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Demonstration of focal physiologic in-vivo somatostatin receptor expression in the caput epididymis of the testes on ^{68}Ga-DOTANOC PET/CT and ^{177}Lu-DOTATATE post-therapy whole body scintigraphy

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ABSTRACT

We present the case of a 60-year-old man with metastatic neuroendocrine tumor of the ileum following ileal resection, being evaluated for ^{177}Lu-based peptide receptor radionuclide therapy. ^{68}Ga-DOTANOC PET/CT showed focal increased tracer uptake in the scrotal region without any morphologic changes on the corresponding CT images. Similar increased tracer uptake was seen on post-therapy whole-body imaging following ^{177}Lu-DOTATATE therapy. An USG guided FNA revealed no malignant cells on cytopathologic examination. This case illustrates that focal testicular tracer uptake, may not always be pathological and can represent a normal physiologic variant, similar to the diffuse testicular somatostatin receptor expression as previously reported in literature.

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Introduction

^{68}Ga-DOTANOC PET/CT has shown to be a useful modality in the detection of tumors of neuroendocrine origin. It also forms the basis of peptide receptor radionuclide therapy (PRRT) as the degree of tumoral somatostatin receptor expression on ^{68}Ga-DOTANOC PET/CT is one of the major factors determining suitability and effectiveness of ^{177}Lu or ^{90}Y based PRRT. A physiologic, low grade, diffuse somatostatin receptor expression has been described in the testes, but we report a case of focal, increased somatostatin receptor expression in the caput epididymis of the testes on ^{68}Ga-DOTANOC

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PET/CT and post ^{177}Lu-DOTATATE therapy imaging that turned out to be physiologic on further work-up.

Cases report

A 60-year-old man, diagnosed with metastatic neuroendocrine tumor of the ileum post-ileal resection with end-to-end anastomosis and enucleation of the liver metastases, six years back presented with progressive disease. He underwent a ^{68}Ga-DOTANOC PET/CT for assessment of disease burden and feasibility of ^{177}Lu-based peptide receptor radionuclide therapy (PRRT). Figure 1 - Maximum intensity projection image (A) and transaxial fused PET/CT images (arrows: B, C) showed increased focal tracer uptake in the scrotal region, likely corresponding to the caput epididymis (SUV_{max} 7.3 on the left side) apart from tracer avid abdominal, mediastinal lymph nodes and liver lesions. There was no abnormal morphologic changes in the testes corresponding to the focal increased tracer uptake on transaxial CT images (Figure 1- D, E). The patient received 7.4 GBq (~200 mCi) of ^{177}Lu-DOTATATE as intravenous infusion under amino-acid renal protection .

Post-therapy whole-body image (Figure 1- F) showed tracer uptake in the liver lesions, abdominal and mediastinal lymph nodes and left supraclavicular lymph node. Focal tracer uptake was also noted in the bilateral scrotal region (arrow: F) correlating with the PET/CT images. In view of the increased focal tracer avidity in the bilateral scrotal region in the ^{68}Ga-DOTANOC PET/CT and ^{177}Lu-DOTATATE post therapy scan, an ultrasound guided fine needle aspiration (FNA) was performed from the testes after reviewing the PET/CT images. The cytopathologic examination revealed no evidence of malignant cells in the aspirate. The ultrasound examination of the bilateral scrotal region also revealed no abnormality.

