Case Report
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The Complementary Roles of ^{18}F-Fluorocholine and ^{18}F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography in an Evaluation of A Patient With Parathyroid Carcinoma: A Case Report

Paratiroid Karsinomlu Bir Hastanın Değerlendirilmesinde ^{18}F-Florokolin ve ^{18}F-Florodeoksiglukoz Pozitron Emisyon Tomografi/Bilgisayarlı Tomografinin Tamamlayıcı Rolleri: Bir Olgu Sunumu

Nikola Pantic[1], Lenka Grujicic[1], Branislava Radovic[1,3], Dragana Sobic Saranovic[1,2], Vera Artiko[1,2], Strahinja Odalovic[1,2]

[1]*University Clinical Center of Serbia, Center for Nuclear Medicine with PET, Belgrade, Serbia*
[2]*University of Belgrade Faculty of Medicine, Department of Nuclear Medicine, Belgrade, Serbia*
[3]*University of Pristina Faculty of Medicine, Department of Internal Medicine, Kosovska Mitrovica, Serbia*

Abstract

^{18}Fluorine-fluorocholine (^{18}F-FCH) is a radiopharmaceutical used in primary hyperparathyroidism. The data about its utility in malignancies other than prostate and hepatocellular carcinoma is limited. We present the case of a patient who was referred for ^{18}F-FCH positron emission tomography/computed tomography (PET/CT) due to the persistently elevated parathormone and calcium levels following total thyroidectomy with left lower parathyroidectomy for parathyroid carcinoma (PTC). Previously, the patient underwent ^{18}Fluorine-fluorodeoxyglucose (^{18}F-FDG) PET/CT. The latter method detected multiple mediastinal and hilar lymph nodes, as well as nodular lesions in lungs and osteolytic bone lesions with an increased tracer uptake, whereas ^{18}F-FCH PET/CT detected an increased tracer uptake not only in lesions at all of the abovementioned areas, but also in the nodular lesion in the neck corresponding to a local relapse as well, with bone lesions showing higher avidity for ^{18}F-FDG than for ^{18}F-FCH. The case we present shows that ^{18}F-FCH PET/CT has an additive value to ^{18}F-FDG PET/CT in an evaluation of patients with PTC.

Keywords: Parathyroid carcinoma, primary hyperparathyroidism, positron-emission tomography, ^{18}F-fluorocholine, ^{18}F-fluorodeoxyglucose

Öz

^{18}F- florokolin (^{18}F-FCH), primer hiperparatiroidizmde kullanılan bir radyofarmasötiktir. Prostat ve hepatosellüler karsinom dışındaki malignitelerdeki kullanımıyla ilgili veriler sınırlıdır. Bu yazıda, total tiroidektomi ve sol alt paratiroidektomi sonrası paratiroid karsinomu nedeniyle sürekli yüksek seyreden parathormon ve kalsiyum düzeyleri olan bir hastanın ^{18}F-FCH pozitron emisyon tomografi/bilgisayarlı tomografi (PET/BT) incelemesi için yönlendirilmesi üzerine bir vaka sunulmaktadır. Hastaya daha önce ^{18}F-florodeoksiglukoz (^{18}F-FDG) PET/BT yapılmıştı. Bu yöntem mediastinal ve

Address for Correspondence: Nikola Pantic, Center for Nuclear Medicine with PET, University of Belgrade Faculty of Medicine, Department of Nuclear Medicine, Belgrade, Serbia
E-mail: nikolapantic944@gmail.com **ORCID ID:** orcid.org/0009-0006-6070-0828
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hiler lenf nodlarında, akciğerlerdeki nodüler lezyonlarda ve osteolitik kemik lezyonlarında artmış tutulum saptamışken, ^{18}F-FCH PET/BT hem bu bölgelerdeki lezyonlarda hem de boyunda lokal nüks ile uyumlu nodüler lezyonda artmış tutulum göstermiştir. Kemik lezyonlarında ise ^{18}F-FDG'ye göre daha düşük FCH tutulumları gözlenmiştir. Bu olguda, paratiroid karsinomu olan hastaların değerlendirilmesinde ^{18}F-FCH PET/BT'nin ^{18}F-FDG PET/BT'ye ek değer sağladığını göstermektedir.

