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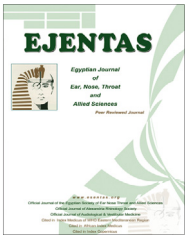

REVIEW

Paraganglioma of the carotid body: Report of 26 patients and review of the literature

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KEYWORDS

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Abstract *Introduction:* Paragangliomas are extra-adrenal tumors originating from the neuroectoderm, occurring from the skull base to the pelvic floor. In the head and neck region, they are found at the jugular bulb, the vagal and tympanic nerves and the aortic glomus.

Objectives: The aim of the present study was to review clinical profile, treatment outcomes and long-term follow-up in patients with paragangliomas of the carotid body.

Materials and methods: It is about a retrospective study of 26 patients (28 paragangliomas) followed and treated in Ear, Nose and Throat Department of La Rabta Hospital. Pre-, intra- and postoperative findings were analyzed.

Results: The present study included 6 men and 20 women. Bilateral involvement of the carotid glomus was noted in 2 cases and tympano-jugular location was associated in 2 other cases. Ultrasound of the neck, computed tomography (CT) and magnetic resonance (MR) tomography were performed in 13, 17 and 10 cases, respectively. 2 patients have had preoperative embolization and 22 patients, in total, were operated. External radiation was an exclusive therapeutic option in 2 patients and adjuvant to incomplete surgery in one patient. Only one case of malignant paraganglioma was noted that evolution was, in fact, rapidly fatal.

Contents

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1. Introduction

Carotid paragangliomas are tumors developed from chromaffin cells of the extra-adrenal tissue. Clinical presentation of these tumors may be misleading and the treatment, often, arduous. Hence, specific pretreatment assessment is the only guarantee of adequate management. The development of diagnostic and interventional radiology techniques has, obviously, improved the prognosis of these tumors.

2. Material and methods

Over a 27-year period (1981–2007), 26 patients were treated for 28 carotid paragangliomas in the Ear, Nose and Throat Department of La Rabta Hospital. Their clinical and operative data were collected and analyzed retrospectively. Preoperative work-up in patients with carotid paraganglioma consisted of careful family history, clinical examination, ultrasound of the neck, computed tomography (CT) or magnetic resonance (MR) tomography. The Shamblin classification was used to grade the tumor size. Treatment modality, including the necessity of preoperative interventional embolization, was assessed by the operating surgeons and vascular radiologist. Postoperative follow-up consisted of clinical evaluation 1 month after surgery, ultrasound 1 year after and CT or magnetic resonance imaging (MRI) if new pathological findings occurred in ultrasound.

3. Results

Our study includes 26 patients. Mean age was 38 years, ranging from 18 to 75 years. There was a female predominance with 20 women and 6 men (sex ratio = 0.3). Carotid paragangliomas were bilateral in 2 cases (10%) and associated with tympano-jugular location in 2 cases.

A family history of paraganglioma was found in 3 cases who were a patient and his 2 nieces.

- This patient and one of his nieces had a double localization. Bilateral carotid localization in one case and a carotid paraganglioma associated with contralateral jugular location in the other case.
- The last patient had a carotid body paraganglioma on a single side.

Consultation average delay was 3 years (6 months–15 years). The chief complaint was a slowly growing, painless lateral neck mass associated with high dysphagia in one case. The carotid paraganglioma was an incidental finding on the occasion of an MRI angiography performed as part of explorations of tympano-jugular paraganglioma in 1 case.

The paraganglioma was discovered intraoperatively during a cervicotomy performed for a supposed chronic lymphadenopathy in 3 cases.

Symptoms related to catecholamines release, giving place to hypertensive crises and arrhythmias, were not reported in our patients.

On physical examination, the mass was located at the high or middle jugulo-carotid region. Its average size was 4 cm (range from 2 to 6 cm). Limited mobility in transverse direction has been reported in 14 cases (54%). Pulse-like sensation and palpated thrill, testifying the vascular character, were noted in 14 (54%) and 2 cases (9%) respectively. Examination of the oropharynx allowed objectifying a parapharyngeal bulge in 1 case.

Otoscopic examination revealed the existence of a bleeding tumor filling the external auditory canal in 2 cases.

Ultrasound of the neck was performed in 13 patients. It was suggestive of the diagnosis in 7 cases showing a well limited hypoechoic solid mass, located in the carotid bifurcation and vascularized in Doppler ultrasound exam. In the other cases, it evoked a cervical lymphadenopathy except in one case where it was in favor of a parotid tumor.

