Letter to the Editor

The diagnostic role of total-body ^{18}F-FDG PET/CT in patients with multiple tumors: a report of the association of thyroid cancer with lung or renal tumors

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Introduction

Multiple primary tumors (MPT) are defined as more than one synchronous or metachronous tumor lesion, histologically different, in the same patient (1). Their incidence has been progressively increasing, probably for the longer life expectancy of the human population as well as for the advances in diagnostic methods (2). Their early identification and the accurate staging are essential to select the appropriate treatment and to anticipate disease progression (3). The imaging detection of MPT may be limited using conventional modalities, such as ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) for their selected regional evaluation (4). Conversely, ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography (PET)/CT, being a total-body imaging technique for the evaluation of malignant tumors, have a wider range (4,5), and may be helpful to detect unexpected malignant tumors or to evaluate patients with MPT (6,7).

In this report, we describe two patients with differentiated thyroid carcinoma (DTC) associated with other cancers in whom tumor lesions were simultaneously detected by total-body FDG PET/CT.

Case 1

A 64-year-old male patient who had radical nephrectomy at the age of 47 for a renal cancer. Histological examination of a large (65 mm) right kidney tumor lesion showed a grade 2 clear cell renal carcinoma (ccRCC), stage pT1b Nx. Initial work-up included abdominal CT and bone scan which showed no metastatic lesions. The patient had no history of thyroid disease or other significant co-morbidities. After 20 years for abdominal pain and weight loss the patient had chest and abdominal CT revealing a pulmonary micro-nodule (5 mm) in the middle lobe, a nodule (19 mm) in the pancreatic head and a perigastric lymph node (22×25 mm). The diagnostic work-up was integrated with FDG PET/CT showing no abnormal uptake in the pulmonary micro-nodule, but two focal areas of hypermetabolism were found in the abdomen (*Figure 1A*). As incidental unexpected finding focal moderate increased FDG uptake (maximum standardized uptake value, SUVmax 3.4) was observed in left thyroid lobe (*Figure 1B*), where a hypodense nodule was detected by co-registered CT. In addition, moderate tracer uptake was found in a perigastric lymph node (SUVmax 2.4) (*Figure 1C*) and in a nodule of the pancreatic head (SUVmax 2.6) (*Figure 1D*). The patient had a total thyroidectomy and neck lymph node dissection; a papillary carcinoma, tall-cell variant, with central cervical lymph nodes metastases was proven. The pathological stage was pT1b (m) pN1aMx. Biopsy evaluation of pancreatic head lesion and perigastric lymph node showed pancreatic and nodal metastases from ccRCC. Before starting tyrosine kinase inhibitor therapy for metastatic ccRCC, the patient underwent radiometabolic therapy with radioiodine (^{131}I). ^{131}I whole-body scan (WBS), obtained 7 days after administration of 1.85 GBq, showed

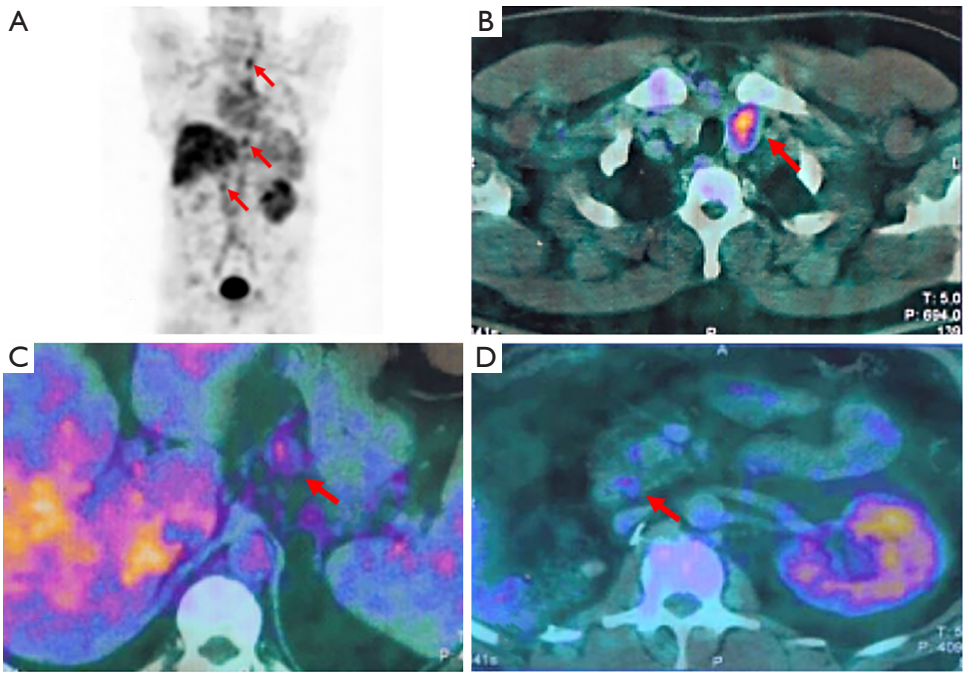

Figure 1 Coronal ^{18}F-FDG PET demonstrates multiple areas of increased uptake (A). Axial ^{18}F-FDG PET/CT images show abnormal tracer uptake in the left thyroid lobe (B), in a perigastric lymph node (C) and in the head of the pancreas (D). Red arrows indicate pathological areas of increased FDG uptake.

