

CASE REPORT

Paget's Disease Mimicking Bone Metastasis in a Patient with Neuroendocrine Tumor on ^{68}Ga -DOTANOC PET/CT

Naciye Sinem Gezer*, Ali Balci*, Özhan Özdoğan† and Dinç Özaksoy*

Somatostatin (SST) is a neuropeptide present in neurons, endocrine cells, and a wide range of neuroendocrine tumors (NETs). ^{68}Ga -DOTATOC, ^{68}Ga -DOTANOC, and ^{68}Ga -DOTATATE are current SST analogues used for PET/CT which bind to SST receptors expressed in NETs. These SST analogues have been used successfully for diagnosis of SST-expressing tumors with a more sensitive detection technique than conventional scintigraphy. However, there is a lack of clinical data on the differentiation between NETs and other malignant tumors or benign pathological conditions. Here, we report a case of Paget's disease mimicking bone metastasis of NET on PET/CT due to increased ^{68}Ga -DOTANOC uptake and review examples of similar cases in the literature.

Keywords: Metastasis; Neuroendocrine tumors; Paget's disease; PET/CT; Somatostatin; ^{68}Ga -DOTANOC

Introduction

Paget's disease (osteitis deformans) is a common, chronic, and metabolic skeletal disorder of unknown etiology characterized by disordered and excessive remodeling of bone due to abnormal osseous resorption and nonuniform mineralization [1–3]. The disease is often asymptomatic and diagnosed incidentally on radiographs obtained for unrelated causes [4]. When symptomatic, skeletal deformities, pathological fractures resulting in pain, and neuromuscular and cardiovascular complications can be seen [5]. Serum alkaline phosphatase level is used for diagnosis, and its elevation is an indicator of the disease activity [1,3]. Conventional radiography is the major and initial imaging technique for diagnosis of Paget's disease. Computed tomography (CT) and magnetic resonance imaging may be used when a fracture or sarcomatous degeneration bone is suspected [3]. Bone scintigraphy with $^{99\text{m}}\text{Tc}$ -labelled bisphosphonate may be more sensitive than conventional radiography in identifying the disease [3]. In up to one-third of patients with Paget's disease, a variable degree of 2-[^{18}F]-fluoro-2-deoxy-D-glucose (FDG) uptake is reported at positron-emission tomography (PET)/CT [6].

Somatostatin (SST) is a neuropeptide present in neurons and endocrine cells which inhibits the secretion of a variety of hormones [7]. It is also present in a wide range of neuroendocrine tumors (NETs) such as carcinoid tumor, pheochromocytoma, renal cell carcinoma, small cell lung cancer, breast cancer, prostate cancer, and malignant

lymphoma [8]. ^{68}Ga -DOTATOC, Gallium-68 (DOTA0-hel-Tyr3) octreotide (^{68}Ga -DOTANOC), and ^{68}Ga -DOTATATE are current SST analogues used for PET/CT which bind to SST receptor subtype 2, predominantly expressed in NETs [8]. However, there is a lack of clinical data on the differentiation between NETs and other malignant tumors or benign pathological conditions [9].

In English literature, four cases have been described with increased uptake of different SST analogues due to Paget's disease. However, to our knowledge, increased ^{68}Ga -DOTANOC uptake in a patient with Paget's disease has not been previously reported. Here, we report a case of Paget's disease mimicking bone metastasis of NET on PET/CT due to increased ^{68}Ga -DOTANOC uptake, which is a somatostatin analogue.

Case Report

A 65-year old male patient who was diagnosed with gastrointestinal stromal tumor at bulbus of duodenum by gastric endoscopy was referred for a ^{68}Ga -DOTANOC PET/CT for investigation of metastasis. PET/CT demonstrated increased tracer uptake in the right ischium, right iliac, and pubic bones (**Figure 1**). He was asymptomatic without any complaint. Subsequent conventional radiography and CT images confirmed the presence of Paget disease in the right hemi-pelvis (**Figure 2**).

