

Case Report

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# Metastatic papillary carcinoma of the thyroid in a patient previously treated for Graves' disease

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## Abstract

Incidental papillary carcinoma of the thyroid in patients treated surgically for benign thyroid diseases including Graves' disease is a known phenomenon. However, the management of these patients remains an issue of concern and controversy for those who care for them. We report a case of metastatic papillary carcinoma of the thyroid in a patient previously treated for Graves' disease. The subject of this presentation is a 50-year-old lady who was diagnosed with Graves' disease at the age of 29, for which she had a subtotal thyroidectomy following failure of medical and radioactive iodine treatment. Three years later, the patient was referred to our nuclear medicine department with a clinical diagnosis of suspected metastatic lymph nodes presumably from a thyroid malignancy. She had an I<sup>123</sup>I diagnostic whole body scan that showed I<sup>123</sup>I avid areas in the thyroid bed as well as left cervical lymph nodes, which later turned out to be metastatic papillary carcinoma of the thyroid on histology. She was treated with therapeutic doses of I<sup>131</sup>I. Follow-up radioactive iodine scans and serum thyroglobulin assays showed no evidence of malignant thyroid tissue. The occurrence of papillary carcinoma of the thyroid after a subtotal thyroidectomy for Graves' disease is hereby reported. The need for vigilance and regular follow-up in patients who receive all forms of treatment for benign thyroid diseases is emphasized.

**Keywords:** Graves' disease, papillary thyroid carcinoma, radioactive iodine

## Résumé

Accessoire de carcinome papillaire de la thyroïde chez les patients traités par chirurgie des maladies thyroïdiennes bénignes, y compris la maladie de Basedow est un phénomène connu. Toutefois, la gestion de ces patients reste une cause de préoccupation et de controverse pour ceux qui s'occupent d'eux. Nous rapportons un cas de papillaire métastatique de la thyroïde chez un patient traité antérieurement pour la maladie de Basedow. L'objet de cette présentation est une dame de 50 ans qui a été diagnostiquée avec la maladie de Basedow à l'âge de 29, pour laquelle elle a eu une thyroïdectomie sous-total après échec du traitement médical et radioactif iode. Trois ans plus tard, le malade a été adressé à notre service de médecine nucléaire avec un diagnostic clinique des ganglions métastatiques présumés vraisemblablement d'un cancer de la thyroïde. Elle avait une I<sup>123</sup>I scan corps entier diagnostique qui a montré de I<sup>123</sup>I avides zones dans la thyroïde de lit ainsi que gauche ganglions cervicaux, qui plus tard s'est avéré pour être métastatique carcinome papillaire de la thyroïde sur l'histologie. Elle a été traitée avec des doses thérapeutiques de I<sup>131</sup>I. suivi scanne d'iode radioactif et dosages de la thyroglobuline sérique ne montrent aucun signe de tissu thyroïdien malin. La présence d'un carcinome papillaire de la thyroïde après qu'une thyroïdectomie sous-total pour maladie de Basedow est signalée par les présentes. Souligne la nécessité d'une vigilance et un suivi régulier chez les patients qui reçoivent toutes les formes de traitement pour les maladies thyroïdiennes bénignes.

**Mots-clés :** Maladie de Basedow, papillaire de la thyroïde, l'iode radioactif

## Introduction

Papillary thyroid carcinoma (PTC) is a well-differentiated thyroid cancer, which is usually considered as potentially curable especially if the diagnosis is established at an early stage. Studies have shown an incidence of between 5 and 15% of papillary carcinomas in patients treated surgically for benign thyroid diseases such as Hashimoto's thyroiditis, follicular adenoma, multinodular goiter, or Graves' disease.<sup>[1,2]</sup> We hereby present a case of metastatic papillary carcinoma of the thyroid arising from a remnant thyroid tissue after a surgical therapy for Graves' disease.

## Case Report

The patient is a 50-year-old lady known with hypertension, hyperlipidemia, type II diabetes mellitus, and previous multiple exposures to X-rays for assessment of a fracture to the mandible, following a motor vehicular accident.

