ORIGINAL ARTICLE

Endoscopic management of pancreatic ascites due to duct disruption following acute necrotizing pancreatitis

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Abstract

Background and Aim: Acute necrotizing pancreatitis (ANP) can be associated with pancreatic duct (PD) disruption. PD disruption can lead to the formation of internal fistulae and consequent pancreatic ascites. Pancreatic ascites is reported very rarely following ANP, and therefore, the role of endotherapy in this setting is not defined. To retrospectively study the safety and efficacy of endoscopic drainage in patients with pancreatic ascites following ANP.

Methods: Over a period of 6 years, 12 patients (10 males; mean age: 35.9 ± 7.1 years) with pancreatic ascites following ANP underwent an attempted endoscopic drainage. Patients with a coexistent pancreatic fluid collection (PFC) underwent endoscopic ultrasound (EUS)-guided transmural drainage of PFC whereas patients with pancreatic ascites alone underwent transpapillary drainage alone.

Results: Nine (75%) patients had coexistent PFC, whereas three patients presented with ascites only. The mean size of PFC was 7.2 ± 1.6 cm. Patients with PFC underwent successful EUS-guided transmural drainage (multiple plastic stents in eight and metal stent in one patient) with complete resolution of PFC as well as ascites within 2–3 weeks. Of three patients with ascites alone, one patient had complete PD disruption, whereas two patients had partial PD disruption. Both patients with partial disruption underwent successful placement of bridging transpapillary stent and resolution of ascites at 6 weeks. In patients with complete disruption, a nonbridging stent was placed into the disruption, and ascites resolved after 8 weeks. There has been no recurrence over 27.5 ± 17.7 weeks.

Conclusion: Endoscopic drainage is a safe and effective treatment modality for the treatment of pancreatic ascites following ANP.

Introduction

The pancreatic duct (PD) disruption can occur following acute or chronic pancreatitis, pancreatic malignancy, abdominal trauma, or abdominal surgery.[1] In acute pancreatitis, ductal disruption usually occurs in the setting of acute necrotizing pancreatitis (ANP), where the necrosis of ductal epithelial cells leads to the loss of integrity of the PD.[2,3] There are limited studies that have looked at the ductal disruption in acute pancreatitis. Neoptolemos *et al.* reported that 25% of patients who had >25% parenchymal necrosis or required surgery for local complications had duct disruption in contrast to none of the patients without these complications, thereby suggesting that ANP was more commonly associated with ductal disruption, and these patients needed surgery more often.[2] Uomo *et al.* reported the frequency of duct disruption to be 31%, whereas Lau *et al.* reported that 37% patients with severe pancreatitis had duct disruption.[4,5]

Ductal disruptions occurring in ANP are significantly associated with pancreatic/extrapancreatic necrosis, prolonged hospital stay, need for intervention, and placement of short-term PD stent.[4,5] These disruptions are not aggressively looked for in patients with ANP as the entire focus of initial management is on treating pancreatic necrosis/walled-off necrosis (WON) and its complications, with little emphasis on PD disruptions. However, the duct disruptions play an important role in determining the long-term outcome after successful initial management of pancreatic necrosis/WON. Patients with duct disruptions, especially complete duct disruptions, tend to have increased frequency of recurrence of pancreatic fluid collections (PFCs) after the removal of transmural stents, placed for endoscopic treatment of WON, especially in patients with presence of considerable amount of viable pancreatic parenchyma upstream to the disruption.[6,7] In addition, occasionally, PD disruption may be associated with minimal necrosis and, therefore, may manifest as pseudocyst or pancreatic ascites/pleural effusion.

The ascites in ANP may be reactionary to acute inflammation or due to internal pancreatic fistula consequent to PD disruption. Significant ascites occurring in the delayed phase of acute pancreatitis is rare and is usually due to PD disruption.[8] This

disruption leads to the formation of internal pancreatic fistula leading to the formation of a pseudocyst that leaks into peritoneum or the fistula directly communicates with the peritoneum, leading to formation of pancreatic ascites. Because of rarity, there is a paucity of published literature on clinical and imaging features as well as the effective management approach of pancreatic ascites in ANP.[8] We retrospectively studied the safety and efficacy of endoscopic drainage in patients with pancreatic ascites developing after an attack of ANP.

