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Title: A case of endoscopic retrograde cholangiopancreatography-related main pancreatic duct perforation salvaged by endoscopic ultrasonography-guided pancreatic duct drainage

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Abstract

We herein report a 78-year-old man who underwent endoscopic retrograde cholangiopancreatography (ERCP) to examine main pancreatic duct (MPD) stenosis. During ERCP, MPD perforation occurred due to the cytology brush maneuver. Endoscopic pancreatic stenting to bridge the perforated site failed because the MPD was bent and formed a loop. Thus, we placed the stent at the proximal perforated side. The patient developed retroperitoneal perforation and pancreatic fistula with infection, showing a worsening condition. Pancreatic duct drainage was not effective, so we performed endoscopic ultrasonography-guided pancreatic duct drainage. Subsequently, he gradually improved and was discharged three months after initial ERCP.

Key words: EUS-guided pancreatic duct drainage, pancreatic duct perforation, ERCP-related perforation

Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) has become essential for both the diagnosis and treatment of pancreaticobiliary disease [1]. Main pancreatic duct (MPD) perforation due to the catheter or guidewire maneuvers is a severe adverse event (AEs) related to ERCP. MPD perforation causes retroperitoneal perforation and pancreatic juice leakage, which can be fatal, so early effective drainage is important.

One treatment for MPD perforation is endoscopic pancreatic stenting (EPS) [2], but it is sometimes technically difficult to place the pancreatic stents at an appropriate site. In such cases, effective pancreatic duct drainage (PD) cannot be obtained. Recently the usefulness of endoscopic ultrasonography-guided PD (EUS-PD) mainly for cases with ERCP failure has been reported [3].

We herein report a case of ERCP-related pancreatic duct perforation salvaged by EUS-PD.

Case report

A 78-year-old man was found to have high pancreatic enzyme levels during a routine health checkup. He had no history of drinking. Contrast enhanced computed tomography (CE-CT) showed dilation of the distal MPD but no obvious pancreatic mass (Fig 1A-C). Magnetic resonance cholangiopancreatography (MRCP) showed short lengths of stenosis of the MPD in the pancreatic body and dilation of the distal MPD (Fig 1D). EUS showed a low echoic pancreatic mass of 9mm in diameter in the pancreatic body (Fig. 1E). An early-stage of pancreatic cancer was mostly suspected from these findings, and differential diagnosis was tumor-forming pancreatitis, so he was admitted to the previous hospital for further examination. Pancreatic juice and brush cytology was chosen for pathological diagnosis in the previous hospital because of the possibility of seeding after EUS-guided fine-needle aspiration (EUS-FNA).

ERCP findings revealed stenosis of the MPD in the pancreatic body, and the MPD at the pancreatic head was bent, forming a loop (Fig. 2A). During insertion of the cytology brush catheter (RX Cytology Brush; Boston Scientific Japan, Tokyo, Japan), the MPD at the pancreatic head was disrupted. Contrast material leaked from the pancreas, and we diagnosed the patient with MPD perforation (Fig. 2B). A plastic stent (5 Fr, 3 cm, GEENEN; COOK Endoscopy, Winston-Salem, NC, USA) was placed near the perforated site because the guidewire could not be inserted into the distal side of the perforated site (Fig. 2C). CT

immediately after ERCP revealed the leakage of contrast material into the retroperitoneum, and two days after the procedure, we noted retroperitoneal air and widespread peripancreatic fat inflammation (Fig. 3A, B). His condition worsened, so he was transferred to our hospital three days after initial ERCP.

On an examination, his blood pressure was 115/65 mm Hg, pulse rate 99/min, and O_2 saturation 93% on 5 L/min of oxygen with a mask. An abdominal examination showed epigastric pain. A blood examination showed that the inflammatory markers, serum pancreatic enzyme, and electrolyte values were abnormal (Table 1). After admission to our hospital, we first discussed the possibility of an operation with the surgeon but decided that pancreaticoduodenectomy was inappropriate because of the patient's poor general condition due to severe pancreatitis. Thus, we reattempted ERCP to place a 5-Fr endoscopic nasopancreatic duct drainage (ENPD) tube under general anesthesia. Although the guidewire was able to be inserted at the distal side of the MPD, placement of the ENPD tube was unsuccessful because the tube deviated from the MPD at the perforated site (Fig. 4A, B). We try to an approach via minor papilla, however we could not find the orifice of minor papilla. Further effective PD was needed to improve his general condition, so we selected EUS-PD.

