

Case Report

Coincidental Thyroid Papillary Microcarcinoma in a Patient Treated for a Toxic Adenoma of the Thyroid

Stergios A. Polyzos MD MSc¹, Dimitrios G. Goulis MD PhD²

Abstract

Thyroid carcinoma is not uncommon in patients with hyperthyroidism. However, the risk of malignancy in patients with autonomously functioning nodules continues to be underestimated in clinical practice, possibly due to the belief of rare co-existence of a “hot” nodule and thyroid carcinoma. We present hereby a man with hyperthyroidism due to a thyroid toxic adenoma, who was subjected to surgery and incidentally found to have a papillary thyroid microcarcinoma on the contralateral thyroid lobe. By reviewing the literature, incidental thyroid carcinoma in patients subjected to thyroidectomy for a hyperfunctioning nodule, both within and out of the nodule is not a rare event. However, the incidental finding of thyroid carcinoma out of a hyperfunctioning nodule is not adequately reviewed in the literature.

Keywords: fine needle biopsy, radionuclide imaging, thyroid carcinoma, thyroid nodule, ultrasonography

Introduction

Thyroid nodules are very common in clinical practice with an estimated prevalence of about 5% by palpation, increasing up to 50% in elderly individuals after the generalized use of thyroid ultrasonography. Although they are usually benign, malignancy should always be excluded.¹

Thyroid carcinoma is not uncommon in patients with hyperthyroidism. The risk of malignancy seems to be increased in patients with concomitant Grave’s disease,²⁻⁴ whereas it is approximately the same in patients with autonomously functioning nodules or toxic multinodular goiters compared to euthyroid patients with thyroid nodular disease.³⁻⁵ Furthermore, incidentally found thyroid carcinoma is not uncommon in patients subjected to surgery for hyperthyroidism^{4,6-9} or apparently benign thyroid disease.^{8,10,11} Nevertheless, the risk of malignancy in patients with autonomously functioning nodules continues to be underestimated in clinical practice, possibly due to the belief of rare co-existence of a “hot” nodule and thyroid carcinoma.¹² This belief continues to lead to abuse of thyroid scintigraphy in euthyroid patients in order to differentiate the “cold” nodules with considerably high malignant potential from the “warm” or “hot” ones with low malignant potential. This practice is more common in Europe than in the USA¹³⁻¹⁶ and in family physicians compared to specialists.¹⁷

We present hereby the case of a gentleman with hyperthyroidism due to a thyroid toxic adenoma, who was subjected to surgery and incidentally found to have a papillary thyroid microcarcinoma on the contralateral thyroid lobe. To our knowledge, the incidental thyroid carcinoma out of a hyperfunctioning nodule, although considered *de facto* a common finding, is not adequately reviewed in the literature. The aim of this case report and review of the literature was to highlight that a hyperfunctioning thyroid nodule cannot exclude thyroid malignancy either within or out of the nodule.

Case Report

A 57-year-old man presented to our clinic in Thessaloniki, Greece in March 2009 for hand tremor and unexplained anxiousness. His personal medical history included coronary artery disease since 2007, hyperlipidemia since 2006 and depressive disorder since 2005. At presentation, he was receiving atenolol 50 mg, acetylsalicylic acid 100 mg, simvastatin 20 mg and paroxetine 10 mg daily. The patient reported no history of head or neck irradiation. Physical examination revealed a large thyroid nodule (approximately 3 cm) within a moderately enlarged thyroid (goiter). No other palpable nodule was found. His weight was 92 kg, height 1.71 m (body mass index 31.5 kg/m²), systolic blood pressure 140 mm Hg and diastolic blood pressure 100 mm Hg. Blood tests revealed primary hyperthyroidism with serum thyroid-stimulating hormone (TSH) 0.1 IU/L (0.4 – 4.0 IU/L), free thyroxine (FT₄) 2.0 ng/dL (0.8 – 1.9 ng/dL), and free tri-iodothyronine (FT₃) 3.9 pg/mL (1.8 – 4.2 pg/mL). Serum thyroid peroxidase (TPO) and thyroglobulin (TG) antibodies were normal (32 IU/mL and 25 IU/mL, respectively, reference range for both: 0 – 60 IU/mL) and erythrocyte sedimentation rate (ESR) was 4 mm/hr. Serum renal

Authors’ affiliations: ¹Second Medical Clinic, Medical School, Aristotle University of Thessaloniki, Ippokraton Hospital, Thessaloniki, Greece, ²Unit of Reproductive Endocrinology, First Department of Obstetrics and Gynecology, Aristotle University of Thessaloniki, Greece.