Anahtar kelimeler: Paratiroid karsinomu, primer hiperparatiroidizm, pozitron-emisyon tomografisi, ^{18}F–florokolin, ^{18}F-florodeoksiglukoz

Introduction

Parathyroid carcinoma (PTC), as one of the rarest malignancies,accounts for less than 0.005% of all cancers and less than 1% of all parathyroid disorders (1,2). Therefore, it is a rare cause of hyperparathyroidism. ^{18}Fluorine-fluorocholine (^{18}F-FCH) is a choline analogue mimicking choline uptake and phosphorylation as a precursor in the biosynthesis of phosphatidylcholine a membrane phospholipid (3). ^{18}F-FCH positron emission tomography/computed tomography (PET/CT) is an established imaging modality for parathyroid localization in primary hyperparathyroidism (PHPT) patients. Studies show its' superior performance in comparison to conventional scintigraphic imaging, ultrasonography, or four-dimensional CT (4). The most recent study showed a sensitivity of 83%, a specificity of 97%, a positive predictive value of 90%, and a negative predictive value of 94% for ^{18}F-FCH PET/CT (5). While the utility of an ^{18}fluorine-fluorodeoxyglucose (^{18}F-FDG) PET/CT for the detection of PTC is well-known and its' sensitivity is high in all disease phases (6), data regarding the usage of ^{18}F-FCH PET/CT in the evaluation of PTC is limited. To the best of our knowledge, there are only a few case reports where ^{18}F-FCH PET/CT was used along with ^{18}F-FDG PET/CT in the evaluation of patients with PTC (7,8,9).

We present a case of a patient with PHPT who was evaluated with both ^{18}F-FCH and ^{18}F-FDG PET/CT during the diagnostic process.

Case Report

A 51-year-old male patient was referred for ^{18}F-FCH PET/CT at the Center for Nuclear Medicine with PET of the University Clinical Center of Serbia due to persistently elevated parathyroid hormone (PTH) and calcium levels following total thyroidectomy with left lower parathyroidectomy for PTC.

Eight months prior, he presented with a pathologic fracture of the left clavicle. Laboratory tests showed hypercalcemia (Ca 4.12 mmol/L, ionized Ca 2.05 mmol/L, PO_4 0.94 mmol/L, vitamin D3 21.9 nmol/L); with significantly elevated PTH levels (11561 pg/mL). The patient has a family history of parathyroid diseases, and a history of nephrolithiasis. After hospitalization, neck ultrasound identified two nodules in the left thyroid lobe. One of the nodules was occupying the majority of the lower pole of the left thyroid lobe and was 30x30 mm in size, while the other one, located caudally in relation to the first one and measuring 22x18 mm, was suspected to be an enlarged parathyroid gland. Thyroid scintigraphy with technetium-99m(Tc-99m)-pertechnetate showed non-functional nodules, while Tc-99m-sestamibi (MIBI) scintigraphy showed focal zone of an increased radiopharmaceutical uptake in the projection of the lower pole of the left thyroid lobe.

Histopathological analysis following total thyroidectomy with lower left parathyroidectomy confirmed PTC adjacent to the lower pole of the left thyroid lobe, which was 22 mm in diameter, with capsular defect, fields of hemorrhage, limited necrosis, and angioinvasion. Immunohistochemistry findings were as follows: GATA3+, CK19+ focal, HMBE1-, calcitonin-, TTF1-, thyroglobulin-, Ki67 index ~13%. A second tumor, containing remnants of the parathyroid gland with dimensions 36x25x15 mm, was identified as an atypical parathyroid adenoma.

Postoperative multi-slice CT (MSCT) of the chest revealed multiple micronodular and nodular lesions in both lungs, with the largest diameter up to 29 mm, which likely corresponded to secondary deposits, as well as multiple enlarged mediastinal lymph nodes, with the largest subcarinal node measuring 20x36 mm, and osteolytic lesions in the left scapula and left clavicle. Following chest MSCT, the patient was referred for an ^{18}F-FDG PET/CT scan for evaluation of lesions detected on MSCT and staging of the disease.

A three-dimensional PET scan (Figure 1a), associated with low-dose non-enhanced CT scan, was acquired from the base of the skull to the mid-thigh. ^{18}F-FDG-avid disease was identified in lymph nodes of the mediastinum and hila of the lungs bilaterally up to 16mm in diameter with the maximum standardized uptake value (SUV_{max}) of 8.3 (Figure 1b), multiple micronodular and nodular lesions in the lungs, which were up to 29 mm in diameter with the SUV_{max} of 14.1 (Figure 1c), as well as multiple zones of an increased metabolism of glucose in lytic lesions in femurs, pubic bones (Figures 1d, 1e), ilia, sacrum, and scapulae bilaterally, left humerus, left clavicle, sternum, and

