ORIGINAL ARTICLE

Report of Three Cases of Chronic Pancreatic Fistulas Treated with Prolamine as a Sclerosing Substance Following Pancreatic Resection

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ABSTRACT

Context Pancreatic fistulas are one of the most common and important complications after pancreatic resection and their consequences are a life-threatening event. Thus, they must be treated in the best way and resolved as soon as possible to avoid their morbidity.

Methods Three cases of pancreatic fistula following pancreatic resection were reported. They were treated with percutaneous embolization using a sclerosing substance, prolamine, injected into the Wirsung duct via drainage catheter.

Results No complications of the technique were revealed and closure of the pancreatic fistula was obtained shortly thereafter.

Conclusions The technique is safe and simple and can be repeated several times. It allows good results without complications. Finally, it avoids additional surgery allowing a shorter recovery time and a lower risk of morbidity.

INTROUCTION

Pancreatic fistulas are a heterogeneous group of disorders in which both disruption of the pancreatic duct and leakage of amylase and lipase-rich fluid to the skin are present. The most common causes include pancreatic inflammation (acute or chronic pancreatitis), pancreatic resection and trauma [1]. Traditionally, they have been classified as high output (secretion of drain fluid greater than 200 mL/day) or low output (less than 200 mL/day), although the utility of this classification remains unclear [2, 3]. Conventional treatment strategy consists in establishing adequate drainage and fistula control, aggressively treating sepsis, providing nutritional support and reducing pancreatic exocrine secretions with total parenteral nutrition or octreotide. The combination of external drainage and medical therapy results in fistula closure in approximately 85% of patients [4]. If closure fails to occur with medical therapy, surgical treatment is necessary [5].

The use of percutaneous injection of a sclerosing substance, prolamine, into the pancreatic duct is reported for the management of three cases of chronic pancreatic fistula following pancreatic resection.

PATIENTS AND METHODS

From 1994 to 2004, 150 pancreatic resections were performed in our Institute; the overall

Table 1. Characteristics of the three cases treated with prolamine.

	Case 1	Case 2	Case 3
Sex	Male	Female	Male
Age (years)	58	26	48
Pancreatic disease	Head cancer	Body-tail cystic lesion	Head cancer
Surgical treatment	PPPD	Excision	PPPD
Fistula manifestation and discover	PC (12 cm), 3 months	PC (9 cm), 2 months	PC (10 cm), 4 months
Fistula output (mL/day)	220	150	200
Fistula persistence (month)	3	3	4

PC: pseudocyst
PPPD: pylorus-preserving pancreaticoduodenectomy

mortality rate was 3.3% (5 cases), while morbidity was of 33.3% (50 cases). Among surgical complications, pancreatic fistulas were the most frequent and were observed in 22 cases (14.7%). Pancreatic fistula was defined as a drainage of more than 50 mL of amylase-rich fluid (more than three times the normal upper limit present in serum) on or after postoperative day 10, or pancreatic anastomotic disruption demonstrated radiographically [6]. They were successfully treated with medical or radiological therapy in 20 cases (90.9%); only in 2 cases (9.1%) was surgical treatment carried out. In 3 out of 20 cases (15.0%) of pancreatic fistulas treated conservatively, a sclerosing substance, prolamine (Ethibloc-Ethicon, Norderstedt, Germany), was used (Table 1).

The patients were 2 males and 1 female 26, 48, and 58 years of age (mean 44 years), respectively, who had undergone pancreatic resection: 2 pylorus-preserving pancreatico-duodenectomies (PPPD) for ductal adenocarcinoma of the pancreatic head and one total excision of a body-tail cystic lesion. In the PPPDs, legation of the Wirsung duct and suture of the pancreatic stump was performed because of a friable pancreatic parenchyma and an undilated Wirsung duct. All cases were treated with octreotide in the postoperative period (0.2 mg/day *tid*) for at least seven days. The postoperative course was uneventful and they were discharged after 8, 15, and 16 days, respectively.

In the follow-up period, a large pancreatic sterile collection, with diameters of 9, 10, and 12 cm, respectively, developed after 2, 3, and 4 months, respectively after the pancreatic resection. In all cases, the first treatment was percutaneous CT-guided drainage of the pseudocyst which resolved the lesion (Figure 1) but it created an external iatrogenic fistula.

Figure 1. Abdominal CT scan shows a large pseudocyst of the head of the pancreas which is treated with percutaneous CT-guided drainage. (Case 1)

Figure 2. Abdominal CT scan showing the fistula and the Wirsung duct after injection of barium via drainage catheter. (Case 1)

Figure 3. Abdominal CT scan showing the Wirsung duct after the injection of 7.5 mL of the sclerosing substance, prolamine, via drainage catheter. (Case 1)

Figure 4. Abdominal CT scan performed three days after treatment with prolamine shows a complete resolution of the pseudocyst and a Wirsung duct occluded by the sclerosing substance (Case 1)

In fact, output from the drainage was 150, 200, and 220 mL/days, respectively, of amylase-rich fluid which persisted for a long time: 2, 3 and 4 months, respectively. In this period, octreotide (0.2 mg/day *tid*) was administered to each patient. In the case treated with total excision of a cystic mass located in the body-tail, an endoscopic sphincterotomy was also performed, but without success.

