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Autonomously hyperfunctioning cystic nodule harbouring thyroid carcinoma – Case report and literature review

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ABSTRACT

INTRODUCTION: Hyperthyroidism is rarely associated with malignancy, but it cannot rule out thyroid cancer. Although there is published data describing this coexistence, thyroid carcinomas inside autonomously functioning nodules are uncommon.
PRESENTATION OF CASE: A 49-year-old woman presented with a cervical mass, unexplained weight loss and anxiousness, sweating and insomnia. On physical examination, she had a palpable left thyroid nodule. Thyroid function tests showed suppressed TSH (<0,1 uUI/mL), thyroxine 1,44 ng/dL (normal range 0,70–1,48) and triiodothyronine 4,33 pg/mL (normal range 1,71–3,71). Ultrasound imaging revealed a left lobe, 4 cm partial cystic nodule. 99mTC thyroid scintigraphy showed a hyperfunctioning nodule with suppression of the remainder parenchyma. Fine-needle aspiration cytology was nondiagnostic (cystic fluid). The patient was started on thiamazole 5 mg daily with subsequent normalization of thyroid function, but she developed cervical foreign body sensation and a left hemithyroidectomy was performed. Histology showed a 4 cm cystic nodule with a follicular variant papillary carcinoma and the patient underwent completion thyroidectomy, followed by radio-iodine ablation.
DISCUSSION: Published literature showed an increased prevalence of autonomously functioning nodules, harbouring thyroid carcinomas in adults. Papillary carcinoma is the most frequently described but the follicular variant is rare.
CONCLUSION: Although rare, thyroid cancer is not definitively excluded in hyperthyroid patients and it should always be considered as differential diagnosis.
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1. Introduction

The most common causes of hyperthyroidism are toxic adenomas and Graves' disease [1,2]. These conditions are usually suggestive of benignity but malignant disease can be present incidentally or in a toxic adenoma [1–11]. Scintigraphy should be performed in all hyperthyroid patients with thyroid nodules: 80–85% of them are "cold", of which 10% are carcinomas [12]. "Hot" nodules correspond to hyperfunctioning adenomas and the likelihood of malignancy is less than 1% [12]. Many authors described thyroid malignant neoplasms in patients with hyperthyroidism, but in the majority of cases, they are incidentally found (out of the index nodule). Toxic thyroid nodules harbouring carcinoma are very rare (1%) [9]. Some studies suggested that nodule size is an independent risk factor of malignancy, but the results are controversial [13,14]. Fine-needle aspiration cytology (FNAC) is a reliable and cost-efficient method to evaluate thyroid nodules, with an overall accuracy of 98% and a false negative rate below 5% [13]. However, its reliability in large nodules is not clear. Published data described a lower sensitivity (65–98%) and higher false-negative rate (4–30%) in nodules larger than 4 cm [12–14]. In cystic thyroid malignancies, performing a diagnostic FNAC is challenging due to the lack of cellularity in cystic areas, presence of nuclear debris and histiocyte/macrophages, that frequently lead to misdiagnosis of a cystic benign nodule [15]. We present an uncommon case of papillary thyroid carcinoma of the follicular variant (PTCFV) in an autonomously hyperfunctioning thyroid nodule. This article has been reported in line with the SCARE criteria [16].

2. Presentation of case

A 49-year-old woman was referred to an endocrinology consultation for evaluation of a cervical mass. The patient described

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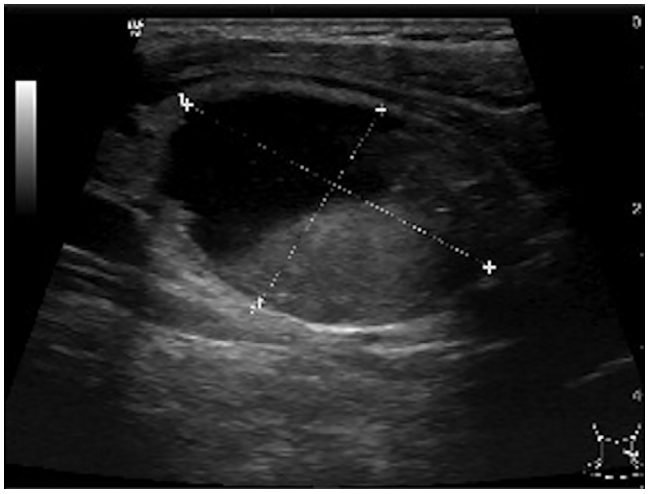

Fig. 1. Thyroid ultrasound imaging revealing a left lobe 4 cm nodule, predominantly cystic.