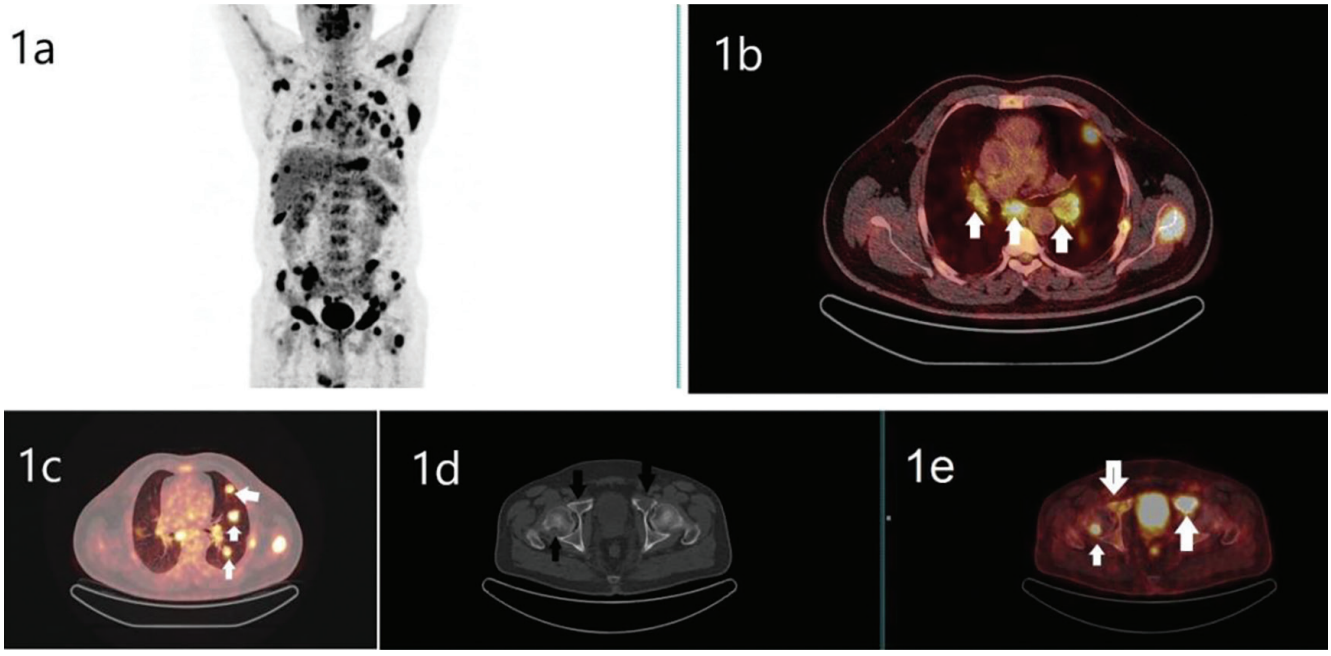

Figure 1. ^{18}Fluorine-fluorodeoxyglucose positron emission tomography/computed tomography (PET/CT): (a) - maximum intensity projection PET image depicts multiple areas of abnormal tracer uptake corresponding to metastatic disease in mediastinal and hilar lymph nodes, pulmonary, and bone lesions; (b) - axial fused image shows increased uptake in enlarged mediastinal and hilar lymph nodes (arrows); (c) - increased metabolism of glucose in pulmonary nodules (arrows); (d) - a low-dose, non-enhanced CT depicts lytic lesions in pubic bones bilaterally and the head of the right femur (black arrows); (e) - increased uptake of the radiopharmaceutical in lytic lesions on the fused image (white arrows)

multiple anterior and posterior rib ends, predominantly on the left side, with the SUV_{max} up to 14.5. All the sites of pathological uptake were interpreted as metastases, and the patient was treated with a chemotherapy regimen combining 5-fluorouracil and dacarbazine.

Due to the persistence of elevated PTH (493 pg/mL), hypercalcemia (Ca 4.05 mmol/L, ionized Ca 2.25 mmol/L), and hypophosphatemia (PO4 0.69 mmol/L), the patient underwent PET/CT with ^{18}F-FCH. A three-dimensional PET scan and a low-dose non-enhanced CT scan were acquired from the top of the head to the mid-thigh, 45 minutes following the injection of 189 MBq of ^{18}F-FCH. The examination revealed multiple sites of pathological radiopharmaceutical uptake in: pretracheal nodular lesion in proximity of the previous intervention in the neck, 22 mm in diameter with the SUV_{max} of 11.8 (Figures 2a, 2e), interpreted asa local relapse; mediastinal lymph nodes with the largest subcarinal node measuring 16x14 mm with the SUV_{max} of 4; multiple nodular lesions in the pulmonary parenchyma bilaterally, more pronounced on the left, up to 30 mm in diameter with the SUV_{max} of 7.3 (Figures 2b, 2f); osteolytic lesions, some with a soft tissue components which were up to 25mm in diameter, in right orbit, scapulae (Figures 2c, 2g) and clavicles bilaterally, ribs (Figures 2d, 2h), sternum, femurs, pelvic bones bilaterally, and sacrum. All the sites of pathological uptake were interpreted as metastases, and a chemotherapy regimen with carboplatin and etoposide was started.

