An unusual presentation of papillary thyroid carcinoma: a case report

Un carcinome papillaire de la thyroïde à révélation inhabituelle : à propos d'un cas

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Abstract

Parathyroid carcinoma (PC) is exceptional cause of primary hyperparathyroidism (PHPT). It has an estimated prevalence of 0.3 to 5.6% and is rarely associated with non-medullary thyroid cancer. We report a case of parathyroid carcinoma resulting in a hyperparathyroidism and revealing a papillary thyroid carcinoma, and emphasize on the management particularities of this entity.

A 37-year-old woman, with prolactin secreting pituitary microadenoma, presented with asthenia and bone pain. Laboratory findings were consistent with PHPT. Neck ultrasonography showed a 3 cm nodule adjacent to the right thyroid lobe with no abnormalities in the thyroid gland. Parathyroid scintigraphy showed a right inferior parathyroid adenoma. Because of the patient age and the decreased renal function, surgical treatment was required. During the intra-operative neck exploration, a juxta-thyroid tumoral right mass was strongly adherent to the right infra-hyoid muscle and the recurrent laryngeal nerve. The frozen examination of the mass demonstrated malignancy features suggesting a poorly differentiated thyroid carcinoma. Thus, a total thyroidectomy with bilateral central neck dissection was carried out. Final histopathological examination showed a 3.5 cm PC infiltrating the thyroid gland with a papillary thyroid microcarcinoma of the left thyroid lobe. External radiotherapy of the neck, indicated for PC, was performed 1 month after surgery. A radioactive iodine therapy was used 6 months postoperatively.

Despite its rarity, PC is to bear in mind in case of PHPT. The association between PC and differentiated thyroid carcinoma is not to be ignored.

Key-words: Primary hyperparathyroidism, parathyroid carcinoma, differentiated thyroid carcinoma, multiple endocrine neoplasia.

Résumé

Le carcinome parathyroïdien, étiologie très peu fréquente de l'hyperparathyroïdie primaire est rarement associé à un carcinome non médullaire de la thyroïde. Nous rapportons un cas doublement rare d'un carcinome parathyroïdien à l'origine d'une hyperparathyroïdie révélant un carcinome papillaire de la thyroïde en insistant sur les particularités de la prise en charge.

Il s'agit d'une patiente de 37 ans, suivie pour un micro-adénome hypophysaire à prolactine et consultant pour une asthénie et des douleurs osseuses. Les explorations biologiques ont conclu à une hyperparathyroïdie primaire. L'échographie cervicale a montré un nodule de 3 cm adjacent à la base du lobe droit de la thyroïde sans anomalie du parenchyme thyroïdien. La scintigraphie parathyroïdienne était en faveur d'un adénome parathyroïdien inférieur droit. L'indication d'un traitement chirurgical a été posée vu l'âge et devant un retentissement rénal. L'examen extemporané de la masse tumorale juxta-thyroïdienne droite qui était fortement adhérente au muscle infra-hyoïdien droit et au nerf laryngé récurrent, montrait des signes de malignité évoquant un carcinome thyroïdien peu différencié. Une thyroïdectomie totale avec curage cervical central bilateral ont été alors réalisés. L'histologie a conclu à un carcinome parathyroïdien de 3.5 cm infiltrant les tissus musculaires et la thyroïde avec un micro-carcinome papillaire thyroïdien lobaire gauche. Un traitement à d'iode radioactif a été indiqué. Cette irathérapie a été réalisée à 6 mois de la chirurgie, postérieurement à une radiothérapie externe de la région cervicale indiquée pour le carcinome parathyroïdien. Bien que rare, le carcinome parathyroïdien est à évoquer devant une hyperparathyroïdie primaire. L'association entre un carcinome parathyroïdien et un carcinome thyroïdien différencié est à ne pas méconnaître.

Mots clés : Hyperparathyroïdie primaire, carcinome parathyroïdien, carcinome différencié de la thyroïde, néoplasie endocrinienne multiple.

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INTRODUCTION

Primary hyperparathyroidism (PHPT) is a common endocrine disorder and its diagnosis frequency has increased since the advent of routine calcium level measurements. Parathyroid carcinoma (PC) accounts for only 0.5 to 5% of the cases (1). Synchronous differentiated thyroid cancer and PC is extremely rare. To our knowledge, 23 cases have been reported in English Medical Literature (2). We share our experience on an unusual case of PHPT revealing a PC associated with a papillary thyroid carcinoma (PTC) and we highlight characteristics of management.

