

DOI: 10.21767/2471-8041.1000031

Outcome of A Non Healing Pancreatico-Cutaneous Fistula, Treated with Local Tetracycline Instillation – A Case Report

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Rec date: May 28, 2016; **Acc date:** Sep 27, 2016; **Pub date:** Sep 30, 2016

Citation: Kumarasinghe NR, Ileperuma SK, Dassanayake BK, et al. Outcome of A Non Healing Pancreatico-Cutaneous Fistula, Treated with Local Tetracycline Instillation – A Case Report. Med Case Rep. 2016, 2:3.

Introduction

Pancreatic fistulas continue to be of significant morbidity, causing longer hospital stay and incur a high cost. It commonly results as a complication of acute pancreatitis, pancreatic surgery and splenectomy [1].

The reported incidence of pancreatic fistula following pancreatico-duodenectomy is 6-14% [2,3]. However, after distal pancreatectomy, it is much lower (0.5%) [4]. Transection at the pancreatic body, splenectomy, failure to close pancreatic duct and non-use of peri-operative somatostatin agonist (Octreotide) are thought to be risks for fistulation following distal pancreatectomy [5-7].

In the absence of sepsis, a majority of pancreatic fistulas are likely to heal with conservative management alone [8,9]. This includes parenteral nutrition (PN) while resting the bowel, drainage of collections, antibiotics and use of octeotride. However clinical trials have shown conflicting evidence regarding the use of octreotide in managing pancreatic fistulas [10-12]. Those which show resistant to healing will need interventions [1]. Surgical techniques for the treatment of intractable pancreatic fistula include percutaneous trans fistulous pancreatic duct drainage (PTPD), percutaneous trans fistulous pancreatojejunostomy (PTPJ), and percutaneous trans fistulous pancreatic duct embolization (PTPE) [1,2].

This report is based on a non-operative therapeutic strategy, in a young male who developed a cutaneous pancreatic fistula following open drainage of a collection of pus in the pancreatic bed and splenic region.

Case Report

A male 39-years of age presented with generalized abdominal pain of 2 days, associated with fever, anorexia and vomiting. Examination findings were consistent with peritonitis. Biochemical indices had neutrophilic leukocytosis and high C-reactive protein. X-ray abdomen has distended bowel loops but no gas under diaphragm. Ultrasonography had limited value due to distended bowel loops.

Emergency laparotomy was undertaken. A retroperitoneal pus collection was noted in the left hypochondrium. It was involving the region of the body and tail of pancreas and the spleen. The pus was drained and the spleen which showed features of necrosis was removed. Following thorough peritoneal lavage a drain was placed in the left hypochondrium (Figure 1).



Figure 1 Healed fistula site.

Post operatively signs of sepsis gradually subsided but a continuous drain of thick material was present through the drain. A daily volume of 50-150 ml. persisted. Drain fluid was positive for amylase and drain culture revealed coliforms.

Decisions on managing this pancreatic fistula was a challenge because though various options are mentioned in literature none was very successful and surgery would have been a daunting task in an abdomen with gross adhesions and in a patient who was in a catabolic state. There was also no clear indication for endoscopic retrograde cholangio-pancreaticography (ERCP) in post-operative imaging.

Hence we opted for non-operative strategies initially. He was commenced on parenteral nutrition with bowel rest. A Somatostatin agonist was added to reduce pancreatic secretions. Drain culture sensitive parenteral antibiotics were started. This trial period was about 2 weeks and little

improvement in fistula output was seen and decline in patients' nutritional state was a concern. Hence we commenced on enteral feeding which helped his general condition improve but not the fistula.

We then resorted to an option of fibrosing the fistula tract. About 6-10 Tetracycline tablets were made in to a powdered solution with isotonic saline and was injected in to the drain. It was noticed that the daily drain volume markedly reduced. Subsequently, following two more tetracycline instillations through the drain on day 03 and day 05 from the first instillation, the fistula output completely ceased (**Figure 2**).



Figure 2 Post-operative pancreatic contrast enhanced CT Abdomen view red arrow- Drain.

