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Detection of thyroid malignancy in a hot nodule by fluorine-18-fluorodeoxyglucose positron emission tomography

S C S Low, A K Sinha, F X Sundram

ABSTRACT

Carcinoma of the thyroid arising in an autonomously functioning or "hot" nodule is uncommon. The majority of thyroid carcinomas present as a "cold" nodule on radionuclide scintigraphy. We report a poorly-differentiated thyroid carcinoma developing in a long-standing "hot" nodule in a 51-year-old Chinese woman. Fluorine-18-fluorodeoxyglucose positron emission tomography (FDG PET) showed focal FDG uptake in the thyroid nodule, as well as in the cervical and pulmonary hilar lymph nodes. This case illustrates that the incidence of thyroid carcinoma in a "hot" nodule is not negligible. The role of FDG PET in the differentiation of benign from malignant thyroid nodules is still unclear. In contrast, FDG PET has been shown to have a role in the follow-up of thyroid cancer patients after thyroidectomy and subsequent radioactive iodine-131 (I-131) ablation. It may be useful in the identification and localisation of recurrent cancer foci in patients with elevated thyroglobulin levels but a negative I-131 whole body scan.

Keywords: positron emission tomography, radionuclide imaging, thyroid gland, thyroid neoplasm, thyroid nodule

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INTRODUCTION

Thyroid nodules are a common problem in clinical practice, occurring in 4-7% of adults in the United States[1,2]. They can be classified on the basis of technetium-99m (Tc-99m) or radio-iodine scintigraphy as "hot" (hyperfunctioning/autonomous) or "cold" (nonfunctioning). About 5-10% of solitary thyroid nodules are hot nodules[3,4]. The hot nodule usually implies a benign entity[4,5] while cold nodules require further investigation due to a significant risk of malignancy. We present the scintigraphical and fluorine-18 (F-18)-fluorodeoxyglucose positron emission tomography (FDG PET) images of a patient with thyroid carcinoma arising, uncommonly, in a long-standing "hot" nodule.

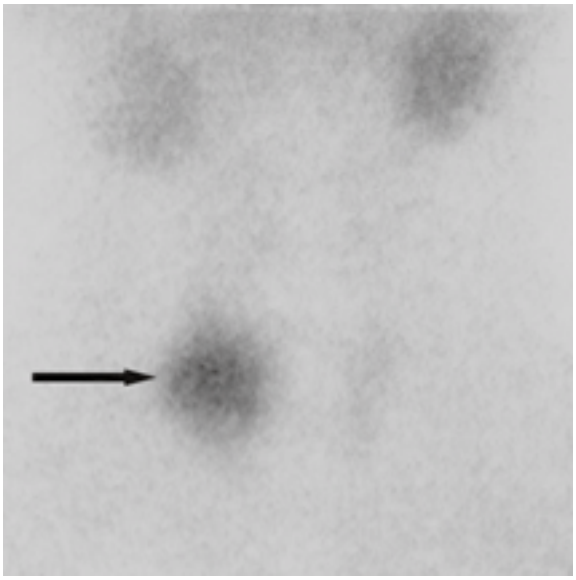

Fig. 1 Tc-99m pertechnetate thyroid scan shows a "hot" nodule in the right lobe of the thyroid gland (arrow). Normal physiological activity is seen in the submandibular salivary glands bilaterally.

CASE REPORT

The patient is a 51-year-old Chinese woman with a long history of thyrotoxicosis diagnosed in 1985 following pregnancy and delivery. She had allergy to carbimazole and propylthiouracil, and was treated with 222 MBq (6 mCi) of radioactive iodine-131 (I-131) in 1985. Since she was toxic again in 1987, a second dose of 222 MBq (6 mCi) of radio-iodine was administered. She subsequently became hypothyroid in 1988, and has been on 0.1 mg of thyroxine replacement daily. However, she was poorly compliant and had persistently elevated levels of thyroid stimulating hormone (TSH). Of note, she had hormone replacement therapy (HRT) in 2001.

