Turkish Journal of Endocrinology and Metabolism, (2003) 1 : 49-52 **CASE REPORT**

Concurrent Metastatic Paraganglioma and Follicular Thyroid Carcinoma

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Paragangliomas are rarely malignant tumors, and they most commonly accompany medullary thyroid tumors as a part of multiple endocrine neoplasia (MEN) syndromes. Rare cases of paraganglioma with papillary thyroid carcinoma, but not follicular carcinoma, has been reported in English literature before. A 52 year-old woman admitted with left-sided neck mass and right pelvic pain. Pathological examination of the surgically excised pelvic mass, which was visualized in pelvic MRI, revealed a paraganglioma which stained positive for NSE, EMA, S-100 and negative for thyroglobulin. The patient also had multinodular goiter and pathology of the dominant nodule in thyroidectomy material, was consistent with follicular carcinoma. The tumor was strongly positive for thyroglobulin and negative for neuroendocrine tumor markers. Metastatic foci of follicular carcinoma and paraganglioma were observed in two bone core biopsies taken from different parts of pelvis. After completion thyroidectomy palliative therapy for bone metastasis was planned.

Key words: Paraganglioma, follicular thyroid carcinoma, toxic nodular goiter.

Introduction

Tumors of chromaffin and nonchromaffin tissues found within the autonomic nervous system-associated extraadrenal paraganglia are called paragangliomas. Most cases of paragangliomas are sporadic but hereditary and familial forms also occur (1). Controversy exists in the classification of paragangliomas. Although rarely malignant (2), there are no characteristic cellular changes of malignancy and the malignant potential can not be determined by pathological examination alone (2). Only when tumor is localized at anatomical sites where chromaffin tissue is not present, metastatic disease can be ascertained. The most common metastatic site is bone (3) and 75% of paragangliomas are nonfunctional (4), irrespective of their malignant potential (5).

Follicular carcinomas are epithelial tumors of the thyroid showing follicular differentiation. Demonstration of insular component in these tumors does not affect the prognosis adversely; however some authors cite it as an independent aggressive risk factor (6). Although their coexistence is not common, it always should be kept in mind that presence of thyrotoxicosis does not preclude concurrent thyroid carcinoma.

A case of metastatic paraganglioma and follicular thyroid carcinoma with insular component and toxic multinodular goiter is presented.

Case Report

A 52 year old woman was admitted to a local hospital with right pelvic pain of six months

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duration and a left-sided neck mass which had been stable in size for many years. Detailed evaluation of pelvic region with magnetic resonance imaging identified multiple hypointense lesions in the pelvic bony architecture extending to the adjacent soft tissue with the largest one reaching a diameter of 8x6x5 on left pubic ramus. An intended incisional biopsy resulted in massive hemorrhage and a 6x5x4,5 cm. tumor was extirpated from the right pelvic region. The pathology of the mass was consistent with paraganglioma. In immunohistochemical analysis, the material stained intensely with NSE-100, scarcely with EMA, moderately with S-100, however thyroglobulin, PAS and chromogranin-A(CgA) were negative. The patient was referred to university hospital for subsequent follow-up and therapy.

On physical examination she was normotensive and had multinodular goiter with a 5x6 cm. dominant nodule on the left. Laboratory evaluation revealed; free T3: 7.1 (3.5-6.5) pmol/L, free T4: 13.1 (9-19.4) pmol/L, TSH: 0.011 (0.3-5) mIU/mL, PTH: 2.6 (1-6.8) pmol/L, calcitonin: 0.2 (<2.9) pmol/L, urinary metanephrine 3.47 (1.5-4.6) µmol/day, noradrenaline 141.8 (59-470) nmol /day and adrenaline 17.2(0-109) nmol /day. Whole body Tc-HMDP bone scan showed increased uptake in the ribs, thoracic vertebra and pelvis which was consistent with metastatic lesions. In thyroid ultrasonography there was multinodular goiter with a dominant nodule on the left lobe 56x64 mm. in diameter. Thyroid scan showed two hyperactive nodules accompanying the hypoactive dominant nodule. Fine needle aspiration biopsy of this nodule disclosed follicular neoplasia. Two core bone biopsies taken from left posterior and right anterior iliac bone lesions confirmed metastasis of paraganglioma and follicular carcinoma. In MIBG scan no uptake was noted in bone lesions and the thyroid nodules.

A left total and right subtotal thyroidectomy was performed and a follicular carcinoma with insular component was diagnosed which stained strongly positive with thyroglobulin and negative with calcitonin, NSE and CgA.

After completion thyroidectomy, high dose radioactive I-131 therapy for ablation of residual thyroid tissue, radiotherapy combined with chemotherapy for the metastatic lesions of paraganglioma was planned.

Pathology

In the thyroidectomy specimen; the insular component, with well-defined tumor nests was seen microscopically (figure 1). The pattern of growth was characteristically infiltrative and blood vessel invasion was reported. Immunohistochemically the tumor cells were positive for keratin, thyroglobulin and negative for calcitonin.

In pathological examination of the pelvic mass, discrete or organoid arrangement of neoplastic cells typical for paraganglioma was seen. The nesting pattern varied in size. Tumor cells were strongly immunoreactive for neuron-specific enolase (figure 2) and S-100 stain deliniated the sustentacular cells. In one of the bone core biopsies taken from pelvis, there were colloid-filled thyroid follicles which stained positive with thyroglobulin (figure 3).

