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Case Report

Comparison of ^{18}F-FDG PET/CT and ^{18}F-DOTATATE PET/CT in the diagnosis of multiple metastases in rectal neuroendocrine neoplasms ☆,☆☆

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ABSTRACT

This case report describes a 62-year-old male with a notable medical history, including surgically treated bladder cancer and the suspicion of metastatic disease. He underwent ^{18}F-FDG PET/CT imaging as part of the initial diagnostic workup, which identified several marginally hypodense hepatic lesions. These lesions exhibited metabolic activity that was slightly lower than the surrounding hepatic parenchyma, raising concerns for metastatic involvement. Subsequent ^{18}F-DOTATATE PET/CT imaging significantly expanded the diagnostic perspective by identifying multiple somatostatin receptor (SSTR)-positive lesions, not only in the liver but also in lymph nodes and bones. This marked an important diagnostic advancement over the initial FDG PET/CT findings, showcasing the superior sensitivity of ^{18}F-DOTATATE PET/CT in detecting SSTR-expressing tumors. Pathological evaluation after these imaging studies confirmed the diagnosis of a rectal neuroendocrine tumor (NET) with extensive hepatic metastasis, altering the clinical management and therapeutic approach for the patient. This case underscores the pivotal role of integrating ^{18}F-DOTATATE and FDG PET/CT in the diagnostic and therapeutic management of neuroendocrine tumors, highlighting the complementary nature of these imaging modalities. The findings advocate for the use of ^{18}F-DOTATATE PET/CT in cases where NETs are suspected, particularly for its enhanced sensitivity in detecting SSTR-positive lesions across various sites, thereby facilitating a more comprehensive disease assessment and informed therapeutic planning.

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Introduction

Rectal neuroendocrine tumors (NETs) are rare, with an incidence of 0.17%, but they represent 12% to 27% of all NETs and 20% of gastrointestinal NETs [1]. They are bifurcated into 2 distinct categories: well-differentiated, low-proliferating NENs, known as NETs or carcinoids, and poorly differentiated, high-proliferating neuroendocrine carcinomas (NECs) [2]. NENs and NECs exhibit considerable differences in their characteristics. NENs are found throughout the body, with about 70% originating in the gastroenteropancreatic system, 25% in the respiratory system, and the remaining 5% in other organs [3]. NETs sometimes manifest symptoms like carcinoid syndrome due to autocrine hormones, although most are nonfunctional, making early detection challenging. They are immunohistochemically positive for neuroendocrine markers, such as chromogranin A or synaptophysin, indicating their neuroendocrine origin and aiding in their classification.

The proliferation rate is a significant prognostic factor for NETs [4]. The WHO grading system classifies NETs into low-grade proliferative (NET-G1) with a favorable prognosis, intermediate grade (NET-G2) with a poorer prognosis, and high-grade (NET-G3) with a poor prognosis, highlighting the importance of accurate grading in patient management [5]. Notably, NETs often exhibit high somatostatin receptor (SSTR) expression, making them amenable to targeted diagnostic and therapeutic approaches. SSTRs are consistently expressed at high levels in both NET-G1 and -G2, regardless of the primary organ, while their expression is markedly reduced in NET-G3 or NEC, affecting the choice of imaging and treatment modalities [6,7].

^{18}F-FDG PET/CT is a predominant functional imaging technique extensively utilized in the diagnosis of tumor, reflecting the metabolic activity of the tumor. ^{68}Ga-DOTATATE, a well-established ^{68}Ga-labeled somatostatin analog (SSA), specifically binds to somatostatin receptors (SSTRs), which are abundantly expressed on neuroendocrine tumor cells. This specific binding facilitates precise imaging of neuroendocrine tumors, enhancing diagnostic accuracy and potentially guiding targeted therapies [8]. Studies have demonstrated varying diagnostic efficacies of FDG and ^{68}Ga-DOTATATE in NENs, contingent upon their grade and degree of differentiation [9]. The comparison between ^{68}Ga-DOTATATE PET/CT and FDG PET/CT in NENs offers a more informed basis for selecting appropriate imaging modalities in nuclear medicine, particularly for newly diagnosed patients or those undergoing follow-up assessments [10].

