
Early Detection of Post-Transplant Pancreatic Graft Dysfunction with Technetium-99m-HMPAO Scintigraphy

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We present two cases of compromised pancreatic graft perfusion on a routine ^{99m}Tc -HMPAO-scan. The radiopharmaceutical, hexamethylpropyleneamine oxime (HMPAO), labeled with ^{99m}Tc -provided high-quality scintigraphic images of transplanted pancreatic grafts. Findings were compared with subsequently performed x-ray digital subtraction angiographs. Pathological examination of both resected grafts revealed venous thrombosis in one case and graft pancreatitis in the other case of disturbed graft perfusion on a ^{99m}Tc -HMPAO-scan. While ^{99m}Tc -HMPAO scans of pancreatic grafts are not specific for early thrombosis, they seem to be a helpful tool in diagnosing pancreatic dysfunction in general, necessitating further diagnostic steps to elucidate the specific cause.

Key Words: pancreas transplantation; technetium-99m-HMPAO scintigraphy; early graft dysfunction

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In combined pancreas and kidney transplantation, pancreatic graft survival is inferior to renal graft survival (1). This discrepancy is most probably related to the higher incidence of technical failures in pancreas transplantation (1). Complications like thrombosis, pancreatitis and the presence of infected peripancreatic fluid collections hamper the success of pancreatic graft survival and often lead to early pancreatectomy. Clinical surveillance of pancreatic function after transplantation is awkward because most physical and laboratory signs cannot accurately diagnose early pancreatic dysfunction. Therefore, other more reliable diagnostic examinations are mandatory. In most centers pancreas biopsy is considered to have considerable risks for inducing iatrogenic lesions. Radiological and scintigraphic evaluation have become increasingly indispensable. Both diagnostic methods share the advantages of minimal invasiveness and therefore, unlike angiography, can be repeated on a regular basis. Technetium-99m-dieth-

ylenetriaminepentaacetic acid (DTPA) is the most frequently used radiopharmaceutical for scintigraphic imaging of pancreatic grafts (2). Hexamethylpropyleneamine oxime (HMPAO) labeled with ^{99m}Tc also provides high quality scintigraphic images and reliably detects early graft thrombosis (3). Extraction of ^{99m}Tc -HMPAO from blood and its uptake in organs is proportional to regional blood flow. HMPAO is converted into a hydrophilic compound by an intracellular reaction with glutathione. In contrast to ^{99m}Tc -DTPA, minimal tracer washout is observed up to 24 hr after injection (3).

From February 1991 through September 1993, 11 cases of combined pancreas and kidney transplantations were performed in our center. Bladder drainage by duodenocystostomy, as introduced by Sollinger (4), was used in all cases. The pancreas was positioned intraperitoneally with arterial anastomoses of the celiac axis or splenic artery and superior mesenteric artery on the common iliac artery. The portal vein was anastomosed with the external iliac vein and the kidney was placed in a retroperitoneal position on the other side with anastomoses between the renal artery and vein and the external iliac artery and vein.

On the first day after transplantation, a ^{99m}Tc -HMPAO-scan was obtained on the last eight patients to gather data about pancreatic graft perfusion. For scintigraphic imaging, 180 MBq of ^{99m}Tc -HMPAO were intravenously injected as a bolus. For 90 sec thereafter, dynamic 1-sec images were recorded. Three-minute static images were obtained 2, 10 and 20 min postinjection. Count density was greater than 500,000 per minute. A normal ^{99m}Tc -HMPAO scan after combined kidney and pancreas transplantation shows clear visualization of the pancreas and the kidney (Fig. 1). For instances of impaired scintigraphic perfusion of the pancreatic graft, x-ray digital subtracting angiography with intra-arterial contrast was performed to depict iliac arteries and arterial anastomoses.