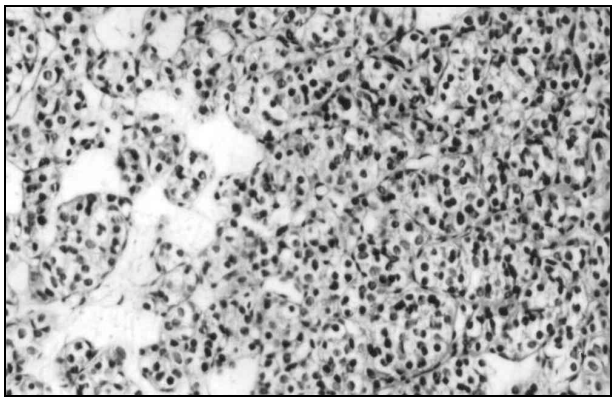

Figure 1. The appearance of insular component in follicular thyroid carcinoma, HE x 200.

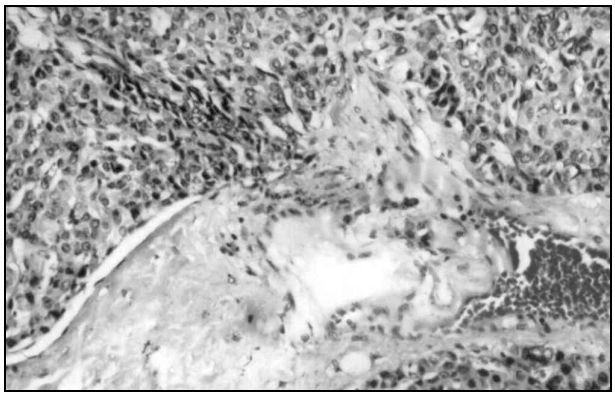

Figure 2. Paraganglioma, HE x 200.

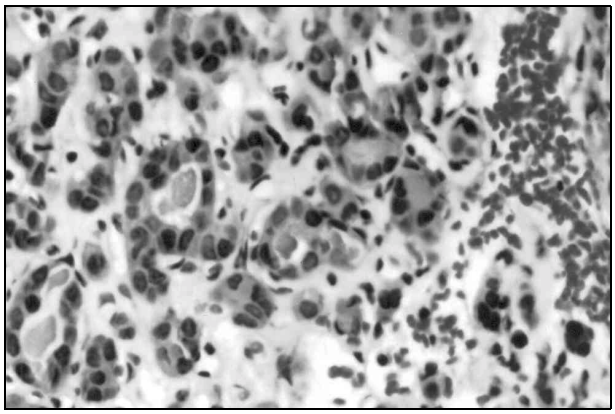

Figure 3. Metastasis of follicular carcinoma to the iliac crest, HE x 400.

Discussion

Papillary thyroid carcinoma coexisting with pheochromocytoma and paraganglioma had been reported previously both sporadically and with MEN syndromes (7), however to the authors' knowledge, this is the first report with concurrent follicular thyroid carcinoma and sporadic malignant paraganglioma.

There were three possible scenarios to elucidate this case; primary thyroid paraganglioma metastatic to the bone, pelvic paraganglioma metastatic to the thyroid and bone or coexistence of follicular thyroid carcinoma and metastatic paraganglioma. As coexistence of these two different neoplasms is a rare situation, the pathologic results of two operation materials have been interrogated intensely.

Primary intrathyroidal paraganglioma is an extremely rare condition (8) which may simulate follicular thyroid carcinoma with invasion of vascular cells; however they stain negative with thyroglobulin and positive with NSE, CgA and S-100 (8). The thyroid mass in our case was strongly positive for thyroglobulin so thyroid paraganglioma was ruled out. However, CgA is known as a universal marker for neuroendocrine tumors, and pelvic lesion of this case was negative for CgA. Procession of CgA into different fragments which is specific for both tissues and tumors, is a disadvantage of this marker. When sequence-specific CgA immunoassays or polyclonal antiserum against both CgA and CgB is not used, the diagnostic sensitivity of the analysis is deeply influenced (4). Unfortunately, such extensive analysis is not possible in our laboratory. As a result, appearance of follicular structures in the pathology of the thyroid nodule, viewing cells organized in "zellballen" pattern typical for paragangliomas in pathological examination of pelvic mass (2) and immunohistochemical analysis of both lesions confirmed existence of two primary malignant tumors in this patient. The patient had normal levels of calcitonin and PTH, hence MEN syndromes were excluded.

Toxic nodular goiter accompanying thyroid carcinoma is another noteworthy point in our case. The incidence of thyroid carcinoma with toxic goiter has a wide range changing from 0.3% to 16.6% and is more prevalent in endemic goiter areas (9) as follicular carcinomas. Turkey is still a country of iodine deficiency where goiter is endemic and this fact at least partially explains their coexistence in this case.

A recent analysis done in Swedish cancer database for evaluation of second primary neoplasms after 19281 endocrine gland tumors, may possibly explain the coexistence of two endocrine tumors in our patient. According to that study, when histologically specified, standardised incidence ratios (SRIs) for paragangliomas after thyroid adenocarcinomas was 41.2* and conversely thyroid adenocarcinoma after paraganglioma was 16.7* which were both significant ratios (10). Combined with these novel findings, our report suggests that apart from incidental concurrence, paragangliomas may be induced by the same enviromental or genetic factors that cause epithelial thyroid carcinomas, vice versa.

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* 95% confidence interval is below 1.00.

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