Case Report

Delayed pancreatic fistula: An unaccustomed complication following pancreaticoduodenectomy- a rare case report

Suvendu Sekhar Jena a,*, Dibyasingh Meher b, Rahul Ranjan b

a Department of Surgical Gastroenterology and Liver Transplantation, Sir Ganga Ram Hospital, New Delhi, 110060, India
b Department of General Surgery, VMMC and Safdarjung Hospital, New Delhi, India

ARTICLE INFO

Keywords:
Post-operative pancreatic fistula
Overt pancreatic fistula
Pancreaticoduodenectomy
Percutaneous drainage
Endoscopic stenting

ABSTRACT

Introduction: and Importance: Post-operative pancreatic fistula is a morbid complication after pancreaticoduodenectomy. Though most of them present in the immediate post-operative period, few case reports have mentioned it even 7 years after index surgery. Here, we report a delayed presentation of pancreatic fistula 6 months after surgery.

Case presentation: A 57 year old female underwent Whipple’s pancreaticoduodenectomy for pancreatic head adenocarcinoma and was discharged with an uneventful post-operative recovery. She presented after 6 months with complaints of abdominal pain and distension which upon evaluation was found to be a pancreatic enzyme rich multiloculated collection. It was managed with per-cutaneous drain placement.

Clinical discussion: Pancreatic fistula remained a major cause of morbidity and mortality even after 100 years of its existence. It can be overt fistula which manifest in the immediate post-operative period or occult fistula which manifests long after primary surgery. Various causes of delayed fistula are anastomotic site stricture, previous chemotherapy, infection. The management options available are percutaneous drainage, endoscopic stenting of anastomotic stricture or redoing the anastomosis.

Conclusion: Pancreatic fistula can have a delayed presentation which can be diagnosed and managed with regular follow up.

1. Background

After its inception by Whipple in 1914, pancreaticoduodenectomy (PD) became preferred choice of surgery in both benign and malignant diseases of periampullary region [1]. Though operative mortality (3-5%) is decreased but morbidity still remained high which around 30-65% [2]. Dealing with pancreatic stump is most important challenge and mostly the cause of postoperative complication [3]. Pancreatic fistula is one of major complication after PD which is around 2-28% [4]. There are lots of literature described about post-operative pancreatic fistula (POPF), but none of them have been mentioned about the timing of presentation apart from few case reports about delayed pancreatic fistula according to our knowledge. Here we present another case of pancreatic fistula presented 6 months after PD.