CT was performed in 17 patients. It helped to advance the diagnosis in 15 cases. The suggestive aspect was that of a carotid space mass which splays the internal and external carotid arteries at the level of the bifurcation and demonstrates intense homogenous enhancement following the intravenous administration of iodinated contrast (Fig. 1).

In one case, the evoked diagnosis was metastatic lymphadenopathy due to the presence of a thyroid suspicious nodule in both ultrasound and cytology.

The MRI was performed in 10 patients. The carotid paraganglioma took the appearance of a lesion sitting at the carotid bifurcation with intermediate and heterogeneous signal on T1 and T2 sequences. Hypointense flow voids of punctuate, serpiginous or channel-like structures on the set of sequences, achieving an aspect of "salt and pepper" is a distinctive feature in MRI. Intense and homogenous enhancement following the intravenous administration of gadolinium is the last character noted in our patients (Fig. 2).

The MR angiography, performed in 2 patients, showed the spacing of the carotid bifurcation and confirmed the permeability of vessels. It also showed the absence of the posterior communicating artery in 1 case. Nevertheless MR angiography was not able to identify the feeding pedicles in our study.

Angiography was performed in 16 patients allowing to confirm the diagnosis in all cases (Fig. 3).

Biologically, measurement of urinary VMA (vanillylmandelic acid) was performed in 12 patients. It was normal in all cases.

A fine needle aspiration was performed in 10 patients without incident, fortunately. It was inconclusive in 9 cases and in favor of metastatic lymphadenopathy in 1 case.

Concerning treatment, 22 patients were operated. Two patients had both large tympano-jugular and carotid paragangliomas. One of them received radiation therapy to the first location and was operated for the second one. The other was lost.

Three patients have already had a cervicotomy in another department for the diagnosis of chronic cervical

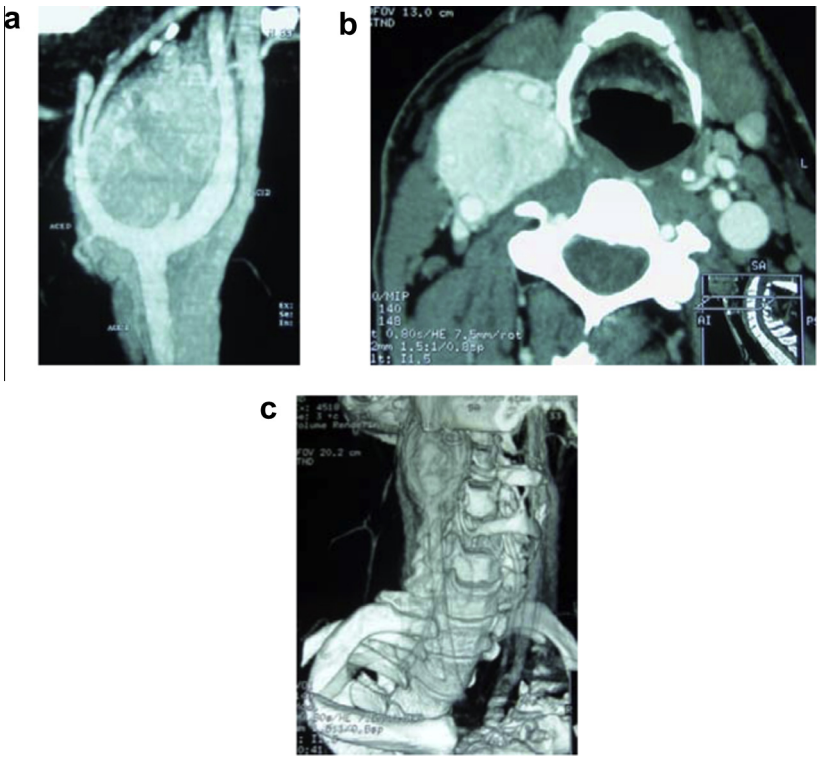

Figure 1 CT sagittal (a) axial (b) sections and 3D view: carotid space mass which splays the internal and external carotid arteries at the level of the bifurcation and demonstrates intense homogenous enhancement following the intravenous administration of iodinated contrast.

