SYNCHRONOUS OCCURRENCE OF THREE DIFFERENT THYROID TUMORS

Y. Darouassi*, A. Aljalil, A. Azami, M. Elakhiri, A. Ennouali, M.A. Hanine, Y. Chebraoui, M. Tayane, M. Mliha Touati, I. Rharrassi, H. Ammar

Hopital Militaire Avicenne, Marrakech, Morocco

Abstract

Background. Thyroid nodules are common; however, the association of two or more different tumors in the thyroid gland is unusual. We present a first case with the association of three histological types of thyroid tumors. To the best of our knowledge, this association has not been reported in the literature before. We aim here to highlight the possible coexistence of many lesions in the thyroid gland and to discuss treatment options.

Case presentation. We report the case of a female patient who presented with a multinodular goiter. The final pathology after total thyroidectomy found the association of a multifocal papillary thyroid microcarcinoma arising within a Hurthle cells adenoma in a lobe and a noninvasive follicular thyroid neoplasm with papillary nuclear features in the other lobe. Due to the very low risk of recurrence, the patient was not treated with radioactive iodine.

Conclusions. Many controversies remain about the management of Hurthle cells tumors and many variants of papillary thyroid carcinoma. Although the management of our case did not change, more studies are necessary to analyze the evolution of patients with multiple thyroid neoplasms. When discussing therapeutic options, the advantages and disadvantages should be considered case by case based on disease staging.

Keywords: Hurthle cell tumor, papillary cells carcinoma, thyroid gland, NIFPT.

INTRODUCTION

Thyroid nodules, characterized by their high frequency, have always aroused great interest. Several controversies persist both in terms of cytological and histological diagnosis and in terms of therapeutic indications. The latest World Health Organization histological classification brought several changes. Regarding the treatment, the current trend is towards de-escalation for both benign and malignant tumors.

Papillary thyroid carcinoma (PTC) represents up to 80% of all thyroid cancers. It presents several

variants dominated by the classical PTC followed by the follicular variant (FVPTC) (1, 2). Encapsulated FVPTC, now called noninvasive follicular thyroid neoplasm with papillary nuclear features (NIFTP) must be distinguished from follicular adenoma (FA) (1). Several controversies remain about Hurthle cell neoplasms, from the nomenclature to the management (3).

The presence of two different tumors associated in the thyroid gland is unusual. Reported cases until now include Hurthle cell adenoma (HCA) with PTC; medullary carcinoma with follicular carcinoma; medullary carcinoma and PTC; tall cell variant of PTC with Hurthle cell carcinoma (HCC); and PTC with FA (4). We present a first case with the association of three histological types: a PTC arising within a Hurthle cells adenoma and an NIFTP. To the best of our knowledge, this association has not been reported before in the literature. We aim here to raise the awareness of possible coexistence of many lesions in the thyroid gland and to discuss treatment options.

CASE PRESENTATION

We report the case of a 55-year-old female patient, without significant medical history, who presented with a swelling of the left lobe of the thyroid gland without evidence of compression or dysthyroidism. There were no lymphadenopathies on palpation. Ultrasonography revealed the presence of a nodule measuring 22 x 48 mm in the left lobe classified EU-TIRADS 3 (European Thyroid Imaging Reporting And Data System), and two small infra-centimetric nodules in the right lobe classified EU-TIRADS 2, without lymphadenopathies. The TSH level was normal. Fine needle aspiration biopsy (FNAB) of the left nodule discovered atypical cells suspected of papillary cancer. We performed a left lobectomy with a frozen section examination, which revealed a follicular adenoma of oncocyctic appearance. We completed

*Correspondence to: Youssef Darouassi MD, Hopital Militaire Avicenne, Marrakech, 40000, Morocco, E-mail: y.darouassi@yahoo.fr

Figure 1. Hurthle cell thyroid tumor with regular nuclei (hematoxylin-eosin staining (HE), medium magnification).

