

Interpreting discordance on dual-tracer positron emission tomography–computed tomography in the setting of metastatic neuroendocrine tumor: Detection of metachronous triple-negative breast carcinoma

ABSTRACT

Second primary malignancies (SPMs) are known to be associated with neuroendocrine tumors (NETs). The association necessitates a careful assessment of the dual-tracer positron emission tomography–computed tomography (PET-CT) imaging findings to identify these malignancies earlier. Such early diagnosis can provide incremental benefit for screening these SPMs apart from their known applications in the management of NETs. A case of incidentally detected metachronous triple-negative breast carcinoma on dual-tracer PET-CT imaging is presented using ^{18}F fluoro-2-deoxy-D-glucose (FDG) and ^{68}Ga -DOTATATE that showed a high uptake on FDG but no uptake on somatostatin receptor-based imaging.

Keywords: ^{68}Ga -DOTATATE, dual-tracer positron emission tomography–computed tomography, fluoro-2-deoxy-D-glucose positron emission tomography–computed tomography, metastatic neuroendocrine tumors, triple-negative breast carcinoma

INTRODUCTION

Second primary malignancies (SPMs) have been reported in the literature in association with neuroendocrine tumors (NETs). In one of the reports, metachronous breast cancer was found in 13% of patients suffering from NETs.^[1] With an increasing number of somatostatin receptor (SSTR)-targeted imaging studies being performed, there is a rising incidence of NETs being reported. Dual-tracer positron emission tomography–computed tomography (PET-CT) (^{68}Ga -DOTATATE and ^{18}F fluoro-2-deoxy-D-glucose [FDG]) is frequently undertaken in the evaluation and management of NETs. There has been also report of SSTR 2-based inhibitory signalling in breast cancer cells.^[2] We herein present a case of metastatic NET who developed a metachronous breast malignancy that was indicated by finding of discordance on dual-tracer PET-CT and hence was diagnosed despite being very small in size.

CASE REPORT

A 53-year-old woman with metastatic NET from jejunal

primary underwent surgery in the form of jejunal resection-anastomosis and adhesiolysis 3½ years previously. The histopathology was suggestive of well-differentiated NET, Grade II with MIB-1 labeling index of 1%. She presented with hepatic and mesenteric nodal metastases 2 years subsequent to her surgery. She was initially treated with long-acting octreotide for flushing and abdominal pain but had poor control of functioning symptoms. Hence, in view of biochemical and symptomatic poor control and

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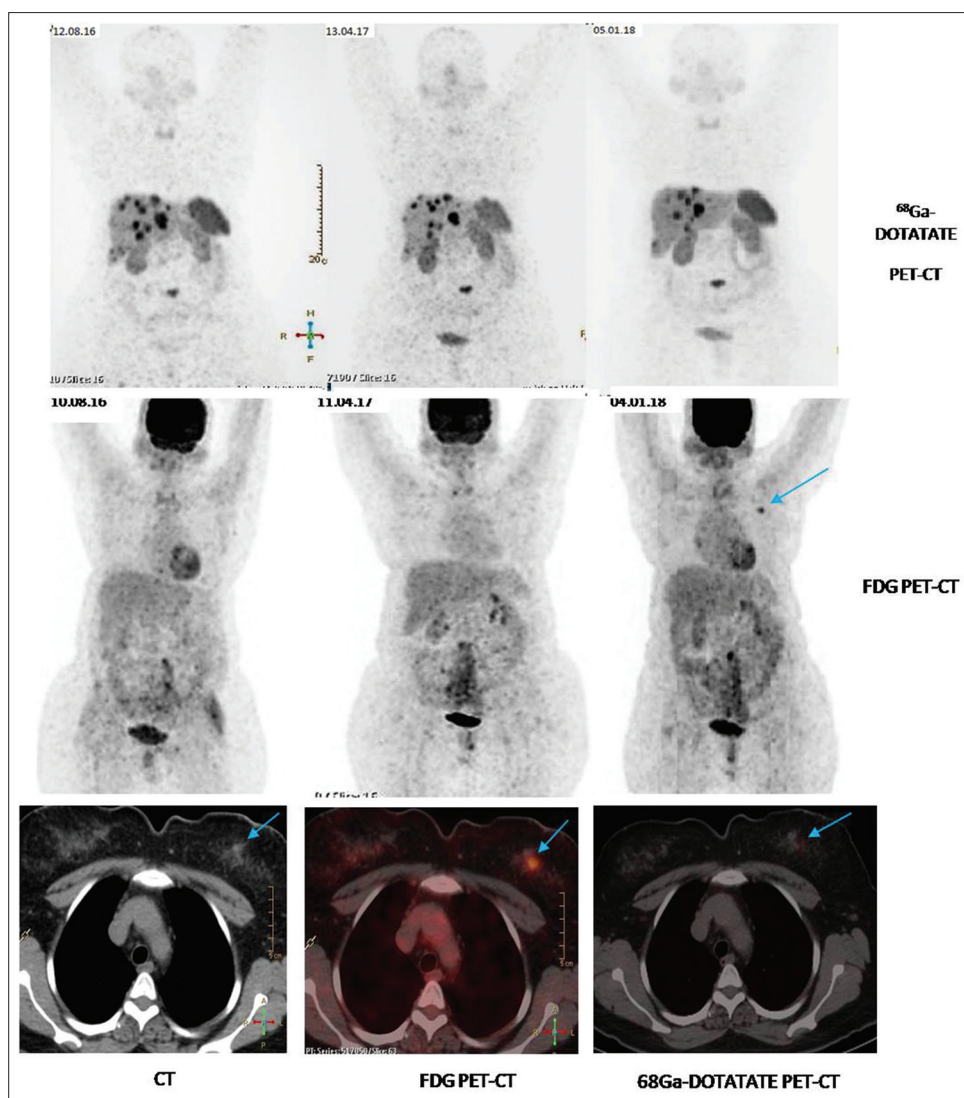


