

ORIGINAL ARTICLE

Pancreatic Leak Related Hemorrhage Following Pancreaticoduodenectomy. A Case Series

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ABSTRACT

Context Delayed arterial hemorrhage, secondary to pancreaticojejunal leakage, is an infrequent complication (2-4%) of pancreaticoduodenectomy but it carries a high mortality rate with more than half of the patients dying from overwhelming sepsis and/or bleeding. Its ideal management remains unclear. **Case reports** We hereby present our experience with respect to the presentation and management of this severe post-pancreaticoduodenectomy complication which occurred in 3/149 patients (2.1%) operated on between 1996 and 2008 in our department and we review the role of endoscopy, interventional radiology and surgery in its management. **Conclusions** The severity of the underlying sepsis and the prompt identification of the sentinel bleed determine surgical and angiographic intervention and define the outcome in the treatment of a pancreatic leak-related hemorrhage. Endoscopy has no role in this setting.

INTRODUCTION

Pancreaticoduodenectomy (PD) was historically considered a formidable procedure with dismal outcome, although excellent results have been reported since the 1990's [1]. Significant progress over the past two decades with a shift to high volume centers providing surgical expertise, perioperative care improvement and interventional radiology modalities has rendered PD a relatively safe operation with a mortality rate not exceeding 5%, albeit with a still high morbidity rate [1, 2, 3, 4, 5].

A delayed hemorrhage, secondary to pancreatic leakage, is an infrequent (incidence less than 4%) complication after PD, but one carrying a high mortality rate, mainly due to septic sequelae. Because of its rarity and devastating course, hard evidence and a uniformly accepted treatment algorithm are lacking. We hereby present our single center experience with this complication and review possible treatment strategies.

PATIENTS

From June 1996 through October 2008, 149 patients (80 males, 69 females; mean age 64 years, range 16-82 years) with a pancreatic head mass underwent a PD in our department. There were 68 classical Whipple and 81 pylorus-preserving pancreaticoduodenectomies (PPPDs). The main histological diagnosis was pancreatic adenocarcinoma in 141 cases and chronic pancreatitis in 8 cases. Minor morbidity was 40% and consisted of urinary tract infection, pneumonia, infection of the surgical wound and delayed gastric emptying. The overall pancreatic leakage incidence was 14.1% (n=21) and delayed hemorrhage occurred in three patients (incidence 2.0%). Postoperative pancreatic fistulae were classified according to the International Study Group on Pancreatic Fistula (ISGPF) definition [2]. We hereby present the case reports.

Case 1

A 74-year-old female underwent a pylorus-preserving pancreaticoduodenectomy (PPPD) for a tumor of the head of the pancreas. The histopathological examination of the specimen showed chronic pancreatitis.

Postoperatively, the patient developed a grade A, high output pancreatic fistula (more than 200 mL/day) due to a leak from the pancreaticojejunal anastomosis; she was treated conservatively with TPN and octreotide analogues. The fistula closed 20 days later without any additional complications. Three months later, the patient presented with an episode of macroscopic lower

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Abbreviations PD: pancreaticoduodenectomy; PPPD: pylorus-preserving pancreaticoduodenectomy

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gastrointestinal (GI) bleeding. Upper GI endoscopy and colonoscopy did not reveal any pathology. The patient was transfused with two packs of red blood cells and was treated conservatively. A few days later, she had a severe episode of lower GI hemorrhage, and upper endoscopy showed that the stomach was full of blood but the source of the bleeding was not identified. During the endoscopy the patient collapsed and was urgently transferred to the operating room. An exploratory laparotomy revealed a small throbbing cyst which was a pseudoaneurysm of the hepatic artery and was the source of the bleeding in the lumen of the intestine. Intraluminal blood was filtered through the intestinal wall adjacent to the pancreaticojejunal anastomosis, as the former was part of the pseudoaneurysm. The pancreaticojejunal anastomosis had healed and was left intact; the hepatic artery was dissected and clamped proximally and distally to the aneurysm. The dissection was possible because the tissue inflammation had subsided since the pancreatectomy had been performed three months earlier. The pseudoaneurysm was opened and the hepatic artery was identified and meticulously repaired in an end to end fashion with interrupted fine Prolene® (Ethicon, Somerville, MA, USA) sutures. We reinforced the eroded intestinal wall with seromuscular sutures and an omental patch, and the area was irrigated and drained. A postoperative angiography showed a sealed and patent hepatic artery. The patient recovered uneventfully and was discharged on the 20th postoperative day.

