Endokrynologia Polska
DOI: 10.5603/EP2015.0030
Tom/Volume 66; Numer/Number 3/2015
ISSN 0423–104X

How often do we see incidental ^{68}Ga-DOTATATE thyroid uptake in PET/CT in patients with neuroendocrine tumours?

Jak często wykrywamy przypadkowe zmiany w tarczycy w badaniu PET/CT z ^{68}Ga-DOTATATE u pacjentów diagnozowanych z powodu nowotworu neuroendokrynnego?

Jolanta Kunikowska[1], Renata Matyskiel[1], Anna Zemczak[2], Janusz Strzelczyk[2], Dariusz Pawlak[3], Leszek Królicki[1], Beata Kos-Kudła[2]

[1]Department of Nuclear Medicine, Medical University of Warsaw, Poland
[2]Division of Endocrinology, Department of Pathophysiology and Endocrinology, Silesian Medical University, Katowice, Poland
[3]National Centre for Nuclear Research, Radioisotope Centre POLATOM, Otwock — Świerk, Poland

Abstract

Introduction: Thyroid diseases, which may occur as focal or diffuse changes in thyroid parenchyma, are most often observed in women.
Aim: Our aim was to assess the prevalence of incidental thyroid uptake of ^{68}Ga-DOTATATE PET/CT in patients referred to the Nuclear Medicine Department for evaluation of neuroendocrine neoplasia (NEN).
Material and methods: We retrospectively evaluated 1150 ^{68}Ga-DOTATATE PET/CT images. Clinical history, serum TSH and thyroid antibody (TAb) concentrations, ultrasonography, and cytological assessment of the material from fine-needle aspiration biopsy (FNA) of the thyroid lesion were investigated.
Results: We found incidental abnormalities in 46/1150 (4.1%) patients (12 men, 34 women). 34/46 patients (8 men, 26 women) showed diffuse ^{68}Ga-DOTATATE thyroid uptake, with mean SUVmax 4.6 ± 1.6. Based on laboratory tests and ultrasound, we found: 38% of patients with an active autoimmune thyroiditis, 27% with benign goitre, and 6% with multinodular goitre with autoimmune thyroiditis. The remaining 29% of patients did not show any pathology. In 12/47 patients (4 men, 8 women) focal uptake in the thyroid with SUVmax 7.3 ± 3.3 was found. During one-year follow-up, category II and category III lesions (according to Bethesda classification) were revealed in 9/12 (75%) patients and in one patient, respectively. Histopathological examination after surgery revealed papillary thyroid carcinoma in one patient and benign multinodular goitre in another patient.
Conclusions: Patients with focal ^{68}Ga-DOTATATE uptake should undergo further examination (FNA) due to potential risk of malignancy. Diffuse ^{68}Ga-DOTATATE uptake was predominantly associated with active autoimmune thyroiditis or benign goitre.
The focal lesions and diffuse pathology diseases were frequently seen in women. **(Endokrynol Pol 2015; 66 (3): 231–236)**

Key words: *somatostatin receptor; ^{68}Ga-DOTATATE; PET/CT; thyroid uptake; neuroendocrine tumors*

Streszczenie

Wstęp: Zmiany w tarczycy mogą występować jako zmiany ogniskowe lub schorzenia dotyczące miąższu tarczycy, częściej stwierdzane są u kobiet. Celem pracy była ocena częstości występowania w badaniu ^{68}Ga-DOTATATE PET/CT przypadkowo stwierdzonego wychwytu w tarczycy u pacjentów, kierowanych w celu oceny stopnia zaawansowania nowotworu neuroendokrynnego (NEN).
Materiał i metody: Analizie poddano 1150 badań ^{68}Ga-DOTATATE PET/CT. Wynik badania PET/CT (ocena wizualna wychwytu, pomiar maksymalnego wychwytu znacznika SUVmax) analizowano wraz z historią kliniczną, stężeniem TSH w surowicy, poziomem przeciwciał przeciwtarczycowych (TAb), badaniem USG i oceną cytologiczną materiału z biopsji cienkoigłowej (BACC).
Wyniki: Przypadkowe zmiany w tarczycy wykryto u 46/1150 (4,1%) pacjentów: 12 mężczyzn i 34 kobiet. U 34/46 pacjentów (8 mężczyzn, 26 kobiet) stwierdzono rozlany wychwyt w tarczycy ze średnim SUVmax 4,6 ± 1,6. W tej grupie w badaniach laboratoryjnych i badaniu USG stwierdzono: u 38% aktywne autoimmunologiczne zapalenie tarczycy, u 27% wole obojętne, u 6% wole guzowate z komponentą autoimmunologiczną; u pozostałych 29% pacjentów nie stwierdzono żadnej patologii. U 12/46 pacjentów stwierdzono ogniskowy wychwyt w tarczycy (4 mężczyzn, 8 kobiet) z SUVmax 7,3 ± 3,3 (zakres 3,9–12,6). U 9/12 w rocznych badaniach kontrolnych stwierdzono kategorię II, u jednego pacjenta kategorię III. W pooperacyjnym badaniu histopatologicznym stwierdzono raka brodawkowatego tarczycy u jednego pacjenta oraz u jednej osoby łagodny rozrost guzkowy.
Wnioski: Ogniskowy wychwyt stwierdzony w badaniu ^{68}Ga-DOTATATE PET/CT wymaga weryfikacji (BACC) ze względu na potencjalne ryzyko wystąpienia nowotworu złośliwego. Rozlany wychwyt ^{68}Ga-DOTATATE PET/CT najczęściej wiąże się z aktywnym autoimmunologicznym zapaleniem tarczycy i wolem guzkowym. Zarówno zmiany ogniskowe, jak i rozlany wychwyt w tarczycy występowały częściej u kobiet. **(Endokrynol Pol 2015; 66 (3): 231–236)**