In 2002, thyroid scintigraphy with both Tc-99m pertechnetate (Fig. 1) and I-131 showed a "hot" nodule in the right lobe. Ultrasonography done during the same visit demonstrated a mixed cystic nodule measuring 1.8 cm by 2.6 cm by 2.7 cm, consistent with

Department of Diagnostic Imaging
National University Hospital
5 Lower Kent Ridge Road
Singapore 119074

S C S Low, MBBS
Medical Officer

A K Sinha, MBBS, MD
Senior Registrar

Department of Nuclear Medicine and PET
Singapore General Hospital
Outram Road
Singapore 169608

F X Sundram, MBBCh, MSc, FAMS
Senior Consultant and Head

Correspondence to:
Dr Felix X Sundram
Tel: (65) 6321 4201
Faxl: (65) 6224 0938
Email: gnmfxs@sgh.com.sg

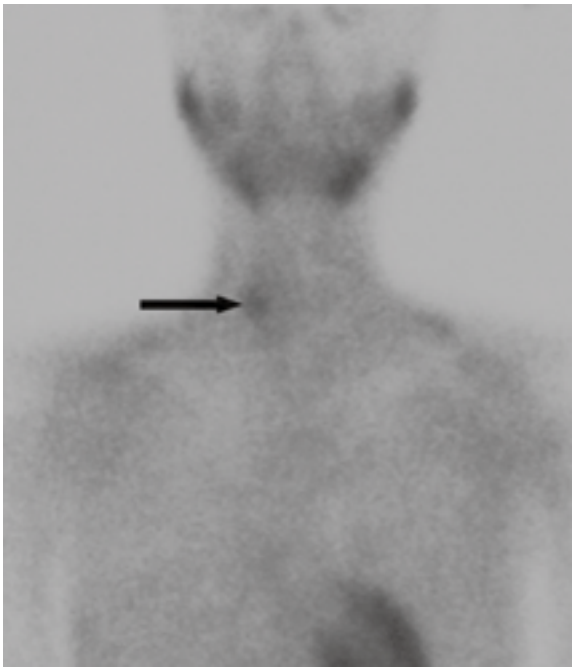

Fig. 2 Tc-99m sestamibi thyroid scan shows a hypermetabolic nodule in the right lobe of the thyroid gland (arrow). No uptake of radio-isotope is seen in the posterior triangle of the neck. The salivary glands and the myocardium of the heart show normal physiological uptake.

an adenoma with early degeneration. A fine-needle aspiration (FNA) biopsy of the nodule revealed "follicular neoplasm". She was offered surgery but the patient refused. In July 2004, she was noted to have an enlarged lymph node in the posterior triangle of the right neck, measuring about 2 cm in diameter. She also gave a history of progressive hoarseness of voice. Serum thyroglobulin level was raised at 4436 μg/L (normal range 2.0 to 70.0 μg/L). Thyroglobulin antibodies (TgAb) were also elevated at 189.4 U/ml (normal range 0 to 60 U/ml).

Tc-99m sestamibi thyroid and whole body scans in July 2004 demonstrated a hypermetabolic nodule in the right lobe of the thyroid gland but no uptake in the right posterior triangle cervical lymph node (Fig. 2). FNA biopsy of the lymph node showed metastatic adenocarcinoma. Computed tomography (CT) of the thorax, abdomen and pelvis failed to demonstrate a primary tumour elsewhere in the body. Subsequently, a whole-body FDG PET/CT was performed using a dedicated whole-body PET scanner (LSO Siemens Biograph, Erlangen, Germany) 60 minutes after 414 MBq (11.2 mCi) of F-18-FDG was administered intravenously. As part of the same examination, unenhanced CT scans were also obtained for the purpose of anatomical localisation.

FDG PET/CT showed focally increased FDG uptake in the right thyroid gland with a standardised uptake value (SUV) of 6.92. This large, hypermetabolic lesion measured 5.3 cm by 3.1 cm by 2.4 cm. Increased focal uptake of FDG was also seen in a lymph node mass in the posterior aspect of the right neck with SUV of 6.2. Hypermetabolic metastatic disease was also seen in the right hilar region (SUV 3.3), left hilar region (SUV 2.7) and in the pre-carinal region (SUV 4.1) in the thorax. No primary tumour was noted elsewhere in the neck, chest, abdomen and pelvis (Fig. 3).

