INTRODUCTION

Paragangliomas are rare tumors derived from the extra-adrenal paraganglionic system, which is composed of cells from the neural crest that are associated with the autonomous nervous system.\(^1,2\) They have been observed at many sites in the head and neck area, including the carotid body, the jugular-tympanic region, and the vagus nerve.\(^2,3\) Unlike pheochromocytomas, head and neck paragangliomas are usually non-functioning tumors; in other words, they do not secrete catecholamines, and the primary symptom is a slow growing mass in the neck.\(^2,4\) Paragangliomas arising within the thyroid gland or the neighboring area are extremely rare, and are believed to derive from the inferior laryngeal paraganglia.\(^5-9\) The laryngeal paraganglia was first described in 1963 by Watzka,\(^10\) who showed the presence of this particular tissue in the upper and anterior third of ventricular folds. One year later, Kleinsasser\(^11\) reported the presence of paraganglia in the subglottic larynx and named it the inferior laryngeal glomus; this author also labeled Watzka’s discovery as the superior laryngeal glomus. In anatomical studies of the human larynges, Zak\(^12\) and Lawson\(^13\) demonstrated that the position of the inferior laryngeal paraganglia can vary from patient to patient. They found paraganglionic tissue to lie between the inferior horn of the thyroid cartilage and the cricoid cartilage, to lie between the cricoid and the first tracheal ring, or to be in intimate contact with the medial aspect of the capsule of the thyroid gland. Aberrant positions, such as in front of the cricoid cartilage and over the cricothyroid membrane, have also been described.\(^11-13\) The association between the inferior laryngeal paraganglia and the inferior laryngeal nerve and its branches has been well documented.\(^11-14\)

The objective of this paper is to report the diagnosis and treatment of a paraganglioma located in the anterior visceral cervical space, between the thyroid gland and the common carotid artery, which during surgery showed no relationship with the recurrent laryngeal nerve and was easily dissected from the thyroid capsule. The origin of the reported tumor, which cannot be explained by the previous anatomical descriptions of the inferior laryngeal paraganglia, is discussed.

CASE DESCRIPTION

A 38-year-old woman complaining of a slowly growing cervical mass was referred to our clinic. Her personal and family histories were unremarkable. In the physical examination, a 5-cm, oval-shaped tumor was noted in the position of the right thyroid lobe. The mass was immobile during deglutition. An ultrasonography suggested a parathyroid mass. A CT scan was performed and showed a well-defined and highly vascularized tumor located beneath the right thyroid lobe, which was displaced in the anterior direction (Figure 1). The mass was located between the common carotid artery and the postero-lateral aspect of the thyroid, and it appeared to share a cleavage plane with the gland. The patient was submitted to a fine needle aspiration biopsy, and the material was analyzed by light microscopy.
or other operative or post-operative complications were observed. The histopathological examination as well as a new immunohistochemical test with a panel of antibodies confirmed the diagnosis of paraganglioma (Table 1, Figures 4 and 5). No tumor recurrence or metastasis was detected six months after surgery, and the patient continues to be observed in regular follow-up exams.

**DISCUSSION**

Paragangliomas may theoretically arise at any site where normal paraganglionic tissue exists. In the head and neck, the carotid body is the most frequently described location of such tumors, but several other sites have been described in the literature.\(^2,3\) Uncommon sites include the laryngeal,\(^14-17\) tracheal,\(^18\) and thyroid paragangliomas.\(^5-9,10-31\) The laryngeal paraganglia has been well described in anatomical studies performed by German researchers,\(^10,11\) and more recently by Zak\(^12\) and Lawson.\(^13\) The latter studies reported that the inferior laryngeal paraganglionic tissue may extend to the

---

**Table 1 - Immunohistochemical panel of antibodies of the present case**

| ANTIGEN                                | RESULT             |
|----------------------------------------|--------------------|
| Vimentin (monoclonal antibody V9)      | positive           |
| Chromogranin                           | positive           |
| Synaptophysin                          | positive           |
| CD56                                   | positive           |
| S-100 Protein                          | positive in sustentacular cells |
| Thyroglobulin                          | negative           |
| Cytokeratins (monoclonal antibodies AE1/AE3) | negative |
| Calcitonin                             | negative           |
medial aspect of the thyroid capsule and may be in contact with the trachea. This finding explained most cases of thyroid paragangliomas.\textsuperscript{5-9,19-29,31} The first remarkable observation in the present case was the asymptomatic anterior neck swelling reported by the patient. This complaint may suggest a benign goiter. However, the immobility of the mass during deglutition caught our attention as a possible indicator of a non-thyroidal disease. The imaging tests, particularly the CT scan, demonstrated clearly that the tumor was not inside the thyroid gland. The fine needle aspiration biopsy together with an immunohistochemical panel of antibodies was essential to figure out the diagnosis. Positive results for chromogranin, synaptophysin, and vimentin, coupled with negative results for thyroglobulin, calcitonin, and cytokeratins were strongly suggestive of a paraganglioma, as described in the literature.\textsuperscript{3,8,14,16,22-31} Among the disorders most easily mistaken for cervical paragangliomas, particularly those arising within the larynx or the thyroid, are the neuroendocrine carcinomas, such as atypical carcinoids and medullary thyroid carcinoma.\textsuperscript{14,16,19,22-29,31} As postulated by Martinez-Madrigal et al.,\textsuperscript{3} the anti-cytokeratin antibody is the single most useful marker for differentiating between paraganglioma and neuroendocrine carcinomas. Both atypical carcinoids and medullary thyroid carcinoma often exhibit diffuse positivity for cytokeratins. Another disorder that may be confused with paragangliomas is hyalinizing trabecular adenoma, a benign thyroid neoplasm that shows a prominent nesting pattern resembling a paraganglioma.\textsuperscript{24,25,29} This rare entity is usually negative for chromogranin and positive for thyroglobulin and cytokeratins.