Słowa kluczowe: *receptory somatostatynowe, ^{68}Ga-DOTATATE, PET/CT, wychwyt w tarczycy, nowotwory neuroendokrynne*

Jolanta Kunikowska M.D., Nuclear Medicine Department, Medical University of Warsaw, Banacha St. 1a, 02–097 Warsaw, Poland, tel.: +48 22 599 22 70, fax: +48 22 599 11 70, e-mail: jolanta.kunikowska@wum.edu.pl

Introduction

Somatostatin receptors (SSTR1 to SSTR5) play an important role not only in the maintenance of normal thyroid physiology, but also in pathologic conditions. Somatostatin (SST) and SSTR1-5 are expressed in medullary thyroid carcinoma (MTC) and differentiated thyroid cancers (DTC), but the role of SSTR subtypes is still not clear [1–3]. Some authors reported that SSTR2 has been found to be the predominant subtype in DTC with a high expression particularly in papillary cancer [4]. SSTR2 also seems to play an important role in the pathophysiology of benign thyroid diseases [5]. Recently published studies suggest that SSTR2 was the most common receptor expressed in benign diseases like multinodular goitre, Graves' disease, Hashimoto disease, or follicular adenoma [6].

On the other hand, ^{68}Ga labelled somatostatin (SST) analogues (like: DOTATATE and DOTATOC) have high affinity to SSTR2. Significant correlation was found between SSTR2 expression and the maximum Standardised Uptake Value (SUVmax) as a semiquantitative parameter on the PET/CT [7]. The visualisation of SSTR2 status *in vivo* with radiolabelled SST analogues help to define the role of SSTR2 in thyroid diseases.

The incidental ^{68}Ga-DOTATATE or ^{68}Ga-DOTATOC uptake seen in the thyroid gland is not an occasional finding on diagnostic PET/CT scans during diagnosis of neuroendocrine neoplasia (NEN). In the published data the problem of unexpected increased uptake of ^{68}Ga-labelled SST analogues in thyroid gland and clinical significance of such findings has not been presented yet and needs further evaluation.

The aim of the study was to evaluate the prevalence of incidental thyroid uptake of ^{68}Ga-DOTATATE PET/CT in patients referred to the Nuclear Medicine Department for evaluation of NEN.

Material and methods

The study was approved by the Ethical Committee of the Medical University of Warsaw. Written informed consent was obtained from all patients.

We retrospectively evaluated 1150 patients with NEN, who underwent ^{68}Ga-DOTATATE PET/CT imaging between January 2010 and March 2013.

Clinical history, serum TSH levels, thyroid antibodies (TAb), ultrasonography, and cytological assessment of the material from fine-needle aspiration biopsy (FNA) of the thyroid lesion were investigated. The cytology examination was described by Bethesda classification [8].

Laboratory examination: serum thyroid-stimulating hormone (TSH), free thyroxine (fT4), free triiodothyronine (fT3), serum thyroperoxidase antibody (ATPO), and thyroglobulin antibody (ATG) were measured using the chemiluminescence method (Immulite 1000 Siemens Healthcare Diagnostics, Architect ci 8200 Abott).

The normal range for TSH level was defined as 0.4–4.0 μIU/mL, for fT4 0.89–1.76 ng/dL, for fT3 1.5––4.1 pg/mL, ATPO < 35.0 IU/mL, and ATG < 115.0 IU/mL.

