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Simultaneous medullary and papillary thyroid carcinoma associated with a primary renal carcinoma: Case report and review of literature

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Abstract

Background: The association of primary two thyroid cancer (TC) and papillary renal carcinoma is an uncommon situation and only few cases have been reported.

Case presentation: We report the case of a 49-year-old man with a papillary, medullary thyroid cancer in whom a papillary renal cancer was subsequently discovered. The patient was treated with total thyroidectomy and dissection of lymph nodes followed by radiotherapy and radioactive iodine.

Conclusions: The simultaneous thyroid and renal carcinomas remains a subject of research, further investigations including tumor mutational status and histopathologic evaluation for each primary tumor are needed.

Key words: Papillary cancer; Medullary cancer; Renal cancer; Surgery; Radioactive iodine.

Introduction

The coexistence of several neoplasias of different origin is a rare situation. Medullary thyroid cancer (MTC) is an uncommon thyroid tumor arising from parafollicular calcitonin (CT)-producing cells which accounts for 3-5% of all thyroid cancers compared to papillary thyroid cancer (PTC), which arises from thyroglobulin (TG)- producing follicular cells representing approximately 85% of all thyroid malignancies [1]. The simultaneous occurrence of these two cancers is rare and observed in 0.28 à 2.6 % [1].

In addition, it has been epidemiologically demonstrated that certain primary malignancies can lead to an increased risk of developing second primary cancers (SPC). Actually, the existing literature supports an increased risk of development of subsequent primary renal carcinoma (RC) in patients treated for thyroid cancer (TC) [2,3]. Conversely, an increased risk of subsequent primary thyroid cancer (SPTC) in patients with RC was not confirmed [2]. We describe a rare case of a patient with a papillary, medullary thyroid cancer in whom a papillary renal cancer was subsequently discovered.

Case presentation

A 49-year-old male was admitted to our department to explore anterior basicervical swelling accompanied with dyspnea, mixed dysphagia and dysphonia evolving for three months. The patient had no apparent family history of endocrine disorders. ENT Physical examination revealed anterior basicervi-

cal swelling of 10 cm of major axis, hard heterogeneous mobile on swallowing with palpable lower pole, associated to a right supra clavicular adenopathy measuring 1 cm of major axis; vocal cords were normal. However, general physical examination revealed an inspiratory bradypnea with cornage. The patient's serum thyroid-stimulating hormone (TSH) and calcium levels were normal. Computed Tomography Cervical imaging revealed a compressive thyroid goiter with infiltration of subcutaneous soft tissue and parasternal acromegaly (Figure 1).

Fine needle aspiration was practiced on the thyroid goiter and revealed a medullary thyroid cancer. The thyrocalcitonin assay revealed a high rate of 29 ng/l. Further examinations, including bone scan and CT of the chest, abdomen, and pelvic confirmed the presence of a suspicious kidney mass associated to a bone metastasis at the seventh rib. Firstly, the patient had an urgent tracheotomy because of the worsening of his respiratory condition. In a second time, he underwent total thyroidectomy, bilateral mediastino-recurrent lymph node dissection and bilateral functional lymph node dissection supplemented by total laryngectomy justified by the infiltration of the cricoid cartilage and the first tracheal rings intraoperatively. The surgical specimen demonstrated two synchronous thyroid tumors: a papillary carcinoma and a medullary carcinoma. Definitive histology showed lymph node metastases from medullary carcinoma in 10 out of 21 central and functional lateral dissection lymph nodes, and one metastatic lymph node from papillary carcinoma among the 11 lymph nodes of the right functional dissection. In addition, the renal biopsies confirmed the diagnosis of low-grade tubulopapillary carcinoma. The postoperative treatment consisted of radioiodine (RAI) therapy at a dose of 200 Mci for his papillary carcinoma and radiotherapy for his medullary carcinoma. The evolution was marked by the appearance of a lymph node metastasis of his medullary carcinoma 4 years later (Figure 2).