uptake in thyroid tissue remnant and also in a lymph node that was previously unknown. During the follow-up, thyroglobulin was near to 0 ng/dL as well as ultrasound of the neck showed no relapse of disease; furthermore, a total-body CT scan demonstrated regression of abdominal lesions, both pancreatic and lymph nodal, and a stable lung finding.

Case 2

A 57-year-old man never-smoker with a long clinical history of thyroid goiter who had dyspnea and chest tightness. The patient was enlisted for total thyroidectomy and before surgery underwent neck and chest CT scan that, further thyroid goiter, showed also an unknown lung nodule. The diagnostic work-up was integrated with FDG PET/CT showing abnormal uptake in the right thyroid lobe (SUVmax 3.4) (*Figure 2A,B*), right latero-cervical node (SUVmax 16.5) (*Figure 2C,D*) and pulmonary right upper lobe nodule (16×15 mm, SUVmax 4.2) (*Figure 2E,F*). Lung nodule was evaluated by fine-needle aspiration cytology, which demonstrated a positivity for thyroid transcription factor-1 (TTF-1). The patient underwent total thyroidectomy with right latero-cervical lymphadenectomy. Histopathological examination showed 3.3 cm nodule of the right lobe with features of papillary carcinoma, follicular variant, infiltrating neural and muscular structures, and lymph node metastases (pT4apN1b according to 8th TNM classification). Metabolic therapy with 3.7 GBq of ^{131}I was performed following L-thyroxine withdrawal. Seven days later, WBS showed an area of ^{131}I uptake in the neck, in the thyroid remnant, but no uptake was visible over the lungs. Three months after radioiodine treatment, the patient underwent upper lobectomy of the right lung; by histology, lung adenocarcinoma of 18×14 mm was detected and classified as pT1, according to TNM staging. In the context of pulmonary adenocarcinoma, rare carcinomatous cells with ground glass nucleus, follicular pattern were detected. This finding was suggestive with the presence of metastasis from DTC. However, immunohistochemistry resulted positive for TTF-1, but negative for thyroglobulin antibodies, excluding the presence of thyroid tissue. Neck and chest CT scan performed 3 months after surgical treatments did not show any thyroid and/or lung abnormalities. One year after radioiodine treatment, thyroglobulin under L-thyroxine therapy was <1 ng/mL and