^{68}Ga -DOTATATE PET/CT scans were performed not earlier than five weeks after the last injection of long-acting SST analogues — octreotide and seven weeks after lanreotide.

Sites of thyroid pathological uptake were noted and confirmed on ultrasound (US) (Voluson E8, linear probe 6 cm/1,0/25Hz) and FNA.

PET/CT imaging

Preparation of radiopharmaceutical ^{68}Ga –DOTATATE and the ^{68}Ga -DOTATATE PET/CT was performed using a previously-described procedure [9].

Image analysis

Image analysis was performed using a Multi-Modality Work Station (MMWS), Syngo (TrueD) (Siemens Medical Solutions). Attenuation-corrected PET images and PET/CT images were analysed. The PET images without attenuation correction were also reviewed. The PET/CT fusion images were used for evaluation of uptake using volume regions of interest (ROIs). The SUV maximum and mean were calculated in all ROIs using the following formula:

SUVmax = Maximum Activity Concentration at time from pixel values/(Injected Dose/Patient Weight)

The thyroid uptake of ^{68}Ga-DOTATATE was analysed: firstly qualitative-visual analysis of distribution pattern and semiquantitative with measurement of SUVmax.

Statistical methods

Patient characteristics, thyroid SUVmax, TAb level, and serum TSH were characterised by the mean (± SD) and median .

To assess the normal distribution data we used the Shapiro-Wilk test and graphical analysis by inspection of the histograms. Spearman's correlation coefficient was used to determine the association of thyroid SUVmax with ATPO and TSH. The tests were two-sided and a p-value of < 0.05 was considered statistically significant.

Calculations were performed using Statistica software (6.0 Stat Soft, Inc. 1984–2002) and Excel (Microsoft Office Professional Edition 2013).

Results

Labelling and imaging procedure

^{68}Ga-DOTATATE was successfully labelled with a radiochemical purity of over 99%. For PET/CT examination a mean injected activity of ^{68}Ga-DOTATATE of 156.4 ± 18.1 MBq, (range: 120–200 MBq) was administered without any major side effects.

Thyroid uptake

Among 1150 patients with histological confirmation of NEN (G1 — 42% and G2 — 58%), referred for staging or restaging after surgery, we revealed abnormalities in the thyroid in 46 (4.1%) patients (12 males and 34 females, mean age 63.8 years ± 10.8; range 25–85 years) with the prevalence significantly higher in women 3.0% than in men 1.1%.

The incidental increased uptake of ^{68}Ga-DOTATATE in the thyroid gland was defined as focal or diffuse, inhomogeneous. A diffuse uptake was noted in 74% of patients and focal in 26% of patients.

Subsequently we analysed the clinical significance of abnormal radiotracer distribution pattern in the thyroid gland and the impact of such a finding on the clinical management of those patients. We compared it with ultrasound, TSH level, TAb, and FNA.

Thyroid diffuse uptake

Increased diffuse, inhomogeneous ^{68}Ga-DOTATATE thyroid uptake was seen in 34/46 patients (8 males, 26 females, mean age 49.5 years ± 16.7; range 25–85). Laboratory tests and ultrasonography revealed: Hashimoto disease in 13 patients (38.2%), multinodular goitre in 9 patients (26.6%), and multinodular goitre coexisting with Hashimoto disease in 2 patients (5.8%) (Figs. 1 and 2). In the remaining 10 patients (29.4%) no abnormalities of laboratory tests and ultrasound were seen.

The mean SUVmax was 4.6 ± 1.6, and median SUVmax was 5.3 (range 2.0–10.9).

The mean TSH level was 1.8 ± 1.2 mIU/L and median 1.7 mIU/L (range: 0.005–5.3 mIU/L). In patients with Hashimoto disease the mean ATPO level was 327.0 ± 733.3 IU/mL, median 67.5 IU/ ml (range: 17.3—2821 IU/mL), the mean ATG level was 99.6 ± 84.0 IU/mL, and median 65.0 IU/mL (range: 19.2–282.0 IU/mL).

Before ^{68}Ga-DOTATATE PET/CT imaging 15/34 (44%) patients had no prior history of thyroid disease. Among them, laboratory test and ultrasound revealed Hashimoto disease in 5 patients, and the remaining 10 patients did not reveal pathology within 6–12-month follow-up.

19/34 (66%) patients had previous history of thyroid disease; 10 patients had long-term supplementation with L-thyroxine, 2 patients Thiamazole therapy.

Spearman correlation coefficient showed no correlation between thyroid SUVmax value and the ATPO level (rho = –0.107, p = 0.547) and SUVmax and TSH value (rho = 0.017, p = 0.924).

