Usefulness of Splenic Scintigraphy in Differentiating Splenosis and Malignancy on Gallium 68 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid-NaI3-octreotide

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Abstract

Somatostatin receptor (SSTR) imaging with gallium 68 (Ga-68) 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-peptide positron emission tomography/computed tomography (PET/CT) has been introduced in clinical routine for the diagnosis and staging of neuroendocrine tumors (NETs) with high SSTR expression. Although it has high sensitivity for NETs, there are some known diagnostic pitfalls one should be aware of. We present a case of suspected NET where Ga-68 DOTA-NaI3-octreotide (NOC) PET/CT showed several abdominal lesions with high SSTR expression suggesting malignancy. On magnetic resonance imaging, the differential diagnosis of the lesions also included splenosis. Subsequent splenic scintigraphy with technetium-99m phytate showed uptake in all suspicious lesions, and biopsy confirmed the diagnosis of splenosis. Splenic scintigraphy with single-photon emission computed tomography/CT can be a helpful noninvasive diagnostic tool when splenosis is suspected on Ga-68 DOTA-peptide PET/CT.

Keywords: Gallium 68 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid-NaI3-octreotide, neuroendocrine tumor, splenic scintigraphy, splenosis

Introduction

Gallium 68 (Ga-68) 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid (DOTA)-peptide positron emission tomography/computed tomography (PET/CT) has improved the diagnostic workup for neuroendocrine tumors (NETs). However, there are limitations because of cellular expression of somatostatin receptors (SSTRs) not related to NETs. One of these pitfalls is the expression of SSTR in normal splenic tissue. This can be a diagnostic problem when ectopic splenic tissue is present (accessory spleens or splenosis) mimicking NET or metastases.

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Case Report

A 42-year-old female patient with a history of pituitary-dependent Cushing's disease was treated neurosurgically more than 20 years ago. Relevant medical history includes splenectomy 8 years ago because of a benign cystic lesion. During a workup for obesity, a low serum potassium level was found. Despite adequate substitution, the hypokalemia persisted. Additional biochemical findings showed increased levels of ectopic production of adrenocorticotropic hormone (ACTH) (165 pg/ml; normal range: 7–63 pg/ml) and cortisol (454 ng/ml at 08:00, normal range 62.4–180 ng/ml) suggesting recurrence of Cushing's

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disease. Magnetic resonance imaging (MRI) suggested the recurrence of a pituitary adenoma. Sinus petrosus sampling (reference standard) was compatible with central Cushing's disease with a basal ratio peripheral/central ACTH > 2 (2:4) and the ratio after stimulation with corticotropin-releasing hormone (CRH) >3 (3:1). However, an endoscopic transnasal transsphenoidal exploration could not confirm the diagnosis. To exclude a NET with ectopic ACTH production or CRH as alternate explanation for the symptoms of the patient, a Ga-68 DOTA-NaI3-octreotide (NOC)-PET/CT was performed. This PET/CT investigation showed a large SSTR expressing abdominal mass in the right fossa and several smaller deposits scattered throughout the abdomen suspect for NET with peritoneal metastases. An additional MRI confirmed the presence of masses, but signal characteristics of the lesions suggested splenunculi due to splenosis rather than malignancy. To further differentiate NET from splenosis, technetium (Tc)-99m phytate single-photon emission computed tomography (SPECT)/CT scan was performed [Figure 1]. All suspicious lesions on Ga-68 DOTA-NOC-PET/CT also demonstrated tracer uptake on Tc-99m phytate scintigraphy making the diagnosis of splenosis more likely [Figure 2]. Finally, laparoscopic exploration with biopsies of several lesions confirmed this diagnosis.

Discussion

Ga-68 DOTA-peptide PET/CT is an important imaging tool for NET.[1] Ga-68 DOTA-peptides bind to the SSTR which are overexpressed not only on NET cells but also on normal and ectopic splenic tissue splenosis or autotransplantation of splenic tissue, is a benign condition caused by previous surgery or, more commonly, after a penetrating or blunt trauma. Abdominal splenosis occurs in up to 65% of splenectomy cases after traumatic spleen rupture.[2] Thoracic splenosis is much less frequent and occurs in about 18% of traumatic splenectomy cases.[3] Splenosis or accessory spleens represent a diagnostic challenge on Ga-68 DOTA-peptide PET/CT. Standard investigations with ultrasound and X-ray have limited value in diagnosing ectopic splenic tissue.[4] CT and especially MRI can help in the differential diagnosis of splenosis[5,6] but are not sufficiently specific to be diagnostic. To date, scintigraphy with Tc-99m-labeled heat-denatured red blood cells (HRBC) is the method of choice for the detection of splenic tissue.[7] Since production of the tracer is labor intensive and not readily available in every nuclear medicine department, Tc-99m sulfur colloid or Tc-99m phytate is often used instead. Compared to Tc-99m sulfur colloid or Tc-99m phytate, the sensitivity of HRBC scintigraphy is higher, which is attributed to a very high sequestration (90%) of HRBCs in splenic tissue.[8,9] In contrast, sulfur colloid and phytate are taken up by the reticuloendothelial system resulting in tracer uptake mainly in the liver (>80%) and only 5%–10% in spleen tissue. Therefore, HRBC scintigraphy is more sensitive in early splenosis, cases where minimal splenic tissue is present, functional hyposplenism or poor splenic uptake, as well as when the liver and spleen overlap, causing poor visualization of splenic tissue.[9] Nevertheless, these shortcomings can be partly overcome with the use of SPECT/CT. This multimodality imaging technique can increase the overall sensitivity of splenic scintigraphy due to better detection of lesions compared to planar imaging,[9] for example, in case of superposition with liver/spleen. It has also improved specificity due to the possibility for anatomical localization and correlation with suspicious lesions seen on Ga-68 DOTA-peptide PET/CT, CT or MRI.[10]

