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HOW-I-DO-IT ARTICLES

Posterior enucleation of the pancreatic head: an alternative route of access for parenchyma-sparing pancreatic resection

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Abstract

Background Enucleation has become an alternative treatment in benign or low-malignant cystic tumors, including intraductal papillary mucinous neoplasms (IPMN). For enucleation to be a safe alternative to the standard procedures, there must be good access to the resection area. In this report, we present such a route for dorsally situated IPMNs.

Methods The head of the pancreas was exposed by an extended Kocher maneuver to the left lateral edge of the aorta. Stay sutures were placed along the second part of the duodenum to allow maximal rotation of the pancreatic head to the left, which exposed the posterior aspect of the pancreatic head. The cystic lesion was then enucleated followed by a protective pancreaticojejunostomy on the resection cavity.

Results Two consecutive patients with IPMNs of the dorsal pancreatic head successfully underwent dorsal enucleation. The postoperative course was uneventful in the first patient, while the course of the second patient was complicated by a clinically relevant pancreatic fistula, delayed gastric emptying, and hospital discharge on day 35.

Conclusion This study shows the feasibility of a dorsal approach to the pancreatic head for enucleation as well as reconstruction by means of posterior Roux-en-Y pancreaticojejunostomy. In very selected cases in specialized centers, cystic lesions in the posterior aspect of the pancreatic head will become amenable to enucleation with preservation of pancreatic functionality. However, more research is needed to clarify postoperative outcomes of this approach.

Keywords Pancreatic resection · Enucleation · Cystic pancreatic lesion · IPMN · Surgical technique

Introduction

The reported incidence of pancreatic cystic neoplasms has been rapidly increasing over the past two decades with the routine use of computed tomography (CT) and magnetic resonance imaging (MRI) [1]. Pancreatic intraductal papillary mucinous neoplasms (IPMN) rank among the most common cystic tumors of the pancreas [2]. According to the international consensus guidelines for the management of IPMN and mucinous cystic neoplasm (MCN) [3], surgical intervention in fit patients is warranted in main-duct and mixed-type IPMN at the time of diagnosis, as the risk of malignant transformation is 60–90% [4]. In selected cases with only minor main-duct dilation of up to 9 mm, surveillance can be considered. The incidence of invasive carcinoma in IPMN is 15% at initial diagnosis and increases over time [5]. Branch-duct (BD) IPMN have a much lower risk for harboring malignancy. For risk stratification and management of all IPMN and MCN, the Fukuoka consensus [3] lists "worrisome features," clinical and radiological signs that warrant further investigative measures and "high-risk stigmata" that call for surgical intervention [6].

Surgical treatment in IPMN requires a differentiated approach with regard to indications and extent of resection. The most common surgical procedures performed for IPMN are pancreaticoduodenectomy (PD), distal pancreatectomy, and total pancreatectomy [7]. Apart from these standard resections, benign or borderline tumors of the pancreas, including cystic lesions and endocrine tumors, may not always require

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extensive pancreatic resection to achieve surgical cure. Several partial resection techniques such as segmental resection, resection of the uncinate process, enucleation, and duodenum-preserving pancreatic head resection (DPPHR) represent tissue-sparing treatment options with minimized risk of endocrine and exocrine pancreatic insufficiency as well as reduced surgical morbidity and mortality [8]. Parenchyma-sparing resections should be considered for the treatment of benign or premalignant lesions.

Enucleation has become an accepted alternative treatment in benign or low-malignant cystic tumors, including neuroendocrine lesions [9, 10] and IPMN [11, 12]. Additionally, it has been proposed that this procedure is particularly well suited for superficial cysts, as the rate of complications, namely grade B or C postoperative pancreatic fistula (POPF), is significantly higher in lesions that are deeply embedded in the pancreatic tissue or located closely to the main pancreatic duct (MPD) [13, 14]. For enucleation to be a safe alternative to the standard procedures, there must be good access to the resection area. In this report, we present such a route for enucleation of dorsally situated IPMNs. We carried out a protective pancreaticojejunostomy (PJ) to reduce the risk of POPF, because both lesions were deeply embedded and a close relationship to the MPD was noted.

Methods

Patients

Two consecutive patients with suspected IPMN of the dorsal pancreatic head underwent dorsal enucleation at the Beau-Site Hospital, Bern, Switzerland in 2016.