During surgery in the present case, the tumor was easily dissected from the thyroid gland and the common carotid artery. No relationship was observed between the tumor and the recurrent laryngeal nerve. Although the patient’s gender (female) and age (40s and 50s), as well as the laterality of the tumor (right side predominance), favored the diagnosis of an inferior laryngeal paraganglioma,\textsuperscript{9,14-16} the site where this tumor developed could not be explained by previous anatomical descriptions of where the inferior laryngeal paranglia was located. The lesion was too far from the carotid body to be considered a displaced carotid body tumor. To our knowledge, only one prior report has described a similar localization for a cervical paraganglioma.\textsuperscript{30} Those authors described a 3.5-cm paraganglioma located immediately posterior to the left thyroid lobe, but they could not dissect it from the gland, which was therefore partially removed. Other previous papers have reported paragangliomas located within the thyroid,\textsuperscript{5,7-9,21-29,31} between the gland and the trachea,\textsuperscript{15} and even over the thyroid cartilage.\textsuperscript{6,20} All of these locations may be explained by anatomical studies documenting the distribution of cervical paraganglionic tissue.

The histopathological and immunohistochemical findings of the specimen confirmed the diagnosis of paraganglioma in the present case. The classic organoid Zellballen pattern, composed of nests of chief cells surrounded by sustentacular cells, was observed, consistent with most previous papers.\textsuperscript{3,5,7,8,14,19,22-27,29-31} The diagnosis was further supported by diffuse positivity for chromogranin and synaptophysin in the chief cells, a focal positivity for S-100 protein in the sustentacular cells, and negativity for cytokeratins. Despite the absence of histopathological signs of aggressiveness, malignance cannot be excluded based only on morphological criteria. The diagnosis of a malignant paraganglioma is based on the detection of regional or distant metastasis and is not related to the histology of the primary tumor. Hence, all patients submitted to a paraganglioma resection must be
observed in regular follow-up exams to rule out recurrence or metastasis. However, according to the literature, the ratio of proven cervical malignant paragangliomas is low: it ranges from 2% to 10% for carotid and vagal body tumors, to less than 2% for laryngeal paragangliomas.\textsuperscript{16,19}

In conclusion, we have described here an atypical location of a cervical paraganglioma. This tumor probably originated from an ectopic inferior laryngeal paraganglia or perhaps from a novel paraganglionic tissue not yet described. This description supports the idea that the anatomical distribution of human paraganglia is incompletely understood. We expect that, with the development and spread of immunohistochemical techniques, new and unusual sites where paragangliomas can arise will be described in the future.

REFERENCES

1. Tischler AS, Kimura N, McNicol AM. Pathology of pheochromocytoma and extra-adrenal paraganglioma. Ann N Y Acad Sci. 2006;1073:557-70.

2. Paris J, Facon F, Thomassin JM, Zanaret M. Cervical paragangliomas: neurovascular surgical risk and therapeutic management. Eur Arch Otorhinolaryngol. 2006;263:860-5.

3. Martinez-Madrigal F, Bosq J, Micheau C, Nivet P, Luboinski B. Paragangliomas of the head and neck: immunohistochemical analysis of 16 cases in comparison with neuroendocrine carcinomas. Pathol Res Pract. 1991;187:814-23.

4. Plouin PF, Gimenez-Roqueplo AP. Initial work-up and long-term follow-up in patients with pheochromocytomas and paragangliomas. Best Pract Res Clin Endocrinol Metab. 2006;20:423-34.

5. Haegert DG, Wang NS, Farrer TA, Schneid MA. Non-chromaffin paragangliomatosis manifesting as a cold thyroid nodule. AJCP. 1974;61:561-70.

6. Kay S, Montague JW, Dodd RW. Nonchromaffin paraganglioma (chemodectoma) of thyroid region. Cancer. 1975;36:582-5.

7. Mitsudo SM, Grajower MM, Balbi H, Silver C. Malignant paraganglioma of the thyroid gland. Arch Pathol Lab Med. 1987;111:378-80.