Methods

The database of patients with ANP seen in our unit over the last 6 years (December 2011–November 2017) was retrospectively searched to retrieve the data of patients with pancreatic ascites. All the enrolled patients had been earlier diagnosed with ANP based on the revised Atlanta classification and had subsequently developed symptomatic pancreatic ascites.[9] Pancreatic ascites was defined as free intraperitoneal fluid visualized either on abdominal ultrasound or computed tomography (CT) scan of the abdomen, with an amylase level higher than the upper limit of normal for serum in a patient with ANP.[10,11] The clinical and imaging features of the patients with pancreatic ascites were also retrieved. On endoscopic retrograde pancreatography (ERP), PD disruption was defined by free extravasation of contrast outside the pancreatic ductal system after retrograde contrast injection into the main PD or dorsal duct (in patients with pancreas divisum). It was defined as complete when the main duct upstream to the disruption was not opacified and as partial when the main duct was visualized upstream from the site of disruption. An abrupt cut-off value of the main PD on pancreatogram with inability to traverse the guide wire across was suggestive of disconnected pancreatic duct syndrome (DPDS).[1] Patients with coexistent pseudocysts/WON underwent an attempted endoscopic transmural drainage, whereas patients with pancreatic ascites alone underwent an attempted endoscopic transpapillary drainage. Informed consent was obtained from all the patients before the procedure.

Endoscopic ultrasound (EUS)-guided transmural drainage of coexistent pseudocyst/WON. The EUS examination was performed with a linear scanning echoendoscope (EG-3870 UTK linear echoendoscope, Pentax Inc., Tokyo, Japan or UCT180 linear echoendoscope, Olympus Optical Co Ltd., Tokyo, Japan). On EUS, the size as well as the detailed morphology of the collection was studied with special emphasis on the presence or absence of the solid necrotic debris. The echogenic material present in the WON was suggestive of solid debris. The PFC with significant amount of solid debris was labeled as WON, whereas PFCs without significant solid debris were labeled as pseudocyst. An attempt to quantify the amount of solid debris as a percentage of the total size of collection was performed. The quantification of the solid debris was an approximate visual judgment of the endoscopist.

The patients received preprocedure intravenous antibiotics that were subsequently continued orally till the PFCs resolved. The procedure was carried out under conscious sedation using intravenous midazolam under EUS and fluoroscopic guidance. The optimal site for drainage was chosen under EUS and color Doppler guidance, ensuring a minimal distance between the PFC and the gastroduodenal lumen, as well as avoiding any intervening blood vessels. One to three, 7, or 10 Fr 3–7 cm double pigtail plastic stents were placed in patients with pseudocyst or WON with less than 40% solid necrotic debris, with a single stent being placed in patients with pseudocyst and multiple stents in patients with WON. In patients of WON with more than 40% solid debris, a fully covered, biflanged, self-expanding metallic stent (BFMS) was placed. Endoscopic necrosectomy was performed only in patients of WON who developed new-onset fever or worsening of existing symptoms with persistent WON on CT after initial endoscopic transluminal drainage.

After the placement of plastic/metal stent, ERP was performed to demonstrate ductal disruption. In patients with partial duct disruption, a transpapillary bridging stent was placed, whereas no transpapillary stent was placed in patients with complete disruption or DPDS.

Endoscopic transpapillary drainage. ERP was performed through a standard technique using a TJF 160 or 180 (Olympus Optical, Tokyo, Japan) side-viewing duodenoscope. Intravenous midazolam was given for conscious sedation and hyoscine butyl bromide for inhibiting duodenal peristalsis. The PD was selectively cannulated, and a pancreatogram was obtained. After confirming ductal disruption, a 5 or 7 Fr pancreatic stent was placed across the papilla into the PD by advancing it over a 0.025″ or 0.035″ hydrophilic guide wire. An attempt was made to place the stent bridging the partial disruption, and if that was not possible, the stent was placed as near as possible to the site of disruption.