Figure 2. Foci within the oncocytic adenoma with cytologic features of papillary carcinoma (HE staining at high magnification).

Figure 3. Immunohistochemical staining of foci of papillary carcinoma in the Hurthle cells adenoma by the anti-cytokeratin 19 antibody.

immediately by a right lobectomy. The post-operative period was uneventful. The final pathology found on the left lobe some millimetric foci of papillary carcinoma with immunohistochemical staining by anti-cytokeratin 19 antibodies; without vascular embolism or capsular invasion; arising within a Hurthle cell adenoma (Figs 1-3). In the right lobe, we found a 5 mm NIFTP and a multiheteronodular thyroid hyperplasia (Figs 4, 5). Due to the very low risk of recurrence, the patient was not treated with radioactive iodine. The evolution was satisfactory with no recurrence at a one-year follow-up.

DISCUSSION

Thyroid nodules are frequent with a prevalence of 5% at palpation and up to 50% on ultrasonography (4). Among thyroid neoplasms, follicular-derived ones are the most common. They comprise benign follicular tumors, borderline follicular tumors (including NIFTP), PTC, follicular carcinoma, Hürthle cell tumors, poorly differentiated carcinoma, anaplastic carcinoma, and squamous cell carcinoma (5).

Carcinoma of the thyroid gland is the most common endocrine carcinoma (6). Our patient had the association of three histological types: a multifocal papillary thyroid microcarcinoma arising within a Hurthle cells adenoma and an NIFTP.

Firstly, PTC is the most frequent thyroid cancer (70% to 85%)(2,5,7-9). It is the seventh most common cancer in women (6). Female patients are two to four times more affected than men and PTC can occur at any age but mostly between the ages of 30 and 60 (9). Dietary iodine concentrations and radiation appear to influence their incidence (9). PTC has fifteen variants with many subtypes. Histopathological diagnosis is based on architectural and nuclear features (10). Imaging techniques and FNAB have allowed for earlier diagnosis, but controversies remain about cytological and histological diagnosis and also management. PTC usually has a very good prognosis with a five-year survival higher than 96.9% in patients without metastasis (2).

Secondly, Hurthle cells neoplasms (HCN) account for 3 to 10 % of thyroid nodules (3). They are composed of cells with large mitochondria and a higher frequency of mitochondrial DNA mutations (2,5,6) with the ability to bind acidic dyes like eosin, explaining the term “oxyphil cells” (3). Other names for Hurthle cells are Askanazy cells and oncocytic cells (6). Oncocytes may appear in different tissues, including endocrine glands (like the thyroid gland), exocrine glands and

Figure 4. NIFTP with well-defined tumor proliferation of vesicular architecture.

Figure 5. NIFTP with enlarged, anisokaryotic, clarified, hunched and incised nuclei (HE at high magnification).

secretory epithelia (3). Hurthle cells may arise in benign conditions like adenomas, nodular goiter, hyperthyroidism, and Hashimoto's thyroiditis, but also in malignant thyroid tumors (2,6). Hurthle cells are commonly thought to have follicular origin based on the detection of thyroglobulin immunoreactivity and TSH receptor adenylate cyclase system; but the parafoallicular origin was also reported based on the more frequent metastatic lymphadenopathies, lower radioactive iodine action, and different oncogene expression (3). HCN is now considered as a separate entity since they have clinical, histopathological, and molecular features different from follicular neoplasms (5). HCNs are divided into Hurthle cell adenomas (HCA) and Hurthle cell carcinomas (HCC) and are generally encapsulated (3). HCA is a benign thyroid neoplasm that shows more than 75% of Hurthle cells(2). Capsular, vascular or peri-thyroid invasion suggests malignancy along with lymph nodes and distant metastasis (2,5,6). Although cytology and molecular tests can sometimes predict malignancy, diagnosis is almost always brought by histology upon discovery of significant capsular or vascular invasion; however, this is not easy given the currently stricter criteria for identifying such invasion (11). Therefore many authors suggest that all HCN have malignant potential and should be managed by total thyroidectomy (2). HCC represents 5 to 40 % of nodules cytologically suspicious for HCN (3,6) and is more aggressive than other well-differentiated thyroid neoplasms (6).