Case 1 A 54-year-old male patient presented with recurrent acute pancreatitis of unknown etiology. Over the course of 8 months, the otherwise healthy patient suffered four attacks. There was no history of regular medication. He stopped drinking alcohol and smoking after the first attack. The laboratory studies showed normal levels of triglycerides, calcium, IgG4, and alpha1-antitrypsin. Serum carcinoembryonic antigen (CEA), carbohydrate antigen (CA) 19.9, and neuron-specific enolase (NSE) levels were within the normal ranges. Genetic testing for hereditary pancreatitis was normal.

Repeated CT showed recurrent exudative pancreatitis of the pancreatic head without necrosis or calcifications. MRI and magnetic resonance cholangiopancreatography (MRCP) during a symptom-free interval showed a 10-mm cyst located in the dorsal pancreatic head, towards the uncinate process. Subsequent endoscopic ultrasound (EUS) showed the lesion to measure 8.5 mm with connection to a normally configured MPD; there were parenchymal signs of chronic pancreatitis with pseudolobulation without calcification. Fine-needle aspiration (FNA) of the parenchyma surrounding the cyst showed subacute to chronic inflammation without atypical cells. Staining for IgG4 was negative. These findings suggested a BD-IPMN; however, autoimmune pancreatitis could not be ruled out. Empirical treatment with steroids was commenced, during which the patient experienced another episode of acute pancreatitis. On follow-up MRI and MRCP 3 months after EUS and 8 months after MRI, progression in cyst size to 13 mm was noted (see Fig. 1a and b). The diagnosis of symptomatic BD-IPMN was made, confirming the indication for surgery—either conventional PD or enucleation depending on the intraoperative and frozen-section findings. In case of enucleation, our approach is to perform a protective PJ as studies have shown to reduce the risk of POPF after enucleation [15].

Case 2 A 76-year-old man suffered two episodes of epigastric pain and unintentional weight loss of 2 kg in 6 months. Abdominal CT revealed a 7-mm cystic pancreatic lesion in the uncinate process. The symptoms cleared and the weight stabilized. Annual follow-up CT showed progression in size to 18 × 12 mm over the course of 3 years. EUS then showed a pluricystoid lesion located in the uncinate process, between the ventral and dorsal rudiments. No solid proliferation or pathology of the MPD was noted. Follow-up EUS 18 months later showed progression in size from 20.8 × 9.5 mm to 22.9 × 14.6 mm. FNA did not reveal atypical cells. Punctate CEA and CA 19-9 were 194 ng/ml and 634 U/ml, respectively, both below the threshold for malignancy. An elevated lipase concentration of 3023 U/l proved the presence of a connection to the pancreatic duct system. Serum CEA and CA 19-9 levels were within normal limits. NSE was slightly elevated, at 17.5 μg/l. Follow-up MRI/MRCP revealed the known lesion to measure 24 mm (see Fig. 2a and b). Surgery was deemed indicated because the lesion measured > 20 mm and was continuing to grow.

The secondary diagnoses included status post robotic-assisted radical prostatectomy for adenocarcinoma of the prostate (pT2 pN0 M0 Pn0 G2/G3 R0 Gleason 3+4), status post bilateral inguinal hernia repair, and stable polymyalgia rheumatica treated with a daily dose of 2.5 mg prednisone (Prednisolon, Streuli).

Surgical technique (video 1)

A vertical midline incision was made, followed by abdominal exploration and cholecystectomy. Wide exposure to the pancreas was obtained by dissecting the gastrocolic ligament and opening the lesser sac, which allowed inspection and palpation of the whole pancreas after dividing the retrogastric adhesions. The head of the pancreas was exposed by dissecting the pancreatic head free from the mesocolic and dorsal gastric attachments. The Kocher maneuver was extended to the left lateral edge of the aorta, taking care to identify the left renal

