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Pancreatic head resection and Roux-en-Y pancreaticojejunostomy for the treatment of the focal form of congenital hyperinsulinism

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Abstract

Purpose—To determine the outcome of patients who underwent pancreatic head resection and Roux-en-Y pancreaticojejunostomy to the remaining normal pancreatic body and tail for the treatment of a focal lesion in the pancreatic head causing congenital hyperinsulinism (HI).

Methods—One hundred thirty-eight patients underwent pancreatic resection for focal HI between 1998 and 2010. Twenty-three patients in the group underwent pancreatic head resection and Roux-en-Y pancreaticojejunostomy.

Results—There were 13 females and 10 males. Median age and weight at surgery were 8 weeks and 5.8 kg, respectively. Twenty-one patients had a near-total pancreatic head resection, and 2 patients had a pylorus-preserving Whipple procedure. The pancreaticojejunostomy anastomosis was performed with interrupted fine monofilament sutures such that the transected end of the pancreatic body was tucked within the end of the Roux-en-Y jejunal limb. Median hospital stay was 22 days. All patients were cured of HI.

Conclusion—We conclude that pancreatic head resection with Roux-en-Y pancreaticojejunostomy is a safe and effective procedure for the treatment of the HI patient with a large focal lesion in the pancreatic head that is not amenable to local resection alone.

Keywords

Congenital hyperinsulinism; Pancreatectomy; Pancreaticojejunostomy; Roux-en-Y

Congenital hyperinsulinism (HI) has an incidence of 1 to 1.4 cases per 50,000 live births, but is more frequent in populations with a high degree of consanguinity [1,2]. Patients who do not respond to medical treatment require surgery. These are predominantly caused by inactivating mutations of ABCC8 or KCHJ11, the 2 genes that encode the β -cell ATP-dependent potassium channel (K_{ATP}). The focal form of HI is associated with isodisomy for a paternally inherited K_{ATP} mutation; diffuse HI is usually associated with bi-allelic K_{ATP} mutations [3]. The surgical strategy is different for each histopathologic subtype: focal HI is cured by selective resection of the affected area, whereas diffuse HI requires a near-total pancreatectomy to facilitate glucose management. A variety of diagnostic modalities have been tried preoperatively to distinguish between focal and diffuse HI, but the standard is now the ^{18}F -fluoro-L-DOPA positron emission tomography scan merged with a computed tomography (^{18}F -PET/CT), which we have used in 163 patients [4–11]. In cases identified as focal on the PET/CT scan, we have found that the correlation between the imaging

location and the actual histological location approaches 100%. However, about 20% of babies with focal disease will have a PET scan that is read as diffuse disease likely because of the very small size of these particular focal lesions [9–12]. These findings make intraoperative assessment by the surgeon and frozen section analysis by the pathologist vitally important.

Superficial or peripheral focal lesions can be completely resected if intraoperative frozen sections confirm clear margins. On the other hand, deep, large, and periductal lesions typically require the resection of a full pancreatic segment. When such lesions are located in the body or tail, a distal pancreatectomy is performed, whereas lesions in the head sometimes require the resection of most of the pancreatic head and a Roux-en-Y pancreaticojejunostomy to preserve the exocrine and endocrine functions of the normal pancreatic body and tail. We report our experience in the management of HI patients that required a pancreatic head resection and a Roux-en-Y pancreaticojejunostomy.

1. Materials and methods

1.1. Study population

Between 1998 and 2010, 138 patients underwent pancreatic resection for the focal form of HI at the Congenital Hyperinsulinism Center of the Children's Hospital of Philadelphia (CHOP). This is a retrospective review approved by the CHOP Institutional Review Board of 23 patients who underwent pancreatic head resection and Roux-en-Y pancreaticojejunostomy. The surgical technical details and outcomes were analyzed.

1.2. Diagnosis

After the diagnosis of HI was established, all patients underwent imaging studies. The first 5 patients in the series had an “Arterial Stimulation with Venous Sampling” (ASVS) test, whereas the other 18 had a ^{18}F -PET/CT. The ASVS test is no longer performed. Neuroendocrine cells have an affinity for taking up and decarboxylating amino acid precursors such as L-dihydroxyphenylalanine (L-DOPA). Decarboxylation of the L-DOPA to dopamine in islet cells allows meaningful localization by means of PET scanning, using the radioactive isomer ^{18}F -fluoro-L-DOPA. The isotope is manufactured by the Cyclotron Facility at the University of Pennsylvania on the day of the PET scan because of the isotope's very short half-life, and it is administered to patients under an IND approved by the Food and Drug Administration. The results are dramatic and visually spectacular for preoperative localization of a focal lesion (Figs. 1, 2).