This case report underscores the significant clinical utility of ^{18}F-DOTATOC-targeted imaging in both the diagnosis and subsequent treatment of well-differentiated NENs, illustrating the pivotal role of advanced imaging techniques in optimizing care for patients with neuroendocrine tumors.

Case report

A 62-year-old male, with a history of surgically treated the bladder urothelial cancer 3 years prior, presented for evaluation. For 3 years postsurgery, he had not undergone any follow-up examinations or treatments. A recent abdominal MRI revealed the presence of multiple hepatic nodules with abnormal signal characteristics and obvious enhancement, raising suspicions of metastasis. Laboratory investigations, including routine blood tests, were within normal limits. Given these findings, the patient's oncologist recommended an FDG PET/CT scan to assess the patient's systemic condition and to investigate the potential spread of disease.

The imaging process was conducted using a PET/CT scanner (Biograph 64, Siemens Healthineers, Germany). Prior to scanning, patients were required to fast for a minimum of 6 hours. Blood glucose levels were carefully maintained below 6.5 mmol/L. After intravenous administration of FDG 407 MBq (11mCi), PET/CT images were acquired following a resting period of 60 minutes. The CT component of PET/CT was executed as a low-dose scan. CT imaging preceded PET scanning, which covered the area from the femur to the skull base. Typically, 5 PET beds were employed. CT settings included a tube current of 110 mAs, voltage of 120 kV, tube rotation time of 0.5 seconds, slice thickness of 5 mm, and a pitch of 1. The PET acquisition time was 2 minutes per bed position, with image reconstruction utilizing CT-based attenuation correction and point spread function. The reconstruction parameters were as follows: 3 iterations, 21 subsets, a matrix of 256 × 256 mm, Gaussian post-filtering with a full width at half maximum (FWHM) of 5.0 mm, a voxel size of 1.65 × 1.65 × 3 mm for the reconstructed images, and scatter correction.

The patient's initial FDG PET/CT examination revealed increased localized radiotracer uptake in the rectum, with SUVmax of 4.5. In the liver, several slightly hypodense areas were observed, the largest measuring approximately 4.4 × 5.6 cm, exhibiting radiotracer uptake lower than the hepatic background (Fig. 1). These findings led the clinician to suspect multiple liver metastases. Due to the suspicious nature of the rectal lesion, further investigation was deemed necessary. Consequently, the patient underwent endoscopic resection of the rectal lesion and a liver biopsy. Pathological analysis confirmed a well-differentiated neuroendocrine tumor (Grade 2) in the rectum, accompanied by multiple hepatic metastases (Figs. 2 and 3). Immunohistochemical results were as follows: CK7(-), p40(-), CgA (+), CK5(+), CD56(+), Syn (+), CK19(-), AFP (+), Hepatocyte (-), PDL1(SP263) (CPS:0), Ki-67(+18%), SSTR1(+), SSTR2(+). Based on these findings, the patient underwent ^{18}F-DOTATATE PET/CT imaging three days later, using the same Siemens Biograph 64 scanner, with unchanged acquisition and reconstruction parameters. The images were acquired 60 minutes postintravenous administration of 222 MBq (6mCi) ^{18}F-DOTATATE. The ^{18}F-DOTATATE PET/CT imaging revealed multiple lesions with high DOTATATE expression in the liver, lymph nodes, and bones (Fig. 4). The diagnostic performance of ^{18}F-DOTATATE PET/CT was significantly superior to that of FDG PET/CT. Additionally, ^{18}F-DOTATATE PET/CT imaging effectively ruled out the possibility of multiple metastases from the bladder tumor.

Finally, the patient received endocrine therapy in an outside hospital. A telephone follow-up 1 year later revealed significant improvements in the patient's condition, with MR Examination indicating a reduction in liver and lymph node lesions.

