CLINICAL CASE

FROM VASOMOTOR SYMPTOMS TO SOLID AND INSULAR PAPILLARY THYROID CANCER WITH OXYPHIL VARIANT AREAS

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Abstract

The thyroid cancer had an increasing frequency during the last decades mostly related to better and accessible detection methods. The papillary type has the major epidemiologic impact. We present a case with mixed symptoms before surgery, a rare combination of both thyrotoxicosis and thyroid malignancy and an unusual pathologic report in a 56-year-old female known with total hysterectomy at age of 42, diagnosed with toxic goiter 2 years ago and under intermittent therapy with thiamazol. She presented for unspecific hot flashes and palpitation at gynaecology and she was referred for endocrine evaluation that revealed unspecific cervical compression complains, and a large goiter. The Thyroid-Stimulating Hormone was normal under thiamazol and so were the thyroid antibodies and calcitonin. The computed tomography pointed an isthmus and left lobe nodule of maximum 7.28 cm with mass effect on trachea. Total thyroidectomy was performed without any significant complications. The patient was hospitalised for 4 days (less than 48 hours postoperatively). The pathological report showed a papillary thyroid cancer (stage III) with oxyphil variant and an insular and solid pattern component. A high proliferative index is detected by vessels invasion and a ki-67 of 15 %. She received radioiodine therapy and then she started suppression levothyroxine treatment. The insular and oxyphilic pattern as well as the large tumour size of 6 cm suggest a severe prognosis. On the other hand, it is still a matter of debate whether non-autoimmune hyperthyroidism and solid pathologic features subscribe to the hypothesis of an aggressive cancer phenotype. Lifelong follow up is needed.

Keywords*: thyroidectomy, thyroid neoplasia, oxyphil, papillary cancer*

Introduction

The thyroid cancer is the most frequent oncologic profile in endocrine patients. The clues to diagnose and treat this disease might not always be so clear depending on the level of population's education to regularly present to a medical evaluation, on the access to current imagery techniques up to the most sophisticated ones as metabolomics, on the pathologic type and the rapidity of its growing and spreading [1]. Except for secondary malignant implants in thyroid, which otherwise is not a frequent site of metastasis, there are mainly four types of primary thyroid cancers: three derived from follicular cells, papillary, follicular and

anaplastic and one coming from C para-follicular cells namely medullar thyroid cancer. Their frequency dramatically increased during the last decades because of widely used detection methods from neck ultrasound to computed tomography, etc.[2].

The prognosis in papillary cancer which is the most frequent subtype of thyroid malignancy, varies largely depending on pathological details, size of the lesion, patient's age, lymph nodes involvement. We present a most interesting multidisciplinary case of a woman with a large panel of symptoms, from menopausal-like vasomotor symptoms to neck intermittent compressive complains and thyrotoxicosis related goiter that underwent surgery. The pathological report was thus provided and it pointed to an unusual combination of features: a background of papillary thyroid cancer with focal oxyphilic variant and both insular and solid pattern.

Case presentation

56-year-old female, non-smoker, coming from an endemic zone, is known with arterial hypertension controlled with hypotensors and with total hysterectomy at age 42 for uterine fibroma. She has been diagnosed with toxic goiter 2 years ago and she is under intermittent therapy with low doses of thiamazol. She presented for unspecific hot flashes and palpitation at gynaecology but after adequate evaluation she was referred to an endocrine consultation. On admission the patient also accused unspecific cervical compression complains and a large goiter especially on the left side was detected.

The blood biochemistry tests were normal. The Thyroid-Stimulating Hormone (TSH) was 1.59 µUI/mL (normal levels between 0.5 and 4.5 µUI/mL) and FreeT4 was 10.54 pmol/L (normal ranges between 9 and 19 pmol/L) under daily 5 mg of thiamazol. The thyroid antibodies were negative. Serum calcitonin (chemolumine-scence) was low of 0.86ng/mL (the normal levels are between 5.15 and 9.82 pg/mL). The thyroid ultrasound showed a left thyroid nodule of 5 centimetres (cm). The anterior cervical and anterior mediastinum computed tomography with contrast medium was performed. (Figure 1) The thyroid had increased dimensions; it was asymmetrical, and spontaneously heterogeneous with microcalcifications. The right thyroid lobe was of 2.19 by 2.35 by 5.03 cm. The thyroid isthmus and the left lobe were occupied by a nodule of 4.05 by 4.42 by 4.44 cm (on the median line) and of 7.28 cm (on the left side) with mass effect over trachea with a minimum diameter of 1.71 by 1.7 cm at the clavicles level of section (Figure 1,2).

