Studies of endoscopic ultrasound-guided drainage for pancreatic pseudocysts and abscesses: a university hospital-based experience

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Background: Recently, endoscopic ultrasound (EUS)-guided drainage is used to treat pancreatic pseudocysts and abscesses. Endoscopic necrosectomy is now rarely performed clinically. We retrospectively studied the effectiveness and complications of these therapeutic procedures.

Methods: The subjects comprised 26 patients with symptomatic pancreatic pseudocysts, pancreatic pseudocysts 5 cm or more in diameter, or pancreatic abscesses from April 2001 through May 2010. The patients underwent EUS-guided drainage alone or combined with other endoscopic techniques. The mean age of the patients was 54.5 years (range, 21-81 years). The male:female ratio was 22:4.

Results: The mean cyst size was 12.9 cm (range, 5.2-30.0 cm) in diameter. The treatment procedures were EUS-guided drainage alone in 11 patients, with adjuvant pancreatic-duct stenting in 7, adjuvant pancreatic-duct stenting and percutaneous drainage in 3, and endoscopic necrosectomy in 5. The technical success rate of EUS-guided drainage was 100% (26/26), and the treatment success rate was 92.3% (24/26). Complications were pneumoperitoneum in 1 patient, bleeding from a fistula after necrosectomy in 2, and cardiac valve vegetation in 1. Regarding long-term outcomes, 2 (9.5%) of 21 patients had recurrent pancreatic pseudocysts.

Conclusions: EUS-guided drainage and endoscopic necrosectomy are relatively safe and effective treatment techniques for pancreatic pseudocysts and abscesses.

Key words: Endoscopic ultrasonography-guided drainage, Endoscopic drainage, Pseudocysts, Pancreatic abscess, Necrosectomy

Abbreviations: EUS, Endoscopic ultrasonography; EPS, Endoscopic pancreatic stenting; FNA, fine needle aspiration; CT, Computed tomography

Introduction

Pancreatic pseudocysts result from the leakage of pancreatic juice from pancreatic tissue or ducts, followed by the retention of such fluid in intrahepatic and extrahepatic tissue. Pseudocysts can be caused by acute pancreatitis, episodes or recurrence of chronic pancreatitis, pancreatic surgery, or abdominal trauma. Infection of a pancreatic pseudocyst leads to the formation of a pancreatic abscess.1-3 Pseudocysts are usually associated with mild symptoms such as abdominal pain and distension, and rarely present with bleeding or infection. Abscesses associated with infection can lead to a high fever and sepsis, resulting in poor outcomes. Treatment is therefore essential.4-10 Necrotizing pancreatitis occurs in about 20% of patients with acute pancreatitis.5-8 Infection of necrotic material is associated with a mortality rate of about 50%. Death is usually caused by sepsis and multiple organ failure.1,5-8,10

Pancreatic abscesses, symptomatic pseudocysts, and pancreatic pseudocysts exceeding 5 to 7 cm in diameter 4 to 8 weeks after the onset of pancreatitis generally require treatment, such as endoscopic pancreatic duct stenting, endoscopic or percutaneous drainage, and endoscopic ultrasound (EUS)-guided drainage. Since the report by Grimm et al.11 in 1992, EUS-guided drainage (EUS-D) has been widely used in clinical practice. In general, surgical debridement remains the standard
EUS-guided drainage of pancreatic pseudocysts

treatment for pancreatic abscesses associated with pseudocyst infection or the removal of necrotic tissue in patients with necrotizing pancreatitis. Recently, necrosectomy, performed by directly inserting an endoscope into an abscess cavity to remove necrotic material, has become a treatment option.12-15 We report the outcomes of treatment for pancreatic pseudocysts and abscesses in a university hospital. We also describe the characteristics of patients who required necrosectomy and complications associated with endoscopic procedures.

Patients and Methods

Study design
This retrospective study was conducted in Kitasato University East Hospital. The study group was comprised of 26 patients, with symptomatic pancreatic pseudocysts, pancreatic pseudocysts 5 cm or greater in diameter, or pancreatic abscesses associated with infection, who were admitted to the Kitasato University East Hospital from April 2001 through May 2010. Treatment was managed by the Department of Gastroenterology and comprised of EUS-D alone or combined with endoscopic pancreatic-duct stenting with or without percutaneous drainage, or endoscopic necrosectomy. EUS-D procedures were done by 5 doctors who have performed at least 50 or more of EUS-FNAs and took commonly 30-60 minutes. The mean age of the patients was 54.5 years (range, 21-81 years). The male:female ratio was 22:4, indicating a preponderance of men. This study was conducted in accordance with the Good Clinical Practice Guidelines. Written informed consent was obtained from all patients before beginning the endoscopic procedures.