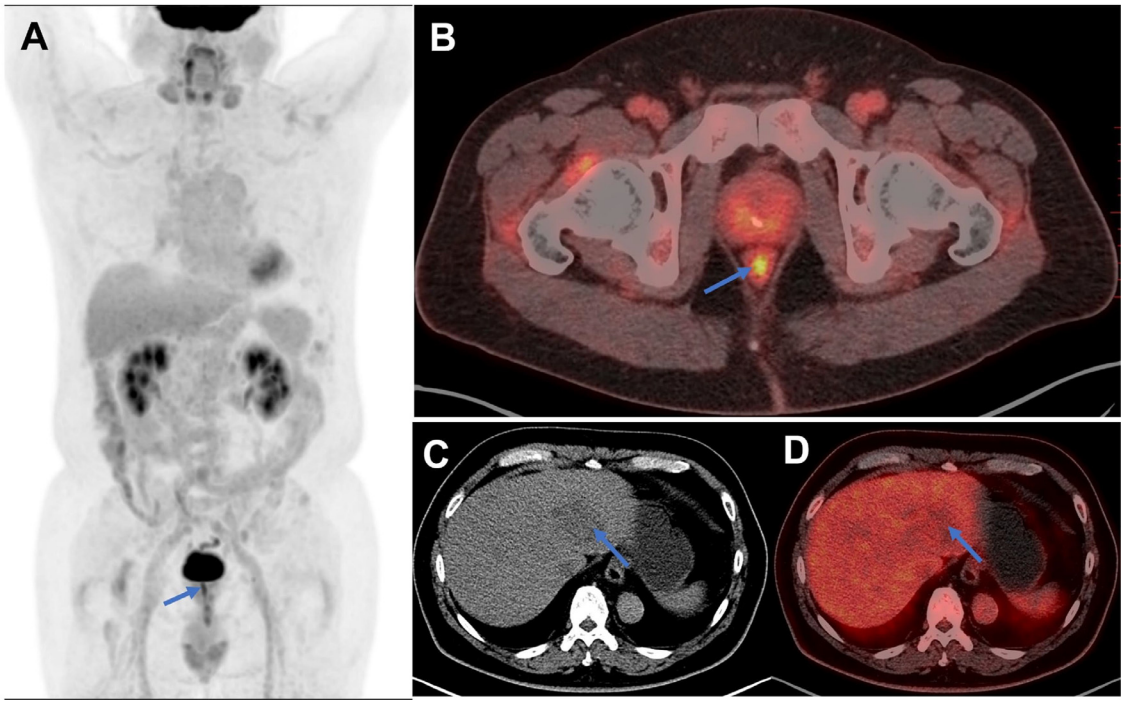

Fig. 1 – The maximum intensity projection (MIP) image (Panel A) displays an elevated radioactive uptake in the rectum (Panel B, fusion PET/CT; SUVmax, 4.5). Additionally, multiple marginally hypodense hepatic shadows are evident, with the largest lesion measuring approximately 4.4 × 5.6 cm (Panel C, CT). These lesions exhibit a radiotracer uptake that is notably lower than the surrounding hepatic parenchyma (Panel D, fusion PET/CT).

