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MANAGEMENT PRINCIPLES OF INCIDENTAL THYROID 18F-FDG UPTAKE IDENTIFIED ON 18F-FDG PET/CT IMAGING

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Abstract

Purpose. The purpose of this study is to determine the clinical significance of incidental thyroid 18F-FDG PET/CT uptake in oncology patients with the focus achieving the most appropriate management of this challenging situation.

Materials and method. Two thousand five hundred and eighty 18F-FDG PET/CT studies performed at our institute in the past 4 years were retrospectively reviewed. Patients with incidental FDG uptake in the thyroid gland were further analysed.

Results. The prevalence of incidental FDG uptake in thyroid gland was 7.6% (129 patients). 26 patients (20.1%) had diffuse 18F-FDG PET/CT uptake, 103 patients (79.1%) had nodular uptake in thyroid gland. All diffuse uptake patients who were further examined diagnosed to be a benign condition. 53 patients in the nodular uptake group were further examined and the final histopathology examinations revealed an 18.8% malignancy rate. SUV max values ranged from 2 to 21.8 with a significant highness in malignant lesions.

Conclusion. 18F-FDG PET/CT uptake in the thyroid gland may be diffuse or nodular. Diffuse uptake needs no further examination as it usually accompanied by benign thyroid disorders. Patients with nodular uptake whose general condition is good should be further examined due to high rates of malignancy.

Keywords: Thyroid incidentaloma, 18F-FDG PET/CT Diffuse uptake, Nodular uptake.

INTRODUCTION

Thyroid nodule is defined as a lesion of the thyroid gland that is differentiated from the normal thyroid parenchyma by physical examination or imaging methods. Detection rates of nodule in thyroid gland were reported to be 2-6% with physical examination, 19-67% with ultrasonography (US) and 8-65% with autopsy series (1). Lesions in the thyroid gland, which are incidentally detected by radiological imaging methods such as US, computed tomography (CT), and magnetic resonance (MR), obtained for other reasons, are called thyroid incidentaloma. The incidence of thyroid incidentaloma has increased significantly due to better diagnostic and therapeutic use of imaging modalities (2). Thyroid nodules are usually asymptomatic unless they affect the thyroid functions or expand to create pressure on the trachea or other surrounding organs. The most important issue in thyroid nodules is to eliminate malignancy. Asymptomatic thyroid nodules do not rule out malignancy. Therefore, the actual rate of malignancy of thyroid nodules in the community is not known exactly (3).

Positron Emission Tomography-Computerized Tomography (PET/CT) scanning has long been used to diagnose and monitor several cancers such as gastric cancer, breast cancer, and malignant melanoma (4). The success of imaging of PET/CT in certain tumors since the late 1970s has increased its use in oncology after 1990s. PET/CT is not a method for screening purposes. It is used in certain oncologic applications such as diagnosis, staging, evaluation of treatment response and recurrence determination (5, 6). One of the advantages of PET/CT is the determination of the incidentalomas holding 18F-fluorodeoxyglucose (18F-FDG) in a tissue other than the known primary tumor. The expanding use of PET/CT has led to the identification of increasing numbers of patients with an incidentaloma in the thyroid gland (7, 8).

The aim of this study was to demonstrate the clinical significance and malignancy potential of incidental thyroid 18F-FDG uptake in oncology patients and to discuss management principles.

MATERIALS AND METHOD

The files of 1677 patients who had 2580

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18F-FDG PET/CT scans in Tokat Gaziosmanpaşa University Hospital between 2014 May - 2018 August were retrospectively examined. In patients with multiple PET/CT scans, the scan with the highest level of 18F-FDG uptake and which needed further examination was taken into account. One hundred twenty-nine patients with incidentally detected focal and diffuse 18F-FDG uptake in the thyroid gland were included in the study. Patients with known primary thyroid tumor and pediatric patients were excluded from the study.

All patients had the same protocol for PET/CT imaging defined by Tokat Gaziosmanpaşa University Nuclear Medicine department. Before the 18F-FDG injection, blood glucose levels of the patients who had been fasting for at least six hours were checked with a finger-stick blood glucose meter, and it was ensured that blood glucose level was less than 150 mg/dL. With a glycemic control, each patient was given 0.10 mCi/kg body weight intravenous 18F-FDG injection. Patients were given at least one liter of water. In the 60th minute, whole body PET/CT of 5 mm spatial resolution was taken using a PET scanner (Siemens Biograph 2, USA) with three minutes of acquisition for each of the five or six bed positions (supine, arms side, vertex to thigh, etc.). A low dose of 70-120 kVp and tube current of 10-90 mAs were used for contrast enhanced CT scan of over one minute without a contrast material. PET images were attenuation-corrected using the CT data. All images were checked visually for the presence of AL. Besides, they were analyzed quantitatively by the same nuclear medicine physician. Increased focal 18F-FDG uptake in the thyroid gland was defined as increased focal 18F-FDG uptake in PET images compared to background thyroid activity. The maximum SUV (SUVmax) values were calculated for each patient with abnormal 18F-FDG uptake in the thyroid gland in 18F-FDG PET/CT imaging.