Under EUS guidance, we punctured the dilated distal side of the MPD with a 19-gauge FNA needle (EZ Shot 3 Plus; Olympus Medical, Tokyo, Japan) and inserted the guidewire into the proximal side of the MPD (Fig. 4C). We performed blunt fistula dilation using an uneven

double lumen cannula (UDC; Piolax Medical, Kanagawa, Japan), and two guidewires were inserted into the proximal side of the MPD (Fig. 4D). A 5-Fr ENPD tube was successfully placed at the perforated site with antegrade stenting (Fig. 4E).

After EUS-PD, he was treated in the intensive-care unit, and his condition gradually improved. On the 10th day, antegrade pancreatography showed a moderate improvement in the leakage of the contrast material. The drainage of the pancreatic juice seemed to be effective, so a 7-Fr plastic stent was placed into the MPD through the fistula (Fig. 4F). We attempted transpapillary placement of the pancreatic stent, but it failed because of guidewire deviation at the perforated site. Conservative treatment and enteral nutrition through a nasogastric feeding tube were then performed, and his condition remained stable.

One month after the procedure, he presented with high-grade fever and epigastric pain again. CT showed an increase in the walled-off pancreatic necrosis (WON), and we performed endoscopic transluminal and percutaneous drainage of the WON. After several drainage attempts, the WON was improved. A transgastric pancreatic stent was relapsed during treatment for WON, but there were no symptoms. Thus, additional stenting was not performed. On the 97th day, his treatment for MPD perforation was finished and transferred to the previous hospital (Fig. 5A-C). Six months after the initial procedure, EUS-FNA for the pancreatic tumor was performed, and the pathological diagnosis was adenocarcinoma. He received chemotherapy with Gemcitabine for pancreatic cancer and no seeding has been observed on

CT for six months. We recommended surgical treatment for pancreatic cancer; however, he refused the surgery. He has now been receiving chemotherapy for one year.

Discussion

ERCP-related Aes mainly include perforation, pancreatitis, and bleeding. Perforation is a severe AE, with a reported frequency of 0.08%-0.6% and associated mortality of 0.06% [4]. Therefore, the diagnosis and appropriate treatment for ERCP-related Aes should be performed as soon as possible [5, 6]. The Stapfer classification developed by Stapfer et al. to predict the need for surgery has been widely used to categorize ERCP-related perforation into type I-IV based on the site and mechanism of perforation [7]: type I, lateral or medial wall duodenal perforation; type II, periampullary perforation; type III, bile duct or pancreatic duct perforation caused by endoscopic devices; type IV, retroperitoneal air alone. According to the Stapfer classification, MPD perforation induced by endoscopic devices is type III, the frequency (including bile duct perforations) of which has been reported to be 13% among all ERCP-related perforation cases [4]. A search for case reports published from 2000 to 2022 in the PubMed, Science Direct, and Google Scholar databases using the keywords “ERCP-related perforation”, and “Stapfer type III” yielded about 50 articles. We targeted 8 case reports that concretely described bile duct or pancreatic duct perforation related to the ERCP procedure (Table 2). A total of 75 cases classified as Stapfer type III were reported. Among the perforated sites, bile ducts were 69 cases and pancreatic ducts were 6 cases. Of the 35 cases in which the cause of perforation was listed, 16 cases were due to the guidewire maneuver, and 19 were due to catheters or endoscopic devices, such as balloon or basket catheters. Most of the patients

improved by endoscopic stenting (48 patients), however, 5 patients underwent surgery. Among patients who underwent surgery, one patient developed severe necrotizing pancreatitis and cardiorespiratory complications. This patient required multiple drainages of intraperitoneal and retroperitoneal fluid collection after exploratory laparotomy, which resulted in his hospital stay being prolonged to 75 days [8]. Although most patients with ERCP-related MPD perforation improve with endoscopic pancreatic stenting (EPS), as in the present case, it was sometimes technically difficult to place pancreatic stents at an appropriate site of the MPD for effective drainage. Moreover, two patients with bile duct perforation were reported to have died: one of tension pneumothorax, the other of multiorgan failure. These incidents supported the fact that Stapfer type III perforation should not be underestimated.

Most cases of MPD perforation are due to trauma, with few reports of ERCP-related incidents noted. ERCP is useful for the diagnosis of traumatic MPD perforation [9], and placement of a pancreatic stent is an alternative to surgery. Ito et al. reported that surgery could be avoided in 89% of cases by placing a pancreatic stent [10]. Considering the mechanism underlying the MPD perforation, EPS for drainage of pancreatic juice is suggested to be useful for managing iatrogenic MPD perforation, including ERCP-related cases, as well as traumatic perforation. Aside from ERCP-related cases, a case of the MPD perforation by EUS-FNA was reported by Reddymasu et al. [11]. The patient also improved in response to EPS in the short term.