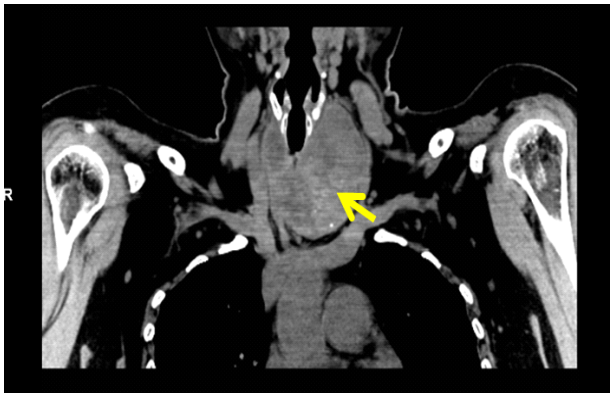

Figure 1 - Computed tomography (coronal plane): left thyroid and isthmus macronodule

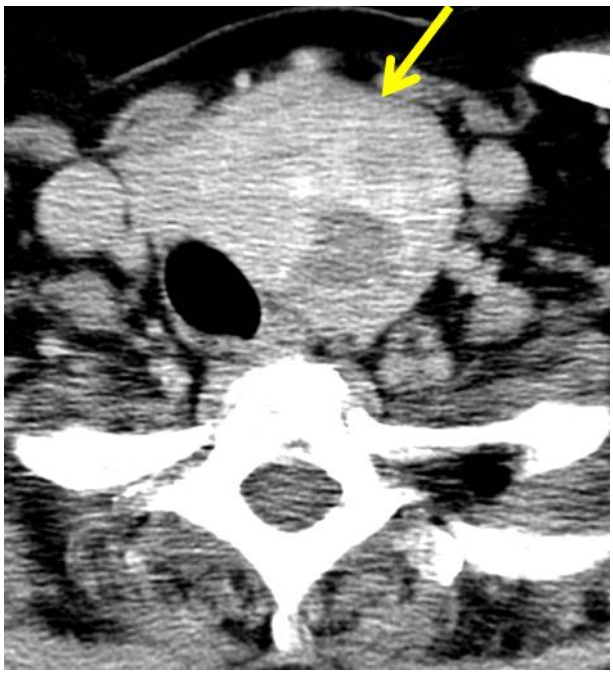

Figure 2 - Computed tomography (transversal plane): heterogeneous aspect of the left thyroid tumour

The patient was referred for surgery. Total thyroidectomy was performed without any major incidents or complications (except for a small hemorrhagic incident at the Berry's ligament on the right; temporary postoperative hypocalcemia). She was hospitalised for 4 days and discharged under levothyroxine therapy

(daily 100 μg). The pathological report showed a papillary thyroid cancer of 6 by 3 by 2.8cm at the left thyroid nodule (stage III). The tumour associates oxiphile variant and an insular and solid pattern component (Figure 3,4).

