J Ped Surg Case Reports 13 (2016) 28–30

Contents lists available at ScienceDirect

Journal of Pediatric Surgery CASE REPORTS

journal homepage: www.jpscasereports.com

Total pancreatectomy and autoislet transplant for chronic recurrent pancreatitis in a 5-year-old boy

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ARTICLE INFO

Article history:
Received 30 April 2016
Received in revised form
22 July 2016
Accepted 24 July 2016

Keywords:
Pediatric
Islet
Autotransplant

ABSTRACT

Childhood chronic pancreatitis is a rare disorder, which can lead to a chronically debilitating condition. The etiology of recurrent hereditary pancreatitis, which previously was classified as idiopathic, has now been attributed in certain cases to specific genetic mutations including abnormalities in the PRSS gene. We describe here the use of total pancreatectomy and autoislet transplant in a 5-year-old with chronic pancreatitis. This represents the youngest patient undergoing the procedure at our institution. The early successful outcomes for this patient, both of symptom relief and glycemic control are detailed.

Pancreatitis in childhood is relatively rare when compared to the adult population and its etiology is also different than the adult counterpart. Chronic recurrent pancreatitis can result from trauma, hereditary, systemic disease, or anatomic etiologies. Several gene mutations have been implicated in hereditary or idiopathic pancreatitis including PRSS, CFTR, and SPNK [1].

Surgical intervention for chronic pancreatitis is typically reserved for refractory symptoms unresponsive to medical or endoscopic management, or in the setting of suspected or confirmed malignancy. Surgical procedures for chronic pancreatitis include drainage, resection, or combined procedures.

Total pancreatectomy for chronic pancreatitis is typically be reserved for rare situations with pre-existing diabetes since the total impact of the loss of endocrine function may be limited. The loss of counter-regulatory mechanisms from this procedure poses significant metabolic implications and glycemic control can be challenging, even life threatening, for these patients. Treatment with pancreatectomy combined with autoislet transplant has been described for chronic pancreatitis [2] and specifically genetic pancreatitis in adult patients [3]. In children, total pancreatectomy with autoislet transplant has been demonstrated to provide pain relief and improved quality of life for children aged 5–19 years old in the setting of failure of medical and endoscopic management [4]. Chinnakotla et al. have specifically described the indications for total pancreatectomy and autoislet transplant used at their institution [4]. The ability to predict successful islet yield in a patient with chronic pancreatitis has also been described [5,6].

Case series examined the application and islet yield of the procedure for school aged and adolescents with chronic pancreatitis [4,5,7]; however, application in a pre-school aged (that is less than 6 years old) is more limited. We describe here our experience with our youngest patient with chronic pancreatitis undergoing total pancreatectomy and autoislet transplant.

1. Case report

1.1. Clinical history

A 5-year-old boy initially presented with recurrent bouts of acute abdominal pain secondary to episodic acute pancreatitis

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http://dx.doi.org/10.1016/j.epsc.2016.07.009

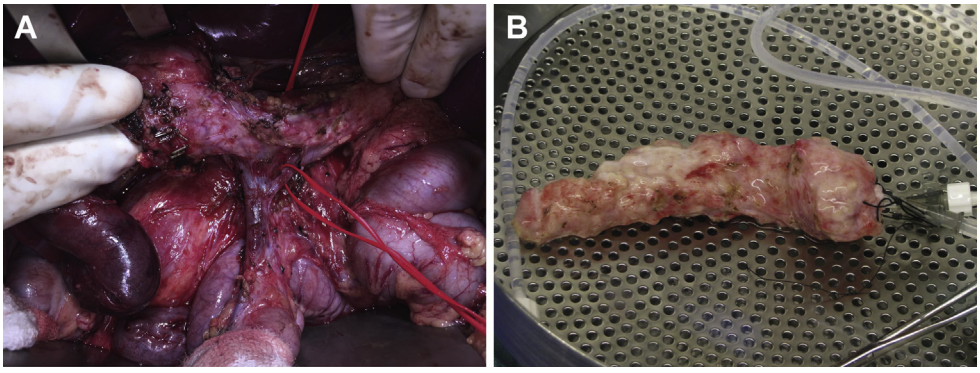

Fig. 1. Total Pancreatectomy. Total pancreatectomy was performed with modification to minimize warm ischemic time to the pancreas. Dissection of the pancreas including isolation of the splenic artery, splenic vein, portal vein was achieved (A). Both the ventral and dorsal pancreatic duct were cannulated on the back table, and the duodenum and spleen removed from the pancreas in the islet laboratory (B).

occurring every two to three months over the course of a year. These episodes were very disruptive resulting in hospitalization for supportive management including narcotic analgesic use. The patient had not required endoscopic management. The patient was therefore thought to be at significant risk of both nutritional and developmental sequelae. Subsequent genetic testing confirmed an underlying PRSS1 mutation.