The reasons for imaging (diagnosis, staging, restaging and response to treatment) were recorded. The patients were grouped into two as metastatic and non-metastatic according to primary illness. 18F-FDG uptake was evaluated as nodular or diffuse. Nodule size was calculated for the nodular uptake. SUVmax value was calculated for each 18F-FDG uptake.

For the statistical analysis, descriptive analyses were used for distribution of 18F-FDG uptake and nodule size. Pearson Chi-square test was used for categorical data. The significance of the SUVmax value for malignant and benign lesions was calculated using the Mann-Whitney U test for nonparametric data distribution. Correlation between classification of the patient groups separated by cut-off value was calculated according to the variables, and real classification was expressed by examining the sensitivity, specificity, area under curve (AUC) value using receiver operating characteristic (ROC) curve analysis.

RESULTS

Increased 18F-FDG uptake in thyroid gland was observed in 129 (7.6%) of the 1677 patients who had PET/CT scan. Nodular 18F-FDG uptake was observed in 103 patients (79.9%) while 26 patients (20.1%) had increased diffuse uptake. Figure 1 and 2 demonstrate diffuse and nodular 18F-FDG uptake. The reasons for imaging were diagnosis in 21 patients, staging in 18 patients, response to treatment and restaging in 90 patients.

Clinical features, further examination with Fine Needle Aspiration Biopsy (FNAB), surgery and histopathology results of 129 patients are shown in Table 1 and Figure 3.

Ten of the 26 patients who had diffuse uptake in thyroid gland with 18F-FDG PET/CT had metastatic primary disease. These patients were not further examined for thyroid gland. Sixteen of the 26 patients in diffuse uptake group who had non-metastatic primary tumor were further examined with thyroid function tests and US. Three patients who had nodules with US were biopsied. FNAB results were Bethesda II and III. These

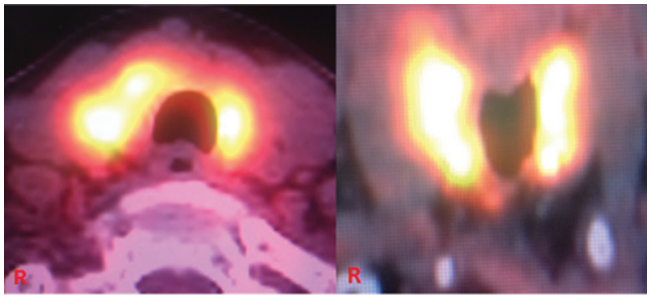

Figure 1. Diffuse 18F-FDG PET/CT uptake with transaxial and coronal sections. (SUV Max: 4.62).

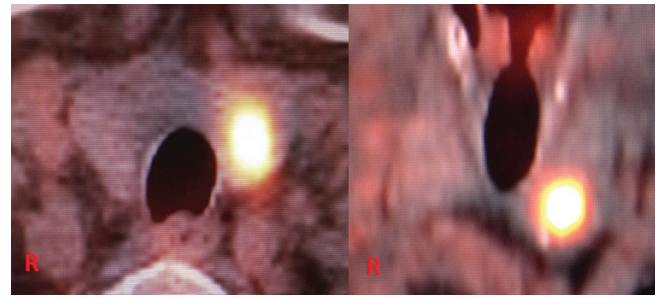

Figure 2. Focal 18F-FDG PET/CT uptake in left thyroid lobe with transaxial and coronal sections. (SUV Max: 5.28).

three patients were followed up without any thyroid problem. Other 13 patients were diagnosed and treated as thyroiditis.

Fifty of 103 patients who had nodular uptake in thyroid gland had metastatic primary disease. Fifteen of these patients whose general condition were good were further examined. Two of these patients had unknown primary cancers. FNAB results of these two patients were Bethesda V. These patients underwent total thyroidectomy and the final histopathology examination revealed thyroid papillary carcinoma. Fifty-three of 103 patients in nodular uptake group had non-metastatic disease. Thirty-eight of these 53 patients were further examined, and 31 of these patients turned out to have FNAB. Eleven of these patients had total thyroidectomy after clinical, radiologic and histopathology evaluation. Eight of these patients had malignant thyroid papillary carcinoma. Final histopathology examinations revealed malignancy in 10 of 53 patients (18.8%) with nodular uptake who were further examined.