Figure 1. EUS-drainage for pancreatic pseudocyst
A. Puncture with 19-guage needle
B. Filling contrast into pseudocyst
C. Placement of internal and external stent
D. The CT revealed a large pseudocyst.
E. After the pseudocyst was treated by EUS-drainage, it was reduced.
Medical records of all patients were reviewed to obtain information on physical findings, such as body temperature, pulse rate, and local tenderness; laboratory data; endoscopic findings; the number of treatment sessions; clinical course; and computed tomographic (CT) findings. Regarding drainage, we examined whether patients underwent internal, external, or internal and external drainage, whether or not percutaneous drainage was performed concurrently, and whether or not a pancreatic-duct stent was used.

Treatment strategy and techniques for endoscopic drainage
Pseudocysts that were symptomatic or more than 5 to 7 cm in diameter: Pseudocysts were first observed for at least 4 weeks after an episode of pancreatitis to confirm that the cysts did not shrink or become asymptomatic. In principle, endoscopic retrograde cholangiopancreatography was then performed to examine any communications with the pancreatic duct. If the cyst communicated with the pancreatic duct, a 7- to 10-French pancreatic-duct stent was emplaced, and CT was performed after about 1 week of observation. If the pseudocyst disappeared or nearly disappeared, treatment was completed. If the response was inadequate, there was no communication with the pancreatic duct, or the cyst was near the gastrointestinal tract (within about 1 cm), EUS-D was performed (Figure 1). If the distance between the cyst and gastrointestinal tract exceeded 1 cm, percutaneous or surgical drainage was performed. EUS-D was performed with 7-French tubes. An internal drain (7-French pigtail catheter) and an external drain (a 7-French endoscopic nasobiliary drainage tube with side vents opened at 3-cm intervals, compatible with the size of the cyst cavity) were emplaced.

Pancreatic abscesses: If the abscess was near the gastrointestinal tract, EUS-guided direct puncture was performed to create a fistula the same as the pseudocyst treatment. At the first necrosectomy session, the fistula was dilated with a 20-mm controlled radial expansion balloon (Boston Scientific Co., Ltd., Boston, MA, USA). After placement of an endoscopic overtube, a video endoscope (model GIF-Q260J; Olympus Optical Co., Ltd., Tokyo) was directly inserted into the abscess cavity.

Figure 2. Necrosectomy for pancreatic abscess with GF-Q260J
A. Dilatation of a fistula with a 20 mm CRE balloon
B. Infected necrotic tissue was revealed.
C. The abscess cavity was cleaned up by a necrosectomy.
D. The removed necrotic tissue
E. The pancreatic abscess before necrosectomy
F. The abscess cavity disappeared after necrosectomy.
Necrotic material was grasped with a 5-pronged forceps, a basket, or a retrieval net. The material was removed by withdrawing and inserting the endoscope (Figure 2). These procedures were repeated to perform treatment. If treatment was inadequate, or the abscess cavity was partitioned, puncture was done via a different route, or a percutaneous fistula was created under ultrasound guidance or CT. The endoscope was then withdrawn and inserted to remove the necrotic material. If cure was not obtained after these procedures, surgical intervention was considered.

For treatment, an intravenous line was set up, and antibiotics were given by infusion. After treatment, the patients fasted. Oral intake of food was resumed from 5-10 postoperation days after confirming that the cysts or abscesses had almost disappeared, with no signs of infection on the CT, blood analysis, or other clinical examinations. Both pancreatic pseudocysts and pancreatic abscesses were followed up by CT at 1- to 3-week intervals to evaluate therapeutic effectiveness.

Statistical analysis
The data collected from the medical records of each patient and EUS-FNA (fine needle aspiration) data sheet were analyzed for sex ratio, averaged age, size, and etiology of pseudocyst/abscess. The comparison of size, number of sessions, necessity of necrosectomy was done using the Mann-Whitney U test and \( \chi^2 \) for independence test. P values less than 0.05 were considered to indicate statistical significance.