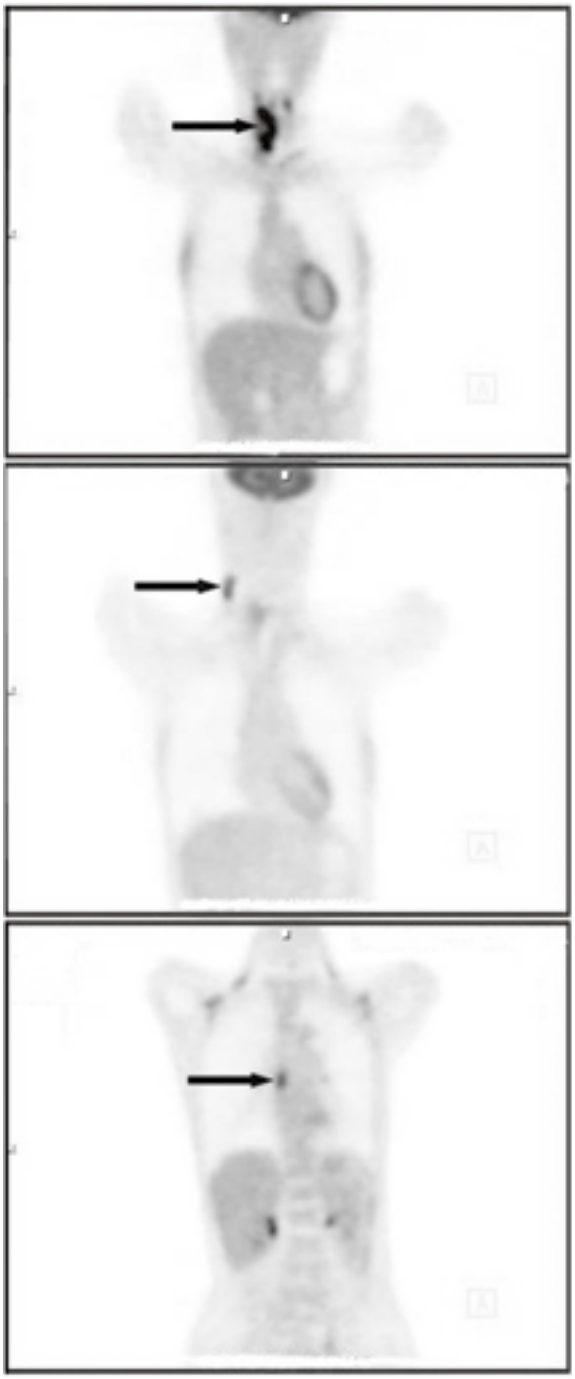

Fig. 3 Attenuation-corrected FDG PET whole body scan obtained after intravenous administration of 414 MBq (11.2 mCi) of 18F-FDG shows focal FDG uptake in the right thyroid gland (top image, arrow), posterior triangle of the right neck (middle image, arrow) and right hilar region (bottom image, arrow). The brain and myocardium of the heart show normal physiological uptake.

The presumptive diagnosis was thyroid carcinoma arising from the right toxic nodule with metastases to the posterior cervical, bilateral hilar and pre-carinal lymph nodes. The patient underwent a total thyroidectomy and modified right radical neck dissection. Operatively, a 5 cm diameter thyroid carcinoma was found in the right lobe. Enlarged cervical lymph nodes were noted on the same side. The recurrent laryngeal nerve was involved by the tumour. Histology showed poorly-differentiated thyroid carcinoma with extension into the perithyroid tissue, adjacent skeletal muscle and margin of resection. Eight lymph nodes were positive for metastatic disease. The patient was discharged and scheduled for 9.3 GBq (250 mCi) of radio-iodine ablation therapy, followed by external-beam radiotherapy to the neck and mediastinum.

DISCUSSION

In the majority of cases, carcinoma of the thyroid presents as a "cold" nodule on scintigraphy. "Hot" nodules have long been thought to be associated with an exceedingly low incidence of malignancy. However, a study by Harach et al on 73 scintigraphically-confirmed "hot" nodules removed during surgery found malignancy in six cases (8.2%)[6]. Five of these were follicular carcinomas while one was papillary in nature. Another study by Daumerie et al found carcinoma in five (11%) of 46 patients with a solitary "hot" nodule removed during surgery[7]. These two studies seem to suggest that the probability of carcinoma in a "hot" nodule is not as rare as was once thought. In our patient, the suspicious ultrasonographical features and the subsequent development of hoarseness of voice and palpable cervical lymph nodes prompted an FNA biopsy. Such signs and symptoms are considered "red flags", even in patients with clinically and scintigraphically proven "hot" nodules.