Discussion

Since SST has very low metabolic stability, its different gamma- or positron-emitting synthetic analogues have been developed for use in diagnostic applications for SST-expressing tumors [7,10]. These SST analogues have been used successfully for the diagnosis of NETs with a more sensitive detection technique than conventional

* Dokuz Eylul University Faculty of Medicine, Department of Radiology, Izmir, Turkey

† Dokuz Eylul University Faculty of Medicine, Department of Nuclear Medicine, Izmir, Turkey

Corresponding author: Naciye Sinem Gezer (drsinemgezer@gmail.com)

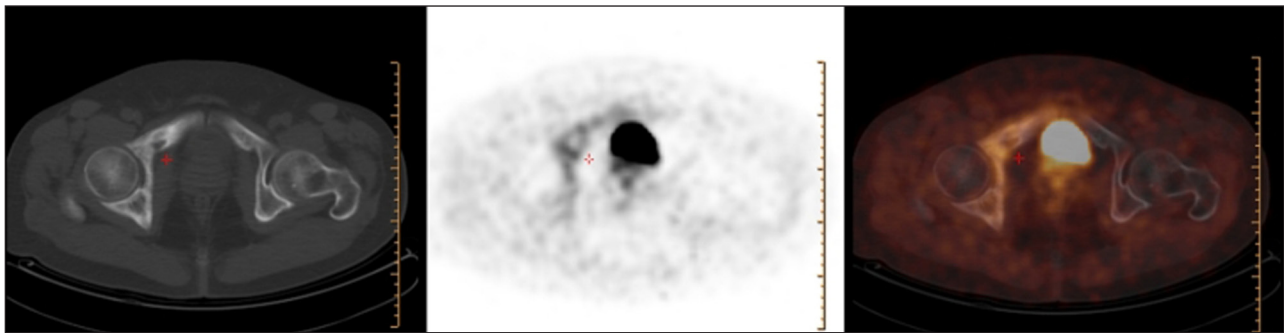


Figure 1: The axial-fused ⁶⁸Ga- DOTANOC PET/CT images show increased uptake in the right pubic bone, superior pubic ramus, and acetabulum.