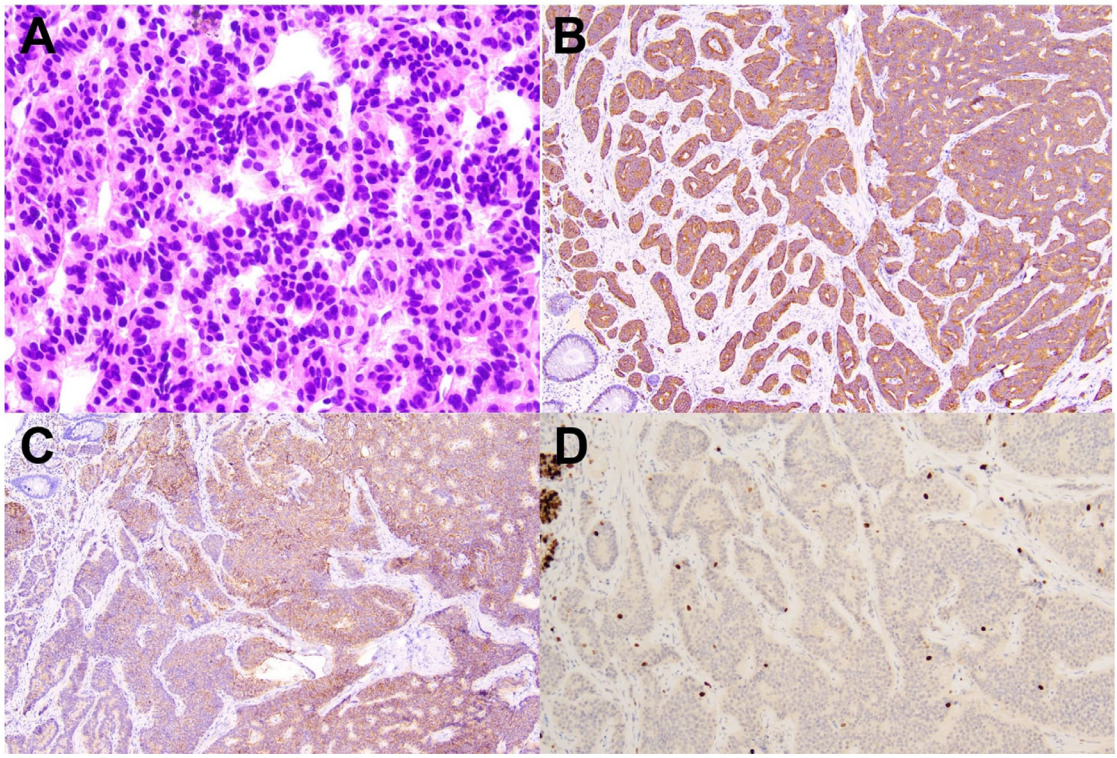

Fig. 2 – Pathological findings from the patient's liver biopsy. (Panel A) shows the histopathology of hepatic metastasis from a neuroendocrine tumor (Grade 2), visualized using hematoxylin and eosin staining (original magnification × 40). Immunohistochemical analysis reveals positive staining for Synaptophysin (Syn) (Panel B, original magnification × 10), CD56 (Panel C, original magnification × 10), and a Ki-67 proliferation index of 18% (Panel D, original magnification × 10).

