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ENDOSCOPIC ULTRASOUND-GUIDED ENDOSCOPIC TRANSMURAL DRAINAGE OF PANCREATIC PSEUDOCYSTS

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ABSTRACT – ***Background*** - Surgery is the traditional treatment for symptomatic pancreatic pseudocysts, but the morbidity is still too high. Minimally invasive endoscopic approaches have been encouraged. ***Aims*** - To evaluate the efficacy of endoscopic ultrasound-guided endoscopic transmural drainage of pancreatic pseudocysts. ***Methods*** - From January, 2003 to August, 2006, 31 consecutive symptomatic patients submitted to 37 procedures at the same endoscopic unit were retrospectively analysed. Chronic and acute pancreatitis were found in, respectively, 17 (54.8%) and 10 (32.3%) cases. Bulging was present in 14 (37.8%) cases. Cystogastrostomy or cystoduodenostomy were created with an interventional linear echoendoscope under endosonographic and fluoroscopic control. By protocol, only a single plastic stent, without nasocystic drain, was used. Straight or double pigtail stents were used in, respectively, 22 (59.5%) and 15 (40.5%) procedures. ***Results*** - Endoscopic ultrasound-guided transmural drainage was successful in 29 (93.5%) patients. Two cases needed surgery, both due to procedure-related complications. There was no mortality related to the procedure. Twenty-four patients were followed-up longer than 4 weeks. During a mean follow-up of 12.6 months, there were six (25%) symptomatic recurrences due to stent clogging or migration, with two secondary infections. Median time for developing complications and recurrence of the collections was 3 weeks. These cases were successfully managed with new stents. Complications were more frequent in patients treated with straight stents and in those with a recent episode of acute pancreatitis. ***Conclusions*** - Endoscopic transmural drainage provides an effective approach to the management of pancreatic pseudocysts.

HEADINGS – Pancreatic pseudocyst. Drainage. Endosonography. Prostheses and implants.

INTRODUCTION

The surgical management of pancreatic pseudocysts (PPC) has traditionally been appreciated for a long time as the treatment of choice for symptomatic and, especially, infected PPC. Although surgery is effective, it may be associated with complications in up to 35% of the cases and with a mortality rate close to 10%[18]. With these results, the development of minimally invasive surgical approaches has been encouraged. Among these alternatives, the endoscopic transmural drainage is surely the major breakthrough over recent years, especially after the advent of the endoscopic ultrasound (EUS) longitudinal scanners for guidance of transmural punctures[3, 4, 8, 11]. This technique makes possible the puncture of cysts under endosonographic control even without bulging of the gastric or duodenal wall, and accidents by puncturing blood vessels can be prevented[7, 12, 15], which used to occur in up to 6% of the cases without endosonographic control[6, 13, 14]. Once established the endoscopic access to the PPC, a plastic stent can be placed between the pseudocyst and the gastric lumen (cystogastrostomy) or the duodenal lumen (cystoduodenostomy) for continuous drainage.

The aim of this study was to evaluate the results of the endoscopic transmural drainage of pancreatic pseudocysts by means of an interventional linear echoendoscope at the same referral center.

METHODS

Patients

Between January 2003 and August 2006, EUS-guided transmural drainage of PPC was carried out in 31 patients (23 men, mean age: 56 years (12-82)), totalling 37 procedures (Table 1). The underlying diagnosis was chronic and acute pancreatitis in, respectively, 17 (54.8%) and 10 (32.3%) patients. Three cases with chronic pancreatitis were suffering from a new attack of acute pancreatitis, and seven patients had no history of inflammatory pancreatic disease. Every patient, except one, had a single anechoic cystic lesion without debris, and the review of the cyst aspirate analyses confirmed the sterile fluid collection. The PPC were originated after surgical interventions in six cases. Esophagogastroduodenoscopy revealed an extrinsic compression for selecting the ideal puncture site in 14 (37.8%) patients. The mean size

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of the lesions was 6.3 (3-15) cm. The criteria for endoscopic drainage, once eliminated the suspicion of malignancy and any communication with the main pancreatic duct by endoscopic retrograde pancreatography or magnetic resonance imaging, were presence of symptomatic pancreatic pseudocyst with no spontaneous resolution after 6 weeks; enlargement of the cyst; absence of multiloculated cystic lesions; distance pseudocyst from enteric wall <1 cm, absence of interposed vessels and good coagulation patterns (prothrombin time >60%, platelets >80.000/mm^3). A cystogastrostomy was performed in 33 cases and a cystoduodenostomy in 4 cases.