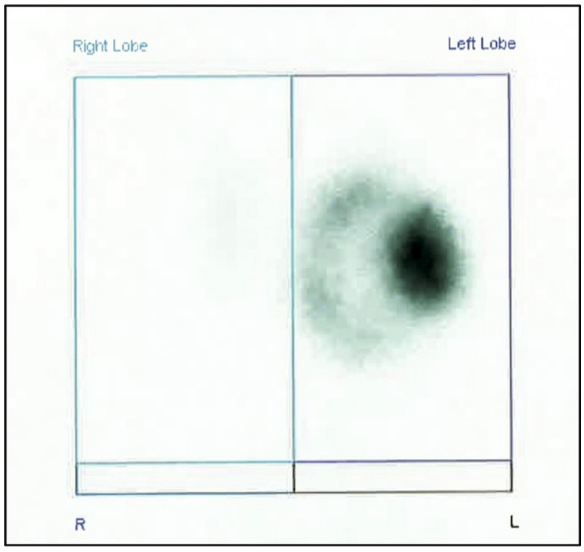

Fig. 2. 99mTC Thyroid scintigraphy image showing a left hyperfunctioning nodule and a suppression of the remainder parenchyma.

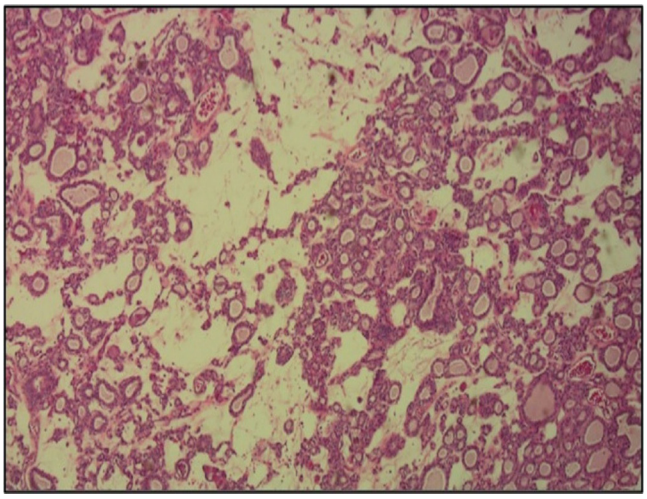

Fig. 3. Histological image showing a malignant neoplasm of follicular pattern with cytological features of papillary carcinoma and cystic degeneration.

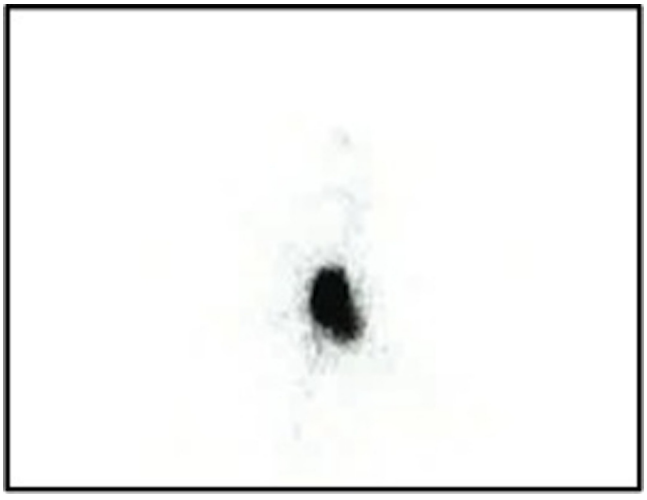

Fig. 4. Post-radioiodine ablation scintigraphy showing one foci of ^{131}I uptake in the thyroid bed.