CASE REPORTS

Patient One

A 42-yr-old male with a 27-yr history of insulin-dependent diabetes mellitus underwent uncomplicated simultaneous pancreas and kidney transplantation. No signs of pancreatic dysfunc-

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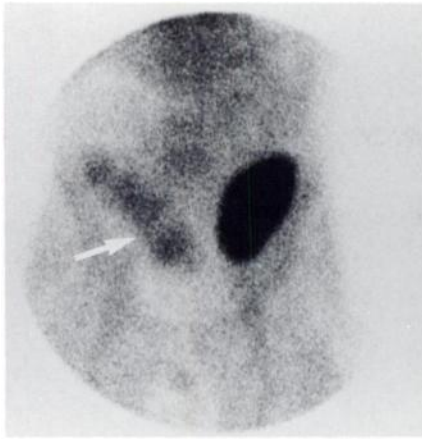


FIGURE 1. Technetium-99m-HMPAO scan of successful simultaneous pancreas and kidney transplantation. The image was recorded 2–5 min postinjection. The pancreas is visualized in the right lower abdomen (white arrow) and the kidney on the contralateral side. No bladder activity can be detected since urine flow has been diverted by prophylactic ureterostomy.

tion were found postoperatively, with blood glucose and urinary pH levels remaining in the normal range. A routine ^{99m}Tc -HMPAO scan revealed a photon-deficient area at the site of the pancreatic allograft, while the cotransplanted kidney on the other side was well visualized (Fig 2A). X-ray subtraction angiography revealed total obstruction of both arterial anastomoses (Fig. 2B). The patient did not complain of abdominal discomfort and blood glucose and urine amylase levels were still in the normal range. A few hours later, the patient developed severe hypotension (80/40 mmHg) and complained of lower back pain. Blood hemoglobin levels dropped rapidly from 6.6 to 4.3 mmole/liter despite infusion of 2 units of packed cells, and blood glucose levels rose above 10 mmole/liter. Relaparotomy revealed intra-abdominal blood collection. Macroscopically, the pancreas were edematous with necrotic changes of the largest part of the gland. After pancreatectomy, the patient remained hemodynamically stable. The excised gland showed necrotising pancreatitis with extensive fat necrosis and thrombosis of the splenic vein. Both the splenic artery and the superior mesenteric artery proved to be patent on pathological examination. Absent arterial flow on angiographs was probably caused by a retrograde high-pressure gradient of the concomitant venous thrombosis.

Patient Two

A 57-yr-old female with a history of more than 25-yr of diabetes mellitus underwent simultaneous pancreas and kidney transplantation. Postoperative blood glucose levels were normal, but urine amylase concentration remained consistently under 1000 U/liter, suggesting exocrine dysfunction. Urine pH was above 7, suggesting adequate bicarbonate secretion by the transplanted pancreatic graft.

A routine ^{99m}Tc -HMPAO scan on the first postoperative day showed normal delineation of the kidney transplant. There was no visualization of the pancreas (Fig. 3A). X-ray digital subtraction angiography revealed adequate perfusion of the pancreas (Fig. 3B). No other interventions were performed at the time. On the second postoperative day, diuresis became marginal and the patient developed severe hypoxemia (7.3 kPa), necessitating hemodialysis and positive end expiratory pressure ventilation. On ultrasonography (US), a large intra-abdominal fluid collection was detected. One week after transplantation, relaparotomy was performed to drain the fluid collection. Macroscopically, the pancreas had an edematous aspect with the presence of peripancreatic fat necrosis, highly suggestive of pancreatitis. After abdominal lavage, the pancreas was left in situ since the endocrine portion was still functioning satisfactorily. The patient died the next day after developing generalized sepsis with severe electrocardiographic changes. At autopsy, a partially necrotic pancreas with signs of acute pancreatitis and fat necrosis in the omentum and mesentery was seen. None of the arterial or venous anastomoses of the transplanted pancreas showed signs of occlusion. A bilateral purulent pneumonia with positive cultures of *Escherichia coli* seemed to be the direct cause of death.

DISCUSSION

These two cases illustrate that ^{99m}Tc -HMPAO scintigraphy is a sensitive method for detecting early pancreatic dysfunction. In our preliminary experience with ^{99m}Tc -HMPAO scintigraphy, specificity for a particular cause of pancreatic dysfunction may not be present.