A CT scan with barium injection via drainage catheter allowed to show disruption of the pancreatic duct, and the distal Wirsung duct (Figure 2). Persistent, intractable pancreatic fistulas were treated as follows: 1) a CT scan with barium injection via drainage catheter which showed disruption of the pancreatic duct, and the distal Wirsung duct (Figure 2); the catheter was not in the duct but just outside of it; 2) Wirsung duct embolization with 7.5 mL of sclerosing substance, prolamine, injected, via the catheter, under CT scan guidance (Figure 3). Three days later, an abdominal CT scan was performed to establish whether or not drainage catheter
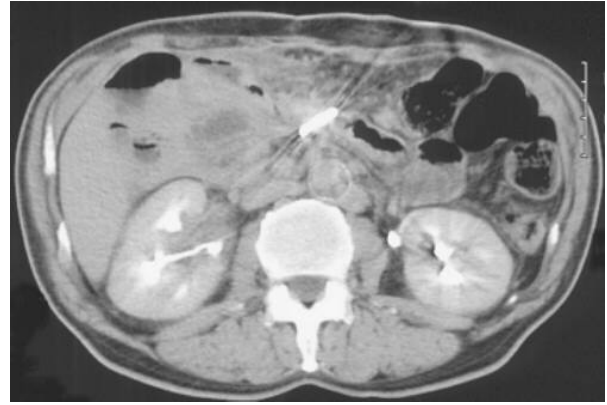
could be removed (Figure 4). The first abdominal ultrasound was performed after one month and the ultrasound examination was performed subsequently every 3 months until 12 months after the treatment.

RESULTS

The results of this method are summarized in Tables 2 and 3. In cases 1 and 2 the fistula output decreased rapidly: from 220 to 10 mL/day in case 1 and from 150 to 20 mL/day in case 2. There were no clinical signs of pancreatitis and no serum amylase level increase after the procedure and the drainage catheter was removed after 4 days. An abdominal ultrasound examination, performed 1 month later, did not show any pseudocysts or other collections. The patients had post-injection diarrhea and required enzyme replacement. They have not experienced recurrence of the pancreatic juice fistula or reduction of glucose tolerance 12 months after the treatment.

In case 3, the fistula output remains high after

Table 2. Results of the prolamine injection into the Wirsung duct in the treatment of a pancreatic fistula after pancreatectomy.

	Case 1	Case 2	Case 3
Fistula output before treatment (mL/day)	220	150	200
Fistula output after 24 hours from the treatment (mL/day)	10	20	100
Complications	None	None	None
Drainage removal (day)	4	4	60

Table 3. Follow-up after prolamine injection in Wirsung duct to treat pancreatic fistula after pancreatectomy.

Case	Follow-up
1	Ultrasound after 1 month: complete resolution. After 12 months: no fistula recurrence, no glucose intolerance
2	Ultrasound after 1 month: complete resolution. After 12 months: no fistula recurrence, no glucose intolerance
3	Ultrasound after 5 months: small pseudocyst (2 cm. in diameter). Complete resolution after 6 months. After 12 months: no fistula recurrence, no glucose intolerance

treatment (100 mL/day). There were no complications in this case, but the patient had post-injection diarrhea and required enzyme replacement. In contrast with cases 1 and 2, the drainage catheter was removed after 60 days because of the persistent high volume fistula output (superior than 50 mL/day). An abdominal ultrasound examination showed a significant decrease in the collection after 5 months and a complete resolution after 6 months. Twelve months after the treatment, there were no recurrences of a pancreatic fistula or reduction of glucose tolerance.

DISCUSSION

The safety of pancreatic resections has increased in recent years but, although the mortality rate has decreased tgo less than 5% in high volume centers [7, 8, 9, 10], morbidity is still high ranging from 10 to 47% [7, 8, 10]. Among surgical complications pancreatic fistulas represent the most common and clinically relevant; in high volume centers, their rate is in the range of 3 to 13% [7, 9] and the consequences are life-threatening (i.e., bleeding, pancreatic fluid collection and abscesses) with a prolonged hospital stay for specialized treatment and increased costs.

