugular lymph nodes were carried out in all cases. Follow-up included CCU examination and radioisotopic scans at, 6 and 12 months postoperatively and every 12 months after the first year to show local recurrence and to control arterial reconstruction. When any abnormal tracers of CBTs were identified, CT or MR scans from those areas were obtained to confirm.

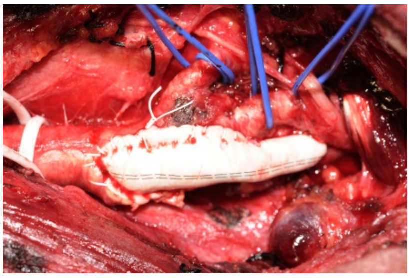

Figure 5: PTFE carotid reconstruction after CBT and internal carotid resection

Results

The CCU failed in a sharp evaluation of tumour size and its superior extension in 4 cases (4/27, 14.8%), when compared with CT and MR techniques data and with Octreoscan SPECT imaging.

Preoperatively the In-111 pentetreotide uptake by nuclear scans was high in all tumourdetected by ultrasounds but conversely in two cases the results were low and in both the intraoperative finding was surprisingly a neurinoma originating from vagus nerve as confirmed by histological data. It must be underline that ultrasound was unable to differentiate this pathology from carotid body tumors. Compared with SRS-SPECT, CCU showed a good diagnostic accuracy with a sensitivity and a specificity of 100% and 93.7% respectively. Preoperatively ultrasounds data and radioisotopic scan findings were combined to group CBTs based on their estimated size and their relationship with the adjacent vessels (Table 1).

CBTs embolization was carried out for the largest 3 tumors of group II and for 4 CBTs of group III (43.7%) and led to shrinkage of tumour and reduction of its vascularity in 6 out of 7 cases (85.7%).

The closure of the majority arteries supplies to the CBT is probably at the basis of the shrinkage of the tumor itself and this is beneficial during the operation because it allows a reduction of blood loss and a more suitable surgery. Nevertheless in 2 young patients a transient neurological ischemic complications were detected during the embolization: one dysarthria and one brachial monoparesis were observed and this is a major concern because this complication have a 35% incidence rate.

Group	Number of patients	Mean size on CCU	Mean size on radioisotopic scans	of CBTs on the ground of size measurements and relationship with adjacent vessels on CCU	of CBTs on the ground of size measurements and relationship with adjacent vessels on radioisotopic scans
I	9	16 mm	18mm	well defined	not adhering
II	11	28 mm	31 mm	partially defined	partially adhering
III	7	43mm	47 mm	undefined	strongly adhering

Table 1: Preoperative classification of CBTs on ground of size measurements and relationship with adjacent vessels on CCU and radioisotopic scans (111In-pentetreotide scintigraphy–SPECT)

At surgery 9 CBTs were classified on size as Shamblin class 1 and they all could be easily dissected from carotid arteries, 11 were in Shamblin class 2 and partially encircled carotid bifurcation; the remaining 7 tumours were in class 3 since they were strongly adherent to carotid vessels and surgical resection in a periadventitial plane was not possible.

Table 2 summarizes intraoperative measures of all tumors; they ranged from1.4 to 2.7 cm for CBTs in class I (mean size of 2.0 cm), tumoursin class II were from 1.8 to 3.6 cm with a mean size 2.7 cm and those in class IIIwere from 4.5 to 5.1 cm with a mean size 5 cm.

Shamblin's class	**n°**	**ranging size**	**mean size**
I	9	1.4-2.7 cm	2.0 cm
II	11	1.8-3.6 cm	2.9 cm
III	7	4.5-5.1 cm	5.0 cm

Table 2: Intraoperative Shamblin's classification and size of CBTs

Preoperative CCDI tumor measurements agree with intraoperative Shamblin's classification. Preoperative CCU imaging and radiosotopic scans suggested the need of a multidisciplinary approach treatment involving vascular and maxillofacial teams in 4 patients; the dimension of the CBT and its extension towards the skull basis and the presence of a high carotid bifurcation suggested this surgical strategy that was confirmed to be useful by intraoperative findings.