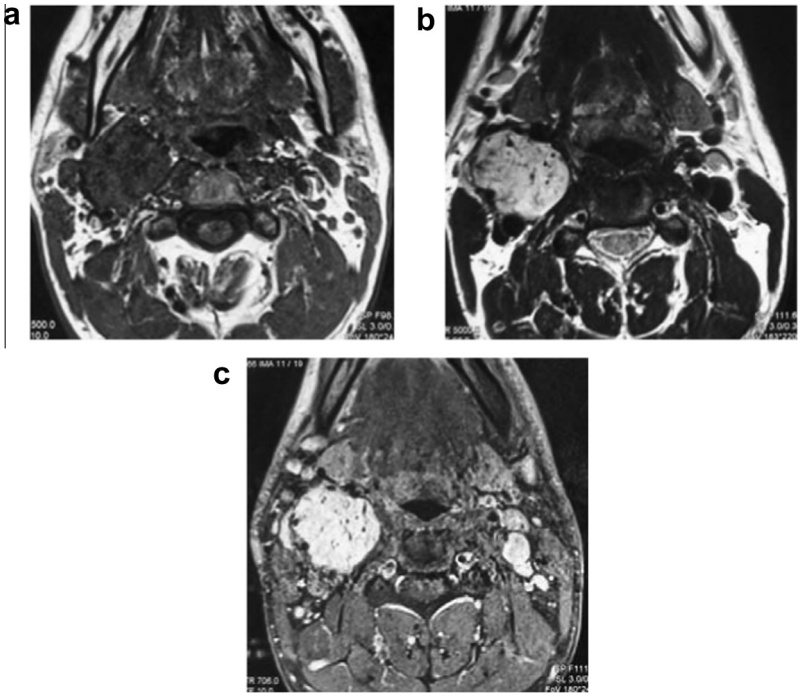

Figure 2 MRI axial sections in T1 (a), T2 (b) sequences and after administration of gadolinium (c): lesion sitting at the carotid bifurcation with intermediate and heterogeneous signal on T1 and T2 sequences achieving an aspect of ''salt and pepper'' with intense and homogenous enhancement following the intravenous administration of gadolinium.

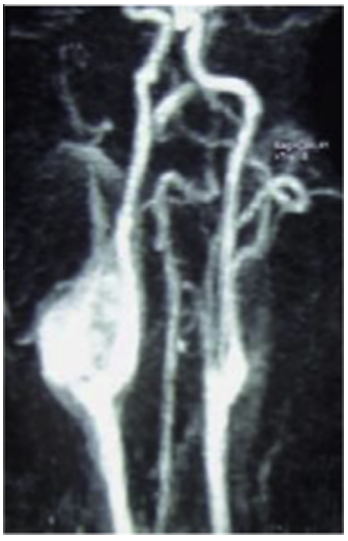

Figure 3 Angiography aspect of a paraganglioma showing the spacing of the carotid bifurcation and confirming the permeability of vessels.

lymphadenopathy. Reoperation was performed within 3–15 days. Tumor size was of 3, 4 and 6 cm. The dissection was complicated by a vascular wound of the external carotid artery which was sutured in the latter two cases.

The latero-cervical approach was performed in all cases. Resection was complete in 21 cases. In one case, residual tumor was left due to vascular wound.

2 cases of bilateral carotid paragangliomas were operated separately with an interval between 6 and 12 months. The first intervention, in fact, was conducted without complications.

Reported intraoperative incidents were:

- Internal carotid artery wound that was sutured by performing an end-to-end anastomosis.
- Common carotid artery wound 2 cm below bifurcation that was, also, sutured.

Otherwise, the external carotid was sacrificed in 7 cases in front of tumor invading this vessel. The internal jugular vein has been sacrificed in two cases and the descending branch of the hypoglossal nerve (XII) was sacrificed in 3 cases.

Early postoperative period was marked by cervical hematoma in one patient, known hypertensive, with hemorrhagic shock requiring rapid surgical revision.

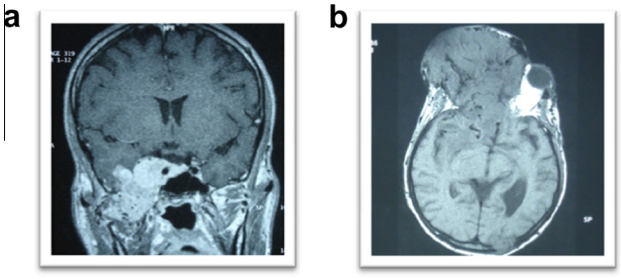

Figure 4 MRI T1 sequences: right temporal metastasis extended to the nasopharynx and parapharyngeal spaces and right frontal metastasis invading the eyeball and superficial planes.