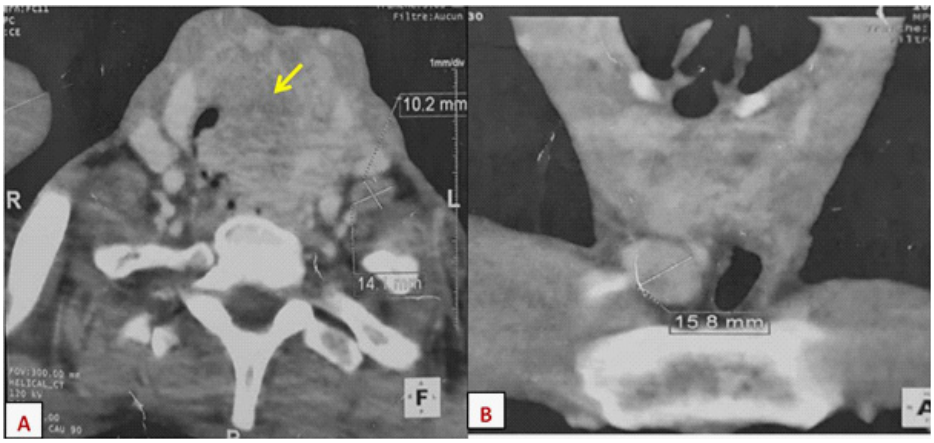

Figure 1: Axial (A) and Coronal (C) Cervical CT showing an enlarged thyroid gland exerting a mass effect on the trachea Right suprasternal adenomegaly with necrotic center.

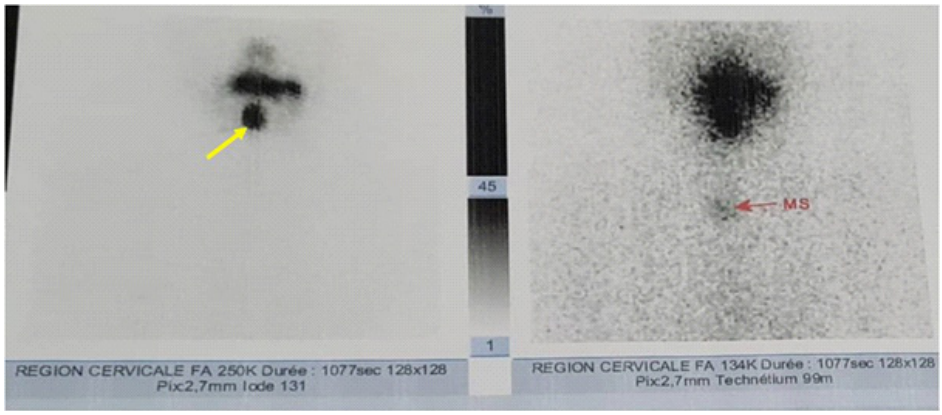

Figure 2: Whole-body scintigraphy with radioiodine-131 performed after IRA therapy which shows a focus of cervical fixation evoking functioning metastases in lymph nodes.

For his renal carcinoma, the patient was taken care of in urology department; he had a partial nephrectomy with simple postoperative course without recurrence.

Discussion

Association of thyroid carcinoma with other neoplasms in different anatomic sites has been mentioned in several studies. It was firstly described in association with paraganglioma of the carotid body [4,5], then mentioned by oscar larraza et al. in a family neoplasic syndrome that associated thyroid papillary carcinoma with pituitary adenoma, bilateral carotid body paraganglioma, gastric leiomyoma, parathyroid hyperplasia, and amyloidosis [5,6].

Actually, it has been proved that patients with thyroid carcinoma have a tendency to develop secondary malignancy especially with younger patients. Therefore, many neoplasms were described notably leukemia, lymphoma, melanoma, carcinoma of salivary glands and kidney, and bone and soft tissue sarcomas [5,7]. In a study conducted by the SEER data, 113389 cases of cancer of the thyroid were identified. Only 9 cases of urothelial

carcinomas of the renal pelvis were found, which represented the second malignant neoplasm. On the other hand, only 3 cases of thyroid carcinomas out of 12047 cases of cancers of the renal pelvis were found during the same period. This study concluded a non-significant O/E Ratio [7]. However, the association of thyroid carcinoma with breast cancer was significantly described [8].

