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CASE REPORT

False aneurysm of a hepatic artery branch complicating intrahepatic islet transplantation

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Summary

Islet transplantation, an innovative treatment strategy for type 1 diabetes mellitus, is a relatively safe procedure, with less morbidity than pancreas transplantation. Vascular injuries have not been reported to date. We report a percutaneous transhepatic intraportal islet transplant infusion that was followed by bleeding from a false aneurysm of an intrahepatic branch of the hepatic artery. The bleeding was controlled by selective embolization. Despite the complication and its treatment, the patient gained insulin independence, which was sustained for 285 days. She is currently on a small dose of insulin with good glycemic control.

Introduction

Pancreatic islet transplantation is an innovative treatment strategy for patients with type 1 diabetes mellitus. In contrast with whole organ pancreatic transplantation, which has associated morbidity and also mortality [1], pancreatic islet transplantation is performed as an interventional radiology procedure and is better tolerated [2]. Complications of the procedure include bleeding and portal vein thrombosis, but to date, there are no reports of arterial injuries associated with the islet infusion. We report the formation of a false aneurysm of a hepatic artery branch following an intrahepatic islet infusion.

Case presentation

A 55-year-old woman with type 1 diabetes mellitus of more than 40 years' duration, complicated by hypoglycemia unawareness, was evaluated and found suitable for deceased-donor, pancreatic islet-only transplantation using a modified Edmonton protocol. The patient underwent a first islet infusion of 4410 islet equivalents (IEq) per kg of body weight. Following this infusion, the patient did not achieve insulin independence; therefore, she was selected for a second islet infusion. Doppler ultrasonography (DUS) performed as part of the investigational protocol the day after the first infusion and 3 weeks and 3 months later did not show any intrahepatic vascular abnormality.

The patient underwent a second islet infusion 143 days after the first infusion using the same approach, i.e. by percutaneous transhepatic cannulation of a portal vein branch using a 5-French catheter (Seldinger technique). Multiple liver punctures using a 22-gauge Chiba needle were necessary to access the portal vein branch. A total of 7686 IEq/kg of islets were infused with the second procedure. Upon completion of the infusion, the catheter was withdrawn, its position was confirmed to be within the

liver tissue tract and the tract was obliterated with a Gelfoam plug by injection. As part of the protocol with both infusions, the islet aliquot contained 70 units of heparin per kg of recipient body weight and the patient was also started on enoxaparin 20 mg twice a day 12 h after the procedure.

The course after the procedure was complicated by intra-abdominal bleeding, which was diagnosed by enlarged abdominal girth, a drop in hemoglobin (Hb) from 12.6 to 8.8 g/dl in the first 24 h, and the finding of intra-abdominal fluid by DUS. DUS did not show any vascular lesions. The enoxaparin was discontinued (two doses of 20 mg administered in total). The patient received 2 units of packed red blood cells and the Hb remained stable above 10 g/dl for 48 h. Therefore, we considered that the bleeding had stopped, and the patient was discharged from the hospital 3 days after the procedure.

On the fifth day, she returned with weakness and enlarged abdominal girth. She was stable hemodynamically, and her Hb was 7.6 g/dl. A computed tomography (CT) scan of the abdomen was obtained, which showed active bleeding on the surface of the right lobe of the liver (Fig. 1). The patient received 4 units of packed red blood cells. A transfemoral hepatic arteriogram showed active bleeding from a false aneurysm of a hepatic artery branch (Fig. 2), which was controlled by embolization of the feeding vessel (Fig. 3). The patient remained stable subsequently. There was no need for surgical exploration of the abdomen. Her aspartate aminotransferase level peaked at 268 mg/dl, and alanine aminotransferase, at 262 mg/dl; both liver enzyme levels subsequently returned to normal.

