A Case of Pancreatic Islet Cell Transplantation in a Patient with Situs Ambiguous: Anatomical and Radiological Considerations

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ABSTRACT

Pancreatic islet cell transplantation is an evolving treatment of severe, refractory type 1 diabetes that has been gaining more use, particularly after one year rates of insulin independence post-transplantation were found to approach 80% under the Edmonton protocol. Islet cell transplantation involves percutaneous delivery of harvested allogeneic β cells into the portal venous circulation for implantation into the liver. We present the case of a 35-year-old woman with type 1 diabetes and situs ambiguous with left isomerism and resultant variant anatomy of her portal venous anatomy who underwent islet cell transplantation, which, to our knowledge, has not been previously reported.

KEYWORDS: Pancreatic islet cell transplantation, situs ambiguous, treatment of diabetes mellitus

Objectives: Upon completion of this article, the reader should gain a basic understanding of pancreatic islet cell transplants and the anatomical considerations for transplantation.

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Type 1 diabetes affects ~1.5 million individuals in the United States and results from the autoimmune destruction of pancreatic β -islet cells and inadequate insulin production.¹ Chronic debilitating complications, including blindness and renal failure, can be prevented or minimized by keeping blood glucose levels under tight control. The current mainstay of treatment, intensified exogenous insulin, cannot approximate normal pulsatile insulin secretory patterns and carries a risk

of major hypoglycemic episodes. Pancreas transplantation is the only therapy shown to stop the progression of diabetic complications without increasing the incidence of hypoglycemic events.² However, it carries a high morbidity and mortality rate. Percutaneous islet cell transplantation is a potentially viable minimally invasive procedure that would avoid the risk of hypoglycemia and life-threatening complications of whole pancreas grafts. To date, fewer than 1000 cases have

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Figure 1 Liver masses detected on computed tomography. (A) Left lobe mass typical of focal nodular hyperplasia (FNH) (open arrow). Note splenules (white arrowheads) and right-sided stomach (black arrow) characteristic of situs ambiguous with polysplenia. (B) Right lobe mass found to be FNH (open arrow).

been performed worldwide as this procedure continues to undergo refinements.^{3,4} Of these, no known cases have been described in patients with significant variant anatomy. We discuss the case of a patient with situs ambiguous who underwent islet cell transplantation.

CASE REPORT

A 35-year-old woman with a history of type 1 diabetes (since age 9) and abdominal heterotaxia presented to the radiology department for evaluation prior to pancreatic islet cell transplantation. Cross-sectional imaging with ultrasound and computed tomography (CT) demonstrated midline liver, polysplenia, inferior vena cava interruption with azygous continuation, levocardia, bilateral bilobed lungs, truncation of the pancreas, and a right-sided stomach, findings consistent with situs ambiguous with polysplenia, or left isomerism.⁵ Incidentally noted were several small hepatic hemangiomas (measuring <1.5 cm each), and a larger (4.8 cm) left lobe liver mass with imaging features typical of focal nodular hyperplasia (FNH). An additional smaller mass (2.5 cm) in the right lobe was suspicious for FNH, but hepatocellular carcinoma

could not be excluded (Fig. 1). Percutaneous biopsy of this lesion confirmed FNH.

Characterization of the portal veins with CT showed the right anterior sectoral branch of the portal vein bifurcating from the main portal vein, with the right posterior sectoral branch arising from the left portal vein (Fig. 2). The peripheral portal veins were patent.

After taking into account the variant anatomy, islet cell transplantation was performed in the interventional radiology suite under moderate sedation. Using ultrasound guidance, a 20-gauge INRAD needle (INRAD, Kentwood, MI) was guided into the right anterior sectoral portal vein followed by a 0.018-inch Cope Mandril wire (Cook, Bloomington, IN). The needle was exchanged for a coaxial 4/6F introducer AccuStick II cannula and sheath system (Boston Scientific, Natick, MA). The inner 4F cannula was removed and over a 0.035-inch Bentson wire (Cook, Bloomington, IN), a longer 5F Berenstein catheter (AngioDynamics, Queensbury, NY) was positioned in the main portal vein. Direct portography was performed (Fig. 3) followed by measurement of intraportal pressure. Two thousand units of heparin were administered into the portal vein. Then purified islet cells

Figure 2 Portal venous anatomy on computed tomography. (A) Right anterior sectoral portal venous branch (black arrow) arises from the main portal vein. (B) Left portal vein (white arrow). (C) Right posterior sectoral portal venous branch arises from left portal vein (open arrow). Note hemangioma in right lobe (arrowhead).