The coexistence of papillary and medullary thyroid cancer can occur in different forms , and can present as a mixed tumor characterized by the presence of PTC and MTC in the same nodule, or as a collision tumor defined by the presence of both cancers in the same gland but separated by normal thyroid tissue. In our case, our patient presents a collision tumor with PTC in an upper polar nodule that measured 1.8 cm, with MTC in a 2.5 cm mediolobar nodule. In fact, the pathogenesis of this phenomenon was enigmatic and many theories have been suggested in order to elucidate it. Most studies support the 'collision' phenomenon suggesting that the existence of two independent tumors in the same lesion is a coincidental event [1].

Genetically, PTC was related to a somatic RET/PTC rearrangements and mutations in RAS and BRAF oncogenes, meanwhile mutation in RET activating point was observed in MTC [9,10]. Furthermore, another theory suggests that intermixed tumors could derive from a common uncommitted stem cell or potentially a common tumorigenic stimuli triggering neoplastic transformation of both follicular and C cells cell , and this theory also demonstrated distinct patterns of RET proto-oncogene mutation, loss of heterozygosity, and X-chromosomal inactivation in the two histological components of mixed tumors [1].

The prognosis of synchronous MTC-PTC is usually determined by the medullary component since PTC has often a favorable prognosis and slow progress[11]. Actually, it is preferable to realize calcitonin in the presurgical work up , since patients with PTC and MTC have more than one thyroid nodule usually, and that, even if the cytology concludes a PTC [9]. Besides, it has been proved that an early diagnosis of MTC offers a better outcome for the patient [11].

In our study, the follow up was characterized by a lymph node recurrence as well as the appearance of bone metastasis, both related to MTC according to histologic results. Appetecchia et al demonstrated, in their recent epidemiological multicenter study in which they investigated the epidemiologic characteristics and clinical outcomes in 183 patients with simultaneous PTC-MTC [12], that 45% of patients were disease-free after >10 years from diagnosis, with 72.5% for PTC and 51.1% for MTC [12]. These results concluded that the treatment of intermixed thyroid tumors should prioritize the management of MTC, which includes total thyroidectomy and central lymph node dissection.

The association of papillary and medullary thyroid carcinomas with renal papillary carcinoma is a very rare combination described few times in the literature. Some authors discussed the possibility of a syndromic association [5].

The development of simultaneous renal and thyroid cancers interested many researchers because of the several disparities in gender distributions, risk factors, age at diagnosis, histologic characteristics and associations with additional malignancies. Aubrey A et al. suggested that epidemiologic associations and biologic connections which have been reported including common carcinogenic exposure (e.g., radiation, tobacco, or alcohol) genetic predispositions or side effects of TC or RC treatments might explain such association [3].

Moreover, papillary thyroid carcinoma and papillary renal carcinoma might have in common some genetic abnormalities such as mutations of Her2/ERBB2, Cyclin D1, Cadherin 1/E-cadherin, and fibroblast growth factor receptor [13].

Malchoff et al. described in their study a tumor syndrome as the familial association of papillary renal neoplasia (PRN), PTC and a nodular thyroid disease, and explained it genetically by a germline mutation in chromosome 1q21 [14]. However, Cybulski et al demonstrated the incrimination of the CHEK2 gene which plays an important role in DNA repair, in a higher risk of breast, colon, kidney, and thyroid cancer [15].

Prognostically, it has been proved in a comparative study conducted by Aubrey A et al, that patients affected by primary TC alone have better survival advantage than patients having both TC and Renal Carcinoma (RC). However, this study showed that patients in the TC/RCC cohort survived longer than patients who developed RC alone [3].

Conclusion

In summary, we illustrate a case of a patient with a rare situation associating a simultaneous PTC and MTC with a renal papillary cancer. This association was mentioned in several studies. When medullary and papillary thyroid cancers are associated, the treatment is driven by the medullary component, which includes essentially total thyroidectomy and central lymph node dissection. However, the simultaneous thyroid and renal carcinomas remains a subject of research, further investigations including tumor mutational status and histopathologic evaluation for each primary tumor are needed. It is essential to diagnose simultaneous primary malignancies in order to provide an earlier diagnostic evaluation and establish the adequate treatment with a better prognosis.

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