Thyroid paraganglioma: report of a case and review of the literature

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Abstract

A case of thyroid paraganglioma is reported. Immunohistochemically the tumor showed negativity for thyroglobulin and calcitonin and positivity for chromogranin A and S-100. Protein positive sustentacular cells were demonstrated.
The authors discuss the previous literature on these tumors.
Key words: Thyroid paraganglioma, paraganglioma, rare thyroid tumor.

Introduction

Paragangliomas are rare neuroendocrine neoplasms of paraganglia. They generally develop near the autonomic nervous system and its branches.
Tumors of the carotid body and glomus jugulare account for > 80% of the cases (1). Other sites are the orbit, larynx, the vagus nerve, mediastinum and great vessels, lung, duodenum, para aortic and retroperitoneal region, cauda equina and urinary bladder (2, 3).
In the head and neck region paragaglia are present as paired orbital, jugulo-tympanic, laryngeal, vagal and carotid bodies. The laryngeal paraganglia are comprised of a small superior pair usually found near the superior edge of the thyroid cartilage and a large pair, less constant in location which can be found between the cricoid cartilage and the first tracheal ring. The latter may be more laterally located and in contact with thyroid gland. These inferior paraganglia can also be seen between the inferior horn of the thyroid cartilage and the cricoid cartilage in close relationship to the inferior thyroid artery and recurrent laryngeal nerve and may extend to or arise within capsule of the thyroid gland (4).
Many authors (4, 5) believe that this location could explain the origin of the rare thyroid paragangliomas.
The first reported thyroid paraganglioma was described by Van Miert in 1964 (6). Since that time 11 cases have been reported in literature (7) but the evaluation of these thyroid paragangliomas is often difficult because many of the cases have been reported without substantiating electron microscopy or immunohistochemistry (8, 5, 9, 10, 11, 12, 13, 3, 14, 6). The literature from the former Soviet Union contains as many as seven reports on thyroid paragangliomas (7) but unfortunately the investigators did not offer substantial histologic, immunohistochemical or EM evidence to support their diagnosis.
It is sure that for their rarity the thyroid paragangliomas often present a difficult diagnostic problem, both for the clinician and the pathologist.
For this reason we believe interesting the report of a new additional case of thyroid paraganglioma.

Case report

A 47 year old woman was admitted in our Surgical Department for a thyroid nodule which was discovered incidentally in the left lobe by ultrasound examination performed for other reasons.
The patient complained since one year of episodes of tachycardia, sweating and flushing.
A repeated ultrasound examination revealed a 3 × 3,5 cm solid parenchymal mass in the left lobe of the gland. The nodule was "cold" on thyroid scan. All thyroid function tests were normal. A fine needle aspiration biopsy specimen revealed small clusters and sheets of small cells having moderate variability in size and shape and it was suspicious for a malignant tumor. A tracheoscopy revealed a slight compression (10%) of the upper third of the tracheal left lateral wall.

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At operation a firm tumor mass was found in the left lobe. An intraoperative frozen section was interpreted as "consistent with follicular carcinoma" and a total thyroidectomy was performed. The tumor mass was of wooden consistence, ill-defined, focally hemorragic and its external surface was partially covered by a thin capsule.
Multiple surgical specimen were fixed in 10% buffered formalin and embedded in paraffin blocks. For histological investigations 5 micron-thick sections were stained with haematoxylin-eosin. For immunohi-stochemical studies, representative sections were examined by the avidin-biotin-peroxidase complex (ABC) technique with appropriate use of positive and negative controls throughout. The following antibodies were used; Chromogranin A, S-100 Protein, Calcitonin and Tyroglobulin.
Hematoxylin-eosin stains showed the presence of neoplastic cells arranged in a organoid pattern characteristic of the "Zellballen" or nesting pattern seen in the classic paragangliomas. The cells shape varied from oval to polygonal with poorly defined cellular margins. Foci of cellular pleomorphism with moderate nuclear atypia, occasional mitosis and focal capsular invasion were noted (Fig. 1).
Immunohistochemical staining for calcitonin and thyroglobulin were negative (Fig. 2). The epithelioid cell nests displayed positive immunoreactivity for chromogranin.
Positivity with S-100 was evident within sustentacular cells at periphery of tumor cell nests (Fig. 3). The immunostaining highlighted the organoid pattern of the tumor and the presence of sustentacular cells.
A diagnosis of thyroid paraganglioma was made.
The patient was dismissed in IV post-operative day. 6 months since surgery the patient is well and without evidence of recurrent disease.