Results
Patients
From April 2001 through May 2010, a total 26 patients were admitted to the Kitasato University East Hospital because of symptomatic pancreatic pseudocysts, pancreatic pseudocysts 5 cm or more in diameter, or pancreatic pseudocysts or abscesses associated with infection. Their mean age was 54.5 years (range, 21-81 years). The male:female ratio was 22:4, indicating a preponderance of men. The underlying causes of pancreatic pseudocysts and abscesses were acute pancreatitis in 3 patients, chronic pancreatitis in 13, and severe pancreatitis in 10. The mean diameter of pancreatic pseudocysts and abscesses at the start of treatment was 12.9 cm (range, 5.2-30.0 cm) in maximum diameter, and there was no significant difference in the mean size among these 4 groups (Table 1).

Treatments outcomes
The treatment procedures were EUS-D alone in 11 patients (42%), EUS-D with adjuvant pancreatic-duct stenting in 7 (27%), with adjuvant pancreatic-duct stenting and percutaneous drainage in 3 (12%), and endoscopic necrosectomy in 5 (19%) (Table 1). The technical success rate of endoscopic treatment based on EUS-D was 100% (26/26) (Table 2). The treatment success rate, based on the number of cases that disappeared or shrank, was 92.3% (24/26). One patient, who was treated in the early phase of the study prior to the introduction of necrosectomy, could not continue the treatment because of reinfection and, therefore, underwent emergency surgical necrosectomy. Another patient was elderly and had chronic heart failure during the early phase of the EUS-D. Septic shock developed on the day the patient was scheduled for surgery. Therefore the surgery could not be performed, and the patient died.

Five (19%) of the 26 patients required necrosectomy owing to the presence of necrotic material inside a pseudocyst or abscess. Treatment required an average of 11.4 sessions (range, 2-18 sessions), and the number of sessions required in the necrosectomy group was significantly larger than those in the other groups (Table 2). The proportion of patients who required necrosectomy after severe pancreatitis (40.0%, 4 of 10 patients) was

<table>
<thead>
<tr>
<th>Treatment</th>
<th>N</th>
<th>Sex</th>
<th>Acute</th>
<th>Chronic</th>
<th>Severe</th>
<th>Mean size (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUS-drainage</td>
<td>11 (42%)</td>
<td>8:3</td>
<td>2</td>
<td>6</td>
<td>3</td>
<td>10.8</td>
</tr>
<tr>
<td>+ EPS</td>
<td>7 (27%)</td>
<td>7:0</td>
<td>1</td>
<td>5</td>
<td>1</td>
<td>13.3</td>
</tr>
<tr>
<td>+ Percutaneous-drainage</td>
<td>3 (12%)</td>
<td>3:0</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>14.2</td>
</tr>
<tr>
<td>+ Necrosectomy</td>
<td>5 (19%)</td>
<td>4:1</td>
<td>0 (0%)</td>
<td>1 (7.7%)</td>
<td>4 (40.0%)</td>
<td>16.2</td>
</tr>
<tr>
<td>Total</td>
<td>26</td>
<td>22:4</td>
<td>3</td>
<td>13</td>
<td>10</td>
<td>12.9 (ave)</td>
</tr>
</tbody>
</table>

EPS, endoscopic pancreatic stent
Table 2. Efficacy of endoscopic treatment for pancreatic pseudocyst and abscesses

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Technical success</th>
<th>Session (mean)</th>
<th>Efficacy of treatment (disappear/shrink/op/death)</th>
<th>Treatment success</th>
<th>Complications</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>EUS-drainage</td>
<td>11/11 (100%)</td>
<td>1.4</td>
<td>8/2/0/1</td>
<td>10/11 (91%)</td>
<td>Pneumoperitoneum: 1</td>
<td>-</td>
</tr>
<tr>
<td>+ EPS</td>
<td>7/7 (100%)</td>
<td>1.6</td>
<td>4/3/0/0</td>
<td>7/7 (100%)</td>
<td></td>
<td>Reccurence: 1</td>
</tr>
<tr>
<td>+ Percutaneous-drainage</td>
<td>3/3 (100%)</td>
<td>3.0</td>
<td>2/0/1/0</td>
<td>2/3 (67%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>+ Necrosectomy</td>
<td>5/5 (100%)</td>
<td>11.4</td>
<td>5/0/0/0</td>
<td>5/5 (100%)</td>
<td>Bleeding fistula: 2</td>
<td>Valvular vegetation: 1</td>
</tr>
<tr>
<td>Total</td>
<td>26/26 (100%)</td>
<td>3.5</td>
<td>19/5/1/1</td>
<td>24/26 (92.3%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

significantly higher than that after chronic pancreatitis (7.7%, 1 of 13 patients; \( P = 0.03 \)) (Table 1).

