ORIGINAL ARTICLES

^{18}F-PET/CT imaging of metastasis to the thyroid gland: Imaging findings and effect on patient management

Giovanni G. Millare[1], Michael Kwon[2], Beth S. Edeiken-Monroe[2], J. Matthew Debnam*[2]

[1] *Department of Diagnostic Radiology, Wilford Hall Ambulatory Surgical Center, San Antonio, Texas, United States*
[2] *Department of Diagnostic Radiology, Section of Neuroradiology, The University of Texas MD Anderson Cancer Center, Houston, Texas, United States*

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ABSTRACT

Purpose: While metastasis to the thyroid from a primary cancer remote to the thyroid is uncommon, current imaging techniques have improved detection of these intrathyroid metastases. The purpose of this study was to evaluate the ^{18}F-PET/CT appearance of intrathyroid metastases and assess the impact of detection on patient management.
Methods: The ^{18}F-PET/CT appearance of intrathyroid metastasis, including standardized uptake value (SUV), disease extent, and the effect on patient management following diagnosis were retrospectively reviewed. Inclusion criteria included ^{18}F-PET/CT imaging and diagnosis of the intrathyroid metastasis matching the remote primary tumor.
Results: Intrathyroid metastasis were detected in 24 patients. The intrathyroid metastases presented on ^{18}F-PET/CT as focal nodular uptake (n = 21), multiple nodular uptake (n = 2), or diffuse uptake/infiltration of the thyroid gland (n = 1). The SUV ranged between 3.9 and 42 (median 12.5 $\pm$ 7.5); in 2 patients, the FDG-avidity was minimal. On ^{18}F-PET/CT, distant metastases were present outside the neck (n = 18), or limited to the neck (n = 6). In 2 of these 6 patients, the thyroid was the only site of metastatic disease. Due to the metastatic disease, the therapy was changed in 23 of 24 patients; 1 patient was lost to follow-up.
Conclusion: In any patient with a previous or current history of an extrathyroid malignancy, an ^{18}FDG-avid thyroid mass or diffuse infiltration of the thyroid on ^{18}F-PET/CT should be considered a potential intrathyoid metastasis until proven otherwise. Knowledge of an intrathyroid metastasis may impact patient management, especially if the thyroid or neck are the only sites of metastatic disease.

Key Words: PET/CT, Thyroid, Metastasis, Standardized uptake value (SUV)

1. INTRODUCTION

Intrathyroid metastasis from an extrathyroid primary cancer is uncommon clinically. In the past, metastases to the thyroid have been most commonly detected at autopsy with a reported incidence ranging from 1.25% to 24%.[1–14] While clinical findings may be subtle, detection of an intrathyroid metastasis from an extrathyroid primary tumor has improved with current imaging techniques, including ^{18}F-PET/CT. To the best of our knowledge, previous descriptions of the ^{18}F-PET/CT of intrathyroid metastases are limited to case reports[15–21] and there are no reports about how detection of an intrathyroid metastasis effects management. As knowledge of metastasis specific to the thyroid gland could potentially change patient management, the purpose of this study is to report on our experience with ^{18}F-PET/CT on intrathyroid metastases.

*Correspondence: J. Matthew Debnam; Email: matthew.debnam@mdanderson.org; Address: Department of Diagnostic Imaging, The University of Texas, MD Anderson Cancer Center, Houston, Texas, United States.

2. MATERIALS AND METHODS

The Institutional Review Board approved this study and waived the requirement for informed consent. Data acquisition was performed in compliance with all applicable Health Insurance Portability and Accountability Act regulations. Fifty-five patients have been diagnosed with a cytologically-proven intrathyroid metastases matching an extrathyroid primary tumor at our institution between 2002 and 2016. From this group, those patients in whom an ^{18}F-PET/CT study was obtained were included in this study. A retrospective review of the patient demographics and ^{18}F-PET/CT appearance of intrathyroid metastases from a remote primary tumor was performed.