Although the role of HRT in the aetiology of thyroid carcinoma has not been fully elucidated, oestrogen and/or progesterone may be important for the development of these neoplasms[8]. Of note, our patient did have HRT in 2001. She also had persistently high levels of TSH for nearly 16 years due to poor compliance to thyroxine therapy. TSH has a central role in thyroid growth and normal function, and appears to play a similar part in the growth and development of thyroid cancer[9].

Whole-body FDG PET reflects glucose metabolism of tissue *in-vivo*. In patients with known thyroid nodules, the differentiation of benign from malignant lesions with FDG PET is not entirely straightforward. Both benign and malignant lesions have been found to show considerable uptake of FDG. Some authors have found good separation of FDG accumulation between benign and malignant lesions. Adler et al[10] studied nine patients with suspicious thyroid nodules with FDG PET prior to surgical excision. Three patients had papillary carcinoma and all had SUVs in excess of 8.5. The benign lesions (follicular adenomas and the dominant nodules of multinodular goitres) all had SUVs ranging between 1.9 and 6.3. The SUV represents the uptake in a given region of interest related to the average uptake throughout the body from the injected dose.

A follow-up study by the same authors[11] showed that four malignant nodules (out of twelve studied) had SUVs greater than 8.5. In contrast, eight benign lesions (all follicular adenomas) had SUVs less than 7.6. In a subsequent paper[12], the authors proposed that a cut-off SUV of 8 could successfully differentiate seven out of seven cases of malignant thyroid nodules and 31 of 33 benign lesions, giving a sensitivity of 100% and a specificity of 94%. Other authors[13] used an SUV cut-off of 5 to successfully differentiate four malignant nodules (out of a total of 11 lesions).

Cohen et al[14] studied fifteen patients with thyroid incidentalomas identified by FDG PET performed as part of a staging protocol for other cancers. Patients with malignant lesions (seven nodules) had a significantly higher SUV on average, expressed as the mean ± standard deviation (6.92 ± 1.54) compared to patients with benign lesions (3.37 ± 0.21, p=0.04). However, all these studies dealt with relatively small numbers of patients. Larger series should be evaluated before any recommendation for the initial evaluation of thyroid nodules with FDG PET can be made. In a recent review, Schoder et al[15] addressed the issue of diffusely or focally increased FDG uptake as an incidental finding in the thyroid gland. They concluded that diffusely increased thyroid FDG was most likely benign and usually due to chronic thyroiditis. In contrast, focal FDG uptake had a significant risk (27-50%) of being malignant.

Patients with thyroid carcinoma treated with total thyroidectomy and subsequent I-131 ablation therapy for destruction of remnants are usually followed-up with I-131 whole body scans. Other conventional imaging modalities such as ultrasonography, CT and magnetic resonance imaging may also be performed. The patient's thyroglobulin levels are also monitored. Elevated thyroglobulin levels are a marker for residual or recurrent disease. Several studies suggest that FDG PET may be useful in the identification and localisation of recurrent cancer foci in patients with elevated thyroglobulin levels and a negative I-131 whole body scan[16-18].

Furthermore, the metabolic profiles of thyroid cancer metastases are varied; some metastases accumulate only FDG, others just I-131 and yet others accumulate both tracers[17].

The I-131 whole body scan has been found to have a high sensitivity in the follow-up of well-differentiated tumours. In contrast, FDG PET was found to be superior in poorly-differentiated tumours[18]. It has also been suggested that FDGPET and Tc-99m sestamibi may be closer in their uptake patterns to each other than to I-131. Tc-99m sestamibi is commonly used when thyroglobulin is elevated and the I-131 whole body scan is negative.

In conclusion, this case report of carcinoma of the thyroid arising in a long-standing toxic nodule illustrates that the possibility of malignancy in a "hot" nodule should not be overlooked. The role of FDG PET in the differentiation of benign from malignant thyroid nodules is still unclear. However, several studies with limited numbers of patients have demonstrated significant differences in the uptake of FDG between benign and malignant lesions. It remains for us to await the results of larger studies before any recommendation for the initial evaluation of thyroid nodules with FDG PET can be made. In contrast, FDG PET has been shown to have a role in the follow-up of thyroid cancer patients after thyroidectomy and subsequent I-131 ablation. It may be useful in the identification and localisation of recurrent cancer foci in patients with elevated thyroglobulin levels but a negative I-131 whole body scan.

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