Discussion

Compared with patients with benign parathyroid adenomas, patients with PTC are more symptomatic and present with significantly higher calcium and PTH levels. PTC is notably challenging to diagnose, with confirmation typically only being possible post-operatively on histopathology (10). A meta-analysis supports the use of ^{18}F-FCH over MIBI in patients with PHPT due to its higher sensitivity (11). PTC and its metastatic sites show significant avidity for ^{18}F-FDG (6), while data on the use of ^{18}F-FCH in the evaluation of patients with PTC are limited to a few cases in which ^{18}F-FCH-avid metastatic disease was detected (8,9,12,13). In the case we presented, lesions in the lungs and mediastinum were positive on both ^{18}F-FDG and ^{18}F-FCH PET/CT, while there was a nodular lesion in the neck that wasn't ^{18}F-FDG-avid but showed choline avidity. Osteolytic bone metastases have been reported in patients with PTC (14). In the case of our patient, the uptake of a radiopharmaceutical in bone lesions was higher on

^{18}F-FDG PET/CT, compared to that of ^{18}F-FCH PET/CT (Figure 3); however, they showed avidity on both examinations. It should be noted that the delay between the two PET/CT scans was four months. Meanwhile, the patient was subjected to chemotherapy, which the ^{18}F-FCH PET/CT showed to be ineffective. However, considering all of the above, this case, along with others mentioned, shows the complementary role of ^{18}F-FCH PET/CT with ^{18}F-FDG PET/CT in the staging and detection of recurrence of the disease in patients with PTC.

Conclusion

This case report demonstrates a potential additive value of ^{18}F-FCH PET/CT to ^{18}F-FDG PET/CT in an evaluation of patients with PTC.