Dalal et al. reported the usefulness of EUS-PD for patients who required pancreatic duct drainage and failed transpapillary access [3]. Their retrospective study revealed the technical and clinical success rates of EUS-PD for patients with failed ERCP (39/44) or a surgically altered anatomy (5/44) to be 88.6% and 81.8%, respectively. A study from multiple databases showed the technical and clinical success rates of EUS-PD were 89.2% (95% confidence interval [CI] 79.1-89.2) and 81.8% (95% CI 82.1-93.7), respectively. The technical and clinical success rates of EUS-PD for patients with failed ERCP or surgically altered anatomy did not significantly differ from those of initial EUS-PD procedure, suggesting that EUS-PD may be a useful salvage method. On the 10th day after EUS-PD, we confirmed the fistula matured by the absence of the contrast material leakage from the punctured site of the MPD and replaced the ENPD tube with a pancreatic stent. There seems to be no clear criteria for fistula maturation, but one report indicated that fistulas form within two weeks [12].

In the present case, initial EPS was not effective because bridging stenting across the perforated site could not be achieved. Thus, pancreatic juice leakage from the perforated site to the retroperitoneum continued. For further effective drainage, we selected EUS-PD. Although a pancreatic stent was unsuccessfully placed to cross the perforated site, EUS-PD was effective for draining the distal side of the pancreatic juice to the stomach. A WON subsequently formed, and several instances of transluminal drainage were required. Appropriate drainage ultimately saved the patient’s life. ERCP-related perforation can

sometimes result in a severe outcome as in the present case. When the MPD is looped on radiographic images and obtaining the pathological samples by usual ERCP is seemed to be difficult, we should consider an approach via minor papilla or EUS-FNA despite of the risk of tumor seeding. Otherwise, if the image findings strongly suggested malignancy, surgery treatment should be selected without pathology.

In conclusion, we experienced a case of ERCP-related pancreatic duct perforation salvaged by EUS-PD. EUS-PD may be useful for managing ERCP-related MPD perforation when drainage by ERCP fails or is ineffective.

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Contributions

RS and KM organized the report and wrote the paper. AM, KM and HT took care of the patient. YF, TY, KT and SH gave us pathological ideas. HK helped by supervising and approving the final manuscript. All authors read and approved the final manuscript.

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Ethic declarations

Conflict of interest

The authors declare no conflicts of interest.

Human/animal rights

Not applicable.

Informed consent

Written informed consent was obtained from the case patient for publication of this report.

Figure legends

Figure 1. (A, B, C) On the arterial phase, portal phase, and delayed phase of contrast enhanced computed tomography (CE-CT) images, respectively. CE-CT showed dilation of the distal main pancreatic duct (MPD) but no obvious pancreatic mass. (D) Magnetic resonance cholangiopancreatography (MRCP) showed short lengths of stenosis of the MPD in the pancreatic body and dilation of the distal MPD. (E) EUS showed a low echoic pancreatic mass of 9mm in diameter in the pancreatic body (arrowhead).

Figure 2. (A) Endoscopic retrograde cholangiopancreatography (ERCP) revealed stenosis of the MPD in the pancreatic body (arrowhead). The MPD in the pancreatic head was bent and formed a loop (arrow). (B) The MPD was disrupted during the insertion of the cytology brush, and contrast material leaked (arrowhead), which convinced us of MPD perforation. (C) A plastic stent was placed (5-Fr, 3 cm) near the perforated site after unsuccessful insertion of the guidewire into the distal MPD.

Figure 3. (A) Abdominal CT immediately after ERCP showed the leakage of contrast material into the retroperitoneum (red arrowhead). (B) Follow-up CT revealed retroperitoneal air and peripancreatic fat inflammation, which indicated retroperitoneal perforation and acute

pancreatitis.

Figure 4. (A, B) First, we attempted transpapillary placement of a 5-Fr endoscopic nasopancreatic duct drainage (ENPD) tube. We were able to insert the guidewire into the distal MPD; however, we unsuccessfully placed the ENPD tube because of the tube deviation at the perforated site (arrowhead). (C) Under EUS guidance, we punctured the dilated MPD with a 19-gauge fine-needle aspiration needle and performed antegrade pancreatography. (D) Assisted by an uneven double lumen cannula, the fistula was dilated bluntly, and two guidewires were inserted into the proximal MPD. (E) A 5-Fr ENPD tube was successfully placed at the perforated site in an antegrade transgastric fashion. (F) On the 10th day, a 7-Fr plastic stent was placed into the MPD through the fistula.

Figure 5. (A) A pancreatic stent was placed into the MPD through the EUS-PD fistula (arrow). (B) Walled-off pancreatic necrosis (WON) formed around the pancreas (arrowheads). (C) After several instances of drainage, the WON had improved. The red arrowhead indicates the tubes for transluminal drainage.