During surgery gamma probe showed no radiotracer uptake from the neurinoma and identified all CBTs which had more than twofold radioisotopic uptake as compared to background (mean tumor/ background ratio: 3.02). After removal, intraoperative Octreoscan showed small residual of tumour tissue with partial involvement of internal carotid artery that required a further resection followed by carotid bifurcation PTFE angioplasty in 1 case (6.6%). In another case radiotracer uptake by an unresectable remnant was recorded at base skull that was not detected by other subsequent imaging methods (6.6%) performed during follow-up. Radioactivity measurements on lymph nodes never revealed tumour invasion. The postoperative histologic data confirmed the diagnosis of CBT in 15 cases and showed no metastasis both in jugular lymph nodes. Lymph nodes sampling showed no residual disease. Perioperative mortality was nil and no intraoperative cerebral ischemia occurred. Deviation of tongue was seen after surgery in 6 cases (6/2, 26%) but disappeared in a few days. Nine patients (9/2, 39.1%) sustained permanent cranial nerve injuries causingdysphonia in 6 case that was associated with dysphagia in 2 and dysphagia andtotal tongue deviation in another case. Postoperative course was uneventful in all cases.

During follow-up (from 6 months to 10 years; median 3.9 years) clinical, CCU and Octreoscan SPECT of carotid arteries were performed at 6 and 12 months after surgery and yearly thereafter. Those controls showed no signs of recurrence in all cases but , in which a second operation was performed to remove a little mass adjacent the common carotid artery; in all the 9 patients operated upon by carotid repair, the patency of carotid axis was detected without significant stenosis. Nuclear scan confirmed in another case, the presence of the intracranial remnant as detected intraoperatively which slightly enlarged without clinical evidence within the following 8 years making further CT or MR controls unnecessary.

Discussion

Although malignant forms CBT seems to be only around 5%, the early surgical excision at presentation is mandatory because of their locally invasive nature and the uncertainty about their natural history. They may grow unpredictably and destroy several nerves (glossopharyngeal, vagus, hypoglossal and recurrent) [7] and they can also invade the adjacent carotid arteries making surgical management problematic.

Lack of clinical diagnosis has been reported in up 30% of patients since those neoplasia can be confused with enlarged lymph nodes or branchial cysts or salivary glands tumors. The advent of new imaging modalities allows their detection at an earlier stage even before they become clinically evident. CT or MR angiography is reliable diagnostic techniques to evaluate CBTs and their potential multicentricity or recurrence. The main problem regarding CT is the usage of iodinated contrast media related to potential side effects (eg. acute renal failure) and radiation burden with their inherent risks. MR angiography cannot be performed when patient has pacemaker or old steel prosthesis.

In our experience CCU proved to be useful and very sensitive for detection of CBTs before the onset of symptoms; it also allows the differential diagnosis with other neck mass avoiding ill-advised biopsy. Our experience is consistent with those of several series that indicate Duplex scanning as a non-invasive method for screening evaluation of even small tumours [9-10]. Early diagnosis is a crucial point: available reports suggest cranial nerves and vessels injuries are more likely related to locally advanced disease rather than surgical trauma.

Ultrasounds study alone may fail in the evaluation of the real size and the relationship with adjacent structures of larger tumours when compared with CT and intraoperative measurements 15. In our experience the only CCU can establish the diagnosis and measures well enough to proceed with surgery for tumours less than 2 cm, while for larger masses an adjunctive instrumental techniques should are needed.

Both CCU and radiological imaging do not provide any information for differential diagnosis between chemodectomas and vagus nerve neurinoma that was obtained by 111In-pentetreotide scintigraphy–SPECT scans. Moreover combination of CCB evaluation and 111In-pentetreotide scintigraphy–SPECT scans may help not only to confirm diagnosis of CBTs, but also to determine the involvement of adjacent structures and the presence of somatostatin receptors [16,17].

Earlier histologic studies indicated an high incidence of CBT malignancy based on their mitotic activity, capsular invasion and pleomorphism, but the reports by Martin [18,19] and Westerband [20] suggest that CBT's metastasis to regional lymph nodes, brain, bone, liver, lungs are the actual hallmark of malignancy; they occur from 5 to 10% and can be reliably detected by radioisotope scans.