1.1. Case presentation

Fifty seven year old female, without any co-morbidity, with past history of cholecystectomy, presented with history of progressively worsening jaundice. It was associated with itching, occasional fever with chills and rigor. There was no significant drug history or family history. She was evaluated with ultrasound abdomen which showed mild dilatation of the intrahepatic biliary tree and the common hepatic duct with a dilated common bile duct measuring 9 mm and main pancreatic duct is dilated and measuring 4.1 mm. Computed tomography (CT) angiography of abdomen showed parenchymal mild heterogeneous enhancing mass of size (2.0 × 1.9 × 1.7) cm mainly involving the lower right side without any vascular invasion. There was narrowing of celiac artery with collaterals between celiac artery and superior mesenteric artery. It was associated with some pancreatitis involving the head and uncinate process with stranding around the distal SMV along the right side without any vascular invasion. There was narrowing of celiac artery with collaterals between celiac artery and superior mesenteric artery over the head of pancreas. In view of features of cholangitis, she was planned for endoscopic stenting of common bile duct but percutaneous transhepatic drainage was done in view of repeated failed cannulation. After optimization, she underwent Whipple’s
pancreaticoduodenectomy with division of median arcuate ligament by the experienced senior surgeon of our hospital. Intra-operatively, there was a pancreatic head mass of size (3 × 1) cm with a large aorto-caval lymph node which on frozen section was negative for metastatic deposit, pancreas was soft with a duct diameter of 3mm. The pancreatico-jejunal anastomosis was a stented duct to mucosa anastomosis done using 6–0 polydiaxone sutures. The histopathological report showed moderately differentiated adenocarcinoma of the head of pancreas with lymphovascular invasion and peri-neural invasion with 5 positive out of 42 lymph nodes with a pathological stage of pT1cN2pMx. The drain fluid amylase sent on post-operative day 3 (POD) from both drains was 8 U/L and 9 U/L. Both the drains were removed and she was discharged on POD 12. The subsequent imaging in the form of CT abdomen did not show any collection. She received adjuvant chemotherapy in the form of 2 cycles of gemcitabine and capecitabine. Post 2nd cycle chemotherapy she developed pain abdomen which was initially of low intensity but gradually worsened. She was admitted to a regional hospital with hypotension and a total leukocyte count of 26,000/cu mm. After optimization, she presented here and on evaluation with CT abdomen there was a large multiloculated collection with enhancing wall in the upper and lower abdomen with haziness around the pancreatic anastomotic site underneath the anterior abdominal wall with a distended stomach (Fig. 1 and 2). Feeding was started through nasojejunal tube. CT guided per-cutaneous drain was placed and drained fluid on analysis had an amylase of 1131 U/L and lipase of 3003 U/L. Somatostatin analogue was started due to raised drain fluid enzyme levels. Drain fluid culture was positive for Klebsiella pneumonia and antibiotics were changed as per sensitivity. Gradually drain output reduced and subsequent CT abdomen showed no significant collection (Fig. 3). She was discharged with per-cutaneous drain in situ which was removed on outpatient basis. Now she is doing well in subsequent follow up 15 months post surgery.

2. Discussion

PD continues to be a difficult surgery even 100 years after its inception by Dr Walter Kausch and its modification by Dr. Allen

Fig. 1. CT abdomen showing a collection with enhancing wall (White arrow).

Fig. 2. Coronal section of CT abdomen showing multiiloculated collection (Double white arrow) with a distended stomach (Single white arrow).

Fig. 3. CTfull a
Oldfather Whipple. With improvement of surgical techniques, though the mortality rate dropped, the morbidity still remained on higher side. Delayed gastric emptying, wound infection, post-pancreatectomy hemorrhage, postoperative pancreatic fistula (POPF), intra-abdominal abscess are amongst the common and serious complications following PD. Pancreatic anastomosis leak causing POPF still remains the leading cause of morbidity following PD even in specialized centers [5]. The main hurdle to manage POPF was lack of standardized and universally accepted definition until 2004 when 37 pancreatic surgeons from 15 countries formed International Study Group of Pancreatic Fistula (ISGPF) and purposed a definition for POPF. According to ISGPF, POPF was defined as measurable fluid output on or after postoperative day 3, with amylase content higher than three times the upper normal serum level [6]. It was revised in 2016 and divided POPF into biochemical fistula and clinically relevant fistula [7].

The risk factors of POPF following PD can be various like etiologies for surgery, pancreatic parenchymal texture, duct diameter, surgical techniques, blood loss, high BMI. In regards to etiologies, PD done for pancreatic adenocarcinoma has a low risk for fistula formation in comparison to ampullary, duodenal, distal cholangiocarcinoma [8]. Risk of POPF increased many fold in patients with soft pancreas and small pancreatic duct diameter \( < (2-3) \) mm [8,9].

Depending upon timing of its presentation, Veillette et al. divided POPF into overt and occult fistula. Overt fistulas are defined by their evidence within first post-operative week and causes major morbidity and mortality. Occult fistulas are those which are not manifested in the initial post-operative period but subsequently resulted in intra-abdominal collection, abscess formation, hemorrhage and death. In

![Image](http://example.com/fig3.png)
their series, there were 13 occult fistulas. They also found that occult fistulas were responsible for repeated hospital admissions but there was no difference between them in relation to intervention, reoperation or mortality. But the occult fistulas in their study presented within 90 days of surgery [10].