8. LaGuette J, Matias-Guiu X, Rosai J. Thyroid paraganglioma: a clinicopathologic and immunohistochemical study of three cases. Am J Surg Pathol. 1997;21:748-53.

9. Aribas OK, Kanat F, Avunduk MC. Inferior laryngeal paraganglioma presenting as plunging goiter. Eur J Cardiothorac Surg. 2004;25:655-7.

10. Watzka M. Über die paraganglien in der plica ventricularis des menschlichen kehlkopfes. Dtsch Med Forsch. 1963;1:19-20.

11. Kleinsasser O. Das glomus laryngicum inferior - Ein bisher unbekanntes, nichtchromaffines Paraganglion vom Bau der sogenannten: Carotisdruse im menschlichen Kehlkopf. Arch Ohren Nasen und Kehlkopfheilk. 1964;184:214-24.

12. Zak FG, Lawson W. Glomic (paraganglionic) tissue of the larynx and capsule of the thyroid gland. Mt Sinai J Med. 1972;39:82-90.

13. Lawson W, Zak FG. The glomus bodies (“paraganglia”) of the human larynx. Laryngoscope. 1974;84:98-111.

14. Barnes L. Paraganglioma of the larynx. A critical review of the literature. ORL J Otorhinolaryngol Relat Spec. 1991;53:220-34.

15. Brandwein M, Levi G, Sop M, Urken ML. Paraganglioma of the inferior laryngeal paraganglia. Arch Otolaryngol Head Neck Surg. 1992;118:994-6.

16. Ferlito A, Barnes L, Wenig BM. Identification, classification, treatment, and prognosis of laryngeal paraganglioma: review of the literature and eight new cases. Ann Otol Rhinol Laryngol. 1994;103:525-36.

17. Peterson KL, Fu YS, Calcaterra T. Subglottic paraganglioma. Head Neck. 1997;19:54-6.

18. Liew SH, Leong ASY, Tang HMK. Tracheal paraganglioma: a case report with review of the literature. Cancer. 1981;47:1387-93.

19. Hinojar AG, Prieto JR, Muñoz E, Hinojar AA. Relapsing paraganglioma of the inferior laryngeal paraganglion: case report and review of the literature. Head Neck. 2002;24:95-102.

20. Banner B, Morecki R, Eviatar A. Chemodectoma in the mid-thyroid region. J Otolaryngol. 1979;8:271-3.

21. Cayot F, Bastien H, Jusbrolo E, Mottot C, Cuisenier J, Bruchon Y, Cabanne F. Paragangliomes multiples du cou avec localization thyroïdienne. Cancer papillaire thyroïdien et adenoma parathyroïdien associés. Sem Hop. 1982;58:2004-7.

22. de Vries EJ, Watson CG. Paraganglioma of the thyroid. Head Neck. 1989;11:462-5.

23. Brownlee RE, Shockley WW. Thyroid paraganglioma. Ann Otol Rhinol Laryngol. 1992;101:293-9.

24. Hughes JH, El-Mofty S, Sessions D, Liapis H. Primary intrathyroidal paraganglioma with metachronous carotid body tumor: report of a case and review of the literature. Pathol Res Pract. 1997;193:791-6.

25. Bizollon MH, Darreye G, Berger N. Paragangliome thyroïdien: à propos d’un cas. Ann Pathol. 1997;17:416-8.

26. Kronz JD, Argani P, Udelman R, Silverberg L, Westra WH. Paraganglioma of the thyroid: two cases that clarify and expand the clinical spectrum. Head Neck. 2000;22:621-5.

27. Vedovnik A. Fine needle aspiration cytology of primary thyroid paraganglioma. Report of a case with cytologic, histologic and immunohistochemical features and differential diagnostic considerations. Acta Cytol. 2002;46:1133-7.

28. Zantour B, Guilhaume B, Tissier F, Louvel A, Jeunemaitre X, Gimenez-Roqueplo AP. Fine needle aspiration cytology of primary thyroid paraganglioma. Report of a case with cytologic, histologic and immunohistochemical features. Acta Cytol. 2002;46:1133-7.

29. Corrado S, Montanini V, De Gaetani C, Borghi F, Papi G. Primary paraganglioma of the thyroid gland. J Endocrinol Invest. 2004;27:788-92.

30. Schmitter GD, Gorman B, van Heerden JA, Gharib H. Inferior laryngeal paraganglioma mimicking a primary thyroid tumor. Endocr Pract. 2006;12:432-5.

31. Yano Y, Nagahama M, Sugino K, Ito K, Kameyama K, Ito K. Paraganglioma of the thyroid: report of a male case with ultrasonographic imagings, cytologic, histologic, and immunohistochemical features. Thyroid. 2007;17:575-8.