Follow up. The patients were followed up clinically as well as by abdominal ultrasound every two weeks. Following the resolution of symptoms as well as ascites and PFCs on ultrasound, CT of the abdomen was performed to document complete resolution. Patients with partial duct disruption had both the transpapillary and transmural stents removed after documenting the healing of ductal disruption on ERP. In patients with DPDS/complete duct disruption and indwelling transmural plastic stents, one or more transmural stents were left indefinitely, whereas BFMS was replaced with a double-pigtail plastic stent that was left indefinitely. The indwelling transpapillary stent in patients with complete disruption and ascites alone was removed after resolution of pancreatic ascites.

Outcome definitions. Treatment success was defined as resolution of symptoms with resolution of pancreatic ascites as well as any associated PFCs on CT, with no need for surgery. Any complications occurring following endoscopic drainage and their outcome were also retrieved.

Results

Over a period of 6 years, 12 patients (10 males; mean age: 35.9 ± 7.6 years) with pancreatic ascites following ANP underwent an attempted endoscopic drainage. The etiology of ANP was alcohol in six, gall stones in three, trauma in one, and idiopathic in two patients, and patients presented 8.8 ± 2.7 weeks after an attack of ANP (Table 1). Nine (75%) patients had

Table 1 Demographic profile of studied patients

Serial no.	Gender/ age	Etiology	Coexistent PFC	Location of PFC	Pancreatic duct disruption	Period of resolution (weeks)	Complications
1	Male/28	Idiopathic	Yes	Body	Complete	3	None
2	Male/42	Alcohol	Yes	Body	Complete	2	None
3	Male/22	Alcohol	No	no PFC	Partial	6	None
4	Female/28	Gall stones	Yes	Head	Complete	3	None
5	Female/32	Gall stones	Yes	Body	Complete	3	None
6	Male/46	Alcohol	Yes	Body	Complete	3	None
7	Male/36	Alcohol	Yes	Body	Complete	2	None
8	Male/39	Alcohol	Yes	Body	Complete	2	None
9	Male/42	Gall stones	Yes	Tail	Partial	3	None
10	Male/38	Idiopathic	Yes	Body	Complete	3	None
11	Male/46	Alcohol	No	no PFC	Complete	8	Fever
12	Male/32	Trauma	No	no PFC	Partial	6	None

PFC, pancreatic fluid collection.

coexistent PFC along with pancreatic ascites, whereas three (25%) patients had presented with pancreatic ascites only. The PFC was pseudocyst in three patients and WON in six patients. The mean size of PFC was 7.2 ± 1.6 cm, and it was located in head, body, and tail in one, seven, and one patient, respectively. The ascitic fluid was exudative in all the patients, with fluid amylase ranging from 3600 to 96 000 IU/l.

Nine patients with PFC underwent successful EUS-guided transmural drainage (multiple plastic stents in 8 and BFMS in one patient) with complete resolution of the PFC as well as pancreatic ascites within 2–3 weeks (Figs 1,2). The ERP documented complete PD disruption in eight patients, and therefore, transmural plastic stents were left indefinitely. One patient with partial disruption underwent successful placement of bridging transpapillary stent followed by removal BFMS as well as transpapillary plastic stent after documenting healing of PD disruption.

Three patients with ascites alone underwent endoscopic retrograde cholangiopancreatography (ERCP), and it demonstrated complete PD disruption in one patient and partial disruption in two patients. The patients with partial disruption underwent successful placement of bridging transpapillary stent followed by resolution of ascites at 6 weeks. The patient with complete disruption underwent placement of nonbridging stent into disruption, and it led to the resolution of ascites after 8 weeks. One patient with pancreatic ascites alone and complete duct disruption developed transient fever that responded to antibiotics. There has been no recurrence of symptoms or ascites in these patients over a follow-up period of 27.5 ± 17.7 weeks.

