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Clinical Experience with Pancreas Graft Rescue From Severe Thrombus After Simultaneous Pancreas-Kidney Transplantation by Early Detection with Doppler Ultrasound: A Case Report

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Patient: Female, 41
Final Diagnosis: Graft thrombosis
Symptoms: None
Medication: —
Clinical Procedure: Doppler ultrasound
Specialty: Transplantology

Objective: Unusual clinical course

Background: Graft thrombosis is the main cause of early graft loss after transplantation. In Japan, pancreases available for transplantation are frequently from marginal donors due to diverse backgrounds in the population. However, marginal tissues increase the risk of early thrombosis in the graft.

Case Report: Here, we describe a 41-year-old woman with type 1 diabetes mellitus who underwent a simultaneous pancreas-kidney transplantation. The pancreas was retrieved from a 34-year-old man who had experienced severe hemodynamic instability. The pancreaticoduodenal graft was implanted in the recipient iliac fossa with enteric drainage. Although the patient had not shown any physical signs or alterations in substances that might indicate functional loss of the pancreas graft, a Doppler ultrasound analysis detected a major thrombus in the pancreas graft on day 7 after surgery. A thrombectomy was performed with a radiological emergent intervention. After percutaneous direct thrombolysis, the patient received adjuvant thrombolytic therapy. Thereafter, the postoperative course was uneventful and the pancreas graft remained functional.

Conclusions: Early detection and treatment of thromboses are required to avoid graft failure and graft pancreatectomy. This case study demonstrates that early detection of severe thrombus with Doppler ultrasound in a grafted pancreas did not increase the risk of graft failure.

MeSH Keywords: Graft Survival • Pancreas Transplantation • Radiology, Interventional • Thrombosis • Ultrasonography, Doppler, Color

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/899673

Background

Graft thrombosis is the most common cause of early graft loss after pancreas transplantation [1,2]. Many studies have described the causes, prevention, and treatment of vascular thrombosis in pancreas transplantation [1–5]. The development of graft thrombosis depends on various factors, including donor factors, recipient factors, and factors associated with perioperative situations [6]. Due to the chronic shortage of donors in Japan, pancreas transplantations have involved mostly marginal donors (64.2%), which is the most common risk factor for early graft thrombosis [4]. Moreover, an early thrombosis sometimes appears unexpectedly, and it causes severe problems, including graft loss. Therefore, we need an effective early detection tool to alert us of this complication in time to apply interventions and avoid graft loss due to early thrombosis.

Here, we describe the case of a patient with a pancreas graft that was successfully rescued from severe thrombosis with interventional radiology, following early detection.

Case Report

A 41-year-old woman with a BMI of 21.8 kg/m^2 and a 28-year history of type 1 diabetes mellitus underwent a simultaneous pancreas-kidney transplantation with organs from a cadaveric donor. The patient received hemodialysis 3 times per week for 1 year. The donor was a 34-year-old man, with a BMI of 20.2 kg/m^2, who died of cerebral hemorrhage. Despite the donor's young age, he was a marginal donor because he had received 2 types of vasopressors (dopamine and noradrenalin) and he had experienced cardiopulmonary arrest for 57 min. The cold ischemic times were 14 h 22 min and 9 h 17 min for the pancreas and kidney, respectively.

The transplantation was achieved by first transplanting the kidney graft in the recipient's left retroperitoneal space; subsequently, the pancreaticoduodenal graft was implanted in the right iliac fossa. A Carrel patch was anastomosed to the recipient's right common iliac artery. The graft gastroduodenal artery was anastomosed to the common hepatic artery with an arterial I-graft derived from the donor iliac artery. The donor portal vein (PV) was anastomosed to the recipient's right common iliac vein without a venous extension. After reperfusion of the pancreatic graft, the graft duodenum was anastomosed to the recipient's jejunum for enteric drainage of graft pancreatic exocrine output and the spleen in the graft was resected. No intraoperative complications were encountered.

The patient's initial course was uneventful. Normal pancreatic and renal functions began immediately and no recombinant insulin or dialysis was required. To prevent early thrombosis, the patient was administered a prophylactic anticoagulant medication (heparin, 5000 units per day), beginning on the day after surgery. We monitored blood flow every 8 h with Doppler ultrasound. From the Doppler data, we calculated the resistive index (RI) by evaluating the difference between the peaks of the systolic (S) and diastolic (D) pulse waves and dividing by the S, as follows: RI=(S-D)/S [7–9]. Thus, the RI is the pulsatile blood flow, which reflects the resistance to blood flow; it has been described as a tool for the early detection of thrombosis [7–9].