Complications
Regarding complications associated with EUS-D, only 1 patient had pneumoperitoneum (Table 2). However, patients undergoing necrosectomy had a high incidence of complications. Bleeding from a fistula dilated with a 20-mm controlled radial expansion balloon catheter (Boston Scientific) occurred in 2 patients, and their hemoglobin concentration decreased about 2 g/dL. In another patient, who underwent necrosectomy, cardiac-valve vegetation, attributed to bacteremia, developed after treatment, so valve replacement was performed.

Follow-up observations
Among the 21 patients who were followed up for at least 6 months (mean, 13.2 months), 2 patients had recurrence of pancreatic pseudocysts after the onset of chronic pancreatitis or severe pancreatitis (pancreatic duct disruption) (Table 2). These pseudocysts were treated by EUS-D alone. There were no other significant complications.

Discussion
Pancreatic pseudocyst is a complication that can be triggered by factors, such as acute pancreatitis, primary and recurrent episodes of chronic pancreatitis, pancreatic surgery, and abdominal trauma. In previous studies, about 40% of pseudocysts disappeared spontaneously within 6 weeks after disease onset, and the incidence of complications was 20%.\(^1\) During weeks 7 to 12, the spontaneous disappearance rate was 8%, with an incidence of complications of 46%. From weeks 13 to 18, the spontaneous disappearance rate was 0%, and the incidence of complications was 75%.\(^1,10\) However, another study reported that pancreatic pseudocysts have a higher spontaneous disappearance rate and a lower incidence of complications.\(^16\)

Treatment is generally indicated for pseudocysts more than 5 to 6 cm in diameter that remain after 4 to 8 weeks of follow-up.\(^1,2,8-10\) Pancreatic abscesses resulting from the infection of a pancreatic pseudocyst can lead to a high fever and sepsis, resulting in potentially fatal outcomes. Emergency treatment is therefore absolutely indicated for this condition. Necrotizing pancreatitis develops in about 20% of patients with acute pancreatitis. Necrotic material is easily infected, creating a pancreatic abscess and potentially triggering sepsis and multiple organ failure. The mortality rate may reach as high as 50%.\(^1,5-8,10\) The removal of necrotic material is therefore imperative in the treatment of necrotizing pancreatitis and comorbid resulting sepsis.

Transpapillary pancreatic-duct stenting is indicated if pseudocysts communicate with the pancreatic duct. Because this procedure is the most minimally invasive, it is considered a first line therapy. However, the initial resolution success rate of this procedure is not 100%; therefore, other procedures are required for patients who have poor response or recurrence.\(^17\) Because we studied patients who underwent EUS-D, we preformed EUS-D for many of our patients who did not respond satisfactorily to transpapillary pancreatic-duct stenting.

Endoscopic drainage is a procedure for internal drainage described by Rogers et al.\(^18\) in 1975. It is a physiological technique designed to return pancreatic juice to the gastrointestinal tract. The risk of causing a pancreatic fistula is negligible in contrast to percutaneous drainage.\(^18\) Generally, the bulge in the gastrointestinal tract is directly punctured under endoscopic guidance, and a drainage tube is emplaced. If there is no bulge in the gastrointestinal tract, it is more difficult to determine the puncture site. To solve such problems, EUS-D was developed by Grimm et al.\(^11\) in 1992. Using endoscopic ultrasonography allows the puncture to be made into the
abdominal wall at the nearest site to the access while, at the same time, avoiding puncturing large vessels by using Doppler ultrasound guidance. Because of these advantages, EUS-D is now widely used to treat pancreatic pseudocysts and abscesses.11,19

Percutaneous drainage is performed by puncturing the abdominal wall under CT or EUS guidance. However, because this procedure carries the risk of creating a pancreatic fistula, it is generally used in patients in whom target lesions are difficult to approach because they are located far from the gastrointestinal tract.