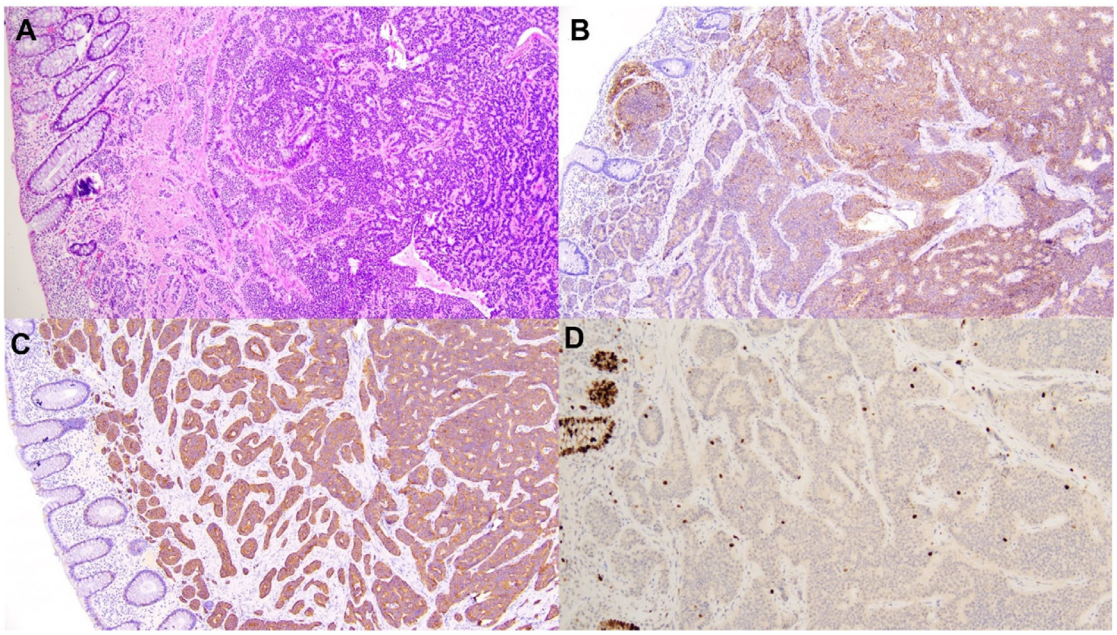

Fig. 3 – Histopathological and immunohistochemical findings following a colonoscopy and endoscopic resection of the rectal lesion. Panel A depicts the well-differentiated neuroendocrine tumor (Grade 2) in the rectum, showing invasion into the mucosa and submucosa, stained with hematoxylin and eosin (original magnification × 10). Immunohistochemical analysis reveals positive staining for CD56 (Panel B, original magnification × 10), Synaptophysin (Syn) (Panel C, original magnification × 10), and a Ki-67 proliferation index of 3% (Panel D, original magnification × 10).

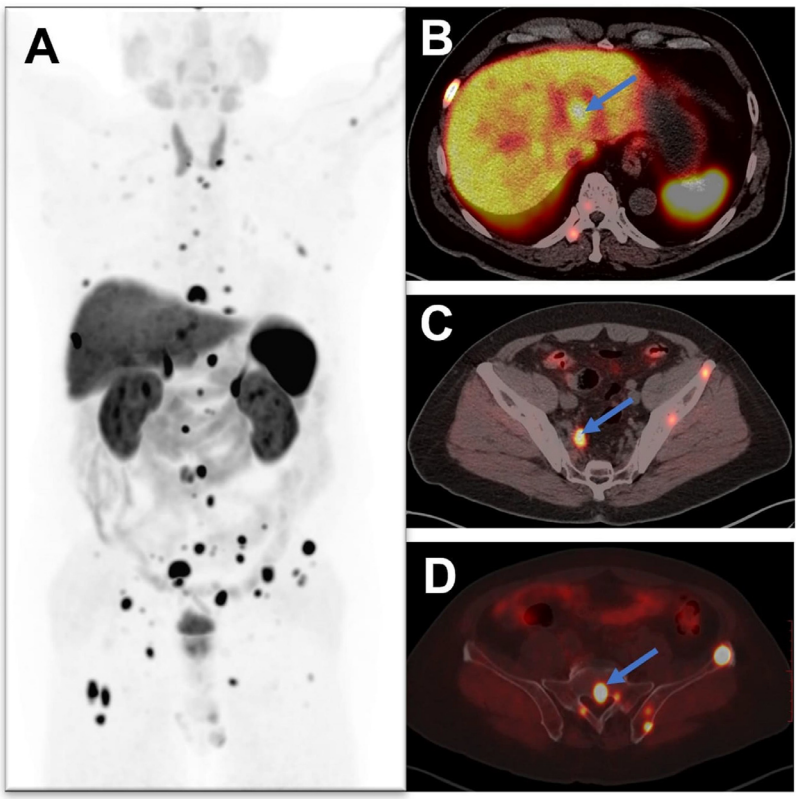

Fig. 4 – Results from the ^{18}F-DOTATATE PET/CT imaging. (Panel A) shows the maximum intensity projection (MIP) image. The imaging revealed multiple DOTATATE-avid lesions, notably in the liver (Panel B, fusion PET/CT), lymph nodes (Panel C, fusion PET/CT), and bones (Panel D, fusion PET/CT). These findings indicate a significantly higher lesion detection rate in comparison to the previous ^{18}F-FDG PET/CT imaging.