CASE REPORT

A 37 year-old female presented with bone pain, deterioration of general status and epigastric pain. A year ago, the patient was followed-up for prolactin secreting pituitary microadenoma discovered in the context of primary infertility. Physical examination showed a right firm cervical mass with no other abnormalities. Biological tests were consistent with PHPT, showing high serum calcium level (3.2 mmol/l), hypophosphatemia with a range of 0.6 mmol/l (0.8-1 mmol/l), high level of parathyroid hormone (PTH) 1292 pg/ml which is 20 times the upper limit of normal (<65 pg/ml). The other biochemical serum markers were normal.

Neck ultrasonography demonstrated a nodule adjacent to the right thyroid lobe measuring 30*9 mm which was hypoechoic, homogenous, well-circumscribed and non-calcified. Otherwise, there were no abnormalities of the thyroid gland.

Tc-99m Sestamibi / Pertechnetate dual tracer with image subtraction parathyroid scintigraphy was also performed. It showed a focal uptake in the inferior pole of the right thyroid lobe suggesting a right inferior parathyroid adenoma (Figure 1).

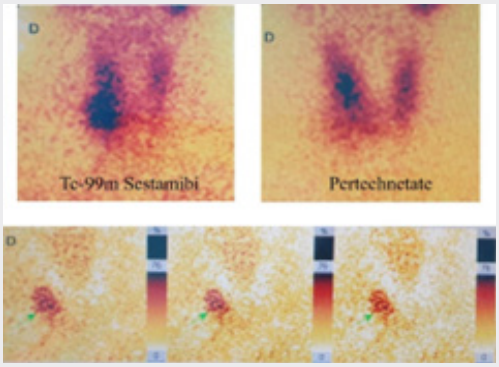


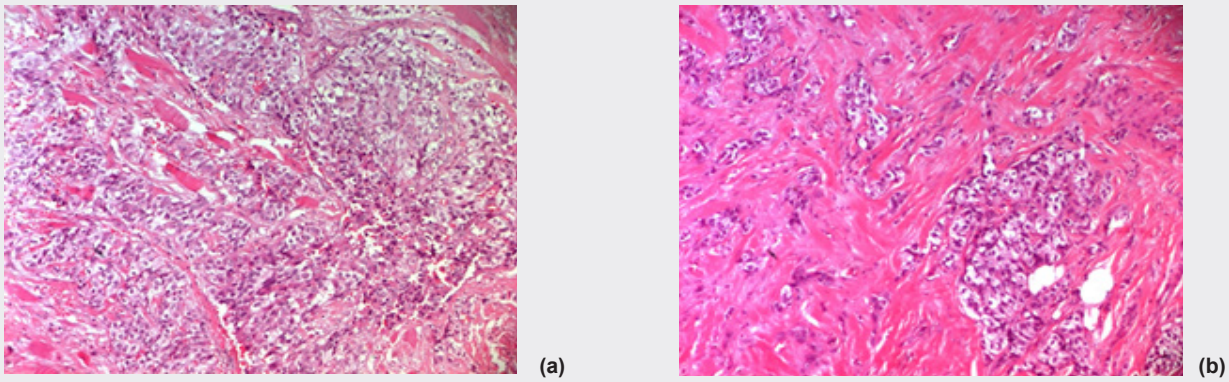
Figure 1. Tc-99m Sestamibi / Pertechnetate Subtraction parathyroid scintigraphy showing an abnormal focal uptake in the inferior pole of the thyroid lobe (Green arrow).

An abdominal ultrasound revealed nephrocalcinosis and a septated ovarien cyst. The pancreas was normal-sized with a homogeneous architecture. Surgical treatment was required due to the patient age and the decreased renal function.

During the intra-operative neck exploration, a juxta-thyroid tumoral right mass was strongly adherent to the right infra-hyoid muscle and the recurrent laryngeal nerve.

The frozen examination of the mass demonstrated malignancy features suggesting a poorly differentiated thyroid carcinoma. Thus, a total thyroidectomy with bilateral central neck dissection was carried out.

Final histopathological examination showed a 3.5 cm PC invading the adjacent muscle (Figure 2a, 2b). Immuno-histological staining of tumoral cells showed a strong and diffuse expression of GATA3, a marker of parathyroid differentiation as well as synaptophysin and chromogranin while thyroglobulin, TTF1 (thyroid Transcription Factor-1) and calcitonin markers were negative. The right central neck dissection yielded one metastatic lymph node among five.



(a) **(b)**

Figure 2. (a) Tumor cells proliferation invading the adjacent muscle / (b) Sclerotic stroma with tumor cells organized in clusters and cords.