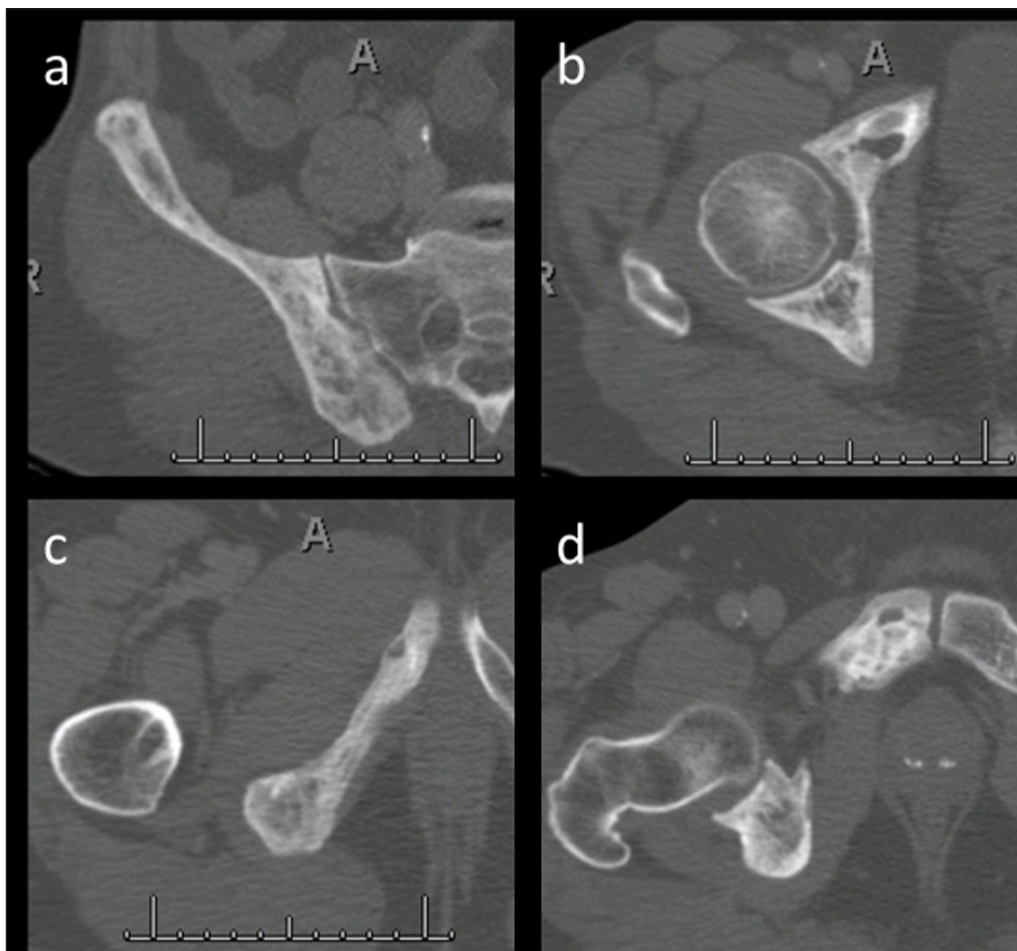


Figure 2: The axial CT images show cortical thickening, trabecular coarsening, and expansion in the right iliac bone (a), acetabulum (b), inferior pubic ramus (c), and pubic bone (d) due to Paget's disease.

scintigraphy. However, it is reported that various subtypes of cellular surface somatostatin receptors are described in osteoblasts and other different cell types, such as leukocytes, fibroblasts, and vessels [11].

In differentiation of NETs from other malignant tumors or benign pathological conditions such as Paget's disease, it should be kept in mind that SST analogues used for PET/CT may lead to false-positive results. In our case, increased ⁶⁸Ga-DOTANOC uptake suspected a metastasis from the NET in the first place. However, radiological and clinical findings led to the diagnosis of Paget's disease. We

suggest that uptake of SST analogues Paget's disease could be associated with markedly increased bone turnover.

In English literature, four cases with increased uptake of different SST analogues due to Paget's disease are described. Kang SK et al. [11] reported two cases of In-111 pentetreotide uptake due to Paget's disease in the humerus and skull. They showed these were the areas of increased osteolytic process. Vandemergel X et al. [12] reported a case of Paget's disease in the femur associated with phosphate diabetes which had positive octreotide scintigraphy. They hypothesized osteoblasts might

manifest somatostatin receptor activity. Minutoli F et al. [13] reported increased ^{177}Lu -DOTATATE uptake due to Paget's disease in the hip bone of a patient who had a surgical resection of a locally invasive NET of ampulla Vater.

Conclusion

The interpretation of skeletal lesions in a patient with NET might be complicated due to the variable uptake of ^{68}Ga -DOTANOC, as in this case. The review of the literature and our case shows Paget's disease should be kept in mind as a benign differential diagnosis when increased uptake is detected on PET/CT with SST analogues.

Competing Interests

The authors declare that they have no competing interests.