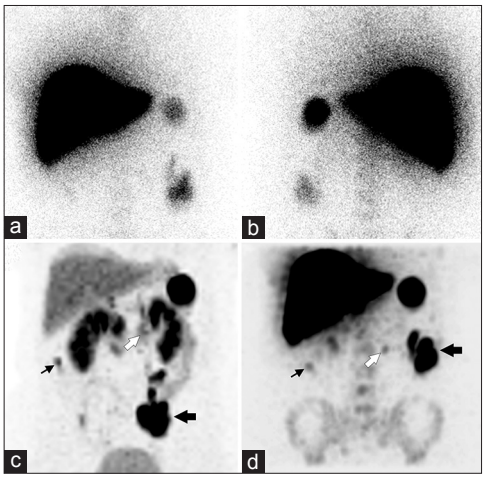

Figure 1: Planar technetium-99m phytate scintigraphy anterior (a) and posterior (b) view. Maximum intensity projection images of gallium 68 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid-NaI3-octreotide-positron emission tomography/computed tomography (c) and technetium-99m phytate single-photon emission computed tomography/computed tomography (b) showing similar lesions. Maximum intensity projection image of single-photon emission computed tomography/computed tomography (d) more lesions compared with planar views (a and b) due to improved sensitivity. Displacement of the biggest lesion in the left flank due to bowel movement

Conclusion

Ga-68 DOTA-peptide PET/CT has improved the diagnosis and staging of NET with high SSTR expression, but splenic nodules can mimic primary or metastatic NETs. Especially, after traumatic spleen rupture, patients have a high incidence of splenosis and splenic scintigraphy can help differentiate splenic tissue from NET in a noninvasive way. The choice of the radiopharmaceutical (99mTc-HRBC, 99mTc sulfur colloid, or 99mTc phytate) is dependent on availability. SPECT/CT has improved the sensitivity as well as the specificity of splenic scintigraphy, and therefore, it is recommended not only for detection but also for better correlation of Ga-68 DOTA-peptide PET/CT.

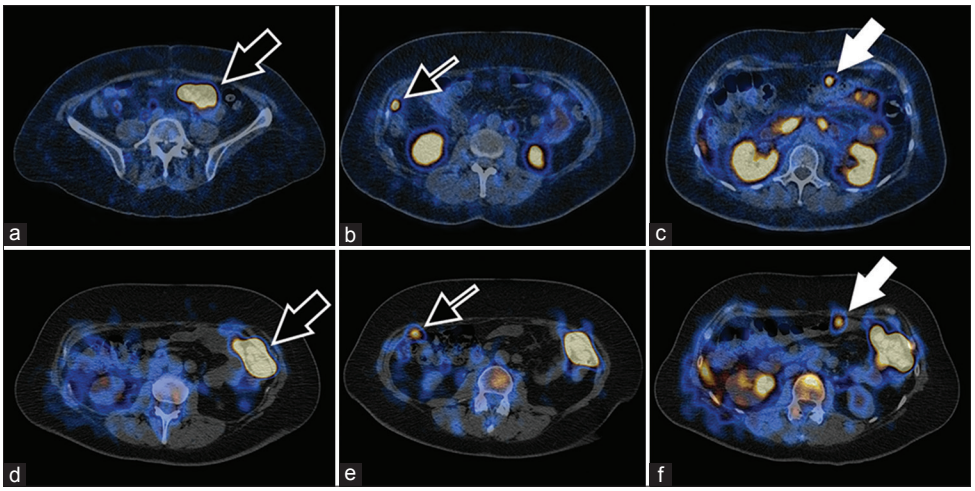

Figure 2: Suspicious lesions on gallium 68 1,4,7,10-tetraazacyclododecane-1,4,7,10-tetraacetic acid- NaI3-octreotide-positron emission tomography/computed tomography (a-c) with respective correlates on technetium-99m phytate single-photon emission computed tomography/computed tomography (d-f) confirming the diagnosis of splenosis

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Conflicts of interest
There are no conflicts of interest.

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