TABLE 1. Characteristics of patients submitted to EUS-guided endoscopic transmural drainage of pancreatic pseudocysts

Patients (n)	31
Procedures	37
Sex (M / F)	23 / 8
Age (years)	56.3 +/- 15.8 (12–82)
Chronic pancreatitis*	17 / 31 (54.8%)
Acute pancreatitis	10 / 31 (32.3%)
Location of the PPCs	
Head	13 (35.2%)
Body	12 (32.4%)
Tail	12 (32.4%)
Cyst diameter (cm)	6.3 +/- 2.8 (3–15)
Bulging	14 / 37 (37.8%)
Post-surgical collections**	6 /37 (16.2%)
Plastic stent	
Straight	22 (59.5%)
Double pigtail	15 (40.5%)

*three patients suffering from recurrent acute pancreatitis
**one patient with chronic pancreatitis

Methods

The EG38UT (Pentax-Hitachi®, Hamburg, Germany) was the interventional EUS endoscope for all procedures. Transmural drainage was performed by the same experienced endoscopist (M.G.) under conscious sedation in the fluoroscopy room under EUS, endoscopic and fluoroscopic guidance with the patient in the left side or prone position after overnight fast before the procedure. Antibiotic prophylaxis was given for all patients during and after the procedure. The sequence of individual steps is delineated as follows[9, 10, 11]:

1. location of the contact zone between the cyst wall and the gastric or duodenal wall;
2. Doppler assessment to check interposed vessels;
3. puncture of the cyst wall by means of a 10Fr cystostome (COOK®, Limerick, Ireland), followed by the insertion of a 0.035 guide wire in case of double pigtail stents, or a needle-wire from the straight stent device (Giovannini Needle Wire Oasis; Ref. NWOA-10; COOK®, Limerick, Ireland). With this last device, the internal rigid part of the tip of the needle-wire is removed and the tip of the needle-wire become flexible;
4. aspiration of a sample of the cyst contents for biochemical, cytological and tumoral markers analysis, as well as for gram stain and culture;
5. widening of the size of the tract by means of the external catheter of the cystostome for double pigtails stents or by the dilator catheter from the needle set for straight stents;
6. instalation of the plastic stent, either straight (Giovannini needle set) or double pigtail (SOLUS; Ref.ZSS-10-4-RB; COOK®, Limerick, Ireland). The type of stent used in each patient was assigned in a non randomized fashion, depending on stent availability.

After stent placement, patients were imaged by computed tomography within 48-72 hours and 3 months later. In case of symptoms reappearance, patients were submitted to a new computed tomography. Stent was removed after 3 months, but, in those cases with chronic pancreatitis complaining of pain before the endoscopic drainage, it was left in place until spontaneous expulsion.

Statistical analysis

Numerical variables were expressed as mean ± standard deviation. Categorical variables were analysed by $\chi 2$ test with Yates correction, relative risk and Fischer exact test. The significance level was 5% for all statistical procedures. The data were processed and analyzed by means of Epi Info version 6.04 statistical software. Thirteen cases whose follow-up was shorter than 4 weeks were taken into account only for evaluation of demographics and procedure-related complications, and were considered ineligible for further analysis. This study was approved by the Research Ethics Board of Paoli-Calmettes Institute and written informed consent was obtained from every patient to undergo the procedure.

RESULTS

EUS-guided puncture of pancreatic pseudocysts and stent placement were successful in all patients, even though two cases have developed procedure-related complications - one pneumoperitonium and another case with peritonitis, both managed surgically. There was no procedure-related mortality. Twenty-four patients were followed-up for more than 4 weeks, with a mean follow-up of 12.6 (1-43) months. During this time frame, six (25%) patients had symptomatic recurrences due to stent clogging (three cases) or migration (three cases). In these cases, there was secondary infection in two PPC. All these cases were successfully managed with new stents. In fact, a single endoscopic procedure was the curative treatment for 23 (74.2%) patients. Solely one patient deceased due to coronary heart disease.

The general number of complications are exposed in the Table 2. The median time for developing late complications, either obstruction or dislocation, followed by the recurrence of the fluid collection was 3 (1-79) weeks. Some predictive factors for the development of late complications and, as a consequence, recurrence were evaluated, but none of them reached statistically significant difference (Table 3). Patients after an episode of acute pancreatitis had more chance to develop complications (50% vs 33.3%; $P = 1.00$). On the other hand, chronic pancreatitis showed a lower risk (18.2% vs 33.3%; $P = 0.58$). The occurrence of complications was a little higher in patients treated with straight stents. No patient with PPC in the pancreatic head developed any sort of complication,

whereas they occurred in 6 of 14 cases with pseudocysts in the body or tail of the pancreas. Finally, neither the size of the pseudocyst nor the presence of bulging influenced significantly the occurrence of complications.