The parathyroid tumor was therefore classified as pT3pN1b. In addition, histopathological examination revealed a papillary thyroid microcarcinoma of the left thyroid lobe with no lymph node involvement (the tumor was classified as pT1pN0).

Postoperatively, levothyroxine was administered to the patient at suppressive doses with calcium and vitamin D supplementation. External radiotherapy of the neck, indicated for PC, was performed one month after surgery. A radioactive iodine therapy was used 6 months postoperatively. The patient was treated with 3700 MBq of Iodine 131. The post-therapy scan of the neck and chest showed accumulation in the thyroid bed (Figure 3) with no other uptake foci elsewhere. Initial stimulated thyroglobulin was undetectable. Clinical and biological follow-up was performed at our department biannually.

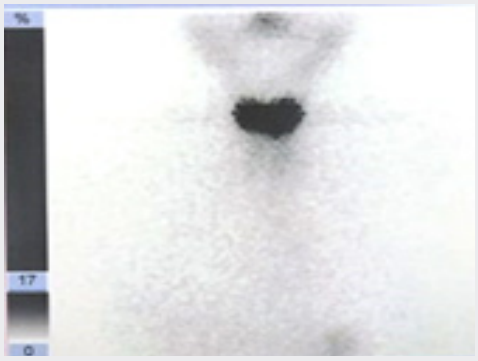


Figure 3. A scintigraphy performed 5 days after the administration of 3700MBq of I-131. A focused image on the neck region showed an intense uptake at the level of thyroid cartilage suggesting a thyroid remnant.

A multiple endocrine neoplasia type 4 was suspected because of papillary thyroid carcinoma, PC and pituitary adenoma. Genetic testing was decided to be performed to confirm the above disorder.

DISCUSSION

The reported case of our patient is particular because of the extreme rarity of parathyroid carcinoma, which accounts for 0.005% of all tumors (3). PC's diagnosis is based on final histological analysis. Nevertheless, in case of PHPT, some clinical and paraclinical features can suggest malignancy which are described in table (4). These elements are not specific to PC but their presence must draw the clinician's attention to optimize the surgical treatment. The preoperative evaluation of a patient with severe hypercalcemia and high PTH levels should include the possible diagnosis of parathyroid carcinoma, especially in symptomatic patients or in case of palpable neck mass (5).

Many studies have shown that an en bloc resection of the tumor along with the ipsilateral thyroid lobe and isthmus is the most effective treatment modality. This surgical approach improves the overall survival, given the high risk of recurrence (6).

Table 1 . Features suspecting parathyroid carcinoma in primary hyperparathyroidism [6]

Palpable neck mass
Association with recurrent severe pancreatitis, peptic ulcer disease and anemia
Recurrent laryngeal nerve palsy in a patient with no previous neck surgery
Concomitant renal and skeletal disease
Hypercalcemia > 3.5 mmol/l
High PTH level : 3-10 times above the upper limit of normal
High alkaline phosphatase level: above the upper limit of normal
Elevated levels of α- and ß-subunits of hCG

The second particularity of our case is the extremely rare association between parathyroid carcinoma and papillary thyroid carcinoma. A review of literature showed that most of the patients were women (75%) and that PTC was found incidentally on final histological examination, in most of the cases (7). This association's prognosis is rather correlated to PC. Physiopathology remains unclear. However, a review of published cases has shown the frequent association of thyroid pathology especially thyroid nodules or goiters and PHPT. Referring to the literature, the incidence of thyroid nodules in these patients ranges from 12 to 57% (8). Cinamon et al. consider PHPT as a noteworthy risk factor for PTC (9). These authors emphasized that patients with PHPT should have cytology of any thyroid nodule, including small subcentimeter lesions.

The third particularity to underline in our case is the possibility of genetic forms. The latest variant of the MEN syndromes is MEN type 4 (MEN4) which is characterized by an overlap of MEN type1 and gonadal, adrenal, renal, and thyroid tumors. Until now, only 19 cases have been reported in English literature. MEN4 is caused by germline mutations of the CDKN1B gene, codifying for p27kip1 which inhibits the cyclin-dependent kinases, involved in the control of cell cycle progression (10). Genetic tests are being carried out for our patient for the suspicion of a MEN4.

CONCLUSION

We present an unusual case of a papillary thyroid carcinoma revealed by PHPT associated with a parathyroid carcinoma. Despite its rarity, PC is to bear in mind in case of unusual presentation or severe PHPT considering that prognosis depends primarily on an early and appropriate surgical treatment. The association between PC and differentiated thyroid carcinoma has recently increased given a better management of the thyroid pathology. Our case reported underlines the need for genetic investigations when multiple endocrine neoplasia is suspected.

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