Case 2

A 65-year-old male underwent a PPPD for a carcinoma of the ampulla of Vater. The patient developed a grade B pancreatic fistula, due to a leak of the pancreaticojejunal anastomosis and was treated conservatively with TPN and octreotide analogues, thus achieving a fistula rate of less than 100 mL daily. On postoperative day 17, the patient became febrile (up to 38.5°C) and CT of the abdomen revealed an upper abdominal fluid collection which was successfully drained under CT guidance. A percutaneous catheter drain was left in place and clinical and laboratory improvement of the patient was recorded thereafter. On day 25, the patient had a mild lower GI bleeding and was scheduled for upper and lower GI endoscopy while closely monitored. A few hours later he experienced severe hematemesis and concurrently collapsed. He underwent an urgent explorative laparotomy and a large hematoma was found in the upper abdomen close to the pancreaticojejunal anastomosis. The source of the bleeding was the gastroduodenal stump of the common hepatic artery. Blood entered the lumen of the intestine through the ruptured pancreaticojejunal anastomosis where the pancreatic stump was exposed. The intestinal loop and the pancreatic remnant were oversewn separately with non-absorbable sutures and the area was drained with two large bore soft drains. Due to the patient's unstable condition and severely

inflamed and distorted tissues, it was not deemed prudent to proceed with a completion pancreatectomy. The patient was transferred to the ICU where he developed septic shock leading to multiorgan failure and died a few days later.

Case 3

A 51-year-old male underwent a PPPD for a pancreatic adenocarcinoma. On postoperative day 12, he was transferred to his residential area hospital in a good general condition, on a normal diet and with a low rate pancreatic fistula (less than 75 mL/day) which discharged through a remaining soft abdominal drain. Five days later, blood was discharged through the abdominal drain. The hemorrhage temporarily stopped and he was hemodynamically stable. He was transfused, closely monitored and during his transfer back to our institution, he collapsed and succumbed to massive hemorrhage through his abdominal drain. There was no autopsy and, therefore, the precise source of the bleeding was not clarified.

DISCUSSION

Delayed gastric emptying, pancreaticojejunal failure and intra-abdominal abscess predominantly account for the steadily increasing morbidity of PD [2, 3, 4, 5, 6, 7, 8]. Post-pancreatectomy hemorrhage is reported less frequently with an incidence ranging from 2 to 18%, nevertheless having conversely high mortality as compared to other complications with the principal cause of death being overwhelming sepsis rather than uncontrolled bleeding [9, 10, 11, 12, 13, 14, 15, 16].

Despite the severity of post-pancreatectomy hemorrhage, a universal classification system and treatment practice is lacking. The most systematic effort in defining post-pancreatectomy hemorrhage comes from a project of the International Study Group of Pancreatic Surgery (ISGPS) [17]. According to the proposed consensus, post-pancreatectomy hemorrhage should be categorized with respect to time of onset (early, within 24 h or delayed, post-24 h), location (intra-luminal or extra-luminal) and severity (grade A, B or C).

In our series of 149 PDs, there were three cases of delayed hemorrhage (2.0%). Two patients presented with intraluminal bleeding and one patient with sanguineous peritoneal drainage. These three patients were among the 21 cases (14.1%) with a pancreatic fistula/abscess due to pancreaticojejunal anastomotic failure.