Discussion

Pancreatic ascites is a very rare complication of ANP and is usually due to PD disruption.[8] Because of the rarity, there is paucity of published literature on this complication of ANP, and most of the cases reported have been managed surgically.[1,8] In a patient with ANP, the treatment is focused on managing organ failure in the initial phase of illness followed by managing the local complications consequent to pancreatic necrosis in the later phase of illness.[9] Several studies involving both endoscopic as well as surgical have focused on the appropriate management of pancreatic

necrosis, including WON.[12–14] However, few studies have looked at the incidence as well as impact of PD disruption on the clinical course of ANP.[2,5,8,15] Jang *et al.* reported that extensive necrosis, enlarging/refractory PFCs, persistence of amylase-rich output from percutaneous catheter, and amylase-rich ascites/pleural effusion were seen more commonly in patients with PD disruption.[15] In addition, the hospital stay as well as recurrence of PFCs were more common in patients with PD disruption.[15] Neoptolemos *et al.* also reported that patients with main duct disruption and extensive necrosis (>25%) more frequently required surgical intervention.[2]

Internal pancreatic fistula because of ductal disruption can lead to pancreatic ascites, and this is seen more commonly in patients with underlying chronic pancreatitis than acute pancreatitis.[16] Although mild reactive inflammatory ascites is seen commonly in patients with ANP, true pancreatic ascites due to leakage of enzyme-rich pancreatic juice into the peritoneum consequent to PD disruption is seen infrequently. This is due to the intense inflammatory reaction accompanied with variable amount of pancreatic/extrapancreatic necrosis leading to the leaking of pancreatic juice from the duct disruption being walled off, in turn leading and forming WON.[8] Rarely, the WON/acute pseudocyst may leak into the peritoneum, and this leads to the formation of pancreatic ascites. Less commonly, the fistula due to duct disruption may directly communicate with the peritoneum, leading to the formation of pancreatic ascites without any associated WON/acute pseudocyst. In our study, a majority of patients with pancreatic ascites had associated PFC, and only 25% of patients had pancreatic ascites due to a directly communicating internal pancreatic fistula.