Figure 1: The last fluoro-2-deoxy-D-glucose positron emission tomography-computed tomography (January 2018: Middle panel right side) demonstrating a new subcentimeter-sized metabolically active lesion in the upper inner quadrant of the left breast that is not ⁶⁸Ga-DOTATATE avid (upper panel: right side). The appropriate transaxial images at the level mentioned are also demonstrated (lowermost panel)

disease progression, she was referred for consideration of peptide receptor radionuclide therapy (PRRT). She received a cumulative dose of 960 mCi ¹⁷⁷Lu-DOTATATE. Dual-tracer PET-CT with ⁶⁸Ga-DOTATATE and ¹⁸F-FDG was undertaken at baseline as part of work-up, post four cycles, and at conclusion of PRRT. The last FDG PET-CT demonstrated a new subcentimeter-sized metabolically active lesion in the upper inner quadrant of the left breast which was not ⁶⁸Ga-DOTATATE avid [Figure 1]. In view of this finding, she was advised mammogram which showed a BIRADS category 4C lesion in the inner central region of the left breast [Figure 2]. Biopsy from the lesion was suggestive of triple-negative infiltrating ductal carcinoma, Grade III. Subsequently, she underwent left modified radical mastectomy and is now being planned for chemoradiation. The findings of discordance on dual-tracer PET-CT compared to other metastatic lesions

in the patient in the present case were noteworthy that warranted clinical suspicion and further radiological and pathological evaluation.

DISCUSSION

The present case study underscores the importance of appropriate interpretation of dual-tracer noninvasive molecular imaging methods for *in vivo* characterization of lesions in patients of metastatic NET. The role of dual-tracer PET-CT in the setting of evaluation of NETs has been reported in the literature earlier including detection of breast metastasis,^[3] and incidental detection of SPMs, including breast cancer;^[4] there has been report of SSTR-based signalling and imaging in breast cancer.^[2,5]

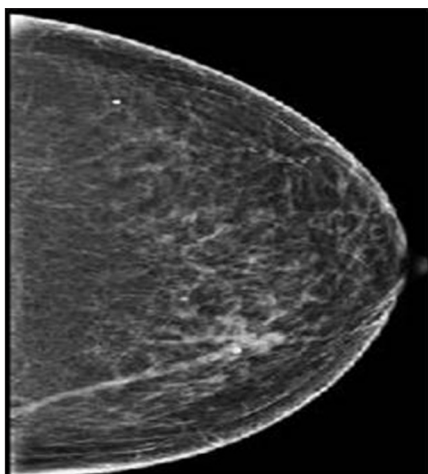


Figure 2: Left craniocaudal projection on mammogram showing the lesion

In this particular case, the absence of SSTR expression in a FDG-avid breast lesion raised a high suspicion of metachronous breast malignancy. Another point which needs to be highlighted is that as we performed dual-tracer PET-CT imaging as part of selective NET work-up, a subcentimeter-sized lesion was picked up earlier giving this patient access to early diagnosis and treatment before she would even become symptomatic. Appropriate interpretation of FDG PET-CT in conjunction with SSTR-based PET-CT thus would be of importance for some patients with NETs showing an inherent predisposition to SPMs. A larger study to critically look at the sensitivity and diagnostic values of such imaging in these patients is necessary to further clarify its role in the management.

A futuristic but relevant aspect that would be worth discussing is the biology of the lesion and the findings on SSTR-based PET imaging. A study by Chereau *et al.*^[6] suggested that SSTR expression and SSTR-mediated imaging can differentiate low-grade breast cancer from high-grade ones. In our case of triple-negative breast carcinoma, the absence of uptake on SSTR-based ⁶⁸Ga-DOTATATE PET and the high uptake on ¹⁸F-FDG was commensurate with the known aggressive biology of the disease. If the SSTR and glucose transporter receptor mismatch could be clinically explored in the future, it may open a new horizon of *in vivo* characterization of primary breast malignancies.

CONCLUSION

The appropriate interpretation of dual-tracer PET-CT with somatostatin analogs (⁶⁸Ga-DOTA-NOC/TATE and FDG) can lead to early identification of developing SPMs in patients with NETs and initiation of treatment for the second malignancy.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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