Simultaneous Medullary and Papillary Thyroid Carcinoma with Lymph Node Metastasis in the Same Patient: Case Report and Review of the Literature

Nidal Younes, Maha Shomaf and Lamia Al Hassan

Departments of Surgery and Pathology, Faculty of Medicine, University of Jordan, Amman, Jordan.

We report a rare case of simultaneous medullary thyroid carcinoma on the left thyroid lobe with lymph node metastasis and papillary thyroid cancer on the right thyroid lobe. The 55-year-old woman was diagnosed with medullary thyroid carcinoma after left hemithyroidectomy for goitre. Completion thyroidectomy, central neck dissection and left modified neck dissection revealed the presence of papillary carcinoma on the right side. The extreme rarity and interesting pathological features are discussed and we raise the question of whether the finding of another thyroid cancer on the opposite side was coincidental or from possible activation of a common tumorigenic pathway for both follicular and parafollicular thyroid cells. [Asian J Surg 2005;28(3):223–6]

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Introduction

Medullary thyroid cancer (MTC) is derived from the C-cells or the parafollicular cells of the thyroid and currently accounts for 5–8% of all thyroid cancers. Histologically, it shows unusual features such as trabeculae, papillae, follicles, oxyphilic small cells and, sometimes, anaplastic features. The presence of amyloid deposits and positive immunohistochemistry usually confirms the diagnosis of MTC.

Papillary thyroid cancer is the most common thyroid cancer, accounting for 75–80% of all thyroid cancers. It arises from the thyroid follicular cells and is characterized by the presence of papillae and specific cellular changes such as pseudonuclear inclusions, nuclear grooves, nuclear clearing and moulding of nuclei.

Simultaneous occurrence of medullary and papillary thyroid carcinomas in the same gland is rare. In fact, there are only 13 reports describing a total of 17 cases of simultaneous occurrence of medullary and papillary thyroid carcinoma in the literature. Although the two cancers have different cells of origin, they share some genetic predisposition. In this paper, we describe a patient with MTC and lymph node metastasis on one side and papillary thyroid cancer on the other side, and raise the question of whether the finding of another thyroid cancer on the opposite side was coincidental or from possible activation of a common tumorigenic pathway for both follicular and parafollicular cells of the thyroid.

Case report

A 55-year-old woman was diagnosed with MTC after left hemithyroidectomy for goitre. Five weeks later, she presented to Jordan University Hospital with cervical neck swelling on the left side. On admission, she was found to have a left cervical mass measuring 5 × 3 cm, her blood pressure was normal, and there was no apparent family history of thyroid cancer or any disease of the parathyroid, adrenal, pituitary or pancreas. Her serum levels of calcium, thyroid stimulating hormone and free
thyroxine were normal. The baseline serum calcitonin level was 767 pg/mL (normal, < 100 pg/mL).

Computed tomography revealed the presence of the thyroid remnant and cervical lymphadenopathy on the left side. Completion thyroidectomy, central neck dissection and left modified neck dissection were performed.

Grossly, the right thyroidectomy specimen measured 4 × 3 cm at the greatest dimensions. Cut sectioning showed a whitish nodule measuring 2 × 1 cm. Microscopically, the sections of the right lobe showed a papillary thyroid carcinoma involving the whole nodule. The tumour comprised well-formed papillae showing fibrovascular cores lined by oval to round nuclei with clearing, grooving and pseudoinclusions consistent with papillary thyroid carcinoma (Figure 1). Immunohistochemical staining of these cells was strongly positive for thyroglobulin (Figure 2) but not for calcitonin.

Remnants of the left lobe, measuring 2 × 1.5 cm at the greatest dimensions, contained multiple irregular whitish areas. It was connected to a 5 × 3 cm mass representing the left deep group of cervical lymph nodes. Microscopic examination of all masses on the left side showed a tumour formed of proliferating sheets of cells with oval hyperchromatic nuclei and prominent nucleoli with scant cytoplasm and a background of a pink homogeneous material that stained positive with Congo red (Figure 3). Immunohistochemically, the tumour cells were reactive for calcitonin and carcinoembryonic antigen (CEA) (Figure 4) but not for thyroglobulin. The patient recovered uneventfully and was discharged on the fifth postoperative day.