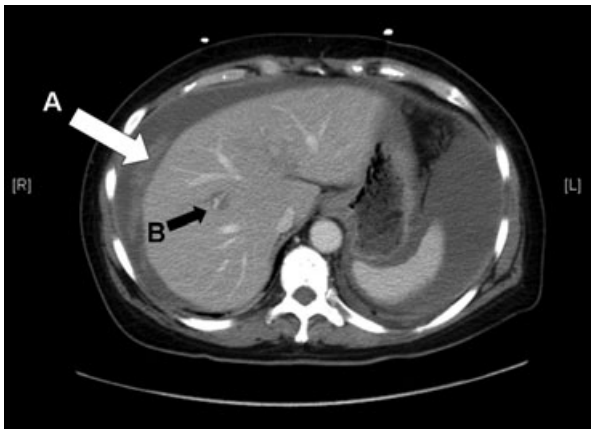

Figure 1 Computed tomography scan of the liver after islet infusion and recurrence of drop in hemoglobin. Arrow A: Area of extravasation of iodine contrast agent indicating arterial bleeding. Arrow B: Area of injury; the false aneurysm is not visualized.

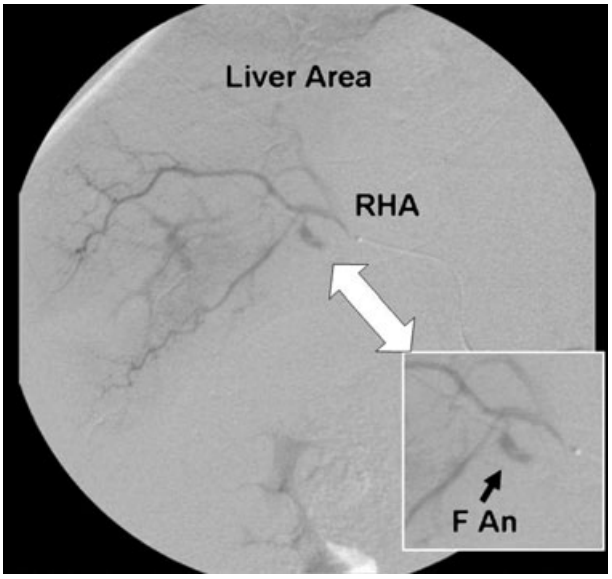

Figure 2 Selective hepatic arteriogram. The false aneurysm (F An) is shown in the insert. RHA, right hepatic artery.

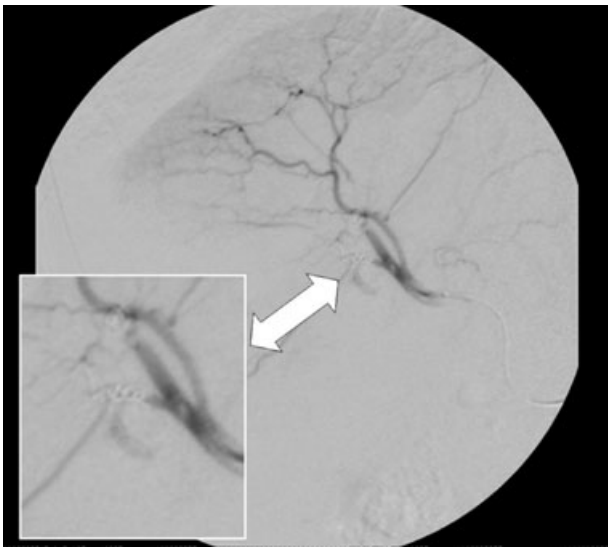

Figure 3 Completion of arteriogram after embolization.

The patient's glycemic control after the second islet infusion was very good. Despite the adverse event, she became insulin independent 42 days after the second islet infusion and maintained insulin independence until day 285 (9 months), when she returned to a small dose of Humalog insulin (2–4 units/day). Hemoglobin A_{1c} levels were checked monthly and ranged from 5.8% to 6.7% (latest: 6.7%), and serum C-peptide levels were 0 before the first infusion, 0.5 ng/ml before the second infusion, and 0.9–5.7 ng/ml afterwards (latest: 0.6 ng/dl at 1 year after transplant).

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Discussion

Pancreatic islet transplantation is a treatment alternative for type 1 diabetes mellitus by beta cell mass replacement. Although most patients do not achieve long-lasting insulin independence [3], they can achieve euglycemia post-transplant [3], and experience improvement in diabetic target organ damage [4]. The risks associated with the transplantation procedure, usually performed in two sessions as a percutaneous transhepatic portal vein infusion in the interventional radiology setting, are smaller than with pancreatic transplantation surgery.