Table 1. Patients' demographics

Patient #	Age/Sex	Primary cancer	PET/CT indication	Staging
1	54/F	Breast	Staging	T1N0M0
2	64/M	Lung	Staging	T2N2M1
3	63/M	Melanoma	Staging	Clark's level II
4	59/F	Melanoma	Staging	Stage III
5	40/F	Neuroendocrine adrenal	Staging	NA
6	79/M	Lung	Staging	T2N2M0
7	45/M	SCC-RMT	Staging	T1N0MO
8	66/M	Lung	Staging	T1N3M0
9	77/F	Colon	Thyroid mass	T1N3M0
10	60/F	SCC-tonsil	Prior US FNA	T1N2CMO
11	52/F	Lung	Prior US FNA	NA
12	44/F	Lung	Staging	T1N0M0
13	48/F	Breast	Staging	NA
14	67/M	Synovial sarcoma C1 ring	Staging	NA
15	49/M	SCC-tonsil	Staging	T2N2bMO
16	50/F	Breast	Staging	T2 N1MX
17	59/F	Lung	Prior US FNA	T3N3M0
18	52/F	Breast	Staging	T1N0M0
19	57/M	Lung	Staging	T2N3M0
20	58/F	Lung	Staging	T4N3M1
21	61/M	SCC-BOT	Prior US FNA	T2N2CMO
22	65/F	Breast	Prior US FNA	T4N0M0
23	51/M	Lung	Staging	Stage IV
24	67/F	SCC nasal cavity	Staging	T2N2M0

Note. SCC: squamous cell carcinoma; RMT: retromolar trigone; BOT: base of tongue; FNA: fine needle aspiration.

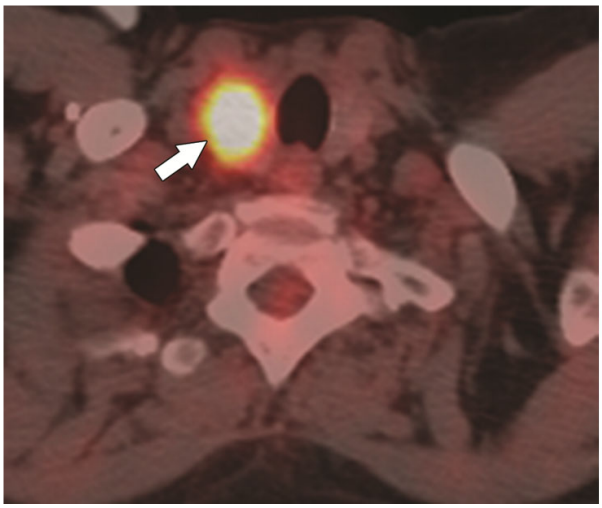

Figure 1. A 54-year-old female with breast cancer (patient #1). ^{18}F-PET/CT, axial plane, shows a solitary nodular focus of uptake in the right thyroid gland (SUV = 15.4) (arrow).

^{18}F-PET/CT scans were performed on a dedicated PET/CT system (Discovery ST, STe, or RX, General Electric Medical Systems, Milwaukee, WI). Scans were acquired to include a region from the orbits through the mid thighs. Scans were acquired 60 to 90 minutes after intravenous administration of ^{18}F-PET/CT. PET studies were acquired in either 2-dimensional or 3-dimensional acquisition mode at 3-5 minutes per bed position (depending on the patient body mass index).

3. RESULTS

3.1 Demographics

Intrathyroid metastases were detected on ^{18}F-PET/CT scans in 24 patients, 10 men and 14 women, age range 44-77 years (median 58.5 $\pm$ 9.8 years). Sites of primary tumor were as follows: lung (n = 9), breast (n = 5), head and neck (n = 5), melanoma (n = 2), colon (n = 1), neuroendocrine tumor

of the adrenal gland (n = 1), and synovial sarcoma of the C1 level (n = 1). The patient demographics, indication for PET/CT imaging and staging, when available, is provided in Table 1.