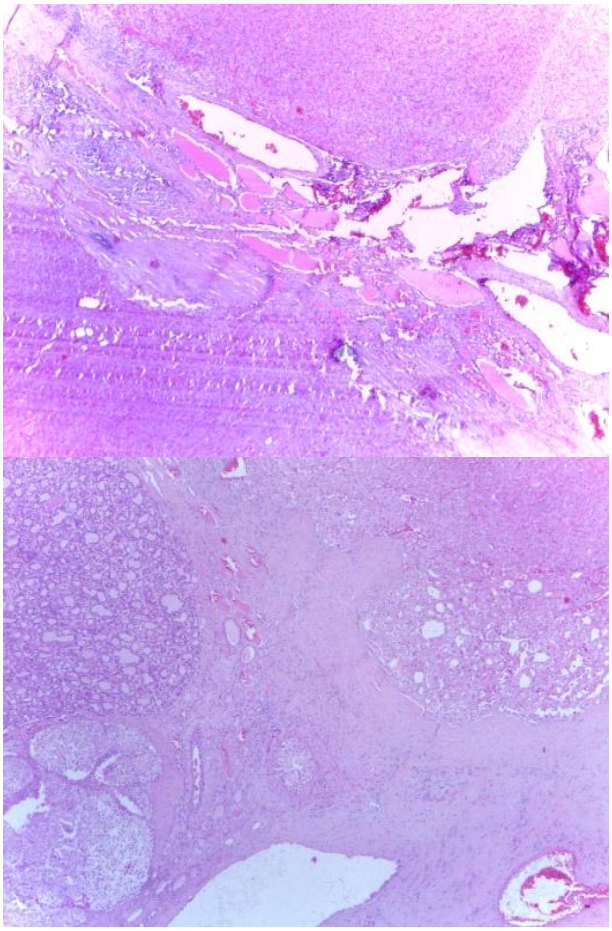

Figure 3 - Pathological exam: papillary thyroid cancer (focal oxyphil variant); hematoxylin – eosin (HE 4X)

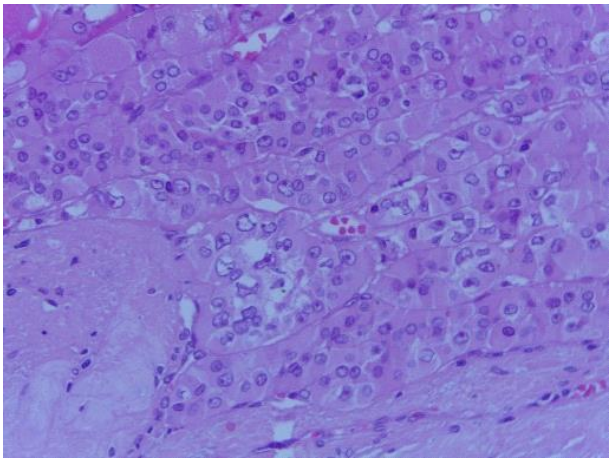

Figure 4 - Pathological exam: papillary thyroid cancer; hematoxylin – eosin (HE 40X)

Immunohistochemistry was performed. Thyroglobulin diffuse positive immunostain was detected in papillary cancer cells, and CK19 locale positive reaction in papillary cancer cells. (Figure 5,6) A high proliferative index is detected by vessels invasion and a ki-67 of 15 %. (Figure 7) After one month she stopped the substitution medication to receive a first dose of radioiodine therapy after which she started suppression levothyroxine treatment. She needs lifelong evaluation.

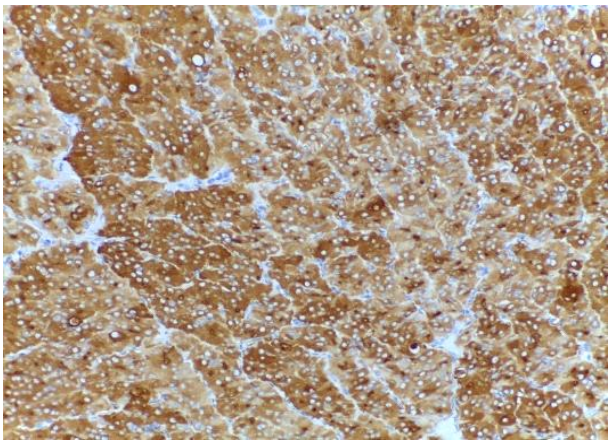

Figure 5 - Thyroglobulin diffuse positive immunostain in papillary cancer cells (10X)

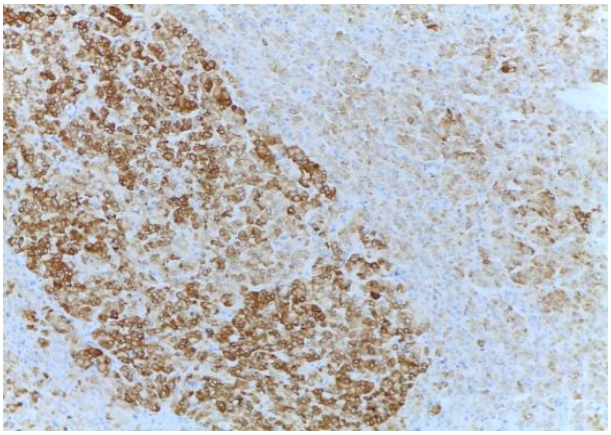

Figure 6 - CK19 locale positive immunostain in papillary cancer cells (10X)

