ABSTRACT

Background Pancreatic leak is one of the most feared complications after duodenopancreatectomy. Treatment depends on the leak’s severity. Conservative treatment is usually effective for leaks of lesser severity. However, conservative treatment prolongs hospital stay, thus increasing hospital cost and decreasing the patient’s quality of life. Surgical treatment is reserved for persistent, high output fistulae but, it is a high risk procedure, often with poor results. There is a plethora of endoscopic methods and devices used to address pancreatic leaks in general. However, in current literature, there is a lack of papers specifically about endoscopic treatment options for pancreatic leaks after duodenopancreatectomy. Methods We present our small series of 4 patients with pancreatic fistula after duodenopancreatectomy and duct-to-mucosa anastomosis. Our patients were treated by implanting a biflanged, fully covered metal stent. The rationale of the treatment, not yet described in the literature, is explained hereafter. Results During the postoperative days, we always documented a significant reduction of the fistula’s output. In all cases, the surgical drain’s output stopped within a few days (range: 2-5 days). One patient died because of severe, preexisting sepsis from multi-resistant Klebsiella pneumoniae five days after the endoscopic procedure. At the time of death, the fistula had already dried out. The remaining three patients had a complete fistula’s healing and no early complication was noted at first follow-up visit (1 month). One patient had a spontaneous yet uneventful migration of the stent, a few weeks after fistula’s healing. The mean follow-up is 24 months. Conclusions The endoscopic interventions were performed successfully rather late in our small study group. This complication is better treated as soon as possible so as to avoid forming a mature fistula or allow for establishment of sepsis. The present method could be a reasonable alternative in selected patients and tertiary referral endoscopic centers.

INTRODUCTION

Pancreatic leaks may occur after pancreatic surgery, trauma or pancreatitis. Pancreatic secretions collect in the peripancreatic area. Subsequently, the collection evolves to forming a pseudocyst, an internal pancreatic fistula or an external pancreatic fistula [1]. External pancreatic fistula result when a tract to the skin is formed. This occurs spontaneously or after percutaneous or surgical interventions to treat the leak.

Pancreatic duct leaks and fistulae can lead to significant morbidity and mortality. Surgical treatment is usually employed for the treatment of high output pancreatic leaks. Recently however, there is a trend towards more aggressive medical management, to avoid surgery. Successful endoscopic treatment of pancreatic leaks, either transpapillary or transmural, is now frequently reported, turning the spotlight on pancreatic endotherapy. However, there is only scarce published data about the endoscopic management of post-pancreaticoduodenectomy fistulas [1, 2, 3, 4, 5].

Pancreaticojejunostomy dehiscence is a major cause for morbidity and mortality following pancreaticoduodenectomy. In the context of Whipple’s procedure, pancreatico-jejunostomy, is generally performed with two different reconstruction techniques. The first is the classic pancreatico-jejunal invagination type anastomosis and the second is the duct-to-mucosa anastomosis. So far, several technical modifications of the above reconstructive techniques have been tested, but ultimately no method has proven superior. Our present experience is specifically focused on leaks after duct to mucosa pancreaticojejunostomy.

In our brief report, we describe our experience on endoscopic management of pancreatic leaks after duct to mucosa pancreaticojejunostomy with the insertion of a biflanged, fully covered metal stent.
MATERIALS AND METHODS

During the period between 2014 and 2016, six patients with pancreatic fistulae after pancreaticoduodenectomy were treated endoscopically in our unit. Four of these patients were treated with biflanged fully covered metal stent placement (Niti-S™ NAGI™ Stent, TaeWoong Medical, South Korea). The main data are resumed in Table 1.

All four patients underwent typical Whipple’s procedure. Pancreaticojejunostomy was accomplished with duct-to-mucosa pancreatic reconstruction. In all cases, during surgery, a pancreatic stent was inserted into the Wirsung duct to protect the anastomosis. The surgical indications were heterogeneous and included both benign and malignant diseases. All four patients developed a high-output pancreatic fistula (type III postoperative pancreatic fistula according to ISGPF classification [2]). Endoscopic treatment was delayed for a mean time of 28 days.