Focal thyroid uptake

12/46 patients (4 males, 8 females, mean age 55.5 ± 17.2 years, range 35–78) had focal uptake in the thyroid. All patients had prior history of thyroid diseases: one patient had Hashimoto disease, six patients had multinodular goitre coexisting with Hahimoto disease, and five patients had multinodular goitre. Among them three patients were receiving substitutive therapy with L-thyroxine and one patient with multinodular goitre Thiamazole therapy. The ultrasound revealed hypoechogenic lesions in 10 patients and irregular echogenicity in 2 patients.

The mean thyroid SUVmax was 7.3 ± 3.1, and median SUVmax 6.6 (range 2.8–12.6). The mean TSH level was 3.0 ± 4.9 mIU/L, and the median was 1.47 mIU/L (range 0.06–19.2 mIU/L).

Based on histopathology 2/12 patients after thyroidectomy revealed the following: one patient had papillary thyroid cancer (SUVmax 11.6) (Fig. 3), and one patient had benign multinodular goitre. Among the remaining 9/12 patients managed with a 12-month follow-up all had category II lesion (Fig. 4). One patient's (with category III lesion) follow-up data was unavailable.

Discussion

The spread of ^{68}Ga-DOTA-somatostatin analogues PET/CT availability as a new standard imaging for the diagnosis of patients with NEN forces us to clarify the clinical role of incidental radiotracer uptake seen in the thyroid gland. In addition, no guidelines have been drawn up for the clinical assessment and management of such abnormalities.

In visual analysis normal ^{68}Ga-DOTATATE uptake tends to be bilateral, diffuse, homogenous, and only slightly visible on maximum intensity projection (MIP), with mean SUVmax 2.9 (± 1.2) [9]. Knowledge of normal ^{68}Ga-DOTATATE distribution in the thyroid gland is crucial for accurate image interpretation, which should not be confused with any pathology. The assessment of the functional SSTR2 receptor status *in vivo* in normal thyroid by ^{68}Ga-DOTATATE PET/CT seems to be partially consistent with the results obtained in vitro, but published studies are still very limited and often controversial [3, 5, 6, 10]. In the normal thyroid, increased expression of SSTR3 and SSTR5 have been documented by molecular methods, whilst SSTR2 expression was at very low levels [1]. In immunochemistry (IHC) some

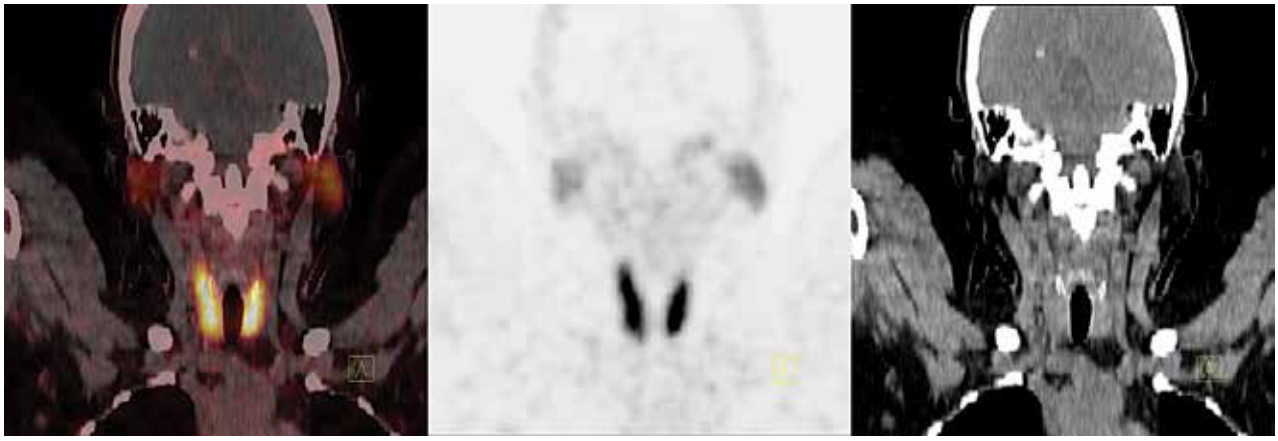

Figure 1. *PET/CT with ^{68}Ga-DOTATATE in patients with pancreatic NEN G2 with diffuse, homogenous uptake in thyroid gland (SUVmax 9.8). US as well, laboratory tests revealed Hashimoto disease (Fusion PET/CT, PET, CT)*