At 7 days after transplantation, the Doppler ultrasound analysis detected a severe thrombus in the splenic vein (SV) of the graft with a high RI score (1.08). However, the patient did not exhibit any signs to indicate the initiation of graft failure (e.g., physical pain in a corresponding abdominal region, a low C-peptide value, a high serum amylase value, or a high blood glucose level) (Figures 1, 2). We immediately performed contrast-enhanced computed tomography and detected a thrombus in the SV, the splenic artery (SA), and the superior mesenteric artery (SMA) (Figure 3). We attempted interventional therapy because the thrombi were progressing, which indicated a high possibility that we could preserve the graft with immediate thrombolysis.

Arterial access was achieved via the left femoral artery. Selective angiography via the Carrel patch revealed that severe thrombi had interrupted blood flow in the SA and SMA (Figure 4). A percutaneous balloon thrombectomy and direct thrombolysis with urokinase (60,000 units in each artery) succeeded dramatically. These interventions eliminated the thrombi, and resulted in reperfusion of the graft. Subsequently, a percutaneous balloon thrombectomy was performed in the graft vein to restore flow as much as possible. Following these interventions, the patient received adjuvant thrombolytic therapy with a continuous urokinase infusion (240,000 units per day) via the graft's SA, concurrent with systemic heparinization (12,000 units per day) for 4 days. The latter treatments were implemented to eliminate the remnant thrombi in the graft veins, and to prevent a relapse of thrombosis. Four days after radiological thrombectomy, a second angiographic analysis did not detect any thrombi in graft vessels; hence, the preventive thrombolysis infusion was exchanged for an anticoagulant treatment of oral warfarin medication for 4 months. Thereafter, the clinical course of the patient was uneventful, and the pancreas graft is currently functioning well. At discharge, a contrast-enhanced computed tomography scan revealed that the pancreas graft was well enhanced and showed no thrombosis. At 11 months after transplantation, the patient exhibited a fasting blood glucose level of 91 mg/dL, a HbA1c of 5.7%, and a serum C-peptide level of 3.7 ng/mL.

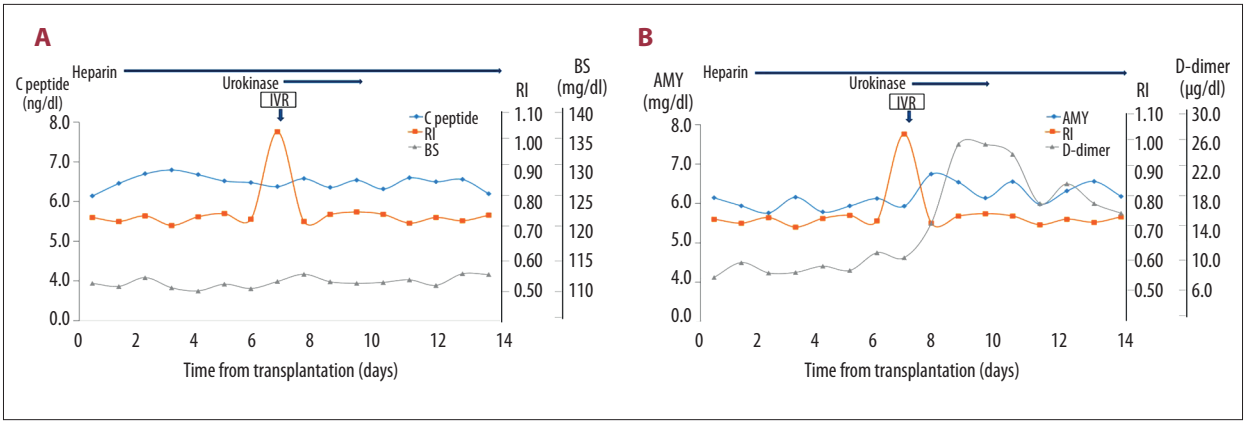

Figure 1. Early thrombosis was detected by the resistive index (RI) before other risk indicators changed. Data from blood and Doppler analyses show changes over time in serum risk factors and resistive index (RI) measured before and after interventional radiology (IVR). (**A**) Transitions in the calculated RI, C-peptide, and blood glucose levels. C-peptide is a short 31-amino-acid polypeptide that connect the A-chain of insulin to its B-chain in the proinsulin molecule; its level in the recipient's serum indicates the level of insulin produced by the pancreas. BS – blood glucose level. RI increased dramatically at the time the severe thrombus developed, but C-peptide and blood glucose levels did not change. Only RI detected the risk of graft loss due to severe thrombus. (**B**) Transitions in the RI, serum amylase (AMY), and D-dimer (a fibrin degradation product). Only RI detected the risk of graft loss due to severe thrombus.