We performed endoscopy under fluoroscopy in the ERCP suite. We used a pediatric colonoscope (Pentax) to reach the pancreatic anastomosis through the afferent loop. After identification of the pancreaticojejunostomy dehiscence site, we inserted, over a guidewire, a short, biflanged, fully covered stent (12 mm diameter 2 cm length) (Niti-S™ NAGI™ Stent, TaeWoong Medical, South Korea) into the retroperitoneal space, in front of the pancreatic stump, through the dehiscence (Figures 1, 2). The aim of the procedure is to divert the associated fluid collection towards the jejunal loop.

The stent was inserted through-the-scope and the deployment was monitored both endoscopically and fluoroscopically. A naso-retroperitoneal catheter for lavage was placed at the first patient (Figures 3a, b). This was not repeated subsequently and was considered unnecessary as the fistula output rapidly decreased.

At the end of the intervention, the surgical drain was pulled slightly back, 4 to 6 cm, away from the origin of the pancreatic leak. This is a very important part of the procedure. By pulling back the external drain, we create a preferential flow of the fluid towards the intestinal lumen taking advantage of the associated high pressure in the retroperitoneal space.

We evaluated the reduction of fistulae’s outputs both measuring the quantity of fluid in the drain and performing an abdominal CT scan when the drain became null (to verify eventually not-drained fluid collections).

RESULTS

After the procedure, the patients were kept nil per os for at least 24 hours. On the first post-procedural day, they started drinking clear liquids and, by the second or third day, if general conditions were good, they were given a light semi-solid diet.

During the postoperative days, we always documented a significant reduction of the fistula’s output. In all cases, the surgical drain’s output stopped within a few days (range: 2-5 days). The surgical drain was removed definitively after cross-sectional imaging control (CT scan) to rule out the possibility of residual, undrained collections. If there were no other contraindications, the patients were discharged the same day.

One patient died because of severe, preexisting sepsis from multi-resistant Klebsiella pneumoniae five days after the endoscopic procedure. At the time of death, the fistula had already dried out. The remaining three patients had a complete fistula’s healing and no early complication was noted at first follow-up visit (1 month). One patient had a spontaneous yet uneventful migration of the stent, a few weeks after fistula’s healing. The mean follow-up is 24 months.

DISCUSSION

After duodenopancreatectomy with duct-to-mucosa anastomosis, the outflow of pancreatic juice follows the same rules of standard pancreatic secretion in normal anatomy: under appropriate stimulation, increased pancreatic juice production leads to elevation of intraductal pancreatic pressure, which in turn overpasses the enteral pressure, leading to pancreatic juice flow towards the enteral lumen.

In the case of pancreatic leak, pancreatic secretions accumulate into the retroperitoneal space where the pressure is higher than the enteric one. Considering the pathophysiology, this condition should promote the leak’s spontaneous resolution. However, in real life, two factors act against spontaneous healing. Firstly, the jejunal orifice diameter is very small and tends to almost close completely shortly after dehiscence of the anastomosis, thus promoting ongoing leak. Additionally, the presence of surgical drains at the region is another key factor in

Table 1. Resumed data of our case series.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Sex</th>
<th>Age</th>
<th>Indication to Whipple procedure</th>
<th>Hospital-stay length (days)</th>
<th>Timing to endoscopy (days)*</th>
<th>Technical success</th>
<th>Clinical success</th>
<th>Complications</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>62</td>
<td>Chronic pancreatitis</td>
<td>35</td>
<td>15</td>
<td>Yes</td>
<td>Yes</td>
<td>Spontaneous stent migration</td>
<td>24</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>72</td>
<td>Gastropancreatic adenocarcinoma</td>
<td>38</td>
<td>25</td>
<td>Yes</td>
<td>Yes</td>
<td>Died because of preexisting sepsis</td>
<td>1</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>69</td>
<td>Chronic pancreatitis</td>
<td>46</td>
<td>32</td>
<td>Yes</td>
<td>No</td>
<td>-</td>
<td>24</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>57</td>
<td>IPMN MD</td>
<td>32</td>
<td>28</td>
<td>Yes</td>
<td>Yes</td>
<td>-</td>
<td>24</td>
</tr>
</tbody>
</table>

*days since the onset of pancreatic fistula till the day of endoscopic procedure

IPMN MD intraductal pancreatic mucinous neoplasm of the main duct
fistula perpetuation. Atmospheric pressure at the level of the drain (which is the lowest of all pressures in this barometric balance) promotes pancreatic juice flow towards the drain. So, in many cases a new circuit is created in which pancreatic juice flows from the pancreatic stump to the peripancreatic area and finally towards the surgical drain. When this circuit is established, the fistula is not about to close.