Corresponding author and reprints: Stergios A. Polyzos MD MSc, 13 Simou Lianidi St., 55134 Thessaloniki, Greece.

Tel: +30-2310-424710; Fax: +30-2310-424710; E-mail: stergios@endo.gr
Accepted for publication: 29 September 2010

and liver function tests were normal.

A thyroid scintigraphy with 6 mCi technetium pertechnetate (^{99m}Tc) revealed an area of increased radioactivity at the middle of the right lobe (uptake 2.7%) with suppression of ^{99m}Tc uptake in the rest of thyroid parenchyma, findings suggestive of a toxic adenoma. Ultrasonography of the neck revealed a 2.0×1.8 cm, hypoechoic, dominant nodule in the right lobe and three hypoechoic nodules in the left lobe of maximum diameter 0.6 cm. No lymph nodes were depicted.

The patient received carbimazole 15 mg daily, in divided doses, which was decreased to 10 mg after two months (May 2009) and 5 mg daily a month later (June 2009). On October 2009, euthyroidism was achieved (TSH 3.6 IU/L, FT₄ 1.1 ng/dL and FT₃ 3.03 pg/mL) and the patient subjected to uncomplicated total thyroidectomy. No suspicious cervical lymph nodes were reported during intraoperative exploration.

Macroscopic pathology examination revealed a nodular goiter (total thyroid weight 50 g) with a dominant yellow-brownish nodule of maximum diameter 3.0 cm on the right lobe and multiple smaller nodules of maximum diameter 0.7 cm. The dominant nodule was microscopically a colloid adenoma, as well as most of the smaller nodules. However, a papillary thyroid microcarcinoma (maximum diameter 0.2 cm) was found in one of the smaller nodules on the left lobe. The carcinoma was of follicular variant without capsular or vascular invasion.

Postoperatively, the patient did not receive radioiodine ablation because of the small carcinoma size and the absence of invasion. There was no evidence of thyroid tissue on postoperative ultrasonography. He received thyroxine sodium 100 µg daily, targeting to a low-normal or mildly suppressed TSH. On March 2010, he was euthyroid and asymptomatic (TSH 0.6 IU/L, FT₄ 1.3 ng/dL).

Discussion

In this report, a man with a thyroid toxic adenoma and papillary thyroid microcarcinoma on the contralateral thyroid lobe is presented. He was subjected to surgery because of a hyperfunctioning nodule on the right thyroid lobe causing hyperthyroidism. The papillary thyroid microcarcinoma was incidentally found after thyroidectomy.

Incidental thyroid carcinoma or microcarcinoma in patients subjected to thyroidectomy for hyperfunctioning (or scintigraphically “hot”) nodules have been encountered in clinical practice,^{4,6,8,9,11} but are rarely described adequately. However, in a recently published series, 88% of microcarcinomas diagnosed between 1993 and 2007 were incidental and 6% of incidental papillary carcinomas were found at surgery performed for a “hot” nodule.⁸ In another series, incidental carcinoma was found in one of the patients (3.7%) subjected to surgery for a hyperfunctioning thyroid nodule.¹¹

In the literature there are many cases^{18–32} and some se-

ries^{3–5,33} reporting carcinomas within hyperfunctioning (or scintigraphically “hot”) thyroid nodules. They are more often unifocal papillary microcarcinomas, but multifocal,²¹ follicular or Hürthle cell hyperfunctioning carcinomas^{25,28} have been reported as well. In our 941 patient series, there was no statistical difference in the rates of malignancy among scintigraphically “hot” (n=4, 9.3%) and “cold” nodules (n=37, 10.7%).⁵

These considerations render the routine use of scintigraphy useless in thyroid nodular disease, since a hyperfunctioning or “hot” nodule may harbor a thyroid carcinoma or a thyroid carcinoma may co-exist out of the hyperfunctioning nodule. This is in accordance with the recently published guidelines,^{34,35} which recommend the use of scintigraphy only in cases of low TSH in order to perform differential diagnosis of hyperthyroidism. Adherence to these guidelines would limit the abuse in thyroid scintigraphy.

Additional indications for thyroid scintigraphy have also been suggested in clinical practice. These include cases of multinodular goiter in iodine-deficient regions,¹² and cases of cytologically follicular neoplasm^{34,36} in order to minimize the number of patients subjected to fine-needle biopsy or surgery, respectively. However, in our opinion, data are limited to strongly support either one of these additional indications.