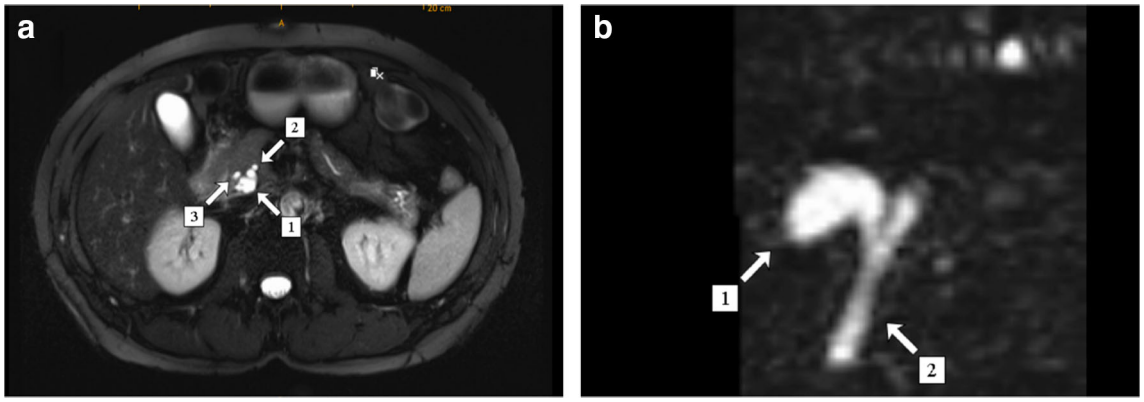

Fig. 1 Preoperative sagittal (**a**) and coronal (**b**) view of the MR/MRCP of case 1. Intraductal papillary mucinous neoplasms (1); main pancreatic duct (2); bile duct (3)

vein. This yielded good visualization of the posterior aspect of the pancreas. Three stay sutures were placed along the second part of the duodenum to allow maximal rotation of the pancreatic head to the left, which exposed the posterior aspect of the pancreatic head. For identification of the intrapancreatic common bile duct, following cholecystectomy, a single-lumen central venous catheter was advanced through the cystic duct into the common bile duct, passing through the major duodenal papilla. The cystic lesion and its relationship to the common bile duct were visualized and confirmed by intraoperative ultrasound (IOUS) if necessary. Dissection of the lesion was performed using a monopolar (Colorado Microdisection Tip, Stryker) and a bipolar cautery (SuperGliss Non-Stick Bipolar Forceps, Sutter Medizintechnik). The dissection was performed along the tissue plane between the pancreatic parenchyma and the cystic lesion, then the lesion was gradually mobilized towards its connection with the MPD. The side branch was ligated using metal clips (Small Titanium Hemostatic Clips, Péters Surgical). Frozen-section examination of the cyst and distal resection margin was performed to exclude malignancy and confirm tumor-free resection margins at the connecting duct. The integrity of the pancreatic duct was evaluated by intravenous administration of the secretin analog secretin pentahydrochloride (Secrelux, Sanochemia Diagnostics; 14.5 μg) at 0.5 to 1 unit per kilogram of body weight.

Reconstruction of the pancreatic resection area began with the formation of a Roux-en-Y jejunal loop. The jejunum was transected 60 cm distal to the ligament of Treitz. A 60-cm jejunal limb was passed through the retrocolic mesenteric cleft to the right of the middle colic artery towards the pancreatic head. A two-layer side-to-side PJ was performed using interrupted stitches with 5-0 absorbable sutures (PDS II, Ethicon). For restoration of intestinal tract continuity, a side-to-side double-layer entero-enteral anastomosis (Roux-en-Y) was carried out. Soft silicon drains (Easy-flow 8 mm, P.J. Dahlhausen) were placed at the resection site.

Postoperative management

The proton-pump inhibitor esomeprazole (Nexium, AstraZenica; 40 mg) was given for 6 weeks postoperatively to prevent stress ulceration. The somatostatin analog octreotide (Sandostatin, Novartis Pharma; 200 μg, subcutaneous injection 3 times per day) was given intra- and postoperatively for a total of 7 days. Postoperative management