Discussion

Pancreatic fistulas have been a major concern following surgical intervention of pancreas because of its significant morbidity, longer postoperative recovery and high cost incurred to health institutions. Case series have shown a 6-14% incidence of developing fistulas from pancreatico-enteric anastomosis following pancreatico-duodenectomy [2,3]. However pancreatic leaks which form after distal pancreatectomy and various enucleation procedures are categorized as pancreatic occlusion failures (POF) [2] and have the low incidence of about 5% amongst specialized centers [4]. These act in a more benign manner and have less morbidity, due to the absence of enzyme acting on pancreatico-enteric anastomosis.

Little is known about risk factors in fistula formation following distal pancreatectomy. BMI >25 kg/m², transection at the pancreatic body, pancreatic necrosis, operative trauma to pancreatic tail during splenectomy, nephrectomy and splenic flexure mobilization, absence of pancreatic duct ligation and non-use of preoperative somatostatin agonist are several of the implicated factors [6,7].

In this patient presence of pus around the pancreatic tail and spleen, difficulty in identifying clear tissue planes with possible iatrogenic pancreatic injury and failure to close the resected part are risk factors which may have contributed to fistula formation.

Studies have shown that more about 90% patients with distal pancreatic fistulas are managed successfully with non-operative measures and they seldom require early surgical intervention [13]. In addition, reopening in to a laparatomized abdomen with purulent infection was a challenge because of the fragile adhesions and difficulty in identifying anatomy with possibility of iatrogenic injury. Hence non operative therapeutic measures were implemented.

The main consequences in gastrointestinal fistulas with high outputs are associated with electrolyte imbalances and nutritional deficiencies. Patients are affected by anorexia, poor oral tolerance and malabsorption from gut. Hence initial conservative measures include resting the bowel (nil per oral), giving adequate hydration and correction of electrolytes. However, there is a place for oral feeding with surgically placed naso-jejunal tubes or feeding jejunostomy, bypassing the fistula origin and if the patient tolerates [1]. On the contrary, prolong fasting will need reinforcement with parenteral nutrition support [8,9]. These measures were adopted on this patient, with very limited success in controlling the fistula.

Those which are resistant to heal will need interventions [1]. Surgical techniques for the treatment of intractable pancreatic fistula include percutaneous trans fistulous pancreatic duct drainage (PTPD), percutaneous trans fistulous pancreatojejunostomy (PTPJ), and percutaneous trans fistulous pancreatic duct embolization (PTPE) [1,2]. Peripancreatic collections are amendable for drainage by intervention radiology or surgically. The latter may involve a complete pancreatectomy but this adds a significant mortality to patients [3].

Endoscopic therapy with endoscopic retrograde cholangio-pancreatography (ERCP) has shown benefit. Transpapillary sphincterotomy and stent placement for obstructed pancreatic ducts have improved healing time in some studies but controversies do exist regarding its effectiveness [14-18].

Octeotide is a peptide with similar amino acid sequence to somatostatin. It reduces gastrointestinal exocrine and endocrine secretions. Randomized control studies have shown conflicting evidence regarding its use for reducing the incidence of developing pancreatic fistulas [10-12]. Much of the promising results were seen in high risk patients.

The agent used to heal this fistulous tract is Tetracycline, derived and chemically modified from Actinomycetes [14]. Apart from been an antimicrobial agent, Tetracycline has sclerosing properties and stimulating fibrosis. It was found to be effective in healing postoperative chylous fistulas and broncho-cutaneous fistulas. Studies have evaluated its ability to heal malignant pleural effusions and suggest the ability of tetracycline to interfere in mesothelial cell repair, induce fibroblast enhancing growth factor secretion and inhibit metalloproteinases as contributory factors [19,20].

Giving consideration to these facts we instilled powdered tetracycline tablets, dissolved in normal saline through the drain tube. A remarkable reduction in drain output was noted and by the 3rd local tetracycline instillation the fistula completely ceased to drain. Hence sclerosing properties of

tetracycline need consideration as an effective mode in the treatment of pancreatic fistulas.

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