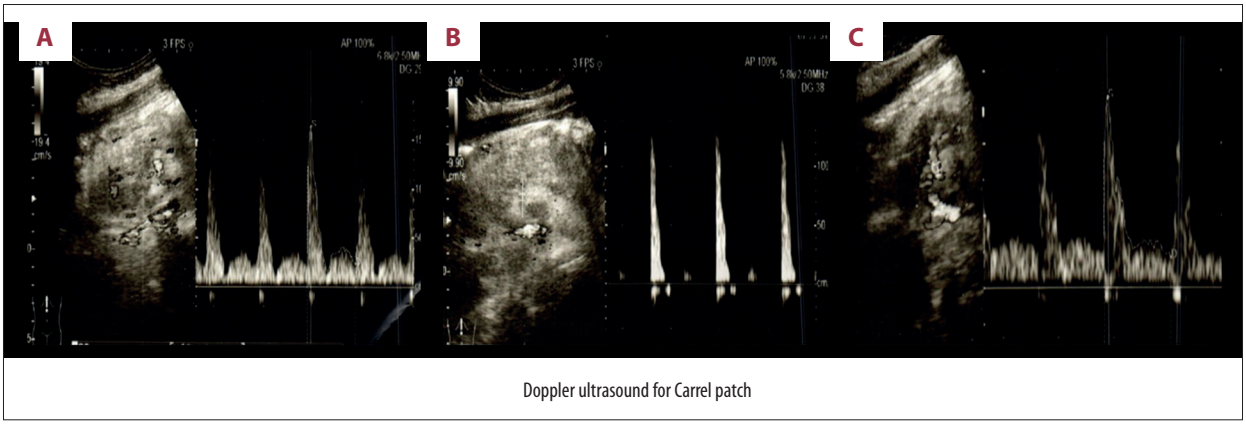

Figure 2. Doppler ultrasound images acquired at the Carrel patch in the pancreas graft before, during, and after thrombosis. The wave pattern on the right of each panel indicates the arterial blood flow measured (**A**) before thrombosis detection and at 6 days after the simultaneous pancreas-kidney transplantation; (**B**) at the time the thrombus was detected; and (**C**) at a time after complete thrombolysis. Panel B shows how the wave shape changed; the gentle slope with 2 phases changed into a single spike wave.

Discussion

The latest reports in the United States and Europe on outcomes of pancreas transplants have shown a 5–10% graft thrombosis rate [6–12]. Despite remarkable improvements in operative techniques, immunosuppression, and postoperative management, the International Pancreas Transplant Registry has reported that vascular thrombosis is responsible for 2.7–6.8% of graft losses [10]. In pancreas grafts, vascular thrombosis is caused by various factors, including the surgical technique (e.g., overextension or flexion of the graft PV), ischemia-reperfusion injury, pancreatitis, a hypercoagulable state (e.g., hyperglycemia, hyperlipidemia, or perioperative dehydration), arteriosclerotic changes at the anastomotic site with low recipient blood pressure, and marginal donor tissues [2–4]. In this case study, a marginal donor was the main risk factor for thrombosis, a relatively common scenario in Japan. The recipient had received anticoagulant therapy on the day after transplantation to prevent early thrombosis. Although we regularly control patient recovery with postoperative water balance and preventive heparin treatment, pancreas grafts sometimes develop thrombosis from an uncertain origin.