Computed tomography is widely available for the assessment of such complications. Fistulography may help in this setting by showing the communication with the main pancreatic duct.. Endoscopic retrograde cholangiopancreatography (ERCP) has lost much of its contribution to the staging of pancreatic fistulas since the development of secretin-enhanced magnetic resonance pancreatography (S-MRCP). This procedure gives a planar reconstruction of the pancreatic duct and, after secretin injection, the preferential direction of the pancreatic flow (through the fistula). Moreover, it allows us to

precisely locate the disruption without any risk of infection due to the external injection of contrast [11].

The goal of fistula treatment is to achieve its closure in the shortest time possible. Several therapeutic modalities should be considered: conservative measures, radiological, endoscopic and surgical treatment. According to previous reports [12], the initial treatment for a pancreatic fistula is conservative and it varies with the severity of the leak. Moreover, it has been well-established that approximately 85% of pancreatic fistulas heal with conservative therapy alone [13] and that the time for closure is from 4 to 18 weeks [13, 14]. Additional therapies have been advocated by some authors in an attempt to speed closure of the leak [15] and to avoid surgical treatment. Endoscopic stenting of the pancreatic duct allows favorable results for incomplete main pancreatic duct disruption [16]. Transpapillary stents can bypass the high resistance of the sphincter of Oddi, ductal strictures and calculi, thereby reducing intraductal pressure and the driving force behind the fistula. Endoscopic pancreatic sphincterotomy should be considered the treatment of choice in patients with a pancreatic fistula after body-tail resection. Percutaneous embolization of the pancreatic duct with different sclerosing substances is a new method for resolving pancreatic fistulas as soon as possible. Embolization of the pancreatic duct was first described by Little *et al*. in 1977 [17]. They reported the technique of intraoperative pancreatic duct embolization for the prevention or treatment of a pancreatic fistula. Embolization of the duct in the pancreatic remnant during pancreatico-duodenectomy for chronic pancreatitis has been shown by Gall *et al*. [18] to reduce the frequency of postoperative recurrent pancreatitis by preventing leakage at the

pancreaticojejunostomy anastomosis. In several series, this approach has been shown to preserve the endocrine function of the pancreas while it caused exocrine atrophy [19]. The percutaneous approach to embolization, using a prolamine solution, was first described in 1997 by Buecker *et al.* [14] in a 54-year-old woman in order to treat a pseudocystoductal fistula following necrosectomy for acute pancreatitis. Subsequently, a few cases of percutaneous embolization of the pancreatic duct have been described but they regarded only single case reports. Some different tissue glues were used for embolization: fibrin glue [20], neoprene, n-butyl cyanoacrylate (NBCA) [19] and prolamine solution [14, 19]. Prolamine solution was the first sclerosing substance proposed in the treatment of persistent pancreatic fistulas as an alternative to surgery [14]. The injection of the prolamine solution into the pancreatic duct causes its occlusion with a decrease in the serum enzyme levels while the endocrine function remains the same [21]. Moreover, this agent can be opacified and observed with a CT scan. The relative disadvantages of this agent for percutaneous use include a high degree of viscosity and complete absorption with recanalization within 14 days [19].

Prolamine injection is usually performed after the unsuccessful insertion of a percutaneous drainage catheter, used to treat pancreatic collections, with or without proven fistulas, between the pancreatic duct and the pseudocyst which are more difficult to treat and need longer drainage time. The question of when to stop unsuccessful catheter drainage is not yet clear. Buecher *et al.* [14] performed percutaneous embolization 6 weeks after catheter drainage insertion because of a persistent pancreatic fistula with 200 mL fluid daily and Findeiss *et al.* [19] performed percutaneous embolization after 11 months in a pancreatic fistula having an output of more than 200 mL daily. In our experience, the patients' drainage catheters yielded 220, 150, and 200 mL fluid, respectively, daily after 2, 3, and 3 months, respectively. In unsuccessful cases, Hirota *et*

al. [15] suggested repeating the embolization at an interval of 1-2 weeks.

Independently of the correct timing and the number of embolizations, the results were good with complete resolution of the pancreatic fistula and no increase in serum glucose levels [14, 15, 18].

In our experience, percutaneous embolization was performed only once and the treatment allowed the complete closure of the pancreatic fistulas shortly thereafter. Moreover, we report a series of three patients with successful outcomes while, until now, only single case reports have, for the most part, been seen.

Chronic pancreatic fistulas following pancreatic resection is a difficult problem often requiring operative intervention due to anatomical causes. However, in selected cases, new techniques such as prolamine ductal injection offer a less invasive option with good results. This is a simple and safe technique which should follow percutaneous catheter drainage of a pseudocyst. It consists of: 1) a CT scan with barium injection via a drainage catheter to show the duct disruption and the whole Wirsung duct; 2) Wirsung duct embolization with 7.5 mL of prolamine, injected, via the catheter, under CT scan guidance. This treatment avoids surgery allowing a shorter recovery time and a lower risk of morbidity.

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