

Concurrent papillary and medullary thyroid carcinomas with mixed metastases to lymph nodes

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ABSTRACT

We report here a rare concurrence of medullary and papillary carcinomas of the thyroid in a 39-year-old Saudi male. He presented with a solitary nodule of the right thyroid lobe and underwent total thyroidectomy based on the cytological diagnosis of papillary carcinoma. Subsequent detailed histopathologic examination of the thyroid revealed 2 different types of malignancies in the 2 lobes (papillary cancer in the right and medullary cancer in the left lobe). A single small lymph node showed metastatic replacement by both cancers. The extreme rarity and the interesting pathological features of such combinations are discussed.

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Medullary carcinoma of the thyroid (MTC) is a rare tumor. It is derived from thyroid C cells with serum calcitonin acts as a specific and sensitive marker.¹ On the other hand, papillary carcinoma is the most common thyroid malignancy seen at our centre. Although concurrent medullary and papillary carcinomas of the thyroid are extremely rare, this pathological entity has already been described.²⁻¹⁰ Medline search of the world literature revealed a total of 15 reported cases to date. We report here yet another case of such concurrence as the first ever reported in the Saudi literature and discuss the interesting pathological features of such a rare combination.

Case Report. A 39-year-old male was first seen in the surgical clinic in November 1998. He initially presented with recurrent upper respiratory tract infection and a right thyroid swelling. He denied any history of voice change, weight loss or previous neck irradiation. There was no history

suggestive of hypo or hyperthyroidism, but there was a family history of benign thyroid disease. On examination, he looked euthyroid with no pallor or cervical lymphadenopathy. There was a palpable small solitary nodule in the right lobe of the thyroid, but the left lobe was normal. Neither serum calcitonin or thyroglobulin levels were measured, but the thyroid function test was normal. Fine needle aspiration cytology of the nodule was highly suspicious of papillary thyroid carcinoma. Ultrasonography showed right thyroid nodule measuring 2 x 1.5 cm with mixed echogenicity; there was also a much smaller nodule with mixed echogenicity in the left lobe. He underwent an uneventful total thyroidectomy and central lymphadenectomy. The histology of the excised thyroid showed papillary carcinoma of the right lobe (**Figure 1**) and a medullary carcinoma in the left lobe of the thyroid (**Figure 2**) with metastatic deposits of both medullary and papillary carcinoma in one of the excised lymph nodes. In view of the findings,

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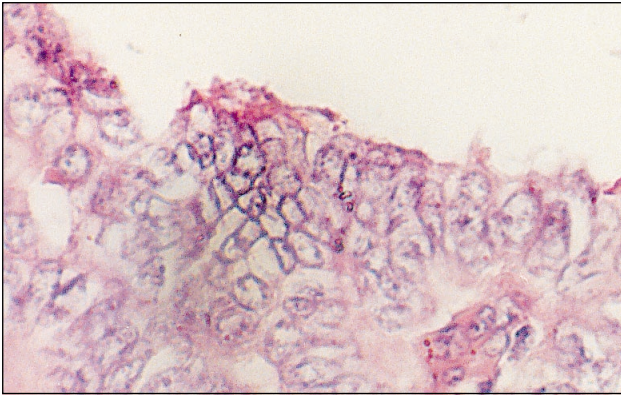


Figure 1 - Papillary carcinoma in the right thyroid lobe (Hematoxylin-Eosin x 400).

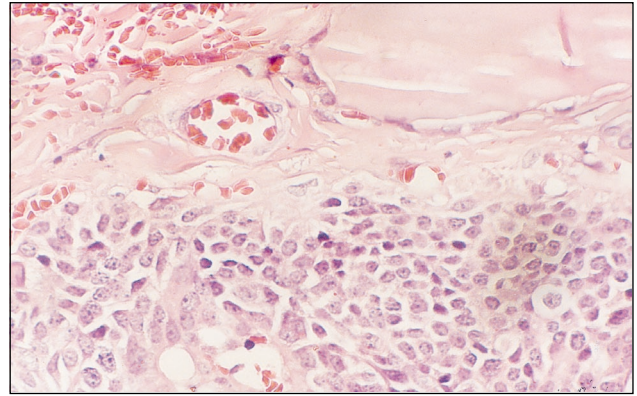


Figure 2 - Solid pattern of medullary carcinoma in the left thyroid lobe (Hematoxylin-Eosin x 400).

calcitonin level was requested but was not available. Computed tomography scans of the chest and abdomen were normal. He was given postoperative radioactive iodine therapy and remained well at 4-year follow up on thyroid replacement therapy.