In our series SPECT scan allows to exclude potential multicentricity and metastasis of CBTs in an accurate fashion [18,19] and it is less invasive than total body CT angiography scanning, avoiding radiation exposure and contrast media toxicity [20].

In our study we appreciate a good correlation between preoperative classification based on CCU imaging and radioisotopic measurement and Shamblin classification determined intraoperatively.

The data from preoperative studies made it possible to plan a preoperative multidisciplinary treatment for Shamblin II and III CBTs with the greatest difficulties in surgical dissection, even in benign forms. CCU and nuclear evaluation could also provide useful information for an eventual selective preoperative embolization. According with other authors [21-24] we believe that the apparent benefits of embolization should be weighed against the risk of stroke. Because of the possible neurological complications related to the embolization procedure, we can consider to avoid this procedure in CBTs smaller than 3 cm.

However an accurate pre-operative evaluation by ultrasounds and nuclear methods can be useful for selection of greater and more invasive tumours that should be treated by embolization. A further advantage of the early detection and resection of smaller lesion is the possibility of lower need of preoperative embolization and its attendant risks [2,25]. Preoperative CBT embolization is advocated to facilitate resection of large tumors and lessen the cranial nerve injury rate but these benefits were offset by a not negligible incidence of TIAs in our series.

In our experience, large CBTs can be resected safely with or without preoperative embolization. Preoperative embolization does not decrease rates of cranial nerve injury, although most are temporary. However, we think it is necessary further multicentric studies and the analysis of wide case studies to confirm this possible therapeutic choice.

Concerning the surgical resection, a reliable radioisotopic evaluation of the distal extension of tumours above the angle of the mandible, suggest the need of a combined surgical team of maxillofacial and vascular surgery for the distal internal carotid exposure as high as possible at the skull base by mandibular osteotomy, in order to reduce the incidence rate of peripheral neurological complications.

In case of use of a general anesthesia in the more difficult cases (Shamblin III) in which a carotid clamping and resection is predictable, a transcranial doppler monitoring is advised.

The vascular reconstruction of the internal carotid artery is mandatory in those cases in which the CBT involve the arterial wall. Good results are obtained with autologous vein graft but, due to the reduction of operative time and to an adequate size, in many cases PTFE graft seems to be a valid alternative. The involvement of the external carotid artery may require, in some cases, its binding, which is generally well tolerated.

The risk of tumour recurrence is related tominimalresidue which can be missed even by an accurate surgical resection [26]. Intraoperative gamma probe radioactivity measurement in vivo on the tumour bed allows to detect invisible remnants, which may be removed by a more radical radioguided dissection. It can also show inoperable residuals, that need a careful surveillance during follow-up [27].

During follow-up ultrasounds and SRS-SPECT may be used to evaluate carotid reconstruction and to detect recurrence of tumour in the order to reduce the need of CT or MR controls.Nuclear controls have also showed to be a reliable modality to follow the growing of unresectable residuals not detectable by CCU.

Conclusions

In management of CBT a multidisciplinary approach should be used involving vascular surgery, otolaryngology, maxillofacially and radiology to treat these patients. The early detection, and accurate measurements of larger lesions appears to provide an additional advantage by decreasing the need for preoperative embolization and its attendant risks. Large CBTs can be resected safely, with or without preoperative embolization. Preoperative embolization raises the risk of stroke and must be restricted to selected cases since, in our hands, it does not decrease the incidence of cranial nerve injury. An accurate technical surgical approach and an early diagnosis can minimize the risk of cranial nerves and vessels injures.

Radioactivity measurements performed during surgery is helpful to detect those microscopic leftovers of tumor tissue, which could be missed by surgeon without the help of Octreoscan and that would led to its recurrence.

Advances in diagnostic modalities based on ultrasounds and radioisotope imaging have increased earlier discovery of those tumours. The nuclear images obtained by Octreoscan SPECT seems to be very accurate to determine the nature of the neck mass and to localize it; SPECT scan also detect areas of potential postoperative early recurrence.

During follow-up, CCU combined to radioisotope imaging is sensitive and less invasive methods to detect potential recurrence and to monitor growth progression of unresectable remnants of "these curious little tumors" as defined by Lund FB [28].

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