After multidisciplinary consultation, the patient was offered total pancreatectomy given the likely pancreatic burnout with progression to diabetes and the concerning long-term risks of developing pancreatic cancer. Endocrine replacement with islet autoislet transplantation was discussed and consent from the child's parents was obtained.

1.2. Pancreatectomy and autoislet transplantation

Total pancreatectomy, with en bloc duodenectomy and splenectomy was performed though transverse laparotomy (Fig. 1). The patient weighed 19.1 kg and measured 107 cm tall at the time of the procedure. Pancreatic specimen was placed in histidine-tryptophan-ketoglutarate (HTK) cold preservations solution on the back table, where the pancreatic duct was cannulated. The organ was then packaged for transportation to the islet isolation laboratory.

Islet isolation was performed without purification using method previously described [8]. The 32.2 g pancreas was digested for 17 min. Non-purified product of 6 cc tissue contained 196,275 islet equivalents (IEQ) (or 10,276 IEQ/kg). The estimated viability was 96.5% and purity was 20%. Total processing time was 91 min.

Heparin at a dose of 70 units/kg body weight was added into the islet preparation. Gravity infusion of the islets into the portal vein was performed and portal pressure was measured at 10 mm Hg prior to infusion and 17 mm Hg after. Biliary and enteric reconstruction was achieved with a roux-en-Y choledochojejunostomy and gastrojejunostomy.

1.3. Post-operative and early outcomes

The child was maintained on 300 units/hour of IV unfractionated heparin for the first two post-operative days. Post-operatively, the patient was advanced to a full diet. The patient did experience gastroparesis while in hospital that was investigated with both an ultrasound and computed tomography imaging of the abdomen and pelvis. Neither demonstrated evidence for obstruction or post-surgery related pathology. The portal vein remained patent on imaging. Domperidone was used to treat the gastroparesis, with good effect and return to normal bowel function.

The patient's early post-operative random glucose levels remained between 5 and 6 mmol/L, and he never required insulin. Serum insulin and c-peptide levels remained positive (Table 1).

At 8-month post-operatively, the patient has remained pain free and had not required any hospitalization. Islet graft function appeared appropriate with random glucose 4.4 and Hgb A1c of 5.6%. He continues to receive pancreatic exocrine replacement therapy without symptoms of either diarrhea or malabsorption. He will be followed clinically with repeat blood work twice annually.

2. Discussion

Total pancreatectomy and autoislet transplant is a treatment option for certain cases of pancreatitis. The use of this in the adolescent population and even school aged child has been described. We present here early success in relief of symptoms and glycemic control when this treatment was offered to a pre-school child debilitated by hereditary pancreatitis.

Case series have demonstrated success of this procedure in children, even demonstrating that younger age was associated with higher rates of insulin independence following the procedure [4], possibly in part related to treatment before islet cell burnout from recurrent chronic pancreatitis.

The current report demonstrates that the procedure can be performed with good short-term outcomes and safety profile in childhood. The expansion of this procedure to an even younger age group (pre-school aged), we believe requires special attention to safety and outcome of the procedure specifically in this cohort.

In addition to the morbidities associated with a major abdominal surgery, there is the concern for portal hypertension resulting from infusion of a non-purified islet preparation directly into the portal circulation. Intra-operative portal pressure monitoring allows for dynamic measurement during the islet transplant procedure. With regards to portal vein thrombosis, consideration must be given to the balancing the risk of systemic heparinization to

Table 1
Perioperative glycemic profile.

	Pre-op	Post-op	8 mo follow-up
Glucose (random) mmol/L	3.4	5.4	4.4
HbA1c (%)	N/A	N/A	5.6s
c-Peptide (mmol/L)		0.23	
Insulin (pmol/L)		18	14.9

prevent thrombosis, which is low in adults (3.7%) [9] and children (0%) [4] undergoing islet transplantation.

Hereditary pancreatitis related to PRSS1 mutations carries an increased risk of life time development of pancreatic adenocarcinoma [10], which is inflated over that seen in chronic pancreatitis due to other etiologies. Pancreatic resection is thought to be protective of cancer development. Available data on pediatric patients with PRSS mutations undergoing total pancreatectomy with autoislet transplantation demonstrate that none have developed malignancy [4].

Though case series, a definition of the indications and contraindications to total pancreatectomy and islet transplantation for hereditary pancreatitis in childhood as well as parameters for the timing for the procedure has been proposed [4]. Expanding this procedure to an even younger aged cohort may provide benefit to early onset chronic pancreatitis in pre-school child.

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