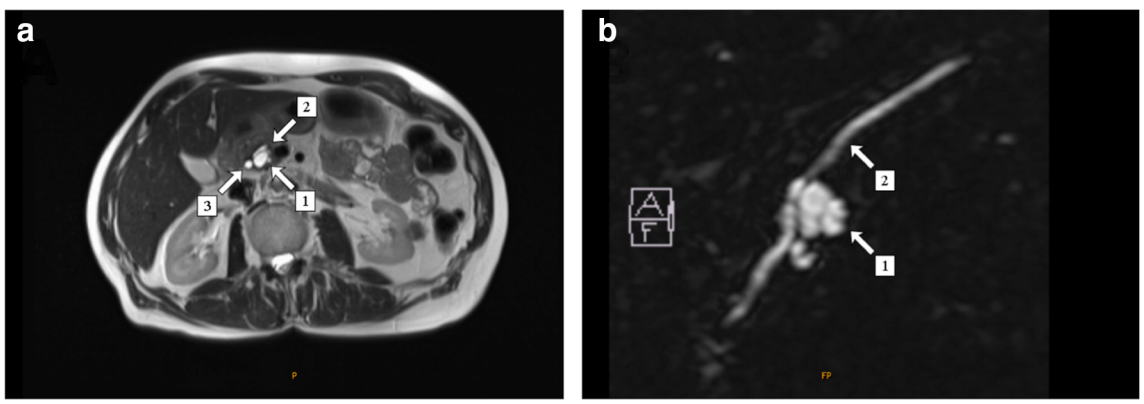

Fig. 2 Preoperative sagittal (**a**) and coronal (**b**) view of the MR/MRCP of case 2. Intraductal papillary mucinous neoplasms (1); main pancreatic duct (2); bile duct (3)

followed the Enhanced Recovery After Surgery (ERAS) guidelines with the aforementioned deviations [16].

Results

Case 1 Intraoperatively, the IPMN did not involve the MPD. However, leakage of pancreatic fluid was noted after clipping of the connecting duct within 1 mm of the MPD and removal of the cystic lesion. Closer examination showed a small semicircumferential lesion of the MPD, and optimal drainage into the resection cavity was observed under secretin stimulation. The pancreatic texture was hardened due to the previous recurrent pancreatitis.

The initial postoperative course was uneventful. Early oral food intake was well tolerated. The silicon drains were removed on postoperative day (POD) 5. The patient later suffered from fatty diarrhea, which improved with the administration of pancreatic enzymes (Pancreatin; Creon, BGP Products; 300 mg, 3 times a day). Serum glucose levels were within normal limits. The patient was discharged on POD 10.

Histopathological analysis of the completely resected lesion showed a gastric-type IPMN with low-grade dysplasia together with a pancreatic intraepithelial neoplasm (PanIN) 1b in an accessory duct.

During the 12-month follow-up period, the patient remained free of symptoms; no acute pancreatitis occurred. The patient reported suspending the daily intake of pancreatic enzymes within a few weeks after discharge, and no sign of exocrine dysfunction was observed. Follow-up CT showed normal postoperative conditions. Annual surveillance was initiated.

Case 2 Contradictory to preoperative imaging, intraoperatively, the IPMN was found to marginally involve the MPD. We therefore decided on segmental resection of the MPD. Frozen-section examination excluded malignancy of the cystic tumor and no atypical cells or dysplasia was noted at the resection margins of the MPD, so we refrained from standard PD. Before reconstruction with a protective PJ, two pancreatic duct plasties were created at both resection margins of the major pancreatic duct with four to six single 6-0 absorbable sutures (PDS II, Ethicon) between the duct and the soft pancreatic parenchyma to form a cone-shaped orifice into the resection cavity for optimal drainage.

The postoperative course was complicated by grade B delayed gastric emptying according to the International Study Group of Pancreatic Surgery [17]. On POD 9, the development of a grade B POPF [18] was noted with secretion of pancreatic juice via the intraoperatively placed drains. No additional drain needed to be placed, and the drains were removed on POD 24. Supplemental parenteral nutrition was necessary until POD 24. Furthermore, the patient developed multiple peripheral lung embolisms. Throughout the hospitalization, there was no sign of endocrine or exocrine pancreatic insufficiency. The patient was discharged on POD 35.

Histopathological analysis showed a mixed-type IPMN with low-grade dysplasia. The MPD and BD components were both of gastric epithelial subtype. The IPMN involved the complete circumference of the MPD. The patient recovered completely over the course of the 12-month follow-up period. MRI/MRCP revealed slight dilation of the MPD without atrophy of the remaining pancreatic parenchyma. Annual surveillance was initiated.