Radiotherapy was the first therapeutic choice in 2 cases. Reasons were a carotid paraganglioma with intracranial extension invading the cavernous sinus in 1 case and a large paraganglioma adjoining the internal carotid with extension to parapharyngeal spaces and compressing the aero-digestive tract in the other case (type III of Shamblin in both cases).

Radiation therapy completed incomplete surgical resection in 1 case.

No recurrence was noted. 8 years after surgery, one patient developed a right temporal lesion extended to the nasopharynx and parapharyngeal spaces and a right frontal lesion invading the eyeball and superficial planes (Fig. 4). Biopsy concluded the paraganglionar tissue. The evolution was rapidly fatal despite external flush radiation therapy. 2 patients were lost to follow up. The mean follow-up was 5 years.

4. Discussion

Paragangliomas are rare neoplasms. Their incidence is estimated at less than 0.03%. Their frequency is underestimated since they are sometimes asymptomatic.[1]

They arise from the neural crest located in extra-adrenal locations. In most cases, they are found in the head and neck region, especially as highly vascularized carotid body (CBT) or glomus tumors.[2] They are related to the parasympathetic nervous system and are found near the arteries and cranial nerves.

Their etiology is still unknown.[1,2] It was noted a high incidence of carotid paraganglioma in patients suffering from chronic pulmonary disease and those living at high altitude.[3] In fact, chronic hypoxia can induce hypertrophy of carotid glomus cells which detect blood pressure changes in oxygen, carbon dioxide and pH.[3] The resulting lesions are referred to as non-heritable or sporadic tumors. In the sporadic form, a female predominance was reported.[1–3]

Regarding family form, it represents 10% of cases.[4,5] Its mode of inheritance is autosomal dominant with variable penetrance and is characterized by the frequency of bilateral forms.[4,5] It is caused by germline mutations of genes associated with the mitochondrial succinate dehydrogenase complex (SDHD, SDHB, SDHC or SDHAF2).

Clinically, patients notice a slowly growing, painless lateral neck mass located just anterior to the sterno-cleido-mastoid muscle at the level of the hyoid bone. Due to the proximity to the visceral axis of the neck, and the 10th and 12th cranial nerve, symptoms like cranial nerve palsies, voice changes or auditory defects are possible but not common.[1,2,6]

Patients with carotid paraganglioma can report clinical signs of catecholamines hypersecretion like high blood pressure, palpitations, and diarrhea.[6–8]

The tumor is typically moveable in the horizontal plane, but mobility is limited vertically (fountain sign). Carotid paragangliomas can be beating, transmitting the carotid pulse and producing a thrill.[6,7]

Differential diagnoses include: cervical lymphadenopathy, carotid aneurysms, laryngeal tumors and metastatic tumors.[6]

In the majority of cases the tumors are benign, but in up to 5% malignant.[1,2,9] Malignancy in paraganglioma is defined by the confirmation of metastases in non-neuro-ectoderm tissue such as lymph nodes.[9,10] Tumor size is not a malignant factor.[9,10] These metastases can affect the kidneys, lungs, brain and pancreas.[9–11] They are, often, limited to the cervical region.[9–11]

CT and MRI are non-invasive and effective means of diagnosis.[12,13] Conventional angiography may show the classic tumor "blush" and is important if embolization is to be attempted to minimize intra-operative bleeding.[12,13]

Radionuclide imaging uses an octreotide marked with Indium, labeled DTPA (pentetreotide). It binds somatostatin type 2 receptors common to paragangliomas. It is advocated if multicentricity is suspected in familial disease or to seek postoperative residual tumor.

The management of cervical paraganglioma has been controversial given morbidity rates (32–44%) and mortality (5–13%) following surgery of this benign tumor.[14–16] Currently postoperative mortality is estimated between 1% and 2%, but the morbidity related to cranial nerve lesions remains high (40%).[14–16] However, surgery remains the only curative treatment.[14–16]

Radiation therapy is indicated only in some patients or following surgery.[17–19] It seems to be a useful alternative in case of unresectable lesions, in patients with anesthetic high risk and in addition to surgery in cases of incomplete resection and finally in malignant paraganglioma.[17–20]

Clinical, biochemical and radiological findings cannot neither distinguish benign from malignant lesions nor predict malignancy evolution. In fact, malignancy is established in the presence of distant metastases mainly to the liver, lymph nodes, lung and/or bone either at diagnosis or during follow-up. Local invasion and various histopathological features can be suggestive. However, these features are not widely accepted. At present there is no universally effective therapy for malignant chromaffin-cell tumors. Most treatments are palliative, although there is a great variability in patients' responses.[21]

5. Conclusion

Carotid paragangliomas are rare neoplasms. They still pose several diagnostic and mainly therapeutic challenges. The lack of firm predictors of malignancy, coupled with the variable course of this rare disease, make life-long follow-up of patients with chromaffin-cell tumors, paragangliomas included, mandatory.