The time from primary tumor diagnosis to ^{18}F-PET/CT imaging demonstrating the intrathyroid metastasis ranged from 2-141 months (median 16 months). Clinically, the patients were asymptomatic (n = 16), presented with a palpable neck/thyroid mass (n = 7), or neck pain (n = 1). The time from ^{18}F-PET/CT to diagnosis of the intrathyroid metastasis ranged between 121 days before the ^{18}F-PET/CT to 53 days after (median 4 $\pm$ 29 days after the ^{18}F-PET/CT).

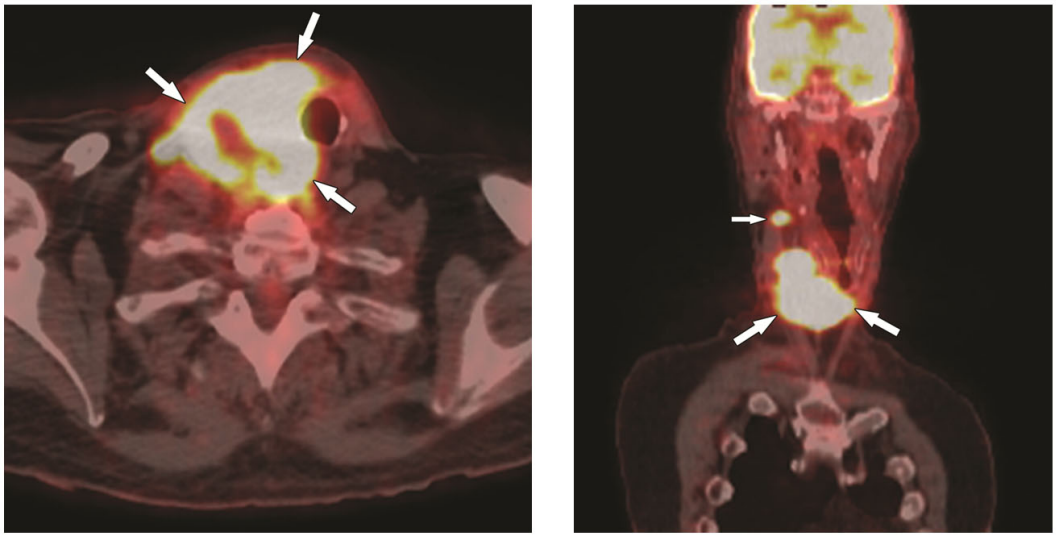

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Figure 2. A 67-year-old male with synovial sarcoma of the C1 ring (patient #14). A) ^{18}F-PET/CT, axial plane, shows multiple nodular foci of uptake (SUV = 21.8) in the thyroid and isthmus (arrows). B) ^{18}F-PET/CT, coronal plane, multiple nodular foci of uptake in the right thyroid (large arrows) and right mid neck node (small arrow). Note lack of FDG activity in the left lobe.