unexplained weight loss (18%) and anxiousness, sweating and insomnia. On physical examination, she had a palpable left thyroid nodule and no lymph nodes were palpable. Thyroid function tests showed suppressed TSH (<0,1 uUI/mL) with normal levels of thyroxine 1,44 ng/dL (normal range 0,70–1,48) and elevated levels of triiodothyronine 4,33 pg/mL (normal range 1,71–3,71). Ultrasound imaging revealed an asymmetrical thyroid with a 4 cm nodule, predominantly cystic, in the left lobe (Fig. 1). 99mTC thyroid scintigraphy showed a left lobe hyperfunctioning nodule (uptake 4,2%) with necrotic and haemorrhagic central area and a suppression of the remainder parenchyma (Fig. 2). Under ultrasound guide, fine-needle aspiration was performed and cytology was only representative of cyst fluid, bearing no epithelial cells. The patient was started on thiamazole 5 mg daily with subsequent normalization of thyroid function. Clinically, the patient developed cervical foreign body sensation and she was referred to surgery consultation. A left hemithyroidectomy was performed. Gross description comprised a 5,1 × 4,8 × 2,8 cm specimen with 14.9 g and irregular surface, exhibiting a 4,2 × 3,2 cm nodule with an extensive cystic area of 1,6 cm. On histological examination, a malignant neoplasm of follicular pattern was observed, with large overlapping nuclei, optically clear chromatin and longitudinal nuclear grooves, reported as a follicular variant papillary carcinoma (with cystic transformation). There was neither multicentricity nor vascular invasion (Fig. 3). The patient underwent completion thyroidectomy followed by radio-iodine ablation (101,9mCi). The post-treatment scintigraphy showed one cervical uptake foci in the thyroid bed (Fig. 4). After two years' follow-up, she is asymptomatic and well substituted.

3. Discussion

Autonomic thyroid carcinomas are very rare, although published literature showed an increase of these cases in adults [2–4,6,9]. Until 2008, 14 relevant case series described 1124 cases of solitary hyperfunctioning nodules submitted to surgery and associated with thyroid cancer, but only in 35 the cancer was in the hyperfunctioning nodule [5]. In 2013, Mirfakhraee et al. published a literature review of 77 malignant hot nodules. They described 44 papillary (8 PTCFV) and 28 follicular carcinomas. Only 23 were biopsied before surgery: 7 (30,4%) cases characterized as benign were false negatives (3 were papillary of which 1 was PTCFV) and 4

(17,4%) were nondiagnostic [5]. Luca Giovanella et al. reported a 68-year-old female with a solid/trabecullar follicular carcinoma inside a 5 cm hot nodule [10]. Seven case reports described papillary carcinomas inside autonomously functioning nodules [1,2,4,6,8,9,11]. Mehmet Uludag et al. published a report of a micropapillary thyroid cancer in a Marine-Lenhart Syndrome nodule [1]. There are two published cases of PTCFV inside solitary hot nodules. Monalisa Azevedo et al. reported a 47-year-old woman with a solitary 2,5 cm nodule and hyperthyroidism. Scintigraphy confirmed a "hot" nodule with no iodine uptake in the remaining tissue and the FNAC was suggestive of papillary carcinoma. After total thyroidectomy, histopathology confirmed a 3 cm PTCFV [9]. Kuan et al. described a case of a 60-year-old woman with hyperthyroidism and a 8 cm solitary nodule, confirmed to be autonomously hyperfunctioning in the scintigraphy. FNAC showed a follicular lesion and a total thyroidectomy was performed. Histological examination described an 8 cm PTCFV [6].

Here, we present a patient that was proposed to surgery because she was clinically symptomatic. Scintigraphic and cytological features of the nodule didn't predict thyroid carcinoma. Scintigraphy described a solitary "hot" nodule, mimicking a toxic adenoma. FNAC was nondiagnostic. The size of the nodule (>4 cm) could have compromised the reliability of the cytological result and this sample was not representative of the malignant nodule. Although a common finding, papillary thyroid carcinomas that undergo cystic transformation are a diagnostic challenge in fine-needle aspiration. The lack of diagnostic epithelial cells in the cystic component aspiration led to false negative interpretation of cytological result. Final diagnosis of PTCFV was unexpected and it was only established post-operatively.

4. Conclusion

The association of thyroid carcinoma and hyperthyroidism is rare and the published evidence showed that systematic exclusion of malignancy is not cost-effective in autonomously functioning nodules. However, hyperthyroidism does not definitively exclude thyroid carcinoma and it should always be considered as differential diagnosis.

Conflict of interest

The authors declare that there are no conflicts of interest.

Sources of funding

The authors declare that there were no sources of funding.

Ethical approval

This article is single case report and the patient gave informed consent for the report and p the publication of this clinical case. Therefore, Ethical Committee approval has been exempted from our institution.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request. There were no altered characteristics that distort scientific meaning.

Author contribution

Maria João Lima – data collection, data interpretation, writing the paper.
Virgínia Soares – data interpretation, writing the paper.
Pedro Koch – data interpretation, writing the paper.
Artur Silva – data collection, writing the paper.
António Taveira-Gomes – data interpretation, writing the paper.

Guarantor

The guarantors of this article are Maria João Lima and António Taveira-Gomes.

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