Case Report
Hyperfunctioning Solid/Trabecular Follicular Carcinoma of the Thyroid Gland

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1. Introduction

Hyperthyroidism due to thyroid carcinoma is an extremely rare phenomenon. It is commonly believed that the diagnosis of a solitary autonomously functioning thyroid nodule (AFTN)—a solitary “hot” nodule in radionuclide imaging—can almost always rule out malignancy in the nodule [1]. In this paper, we present the rare case of follicular carcinoma manifesting as an AFTN.

2. Case Report

A 68-year-old female, affected by a long-standing asymptomatic normally functioning nodule in the right lobe of the thyroid, developed symptoms of neck swelling and palpitations. The patient presented a resting pulse rate of 108 and blood pressure of 145/90 mmHg. A large, well-defined, hard nodule was palpable in the right lobe of the thyroid; the left lobe was normal, and there were no cervical lymphadenopathies. Ultrasonography (US) of the thyroid revealed a large and slightly hypoechoic nodule (diameters: 33 × 38 × 53 mm). Thyroid function tests showed elevated free triiodothyronine (fT3) of 7.60 pmol/L (reference range 2.30–6.30 pmol/L) and undetectable thyroid-stimulating hormone (TSH) of 0.006 mIU/L (normal 0.4–4.0 mIU/L). The free thyroxin (fT4) was normal at 11.4 pmol/L (reference range 7.5–21.1 pmol/L), and both thyroperoxidase and thyrotropin-receptor autoantibodies were negative (<60 U/I/mL and <1 U/L, resp.). A 99mTc-perthecnetate scan demonstrated a large hot area with inhomogeneous uptake and no cold areas inside corresponding to the nodule, with a suppressed uptake in the remaining thyroid tissue. Histopathological examination of the nodule revealed a solid/trabecular follicular thyroid carcinoma. To the best of our knowledge, this is the first case of hyperfunctioning follicular solid/trabecular carcinoma reported in the literature. Even if a hyperfunctioning thyroid carcinoma is an extremely rare malignancy, careful management is recommended so that a malignancy will not be overlooked in the hot thyroid nodules.
revealed a follicular carcinoma with solid and trabecular parts and focal signs of angioinvasivity (Figures 2(a), (b)). The surrounding thyroid tissue showed a follicular architecture with no signs of tumour infiltration or spreading. Since the patient declined further surgery, a radioiodine ablation was directly performed by administering $^{131}$I (2.5 GBq). Serum thyroglobulin was 9.4 ng/mL before $^{131}$I treatment, with a corresponding TSH level of 36 mUI/L. Six months after thyroid ablation, a $^{131}$I whole-body scanning after recombinant human TSH administration was negative with a corresponding undetectable serum Tg (i.e., <0.2 ng/mL). Further followup by clinical examination, including neck US and Tg measurement, every 6 months, is negative up to now (3.4 years follow-up).

3. Discussion

Our patient presented with a palpable thyroid nodule and hyperthyroidism with the absence of TRAb and TPOAb. The nodule was proved to be functionally autonomous by $^{99m}$Tc-pertechnetate imaging and RAIU. However, a follicular solid/trabecular carcinoma was finally proved by histological examination. Hyperthyroidism due to thyroid carcinoma is a rare, but well-recognized phenomenon. This situation has been generally described as resulting from excessive production of thyroid hormone by extensive functioning metastases, usually from follicular carcinoma [2, 3]. The incidence of thyroid carcinoma in a hot nodule is reported to be very low by most authors [4–6], but the incidence

Figure 1: $^{99m}$Tc scan: hot thyroid nodule in the right thyroid lobe with suppressed extranodular thyroid tissues (a). Surgical specimen from right lobectomy and isthmectomy (b).

Figure 2: Hematoxylin/eosin histological stains: follicular carcinoma with solid (a) and solid-trabecular (b) features.
is somewhat higher in other retrospective studies [7, 8]. Actually, thyroid carcinoma in a hot nodule has been described in numerous case reports prior to ours. However, unlike our case, most of these cases show a cold area within a hot nodule, indicating that the thyroid carcinoma itself did not produce thyroid hormone [9]. Women are far more often affected than men, but no significant peak with regard to age was noted [10]. Interestingly, the histological features of these tumors correspond in principle to the papillary carcinoma, as opposed to the metastatic functioning carcinomas, essentially being of follicular type [11–15]. Classical follicular histology is described in the few reported cases of hyperfunctioning follicular carcinoma while only one case with a clear-cell variant histotype is described [16–18]. To the best of our knowledge, we are the first to report a case of hyperfunctioning aggressive follicular carcinoma with solid and trabecular features. This case underlines the clinical importance of predicting the incidence of malignancy in hot thyroid nodules. However, reports in the literature indicate significant difficulty in determining the risk that AFTN will undergo malignant degeneration. Some clinical findings set forth the risk factors for malignancy in thyroid nodules: age <20 or >60 years, male sex, the family history of differentiated or medullary thyroid carcinoma or of familial adenomatous polyposis (Gardner’s syndrome), past history of head and neck radiation, rapid tumor growth, irregular outline, fixation to adjacent structures, and symptoms of tumor invasion [1, 15, 19]. In actual practice, however, few patients have these symptoms, and most nodules are nearly asymptomatic [1]. The classical benign AFTN presents itself as a smooth, well-defined, round or ovoid mass that moves freely and occurs in patients aged 40 or over with a history of long-standing and slowly expanding mass in the neck [19]. The US pattern, as well as the vascular signals in power or color-Doppler samplings, is largely overlapped in malignant nodules and AFTN, as occurred in our patient [1]. An incomplete suppression of radionuclide uptake in extranodular thyroid tissues was reported as a risk factor of malignancy, but this did not occur in our patient [20]. Differentiating a benign follicular adenoma from a malignant follicular carcinoma is challenging by cytology, and a thyroid scan is advocated in these cases, considering functioning nodules as being benign [1, 21]. Hot nodules outside the thyroid can be helpful in diagnosis of malignancy in the case of metastatic thyroid carcinoma, but this is rare in practice [22]. In our patient, surgical treatment was preferred to radiiodine ablation considering her symptoms and the nodule's size. However, 131I could be administered under medical guidelines for clinical practice for the diagnosis and management of thyroid nodules [1]. K. Kasagi, R. Takeuchi, S. Miyamoto et al., “Metastatic thyroid cancer presenting as thyrotoxicosis: report of three cases,” Clinical Endocrinology, vol. 40, no. 3, pp. 429–434, 1994.

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