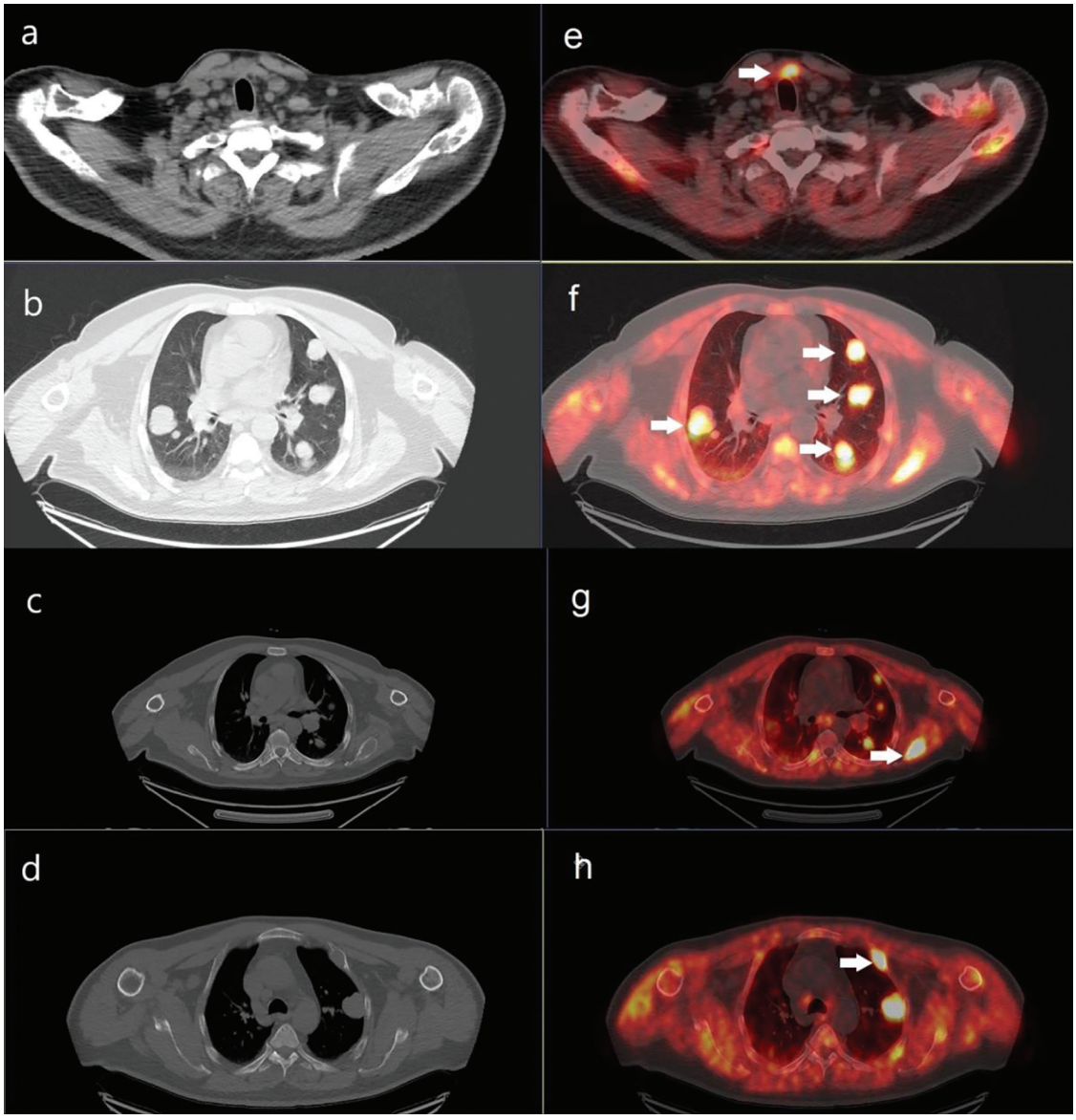

Figure 2. ^{18}Fluorine-fluorocholine positron emision tomoraphy/computed tomography: the axial images depict an increased uptake of the radiopharmaceutical in the pretracheal nodular lesion (a,e), coresponding to a local relapse; pulmonary nodules (b,f), corresponding to metastasis of the parathyroid carcinoma; osteolytic lesions in the left scapula (c,g) and the second rib on the left (d,h), coresponding to metastatic disease

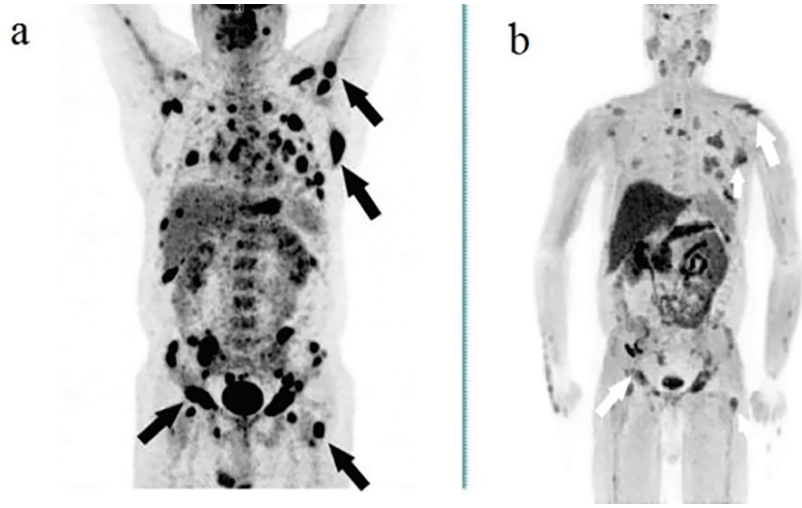

Figure 3. ^{18}Fluorine-fluorodeoxyglucose (^{18}F-FDG) and ^{18}Fluorine-fluorocholine (^{18}F-FCH) positron emission tomography (PET): maximum intensity projection PET images depict higher uptake of ^{18}F-FDG (black arrows) (a) compared to ^{18}F-FCH (white arrows) (b) in multiple bone lesions coresponding to metastatic disease

Ethics

Informed Consent: Informed consent was obtained from a patient.

Footnotes

Authorship Contributions

Surgical and Medical Practices: N.P., L.G., B.R., D.S.S., V.A., S.O., Concept: N.P., L.G., B.R., D.S.S., V.A., S.O., Design: N.P., L.G., B.R., D.S.S., V.A., S.O., Data Collection or Processing: N.P., L.G., B.R., D.S.S., V.A., S.O., Analysis or Interpretation: N.P., L.G., B.R., D.S.S., V.A., S.O., Literature Search: N.P., L.G., B.R., D.S.S., V.A., S.O., Writing: N.P., L.G., B.R., D.S.S., V.A., S.O.

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