Rycina 1. *Badanie ^{68}Ga-DOTATATE PET/CT u pacjenta z NEN G2 trzustki, z widocznym rozlanym, jednorodnym gromadzeniem znacznika w gruczole tarczowym (SUVmax 9.8). W badaniu USG oraz w badaniach laboratoryjnych potwierdzono chorobę Hashimoto (Fuzja PET/CT, PET, CT)*

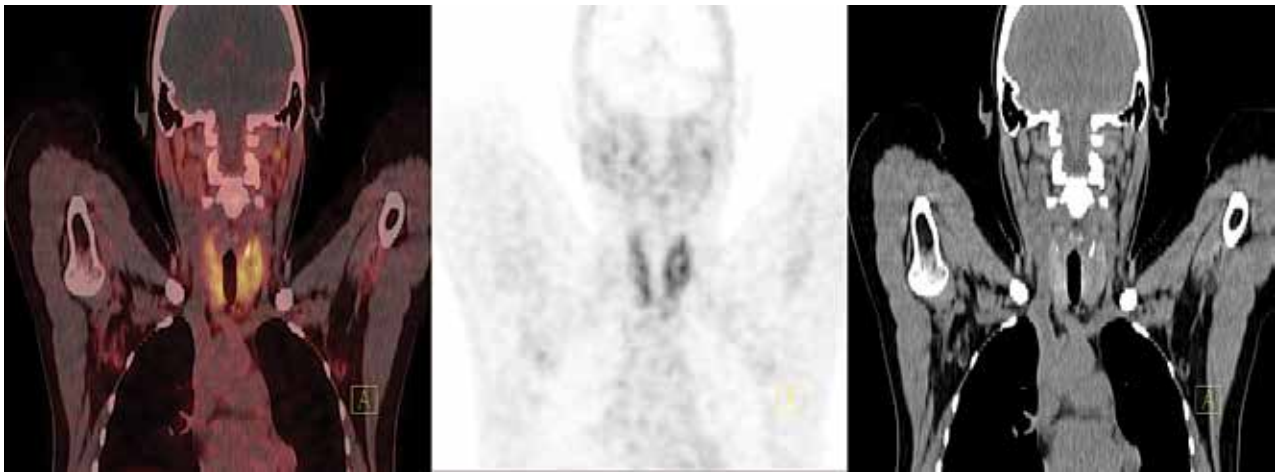

Figure 2. *PET/CT with ^{68}Ga-DOTATATE in patients with ileal NEN G1 with diffuse, nonhomogeneous uptake (SUVmax 3.3). US as well, laboratory test revealed Hashimoto disease (Fusion PET/CT, PET, CT)*

Rycina 2. *Badanie ^{68}Ga-DOTATATE PET/CT u pacjenta z NEN G1 jelita cienkiego, z widocznym rozlanym, niejednorodnym gromadzeniem znacznika w gruczole tarczowym (SUVmax 3.3). W badaniu USG oraz w badaniach laboratoryjnych potwierdzono chorobę Hashimoto (Fuzja PET/CT, PET, CT)*

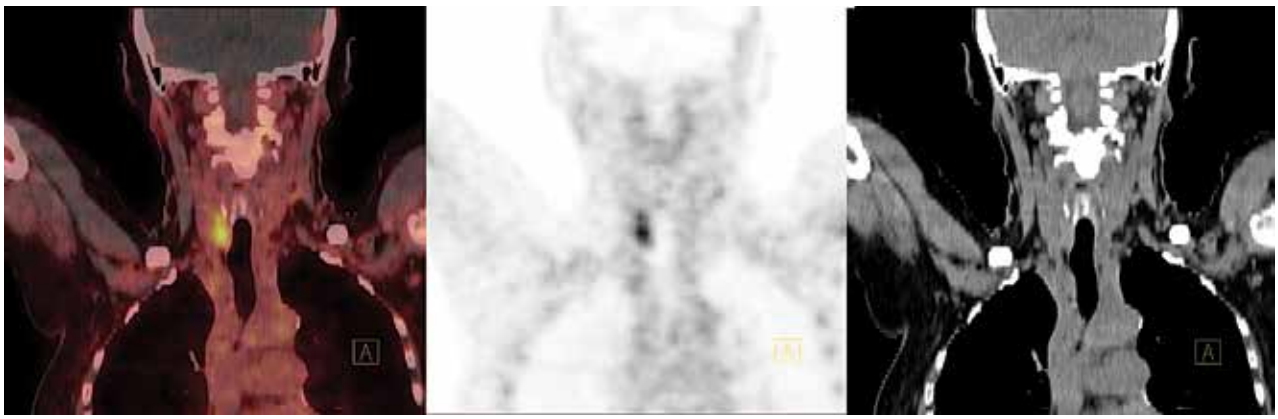

Figure 3. *PET/CT with ^{68}Ga-DOTATATE in patients with gastric NEN G1 with focal uptake in the right lobe (SUVmax 11.6). FNA biopsy as well as post-surgical examination revealed papillary carcinoma (Fusion PET/CT, PET, CT)*