So, delayed presentation of POPF is a rare presentation which is rarer after PD and is only limited to individual case reports [11]. There are few case reports of delayed POPF after splenectomy [12,13]. Though the cause of delayed presentation of fistula is yet to be established, there are various plausible explanations. Pancreatic duct obstruction, recurrent pancreatitis, ischemia and fibrosis may lead to anastomotic disruption causing delayed POPF [14]. Pancreatojejunal anastomotic site stricture secondary to chemotherapy for pancreatic carcinoma may be another explanation [15]. Smoking which creates a thrombogenic environment along with its vasoconstrictive property may be another factor responsible for delayed POPF [16]. Small amount of initial leakage which often goes unnoticed may be aggravated by infection causing delayed fistula is another theory behind POPF. Gray zone between POPF and post-operative collections was described by Barreto et al. They proposed drains failing to drain properly due to blockage, displaced or misplaced drains and vascular factors may be responsible for delayed presentation of POPF [17]. In this case, though her immediate post-operative drain fluid amylase levels were normal ruling out an overt fistula, she presented with collections after receiving chemotherapy which may be the cause of delayed POPF by causing pancreatojejunal anastomotic stricture.

Due to its rarity, the exact time duration of its presentation from index surgery is yet to be elucidated. Veillette et al. in their series found all occult fistulas presented within 90 days of index surgery [10]. In a case report by Faraj et al. the duration was 7 years which is by far the longest interval reported in literature [14]. Ito et al. reported a gap of 1 year and it was 8 months by Perez et al. In our case, patient presented to us after 6 months of index surgery [3,18].

Management of this unique condition may range from percutaneous drainage, endoscopic stenting of anastomotic stricture to redo of the anastomosis [3,14,18]. Patient was managed with antibiotics and percutaneous drainage in our case.

3. Conclusion

A delayed pancreatic fistula after PD is a rare complication and is limited to only individual case reports. This is the fourth case report on delayed POPF in literature to our best of knowledge. A little is known about its etiopathogenesis and few plausible explanations are available regarding the same without any concrete evidence. Few management options are available in the form of percutaneous drainage, stenting of anastomotic stricture and redoing the anastomosis. Though this study provides a different perspective to the existing literature about the delayed presentation of pancreatic fistula, a case series involving large number of patients is required to establish its etiopathogenesis and management.

The work has been reported in line with the SCARE 2020 criteria [19].

Provenance and peer review

Not commissioned, externally peer-reviewed.

Ethical approval

Not required as per local ethical committee protocol.

Source of funding

This study has not received any funding from any government or non-government organization.

Author contribution

All authors have read and approved the manuscript. Dr Suvendu Sekhar Jena - Data collection and analysis, Writing Case report and Discussion. Dr Dilibisingh Meher – Writing abstract, introduction and article name. Dr Rahul Ranjan – Study designing and Final proofing.

Research registration

Not applicable.

Guarantor

Dr Suvendu Sekhar Jena.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Conflicts of interest

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2021.102460.

References

[1] G. Conzo, C. Gambardella, E. Tartaglia, V. Sciaccia, C. Masiello, S. Napolitano, et al., Pancreatic fistula following pancreatoduodenectomy. Evaluation of different surgical approaches in the management of pancreatic stump. Literature review, Int. J. Surg. 21 (Suppl 1) (2015) S4–S9.

[2] N.O. Machado, Pancreatic fistula after pancreatotomy: definitions, risk factors, preventive measures, and management review, Int J Surg Oncol (2012) 602479.

[3] N.P. Perez Jr., D.G. Forcione, C.R. Ferrone, Late pancreatic fistula after pancreatoduodenectomy: a case report and review of the literature, Case Rep Pancreat Cancer 2 (2016) 65–70.