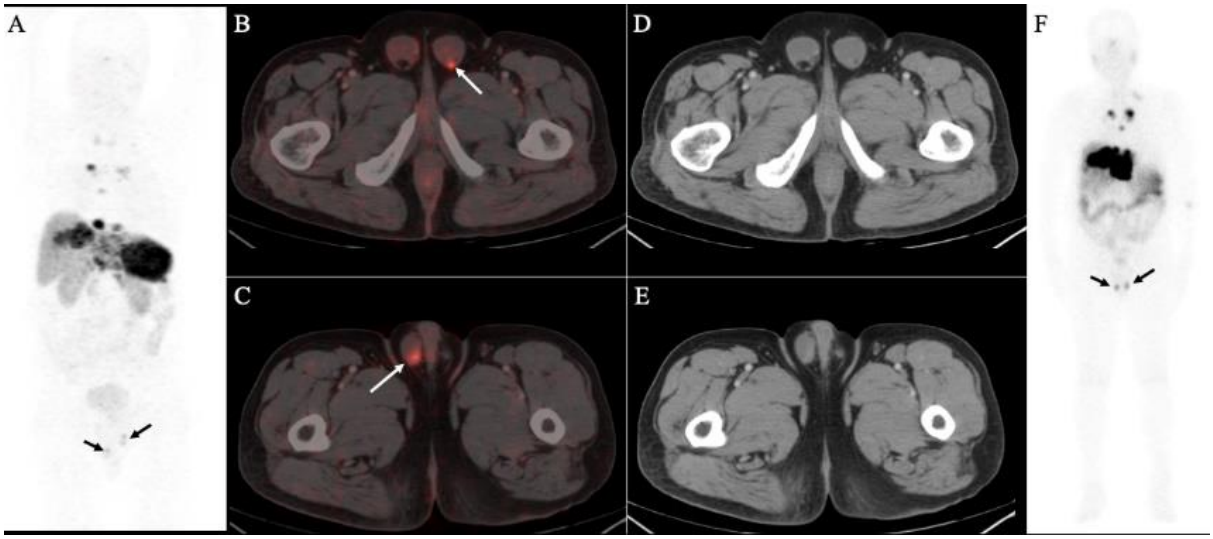

Figure 1. ^{68}Ga-DOTANOC PET/CT maximum intensity projection image (A) and transaxial fused PET/CT images (arrows: B, C) showing increased focal tracer uptake, likely in the caput epididymis of the testes (SUV_{max} 7.3 on the left side) apart from tracer avid abdominal, mediastinal lymph nodes and liver lesions. No abnormal morphologic changes in the testes noted on transaxial CT images (D, E). Post ^{177}Lu-DOTATATE therapy whole-body image (F) showing tracer uptake in the liver lesions, abdominal and mediastinal lymph nodes and left supraclavicular lymph node. Focal tracer uptake also noted in the bilateral scrotal region (arrow: F) correlating with the PET/CT images

Discussion

^{68}Ga-DOTANOC expresses increased affinity for somatostatin receptor (SSTR) subtypes 2, 3 and 5 (1). ^{68}Ga-DOTANOC PET/CT has proven to be a sensitive imaging modality for detection of tumors with neural crest origin, such as gastro-pancreatic neuroendocrine tumors, carcinoids and medullary thyroid carcinoma among others (2-5). Apart from this, tumors such as meningioma, medulloblastoma, low grade gliomas, hemangioblastoma, pituitary adenomas are also avid on ^{68}Ga-DOTANOC PET/CT (6-8). Physiologic uptake of the tracer is seen in the pituitary gland, thyroid, liver, spleen, adrenals, kidneys and excretory activity in the urinary tract (9-12). Apart from the uncinate process of the pancreas, a focal tracer uptake, with intensity similar to the liver has also been described in the pancreatic head (13). A varying degree of tracer uptake is also noted in the stomach, small and large intestine, likely attributable to neuroendocrine cell hyperplasia (14). Physiologic somatostatin receptor expression is also reported in the splenunculus, albeit to a lesser intensity than that on the spleen

and on the white blood cells, in a setting of an inflammatory/ infective process (14). Somatostatin receptor expression (SSTR 3 and 5) has been documented in testis, though testicular tracer uptake on ^{68}Ga-DOTANOC is usually diffuse and of low grade (15, 16). Similarly low grade tracer avidity in testes, just slightly higher than the background tracer activity has also been shown on ^{68}Ga-DOTATOC PET/CT (17). On the other hand, though very rare, testes are a known site for metastasis from gastrointestinal neuroendocrine tumors and primary carcinoids (18, 19). Thus, focal and significantly increased testicular tracer uptake on PET/CT might raise the suspicion of a malignant entity. The present case showed that focal increased tracer avidity in the caput epididymis of the testes on ^{68}Ga-DOTANOC PET/CT as well as on ^{177}Lu-DOTATATE post-therapy scan does not necessarily denote a malignancy and can be a physiologic finding. Therefore, any increased tracer uptake at unusual sites on diagnostic and post-therapy imaging requires accurate interpretation to avoid the potential pitfalls associated with somatostatin receptor imaging.

Conflict of interest

Ashwin Singh Parihar, Apurva Sood, Ashwani Sood, Ajay Gulati, Rajender Kumar and Bhagwant Rai Mittal declare that they have no conflict of interest. There is no source of funding .

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. For this type of study formal consent is not required .

Informed consent

The institutional review board of our institute approved this retrospective study, and the requirement to obtain informed consent was waived.