Rycina 3. *Badanie ^{68}Ga-DOTATATE PET/CT u pacjenta z NEN G1 żołądka, z widocznym ogniskiem gromadzenia znacznika w prawym płacie tarczycy (SUVmax 11.6). W biopsji cienkoigłowej oraz w pooperacyjnym badaniu histopatologicznym – rak brodawkowaty tarczycy. (Fuzja PET/CT, PET, CT)*

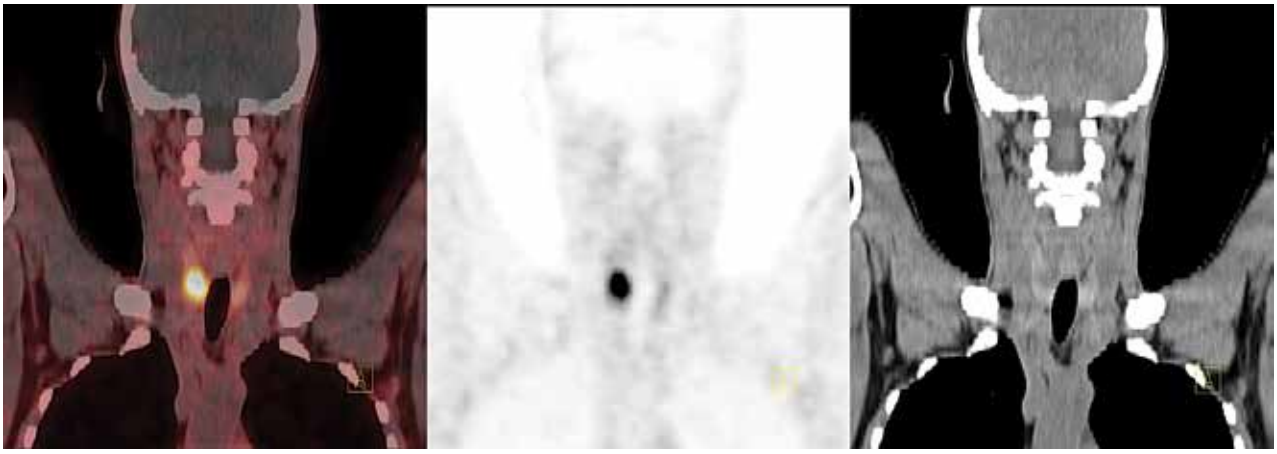

Figure 4. *PET/CT with ^{68}Ga-DOTATATE in patients with unknown primary NEN with focal uptake in the right lobe (SUVmax 4.2). US and FNA biopsy examination revealed category II lesion in multinodular goitre (Fusion PET/CT, PET, CT)*

Rycina 4. *Badanie ^{68}Ga-DOTATATE PET/CT u pacjenta z NEN o nieznanym punkcie wyjścia z widocznym ogniskiem gromadzenia znacznika w prawym płacie tarczycy (SUVmax 4.2). W badaniu USG oraz biopsji cienkoigłowej- zmiana kategorii II w wolu wieloguzkowym (Fuzja PET/CT, PET, CT)*

authors found that in the normal thyroid tissue SSTR2 was expressed in 13%, SSTR3 in 24%, and SSTR5 only in 2%, without expression of SSTR1or SSTR4 [10]. Conversely, in a recently published study SSTR expression was highly expressed in normal thyroid tissue for SSTR1, SSTR3, SSTR4, and SSTR5, whilst SSTR 2a was not expressed at all [6]. Results depend on the investigation method used - expression of receptors at the level of mRNA SSTRs or IHC [1, 6, 10–12].

A study of the Polish population revealed thyroid dysfunctions in over 10% of older patients, but 80% of them were subclinical [13]. In our study an unexpected increase of ^{68}Ga-DOTATATE uptake in the thyroid gland was seen in 4.1% of patients.

Most of them presented a diffuse pattern as predominantly seen in Hashimoto disease and less frequently in multinodular goitre and normal thyroid gland. Data in the literature regarding SSTR2 expression in vivo in benign thyroid pathologies are still limited with a very small sample size [14–20].