Endoscopic transpapillary drainage has been shown to be a safe and effective treatment for pancreatic ascites and pleural effusions occurring in chronic pancreatitis.[1,10] The transpapillary drainage facilitates the drainage of pancreatic juices through the papilla by traversing the pancreatic sphincter, thus converting the high-pressure pancreatic ductal system to a low-pressure system.[17] This leads to the diversion of the pancreatic juices from the disruption and thus promotes the healing of ductal disruption and consequent pancreatic ascites. Endoscopic transpapillary drainage has the best results in the presence of partial duct
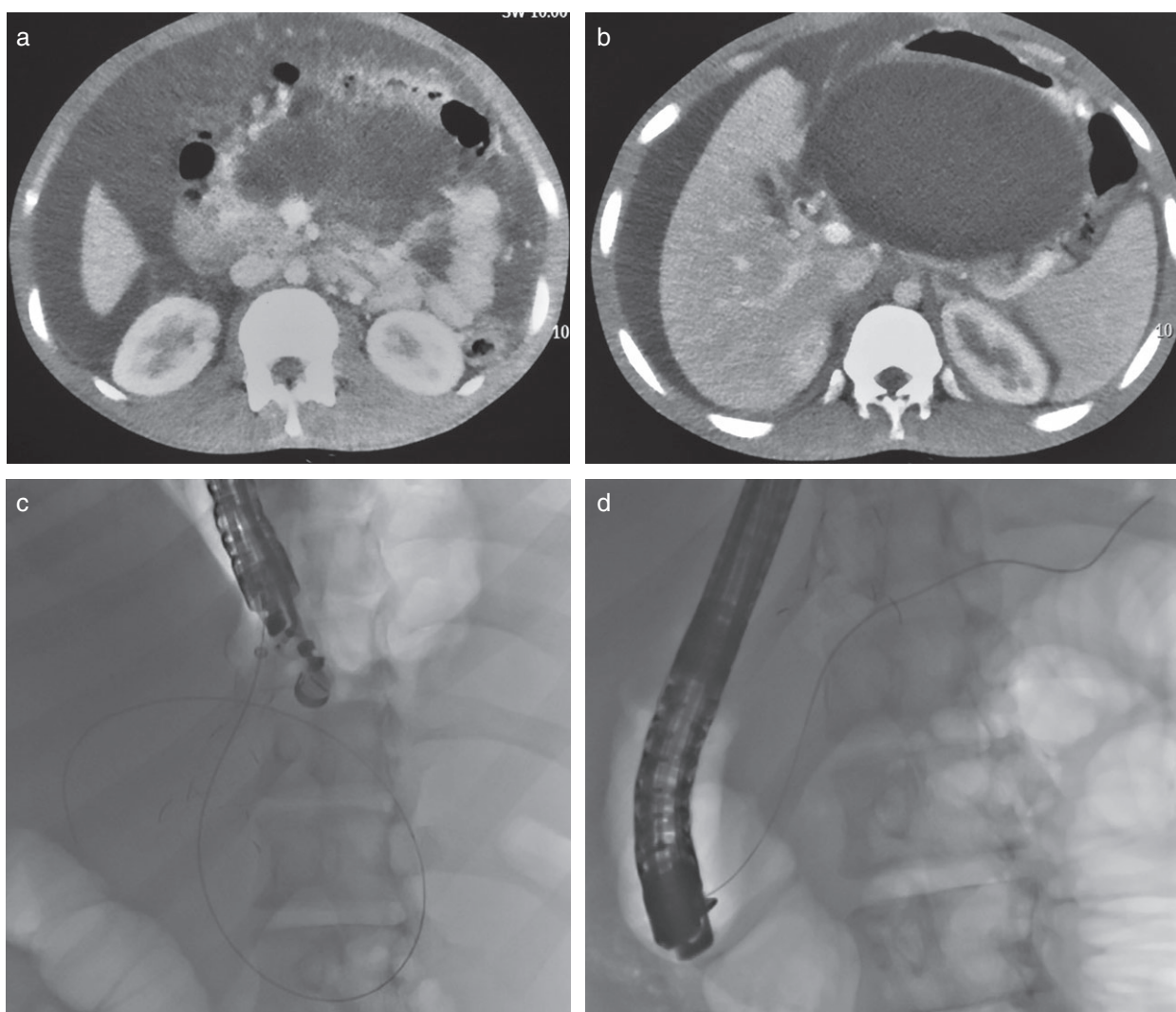
Figure 1 (a) Computed tomography (CT): Pancreatic ascites. (b) CT: Large walled-off necrosis. (c) Biflanged metal stent being placed. (d) Endoscopic retrograde pancreatography: Guide wire negotiated across the partial disruption. Transmural metal stent is also noted.

disruption that can be bridged with an endoprosthesis.[1,10,18] The presence of complete duct disruption usually leads to the failure of endoscopic transpapillary drainage because of an inability to drain the leaking disconnected segment of pancreas.[1] Complete duct disruption is seen more commonly in acute pancreatitis than chronic pancreatitis, and therefore, endoscopic transpapillary drainage is less effective in treating consequences of PD disruptions in acute pancreatitis. Jang *et al.* reported that endoscopic transpapillary stenting was associated with lower success rates in the presence of complete duct disruptions (20 vs 92%).[15]

The presence of associated PFC with complete duct disruptions makes endoscopic treatment possible by enabling the creation of a fistula between the gastrointestinal tract and the PFC using endoscopic transmural drainage, and this fistula facilitates the drainage of a disconnected segment into the gastrointestinal tract lumen.[1] This fistula can be maintained by placing permanent indwelling transmural stents, thus preventing the leakage of pancreatic juice from PD disruption.[6,7] In our study, a majority of patients with ANP had complete duct disruption, but a majority of patients had associated PFC that could be successfully drained by endoscopic transmural drainage. The endoscopic transmural drainage of acute pseudocyst or WON also led to the resolution of pancreatic ascites. Moreover, as described by us previously, leaving transmural stent/stents for an indefinite period prevented recurrence of PFC/pancreatic ascites.[6,7]

