^{68}Ga-DOTATATE PET/CT Can Be an Alternative Imaging Method in Insulinoma Patients

Sadiye Altun Tuzcu[1], Zafer Pekkolay[2], Faruk Kılınç[2], and Alpaslan Kemal Tuzcu[2]

[1]*Department of Nuclear Medicine, Gazi Yasargil Education and Research Hospital, Diyarbakır, Turkey; and* [2]*Department of Endocrinology, Dicle University Faculty of Medicine, Diyarbakır, Turkey*

Insulinomas are the most common cause of hypoglycemia, resulting from endogenous hyperinsulinism. The diagnosis of insulinoma is established by demonstrating inappropriately high serum insulin concentrations during a spontaneous or induced episode of hypoglycemia. Most insulinomas are islet-cell tumors. They are often small (<2 cm), benign, and difficult to localize with current imaging techniques. Insulinomas can be detected using either noninvasive procedures (e.g., transabdominal ultrasonography, spiral CT, MRI, ^{111}In-pentetreotide imaging, and ^{18}F-L-dihydroxyphenylalanine PET) or invasive procedures (e.g., endoscopic ultrasonography) or a selective arterial calcium stimulation test with hepatic venous sampling. **Methods:** We performed ^{68}Ga-DOTATATE PET/CT on 3 patients with insulinoma. **Results:** All patients' insulinomas were shown clearly with ^{68}Ga-DOTATATE PET/CT. **Conclusion:** ^{68}Ga-DOTATATE PET/CT imaging may be a useful noninvasive imaging technique to localize insulinomas preoperatively.

Key Words: ^{68}Ga-DOTATATE PET/CT; insulinoma; neuroendocrine tumor

J Nucl Med Technol 2017; 45:198–200
DOI: 10.2967/jnmt.117.192708

The common clinical manifestations of insulinoma are fasting hypoglycemia and neuroglycopenic symptoms. The diagnosis of insulinoma is established by demonstrating inappropriately high serum insulin concentrations during a spontaneous or induced episode of hypoglycemia (72-h fast). Virtually all insulinomas are islet-cell tumors; after biochemical diagnosis, imaging techniques are used to localize the tumor. Accurate preoperative localization of an insulinoma is desirable because some tumors may not be palpable at the time of surgery (*1*). The noninvasive procedures available include transabdominal ultrasonography, spiral CT, MRI, ^{111}In-pentetreotide imaging, and ^{18}F-L-dihydroxyphenylalanine PET. Positron-emitting radiopharmaceuticals for somatostatin receptor (SSTR) imaging—DOTA analogs, which include ^{68}Ga-DOTATATE, ^{68}Ga-DOTATOC, and ^{68}Ga-DOTANOC—have a high affinity to SSTRs, especially to SSTR2. Recently, several studies have demonstrated that when ^{68}Ga-labeled somatostatin analog PET is combined with CT, sensitivity for detecting neuroendocrine tumors is higher than with SSTR scintigraphy. A metaanalysis study suggested that ^{68}Ga-DOTATATE is most accurate for detecting neuroendocrine tumors (*2*).

Received Dec. 8, 2016; revision accepted May 31, 2017.
For correspondence or reprints contact: Sadiye Altun Tuzcu, Department of Nuclear Medicine, Gazi Yasargil Education and Research Hospital, Diyarbakır 21070, Turkey.
E-mail: sadiyetuzcu@yahoo.com.tr
Published online Aug. 10, 2017.

MATERIALS AND METHODS

We performed ^{68}Ga DOTATATE PET/CT on 3 patients with insulinoma and evaluated its usefulness as a first-choice imaging method. Written informed consent was obtained from all patients. All 3 patients had fasting hypoglycemia and received a biochemical diagnosis of insulinoma when they experienced inappropriately high serum insulin concentrations during a 72-h fast. Imaging techniques were then used to localize the tumor.

The first patient was a 49-y-old woman who had complaints of repeated episodes of hypoglycemia and weight gain. Capillary glucose measured by a health professional was 47 mg/dL, and the patient improved after receiving intravenous glucose. After fasting for 10 h, she became diaphoretic and confused. Serum values at that time were as follows: glucose, 44 mg/dL; insulin, 22.3 microunits/mL; and C-peptide, 3.06 ng/mL. Spiral CT of the abdomen revealed a mass at the body of the pancreas, and ^{68}Ga-DOTATATE PET/CT was performed.

The second patient was a 59-y-old woman who had complaints of headache and sweating. After fasting for 6 h, she became hypoglycemic. Serum values at that time were as follows: glucose, 53 mg/dL; insulin, 37 microunits/mL; and C-peptide, 4.14 ng/mL. Spiral CT of the abdomen showed no visible mass, and ^{68}Ga-DOTATATE PET/CT was performed.