TABLE 2. Complications in patients submitted to EUS-guided endoscopic transmural drainage of pancreatic pseudocysts (n = 24)

Procedure-related complications §	2 (5.4%)
Late obstruction	3 (12.5%)
Late migration	3 (12.5%)
Recurrence	6 (25%)
Secondary infection *	2 (8.3%)

§ one pneumoperitonium, and one peritonitis (n = 37)
* Both cases in patients developing recurrence due to obstruction or migration of the stent

TABLE 3. Predictive factors of late complications in patients submitted to EUS-guided endoscopic transmural drainage of pancreatic pseudocysts (n = 24)

	Complications	RR	CI95%	*P*
Acute pancreatitis §	2/4 vs 2/6	1.50	0.34–6.70	1.00
Chronic pancreatitis §	2/11 vs 2/6	0.55	0.10–2.95	0.58
Presence of bulging	3/10 vs 3/14	1.40	0.35–5.56	0.66
Straight or pigtail stent	4/13 vs 2/11	1.69	0.38–7.55	0.64
Head vs body/tail PPC	0/8 vs 6/16	---	------	0.06
PPC ≥5 cm	4/16 vs 2/8	1.00	0.23–4.35	1.00

§ patients with acute pancreatitis in the setting of chronic pancreatitis were excluded from the analysis (n = 3)

DISCUSSION

In this study evaluating the endoscopic management of PPC, patients were constituted mostly by men over the sixth decade of life, with chronic pancreatitis, and cystogastrostomy was the most common endoscopic procedure. Puncture of pancreatic pseudocysts and stent placement were successful in all patients, with two procedure-related complications, both requiring surgical intervention, but with no mortality related to the endoscopic approach. The symptomatic recurrence rate was lower than 30%, either due to stent clogging or migration, but all these cases were successfully managed by a new endoscopic drainage. A single endoscopic procedure was the curative approach for almost three-quarters of these patients.

Our results are in line with the literature about endoscopic management of pancreatic pseudocysts. In the experience of DOHMOTO et al.[7], 47 patients with PPC were treated by endoscopic drainage. The resolution of the pseudocysts was 89%. Other six (13%) patients suffered a relapse after removal of the stent, and a new stent was necessary in six (13%) cases due to occlusion or migration. Overall, six (13%) patients had to undergo surgery. SMITS et al.[16] evaluated the results of the endoscopic drainage in 37 patients with pseudocysts and chronic pancreatitis. The success of the endoscopic drainage was 92%. The procedure-related complications rate was 16%. Seven (19%) patients developed secondary infection, and three (8%) patients had recurrences. Overall, 10 (27%) cases were submitted to surgery. Our study had not a long follow-up, but in relation to this point, SHARMA et al.[15] evaluated the long-term outcome of the endoscopic management of PPC. Over a mean follow-up of 44 months, the symptomatic recurrence was 8%, and all these cases were successfully managed with a new endoscopic procedure.

VOSOGHI et al.[18] reported their results of EUS-guided pseudocyst drainage and performed a literature review of other 11 studies. Specifically about transmural drainage, 99 patients were analysed. Endoscopic drainage was successful in 94% of these cases, with 9% of symptomatic recurrence, and a complication rate of 1.4%, ranging from 0% to 7%. The most common complications with the endoscopic procedure were infection (5%), bleeding (1%) and perforation (1%), and there was no death related to the endoscopic treatment. In relation to our experience, our global success was in line with the results reviewed by VOSOGHI et al.[18].

Patients with chronic pancreatitis responded most positively to the endoscopic procedure, with fewer complications, but not in a statistically significant manner. The importance to differentiate acute from chronic PPC for guiding the best therapeutical approach is reinforced by other authors[1, 2]. BARON et al.[2] evaluated the outcomes for patients with symptoms caused by pancreatic fluid collections referred to endoscopic drainage. Resolution was significantly more frequent in patients with chronic pseudocysts (92%) than acute pseudocysts (74%). Besides, complications rates were similar for patients with chronic (17%) and acute pseudocysts (19%). At a median follow-up of 2 years after successful endoscopic treatment, for patients with acute and chronic pseudocysts, pancreatic fluid collections had recurred in, respectively, 9% and 12% of these cases. In the experience reported by BARON et al.[2], the endoscopic approach was not more hazardous for acute pseudocysts. Nevertheless, in our experience[11] recently published dealing with EUS-guided transmural drainage of 62 pancreatic collections (36 pseudocysts and 26 abscesses), patients were more likely to develop complications after an episode of acute pancreatitis (38.4% vs 10%; $P = 0.083$). Despite the small number of patients, the same was true (50% vs 33.3%; $P = 1.0$) in this new study with a more selected group of patients.