Only one of our patients with pancreatic ascites had complete duct disruption without any associated PFC, and the ascites resolved by 5 weeks after placement of a nonbridging transpapillary stent. It is unlikely that the transpapillary stent led to the resolution of pancreatic ascites in this patient, and the resolution would have been triggered by the gradual atrophy of the disconnected segment. Nonresolving consequences of complete duct disruptions usually require surgery or EUS-guided transmural PD drainage.[1] Small
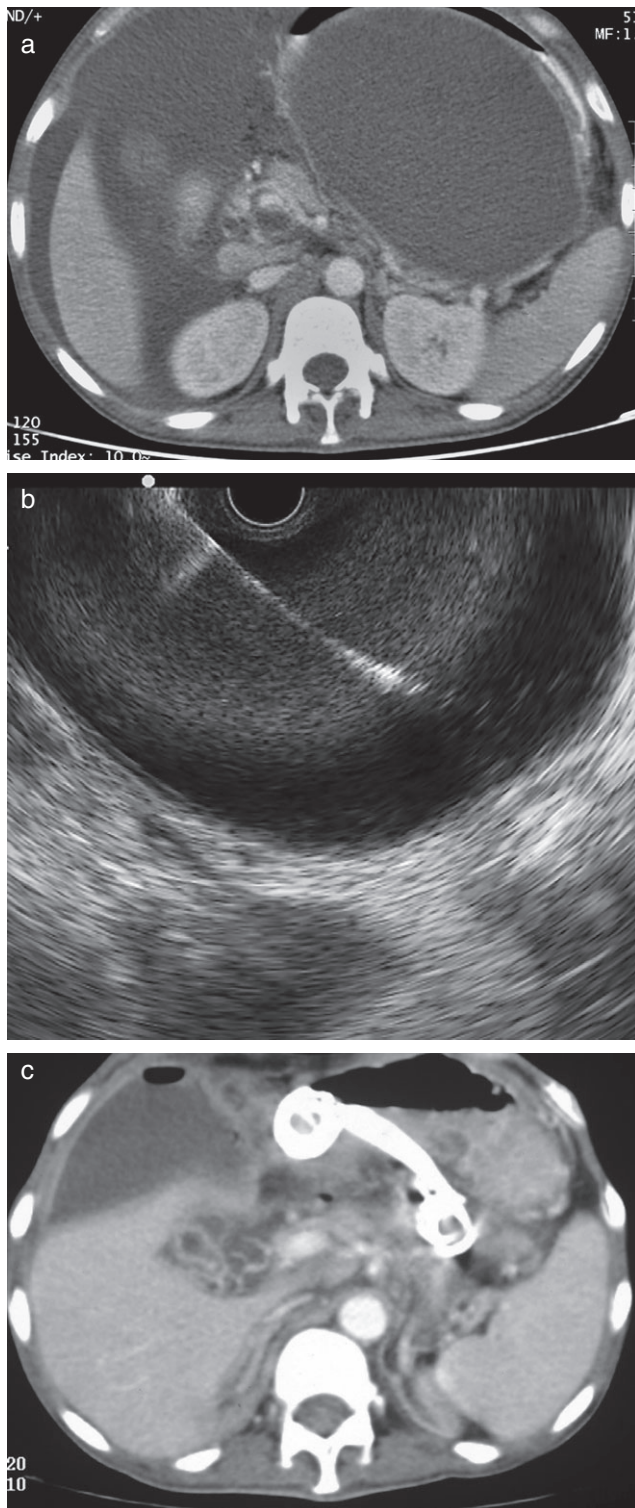
Figure 2 (a) Large walled-off necrosis (WON) with pancreatic ascites. (b) Endoscopic ultrasound-guided puncture of WON. Guide wire coiled in the cavity. (c) Multiple transmural stents with resolved WON. Minimal ascites noted.

sample size, being a single-center study, and retrospective study design are important limitations of the current study. However, pancreatic ascites following ANP is very rare, and to the best of our literature search, the current study is the largest study describing results of endoscopic therapy in these difficult-to-treat patients.

In conclusion, pancreatic ascites following ANP is rare and is commonly associated with complete duct disruption. Endoscopic transmural drainage of associated PFC leads on to successful resolution of pancreatic ascites even in presence of complete duct disruption.

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