Histology. The right lobe showed a tumor measuring 2 cm in the greatest dimension. It was firm, well defined and exhibited granular grey-white gross appearance. The left lobe and isthmus showed multiple firm, fleshy nodules, the greatest of which measured 1.5 cm in maximum dimension. In addition, a small cervical lymph node was seen which measured 0.5 cm in maximum dimensions. For light microscopic examination, multiple sections of both lobes and lymph node were fixed in 10% formalin, embedded in paraffin and stained with hematoxylin-eosin and congo red. Additional sections were obtained from the paraffin blocks and immunostained for calcitonin, thyroglobulin and keratin using avidin-biotin method. The antisera were obtained commercially (Dako Corporation, Santa Barbara, California, United States of America). Multiple sections from the right lobe of thyroid showed papillary carcinoma made up of complex papillae and follicles lined by cuboidal to columnar cells with the overlapping nuclei exhibiting typical ground glass appearance and nuclear grooves. Sections from the left lobe and isthmus showed typical histological features of medullary carcinoma. The tumor cells were arranged in lobules and small nests separated by thin fibrovascular septae. The surrounding thyroid tissue showed small foci of papillary carcinoma consisting predominantly of follicular pattern. Sections from the cervical lymph node showed metastatic deposits of both papillary and medullary carcinoma. Immunohistological stains conducted at King Faisal Specialist Hospital, and Research Center, Riyadh, Kingdom of Saudi Arabia, (KSA) have confirmed that the 2 tumors were indeed medullary and papillary carcinomas.

Discussion. Concurrence of 2 cancers of the thyroid arising from 2 different cell lines has been described, however, very rare. The most commonly described combination is the medullary-papillary carcinoma.²⁻¹⁰ The second most commonly reported concurrence is medullary-follicular carcinoma; review of literature however revealed only 5 reported cases to date.¹¹⁻¹⁴ It has been suggested that the 2 cancers arise from common stem cell origin.^{2,7} To the contrary, Ishida et al suggested that the tumors were derived from different cell origins.⁴ The light microscopic features and immunohistologic results of the present case support this view, bearing in mind that electron microscopy was not carried out in our case. The World Health Organization in its most recent classification of thyroid neoplasms did not include concurrent carcinoma as a special subtype of thyroid cancer.¹⁵ Such lesions could consist of medullary carcinoma composed of parafollicular C cells and well differentiated carcinoma showing papillary or follicular epithelial cell differentiation.⁷ They commonly metastasize to regional lymph nodes, where they form foci of composite medullary and papillary carcinoma, with each component maintaining a distinct immunophenotypic profile as seen in this case.⁷ This composite metastases are best regarded as collision tumors, as each primary neoplasm exhibited only one line of differentiation.⁷ This further supports the different cell origin theory suggested by Ishida et al.⁴ As the incidence of papillary carcinoma is high in comparison to medullary carcinoma, the occurrence of the 2 tumors may be a coincidence. Alternately, a common tumorigenic stimulus triggering neoplastic transformation of both parafollicular C cells and follicular epithelial cells is another common explanation for such a phenomenon.⁷ Others suggested such coexistence to be a distinctive variant of mixed medullary papillary carcinoma that can be recognized by routine stains.⁸ Such

coexistence can occur in patients with Grave's disease⁹ declaring itself as a recurrence of thyrotoxicosis, or presenting many years after thyroidectomy.² The recommended treatment for such concurrent thyroid cancer is total thyroidectomy, central lymph node dissection and thyroid hormone replacement therapy. Serum calcitonin level needs to be monitored regularly as a marker for the recurrence of the medullary component. Our patient has been followed up closely for 4 years at King Faisal Specialist Hospital and Research Center, Riyadh, KSA (a tertiary oncology centre) without evidence of recurrence.

We report this case to highlight the simultaneous coexistence of 2 types of thyroid cancers and to the best of our knowledge; we believe that this could be the first case to be ever reported in the Saudi literature.

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