Dual-time-point 18F-FDG PET/CT Imaging Unveiled Occult Hepatic Metastasis of Breast Cancer with Neuroendocrine Differentiation: A Case Report

Mohamed Hossameldin Mustafa[1]*, Moumen Taha Katamesh[1], Yousry Wasif Nada[2], Batool Essa Albalooshi[3], Mohamad Mosaad ELLabban[4], Mohamed Ali Elbeltagy[5], Sherin Yassin Wagih[1], Raafat Ali Saber[1]

[1] Nuclear Medicine Department, Armed Forces College of Medicine, Cairo, Egypt

[2] Medical Oncology Department, Military Medical Academy, Cairo, Egypt

[3] Dubai Health, Dubai, United Arab Emirates

[4] Department of Anatomic Pathology, Faculty of Medicine, University of Port Said, Port Said, Egypt

[5] Pathology Department, Military Medical Academy, Cairo, Egypt

*Corresponding author: Mohamed Hossameldin Mustafa · ORCID 0009-0006-1269-1269

Received: 19 April 2026 · Peer reviewed, accepted and published: 30 July 2026

Swiss Journal of Radiology and Nuclear Medicine · www.sjoranm.com · SJORANM GmbH · Rosenweg 3 · CH-6340 Baar · Switzerland

Abstract

Breast cancer with neuroendocrine differentiation is a rare entity that may present diagnostic challenges. A 57-year-old woman with a history of right-sided invasive ductal carcinoma (estrogen receptor (ER) positive, progesterone receptor (PR) positive, human epidermal growth factor receptor 2 (HER2) negative) presented seven years after initial management with rising serum carcinoembryonic antigen (CEA) levels. Conventional imaging, including contrast-enhanced CT of the chest, abdomen and pelvis and standard-time 18F-FDG PET/CT, was negative. Delayed PET/CT imaging at 120 minutes revealed a solitary metabolically active hepatic lesion with a maximum standardized uptake value (SUVmax) of 7.6. Core biopsy was reported as large cell neuroendocrine carcinoma (LCNEC) of breast origin, WHO grade 3. In this patient, delayed imaging localized a biopsy target that was not apparent on the standard acquisition. Histopathological and immunohistochemical assessment supported breast origin with neuroendocrine differentiation and informed the reported systemic treatment plan. This single case does not establish diagnostic accuracy or improved clinical outcomes.

Keywords: Delayed PET/CT, breast cancer, neuroendocrine differentiation, liver metastasis, tumor markers, diagnostic imaging, occult metastasis.

Background

Tumour markers are commonly used in practice in the surveillance of breast cancer patients. However, elevated markers such as carcinoembryonic antigen (CEA) in the absence of elevated primarily breast-cancer-associated tumour markers (i.e. Ca-15-3) and clear radiological evidence of recurrence often pose a diagnostic challenge.

Breast cancer is among the most prevalent malignancies in women worldwide. While metastatic spread is well-documented, transformation or progression to neuroendocrine-differentiated subtypes is exceptionally rare and may present diagnostic difficulties.

Traditional imaging modalities may miss early or atypical metastatic lesions, especially when serum markers such as CEA rise in isolation. In this context, dual-time-point 18F-FDG PET/CT imaging, acquiring delayed images, can play a pivotal role in uncovering metabolically active disease that evades standard detection.

Open Access · CC BY 4.0 · © 2026 The Author(s) · Published by SJORANM GmbH, Switzerland
ISSN 2813-7221 · Swiss J. Radiol. Nucl. Med. 2026 32(2):1-7 · DOI 10.59667/sjoranm.v32i2.14

Case Presentation

A 57-year-old female with a history of right-sided grade III invasive ductal carcinoma (ER positive, PR positive, HER2 negative, Ki67 35%) underwent right modified radical mastectomy in July 2017, followed by radiotherapy and two years of hormonal therapy. IHC stains for neuroendocrine differentiation were not performed, as they are not requested routinely.