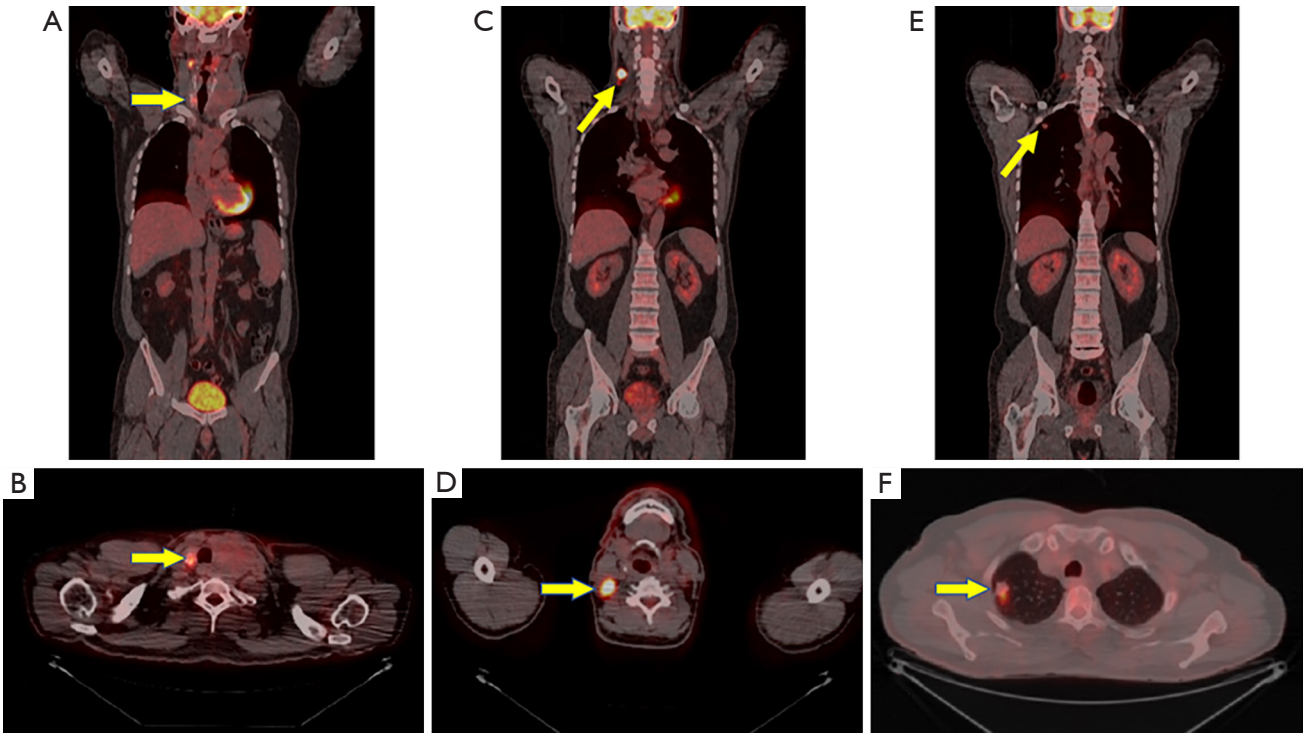

Figure 2 Coronal and axial ^{18}F-FDG PET/CT slices show increased focal uptake in the right thyroid lobe (SUVmax 3.4) (A,B), latero-cervical lymph node (SUVmax 16.5) (C,D), and lung parenchymal nodule (SUVmax 4.2) of the apical segment at the right upper lobe (E,F).

not increased after recombinant human thyroid-stimulating hormone administration.

The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by our Institutional Review Board and written informed consent was obtained.

Discussion

MPT have different histology, involving different organs, and thus may be located in all anatomic sites of the body (1,2). Total-body imaging techniques are helpful to detect tumor lesions in such patients (4,5), and there are several studies on the utility of FDG PET/CT in the identification of MPT (7). FDG PET/CT have numerous advantages in the evaluation of neoplastic diseases such as the possibility to identify local and distant metastases, to differentiate active disease from scar or necrotic tissues after treatment and to detect simultaneously MPT (8). Thyroid incidentalomas detected on FDG PET/CT are quite frequent with an incidence of 2–5% (9) and focal uptake, especially with high SUVs, carries a high risk of malignancies, the originality of the two cases reported in our manuscript consisted of different presentation of thyroid cancer incidentalomas; in this regard, in a patient the thyroid tumor was discovered during the follow-up of a previously resected renal cell carcinoma, while in the other patient the thyroid cancer was detected simultaneously with lung cancer. In both cases FDG PET/CT precisely detected the anatomic location of tumor lesions; therefore, we underlined and confirmed the diagnostic role of such imaging modality for this purpose.

In detail, we describe two patients with MPT both with the association of DTC and other malignancies: in one case abdominal metastases from ccRCC and in the other case with a T1 lung adenocarcinoma. Even if the association of DTC with ccRCC or lung cancer has been previously described (10,11), in these patients, tumor lesions were discovered and simultaneously detected by total-body FDG PET/CT demonstrating the great value of this imaging technique in performing tumor diagnosis. In the first case, DTC was discovered using FDG PET/CT many years later after nephrectomy for ccRCC. PET/CT integrated the information obtained by CT and DTC and pancreatic and nodal metastases from ccRCC were proven. Thus,

the diagnosis of MPT was performed also on the basis of FDG PET/CT findings. In the second patient a DTC was associated with a lung cancer, that simulated a metastasis from DTC: the lung nodule demonstrated a positivity for TTF-1, but no ^{131}I uptake was found in the lung nodule on WBS and therefore other malignancy was suspected. Histology demonstrated T1 lung adenocarcinoma. FDG PET/CT was able to identify all tumor lesions: the right thyroid lesion, the right latero-cervical lymph nodes and the pulmonary right upper lobe nodule, helping in the diagnosis of MPT.

The role of total-body imaging modalities is clinically important in patients with MPT since tumor lesions may be located anywhere in the body (1,2). Conventional imaging techniques may have limited diagnostic accuracy in patients with MPT, since select limited anatomic sites to be evaluated (4). Conversely, FDG PET/CT, a total-body imaging method, is particularly useful to evaluate patients with MPT in which tumor lesions may be located in different organs as occurred in the two cases presented in this brief report and previously also described (7,8,12,13); integrated metabolic imaging provided by FDG PET/CT offers functional and morphological assessment of tumor in unexpected or unknown anatomic locations. For this purpose, hybrid imaging using FDG PET combined with MRI may be also considered providing similar data to PET/CT (14,15).

In conclusion, DTC may be associated with other tumors such as ccRCC or lung cancer and thus classified as MPT. In these patients FDG PET/CT total-body imaging is clinically useful to simultaneously detect tumor lesions as well as to accurately perform the diagnosis of MPT.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/qims-21-36). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by our Institutional Review Board and written informed consent was obtained.

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