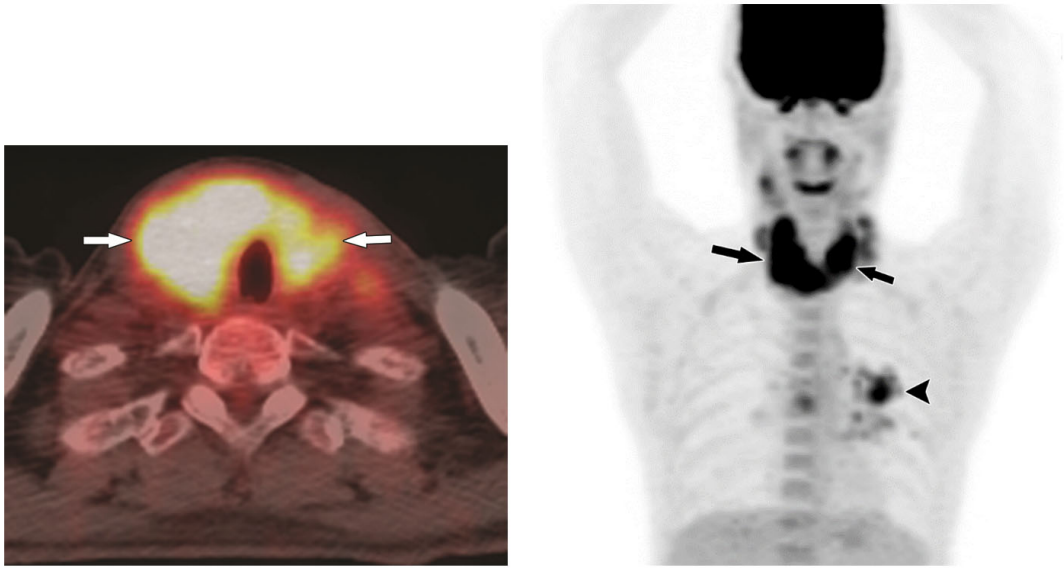

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Figure 3. A 51-year-old male with history of lung cancer (patient #23). A) ^{18}F-PET/CT, axial plane, show diffuse uptake throughout the thyroid gland (SUV = 9.4) (arrows). B) ^{18}F-PET/CT, 3D image, diffuse uptake in the thyroid gland (large arrows) and a left lung metastasis (small arrow).

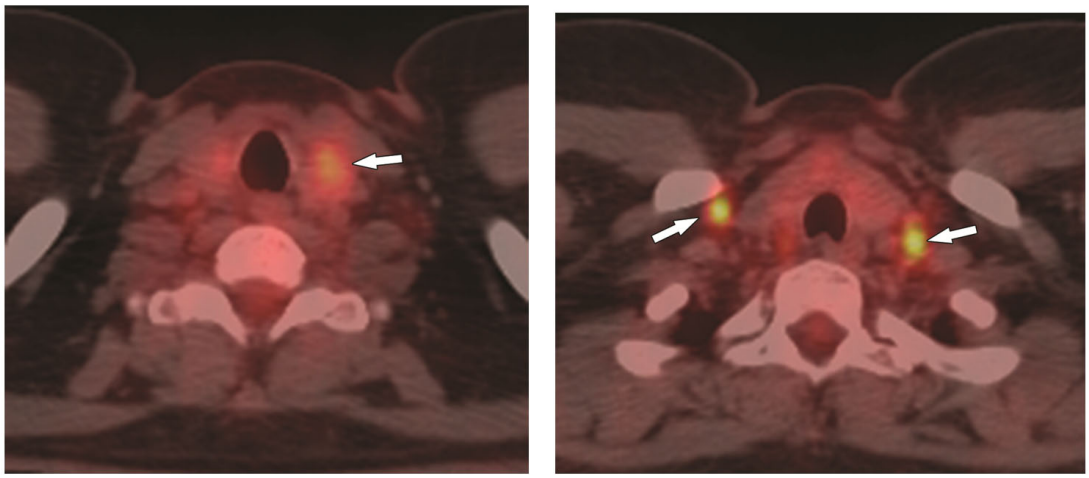

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Figure 4. A 44-year-old female with lung cancer (patient #12). A) ^{18}F-PET/CT, axial plane, demonstrates minimal FDG avidity in the left lobe of the thyroid gland (arrow). B) ^{18}F-PET/CT, axial plane, shows bilateral lower neck FDG avid nodes (arrows).

3.2 Imaging appearance

The intrathyroid metastases presented on ^{18}F-PET/CT as a focal, solitary nodular uptake (n = 21) (see Figure 1), multiple discrete nodular uptake (n = 2) (see Figure 2), or diffuse uptake/infiltration of the thyroid gland (n = 1) (see Figure 3). The SUV ranged between 3.9 and 42 (median 12.3 $\pm$ 7.5); in 2 patients, the FDG-avidity was minimal (see Figure 4). On ^{18}F-PET/CT, sites of extrathyroid metastasis included neck nodes (n = 13) and distant metastases outside the neck (n = 18). Metastatic disease was limited to the neck in 6 patients. In 2 of these 6 patients (patients #11 and #22), the thyroid was the only site of metastatic disease (see Table 2).