She was diagnosed clinically with Graves' disease at the age of 29, when she presented with history of excessive sweating, tremors, palpitations, and menstrual irregularities. On examination, she was wasted and the thyroid gland was diffusely enlarged bilaterally with bruit on auscultation. She had exophthalmos and lid retraction, but no lid lag. Laboratory investigation revealed low serum thyroid-stimulating hormone (TSH = 0.07 mIU/L; normal range, 0.27-4.20 mIU/L), elevated serum free tri-iodothyronine (fT3 = 28.9 pmol/L; normal range, 2.8-7.1), and elevated serum free thyroxine (fT4 = 42 pmol/L; normal range, 12.0-22.0 pmol/L). Serum assay for thyroid auto-antibodies was positive for antimicrosomal antibodies-HA with a titer of 100. She was commenced on neomercazole 40 mg daily, and propranolol 40 mg three times a day. Neomercazole was replaced with propylthiouracil 150 mg twice a day when she developed allergy to it. Patient remained thyrotoxic warranting administration of three separate doses of 370 MBq radioactive iodine-131 at 6 and 4 month's intervals. Subsequently, she has to undergo a subtotal thyroidectomy following failure of medical and radioactive iodine treatments. Histological examination of the surgical specimen showed features of inflammation as the only significant finding. There was no evidence of malignancy.

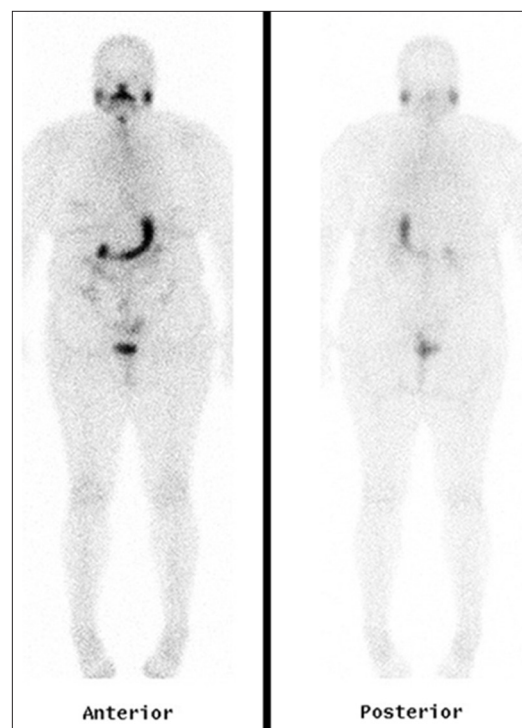
She then presented to our institution at the age of 32 with palpable nodes in her neck and was referred to nuclear medicine with a clinical diagnosis of suspected metastatic lymph nodes, presumably

from a thyroid malignancy. She had a diagnostic iodine-131 whole body scintigraphy (WBS), which showed focal areas of iodine avid uptake in the thyroid bed as well as level IV left cervical lymph nodes. Fine-needle aspiration and cytology from the cervical node revealed metastases from papillary carcinoma of the thyroid. She was treated with 3 GBq of radioactive <sup>131</sup>I.

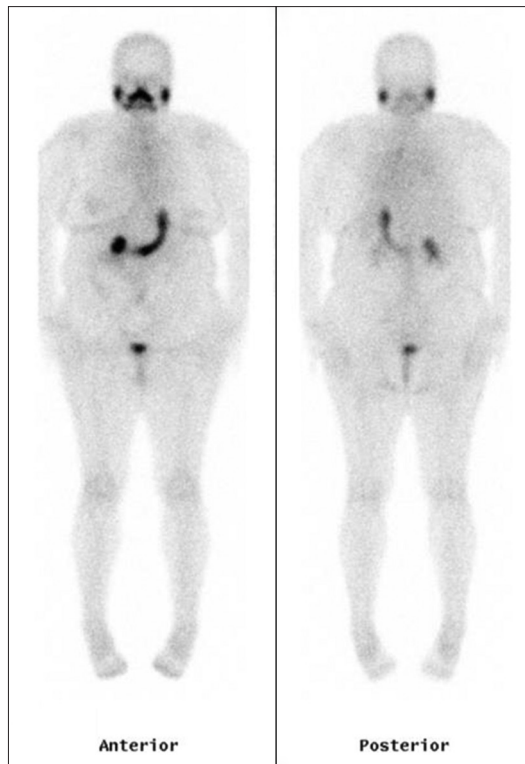
The patient was followed up with TSH suppression with levothyroxine, regular monitoring of serum thyroglobulin and antithyroglobulin antibodies, as well as diagnostic radioiodine whole body scans during the first 2 years. Five years later a rising serum thyroglobulin warranted an <sup>123</sup>I WBS that showed tumor recurrence in the thyroid bed [Figure 1]. She was treated with 5.5 GBq of <sup>131</sup>I. Subsequent follow-up diagnostic scans with <sup>123</sup>I showed no residual iodine avid thyroid tumor remnant [Figure 2]. Patient is still being followed up. She has shown good TSH suppression (TSH < 0.1 pmol/L), has remained disease free, and the serum thyroglobulin levels have remained low (<0.2 µg/L).