In patients with NEN, who underwent ^{111}In-octreotide scintigraphy for tumour localisation, the increased uptake of radiotracer was seen predominantly in endemic goitre with or without thyroid autonomy [14]. The diffuse, bilateral uptake of ^{111}In-octreotide or ^{111}In-pentetreotide as a dominant pattern in patients with autoimmune thyroiditis (AITD): Graves' disease and Hashimoto disease [15–18], was reported by other authors. Thyroid ^{111}In-pentetreotide accumulation in Graves' disease patients was increased seven fold compared to the control group and was almost absent after radioiodine-induced hypothyroidism [15]. In untreated hyperthyroid patients a positive correlation between ^{111}In-pentetreotide uptake in the thyroid and TSH, fT4, fT3, as well receptor autoantibodies levels was found. These correlations were absent after treatment with Thiamazole [17].

Currently, because of its higher sensitivity, PET/CT with ^{68}Ga-labelled somatostatin analogues is the preferred diagnostic method for detection of SSTR2 in vivo [24]. The majority of published studies focus on the clinical value ^{68}Ga-labelled somatostatin analogues PET/CT in patients with non-radioiodine-avid DTC and high thyroglobulin levels [21–23].

The both studies suggest that increased ^{68}Ga-labelled SST analogues uptake in thyroid in patients with AITD might be related to the activity of autoimmune diseases [18, 19]. Both studies suggest that increased ^{68}Ga-labelled SST analogues uptake in thyroid in patients with AITD might be related to the activity of autoimmune disease. Intense tracer uptake was found in some cases (4.8%) of structurally and functionally normal thyroid lobes, but follow-up after 6–14 months did not show any thyroid pathology [20].

Normal thyroids as well as ones with non-toxic nodules and goitres showed a clearly detectable radiotracer uptake with large variability [19]. The radiotracer uptake seen in thyroid can reflect a dense infiltration of lymphocytes that express SSTR2 on their plasma membrane [16, 17, 19, 20].

Contrary to published studies, we found the diffuse pattern with nearly the same frequency for multinodular goitre as for normal thyroid gland. In our series about 30% of patients with increased, inhomogeneous ^{68}Ga-DOTATATE uptake had normal thyroid gland, and 12-month follow-up did not reveal any pathology. Longer follow-up studies are needed to determine whether increased ^{68}Ga-DOTATATE uptake in these

patients can predict future autoimmune thyroiditis or demonstrate normal distribution pattern.

A fundamental problem is differential diagnosis between malignant and benign lesions in focal ^{68}Ga-DOTATATE uptake in thyroid gland, which was noted in 26% of patients.

The prevalence of malignancy among this group was 8% (papillary thyroid cancer). Subsequent biopsy recommended after ^{68}Ga-DOTATATE PET/CT critically changed in the management of this patients. Interestingly, in published studies the focal pattern was associated mainly with hot thyroid nodule (in ^{99m}Tc) and less frequently with benign cold nodules [19, 20]. Due to the high expression of SSTR2 reported in papillary thyroid cancer and benign thyroid nodules in vitro and in vivo studies is probable that the high value of SUVmax could be seen in both conditions [5, 6, 19, 20]. Therefore, in the case of focal uptake of ^{68}Ga-DOTATATE, the patient should undergo further examination, including ultrasonography and FNA, to exclude a thyroid carcinoma.

Our study, for the first time, underlined the clinical significance of an unexpected increase in ^{68}Ga-DOTATATE uptake in the thyroid gland seen on PET/CT. One of the main limitations of this study is its retrospective design, which may have introduced potential selection bias. For some of the variables the follow-up data were scarce. Another important limitation is that the study population included a small percentage with incidental, abnormal thyroid uptake seen in all performed examinations. In particular, due to the small number of patients, the methods of statistical analysis used were limited. For all of the above-mentioned reasons the results should be interpreted with appropriate caution.

Conclusions

Patients with focal ^{68}Ga -DOTATATE uptake should undergo further examination due to potential risk of malignancy. Diffuse ^{68}Ga-DOTATATE uptake was predominantly associated with active autoimmune thyroiditis or benign goitre.

Both focal and diffuse thyroid pathologies were often seen in women.

Acknowledgments

Special thanks to Michał Najdzik for graphic processing.