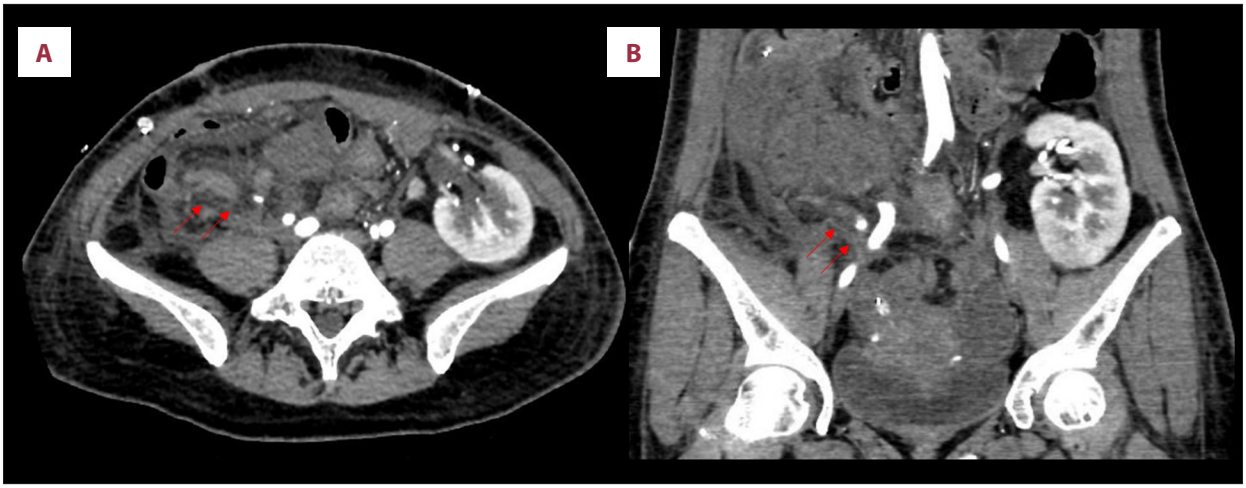

Figure 3. Computed tomography angiography acquired on posttransplant day 7 shows thrombosis. The splenic artery (red arrows) of the grafted pancreas showed a contrast defect along the total length. (**A**) Coronal view; (**B**) sagittal view.