On the other hand, FVPTC accounts for 9 to 22.5% of PTCs and is characterized by the presence of follicles lined by cells with PTC nuclear features (2). It has a better risk profile but a long-term outcome similar to classical PTC (8). Encapsulated FVPTC is now reclassified as NIFTP (2). The reason for this separation is to reduce overtreatment in regard to its highly indolent behavior compared to other variants of PTC (2,5). NIFTP is now considered a low- risk tumor which still can show aggressive behavior requiring follow-up (2). This entity first appeared in the literature in 2016 and is defined as a noninvasive neoplasm of follicular thyroid cells with nuclear features of PTC and a follicular configuration (5). Diagnosis criteria include encapsulation or clear separation from the surrounding tissue, follicular tumor growth, nuclear features of PTC, complete visualization of the capsule and no vascular or capsular invasion (2,5).

FNAB is an effective screening test for patients with thyroid nodules, with a 65-98% sensitivity and a 72-100% specificity but the diagnostic accuracy

is affected by nodule heterogeneity (1). In Bethesda System for Reporting Thyroid Cytopathology, there are six diagnostic categories: benign, atypia of undetermined significance/follicular lesion of undetermined significance (AUS/FLUS), follicular neoplasm/suspicious for follicular neoplasm, suspicious for malignancy, malignant and nondiagnostic (1). However, cytology is often unreliable in diagnosing HCNs (2). Even intraoperative frozen section examination is reported to be unhelpful and the only histopathology in the paraffin section is reliable (3). In our case, FNAB of the left nodule discovered atypical cells suspected of papillary cancer.

Ultrasound, FNAB and intraoperative frozen sections help to decide the extent of surgery. Management of incidental carcinomas (with a diameter smaller than 1 cm) is still controversial. Some authors indicate total thyroidectomy since those tumors are frequently associated with multifocal or bilateral lesions or occult lymph node metastasis; while others indicate conservative surgery (2). Some authors consider treating HCA only by lobectomy with follow-up, indicating total thyroidectomy only in cases of carcinoma (2, 3). Management of NIFTP is now less aggressive reducing psychological impact and costs. For instance, no radioactive iodine treatment is needed after lobectomy (5). However, some authors believe that NIFTP should be treated more seriously. Baloch reported a case of NIFTP with distant metastasis (2,12).

Thyroid gland neoplasms occur generally in a single type, and rarely in more than one type at the same time (4). PTC arising within HCA represents a rare, but important finding, due to controversies about the management of these two lesions (1,2,7). The hypothetical common follicular origin of HCA and PTC may explain the possible synchronicity of these two lesions (4). In our case, given the result of cytology, and to help to decide the extent of surgery, we performed a left lobectomy with a frozen section examination. It revealed a follicular adenoma of oncocyctic appearance. We completed immediately by a right lobectomy because many authors suggest that all HCN have malignant potential and should be managed by total thyroidectomy (2). We finally found a NIFTP in the other lobe. Given the very low risk of recurrence, no further therapy was needed after surgery.

In conclusion, the association of Hurthle cell adenoma and papillary microcarcinoma has been reported only one time before in the literature (4). We report here the association of a multifocal papillary microcarcinoma arising within an HCA synchronous

to an NTIFP that occurred in the other lobe, which has not been reported in the literature before. Many controversies remain about the management of HCA, PTC, and NFIPT. Although the management of our case did not change, more studies are necessary to analyze the evolution of patients with multiple thyroid neoplasms. When discussing therapeutic options, the advantages and disadvantages should be considered case by case based on disease staging.

Conflict of interest

The authors declare that they have no conflict of interest.

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