The third patient was a 55-y-old woman who had complaints of headache. After fasting for 12 h, she became hypoglycemic. Serum values at that time were as follows: glucose, 36 mg/dL; insulin,11.43 microunits/mL; and C-peptide, 2.32 ng/mL. Spiral CT of the abdomen showed no visible mass, and ^{68}Ga-DOTATATE PET/CT was performed.

RESULTS

In all 3 patients, insulinoma was clearly shown on ^{68}Ga-DOTATATE PET/CT: at the body of the pancreas in patient 1

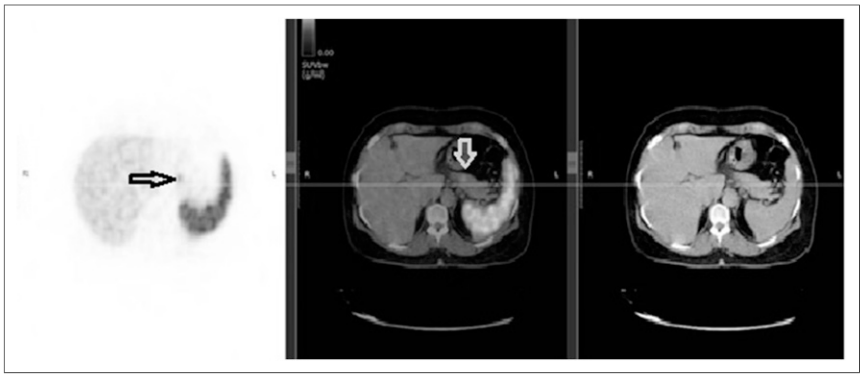

FIGURE 1. ^{68}Ga DOTATATE PET/CT showing lesion at body of pancreas (patient 1). A color version of this figure is available as a supplemental file at http://tech.snmjournals.org.

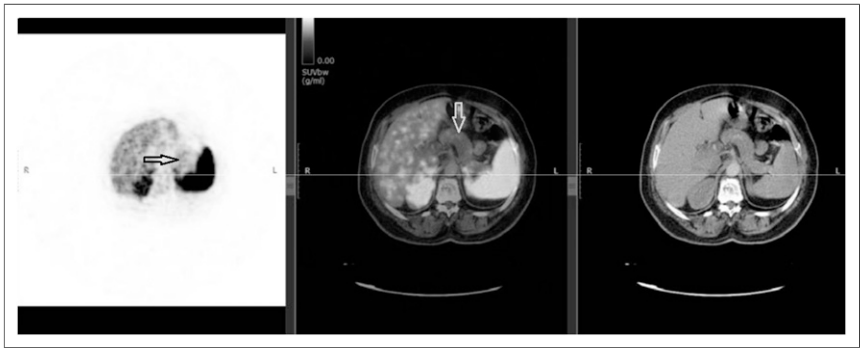

FIGURE 2. ^{68}Ga DOTATATE PET/CT showing lesion at body of pancreas (patient 2). A color version of this figure is available as a supplemental file at http://tech.snmjournals.org.

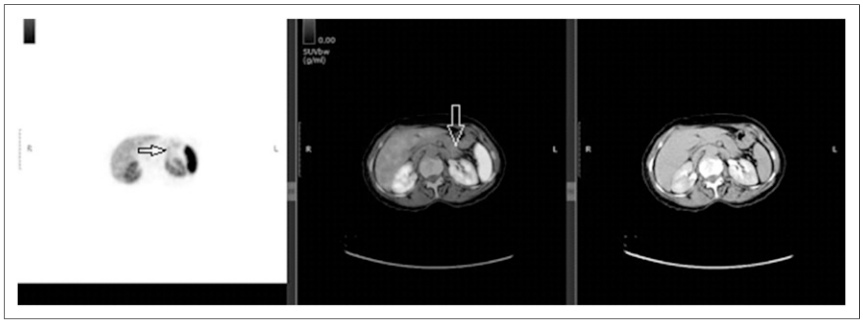

FIGURE 3. ^{68}Ga DOTATATE PET/CT showing lesion at tail of pancreas (patient 3). A color version of this figure is available as a supplemental file at http://tech.snmjournals.org.

(Fig. 1), at the body of the pancreas in patient 2 (Fig. 2), and at the tail of the pancreas in patient 3 (Fig. 3).

In the first patient, the insulinoma was confirmed by intraoperative ultrasonography, enucleated, and confirmed pathologically. In the second, oral diazoxide was started after the ^{68}Ga-DOTATATE PET/CT examination, and surgery was planned. In the third, the insulinoma was confirmed by intraoperative ultrasonography, and distal pancreatectomy was performed; pathologic examination confirmed insulinoma.

DISCUSSION

Accurate preoperative localization of an insulinoma is desirable because some tumors may not be palpable at the time of surgery (*1*). The noninvasive procedures available include spiral CT, MRI, transabdominal ultrasonography, ^{111}In-pentetreotide imaging, and ^{18}F-L-dihydroxyphenylalanine PET. Our patients had biochemically proven insulinomas, but noninvasive procedures were able to show insulinoma in only 1 of the 3 patients.