The goal of endoscopic therapy is to restore the correct pressure gradient to facilitate pancreatic juice flow towards the intestine. The same principles work for EUS-guided transgastric drainage of peripancreatic fluid collections or cystogastrostomy: the stents promote fluid movement from the retroperitoneal space towards the gastric lumen but do not let the gastric content reach the peripancreatic area. The retroperitoneal pressure drives the fluid towards the gastric lumen (Figure 4).

There are only a few reported cases of endoscopic treatment for pancreatic leak after duodenopancreatectomy. Published data suggest that EUS-guided transmural drainage of the collection or EUS-guided pancreaticogastrostomy (in the presence of a dilated pancreatic duct) are valid options [3, 4].

Our technique is a slight modification of the EUS-guided drainage technique: i.e instead of puncturing the intestinal wall, we rather use the jejunal dehiscence site to place the stent right in front of the pancreatic stump. In most cases we found the surgical pancreatic stent in the jejunum, outside the pancreatic duct. Reinserting a new pancreatic stent is not necessary for treatment completion.

The main indication of the particular stent we used is for drainage of pancreatic pseudocyst or walled-off necrosis [5]. Inserting a biflanged, fully covered SEMS, for the treatment of post-duodenopancreatectomy leaks has never been described in the current literature. Cannulation and stenting of the main pancreatic duct is not mandatory because the SEMS helps decrease the pressure gradient between the retroperitoneal space and the intestinal lumen. Pulling the surgical drain a few centimeters back is important to re-establish the normal intra-abdominal pressure at the site of the anastomosis and drive the fluid towards the intestinal lumen.

The biflanged fully covered SEMS placement has some advantages: there is no discomfort for the patient as compared with naso-pancreatic drains. Moreover, the risk of stent occlusion is significantly lower than with plastic double-pigtail stents, so repeat interventions are avoided.
The main disadvantage is the risk of migration. All fully covered stents have a high risk of migration. Moreover, in this particular clinical setting, the stent is not placed through a stricture. On the other hand, the biflanged design of the stent provides adequate stability. We experienced one case of stent dislocation. Fortunately, it was uneventful and did not influence the clinical result. Another inconvenience that we encountered is difficulty opening the stent because of tight jejunal angulation after the surgical reconstruction, at least in our cases. Long-term side effects of using metal stents are few because, as explained before, for this type of complication, they guarantee better patency than plastic ones and naso-retroperitoneal drains. However, a decubitus on the near vascular structures can cause bleeding. In our experience, migration can be a long-term side effect and it can virtually cause a pseudocyst formation if the stent displaces early and the fistula is not well consolidated. The main limitation of the present paper is represented by the small number of cases and on the fact that the procedures were performed in a tertiary referral endoscopy center. Randomized controlled studies would be desirable although difficult to realize in these clinical sets.

The outcomes about re-do surgery are available in the international literature [2, 6]. Our method has the main advantage to shorten the time of fistula's healing in comparison with standard conservative therapy.

CONCLUSION

The endoscopic interventions were performed rather late in our small study group. This complication is better treated as soon as possible to avoid forming a mature fistula or allow for establishment of sepsis. Further studies are also needed to sensitize surgeons to refer patients early for endoscopic treatment.

Authors’ Disclosures

Drs Massimiliano Mutignani, Lorenzo Dioscoridi, Edoardo Forti, Francesco Pugliese, Marcello Cintolo, Alberto Tringali and Stefanos Dokas have no conflicts of interest or financial ties to disclose.

Conflict of Interest

The authors declare that they have no conflict of interest.

References