Discussion

Neuroendocrine neoplasms (NENs) are a distinct group of tumors originating from peptidergic neurons and neuroendocrine cells [11–13]. They are classified into functional and nonfunctional types, based on their hormone secretion capabilities. While the majority of NENs are nonfunctional and often remain asymptomatic, potentially leading to delayed diagnosis, functional NENs, which account for about 20% of all cases, may present with symptoms due to hormone secretion [14,15]. In the diagnostic landscape, the integration of functional imaging with morphological imaging, notably through molecular imaging techniques, is crucial for accurately staging NENs and guiding treatment strategies [16].

FDG PET/CT is instrumental in assessing the glucose metabolism of tumors, providing valuable insights into tumor aggressiveness and proliferation. On the other hand, ^{18}F-DOTATATE PET/CT offers a window into the cellular level by reflecting the expression of somatostatin receptors (SSTR) in NENs [15]. The prominence of ^{68}Ga-DOTATATE PET/CT in diagnosing NENs, evaluating treatment efficacy, and identifying candidates for peptide radionuclide receptor therapy (PRRT) underscores the significance of SSTR expression as a therapeutic target and diagnostic marker. High SSTR expression in patients suggests a potential benefit from PRRT, making it an essential factor in the management of NENs. Prior studies indicate that the detection rates for ^{68}Ga-DOTATATE PET/CT and FDG PET/CT differ significantly between well-differentiated and poorly differentiated NENs [17]. This variance underscores the distinct biological behaviors of these tumors, with well-differentiated NENs showing higher SSTR expression and lower metabolic activity, and poorly differentiated NENs exhibiting the opposite trend [18,19]. This difference in imaging outcomes suggests that combining both imaging modalities could provide a more comprehensive disease assessment, particularly in cases of tumor heterogeneity [20].

In low-grade NENs, which typically exhibit high SSTR expression, ^{18}F-DOTATATE shows high diagnostic accuracy and specificity for both primary and metastatic lesions. However, in cases of advanced-stage NENs or neuroendocrine carcinoma (NEC), where SSTR expression may be reduced, the sensitivity of ^{177}Lu-DOTATATE decreases, highlighting the complexity of imaging and treating these tumors [21]. The higher SSTR expression in well-differentiated NENs implies greater efficacy of ^{18}F-DOTATATE PET/CT imaging and a likelihood of benefiting from PRRT. Conversely, for poorly differentiated NENs, while FDG PET/CT may yield better results, some cases still exhibit high SSTR expression, indicating potential benefit from PRRT. Higher FDG uptake in tumors correlates with a higher Ki-67 index, indicating a more aggressive nature and poorer prognosis [22]. Conversely, while FDG PET/CT may yield better results for poorly differentiated NENs, it is noteworthy that some cases still exhibit high SSTR expression, indicating a potential benefit from PRRT. The correlation between higher FDG uptake in tumors and a higher Ki-67 index signifies a more aggressive tumor phenotype and a poorer prognosis [23]. Conversely, low ^{18}F-DOTATATE uptake by tumors suggests a similarly poor prognosis, reinforcing the complementary roles of ^{18}F-DOTATATE PET/CT and FDG PET/CT in the comprehensive assessment of NENs.

Conclusion

This case emphasizes the synergistic application of both ^{18}F-DOTATATE and FDG PET/CT, enhancing the diagnostic sensitivity and specificity for NENs. The combined use of these imaging modalities holds substantial clinical value for accurately staging the disease, determining appropriate treatment strategies, and prognosticating outcomes, thereby offering a nuanced approach to the management of patients with NENs.

Patient consent

Informed consent was obtained from all subjects involved in the study.

Author contributions

Conceptualization and investigation: Z. H. S; writing—original draft preparation: Z. H. S; writing—review and editing: R. M. W, X.J.Z, and Q. X. L. All authors have read and agreed to the published version of the manuscript.

Institutional review board statement

This study was approved by the Human Ethics Committee of the XXXX General Hospital. (Ethics Committee Approval code: S2018-167-01).

Data availability statement

The data are not publicly available due to privacy regulations regarding patients.

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