In patients with an established insulinoma and negative results on noninvasive radiologic localization studies, endoscopic ultrasonography or selective arterial calcium stimulation testing with hepatic venous sampling can be performed to localize the tumor. These procedures are invasive, and skilled personnel are necessary. The choice of procedure depends on which test is available and local level of radiologic skill. In our center, we cannot use these invasive procedures. Because most neuroendocrine tumors express SST receptors, they can be effectively targeted and visualized with radiolabeled SST analogs in vivo. Pentetreotide scintigraphy can be used to localize insulinomas but will miss 40% of them.

Most studies have demonstrated the potential of PET technology using ^{68}Ga-DOTATOC, ^{68}Ga-DOTANOC, and ^{68}Ga-DOTATATE. In particular, PET clearly offers higher resolution and better pharmacokinetics than SST receptor scintigraphy, with promising results for detecting SST receptor–expressing tumors and providing prognostic information (*2*). Recently, PET with the ^{68}Ga-DOTA–conjugated peptides ^{68}Ga-DOTATOC, ^{68}Ga-DOTANOC, and ^{68}Ga-DOTATATE has brought about dramatic improvements in spatial resolution. Use of these agents in specialized centers is increasing. ^{68}Ga-DOTATOC, ^{68}Ga-DOTANOC, and ^{68}Ga-DOTATATE can bind to SST receptor 2, but they have different affinity profiles for other SST receptor subtypes. In particular, ^{68}Ga-DOTANOC also shows a good affinity for SST receptors 3 and 5, ^{68}Ga-DOTATOC also binds to SST receptor 5, and ^{68}Ga-DOTATATE has a predominant affinity for SST receptor 2. A study demonstrated that SSTR2 and SSTR5 are the major SSTRs

expressed in insulinomas (*3*). These findings suggest that ^{68}Ga-DOTATATE has high affinity for SSTR2 and SSTR5 and thus, when positive in a biochemically proven patient, is specific for insulinomas as observed in our patient. It has been previously reported that ^{68}Ga-DOTATATE PET/CT can detect neuroendocrine tumors as small as 6 mm. ^{68}Ga-DOTATATE PET/CT can be helpful to localized small insulinomas.

In the literature, there are two case reports on the use of ^{68}Ga-DOTATATE PET/CT as a successful imaging method to detect insulinomas (*4,5*). In our study, all patients' insulinomas were shown clearly with ^{68}Ga-DOTATATE PET/CT. In a study by Prasad et al., it was observed that tumor localization was compatible with DOTATATE in patients with insulinoma (*6*). A study by Nockel et al. showed localization to be accurate in pathologically proven patients with ^{68}Ga-DOTATATE PET/CT insulinoma (*7*).

CONCLUSION

^{68}Ga-DOTATATE PET/CT can be alternative imaging method for patients with negative results on noninvasive radiologic localization studies, as well as an alternative to invasive methods such as selective arterial calcium stimulation testing. To our knowledge, ours was one of the first attempts to detect insulinoma by the use of ^{68}Ga-DOTATATE PET/CT. Larger studies are needed to confirm our results.

DISCLOSURE

No potential conflict of interest relevant to this article was reported.

REFERENCES

1. Fedorak IJ, Ko TC, Gordon D, Flisak M, Prinz RA. Localization of islet cell tumors of the pancreas: a review of current techniques. *Surgery.* 1993;113:242–249.
2. Yang J, Kan Y, Ge BH, et al. Diagnostic role of gallium-68 DOTATOC and gallium-68 DOTATATE PET in patients with neuroendocrine tumors: a meta-analysis. *Acta Radiol.* 2014;55:389–398.
3. Bertherat J, Tenenbaum F, Perlemoine K, et al. Somatostatin receptors 2 and 5 are the major somatostatin receptors in insulinomas: an in vivo and in vitro study. *J Clin Endocrinol Metab.* 2003;88:5353–5360.
4. Klinaki I, Al-Nahhas A, Soneji N, Win Z. ^{68}Ga DOTATATE PET/CT uptake in spinal lesions and MRI correlation on a patient with neuroendocrine tumor: potential pitfalls. *Clin Nucl Med.* 2013;38:e449–e453.
5. Sadowski SM, Neychev V, Cottle-Delisle C, et al. Detection of insulinoma using ^{68}gallium-DOTATATE PET/CT: a case report. *Gland Surg.* 2014;3:E1–E5.
6. Prasad V, Sainz-Esteban A, Arsenic R, et al. Role of ^{68}Ga somatostatin receptor PET/CT in the detection of endogenous hyperinsulinaemic focus: an explorative study. *Eur J Nucl Med Mol Imaging.* 2016;43:1593–1600.
7. Nockel P, Babic B, Millo C, et al. Localization of insulinoma using ^{68}Ga-DOTATATE PET/CT scan. *J Clin Endocrinol Metab.* 2016;102:195–199.