Baseline Pancreatic Beta Cell Imaging After Pancreatic Transplantation Using Whole-Body ^{68}Ga-DOTA-Exendin-4 PET/CT

A Spectrum of 2 Cases of Diabetes Mellitus

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Abstract: Whole pancreatic transplant and islet cells transplantation are currently available strategies aiming toward diabetes cure. Beta cell specific noninvasive functional imaging using novel PET radiotracers are now available and can be used for beta cell imaging and quantification. Herein we describe a spectrum of 2 cases demonstrating beta cell targeted imaging using ^{68}Ga-DOTA-exendin-4 PET/CT in patients with diabetes after simultaneous pancreas-kidney transplantation.

Key Words: ^{68}Ga-DOTA-exendin-4 PET/CT, GLP-1 receptor, pancreatic transplantation, diabetes mellitus, beta cell imaging

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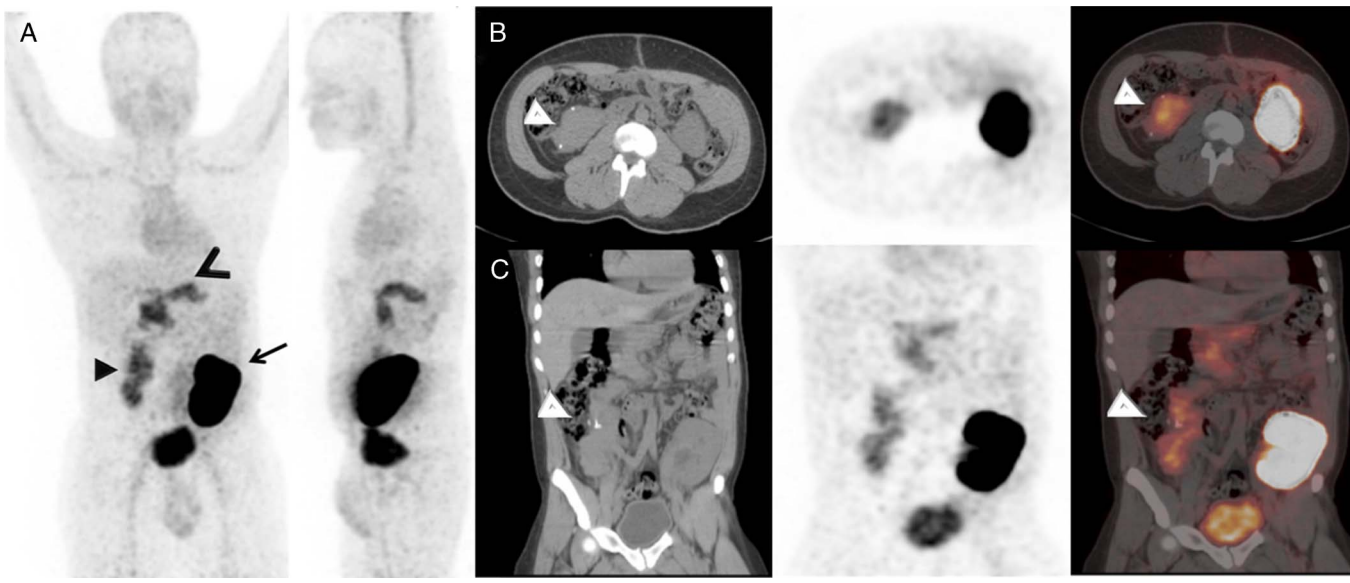

FIGURE 1. A 27-year-old man with progressive type I diabetes mellitus (DM) and associated diabetic nephropathy after simultaneous pancreas-kidney transplantation was referred for baseline beta cell imaging 3 months after surgery. This was part of a small pilot study exploring the use of exendin imaging for follow-up of patients after pancreatic transplantation. Sixty minutes after intravascular administration of 3 mCi of ^{68}Ga-DOTA-Exendin-4, PET/CT was performed. Anterior and lateral MIP (**A**) images demonstrated diffuse heterogeneous glucagon-like peptide-1 receptor (GLP-1R) expression in native pancreas (open arrowhead; SUV_{max}, 7.6) and similar intensity uptake in the vertically oriented transplanted pancreas in right iliac fossa and lumbar region (closed arrowhead; SUV_{max}, 7.9). Intense physiological tracer uptake was noted in transplanted kidney in left iliac fossa (arrow) with no uptake visualized corresponding to the native atrophic kidneys. Faint blood pool tracer activity in mediastinum, liver, spleen, and bowel loops and moderate bladder activity confirmed normal biodistribution of the radiopharmaceutical. Corresponding axial (**B**) and coronal (**C**) CT, PET, and PET/CT images demonstrated a transplanted pancreas (white arrowhead) measuring 9.8 (CC) × 4.7 (AP) × 4.3 (TR) cm with no calcification, fluid collection, necrosis, or peritransplant fat stranding.