References

1. Zatelli MC, Degli Uberti EC. Somatostatin receptors: from basic science to clinical
2. Approach — thyroid. Digestive and Liver Diseases 2004; 36: S86–S92.
3. Treglia G, Rindi G, Rufini V. Expression of somatostatin receptors may guide the use of somatostatin receptor imaging andtherapy in differentiated thyroid cancer. Hormones 2012; 11 (3): 230–232.
4. Druckenthaner M, Schwarzer C, Ensinger C et al. Evidence for somatostatin receptor 2 in thyroid tissue. Regulatory peptides 2007; 138: 32–39.
5. Klagge A, Krause K, Schierle K et al. Somatostatin receptor subtype expression in human thyroid tumours. Horm Metab Res. 2010; 42: 237–240.
6. Sancak S, Hardt A, Singer J et al. Somatostatin receptor 2 expression determined by immunohistochemistry in cold thyroid nodules exceeds that of hot thyroid nodules, papillary thyroid carcinoma, and Graves' disease. Thyroid 2010; 20: 505–511.
7. Atkinson H, England JA, Rafferty A et al. Somatostatin receptor expression in thyroid disease. Int J Exp Pathol 2013; 94: 226–229.
8. Miederer M, Seidl S, Buck A et al. Correlation of immunohistopathological expression of somatostatin receptor 2 with standardised uptake values in ^{68}Ga-DOTATOC PET/CT. Eur J Nucl Med Mol Imaging 2009; 36: 48–52.
9. Cibas ES, Ali SZ. The Bethesda System for Reporting Thyroid Cytopathology. Thyroid 2009; 19: 1159–1165.
10. Kunikowska J, Królicki L, Pawlak D et al. Semiquantitative analysis and characterization of physiological biodistribution of (68)Ga-DOTA-TATE PET/CT. Clin Nucl Med 2012; 37: 1052–1057.
11. Pazaitou-Panayiotou K, Tiensuu Janson E, Koletsa T et al. Somatostatin receptor expression in non-medullary thyroid carcinomas. Hormones (Athens) 2012; 11: 290–296.
12. Boy C, Heusner TA, Poeppel TD et al. 68Ga-DOTATOC PET/CT and somatostatin receptor (sst1-sst5) expression in normal human tissue: Correlation of sst2 mRNA and SUV max. Eur J Nucl Med Mol Imaging 2011; 38: 1224–1236.
13. Pisarek H, Stępień T, Kubiak T et al. Expression of somatostatin receptor subtypes in human thyroid tumors: the immunohistochemical and molecular biology (RT-PCR) investigation. Thyroid Res 2009; 2: 1.
14. Bar-Andziak E, Milewicz A, Jędrzejuk D et al. Thyroid dysfunction and thyroid autoimmunity in a large unselected population of elderly subjects in Poland — the 'PolSenior' multicentre crossover study. Endokrynol Pol 2012; 63: 346–355.
15. Becker W, Schrell U, Buchfelder M et al. Somatostatin receptor expression in the thyroid demonstrated with 111In-octreotidescintigraphy. Nuklearmedizin 1995; 34: 100–103.
16. Krenning EP, Gel HY, Kooij PPM et al. Thyroid and orbital radiolabelled somatostatin accumulationin Graves' diseaseand Graves' ophthalmopathy. JNUC1Med 1992; 33: 894.
17. Postema PTE, Krenning EP, Wijngaarde R et al. [111In-DTPA-D-Phe1] octreotide scintigraphy in thyroidal and orbital Graves' disease: a parameter for disease activity? J Clin Endocrinol Metab 1994; 79: 1845–1851.
18. Kahaly G ,Görges R, Diaz M et al. Indium-111-pentetreotide in Graves' disease. J Nucl Med 1998; 39: 533–536.
19. Mansi L, Rambaldi PF, Bizzarro A et al. 111In-octreotide in the evaluation of autoimmune thyroid diseases. Q J Nucl Med 1995 ; 39 (4 Suppl. 1): 127–130.
20. Lincke T, Singer J, Kluge R et al. Relative Quantification of Indium-111 Pentetreotide and Gallium-68 DOTATOC Uptake in the Thyroid Gland and Association with Thyroid Pathologies. Thyroid 2009; 19: 381–389.
21. Lincke T, Orschekowski G, Singer J et al. Increased gallium-68 DOTATOC uptake in normal thyroid glands. Horm Metab Res 2011; 43: 282–286.
22. Mittal BR, Agrawal K, Shukla J et al. Ga-68 DOTATATE PET/CT in neuroendocrine tumors: initial experience. Journal of Postgraduate Medicine Education and Research 2013; 47: 1–6.
23. Versari A, Sollini M, Frasoldati A et al. Differentiated thyroid cancer: a new perspective with radiolabeled somatostatin analogues forimaging and treatment of patients. Thyroid 2014; 24: 715–726.
24. Kos-Kudła B, Blicharz-Dorniak J, Handkiewicz-Junak D et al. Diagnostic and therapeutic guidelines for gastro-entero-pancreatic neuroendocrineneoplasms (recommended by the Polish Network of Neuroendocrine Tumours). Endokrynol Pol 2013; 64: 418–443.