1.3. Surgical technique

All operations are performed using a transverse supraumbilical laparotomy under general anesthesia with frequent glucose monitoring. An epidural catheter is placed for postoperative analgesia. The pancreas is exposed by an extended Kocher maneuver, entry into the lesser sac, and the entire pancreas is inspected under 3.5× loupe magnification in an attempt to visualize a focal lesion. The pancreas is also palpated because some focal lesions are firmer than the surrounding normal pancreas. If no focal lesion is seen or felt, a 2- to 3-mm diameter biopsy is taken from each of the pancreatic head, body, and tail for frozen section analysis to rule out diffuse disease. If these biopsies show normal pancreatic histology, a further search for the focal lesion is performed. Although focal lesions may maintain a lobular structure similar to that of the normal pancreas, subtle visual clues (ranging from a slightly reddish color to a marble-like appearance) may permit visual detection of the lesion intraoperatively, and preoperative PET/CT greatly facilitates the visual search for a focal lesion. However, a tiny focal lesion can be buried within the pancreas and be impossible to see or feel. Additional biopsies of suspicious areas are

obtained until the focal lesion is diagnosed by frozen section. Expert pediatric pathologic interpretation is vitally important. Focal lesions tend to be less than 10 mm in size (although they can be much larger) and frequently are irregularly shaped. Some lesions have octopus-like tentacles so intraoperative confirmation of clear margins by frozen section analysis is imperative. Insulinomas differ from focal lesions because they are usually straightforward to identify intraoperatively and occur in older children.

If a large/deep focal lesion is identified in the head of the pancreas and a substantial portion needs to be resected to ensure clear margins, a near-total head resection is performed and a Roux-en-Y pancreaticojejunostomy is constructed to preserve the normal endocrine and exocrine functions of the pancreatic body and tail. The same approach is used for pancreatic head lesions close to the common bile duct or pancreatic duct, where it can be tricky to excise the entire lesion, particularly if there are tentacles of diseased tissue that emanate from the lesion. In babies, the pancreatic duct on the cut surface of the transected pancreatic body is not visible, and the resection on the pancreatic body side is performed sharply with minimal use of electrocautery. The end of a retrocolic, 25-cm-long Roux-en-Y jejunal limb is then meticulously anastomosed to the capsule of the pancreatic body (just beyond the cut surface of the pancreas) with fine interrupted 5–0 monofilament suture to effectively tuck the cut end of the pancreas into the jejunal lumen (Fig. 3). The posterior aspect of the anastomosis is performed first, with all sutures placed first and then tied serially leaving the knots on the inside of the anastomosis. The anterior aspect is performed in the same manner, but leaving the knots on the outside. The omentum is then freed from the transverse colon, wrapped around the anastomosis and sutured into place for additional security. A drain is not used. Rarely, a focal lesion in the head will extend into the duodenal wall in which case a pylorus-preserving Whipple procedure may be needed. If a Whipple is performed, a 4F 2-cm-long silastic stent is placed across the biliary-jejunal anastomosis and secured with a single absorbable 6–0 stitch, which permits the stent to pass through the gastrointestinal tract weeks later once the absorbable retaining suture dissolves.

There are 3 technical aspects that are important for successful pancreatic head resection in a baby with a focal lesion. First, placing a vessel loop around the extrahepatic common bile duct and then bringing that vessel loop superiorly within the duodenal C-loop just to the patient's left of the gastroduodenal artery can help with dissection of the tiny common bile duct if it is buried in the pancreatic head. The intrapancreatic course of the common bile duct should be completely defined for performance of an adequate near-total head resection. At the completion of this dissection, the gallbladder is milked to ensure that there is no bile leak from the common bile duct. A cholangiogram is not needed. Second, it is important to preserve the gastroduodenal artery and anterior superior pancreaticoduodenal artery proximally as well as the vessels supplying the third and fourth portions of the duodenum distally to prevent duodenal devascularization. Third, meticulous frozen section analysis is needed to ensure that the surgical resection margins are free of disease.