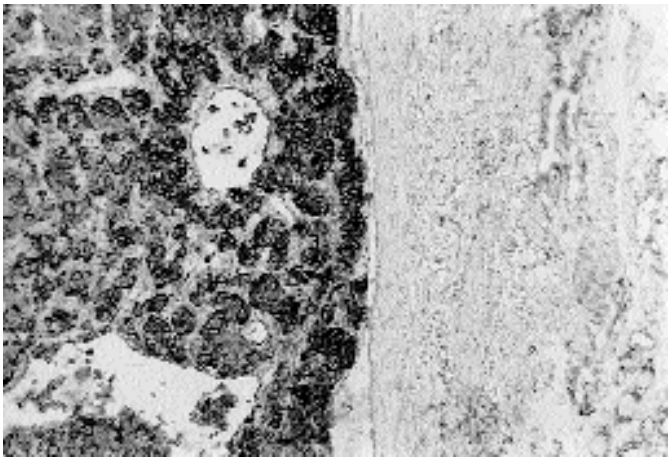

Fig. 2: Chromogranin A × 100 Photomicrograph showing both normal thyroid tissue only slightly positive for chromogranin A (C cells) (left), and paraganglioma with positive immunostaining for chromogranin A (right).

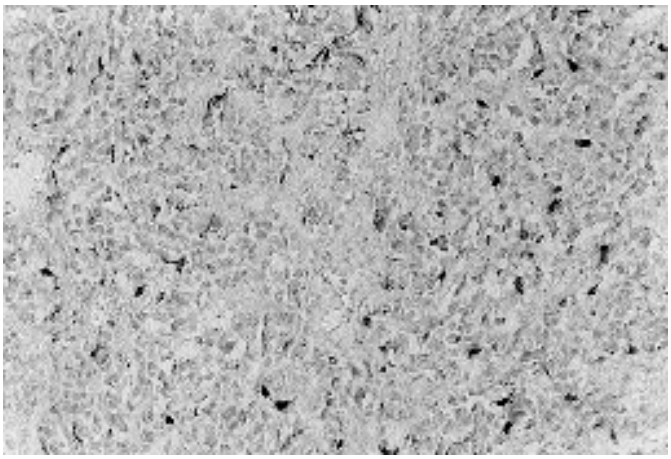

Fig. 3: S-100 × 200 S-100 positive sustentacular cells.

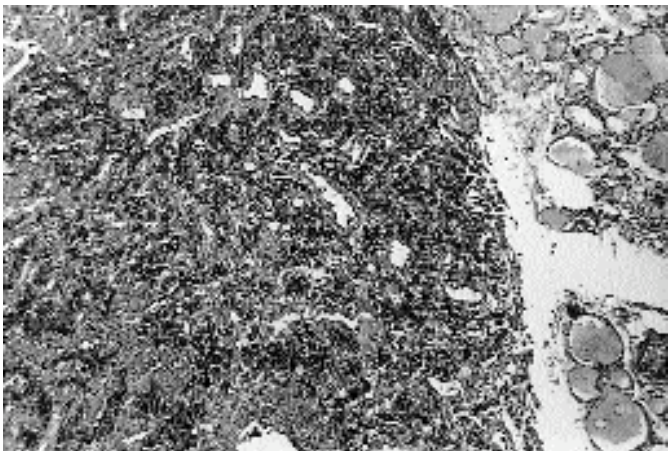

Fig. 1: H&E × 100 Photomicrograph showing both normal thyroid tissue (right) and adjacent paragnglioma (left).

Discussion and Conclusion

Thyroid paragangliomas are very rare and the possibility of misdiagnosing them is very common. The clinical diagnosis of the tumor in this location is almost impossible and also the pathologic diagnosis is difficult and will certainly be missed unless a conscious effort is made to differentiate paragangliomas, hyalizing trabecular adenoma and medullary thyroid carcinoma.
Hyalizing trabecular adenoma of thyroid presents a nesting pattern resulting in a striking paraganglioma-like appearance but presence of occasional follicles, immunoreactivity for thyreoglobulin and over all negativity for chromogranin should establish the distinction.
The distinction between paraganglioma and the medullary thyroid carcinoma with a nesting pattern of growth is

difficult but the most important criterion in favour of medullary carcinoma is the immunohistochemical demonstration of calcitonin and the negativity for chromogranin and for sustentacular cells (S-protein staining) at the edges of the tumor nests.
All the cases reported, including ours, occurred in women between the ages of 9 and 73 years. In the cases described by Haegert (11), by Hughes (15) and by Van Miert (6) the thyroid tumor occurred in association with a synchronous carotid body tumor. Most paragangliomas are confined to the thyroid gland but in three cases (14, 3, 4) the tumor was infiltrative and invaded through the tracheal wall. In one case (9) it was associated with parathyroid adenoma and papillary carcinoma.
In all reported cases, and in ours, there was no evidence of recurrence or metastatic disease following surgical excision. However the follow-up period in our case is too short and it should be emphasized that the literature experience is too limited to allow generalizations about the biological behaviour of the thyroid paragangliomas (15).

