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Incidental ^{18}F-FDG uptake in the thyroid in patients diagnosed with PET/CT for other malignancies

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Abstract

BACKGROUND: The value of PET/CT imaging in diagnosis of different cancers has been widely described. PET/CT may contribute to visualization of additional findings that were not the indication to the study and did not refer to initial diagnosis. In a small number of PET/CT scans an incidentally found focal ^{18}F-FDG uptake in the thyroid gland is found.
The goal of the study was to estimate the prevalence and evaluate the clinical significance of incidental thyroid 18F-FDG uptake in a cohort of patients diagnosed for different malignancies.
MATERIAL AND METHODS: 2478 PET/CT scans using ^{18}F-FDG were performed in 1925 subjects for evaluation of different, non-thyroid malignancies. For PET/CT examination, a Discovery ST (General Electric) PET/CT scanner was used. Patients with focal ^{18}F-FDG activity were further evaluated by means of fine needle aspiration biopsy (FNAB). If cytological examination disclosed malignancy or suspicion of malignancy, thyroidectomy was performed. Both cytological and histopathological results were then analyzed.
RESULTS: Focal increased ^{18}F-FDG uptake was found in 71 patients (3.7%), and cytological or histopathological results were evaluable in 20 of them. In general, 8 cases of thyroid cancer were found, which accounts for 40% probability of malignancy. The predominant histopathological diagnosis was papillary thyroid carcinoma (5 out of 8 cases). Additionally, in one case (5%) thyroid metastasis of lung cancer was detected.
Diffused ^{18}F-FDG activity in both thyroid lobes was observed in 120 subjects (6.2%) — in most cases chronic thyroiditis was confirmed.
CONCLUSIONS: The probability of malignancy of focal thyroid incidentalomas in ^{18}F-FDG PET/CT scans is rather high. Therefore, thorough evaluation of such lesions is highly recommended in each case. Most thyroid malignancies incidentally detected in PET/CT are papillary carcinomas.
Key words: thyroid nodule, PET, ^{18}F-fluorine-deoxyglucose, thyroid carcinoma

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Introduction

In the last decade, positron emission tomography (PET) imaging became one of the most beneficial and accurate diagnostic tools in oncological diagnosis. Especially when combined with computed tomography (PET/CT), its accuracy in imaging malignant tissue increases up to 93% compared to PET scan only (78–85%) [1, 2]. There are many reports confirming its utility in patients with lymphoma, lung cancer, breast cancer, colorectal cancer and liver metastases, oesophageal cancer, head and neck tumours, and melanoma as well as tumours of unknown origin [3–10]. The role of PET in thyroid cancer management has been widely described. It should be routinely performed in patients previously treated for well-differentiated (follicular or papillary) thyroid cancer when the whole-body scan performed with radioiodine is negative and the thyroglobulin is markedly elevated [11].

Apart from this situation, PET/CT may contribute to visualization of additional findings that were not the indication to the study and did not refer to initial diagnosis. About 1-2% of such incidental findings localize in the thyroid gland [12–15]. Significantly increased ^{18}F-fluorodeoxyglucose (^{18}FDG) uptake in these patients still seems not to be clarified. As sufficient data is missing, fine needle aspiration biopsy still remains conclusive in the final diagnosis.

Aim of the study

The purpose of the study was to assess the prevalence and evaluate the clinical significance of incidental thyroid ^{18}F-FDG uptake in a cohort of patients diagnosed for other malignancies.

Material and methods

PET/CT scans using ^{18}F-FDG performed between May 2008 and January 2010 for non-thyroid malignancies were retrospectively analysed. Oncological diagnoses were: non-small cell lung cancer, colorectal cancer, non-Hodgkin or Hodgkin lymphoma, breast cancer, head and neck cancer, and cancer of unknown origin. The main indications for PET/CT comprised: staging of the disease, detection of recurrence in patients treated previously with surgery, chemotherapy and radiotherapy, and detection of the primary focus in subjects with metastases of unknown origin.

For PET/CT examination, a Discovery ST (General Electric) PET/CT scanner was used. All subjects fasted for at least 6 hours. Diabetic patients with blood glucose level > 160 mg/dl were rescheduled. Image acquisition for the whole body scan started 60 ± 10 min after intravenous administration of 550 MBq of ^{18}F-FDG. Whole body emission scans included 7–8 bed positions for 3 min in each position. In this study, a focal thyroid lesion was defined as a focally increased 18F-FDG uptake on the PET images while diffuse thyroid lesion was defined as ^{18}F-FDG uptake in the whole thyroid gland.