In November 2024, serum tumour markers, particularly CEA, slightly rose to 5.49 ng/mL from 3.82 ng/mL in August. Standard 18F-FDG PET/CT was negative. By March 2025, CEA reached 9.25 ng/mL raising concern despite a normal bilateral sonomammography and multiphase contrast-enhanced CT [Figure 1]. This period of diagnostic uncertainty, stretching over several months with conflicting biochemical and imaging results, was a source of significant anxiety for the patient, who remained otherwise asymptomatic.



Figure 1. Axial contrast-enhanced CT image of the abdomen showing no definitive hepatic lesion.

A second standard PET/CT (45 minutes post-injection) showed no uptake [Figure 2], but delayed imaging (120 minutes) revealed a solitary hepatic lesion in segment IV (SUVmax 7.6) [Figure 3]. It was not confidently visualized on prior multiphasic contrast-enhanced CT, likely due to its peri-portal location and minimal density gradient relative to the adjacent parenchyma, making it radiologically inconspicuous. The mastectomy bed, both lung fields, and the remainder of the body showed no suspicious masses or hypermetabolic lesions.

Open Access · CC BY 4.0 · © 2026 The Author(s) · Published by SJORANM GmbH, Switzerland
ISSN 2813-7221 · Swiss J. Radiol. Nucl. Med. 2026 32(2):1-7 · DOI 10.59667/sjoranm.v32i2.14