In the case reported here, the islet transplantation procedure led to the formation of a false aneurysm of a branch of the hepatic artery, with ongoing bleeding that was controlled by embolization of the feeding vessel. Intra-abdominal bleeding is the most common complication associated with the procedure [5]. However, to the best of our knowledge, intrahepatic arterial injuries after islet transplantation have not yet been reported in the literature.

False aneurysms of the hepatic artery and its branches are rare occurrences and are mostly described as case reports or small series in the literature. Although some may occur as a result of a pathologic process, such as with polyarteritis nodosa [6], cholecystitis [7] or amebiasis [8], others have occurred as complications of trauma [9] and surgery, such as pancreaticoduodenectomy [10], laparoscopic cholecystectomy [11] and liver transplantation [12].

Other invasive procedures involving the passage through liver parenchyma, the biliary system, or the hepatic vasculature have resulted occasionally in the formation of false aneurysms of the hepatic artery and its branches. These diagnostic or therapeutic procedures include standard percutaneous liver biopsy [13], transjugular liver biopsy [14], percutaneous transhepatic cholangiogram [15], endoscopic retrograde cholangiogram [16], intra-arterial chemotherapy, radiofrequency ablation of hepatic tumors [17], transjugular intrahepatic portosystemic shunt placement [18], and even right-sided thoracentesis. The diagnosis of a false aneurysm in these settings is very difficult and is frequently delayed for days after the initial procedure [13]. Some false aneurysms can be diagnosed by DUS, CT scan, or even endoscopic ultrasonography, but most are recognized by arteriography or during surgery.

Depending on their size and location, false aneurysms are treated either surgically [19], by percutaneous embolization [10], or by direct thrombin injection [9]. The prognosis of a peripheral arterial injury in the liver from an invasive procedure is better than with more central, extrahepatic false aneurysms, and some intrahepatic false aneurysms undergo spontaneous thrombosis [17]. However, the islet transplantation procedure offers particular challenges, as it involves delivery of fresh tissue into the portal venous system, which activates the coagulation system. Indeed, portal vein thrombosis and portal vein branch thrombosis have been described early after the islet infusion [20]. Therefore, all transplant centers add heparin to the islet suspension, and most are using low-molecular-weight heparin for up to 2 weeks after transplant. This obviously increases the risk of bleeding after the procedure. To avoid bleeding from the liver access site, most centers obliterate the infusion catheter tract with a fibrin plug. However, if multiple needle sticks are necessary to access the portal vein (as happened in our case), only the last tract is sealed with fibrin. Bleeding can occur from another tract, especially with an arterial lesion and anticoagulation.

Nevertheless, given the peripheral injury, the impact of the embolization procedure on the liver parenchyma or the islet graft is minimal, as demonstrated by the early normalization of the liver enzyme levels and the achievement of insulin independence after the transplant.

As false aneurysms of a hepatic artery branch are rare, we cannot formulate a definite diagnosis and treatment algorithm at this time. Early bleeding after an islet infusion usually subsides after discontinuation of the anticoagulation. The rare refractory cases require surgical hemostasis, preferably using the laparoscopic approach. However, if bleeding stops and recurs days later, a vascular injury should be excluded by angiogram. Notably, intraparenchymal vascular injuries cannot be effectively approached by surgery, whether laparoscopic or open.

Prevention of vascular injuries can be achieved by limiting the number of liver punctures used to achieve access to the portal venous system for the islet infusion, ideally to one needle pass per procedure.

To summarize, we report the first case of intrahepatic arterial injuries after islet transplantation. This complication can be adequately controlled by coil embolization without compromising insulin independence.

Authorship

NO: all aspects. BN: paper design, islet isolation data. HBR: inpatient clinical data. JDM: interventional radiology and diagnostic radiology data. EQS: inpatient clinical data. SM: islet isolation. HN: islet isolation. AJ: data collection. NGD: interventional radiology aspects. GBK: paper design and editing. MFL: paper design, clinical post-transplant data and follow-up and monitoring.

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