2. Results

The Congenital Hyperinsulinism Center at CHOP was established in October 1998 and since then we have evaluated and treated 454 HI patients. Forty-one percent of patients were managed medically ($n = 187$) and 59% required surgery ($n = 267$). Within the surgical group, 48% ($n = 129$) had diffuse HI, whereas 52% ($n = 138$) had focal HI. Within the focal HI group, 43% of the lesions were located in the pancreatic head ($n = 59$): 36 were amenable to local resection alone, whereas 23 required a complete or near-complete head resection and Roux-en-Y pancreaticojejunostomy (Roux-en-Y group) to preserve the distal pancreas (2 had a Whipple procedure).

2.1. Roux-en-Y group

There were 13 females and 10 males. Median age at surgery was 8 weeks (range, 3–56 weeks). Median weight at surgery was 5.8 kg (range, 4.3–9.8 kg). In 4 patients, the Roux-en-Y reconstruction was done after a previous local resection was incomplete. Two patients underwent reoperation after the Roux-en-Y because of residual disease in the pancreatic head remnant along the duodenal wall. All 6 patients who underwent 2 operations had clear margins by frozen section at the time of the first resection, but their clinical course with recurrent hypoglycemia mandated re-exploration. Mean blood loss was 25 mL (range, 5–75 mL). Two patients had a focal lesion involving the duodenal wall and required a pylorus-preserving Whipple procedure after lesion resection led to duodenal ischemia. Median operative time from incision to closure was 241 min, which invariably includes numerous biopsies for time-consuming frozen section analysis. There were no intraoperative complications. Postoperatively, one patient had a partial duodenal obstruction from a fluid collection, and 15 cc of sterile pancreatic fluid was percutaneously aspirated under ultrasound guidance without sequelae; the same patient developed an adhesive small intestinal obstruction 4 months postoperatively, which required adhesiolysis. The median hospital stay was 22 days (range, 13–60 days), including endocrine service evaluation for metabolic and fasting studies. All patients are cured of HI, and none have diabetes or pancreatic exocrine insufficiency.

3. Discussion

Congenital HI was first described in 1954 and termed *syndrome of idiopathic hypoglycemia of infants*; its association with hyperinsulinism was unknown at that time [13,14]. Early diagnosis of HI is critical to prevent the devastating neurological consequences of neonatal hypoglycemia. Once the diagnosis of HI is confirmed, genetic and imaging studies are performed to help determine the histopathologic form (diffuse or focal) and whether the disease can be managed medically. According to our own experience at CHOP, 59% of babies with HI do not respond to medical treatment and require surgery. The first pancreatectomy performed on a child with HI was reported in 1934 by Evarts Graham, 20 years before the disease was first described. The pancreas was explored to search for an adenoma, but no adenoma was found; virtually the entire pancreas was resected, and the patient's hypoglycemia disappeared [15].

The focal form of HI can be cured by complete resection of the affected area. The most favorable cases are those in which the focal lesion is superficial and amenable to simple excision. Large or deep lesions in the body or tail of the pancreas often require a distal pancreatectomy, in which case endocrine and exocrine pancreatic functions are preserved with the remaining pancreas. Large or deep lesions in the head of the pancreas are more challenging because they often require the resection of most (if not all) of the pancreatic head leaving the normal distal pancreas disconnected from the intestinal tract. Historically, pancreatocenteric anastomosis was not performed because it was believed that active pancreatic enzymes would produce anastomotic failure, pancreatic fistulae, and mortality. By the 1940s, better results were obtained with pancreatocenteric anastomosis, and the importance of draining the normal distal pancreas into the gastrointestinal tract became clear [16].

Babies with focal HI lesions who require a substantial resection of the pancreatic head should be reconstructed with a Roux-en-Y pancreatojejunostomy. Improvements in HI medical management, preoperative imaging with PET/CT, intraoperative pathology assessment, surgical technique, and postoperative care have made this procedure safe and effective.