References

1. Ambrosini V, Campana D, Bodei L, Nanni C, Castellucci P, Allegri V, et al. ^{68}Ga-DOTANOC PET/CT clinical impact in patients with neuroendocrine tumors. J Nucl Med. 2010; 51: 669–673 .
2. Wild D, Mäcke HR, Waser B, Reubi J C, Ginj M, Rasch H, Müller-Brand J, et al. ^{68}Ga-DOTANOC: a first compound for PET imaging with high affinity for somatostatin receptor subtypes 2 and 5. Eur J Nucl Med Mol Imaging. 2005; 32:724–724 .
3. Sharma P, Dhull VS, Arora S, Gupta P, Kumar R, Durgapal P, et al. Diagnostic accuracy of ^{68}Ga-DOTANOC PET/CT imaging in pheochromocytoma. Eur J Nucl Med Mol Imaging. 2014; 41: 494–504 .
4. Parihar AS, Mittal BR, Vadi SK, Basher RK, Bhansali A. Ectopic Cushing Syndrome (ECS). Clin Nucl Med. 2018; 43:769–770 .
5. Ashwathanarayana AG, Biswal CK, Sood A, Parihar AS, Kapoor R, Mittal BR. Imaging-guided use of combined ^{177}Lu-DOTATATE and capecitabine therapy in metastatic mediastinal paraganglioma. J Nucl Med Technol. 2017; 45:314–316 .
6. Sharma P, Mukherjee A, Bal C, Malhotra A, Kumar R. Somatostatin Receptor–Based PET/CT of Intracranial Tumors: A Potential Area of Application for ^{68}Ga-DOTA Peptides? Am J Roentgenol. 2013; 201:1340–1347 .
7. Parihar A S, Basher R K, Rana N, Mittal B R. Incidental Meningioma on ^{68}Ga-DOTANOC Positron-Emission Tomography. Indian J Nucl Med. 2018; 33:182 .
8. Vadi SK, Mittal BR, Parihar AS, Kumar R, Singh H, Singh G. ^{68}Ga-DOTANOC PET/CT in an Atypical Extraskeletal Paravertebral Hemangioma Mimicking as Neurogenic Tumor in a Known Case of Breast Cancer. Clin Nucl Med. 2019; 44:E364–E366 .
9. Pettinato C, Sarnelli A, Di Donna M, Civollani S, Nanni C, Montini G, et al. ^{68}Ga-DOTANOC: biodistribution and dosimetry in patients affected by neuroendocrine tumors. Eur J Nucl Med Mol Imaging. 2008; 35:72–79 .
10. Wild D, Bomanji JB, Benkert P, Maecke H, Ell PJ, Reubi JC, et al. Comparison of ^{68}Ga-DOTANOC and ^{68}Ga-DOTATATE PET/CT within patients with gastroenteropancreatic neuroendocrine tumors. J Nucl Med. 2013; 54:364–372 .
11. Gabriel M, Decristoforo C, Kendler D, Dobrozemsky G, Heute D, Uprimny C, et al. ^{68}Ga-DOTA-Tyr3-octreotide PET in neuroendocrine tumors: Comparison with somatostatin receptor scintigraphy and CT. J Nucl Med. 2007;48:508–518 .
12. Hofmann M, Maecke H, Börner R, Weckesser E, Schöffski P, Oei L, et al. Biokinetics and imaging with the somatostatin receptor PET radioligand ^{68}Ga-DOTATOC: Preliminary data. Eur J Nucl Med. 2001; 28:1751–1757 .
13. Al-Ibraheem A, Bundschuh RA, Notni J, Buck A, Winter A, Wester HJ, et al. Focal uptake of ^{68}Ga-DOTATOC in the pancreas: Pathological or physiological correlate in patients with neuroendocrine tumours? Eur J Nucl Med Mol

Imaging. 2011; 38:2005–2013 .
14. Hofman MS, Eddie Lau WF, Hicks RJ. Somatostatin receptor imaging with ^{68}Ga DOTATATE PET/CT: Clinical utility, normal patterns, pearls, and pitfalls in interpretation1. Radiographics. 2015; 35:500–516 .
15. Baou N, Bouras M, Droz JP, Benahmed M, Krantic S, et al. Evidence for a selective loss of somatostatin receptor subtype expression in male germ cell tumors of seminoma type. Carcinogenesis. 2000; 21:805–810 .
16. Kagna O, Pirmisashvili N, Tshori S, Freedman N, Israel O, Krausz Y, et al. Neuroendocrine Tumor Imaging with ^{68}Ga-DOTA-NOC: Physiologic and Benign Variants. Am J Roentgenol. 2014; 203:1317–1323 .
17. Todorović-Tirnanić MV, Gajić MM, Obradović VB, Baum RP, et al. Gallium-68 DOTATOC PET/CT in vivo characterization of somatostatin receptor expression in the prostate. Cancer Biother Radiopharm. 2014; 29:108–115 .
18. Degnan AJ, Tadros SS, Tocchio S. Pediatric Neuroendocrine Carcinoid Tumors: Review of Diagnostic Imaging Findings and Recent Advances. Am J Roentgenol. 2017; 208:868–877 .
19. Carreras C, Kulkarni HR, Baum RP. Rare Metastases Detected by ^{68}Ga-Somatostatin Receptor PET/CT in Patients with Neuroendocrine Tumors. Recent Results Cancer Res. 2013. 379–384 .