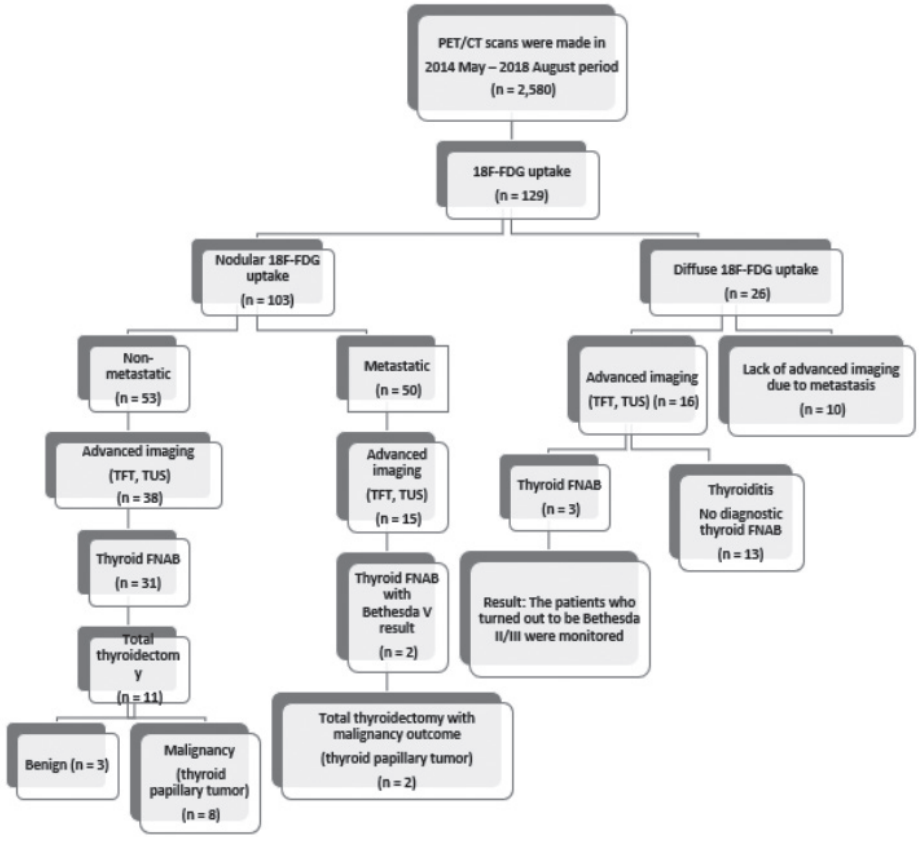

Figure 3. Evaluation of patients who had 18F-FDG PET/CT scan and were found to have 18F-FGD uptake (TFT: Thyroid function tests, TUS: Thyroid Ultrasonography, PET/CT: Positron Emission Tomography - Computerized Tomography, 18F-FGD: 18F-fluorodeoxyglucose).

Table 1. Main clinical features of patients with high 18F-FDG uptake in PET/CT

Primary tumor site	Number of patients			Result of thyroidectomy	
	18F-FDGuptake↑(n)	FNAB(n)	Thyroidectomy(n)	Benign(n)	Malignancy(n)
Gastrointestinal	32	3	3	1	2
Lung	24	6			
Gynecologic	13	3	2		2
Head and neck	12	3	1		1
Urinary system	9	2			
Breast	8	2			
Lymphoma	7	3			
Multiple myeloma	2	1			
Mesothelioma	1				
Cancer of unknown primary	21	13	7	2	5
Total(n)	129	36	13	3	10

(FNAB: Fine needle aspiration biopsy).

Average SUVmax value of 53 patients (38 non-metastatic and 15 metastatic) who were incidentally found to have increased focal 18F-FDG uptake in thyroid gland was 6.93±4.20. SUVmax value of 10 patients with malignancy diagnosis was 12.5±9.1 while SUVmax values of benign lesions (patients who were considered to be non-malignant based on advanced examination results) was 4.97±2.24. Difference in SUVmax values between malignancy and benign groups was statistically significant ($p<0.001$). Using a cutoff value of > 6.15 for SUVmax for nodular 18F-FDG uptake in thyroid tissue of our patients in PET/CT, sensitivity and specificity for predicting the malignancy were 84 and 74%, respectively (accuracy rate = 76%, AUC±SE = 0.774±0.070, $p<0.002$).

Sixty-nine of 129 patients in the study (16 of the 26 patients with diffuse uptake and 53 of the 103 patients with nodular uptake) were further examined using thyroid US, scintigraphy (Thyroid scintigraphy with Technetium 99m pertechnetate), thyroid function tests and FNAB. The mean life span of patients who did not have further examination was 455.72±327.43 days while that of the 69 patients who had further examination was 866.83±468.38 days, and the difference was significant ($p=0.041$).