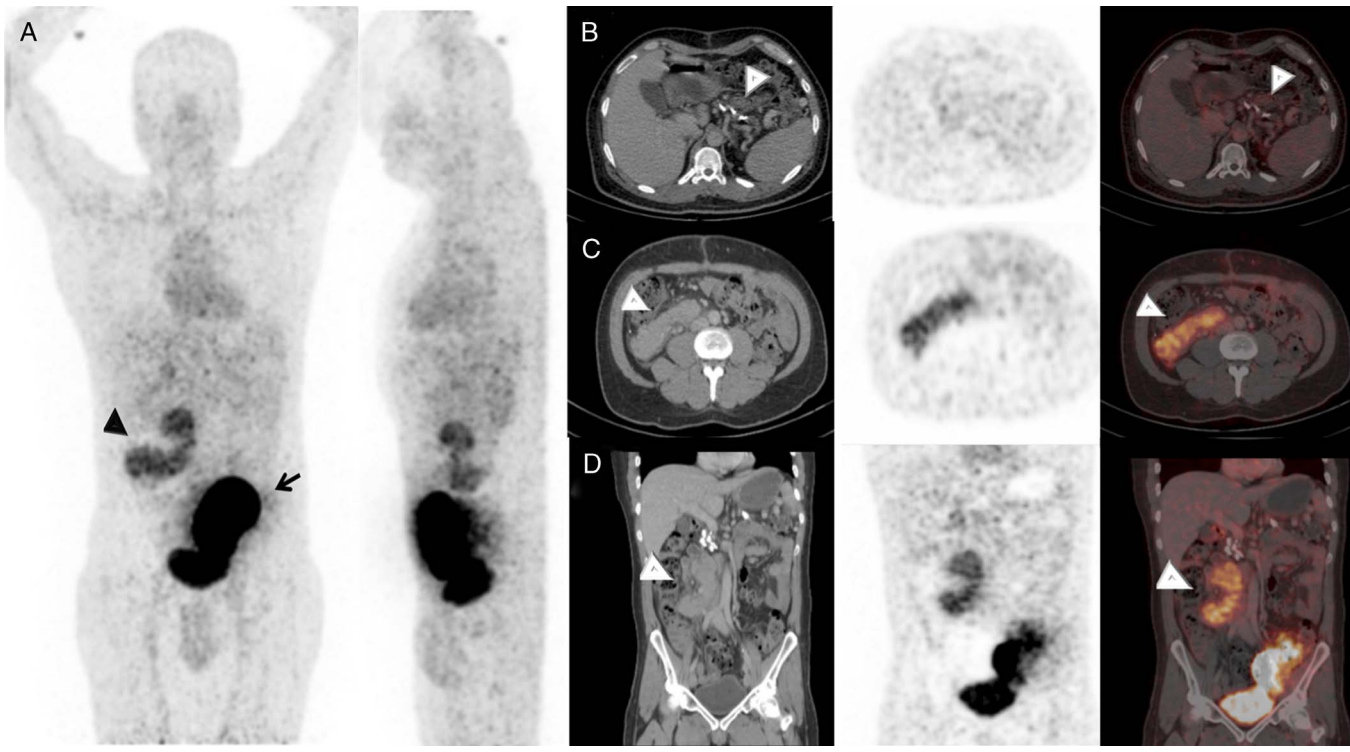

FIGURE 2. A 42-year-old man with rapidly worsening type II DM and associated chronic kidney disease after simultaneous pancreas-kidney transplantation was similarly referred for baseline beta cell imaging 2.7 months after surgery. A PET/CT was performed 60 minutes after intravascular administration of 4.2 mCi of ^{68}Ga-DOTA-exendin-4. Anterior and lateral MIP images (**A**) demonstrated diffuse heterogeneous GLP-1R expression in vertically oriented transplanted pancreas in right abdomen (black arrowhead; SUV_{max}, 4.3) and physiological intense tracer uptake in the transplant kidney in left iliac fossa (arrow) with no significant native renal uptake. Axial (**B** and **C**) and coronal (**D**) CT, PET, and PET/CT images reveal no significant tracer uptake in an atrophic and diffusely calcified native pancreas (white arrowhead, **B**) with tracer-avid transplanted pancreas measuring 10.1 (CC) × 4.9 (AP) × 5.0 (TR) cm (white arrowhead, **C** and **D**). A formal written consent was obtained from both patients regarding participation in this small pilot study. Experimental treatment strategies aiming to cure diabetes include either modification of autoimmune processes or beta cell mass replacement, or both.[1] Whole-pancreatic transplant is considered the current standard of care for diabetes with less invasive alternatives such as islet cells transplantation.[2] Multiple beta-cell–specific PET imaging based biomarkers targeting GLP-1R,[3] vesicular monoamine transporter,[4] sulfonylurea receptor-1,[5] glucose transporter-2, glucokinase (GK),[6] and so on labeled with ^{18}F, ^{11}C, ^{64}Cu, and ^{68}Ga. Although expressed at multiple sites, GLP-1R has significantly high expression on the pancreatic beta cells, suggesting its role as an ideal target for beta cell imaging using dipeptidyl peptidase-IV resistant agonist or antagonist PET tracers. Although clinically used for insulinoma localization[7,8] with recently described potential in temporal assessment of response to nonsurgical ablative therapies,[9] its use as a beta cell surrogate in animal studies has been described. Herein we illustrate a limited spectrum of 2 cases with each of type I and type II DM with one showing uptake in both native and transplanted pancreas and other showing predominant uptake within transplanted pancreas. We hypothesize the future use of beta cell imaging using exendin-4 PET/CT can be used for baseline and follow-up graft imaging and quantification of beta cell mass.