[4] L.B. Haddad, O. Scanton, B. Randone, W. Andrus, P.P. Massault, B. Douset, et al., Pancreatic fistula after pancreatoduodenectomy: the conservative treatment of choice, HPB 11 (2009) 203–209.

[5] B. Rumschmidt, M. Schwab, P. Korth, M. Samman, M. Tredé, Hemorrhage after pancreatoduodenectomy, Ann. Surg. 227 (2) (1998 Feb) 236–241.

[6] C. Bassi, G. Butturini, E. Molinari, G. Mascetta, R. Salvia, M. Falconi, et al., Pancreatic fistula rate after pancreatic resection. The importance of definitions, Dig. Surg. 21 (2004) S4–59.

[7] C. Bassi, C. Dervenis, G. Butturini, et al., Postoperative pancreatic fistula: an international study group (ISGPF) definition, Surgery 138 (2005) 8–13.

[8] M.P. Gallyer, W.B. Pratt, T.S. Kent, et al., A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy, J. Am. Coll. Surg. 216 (2013) 1–14.

[9] F. Muscari, B. Suc, S. Kızırlar, J.M. Hay, G. Fourtanier, Fingerhut Aet al, Risk factors for mortality and intraabdominal complications after pancreatoduodenectomy: multivariate analysis in 300 patients, Surgery 139 (2006) 591–598.

[10] G. Veillette, I. Dominguez, C. Ferrone, S.P. Thayer, D. McGrath, A.L. Warshaw, et al., Implications and management of pancreatic fistulas following pancreatoduodenectomy: the Massachusetts General Hospital experience, Arch. Surg. 143 (2008) 476–481.

[11] R. Canadie, F. Basni, L. Calculli, N. Zanini, V.M. Greco, F. Minni, Report of three cases of chronic pancreatic fistulas treated with prolamine as a sclerosing substance following pancreatic resection, JOP 7 (2006) 41–46.

[12] S.G. Jin, Z.Y. Chen, J.N. Van, Y. Zeng, Delayed internal pancreatic fistula with pancreatic pleural effusion postpancreatectomy, World J. Gastroenterol. 16 (2010) 4494–4496.

[13] M.C. Yagmurdur, G. Gür, C. Aytekin, H. Karakayali, S. Boyacioglu, N. Bilgin, Atypical presentation of chronic pancreatic fistula: a case successfully managed with long-acting somatostatin, Turk. J. Gastroenterol. 14 (2003) 200–203.

[14] W. Faraj, Z. Abou Zahr, D. Mukherji, A. Zaghal, M. Khalife, Pancreatic anastomosis disruption seven years postpancreatectoduodenectomy, Case Rep Med 2010 (2010) 436739.
[15] J.L. Cioffi, L.A. McDuffie, A.M. Roch, N.J. Zyromski, E.P. Ceppa, C.M. Schmidt, et al., Pancreaticojejunostomy stricture after pancreatoduodenectomy: outcomes after operative revision, J. Gastrointest. Surg. 20 (2016) 293–299.

[16] A.K. Mathur, D.N. Ranney, S.P. Patel, D.S. Lee, F. Bednar, R.J. Lynch, et al., The effect of smoking on biliary complications following liver transplantation, Transpl. Int. 24 (2011) 58–66.

[17] G. Barreto, M.A. D’Souza, P.J. Shukla, S.V. Shrikhande, The gray zone between postpancreatoduodenectomy collections and pancreatic fistula, Pancreas 37 (2008) 422–425.

[18] Y. Ito, T. Irino, T. Egawa, S. Hayashi, A. Nagashima, Delayed pancreatic fistula after pancreaticoduodenectomy. A case report, JOP 12 (2010) 410–412.

[19] R.A. Agha, T. Franchi, C. Sohrabi, G. Mathew, for the Scare Group, The SCARE 2020 guideline: updating consensus surgical CAse REport (SCARE) guidelines, Int. J. Surg. 84 (2020) 226–230.