In a study by Snider et al., scintigraphy with ^{99m}Tc -DTPA appeared to be reliable for screening suspected graft thrombosis in pancreas transplantation (5). In 78 scintigraphic flow studies, sensitivity was calculated to be 93% in the evaluation of graft thrombosis. However 36% of the cases of compromised perfusion were nonspecific, caused

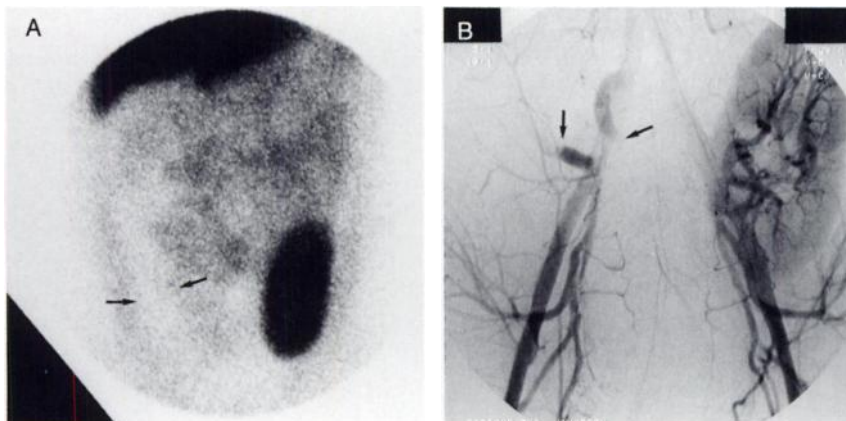
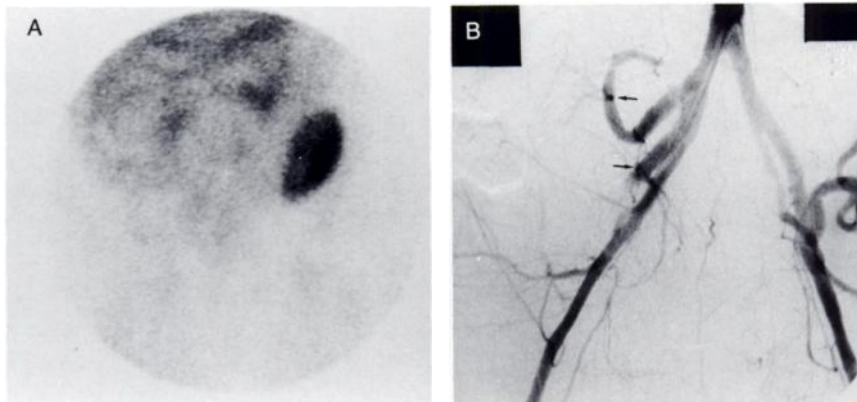


FIGURE 2. (A) Technetium-99m-HMPAO scan recorded 2–5 min postinjection after simultaneous transplantation. A photon-deficient area in the right lower abdomen depicts absence of perfusion due to thrombosis of the pancreatic graft (small arrows). The contralateral kidney is well perfused. The activity immediately adjacent to the photon-deficient area most probably represents ^{99m}Tc in the intestinal structures. (B) X-ray digital subtracting angiography of iliac arteries. Total obstruction is seen at the proximal anastomosis and subtotal obstruction is seen at the peripheral arterial anastomosis due to thrombosis (arrows). Renal perfusion is not compromised.