Riassunto

Viene riportato un raro caso di paraganglioma riscontrato nel contesto della ghiandola tiroide. Le colorazioni istochimiche hanno dimostrato una negatività per la tireoglobulina e per la calcitonina ed una positività per la chromogranina A e S-100. Si è anche riscontrata la presenza di cellule sustentaculari.
Gli Aa. esaminano anche la letteratura più recente su questa rara localizzazione del paraganglioma.
Parole chiave: Paraganglioma tiroideo, paraganglioma, tumori rari della tiroide.

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Commento Commentary

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Il commento dello studio di questo raro caso è sostanzialmente superfluo, data la assoluta rarità dell'evenienza che gli Autori hanno dovuto fronteggiare, e l'ottimo studio postoperatorio che ha consentito la corretta diagnosi finale.
Qualche riflessione è comunque doverosa circa il ruolo della citologia aspirativa in fase preoperatoria e quello dello studio

istologico peroperatorio al congelatore nel caso della patologia tiroidea. È chiaro che entrambe queste metodiche non hanno fornito in questo caso all'operatore gli elementi indispensabili per risparmiare alla paziente la tiroidectomia totale, che in questo caso all'epicrisi si dimostra essere stata un eccesso di trattamento.
Se il chirurgo non avesse avuto altra informazione preoperatoria oltre il fatto che esisteva un nodulo solido nel contesto dell'immagine ecografica della tiroide, muto alla captazione dello iodio radioattivo, certamente egli si sarebbe limitato ad eseguire una lobectomia extracapsulare, rimandando l'eventuale totalizzazione ad un successivo reintervento dopo acquisizione del responso dell'esame istologico definitivo. Questo, con l'acquisizione di una così brillante diagnosi istologica ed istochimica, avrebbe – come ha fornito – la corretta diagnosi di natura del nodulo in questione, dimostrando così che il trattamento limitato già effettuato era del tutto adeguato al caso in esame. Sarebbe stato pertanto conservato alla paziente il lobo destro normale, rendendo superflua l'opoterapia postoperatoria oggi invece obbligatoria.
In fase preoperatoria dunque la citologia aspirativa non è stata in grado di fornire dati che consentissero un corretto orientamento diagnostico, che avrebbe risparmiato una tiroidectomia totale, dimostratasi certamente un eccesso di trattamento nell'epicrisi.

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The comment of the study of this rare case report is substantially superfluous, if we consider the absolute rarity of the eventuality that the authors must have faced, and the excellent postoperative study that gave the correct final diagnosis.
Any reflection is however mandatory about the role of the cytologic FNAB in the preoperative phase and that of the histologic perioperative study with cryostate in the case of thyroid pathology. It is evident that both these methodologies didn't give the surgeon the needed information to avoid to the patient the total thyroidectomy, that in this case at the end demostrated have been an excess of treatment.
If the surgeon has not had other preoperative information beyond the echographic demonstration of a solid nodule in the context of the thyroid, silent to the uptake of the radioactive iodine, certainly he would limitate the operation in performing only a simple extracapsular thyroid lobectomy, with the program to eventually complete the treatment with a total thyroidectomy in a second time, only after the histologic final confirmation of the possible carcinomatous nature of the nodule. This, with such a brilliant histologic and histochemical diagnosis, would have given – as in effect did – the correct benign diagnosis of the nodule taken away with the lobe, demonstrating that the hemi-thyroidectomy already performed was the correct and complete therapy to do. Therefore it would have been preserved the controlateral normal thyroid lobe, avoiding to the patient the now necessary hormonal substitutive therapy.
In preoperative phase the FNAB was then not able to give those needed data for a correct diagnosy of certainty to orientate the sufficient conservative operation that would have spared a total thyroidectomy, demostrated certainly at the end as an excess of treatment. And the same is true for the perioperative histologic study.

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