Table 2. PET/CT findings

Patient #	PET/CT Findings	SUV	Neck nodes	Distant metastasis
1	Solitary uptake	15.4	None	Lung, axilla
2	Solitary uptake	42	None	Subcarinal, chest wall
3	Solitary uptake	12.7	None	Brain
4	Solitary uptake	9	None	Brain
5	Solitary uptake	3.9	None	Thyroid, adrenal
6	Solitary uptake	9.2	None	Larynx, mediastinum
7	Solitary uptake	8.6	None	Tongue base, lung, adrenal
8	Solitary uptake	12.8	None	Adrenal
9	Solitary uptake	10.4	Right	Adrenal
10	Solitary uptake	13.3	Bilateral	Hilum
11	Multiple nodular	15.8	None	None
12	Solitary uptake	Minimal	Bilateral	Lung, pelvis
13	Solitary uptake	Minimal	Left	Lung, mediastinum
14	Solitary uptake	21.8	Right	Lung
15	Solitary uptake	12.4	Right	Retropharyngeal nodes
16	Multiple nodular	6.6	Right	Live, bone
17	Solitary uptake	12.1	None	Brain
18	Solitary uptake	16.5	Right	None
19	Solitary uptake	13.4	Right	Mediastinum
20	Solitary uptake	15.3	Bilateral	Breast, mediastinum
21	Solitary uptake	12.2	Midline	None
22	Solitary uptake	7.9	None	None
23	Diffuse	9.4	Bilateral	Lung, subcarinal
24	Solitary uptake	9	Right	None

Table 3. Initial management and change in management

Patient #	Inintial manangement	Change in management
1	None	Doxil, Cytoxan
2	None	Paclitaxel, Carboplatin, Tarceva
3	Temodar, Thalidomide	Docetaxel
4	None	Temodar
5	None	Chemotherapy
6	None	Chemotherapy
7	None	Docetaxil, Caroplatin
8	Pemetrexed, Carboplatin	Erlotinib
9	None	Folfiri, Avastin
10	None	Thyroidectomy, bilateral neck dissection
11	None	Emetrexed, Carboplatin
12	None	Arboplatin, Paclitaxel
13	None	Xeloda
14	None	Hospice
15	None	Carboplatin, Certuximab
16	None	Capecitabine, Ixabepilone
17	None	Carboplatin, Paclitaxel
18	Trastuzumb, Arimidex	Trastuzumab, radiation
19	None	Erbitux with Gemcitabine
20	None	Lost to follow-up
21	None	Taxotere, Cisplatin, Tarceva
22	Aarimidex	Ixabepilone, Bevacizumab
23	None	Pemetrexed, Carboplatin,Bevacizumab
24	None	Doxetaxel, Cisplatin

3.3 Patient management and survival

Due to the metastatic disease, the patient's therapy was changed in 23 of 24 patients; 1 patient was lost to follow-up. The treatment in these 23 patients included the addition of chemotherapy (n = 20), chemotherapy with neck radiation (n = 1), and total thyroidectomy and neck dissection (n = 1) and hospice referral (n = 1). Four of the 23 patients were undergoing chemotherapy at the time that the intrathyroid metastasis was discovered and was subsequently changed (see Table 3). As of this writing, 19 of the 23 (83%) patients are deceased. These patients lived from 13 days to 8 years 5 months (median 1 year 2 months) after the diagnosis of the intrathyroid metastases. Four patients (17%) are still alive at the time of this report.