Standard-time PET/CT

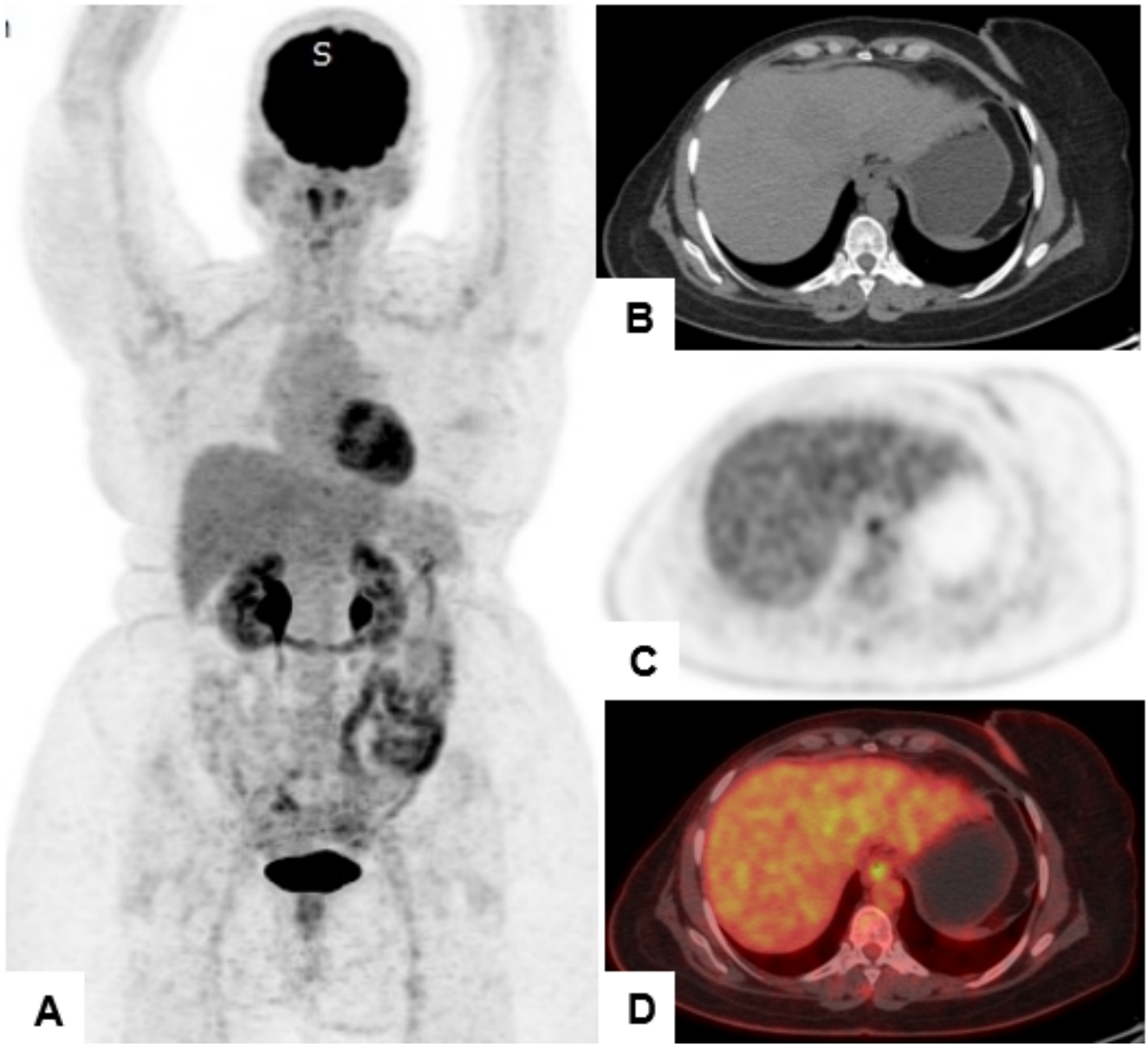


Figure 2. Standard-time-point 18F-FDG PET/CT images showing no definitive hepatic lesion. (A) Maximum-intensity-projection FDG-PET image; (B) axial CT image; (C) corresponding axial PET image; and (D) fused PET/CT image acquired 45 minutes after injection. Physiological hepatic uptake is present.

Based on the 18F-FDG PET/CT images we provided to the interventional radiology team, a successful ultrasound-guided liver biopsy was performed and histopathologic examination revealed a high-grade neuroendocrine neoplasm (NEN); CK7: Positive, CK20: Negative, Chromogranin: Positive, Mammaglobin: Negative, Ki67: 20% [Figure 4].

The findings so far suggested a neuroendocrine tumour (WHO grade 3), either of an unknown primary source or a primary liver origin, a situation much less likely according to literature [1]. To add to this diagnostic dilemma, clinical suspicion remained that it could be a metastasis from the prior breast cancer, partly due to undetected primary location of NET in the surveyed body, specifically the pancreas, lungs and GIT. Furthermore, no hormonal syndromes (functional symptoms) were noted and the patient was asymptomatic, prompting more suspicion in the pathological diagnosis.

Open Access · CC BY 4.0 · © 2026 The Author(s) · Published by SJORANM GmbH, Switzerland
ISSN 2813-7221 · Swiss J. Radiol. Nucl. Med. 2026 32(2):1-7 · DOI 10.59667/sjoranm.v32i2.14