Interestingly, hemorrhage occurs in a few cases of pancreatic leak, although the latter is characterized as the major risk factor of fatal delayed post-pancreatectomy hemorrhage. Pathophysiology may entail the exposure of skeletonized vessels to erosive enzymes [18], inflammatory or traumatic pseudoaneurysms [19] and pancreatic pseudocysts [20]. It can misleadingly manifest as severe upper GI hemorrhage (Cases 1 and 2), collapse with or without evident bleeding or as a less dramatic clinical and

laboratory patient deterioration. The most pivotal sign is an asymptomatic bloody drain or minor hemoglobin decrease in patients with concomitant pancreaticojejunal leakage complications (Case 3). The importance of “sentinel bleed” has been emphasized as a heralding mark for this abdominal catastrophe [16, 21, 22, 23]. Crucial management latency is evident regarding our Cases 1 and 3. Prompt identification and treatment with embolization, stenting or surgery is imperative because it is very unlikely that a patient with a pancreatic leak-related hemorrhage will be treated successfully with conservative measures [9, 10].

Endoscopy has been established as the first line diagnostic option of upper gastrointestinal bleeding, but its role in delayed post-pancreatectomy hemorrhage is very limited, if any. Although intraluminal presentation in the form of hematemesis or melena is not uncommon [12, 24], appearing in 2 of our 3 cases, the source of bleeding in this setting is far beyond endoscopic diagnosis and intervention. Cumulative experience has made clear that “positive” endoscopic findings are misleading and delay definitive treatment. Angiography with subsequent occlusion of arterial pseudoaneurysms has been widely reported with an encouraging success rate [13, 23, 24, 25, 26]. The feasibility and efficacy of transarterial embolization depends on several factors, such as the patient’s hemodynamic stability, bleeding etiology, site, intermittent pattern and institutional facilities and expertise. As a minimal invasive technique, it may spare debilitated patients extensive operations; this rationale is documented by the lower mortality in the series treated successfully with transarterial embolization. However, a pancreatic leak-related post-pancreatectomy hemorrhage is a “secondary” complication and some form of source-control intervention is essential. In addition, the occlusive result of transarterial embolization may have detrimental effects regarding organ perfusion. Fuji *et al.* [27] reported a series of 9 cases treated with super selective celiac axis transarterial embolization with 44% mortality; 75% of the fatal outcomes were attributed to ischemic hepatic failure. The report of Khorsandi *et al.* with no mortality [24] incorporated only cases with distal, non-vital vessels. Endovascular stenting would be an alternative option [28, 29, 30], but is still technically more demanding.

Surgical exploration is considered to be the gold standard for post-pancreatectomy hemorrhage and remains the only option for an unstable, rapidly deteriorating patient or after failed angiography. Operative strategy depends on clinical status and personal experience. Typically, damage control procedures, including bleeding control and abscess drainage, pancreatic duct fistulation or completion pancreatectomy are the cornerstone procedures [31, 32, 33]. In our series, the extent of the local sepsis determined surgical intervention. Case 1 underwent successful sutured arterial reconstruction without the

need for pancreaticojejunal breakdown whereas, in Case 2, only damage control was possible. A completion pancreatectomy in the latter case might have had a more favorable outcome, but the patient’s status and local conditions prohibited it.

Operating on severely ill patients in a difficult surgical field, with severe inflammation and tissue friability, accounts for mortality rates which parallel delayed post-pancreatectomy hemorrhage mortality. Successful angiography could allow more selective laparotomies with vascular reconstruction, but relevant evidence is lacking.

Conclusively, surgical treatment of a pancreatic leak-related post-pancreatectomy hemorrhage is a salvage procedure for severely compromised patients and has high mortality rate. Prompt identification of the “sentinel bleed” is critical, allowing for minimally invasive intervention on a still stable patient. Favorable results of an angiography should be interpreted cautiously, regarding patient selection and side effects. Multimodality treatment with ‘on table’ angiography followed by laparotomy could comprise the ideal setting. However, close observation, early diagnosis and aggressive management of pancreatic leakage is the most effective way to minimize devastating bleeding complications.

Conflict of interest The authors have no potential conflicts of interest

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