A man with thyroid toxic adenoma subjected to surgery and incidentally found to have a papillary thyroid microcarcinoma on the contralateral thyroid lobe is hereby presented. By reviewing the literature, incidental thyroid carcinoma in patients subjected to thyroidectomy for hyperfunctioning nodules both within and out of the nodule is not a rare event. Thyroid scintigraphy can be used in the differential diagnosis of hyperthyroidism, but it cannot exclude thyroid malignancy either within or out of a “hyperfunctioning” thyroid nodule.

References

1. Polyzos SA, Kita M, Avramidis A. Thyroid nodules—stepwise diagnosis and management. *Hormones* (Athens). 2007; **6**: 101–119.
2. Shu X, Ji J, Li X, Sundquist J, Sundquist K, Hemminki K. Cancer risk in patients hospitalised for Graves’ disease: A population-based cohort study in Sweden. *Br J Cancer*. 2010; **102**: 1397–1399.
3. Cappelli C, Braga M, De ME, Castellano M, Gandossi E, Agosti B, et al. Outcome of patients surgically treated for various forms of hyperthyroidism with differentiated thyroid cancer: experience at an endocrine center in Italy. *Surg Today*. 2006; **36**: 125–130.
4. Gul K, Di Ri KA, Ki YG, Ersoy PE, Ugras NS, Ozdemi D, et al. Thyroid carcinoma risk in patients with hyperthyroidism and role of preoperative cytology in diagnosis. *Minerva Endocrinol*. 2009; **34**: 281–288.
5. Polyzos SA, Kita M, Efstathiadou Z, Goulis DG, Benos A, Flaris N, et al. The use of demographic, ultrasonographic and scintigraphic data in the diagnostic approach of thyroid nodules. *Exp Clin Endocrinol Diabetes*. 2009; **117**: 159–164.
6. Cakir M, Arici C, Alakus H, Altunbas H, Balci MK, Karayalcin