Delayed PET/CT

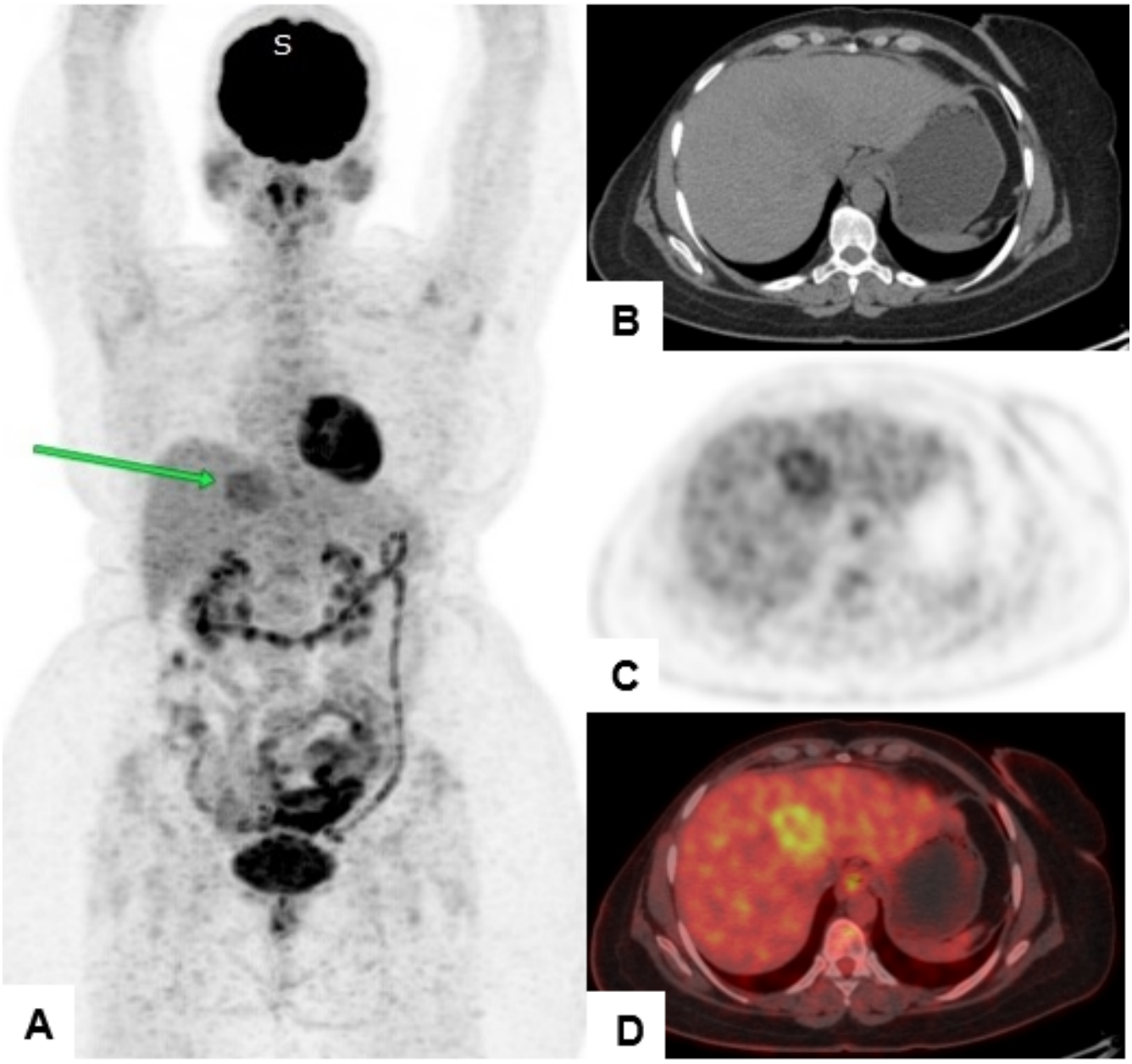


Figure 3. Delayed 18F-FDG PET/CT images highlighting a hypermetabolic lesion in segment IV of the liver. (A) Maximum-intensity-projection FDG-PET image; (B) axial CT image; (C) corresponding axial PET image; and (D) fused PET/CT image acquired 120 minutes after injection. The solitary lesion demonstrates an SUVmax of 7.6, with reduced hepatic background activity.

Further histopathological and immunohistochemical analysis were requested. A review of pathology slides for a second opinion also suggested a neuroendocrine tumour. Additional immunohistochemical analysis revealed strongly positive GATA3 [Figure 4d], a relatively high sensitivity and specificity marker for urothelial and breast carcinoma, including expression in all histological subtypes of breast carcinoma [2]. The hepatic lesion showed strong ER and PR positivity and a Ki67 index of 20% [Figure 4].

These findings were consistent with large cell neuroendocrine carcinoma (LCNEC) of breast origin, WHO grade 3, based on immunophenotyping and clinical context. Management was adjusted accordingly. The patient was referred for systemic therapy, after which the need for local therapy to the liver lesion would be determined. The medical oncology team decided to start with the weekly paclitaxel 80 mg/m^2 and 3-weekly carboplatin AUC 5 doublet.

Open Access · CC BY 4.0 · © 2026 The Author(s) · Published by SJORANM GmbH, Switzerland
ISSN 2813-7221 · Swiss J. Radiol. Nucl. Med. 2026 32(2):1-7 · DOI 10.59667/sjoranm.v32i2.14