Patients with focal ^{18}F-FDG activity were further evaluated by means of fine needle aspiration biopsy (FNAB). Ultrasound-guided FNAB was performed by an experienced endocrinologist using needles with diameter Ø 0.42 mm. The specimens were analyzed by an experienced cytologist. Patients in whom FNAB was positive or suspected for thyroid malignancy were subjected to thyroidectomy. Both cytological and histopathological results were then analyzed.

Results

A total of 2478 PET scans with the use of ^{18}F-FDG in 1925 subjects were performed in the study period. 1003 men and 922 women aged 1–85 years (mean 54.4 ± 29.6 yrs) were evaluated. Focal increased ^{18}F-FDG uptake was found in 71 patients (3.7%) (Figure 1). Thyroid FNAB cytological results were available in 20 out of 71 subjects.

The cytological diagnoses in this group were as follows: 7 colloid nodules (benign lesions), 2 oxyphilic nodules (1 malignancy — papillary thyroid cancer in post-surgery evaluation), 5 papillary cancers, and one case of metastatic lesion with primary origin in lungs. In one case, immunohistochemical staining of FNAB specimen diagnosed medullary thyroid carcinoma (Figures 1 and 2).

In 2 cases FNAB was inconclusive and repetition of the procedure was recommended (results unavailable). In 2 cases follicular tumours were diagnosed in FNAB. One of them appeared to be follicular adenoma in post-surgical evaluation, in the second case the surgery was not performed due to medical contraindications.

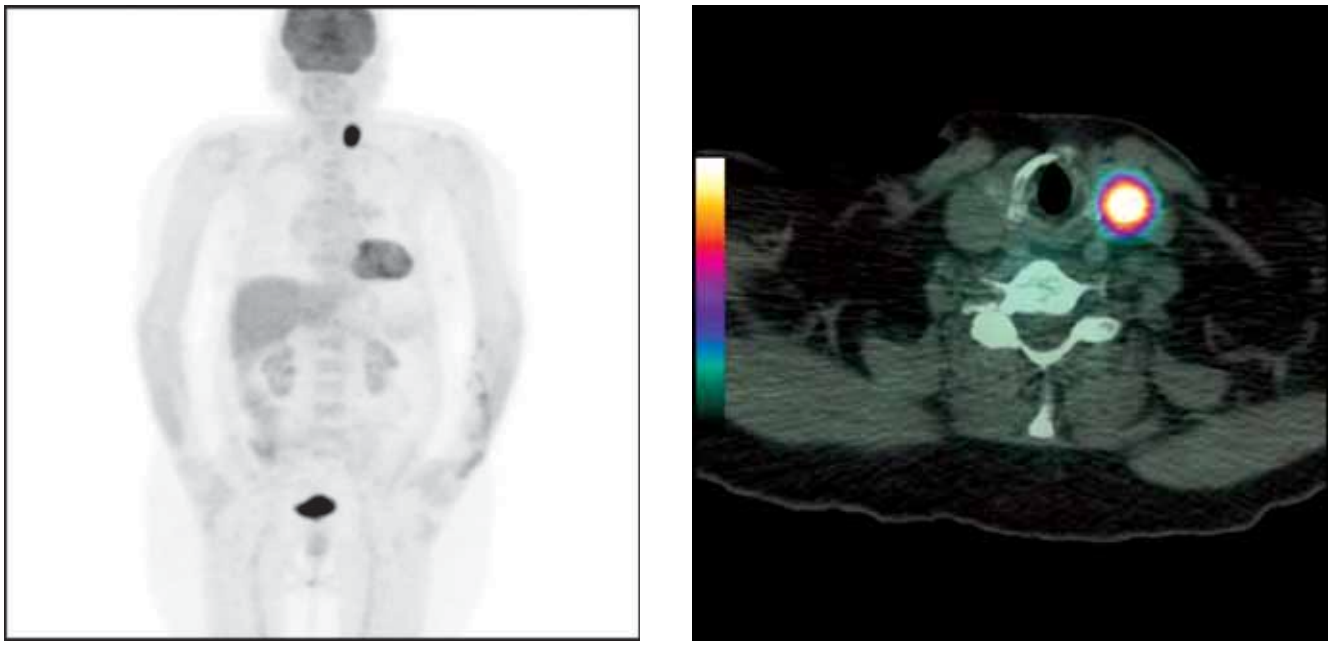

Figure 1. Incidentally found focus of increased ^{18}F-FDG uptake in a patient diagnosed due to a pulmonary nodule that appeared benign in the PET/CT scan (MIP image and fused axial image are presented). FNAB diagnosed benign thyroid nodule.