- U. Incidental thyroid carcinoma in thyrotoxic patients treated by surgery. *Horm Res.* 2007; **67**: 96 – 99.
7. Phitayakorn R, McHenry CR. Incidental thyroid carcinoma in patients with Graves' disease. *Am J Surg.* 2008; **195**: 292 – 297.
 8. Alevizaki M, Papageorgiou G, Rentziou G, Saltiki K, Marafelia P, Loukari E, et al. Increasing prevalence of papillary thyroid carcinoma in recent years in Greece: the majority are incidental. *Thyroid.* 2009; **19**: 749 – 754.
 9. Daumerie C, Ayoubi S, Rahier J, Buyschaert M, Squifflet JP. Prevalence of thyroid cancer in hot nodules. *Ann Chir.* 1998; **52**: 444 – 448.
 10. Bradly DP, Reddy V, Prinz RA, Gattuso P. Incidental papillary carcinoma in patients treated surgically for benign thyroid diseases. *Surgery.* 2009; **146**: 1099 – 1104.
 11. Miccoli P, Minuto MN, Galleri D, D'Agostino J, Basolo F, Antonangeli L, et al. Incidental thyroid carcinoma in a large series of consecutive patients operated on for benign thyroid disease. *ANZ J Surg.* 2006; **76**: 123 – 126.
 12. Gharib H, Papini E, Paschke R, Duick DS, Valcavi R, Hegedus L, et al. American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules: executive summary of recommendations. *Endocr Pract.* 2010; **16**: 468 – 475.
 13. Bonnema SJ, Bennedbaek FN, Wiersinga WM, Hegedus L. Management of the nontoxic multinodular goitre: a European questionnaire study. *Clin Endocrinol (Oxf).* 2000; **53**: 5 – 12.
 14. Bennedbaek FN, Hegedus L. Management of the solitary thyroid nodule: results of a North American survey. *J Clin Endocrinol Metab.* 2000; **85**: 2493 – 2498.
 15. Bennedbaek FN, Perrild H, Hegedus L. Diagnosis and treatment of the solitary thyroid nodule. Results of a European survey. *Clin Endocrinol (Oxf).* 1999; **50**: 357 – 363.
 16. Bonnema SJ, Bennedbaek FN, Ladenson PW, Hegedus L. Management of the nontoxic multinodular goiter: a North American survey. *J Clin Endocrinol Metab.* 2002; **87**: 112 – 117.
 17. Kassum TA, Goldstein DP, Rafferty MA, Rotstein LE, Irish JC. Thyroid scintigraphy in the assessment of the solitary thyroid nodule: differences in practice patterns between family physicians and specialists. *J Otolaryngol.* 2007; **36**: 49 – 53.
 18. Uludag M, Yetkin G, Citgez B, Isgor A, Basak T. Autonomously functioning thyroid nodule treated with radioactive iodine and later diagnosed as papillary thyroid cancer. *Hormones (Athens).* 2008; **7**: 175 – 179.
 19. Azevedo MF, Casulari LA. Hyperfunctioning thyroid cancer: a five-year follow-up. *Arq Bras Endocrinol Metabol.* 2010; **54**: 78 – 80.
 20. Heman-Martinez J, Uzcategui M, Corder E, Castillo M, Sostre S, Alicea L. Hyperthyroidism, hyperfunctioning thyroid nodule, and thyroid cancer in a young female: a rare and unusual coexistence. *P R Health Sci J.* 2010; **29**: 78 – 82.
 21. Nishida AT, Hirano S, Asato R, Tanaka S, Kitani Y, Honda N, et al. Multifocal hyperfunctioning thyroid carcinoma without metastases. *Auris Nasus Larynx.* 2008; **35**: 432 – 436.
 22. Majima T, Doi K, Komatsu Y, Itoh H, Fukao A, Shigemoto M, et al. Papillary thyroid carcinoma without metastases manifesting as an autonomously functioning thyroid nodule. *Endocr J.* 2005; **52**: 309 – 316.
 23. Bitterman A, Uri O, Levanon A, Baron E, Lefel O, Cohen O. Thyroid carcinoma presenting as a hot nodule. *Otolaryngol Head Neck Surg.* 2006; **134**: 888 – 889.
 24. Kim TS, Asato R, Akamizu T, Harada D, Nakashima Y, Higashi T, et al. A rare case of hyperfunctioning papillary carcinoma of the thyroid gland. *Acta Otolaryngol Suppl.* 2007; **557**: 55 – 57.
 25. Wong CP, AuYong TK, Tong CM. Thyrotoxicosis: a rare presenting symptom of Hürthle cell carcinoma of the thyroid. *Clin Nucl Med.* 2003; **28**: 803 – 806.
 26. Lupi A, Orsolon P, Cerisara D, Deantoni MG, Vianello DA. "Hot" carcinoma of the thyroid. Case reports and comments on the literature. *Minerva Endocrinol.* 2002; **27**: 53 – 57.
 27. Mircescu H, Parma J, Huot C, Deal C, Oligny LL, Vassart G, et al. Hyperfunctioning malignant thyroid nodule in an 11-year-old girl: pathologic and molecular studies. *J Pediatr.* 2000; **137**: 585 – 587.
 28. Sasaki J, Odaka Y, Kato R, Tada T, Yagawa K, Kowata T, et al. Hyperfunctioning follicular carcinoma of the thyroid. A case report. *Nippon Geka Gakkai Zasshi.* 1988; **89**: 286 – 291.
 29. Abdel-Razzak M, Christie JH. Thyroid carcinoma in an autonomously functioning nodule. *J Nucl Med.* 1979; **20**: 1001 – 1002.
 30. Hoving J, Piers DA, Vermey A, Oosterhuis JW. Carcinoma in hyperfunctioning thyroid nodule in recurrent hyperthyroidism. *Eur J Nucl Med.* 1981; **6**: 131 – 132.
 31. Khan O, Ell PJ, MacLennan KA, Kurtz A, Williams ES. Thyroid carcinoma in an autonomously hyperfunctioning thyroid nodule. *Postgrad Med J.* 1981; **57**: 172 – 175.
 32. Tfiayli HM, Teot LA, Indyk JA, Witchel SF. Papillary thyroid carcinoma in an autonomous hyperfunctioning thyroid nodule: case report and review of the literature. *Thyroid.* 2010; Epub ahead of print.
 33. Pazaitou-Panayiotou K, Perros P, Boudina M, Siardos G, Drimonitis A, Patakiaouta F, et al. Mortality from thyroid cancer in patients with hyperthyroidism: the Theagenion Cancer Hospital experience. *Eur J Endocrinol.* 2008; **159**: 799 – 803.
 34. Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid.* 2009; **19**: 1167 – 1214.
 35. Camargo R, Corigliano S, Friguglietti C, Gauna A, Harach R, Munizaga F, et al. Latin American Thyroid Society recommendations for the management of thyroid nodules. *Arq Bras Endocrinol Metabol.* 2009; **53**: 1167 – 1175.
 36. Lumachi F, Fabbro M, Tregnaghi A, Antunovic L, Bui F, Cecchin D, et al. Fine-needle aspiration cytology and (99m)Tc-pertechnetate scintigraphy together in patients with differentiated thyroid carcinoma. *Anticancer Res.* 2010; **30**: 3083 – 3086.