Histopathology and Immunohistochemistry

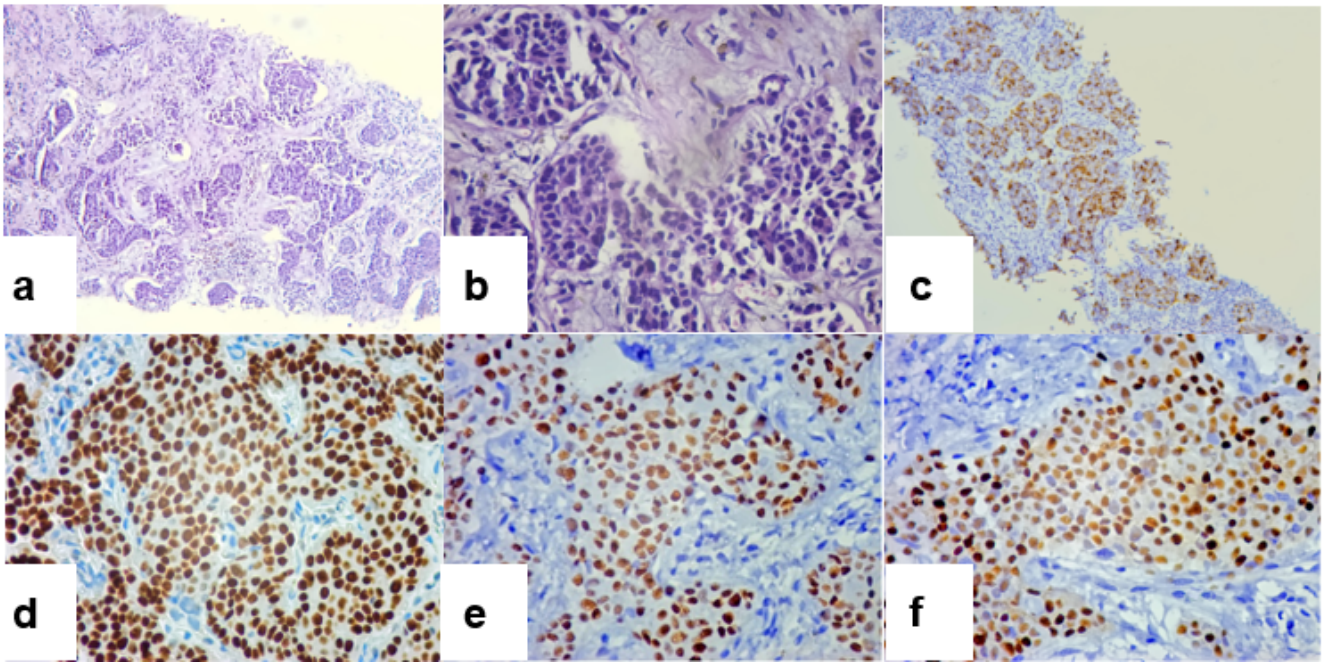


Figure 4. Histopathology and immunohistochemistry of the liver-lesion biopsy. (a, b) Hematoxylin and eosin staining shows a poorly differentiated carcinoma with neuroendocrine features, including nesting and granular chromatin (original magnification ×100 and ×400). (c) Chromogranin A positivity in tumour cells (×100). (d) Strong nuclear GATA3 positivity in tumour cells (×400). (e, f) Positive ER and PR staining in tumour cells.

Discussion

Delayed 18F-FDG PET/CT Imaging in Breast Cancer

This case illustrates the added diagnostic value of delayed-time-point 18F-FDG PET/CT imaging. In hepatic lesions, especially those surrounded by physiologic background uptake, early imaging can be inconclusive. Delayed imaging improves lesion-to-background contrast, enhancing the detection of metabolically active lesions that may otherwise be obscured in early images [3].

Studies have found that delayed imaging can improve lesion detection, especially in the liver, by increasing the contrast between lesions and normal tissue thus enhancing lesion to background ratio [3, 4, 5].

Of note, the lesion in our patient demonstrated FDG avidity, which aligned with the high-grade and poorly differentiated nature of the neuroendocrine tumour. This is consistent with established evidence showing that 18F-FDG PET/CT is more sensitive for high-grade (G3) and poorly differentiated NETs, whereas well-differentiated (G1–G2) NETs often have low or absent FDG uptake [6,7]. In contrast, 68Ga-DOTATATE PET/CT has emerged as the imaging modality of choice for well-differentiated NETs due to its high sensitivity and specificity for somatostatin receptor expression [8].