Figure 3 Unsubtracted (A) and subtracted (B) portal venogram images demonstrate right anterior sectoral branch (black arrow), right posterior sectoral branch (open arrow), and left branch (white arrow) of portal vein.

were delivered in 60-mL syringes using slow manual injection. After each syringe of cells, an additional 1000 units of heparin were delivered for a total intraprocedural dose of 5000 units. Intermittent portal pressures ranged from 4 to 15 mm Hg. Following the completion of islet cell delivery, the catheter was withdrawn into the parenchymal tract. Gelatin foam pledgets (Johnson & Johnson, Somerville, NJ) were delivered into the parenchymal tract until hemostasis was obtained. The catheter was then removed. The patient was transferred to the transplant ward. A 24-hour postprocedure ultrasound showed a right intrahepatic hematoma requiring transfusion of 2 U of packed red blood cells. The patient was conservatively managed and discharged from the hospital 1 week after the procedure.

DISCUSSION

Pancreatic islet cell transplantation was first successfully reported in humans in the 1980s. Initial studies were promising, but showed mixed results until Shapiro et al.⁶ in 2000 demonstrated 100% insulin independence in a study of seven patients from 4 to 15 months following transplantation. Their method required a meticulous preparation of islet cells, injection of a large mass of cells, and a glucocorticoid-free immunosuppressive regimen that came to be regarded as the “Edmonton protocol.” Two or more islet cell transplants were required. A recent multicenter international trial using the Edmonton protocol confirmed the glycemic stability with islet cell transplantation and 1-year insulin independence rate of 44%.⁷ Long-term studies have shown a reduction of the insulin-free rate to 10% at 5 years. Encouragingly, all patients who returned to insulin use required lower doses, with 80% maintaining graft viability as evidenced by measurable C-peptide levels.⁸

The results of the Edmonton protocol have led to an increase in patients undergoing the procedure. As a

result, increased awareness of variant anatomy has become necessary to avoid complications. In the patient presented, careful mapping of the portal venous circulation was performed with CT to determine the optimal route for access. Atri et al.⁹ described variations in the portal venous anatomy to occur in ~20% of the general population, with the most common variant as a trifurcation of the main portal vein into the right posterior sectoral branch, right anterior sectoral branch, and left portal vein (~10% incidence). Other variants include right posterior sectoral from the main portal vein (5%), right anterior sectoral from the left portal vein (4%), and absence of horizontal segment of left portal vein (0.2%). In this patient with situs ambiguous, a right posterior sectoral branch arose from the left portal vein, which, to our knowledge, has not been described in the literature. This is of clinical significance because Kodama et al.¹⁰ have described that percutaneous access in the right posterior branch has increased risk for hemorrhagic complication. Therefore, when accessing the right portal vein branches, an anterior portal vein approach is preferred with awareness that patients with situs ambiguous can have a right posterior sectoral branch arising from the left portal vein. The left portal vein was not accessed given the presence of the large focal nodular hyperplasia. Although a bleeding complication did occur in this patient, this may have been from inadvertent puncture of a small hemangioma coupled with periprocedural heparin administration. Procedure-related complication rate from hemorrhage is 9%, and branch portal vein thrombosis is 6%.⁷

In addition to properly choosing a third or fourth order portal vein branch to minimize complications, ultrasound guidance for access is also a vital aspect of the procedure in patients with variable positioning of the gallbladder, such as those with situs ambiguous. Ultrasound is a valuable tool in determining a safe single-access entry into the portal vein and preventing biliary

puncture, particularly because no cases of biliary injury or gallbladder punctures have been reported with its use.¹¹

CONCLUSION

Pancreatic islet cell transplantation is an evolving therapy in the treatment of type 1 diabetes with refractory hypoglycemia. In patients undergoing this procedure with situs ambiguous, additional factors need to be considered, including variant portal venous anatomy and percutaneous portal vein access for a successful outcome.

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