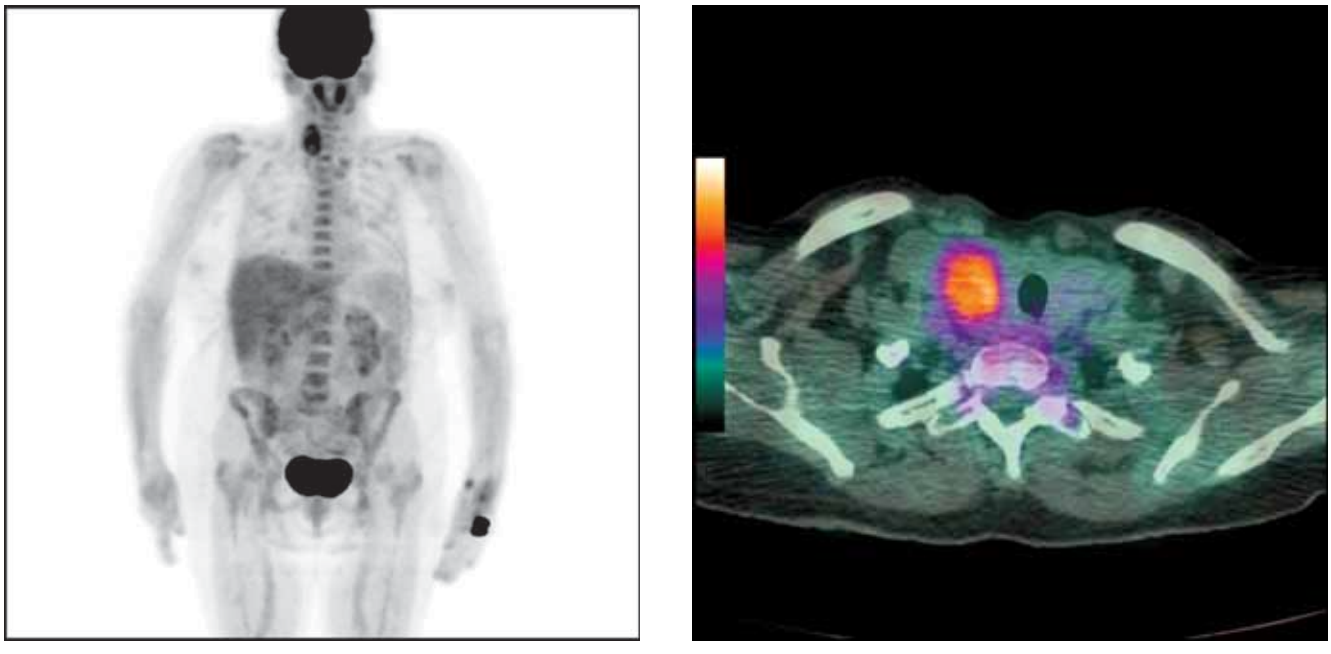

Figure 2. In a patient with colorectal cancer PET/CT did not detect any cancer recurrence. Incidentally found metabolically active thyroid nodule was diagnosed as a medullary thyroid carcinoma (MIP image and fused axial image are presented).