## Discussion

Incidental papillary cancer (IPC) of the thyroid in patients treated operatively for presumably a benign disease is now a well-recognized finding. Bradly *et al.*,<sup>[1]</sup> found an overall incidence of PTC



**Figure 1:** Diagnostic Iodine-123 whole body scintigraphy showing iodine avid uptake in the anterior neck



**Figure 2:** Follow-up Iodine-123 whole body scintigraphy showing no abnormal iodine avid tissue

in this group of patients to be 12%, whereas the incidence among patients with Graves' disease was 8%. However, this study entertained the possibility of underestimation of the incidences due to inconsistent operative sectioning techniques and the fact that more than half of the patients had subtotal thyroidectomy. Our patient justifiably had surgery following failure of both medical and radioactive iodine therapies. Surgery was limited to a subtotal thyroidectomy due to technical difficulties encountered intraoperatively. This may explain why the carcinoma was missed *ab initio*, and this agrees with the findings by Bradly *et al.*,<sup>[1]</sup> that the incidence of IPC is likely to be higher if this group of patients was treated with a total thyroidectomy.

Incidental papillary microcarcinomas of the thyroid are usually not palpable, but are mostly detected during pathological examination of the postoperative surgical specimen. Despite existing controversies surrounding the appropriate operative management of benign thyroid diseases, there are studies that are in favor of both partial and total thyroidectomy.<sup>[2,3]</sup> In patients presenting with proven poorly controlled thyrotoxicosis secondary to Graves' disease, like in our patient, the accepted elective therapy has been a near-total or total thyroidectomy because this offers rapid and durable control of hyperthyroidism.<sup>[4]</sup> Partial thyroidectomy has the advantage of preserving thyroid function

and sparing the patient's need for lifelong thyroid hormone replacement in some cases, whereas total thyroidectomy has the additional advantage of addressing the presence of a potentially existing microcarcinoma. However, associated morbidity, such as hypoparathyroidism, recurrent laryngeal nerve injury, and occasional hypocalcemia are all factors worth considering before performing an elective surgical therapy in a young patient like ours. The best option of surgical therapy for our patient would have been a total thyroidectomy, which was not possible due to difficulty in mobilizing the gland and excessive intraoperative bleeding.

There was no record of ancillary diagnostic imaging in this patient at the time the diagnosis of Graves' disease was made. Preoperative ultrasonography and thyroid scintigraphy where available, coupled with fine-needle aspiration of suspicious nodule have been shown to play a significant role in early detection of microcarcinomas. These methods have led to the detection of nodules that are too small to be palpated, and are said to be responsible for the increasing incidence of IPC over the past few decades.<sup>[5-7]</sup>

The diagnosis of a papillary carcinoma in this patient might have been established before it became metastatic if the aforementioned diagnostic techniques were utilized promptly and appropriately.<sup>[8]</sup>

Radioactive iodine WBS was utilized to establish the presence of a thyroid carcinoma, localize the lymph nodes involved, as well as establish the presence or absence of iodine avid distant metastases. In our patient, the initial diagnostic WBS localized the lesions to the remnant thyroid tissue and left cervical lymph nodes. This is consistent with the suspected nodal metastasis that was reported to have a frequency of up to 90% depending on the sensitivity of the detection method.<sup>[9]</sup>

Following the diagnosis of papillary carcinoma and adequate staging, our patient would have benefited from a therapeutic completion thyroidectomy with lymph node dissection.<sup>[9,10]</sup> However, patient has had previous surgeries; initially a subtotal thyroidectomy and later open reduction and fixation of mandibular fractures. These factors coupled with her age and sex as well as anticipation of possible difficulties during a second neck surgery influenced the patient's decision not to consent for the surgical therapy, but instead she opted for radioiodine therapy. Therefore, this patient was offered the available option of radioactive iodine ablation.

The patient was treated with 3 GB initially and later with 5.5 GB when a follow-up <sup>123</sup>I WBS, prompted by a rising serum thyroglobulin levels,

showed tumor recurrence in the thyroid bed. The activities of radioactive iodine given to this patient were determined empirically because up to now the most appropriate dose is yet to be established from evidence-based data.<sup>[11,12]</sup> However, the generally recommended and accepted dosimetry was that of a tumor dose of above 80 Gy and limiting the absorbed blood dose to below 2 Gy.<sup>[13]</sup>

## Conclusion

Thyroid malignancy occurs in patients with benign thyroid disease. A high level of suspicion for thyroid malignancy in all patients with benign thyroid diseases and appropriate utilization of preoperative imaging are recommended.

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