References

- [1]. Stanley CA. Hyperinsulinism in infants and children. *Pediatr Clin North Am.* 1997; 44:363–74. [PubMed: 9130925]
- [2]. Arnoux JB, de Lonlay P, Ribeiro MJ, et al. Congenital hyperinsulinism. *Early Hum Dev.* May. 2010 86:287–94. [PubMed: 20550977]
- [3]. De León DD, Stanley CA. Mechanisms of disease: advances in diagnosis and treatment of hyperinsulinism in neonates. *Nat Clin Pract Endocrinol Metab.* 2007; 3:57–68. [PubMed: 17179930]
- [4]. Brunelle F, Negre V, Barth MO, et al. Pancreatic venous samplings in infants and children with primary hyperinsulinism. *Pediatr Radiol.* 1989; 19:100–3. [PubMed: 2537942]
- [5]. Abernethy LT, Davidson DC, Lamont GL, et al. Intra-arterial calcium stimulation test in the investigation of hyperinsulinaemic hypoglycaemia. *Arch Dis Child.* 1998; 78:359–63. [PubMed: 9623401]
- [6]. Huopio H, Jaaskelainen J, Komulainen J, et al. Acute insulin response tests for the differential diagnosis of congenital hyperinsulinism. *J Clin Endocrinol Metab.* 2002; 87:4502–7. [PubMed: 12364426]
- [7]. Ribeiro MJ, De Lonlay P, Delzescaux T, et al. Characterization of hyperinsulinism in infancy assessed with PET and 18F-fluoro-L-DOPA. *J Nucl Med.* 2005; 46(4):560–6. [PubMed: 15809476]
- [8]. Stanley CA, Thornton PS, Ganguly A, et al. Preoperative evaluation of infants with focal or diffuse congenital hyperinsulinism by intravenous acute insulin response tests and selective pancreatic arterial calcium stimulation. *J Clin Endocrinol Metab.* 2004; 89(1):288–96. [PubMed: 14715863]
- [9]. Otonkoski T, Näättö-Salonen K, Seppänen M, et al. Noninvasive diagnosis of focal hyperinsulinism of infancy with [18F]-DOPA positron emission tomography. *Diabetes.* 2006; 55(1):13–8. [PubMed: 16380471]
- [10]. Hardy OT, Hernandez-Pampaloni M, Saffer JR, et al. Diagnosis and localization of focal congenital hyperinsulinism by 18F-fluorodopa PET scan. *J Pediatr.* 2007; 150(2):140–5. [PubMed: 17236890]
- [11]. Peranteau WH, Bathaai SM, Pawel B, et al. Multiple ectopic lesions of focal islet adenomatosis identified by positron emission tomography scan in an infant with congenital hyperinsulinism. *J Pediatr Surg.* 2007; 42(1):188–92. [PubMed: 17208563]
- [12]. Ismail D, Hussain K. Role of 18F-DOPA PET/CT imaging in congenital hyperinsulinism. *Rev Endocr Metab Disord.* 2010; 11(3):165–9. [PubMed: 20878481]
- [13]. McQuarrie I. Idiopathic spontaneously occurring hypoglycemia in infants; clinical significance of problem and treatment. *Am J Dis Child.* 1954; 87(4):399–428.
- [14]. Stanley CA, Baker L. Hyperinsulinism in infants and children: diagnosis and therapy. *Adv Pediatr.* 1976; 23:315–55. [PubMed: 795282]
- [15]. Graham EA, Hartmann AF. Subtotal resection of the pancreas for hypoglycaemia. *Surg. Gynecol. Obstet.* 1934; 59:474–9.
- [16]. Kakita A, Yoshida M, Takahashi T. History of pancreaticojejunostomy in pancreaticoduodenectomy: development of a more reliable anastomosis technique. *J Hepatobiliary Pancreat Surg.* 2001; 8:230–7. [PubMed: 11455485]

Fig. 1. ^{18}F Fluoro-L-DOPA positron emission tomography scan merged with a computed tomography (^{18}F -PET/CT) showing a large focal lesion in the head of the pancreas. SMV: superior mesenteric vein.

Fig. 2.
 ^{18}F -PET/CT scan showing diffuse disease. Note the homogeneous distribution of the contrast throughout the pancreatic head (small white arrow) body and tail (long white arrows). LK: left kidney; RK: right kidney.

Fig. 3.

Surgical technique. A, Focal lesion in the head of the pancreas that has octopus-like tentacles that extend into the normal tissue. B, Near-total pancreatic head resection. The common bile duct is skeletonized and the duodenal vasculature is preserved. A very small portion of the pancreatic head (<5%) is left between the common bile duct and the duodenal wall, along the superior pancreaticoduodenal artery. C, Pancreaticojejunostomy. In babies, the pancreatic duct is not visible even under 4× loupe magnification. Fine interrupted 5–0 monofilament sutures are placed from the end of the Roux-en-Y jejunal limb (full thickness) to the capsule of the pancreas just beyond the cut edge so that the cut end of the pancreatic body is tucked into the jejunal lumen. The posterior aspect of the anastomosis is performed first, with all sutures placed first and then tied serially leaving the knots on the inside of the anastomosis. The anterior aspect is performed in the same manner, but leaving the knots on the outside.