A more detailed evaluation of 103 patients with high level of nodular 18F-FDG uptake by thyroid tissue in PET/CT showed a positive, but not significant, correlation between nodule diameter and SUVmax value ($r=0.068$, $p=0.497$) (Table 2).

DISCUSSION

It has been known since 1930s that the consumption of glucose in tumor tissues is higher. 18F-FDG is a glucose anolog in which the OH group is replaced with 18F. However, 18F-FDG accumulation is not specific to malignancy, and glucose metabolism is also higher in inflammatory lesions (9).

In oncological PET/CT studies, incidental uptake of 18F-FDG is more frequent in breast, adrenal glands, gastrointestinal tract, parotid gland, prostate gland and thyroid gland than other areas of the body (10-12). The uptake of 18F-FDG in thyroid tissue is homogeneous with low density under normal conditions and the thyroid gland cannot be distinguished on PET/CT imaging (13). The absence of 18F-FDG uptake in the thyroid gland depends on the preference of fatty acid oxidation for healthy thyrocytes to produce ATP. 18F-FDG uptake in the thyroid gland is roughly divided into two groups: focal and diffuse. Some researchers suggested that diffuse uptake is a variation of normal (5, 8). Some studies suggested that this uptake could be related to lymphocyte infiltration, fibrosis process, chronic thyroiditis and hypothyroidism (14).

Table 2. Relationship between thyroid nodule diameter and SUV max uptake in 103 patients with nodular uptake in 18F-FDG PET/CT

		SUVmax
Nodulediameter	r	0.068
	p	0.497
	n	103

(Correlation is significant at <0.05 level, r: Pearson Correlation Coefficient, P: significant P value, n: number of patients with nodular involvement on 18F-FDG PET/CT).

The incidental thyroid uptake of 18F-FDG in oncologic PET/CT scan was reported to have incidence rates between 0.2% and 8.9% (15-17). In the present study, the incidence of incidentaloma in the thyroid gland was 7.6%, which was consistent with the literature. Bertegna and colleagues (5) attributed the differences in populations to the endemic characteristic of thyroid diseases. The prevalence of thyroid disease in the world is 12% on the average, whereas in the Eastern Black Sea region of Turkey, this rate was reported to be up to 42% (18,19). Tokat Gaziosmanpaşa University is located in the Eastern Black Sea region where endemic thyroid diseases are common. Our results may be significant in this regard.

Although there are studies reporting that the SUVmax value measured in the thyroid tissue is significantly different in benign and malignant tissues (18,19), there are also studies indicating that SUVmax value cannot be used for this differentiation (20, 21). There is also no standard SUVmax value across different centers due to reasons such as different software and imaging systems used in different centers. An evaluation of the patients in the present study with high level of 18F-FDG uptake by thyroid tissue showed that SUVmax values were higher in the malignant nodules compared to the benign ones ($p<0.001$). With a cutoff value of >6.15 for SUVmax, sensitivity and specificity for predicting the malignancy were 84 and 74%, respectively, while the accuracy rate was 76% and AUC±SE was 0.774±0.070 ($p<0.002$).

18F-FDG uptake in PET/CT may be diffuse or focal in the thyroid. Diffuse 18F-FDG uptake is usually associated with autoimmune thyroiditis or Graves' disease (22-24) whereas focal 18F-FDG uptake may be due to a benign or malignant lesion in the thyroid. In our study, 13 of 16 patients with diffuse 18F-FDG uptake in PET/CT had US outcomes compatible with thyroiditis. The results of the biopsy of three patients who had FNAB turned out to be Bethesda 2 and 3. It was indicated in the literature that approximately 5-15% of the thyroid

nodules in the healthy individuals who undergo further examination are malignant. The reported incidence of malignancy in increased focal 18F-FDG uptake, detected incidentally on PET/CT, is highly variable in the literature ranging from 10 to 80% (25, 26, 27). In our study, the rate of malignancy in our patients who underwent further examination and surgery was 18.8%, which is consistent with the literature.

In conclusion, 18F-FDG uptake in the thyroid can be diffuse or nodular. Diffuse uptake in the thyroid gland is usually accompanied by benign thyroid diseases while nodular uptake is a condition that should be further examined. The status of the primary disease and surveillance are also important in patients with nodular 18F-FDG uptake. Patients with a long-life expectancy and nodular 18F-FDG uptake on PET/CT should be evaluated with thyroid US, thyroid function tests, scintigraphy (thyroid scintigraphy with Technetium 99m pertechnetate) and, if necessary, FNAB.

Conflict of interest

The authors declare that they have no conflict of interest.

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