FIGURE 3. (A) Technetium-99m-HMPAO scan recorded 2–5 min postinjection after simultaneous transplantation. There is no clear visualization of the pancreas due to postoperative graft pancreatitis. The contralateral kidney is well perfused. (B) X-ray digital subtracting angiography of the iliac arteries. The splenic artery and superior mesenteric artery are situated on one arterial patch. The pancreas is well perfused by smaller branches in a patient with postoperative graft pancreatitis (small arrows). The renal arterial perfusion is not compromised.



by either infection or rejection. Ultrasonography of pancreatic transplants is, however, an adequate diagnostic method for discovering early graft abnormalities. Changes in graft size, graft texture and the presence of peripancreatic fluid collections may be accompanying features of an ongoing graft thrombosis (5,6). The presence of graft inhomogeneity and/or peripancreatic fluid in the evaluation of graft thrombosis correlated with a sensitivity of 100% and a specificity of only 30% in 27 cases of US (5). Computed tomography (CT) is reportedly helpful in detecting post-transplantation fluid collections, but not in assessing pathological parenchymal changes (6). In the same comparative study, the use of CT in 40 abdominal scans showed a sensitivity of 74% and a specificity of 33% in the evaluation of thrombosis in the presence of perigraft fluid collections (5).

Routine scintigraphic scans on the first post-transplant day at our center were aimed at the exclusion of the presence of pancreatic vascular thrombosis. According to our data and that of others (5,7,8) scintigraphy is a sensitive, albeit nonspecific, indicator of normal transplant function. An abnormal scintigram did not differentiate vascular thrombosis from graft pancreatitis in our series. Patel et al. advocate the use of US in cases of abnormal scintigrams in order to differentiate cases of pancreatitis from other causes of poor perfusion (7). The additional value of color Doppler in analyzing the vascular patency seems promising in the discrimination of vascular causes from parenchymal abnormalities in cases of disturbed pancreatic perfusion (5,8). In a preliminary series of eight color Doppler examinations, five true-positive and three true-negative results were recorded in the evaluation of graft thrombosis (5).

Thus, ^{99m}Tc -HMPAO scintigraphy with subsequent

color Doppler examination is probably a reliable method to survey transplant function in the early postoperative period. As long as our experience with color Doppler examinations of pancreatic grafts is fragmentary, we will rely on invasive angiography to exclude vascular thrombosis in cases of disturbed perfusion, which carries the risk of iatrogenic lesions and nephrotoxic effects by the injected contrast agent. ^{99m}Tc -HMPAO scintigraphy also seems to be a reliable method to assess vascular integrity of pancreatic grafts in the early postoperative period. HMPAO has the theoretical advantage of a better intragraft cumulation than DTPA. This allows the processing of static images in which extraction of the radiopharmaceutical is proportional to graft perfusion. A comparative study between these different radiopharmaceuticals should be the subject of future studies on pancreatic allograft imaging.

REFERENCES

1. Sutherland DER. Report from the International Pancreas Transplant Registry (suppl 1). *Diabetologia* 1991;34:S28–S39.
2. Shulkin BL, Dafoe DC, Wahl RL. Simultaneous pancreatic-renal transplant scintigraphy. *AJR* 1986;147:1193–1196.
3. Booster MH, Peltenburg HG, van Kroonenburg MHPG, et al. Perfusion imaging of pancreas allografts using ^{99m}Tc -hexamethylpropylene amine oxime (HMPAO) *Transplant Int* 1992;5(Suppl 1):S265–S267.
4. Sollinger HW, Glass NR, Belzer FO. Clinical experience with pancreaticocystostomy for exocrine pancreatic drainage in pancreas transplantation. *Diabetic Nephropathy* 1983;2:23–25.
5. Snider JF, Hunter DW, Kuni CC, Castaneda-Zuniga WR, Letourneau JG. Pancreatic transplantation: radiologic evaluation of vascular complications. *Radiology* 1991;178:749–753.
6. Yuh WTC, Wiese JA, Abu-Yousef MM, et al. Pancreatic transplant imaging. *Radiology* 1988;167:679–683.
7. Patel B, Markivee CR, Mahanta B, Vas W, George E, Garvin P. Pancreatic transplantation: scintigraphy, US, and CT. *Radiology* 1988;167:685–687.
8. Low RA, Kuni CC, Letourneau JG. Pancreas transplant imaging: an overview. *AJR* 1990;155:13–21.