In our case, the clear FDG uptake helped localize the lesion and guide the biopsy that led to a definitive diagnosis. This case also adds to the limited body of evidence supporting 18F-FDG PET/CT use in rare breast cancer subtypes.

Open Access · CC BY 4.0 · © 2026 The Author(s) · Published by SJORANM GmbH, Switzerland
ISSN 2813-7221 · Swiss J. Radiol. Nucl. Med. 2026 32(2):1-7 · DOI 10.59667/sjoranm.v32i2.14

Neuroendocrine Differentiation in Breast Cancer

The 2019 World Health Organization (WHO) 5th edition categorizes breast NENs into well-differentiated neuroendocrine tumors (NETs) and poorly differentiated neuroendocrine carcinomas (NECs). [9]

Well-differentiated NETs of the breast typically resemble luminal-type breast cancers, being hormone receptor-positive and HER2-negative. In contrast, poorly differentiated NECs are aggressive, high-grade malignancies, further divided into small cell and large cell types [9].

Diagnosing a primary breast NEN requires a diffuse neuroendocrine marker expression (in > 90% of cells) and comprehensive clinical and radiological exclusion of metastases from extramammary neuroendocrine primaries [10].

A population-based study states that breast NEC accounts for less than 0.1% of all breast cancers and is often underdiagnosed due to overlapping histological and clinical features with conventional subtypes [11]. Breast NENs may present with aggressive behaviour and atypical metastatic patterns, particularly when associated with high-grade features [12].

Immunohistochemical profiling is crucial for accurate diagnosis. Markers such as GATA3 positivity and mammaglobin negativity can help distinguish breast origin from other primary sites. [9]

Limitations

Single case report limits generalizability. Neuroendocrine differentiation contribution to imaging remains speculative; no long-term follow-up.

Clinical Implications

In this case, delayed imaging identified a hepatic biopsy target after negative standard-time PET/CT. The observation supports further evaluation of delayed imaging in selected clinical settings; it does not establish routine use, diagnostic accuracy, or an improvement in patient outcomes.

Conclusion

In this patient, delayed 18F-FDG PET/CT demonstrated a hepatic lesion that was not apparent on the standard-time acquisition and provided a target for biopsy. Histopathological and immunohistochemical assessment supported metastatic breast carcinoma with neuroendocrine differentiation and informed the reported systemic treatment plan. This single case does not establish the diagnostic accuracy of dual-time-point imaging or improved clinical outcomes.

Open Access · CC BY 4.0 · © 2026 The Author(s) · Published by SJORANM GmbH, Switzerland
ISSN 2813-7221 · Swiss J. Radiol. Nucl. Med. 2026 32(2):1-7 · DOI 10.59667/sjoranm.v32i2.14

Declarations

Ethics approval and consent to participate: This study was conducted in accordance with the Declaration of Helsinki. As this was a single-case report, ethical review and approval were waived. The Armed Forces College of Medicine Institutional Review Board waived the need for ethics approval.

Consent for publication: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Competing interests: The authors declare that they have no competing interests.

Funding: This research received no external funding.

Availability of data and material: The data presented in this study are not publicly available due to institutional policies but are available on request from the corresponding author, MHM.

Authors' Contributions

Conceptualization, MHM and MTK.; collection of patient data, MHM; contribution to imaging interpretation, MTK, SYW, RAS; performing the histological examination, MME and MAE; writing: original draft preparation, MHM.; writing: review and editing, SYW, YWN, and BEA.; supervision, SYW and RAS. All authors have read and agreed to the published version of the manuscript.

Acknowledgements: Not applicable.

Correspondence

Mohamed Hossameldin Mustafa · Nuclear Medicine Department, Armed Forces College of Medicine, Cairo, Egypt. Email: mohammedhussam98@gmail.com · Phone: +20 1012179366.

ORCID: 0009-0006-1269-1269

Disclaimer/Publisher's Note

The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of Swiss J. Radiol. Nucl. Med. and/or the editor(s). Swiss J. Radiol. Nucl. Med. and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.

This work is licensed under a Creative Commons Attribution 4.0 International License. Reusers must give credit to the creator. Redistribution and adaptation are permitted in any medium or format, including commercial use.