Moreover, the size of the pseudocysts was not a key factor for the occurrence of procedure-related or late complications. The same was true in the study of SOLIANI et al.[17], where hospital mortality, morbidity, recurrence rate and hospital stay were not influenced by the size of the PPC, although large cysts (>10 cm) following an episode of acute pancreatitis had usually required invasive treatments due to persistent symptoms or complications. In addition, our experience is still too scarce to conclude about the safety of this endoscopic procedure for patients harbouring pseudocysts bulging into the stomach or duodenum, as well as for those collections located in the body and tail of the pancreas, but our initial results suggest that both conditions might increase the occurrence of late complications. Further clinical trials must be conducted to answer these questions.

Specifically concerning the particular types of plastic stents, there was a trend showing a higher complications rate of the straight stents over the double pigtail stents. However, the occurrence of stent-related complications, as well as symptomatic recurrence, for both kinds of stents did not reach a significant difference, probably due to the retrospective design of the study, and the small number of patients. CAHEN

et al.[5] suggest that complications could be reduced by using double pigtails instead of straight stents, but this hypothesis was not tested in a randomized controlled trial. On the other hand, even with a complication rate of 34%, the success of the endoscopic drainage with straight stents performed by these authors was 97%, with surgery being required in only 9%. During a median follow-up of 43 months, 16% of these patients underwent an additional nonendoscopic treatment for a persistent or recurrent cyst. Overall, the endoscopic drainage was successful in 71% of the cases. NORTON et al.[12], evaluating 19 patients in a non-comparative study, believe that multiple double pigtail stents seem to be the best option for resolution of PPC. Nonetheless, we have recently reported that the insertion of two stents into the same pseudocyst increased the complications rate (40% vs 13%; $P = 0.185$)[11]. This way, in order to arrange an homogeneous study group, we decided by protocol to use a single plastic stent without an auxiliary nasocystic drain. Adopting this routine, almost 75% of these patients have been successfully managed with a single procedure. As we can see, the number of stents and the value of the double pigtails in relation to the straight stents for the treatment of PPC are too far to reach a consensus. Prospective randomised controlled trials with a larger number of patients, employing different types and number of plastic stents for the treatment of pancreatic pseudocysts are necessary to define the ideal management of these pancreatic collections in the setting of acute or chronic pancreatitis.

CONCLUSIONS

Given the absence of mortality, as well as the low complication and recurrence rates associated with endoscopic drainage, which can be successfully managed endoscopically, we believe that these aspects make the internal drainage by EUS-guide endoscopic transmural drainage the first choice of treatment for patients with single noninfected pseudocysts, though further studies are required to stablish the standardisation of this endoscopic procedure for the ideal management of these pancreatic collections.

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Lopes CV, Pesenti C, Bories E, Caillol F, Giovannini M. Drenagem transmural de pseudocistos de pâncreas guiada por ecoendoscopia. Arq Gastroenterol. 2008;45(1):17-21.

RESUMO – ***Racional*** - A abordagem cirúrgica é o tratamento tradicional para os pseudocistos sintomáticos de pâncreas, contudo a morbidade permanece elevada. Terapêuticas endoscópicas minimamente invasivas têm sido encorajadas. ***Objetivo*** - Avaliar a eficácia da drenagem endoscópica transmural de pseudocistos de pâncreas guiada por ecoendoscopia. ***Métodos*** - De janeiro de 2003 a agosto de 2006, 31 pacientes sintomáticos submetidos a 37 procedimentos no mesmo centro de referência foram analisados retrospectivamente. Pancreatite crônica e aguda foram detectadas em, respectivamente, 17 (54,8%) e 10 (32,3%) pacientes. Abaulamento da parede esteve presente em 14 (37,8%) casos. Cistogastrostomias ou cistoduodenostomias foram criadas com um ecoendoscópio linear sob controle endosonográfico e fluoroscópico. Como rotina, apenas uma única prótese plástica foi empregada, sem dreno nasocístico. Próteses retas ou "double pigtail" foram empregadas em, respectivamente, 22 (59,5%) e 15 (40,5%) procedimentos. ***Resultados*** - A drenagem endoscópica foi adequada em 29 (93,5%) pacientes. Dois casos necessitaram intervenção cirúrgica por complicações do procedimento. Não houve mortalidade relacionada ao procedimento. Vinte e quatro pacientes contaram com seguimento superior a 4 semanas. Durante seguimento médio de 12,6 meses, ocorreram seis (25%) recurrências sintomáticas por obstrução ou migração da prótese, com infecção secundária em dois casos, todos manejados com novas próteses. O tempo mediano para ocorrência de complicações foi de 3 semanas. Complicações tardias foram mais freqüentes em pacientes tratados com próteses retas e naqueles com história recente de pancreatite aguda. ***Conclusões*** - A drenagem endoscópica transmural constitui abordagem efetiva para o manejo dos pseudocistos de pâncreas.

DESCRITORES – Pseudocisto pancreático. Drenagem. Endossonografia. Próteses e implantes.

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