**Discussion**

Papillary thyroid carcinoma is the most common malignant tumour of the thyroid. It is a well-differentiated neoplasm characterized by papillary architecture and distinctive cytological features. Papillary carcinoma tends to metastasize...
via the lymphatic channels, and its prognosis is generally favourable. Medullary carcinomas, which are of different embryological origin, differ from papillary thyroid carcinoma in their growth pattern and their greater propensity for locoregional invasion. The prognosis of MTC is generally worse than that of papillary thyroid cancer.\textsuperscript{16}

Papillary thyroid cancers arise from the follicular cells of the thyroid, which are derived from a median endodermal anlage from the tongue. Papillary thyroid cells produce thyroglobulins and thyroid hormones. MTCs arise from the parafollicular cells of the ultimobranchial body derived from the neural crest. Medullary carcinomas produce calcitonin and other hormonal peptides and are considered part of the amine precursor uptake and decarboxylation system.\textsuperscript{17}

The concurrence of MTC and papillary thyroid carcinoma within the same thyroid has been sporadically reported. Only 17 cases of mixed and simultaneous thyroid tumours have been reported in the literature.\textsuperscript{3–15} Most of these reports describe mixed tumours with morphological and immunohistochemical traits of both carcinomas.\textsuperscript{4–8} In one report, the diagnosis was made from fine-needle aspiration cytology of two nodules, one on the right side that was positive for calcitonin and CEA and the other on the left that was consistent with papillary thyroid carcinoma. In another report by Mazzotti et al, simultaneous medullary and papillary thyroid carcinoma was found in a patient with Graves’ disease.\textsuperscript{13} To the best of our knowledge, this is the first reported case from Jordan and possibly the second case from the region (personal communication with colleagues in Saudi Arabia).

Although the thyroid gland is not considered part of the diffuse endocrine system, it is worth noting that the concurrence of both tumours in the same gland may suggest that these tumours have a common stem cell origin. The theory of a common stem cell that gives rise to both parafollicular C-cells and follicular epithelial cells was proposed by Ljunberg in 1983.\textsuperscript{18} According to this theory, the ultimobranchial body is the most likely source of this putative common stem cell because the nests of these cells in the thyroid gland show immunoreactivity for both thyroglobulin and calcitonin, suggesting that the ultimobranchial body may have contributed to both the parafollicular cells and the follicular epithelial cells.

The second hypothesis regarding the tumorigenesis of thyroid cancers showing features of both medullary and papillary carcinomas is the possibility of a common tumorigenic stimulus triggering neoplastic transformation for both cell lines, leading to medullary and papillary thyroid carcinoma. Both tumours occur in familial forms, especially MTC, of which 10% are familial. In our case, there was no family history to suggest the familial variety of MTC.

Familial MTC is associated with a positive RET oncogene mutation. Specific mutations of RET are responsible for the inherited cancer syndromes MEN2A, MEN2B and familial MTC.\textsuperscript{19} Rearrangement of the RET proto-oncogene represents one of the most common genetic alterations found in papillary thyroid carcinoma. Unfortunately, we could not perform either a RET oncogene or a RET/papillary thyroid carcinoma analysis in our patient because of technical problems.

The third explanation for this rare presentation is that it is just a coincidental finding since the incidence of papillary thyroid carcinoma is high and there is some evidence to suggest that these two cancers have different patterns of RET proto-oncogene mutation, loss of heterozygosity and X-chromosomal inactivation according to Volante et al.\textsuperscript{20}

In conclusion, simultaneous occurrence of MTC and papillary thyroid carcinoma in the same thyroid gland is extremely rare. Controversies still exist regarding whether this is just a coincidence or related to a common stem cell origin or possible common triggering genetic factors.

References