SJORANM-LinkedIn: Journal profile

References

1. Yang XR, Li YL, Li ZY, Chai XM. Primary hepatic neuroendocrine neoplasms: imaging characteristics and misdiagnosis analysis. Front Oncol. 2024 May 14;14. https://doi.org/10.3389/fonc.2024.1391663
2. Liu H, Shi J, Wilkerson ML, Lin F. Immunohistochemical Evaluation of GATA3 Expression in Tumors and Normal Tissues. American Journal of Clinical Pathology. 2012 Jul 1;138 (1):57–64. https://doi.org/10.1309/AJCP5UAFMSA9ZQBZ
3. Al-Faham Z, Jolepalem P, Rydberg J, Wong CYO. Optimizing 18F-FDG Uptake Time Before Imaging Improves the Accuracy of PET/CT in Liver Lesions. J Nucl Med Technol. 2016 Jun;44 (2):70–2. https://doi.org/10.2967/jnmt.115.169953
4. Lee JY, Song HS. Detection of Hepatic Metastasis from Early Delayed Images of Modified Dual-Time-Point 18F-FDG PET/CT Images in a Patient with Breast Cancer. Diagnostics. 2024 Jul 31;14 (15):1653. https://doi.org/10.3390/diagnostics14151653
5. Annovazzi A, Rea S, Vici P, Fabi A, Sciuto R. Dual-time 18F-FDG PET/CT for the detection of liver metastases in breast cancer. Nuclear Medicine Communications. 2018 Dec;39 (12):1183–9. https://doi.org/10.1097/MNM.0000000000000918
6. Kayani I, Bomanji JB, Groves A, Conway G, Gacinovic S, Win T, et al. Functional imaging of neuroendocrine tumors with combined PET/CT using 68Ga-DOTATATE (DOTA- D Phe1 ,Tyr3 -octreotate) and 18F-FDG. Cancer. 2008 Jun;112 (11):2447–55. https://doi.org/10.1002/cncr.23469
7. Zhou J, Zhao R, Pan Y, Ju H, Huang X, Jiang Y, et al. The Diagnostic and Grading Accuracy of 68Ga-DOTATATE and 18F-FDG PET/MR for Pancreatic Neuroendocrine Neoplasms. Front Oncol. 2022 Feb 22;12:796391. https://doi.org/10.3389/fonc.2022.796391
8. Tirosh A, Kebebew E. The Utility of 68Ga-DOTATATE Positron-Emission Tomography/Computed Tomography in the Diagnosis, Management, Follow-Up and Prognosis of Neuroendocrine Tumors. Future Oncol. 2018 Jan 31;14 (2):111–22. https://doi.org/10.2217/fon-2017-0393
9. Vegni F, De Stefano IS, Policardo F, Tralongo P, Feraco A, Carlino A, et al. Neuroendocrine neoplasms of the breast: a review of literature. Virchows Arch. 2024 Aug;485 (2):197–212. https://doi.org/10.1007/s00428-024-03856-y
10. Rosen LE, Gattuso P. Neuroendocrine Tumors of the Breast. Archives of Pathology & Laboratory Medicine. 2017 Nov 1;141 (11):1577–81. https://doi.org/10.5858/arpa.2016-0364-rs
11. Wang J, Wei B, Albarracin CT, Hu J, Abraham SC, Wu Y. Invasive neuroendocrine carcinoma of the breast: a population-based study from the surveillance, epidemiology and end results (SEER) database. BMC Cancer. 2014 Dec;14 (1):147. https://doi.org/10.1186/1471-2407-14-147
12. Sun H, Dai S, Xu J, Liu L, Yu J, Sun T. Primary Neuroendocrine Tumor of the Breast: Current Understanding and Future Perspectives. Front Oncol. 2022 May 25;12:848485. https://doi.org/10.3389/fonc.2022.848485

Open Access · CC BY 4.0 · © 2026 The Author(s) · Published by SJORANM GmbH, Switzerland
ISSN 2813-7221 · Swiss J. Radiol. Nucl. Med. 2026 32(2):1-7 · DOI 10.59667/sjoranm.v32i2.14