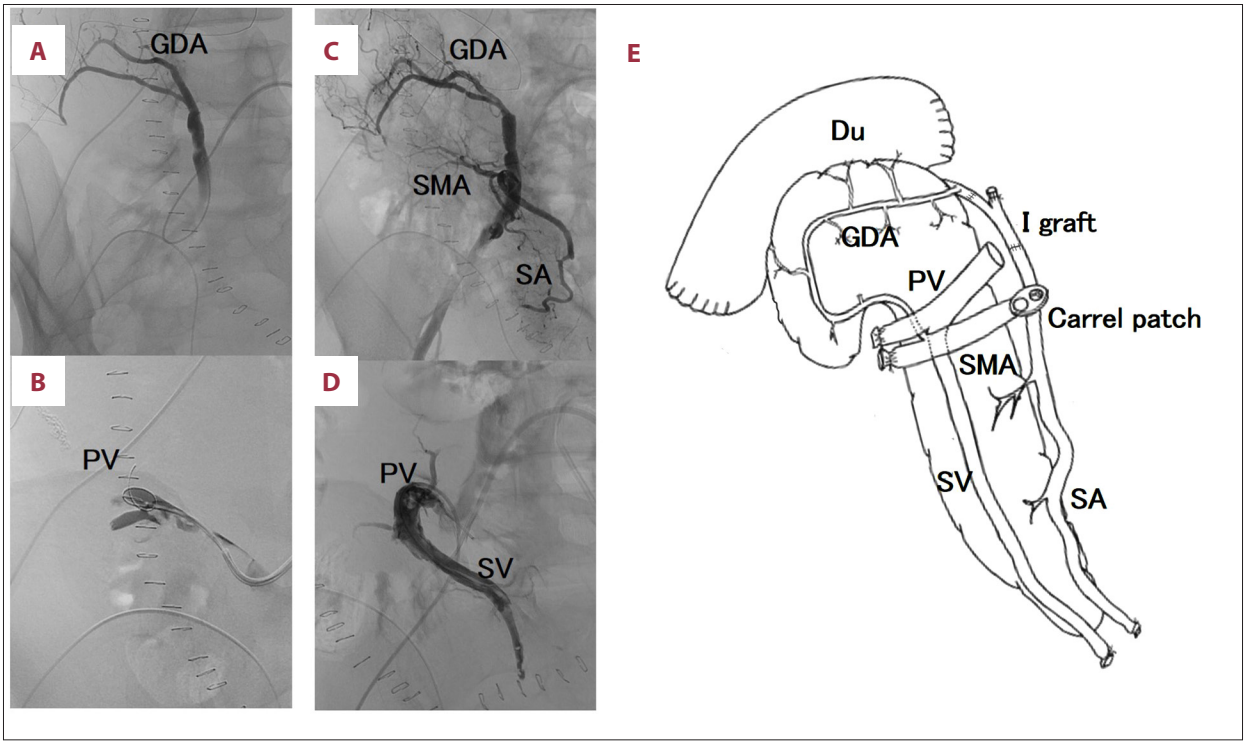

Figure 4. Selective arteriographic and venographic images of the pancreas graft via the Carrel patch and the portal vein (PV). (**A**) Selective arteriography via the Carrel patch before thrombolysis or thrombectomy. Blood flow was clearly observed in the gastroduodenal artery (GDA), but the flow was interrupted in the splenic artery (SA) and superior mesenteric artery (SMA) of the graft due to thrombosis. Pancreatic graft perfusion was maintained via the I-graft anastomosis. (**B**) Selective venography via the PV before thrombectomy. Blood flow was completely blocked in the splenic vein (SV). (**C**) Selective arteriography via the Carrel patch after the thrombus was resolved. (**D**) Selective venography via the PV after thrombectomy. (**E**) Diagram of the pancreas graft indicates the general patterns of the vessel courses. Severe thrombus in the pancreas graft was successfully eliminated with an interventional approach.

In Japan, from 1997, when the organ transplant law was established, through the end of 2015, a total of 246 pancreatic transplantations were performed with organs from deceased donors. An investigation of all 246 cases revealed that pancreas transplantations in Japan were mostly derived from marginal donors (63.8%) [4]. At a local Japanese meeting, graft thromboses were reported to occur in 5–13% of cases, and a total of 42 cases resulted in graft loss. The major reasons for graft

loss were rejection (21 cases, 50%) and graft thrombosis (11 cases, 26%). Thus, in Japan, approximately one-quarter of graft losses were due to thrombosis, but this rate was comparable to that in the United States and Europe (27%) [5]. The 5-year survival rates of pancreas transplants were not significantly different from those derived from a marginal donor (70.7%) and those from a non-marginal donor (81.1%). Although the thrombosis incidence is high in Japan, due to the unpredictable occurrence of thrombosis, the graft survival rate was not impaired compared to that of Western countries, where marginal donors are not typically used. Thrombosis is associated with a high risk of graft removal; therefore, we remain alert with careful monitoring for the detection of graft thrombosis. This regular monitoring may explain why the graft survival rate in Japan was comparable to that of other countries, despite the high number of grafts from marginal donors in Japan.

The results of the present case study suggest that routine, strict monitoring of patients with pancreas transplantations for early thrombosis detection requires frequent checks of blood flow. We demonstrated that monitoring with color Doppler ultrasound is a convenient, non-invasive, effective tool. In previous reports, elevated pancreatic enzymes and blood glucose levels were observed when a complete thrombus blocked the blood flow; however, that method was not effective for the early detection of thrombus formations [6,7]. Previous reports have also indicated that color and pulsed Doppler blood flow monitoring was useful for detecting the early phase of venous thrombus formations [6–9], and that an increase in the RI could be detected prior to a venous thrombus formation [7]. The earlier report showed that the early phase of thrombosis could be detected in 6% of 175 cases. Therefore, we employed that monitoring method as one of several routine monitoring systems, and we typically checked the graft blood flow every 8 h. In the present case study, this monitoring method successfully detected the early phase of thrombus formation, based on an increase in the RI.

Several treatment options are available for graft thromboses. The surgical approach is a surgical thrombectomy [13–18]; non-surgical interventional approaches include pharmacomechanical thrombolysis, transarterial thrombolysis, or catheter-directed thrombolysis combined with balloon thrombectomy [19–21]. Recently, the non-surgical interventional approaches have been considered preferable to the surgical approach. A few previous reports have shown that non-surgical interventions could salvage a graft from thrombosis when the thrombus was detected at an early phase [18–22]. In the present case study, the fact that we detected the thrombosis at an early phase was the dominant reason that the graft was successfully salvaged from severe thrombosis.

Conclusions

We described a rare case in which frequent ultrasound monitoring was able to detect severe thrombosis in a pancreatic graft, even when other findings did not indicate a risk of graft loss.

Abbreviations

SA – splenic artery; **SMA** – superior mesenteric artery; **SV** – splenic vein; **PV** – portal vein; **GDA** – gastroduodenal artery; **SPK** – simultaneous pancreas-kidney transplantation; **RI** – Resistive Index; **IVR** – interventional radiology

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