References

1. **Antunes, P, Ginj, M, Zhang, H,** et al. Are radiogallium-labelled DOTA-conjugated somatostatin analogues superior to those labelled with other radiometals? *Eur J Nucl Med Mol Imaging.* 2007; 34: 982–93. DOI: <http://dx.doi.org/10.1007/s00259-006-0317-x>. PMID: 17225119.
2. **Bombardieri, E, Maccauro, M, De Deckere, E,** et al. Nuclear medicine imaging of neuroendocrine tumours. *Ann Oncol.* 2001; 12: 51–61. DOI: http://dx.doi.org/10.1093/annonc/12.suppl_2.S51. PMID: 11762353.
3. **Bone, H.** Nonmalignant complications of Paget's disease. *J Bone Miner Res.* 2006; 21: 64–68. DOI: <http://dx.doi.org/10.1359/jbmr.06s212>. PMID: 17229011.
4. **Cortis, K, Micallef, K and Mizzi, A.** Imaging Paget's disease of bone—from head to toe. *Clin Radiol.* 2011; 66: 662–72. DOI: <http://dx.doi.org/10.1016/j.crad.2010.12.016>. PMID: 21524738.
5. **Cook, GJ, Maisey, MN and Fogelman, I.** Fluorine-18-FDG PET in Paget's disease of bone. *J Nucl Med.* 1997; 38: 1495–97. PMID: 9293817.
6. **Kang, S and Mishkin, FS.** Visualization of Paget's disease during somatostatin receptor scintigraphy. *Clin Nucl Med.* 1999; 24: 900–902. DOI: <http://dx.doi.org/10.1097/00003072-199911000-00023>. PMID: 10551483.
7. **Kanis, JA.** Paget's disease of bone (osteitis deformans). In: Goldman, L, Bennett, JC, eds. *Cecil Textbook of Medicine.* 21st ed. Philadelphia, PA: Saunders; 2000: 1413–16.
8. **Kuyumcu, S, Özkan, ZG, Sanli, Y,** et al. Physiological and tumoral uptake of (^{68}Ga) Ga-DOTATATE: standardized uptake values and challenges in interpretation. *Ann Nucl Med.* 2013; 27: 538–45. DOI: <http://dx.doi.org/10.1007/s12149-013-0718-4>. PMID: 23543506.
9. **Minutoli, F, Sindoni, A, Cardile, D,** et al. Increased ^{177}Lu -DOTATATE uptake in Paget disease. *Clin Nucl Med.* 2013; 38: 832–34. DOI: <http://dx.doi.org/10.1097/RLU.0b013e31829f8ea6>. PMID: 23877528.
10. **Paget, J.** On a form of chronic inflammation of bones (osteitis deformans). *Med Chir Trans.* 2013 (1877); 60: 37–64. PMID: 20896492.
11. **Resnick, D.** Paget's disease. In: Resnick, D, ed. *Diagnosis of Bone and Joint Disorders.* 4th ed. Philadelphia, PA: Saunders; 2002: 1947–2000.
12. **Reubi, JC and Waser, B.** Concomitant expression of several peptide receptors in neuroendocrine tumors: molecular basis for in vivo multireceptor targeting. *Eur J Nucl Med Mol Imaging.* 2003; 30: 781. DOI: <http://dx.doi.org/10.1007/s00259-003-1184-3>. PMID: 12707737.
13. **Vandemergel, X, Blocklet, D and Decaux, G.** Positive octreotide scintigraphy and determination of lanreotide activity in Paget's disease of bone associated with phosphate diabetes: a case report. *Ann Endocrinol.* 2004; 65: 201–204. DOI: [http://dx.doi.org/10.1016/S0003-4266\(04\)95671-5](http://dx.doi.org/10.1016/S0003-4266(04)95671-5). PMID: 15277976.

How to cite this article: Gezer, NS, Balcı, A, Özdoğan, Ö and Özaksoy, D 2016 Paget's Disease Mimicking Bone Metastasis in a Patient with Neuroendocrine Tumor on ^{68}Ga -DOTANOC PET/CT. *Journal of the Belgian Society of Radiology*, 100(1): 66, pp. 1–3, DOI: <http://dx.doi.org/10.5334/jbr-btr.903>

Published: 11 July 2016

Copyright: © 2016 The Author(s). This is an open-access article distributed under the terms of the Creative Commons Attribution 4.0 International License (CC-BY 4.0), which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited. See <http://creativecommons.org/licenses/by/4.0/>.

Ju *Journal of the Belgian Society of Radiology* is a peer-reviewed open access journal published by Ubiquity Press.

OPEN ACCESS 