Vosoghi et al.20 performed a meta-analysis of treatment methods for pancreatic pseudocysts. Surgical treatment had a high success rate (100%), a low recurrence rate (range, 6.0%–8.5%), but a high mortality rate (range, 1.0%–8.5%). In contrast, treatment with endoscopic and EUS-D had a lower success rate (range, 90%–94%), a slightly higher recurrence rate (range, 9%–12%), but the mortality rate was 0%. Recently, these endoscopic procedures are widely used in clinical practice.

Varadalajulu et al.21 conducted a retrospective case-controlled study comparing surgical intervention with EUS-D. Although therapeutic effectiveness did not differ significantly between EUS-D and surgical treatment, the former was associated with a significantly shorter hospital stay, as well as a significantly lower cost. EUS-D was, therefore, recommended as the first line treatment for pancreatic pseudocysts.21

Kahaleh et al.22 and Park et al.23 conducted prospective studies comparing endoscopic drainage with EUS-D and reported that therapeutic effectiveness did not differ significantly between these procedures. Park et al.23 concluded that EUS-D should be employed for the treatment of non-bulging pseudocysts. Seewald et al.24 summarized the outcomes of EUS-D. In their study, its technical success rate was 91% to 100%, and the pseudocyst/abscess cure rate was 73% to 100%.24 In the present study, we obtained a technical success rate of 100% and a cure rate of 92.3% (24 of 26 cases) which was consistent with previously reported results.

Endoscopic necrosectomy is a minimally invasive technique, to our knowledge, first reported by Seifert et al.25 in 2000. In general, surgical necrosectomy is effective, but can cause serious major complications in the acute phase, lead to long-term complications, or even death. In a recent study of 88 patients with necrotizing pancreatitis who were randomly assigned to receive surgical necrosectomy or a minimally invasive, step-up approach consisting of EUS-D or percutaneous drainage followed, if necessary, by minimally invasive retroperitoneal necrosectomy, the step-up approach significantly reduced the incidence of complications, the length of hospital stay, and the incidence of long-term complications.26

We started to perform endoscopic necrosectomy in February 2008 in the Kitasato University East Hospital. Since then, we have aggressively used this procedure in patients with necrotizing pancreatitis and infected peripancreatic necrosis. All of our patients were successfully treated. Prior to the introduction of endoscopic necrosectomy, the patient who was switched to surgical intervention, and the elderly patient with chronic heart failure who died of sepsis, could possibly have been successfully treated if endoscopic necrosectomy had been performed. To our knowledge, few studies have focused on a series of patients with pancreatic pseudocysts, abscesses, or necrotizing pancreatitis treated by EUS-D and endoscopic necrosectomy. The frequency at which these procedures are used in actual clinical practice remains unclear. In the present study, 5 patients underwent endoscopic necrosectomy, 1 patient underwent surgery, and 1 patient died. We estimated that 20% to 30% of patients who are admitted to a university hospital might require endoscopic necrosectomy. Considerably more patients would require endoscopic necrosectomy after severe pancreatitis. A recent study reported the long-term outcomes and advantages of endoscopic necrosectomy.27

Endoscopic necrosectomy is very effective in patients with necrotizing pancreatitis or infection, but some deaths have been caused by factors such as massive bleeding, pulmonary embolism, and sepsis.12-15,21,25,26 Because pulmonary embolism can be caused by air embolism, we have recently started to endoscopically remove necrotic material under carbon dioxide insufflation in our hospital to prevent pulmonary embolism. We perform endoscopic necrosectomy using such devices as a 5-pronged forceps, a basket, and a retrieval net. Because only small amounts of necrotic material can be removed in one session, multiple sessions of endoscopic necrosectomy were required in the present study. One patient in our series had cardiac valve vegetation, probably caused by prolonged bacteremia. Improved devices should be developed to increase the amount of necrotic material that can be removed in one session.

Because our study group was small, further studies are warranted. However, our results suggest that EUS-D is effective for the treatment of pancreatic pseudocysts and abscesses. This procedure should be considered as a viable treatment option prior to surgical necrosectomy. Clinically, 20% to 30% of patients with pancreatic pseudocysts and abscesses have necrotic material
remaining after severe pancreatitis or are refractory to treatment because of infection or other related factors. Endoscopic necrosectomy should therefore be aggressively performed for such patients. And, in order to achieve a higher rate of success, it will be necessary to develop and further refine devices that will enable safe removal of larger quantities of necrotic material at a single session of endoscopic necrosectomy.

References