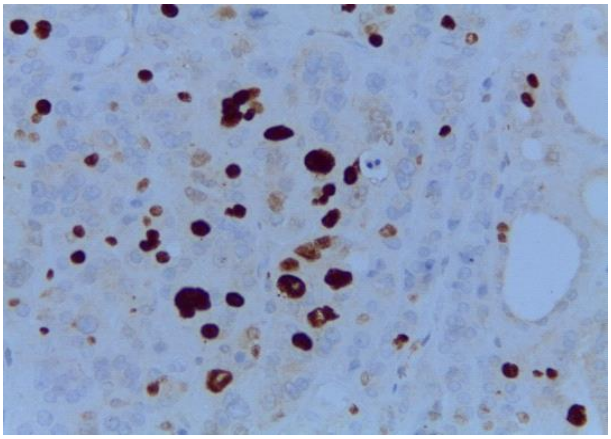

Figure 7 - ki-67 positive of 15% in thyroid cancer cells (40X)

Discussions

The surgery is the gold standard therapy in papillary cancer. This is a life saving first line option. The total thyroidectomy is preferred to thyroid lobectomy for longer safety reasons [3]. Complications may be found regardless the approach, but mostly in less than 1% of cases [4]. The most frequent complications are hypocalcemia and recurrent laryngeal nerve injury [5]. In this case although the post – thyroidectomy total calcium level was less than normal (7.5 mg/dL first day after surgery and 7.2 mg/dl postoperative day 2) it became normal within one month after the procedure. One month after surgery the intact blood parathormone was normal of 31.8 pg/mL (normal levels between 15 and 65 pg/mL), so no permanent hypoparathyrodism was detected.

A poorer prognosis is seen in tumors larger than 2 cm diameter, as in the present case, thus, after surgery, radioiodine remnant ablation is essential to be associated with suppression levothyroxine therapy based on serum thyrotropin levels. A lifelong follow-up is necessary. Constant neck ultrasound and thyroglobulin level checks up are also indicated [6].

A rare situation is like the one we have presented, that before surgery the patient was diagnosed with thyrotoxicosis that mimicked menopausal vasomotor symptoms although our patient had previous surgical menopause, with no estrogen substitution therapy. Studies regarding hyperthyroidism related papillary cancer prognosis are inconclusive, most probably the thyroid dysfunction before surgery does not correlate with a more severe outcome [7].

The ki-67 reaction has an increased value in this case. The correlation with the tumour size and severe prognosis has been suggested [8]. The solid pattern as seen in this case is controversially related to a higher risk of recurrence. Some authors consider that its prognosis should be assimilated in classical papillary form [9].

Up to this moment in this case distant metastases were not found. Despite classical lines of therapy, 5% of papillary thyroid cancers metastasize. Some genetic anomalies as RET/PTC mutations, MAP-Kinase pathway dysfunction, mTOR and VEGFR pathway disruptions have been found behind this aggressive pattern in association to pathologic features that are closer to mostly aggressive type as anaplastic thyroid cancer as oxyphilic areas or insular structures in the classic papillary pattern [10,11]. Targeted therapies should be an option. Second surgery is rarely necessary [12]. The second line therapeutic options if the disease spreads are proteasome inhibitors as sorafenib, vandetanib, cabozatinib with clinical approval [10,11]. Some of these inhibitors may be currently used and some are under evaluation as carfilzomib [13].

The thyroid fine needle aspiration before surgery is very useful but in this case it was not necessary since the patient had surgical indication from the beginning, based on the high dimensions of the left thyroid nodule with mass effect, the thiamazol use for more than 2 years and the suspect aspects in thyroid ultrasound and computer tomography [14].

Conclusions

This adult female case highlights the usefulness of a multidisciplinary approach in a case of thyroid cancer that has a complex pathologic profile, surgery being the major step in treating the patient.

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