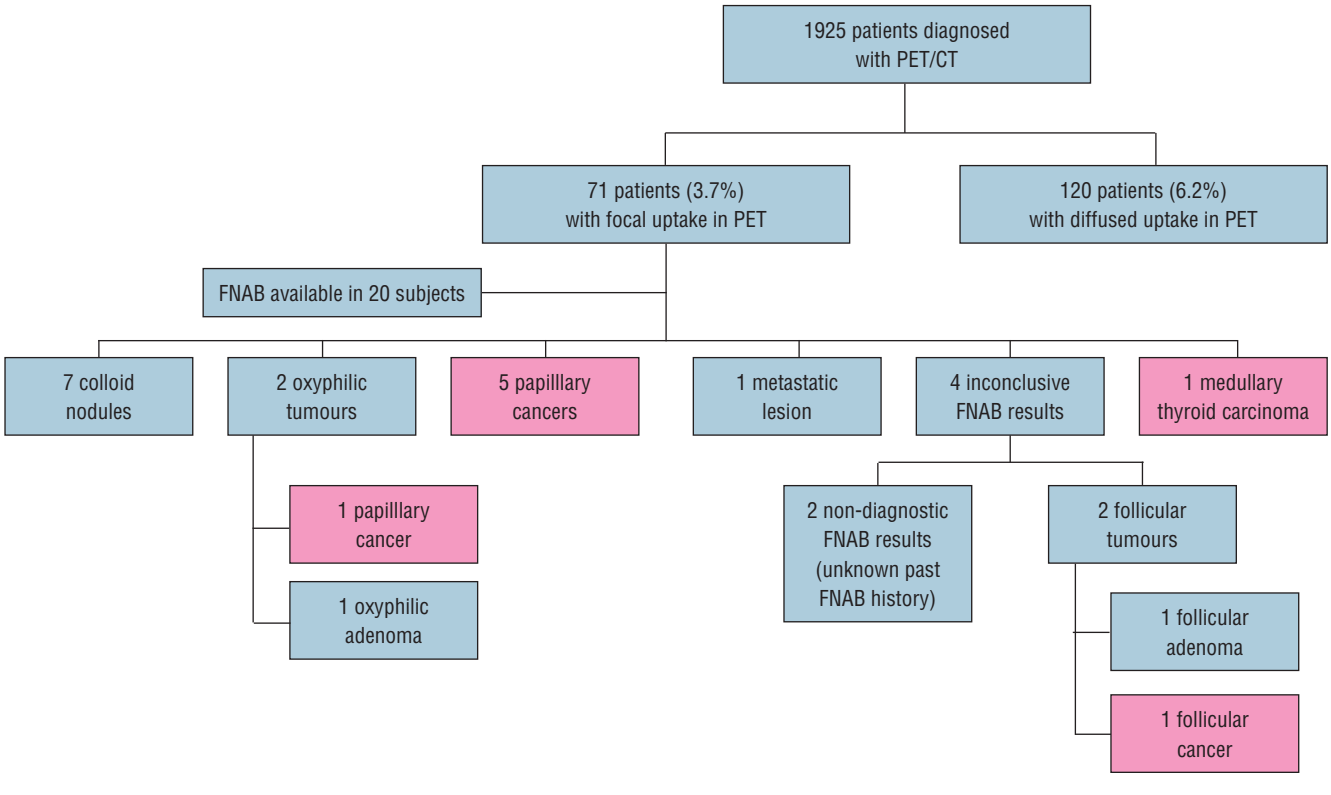

Figure 3. Distribution of FNAB and histopathological diagnoses in the study group.

In general, after both cytological and histological examinations, 8 malignancies were found, which accounts for 40% of malignancies out of all 20 examined ^{18}F-FDG-avid focal lesions (Figure 3).

Diffused 18F-FDG activity in both thyroid lobes was observed in 120 subjects (6.2%). Patients presenting diffused ^{18}F-FDG uptake in the thyroid were suspected of autoimmune thyroid disease that was then confirmed in laboratory findings (elevated serum thyroid antibodies) and characteristic hormonal and clinical status. These patients were not evaluated in the current study.

Discussion

Our study seems to confirm previous studies conducted in other centres. The prevalence of incidental focally increased ^{18}F-FDG metabolism ranges, depending on study cohort, from 1.0% to 4.3% [16, 17]. In the biggest retrospective study developed thus far, Shie et al. estimated the occurrence of thyroid incidentaloma in more than 55,000 subjects evaluated with PET for 1%, whereas 33.2% of focal thyroid lesions were found to be malignant. Moreover, Chen et al. revealed incidental focal ^{18}F-FDG thyroid uptake in 1.2% of a healthy population proving no link with the initial malignancy [15].