4. DISCUSSION

While intrathyroid metastases are rare, we have noticed an increased number of cases at our institution. This is likely due to increased awareness and improved detection with advancing technology. Our results demonstrate that intrathyroid metastases present on ^{18}F-PET/CT predominately as solitary nodules, but can also occur as multiple nodules or as diffuse uptake/infiltration throughout the gland with a median SUV of 12.3. This is in contradistinction to the normal thyroid gland that usually shows low or absent ^{18}F-FDG uptake.[22,23]

Autopsy series show that the breast and lungs are the most common tumors that metastasize to the thyroid gland.[1,24–26] In clinical series however, renal cell carcinoma was the most frequent source of the metastasis.[4,9,27,28] In our series, the lung was the most common primary site of an intrathyroid metastasis (see Table 1). As we are a referral center for cancer, with subspecialization for certain cancer types, an estimation of the frequency of metastasis would be biased. No relation was noted in our series between the type of intrathyroid metastases or SUV, the site of the primary lesion, or the stage of the primary tumor on initial diagnosis.

In our study, the majority of intrathyroid metastases presented on ^{18}F-PET/CT as focal solitary nodular uptake, similar to other benign or malignant primary thyroid lesions.[10,14] While analysis of the neck nodes was not the focus of this study, abnormal neck lymph nodes were present in 13 of 24 (54%) patients. In contradistinction, metastasis to regional neck lymph nodes has been reported to occur in only 19.4% of primary thyroid malignancies.[29] In addition, metastases to locations outside the neck were present in 18 of 24 (75%) patients. The presence of FDG avid nodules in the thyroid in patients with an extrathyroid malignancy, abnormal neck nodes, and/or lesions outside the neck, should further in-

crease suspicion for intrathyroid metastasis. Both patients in our series that presented with thyroid nodules demonstrating minimal ^{18}FDG-avidity had cervical adenopathy and distant metastasis.

Intrathyroid metastases can also present as multiple discrete nodular uptake or diffuse thyroid uptake/infiltration mimicking thyroiditis. In the absence of metastatic adenopathy, diffuse metastatic infiltration of the thyroid from an extrathyroid primary disease cannot be distinguished from thyroiditis.[30–33]

The SUV of a thyroid nodule is not predictive of malignancy. On PET/CT, imaging obtained for non-thyroid disorders, incidental thyroid uptake is either focal or diffuse, often seen with primary thyroid carcinoma or thyroiditis with an SUV of 10.7 $\pm$ 7.8 for focal lesion and mean of 7.7 (4.3-13.4) for diffuse lesions.[10,14] This is similar to our series, were the SUV of intrathyroid metastases were median 12.3 $\pm$ 7.5 and 9.4, respectively. The optimal SUV max cutoff value to differentiate benign from malignant lesions however, has not been fully defined, and could be the subject of further study.

Radiologists interpreting ^{18}F-PET/CT should be aware of these different uptake patterns at presentation. This is especially true for metastases limited to the thyroid and neck which may be confused for primary thyroid cancer. Alternate imaging such as ultrasound with fine needle aspiration may be used as the next step to differentiate between these findings.

Limitations of the study include the retrospective nature of the review and the relatively small number of cases. Future directions could include attempts to differentiate metastasis presenting a solitary or multiple nodules from primary thyroid cancer, and the infiltrative pattern of metastatic disease from thyroiditis based on SUV. As we are a tertiary referral center for cancer, subspecializing in certain types of cancers, many patients are initially diagnosed at outside institutions. In none of the 24 patients was the initial SUV of the lesion at the primary site available to us. An interesting addition to future studies could include this comparison.

5. Conclusions

In any patient with a previous or current history of an extrathyroid malignancy, an ^{18}FDG avid solitary nodule, multiple discrete nodules, or diffuse infiltration of the thyroid on ^{18}F-PET/CT should be considered a potential intrathyroid metastasis until proven otherwise. Knowledge of an intrathyroid metastasis may impact patient management, especially if the thyroid or neck are the only sites of metastatic disease as this may be mistaken on imaging as a primary thyroid cancer.

Conflicts of Interest Disclosure

The authors declare that there is no conflict of interest statement.

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