Discussion

With the increase in incidence of benign or borderline pancreatic lesions due to advances in radiological imaging, the need for a differentiated approach to these pancreatic cystic neoplasms has become apparent. If radical resection is warranted, the surgeon's focus shifts to preservation of healthy pancreatic tissue. Although postoperative exocrine and endocrine pancreatic insufficiency may depend on several factors, it is a reasonable assumption that the extent of pancreatic resection largely determines pancreatic function thereafter [19]. Furthermore, every attempt must be made to reduce morbidity and mortality in the treatment of benign and borderline lesions. Both morbidity and mortality are directly linked to the extent of resection and the complexity of reconstruction.

Enucleation is a surgical technique with maximal preservation of healthy endocrine and exocrine pancreatic function, so it represents an eminently suitable treatment option for these lesions. With cystic tumors located in the pancreatic head, the commonly used techniques of enucleation with Roux-en-Y reconstruction or modified DPPHR utilize an anterior approach to the pancreatic head because surgical control depends on good access to the cystic lesion. By virtue of an extended Kocher maneuver providing extensive mobility of the pancreatic head, the procedure described here allows for good visualization of the dorsal aspect of the pancreatic head. This allows for a direct approach to lesions located dorsal of the MPD plane, permits safe enucleation, and grants access adequate for effective PJ. Furthermore, should intraoperative inspection uncover any signs of malignancy or dysplasia along the resection margins that require radical oncological control, the procedure can be extended to standard PD. If malignancy is discovered postoperatively, a second intervention is warranted.

The oncological validity of enucleation in BD-IPMN has recently been shown [20]. Kaiser et al. assessed the outcomes of 115 patients with presumed noninvasive IPMN after parenchyma-preserving resections. They concluded that enucleation was eminently feasible and effective in selected patients with IPMN [21]. Sahora et al. re-examined the

pathological findings in 404 resected IPMN. They showed that mixed-type IPMN with minimal invasion of the MPD share the pathological features of BD-IPMN, with less aggressive biology and favorable clinical outcome—5- and 10-year-survival rates of 97%—and suggested that the entity of mixed-type IPMN should be further differentiated [22]. However, this subclassification is only possible postoperatively. Nevertheless, in our second case, we decided not to proceed with standard PD due to the macroscopically minimal involvement of the MPD and in light of the patient's advanced age. We are aware that the indication to perform surgery was based on relative indications in both patients, namely the recurrent acute pancreatitis presumably due to a growing BD-IPMN in the first case and the cyst size of > 2 cm with a growth rate of > 5 mm/year in the second case [23].

Even tough enucleations are associated with less blood loss and shorter operating time compared with standard pancreatic resections, a recent systematic review found higher rates of POPF, clinically relevant POPF, and a similar morbidity [24]. The postoperative course of the second patient was complicated by a clinically relevant POPF, DGE with parenteral nutrition until POD 24, and hospital discharge on POD 35, which is the main limitation of the herein described posterior enucleation. Patients with cystic lesions show a higher rate of POPF after enucleation than those undergoing enucleation of solid masses [25], owing to the soft pancreatic texture. In this setting, Xiao and colleagues propose enucleation followed by Roux-en-Y PJ, thus greatly reducing the POPF rate of enucleation in delicately located lesions while still preserving a maximum amount of healthy tissue [15]. In cases without MPD involvement, the efficacy of protective Roux-en-Y PJ has yet to be shown. Ohtsuka et al. retrospectively reviewed 32 patients with and without protective PJ and found no difference in prevalence of POPF; both operation time and hospital stay were significantly longer in the PJ group [26].

Conclusion

This study shows the feasibility of a dorsal approach to the pancreatic head for enucleation as well as reconstruction by means of posterior Roux-en-Y PJ. In very selected cases, this technique widens the indication for parenchyma-sparing surgery and may avoid the necessity for PD. In high-volume pancreatic cancer centers, these cystic lesions in the posterior aspect of the pancreatic head will become amenable to enucleation with maximal preservation of pancreatic endocrine and exocrine functionality. However, more research is needed to clarify the postoperative outcome of this approach, as our study demonstrated a considerable risk of postoperative morbidity and POPF.

Authors' contributions Study conception and design: Müller SA, Müller PC, and Z'graggen K. Acquisition of data: Z'graggen K, Müller SA, and Pärli MS, Razza C. Analysis and interpretation of data: Pärli MS, Müller PC, and Ruzza C. Drafting of manuscript: Pärli MS, Müller SA, and Müller PC. Critical revision: Ruzza C and Z'graggen K.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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