Obviously, the crucial problem of the thyroid incidentalomas is the differential diagnosis between benign and malignant lesions. There have been several studies trying to clarify why only some benign lesions present increased ^{18}F-FDG uptake, while the majority of papillary cancers are ^{18}F-FDG-avid. The potential role of maximal standardized uptake value (SUV_{max}) seems to be the most commonly investigated aspect. Conclusions of published studies are inconsistent. Zhai et al. demonstrated significantly higher SUV_{max} values in malignant than in benign lesions, estimating SUV_{max} above 8 as a strong predictor of malignancy. In other studies, the highest SUV_{max} of malignant thyroid lesions was also significantly higher than that of benign lesions [23]. A significant correlation between SUV_{max} and maximal diameter of the thyroid incidentaloma was also found [24]. However, it has also been demonstrated that low SUV_{max} in a thyroid focus does not exclude malignancy. Other authors concluded no significant difference in SUV_{max} between benign and malignant nodules [19, 25]. In another study, Kim et al. tried to evaluate the utility of ^{18}F-FDG PET in predicting malignancy in thyroid nodules cytologically diagnosed as follicular neoplasm. Unfortunately, in this case glucose metabolic activities of benign follicular nodules were as high as those of malignant nodules [13]. These conflicting data suggest that SUV_{max} alone is not an adequate tool in differential diagnosis of malignant and benign thyroid nodules. Kwak et al. showed the added value of sonography in the evaluation of ^{18}F-FDG-positive thyroid lesions. The probability (13.2%) of malignancy in such cases was much lower when the sonographic findings appeared benign, as compared with patients with nodules sonographically suspected of malignancy (75.5%) [26]. Unfortunately, the malignant sonographic appearance is still operator-dependant, even if these suspicious features are defined by some ultrasound guidelines. As shown above, the problem of incidentally found thyroid nodules has not been adequately solved and needs further evaluation. Our centre continues to collect a database of such lesions in order to obtain data sufficient for more profound evaluation.

Eight out of 20 patients (40%) with ^{18}FDG-avid lesions were eventually diagnosed with thyroid cancer. In 6 of 20 subjects papillary carcinoma was diagnosed. According to previous reports, most of the malignancies in focal ^{18}F-FDG-avid lesions are well-differentiated papillary carcinomas. Are et al. found this diagnosis in 19 out of 20 examined patients [27]. In our opinion, in spite of all those facts, FNAB should remain the crucial diagnostic tool in the evaluation of focal thyroid lesions.

Sebastianes et al. reported a high negative predictive value of PET in detecting malignancies in preoperative evaluation of suspected nodules if the preoperative FNAB result was inconclusive. All ^{18}FDG-avid nodules were confirmed to be cancers (100%), while almost 39% of benign lesions appeared to present increased ^{18}F-FDG uptake. In our study only one out of 4 patients with previous inconclusive FNAB result was diagnosed with follicular adenoma in histopathological examination. Currently, data is being collected to analyze whether PET/CT is helpful in decreasing the amount of unnecessary thyroidectomies due to inconclusive cytological findings.

Distant metastases that locate in the thyroid gland are rather rare. Occasionally, some of the malignant lesions found in thyroid with the means of PET/CT appear to be metastatic [30]. These data are confirmed in our study population of oncological patients: only one focus of an extrathyroid origin was detected — it was a metastasis of non-small cell lung carcinoma.

In 6.2% of our patients diffused thyroid uptake of 18F-FDG was found. The most likely diagnosis is chronic thyroiditis. In fact, many of these patients had already been treated with L-thyroxin before performing the scan. Although diffused ^{18}F-FDG uptake seems to be quite accurate in confirming the diagnosis of Hashimoto thyroiditis [19, 21], a risk of thyroid cancer in both diffuse and combined ^{18}F-FDG uptake should be kept in mind [18, 22]. Additionally, the presence of Hashimoto disease with a large goitre may impair the diagnostic value of ^{18}FDG PET in primary thyroid lymphoma [20]. Therefore, thyroid FNAB seems to be obligatory in cases of coexisting diffused ^{18}F-FDG uptake in PET scans and the occurrence of lesions seen in thyroid sonography. In our study FNAB results were available only in a few cases of diffused ^{18}FDG uptake; all of them reported Hashimoto thyroiditis.

Conclusions

The probability of malignancy in the case of focal ^{18}F-FDG accumulation in the thyroid gland is rather high. Therefore, thorough evaluation of such lesions is highly recommended in each case. Most thyroid malignancies incidentally detected in PET/CT are papillary carcinomas.

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