References

1. Gad Amr, Sayed Ahmed. Carotid body tumors: a review of 25 years experience in diagnosis and management of 56 tumors. *Ann Vasc Dis*. 2014;7(3):292–299.
2. Wienek Jacqueline A, Smith Alice. Paraganglioma: carotid body tumor. *Head Neck Pathol*. Dec 2009;3(4):303–306.
3. Kay JM, Laidler P. Hypoxia and the carotid body. *J Clin Pathol Suppl (R Coll Pathol)*. 1977;11:30–44.
4. Hensen Erik F, Bayley Jean-Pierre. Recent advances in the genetics of SDH-related paraganglioma and pheochromocytoma. *Fam Cancer*. Jun 2011;10(2):355–363.
5. Baez Juan C, Jagannathan Jyoyhi P. Pheochromocytoma and paraganglioma: imaging characteristics. *Cancer Imaging*. 2012;12(1):153–162.
6. Boedeker Carsten Christol. Paragangliomas and paraganglioma syndromes. GMS Curr Top Otorhinolaryngol Head Neck Surg. 2011;10 :Doc03.
7. Nazari I, Aarabi Moghaddam F, Zamani MM, et al. Clinical characteristics and remedies in 45 Iranians with carotid body tumors. *Acta Med Iran*. 2012;50:339–343.
8. Martin Rute. Paragangliomas/pheochromocytomas: clinically oriented genetic testing. *Int J Endocrinol*. 2014;2014:794187.
9. Lowery Aoife J, Walsh Siun. Molecular and therapeutic advances in the diagnosis and management of malignant pheochromocytomas and paragangliomas. *Oncologist*. Apr 2013;18(4):391–407.
10. Saddoud N, Turki I, Chammakhi R. Paragangliome malin avec métastases vertébrales et de la voûte crânienne. J Radiol. 2006;87 (12 (Part 1)):1887–1890.
11. Rachid H, El Biaze M. Paragangliome médiastinal avec métastase pleurale: A propos d'un cas. *Rev Pneumol Clin*. November 2005;61(5):315–318.
12. El Abed R, Farukh U. Imagerie des paragangliomes cervicaux. A propos de 4 cas. J Radiol. October 2005;86 (10):1551.
13. Aydi Z, Daoud F. Imagerie des paragangliomes latéro-cervicaux et abdominaux. Ann Endocrinol. October 2014;75 (5–6):364.
14. Makaieff M. Traitement des paragangliomes cervicaux. *An Fr d'otorhinolaryngolo Pathol Cervicofac*. 2012;129(6):361–367.
15. Tijani Y. Les paragangliomes cervicaux. Une expérience chirurgicale à propos de 12 cas. *J Mal Vasc*. 2012;37(6):291–294.
16. Koskas Fabien. Chémodectomes carotidiens: résultats à long terme de l'exérèse sous-adventitielle avec sacrifice premier de l'artère carotide externe. Ann Chir Vasc. January–February 2009;23 (1):72–81.
17. Lalya I. Efficacité de la radiothérapie en première intention d'un paragangliome carotidien non résécable. *J Mal Vasc*. 2011;36(3):185–188.
18. Kabbali N, Himmich M. Place de la radiothérapie exclusive dans les paragangliomes non opérables de la tête et du cou, à propos d'une série de dix cas. Cancer/Radiothérapie. September 2012;16 (5–6):576.
19. Chekrine T. Á propos de deux cas de paragangliome cervical traités irradiation exclusive. Cancer/Radiothérapie. October 2011;15 (6–7):637.
20. Nasr Ch. Á propos de six cas de paragangliome cervical. Cancer/Radiothérapie. October 2010;14 (6–7):622.
21. Chrisoulidou Alexandra, Kaltsas Gregory, Ilias Ioannis, Grossman Ashley B. The diagnosis and management of malignant phaeochromocytoma and paraganglioma. *Endocr Relat Cancer*. 2007;14:569–585.