

CASE REPORT

Cholangitis Due to Pancreaticobiliary Fistula and Intraductal Papillary Mucinous Neoplasm: Thick Mucus Alters the Effectiveness of Biliary Drainage

Théophile Guilbaud¹, François Portier², Marie Pierre Mathoulin-Portier³, Yves Rinaldi⁴, Régis Fara¹

Departments of Digestive Surgery¹, Radiology², Histopathology³, and Gastroenterology⁴,
Hôpital Européen, Marseille, France

ABSTRACT

Context Fistula formation between the pancreas and adjacent organs has been reported in up to 6.6% of Intraductal papillary mucinous neoplasm cases of the pancreas. Pancreaticobiliary fistulas connect the intrapancreatic portion of the common bile duct and the main pancreatic duct. **Case report** Herein we report a case of an eighty-year-old man presented with a main pancreatic duct - intraductal papillary mucinous neoplasm complicated by PB fistula and obstructive cholangitis caused by the impaction of thick mucus protruding from the pancreas into the bile duct. In the present case, the main difficulty was the control of sepsis and jaundice related to the PB fistula. Endoscopic retrograde cholangiopancreatography was undertaken to confirm pancreaticobiliary fistulas and perform common bile duct drainage. Thick mucus flowing from the papilla revealed “pig-nose” appearance. Three endoscopic procedures were required because of failure to obtain effective common bile duct drainage due to stent migration and obstruction. Eventually a large covered biliary metallic stent was positioned to treat recurrent obstructive cholangitis. Combined with prolonged antibiotherapy these manoeuvres allowed biliary sepsis control, but jaundice persisted. A surgical approach was then decided to treat both persistent obstructive jaundice and the intraductal papillary mucinous neoplasm. **Conclusion** Pancreaticobiliary fistulas presenting as jaundice and /or cholangitis is a rare condition and is associated with malignancy in half of the patients. Biliary stenting remains the first line treatment but fails to control symptoms in half of the cases. Under such circumstances resective surgery is a radical treatment that resolves both the symptoms and the cause of PB fistula and should not be delayed.

INTRODUCTION

Intraductal papillary mucinous neoplasms (IPMN) of the pancreas are increasingly recognized and currently account for 20% of resected pancreatic neoplasms. Symptomatic IPMN commonly present with recurrent pancreatitis, chronic abdominal pain, or jaundice. Fistula formation between the pancreas and adjacent organs has been reported in up to 6.6% of IPMN cases, with the duodenum (67%), the stomach (44%) and the common bile duct (CBD) (33%) being the most frequently affected sites; up to 39% of the patients show multiple fistula formation [1, 2, 3]. Pancreaticobiliary fistulas (PB) connect the intrapancreatic portion of the CBD and the main pancreatic duct (MPD). Reports of PB associated with

IPMN and manifesting as obstructive jaundice are scarce in the literature [1, 4, 5, 6, 7, 8]. Herein we report a case of a MPD-IPMN complicated by PB fistula and obstructive cholangitis caused by the impaction of thick mucus protruding from the pancreas into the bile duct. A written informed consent was obtained from the patient.

CASE REPORT

An eighty-year-old man presented with right upper quadrant pain, jaundice, fever and weight loss. He had a 15-years history of type-2 diabetes mellitus. On admission, physical examination revealed obstructive cholangitis. The initial biological investigations revealed deranged liver function tests consistent with cholestasis and increased inflammatory tests (white blood count, C reactive protein). Computed tomography of the upper abdomen showed dilatation of the intrahepatic bile duct, CBD, and MPD without evidence of pancreatic head mass. Magnetic resonance imaging (MRI) also showed dilatation of the CBD and MPD, and multiple cystic masses located in all pancreatic segments; cholelithiasis was not demonstrated in the gallbladder and the common bile duct. Both radiological exams showed a large PB fistula connecting the intrapancreatic portion of the CBD and the MPD (**Figures 1a, b**). Endoscopic retrograde

Received May 19th, 2018 - Accepted June 29th, 2018

Keywords Jaundice, Obstructive; Pancreatic Ducts; Pancreatic Fistula

Abbreviations CBD common bile duct; IDUS intraductal ultrasonography; IPMN intraductal papillary mucinous neoplasm; MPD main pancreatic duct; PB pancreaticobiliary fistulas

Correspondence Théophile Guilbaud
Hôpital Européen, 6 Rue Désirée Clary
13003 Marseille, France

Phone + 336 42 57 52 85

Fax + 334 13 42 75 35

E-mail theo.guilbaud@gmail.com

cholangiopancreatography (ERCP) was undertaken to confirm PB fistula and perform CBD drainage. Thick mucus flowing from the papilla revealed “pig-nose” appearance, and selective cholangiography showed a short distal CBD stricture with proximal filling defects and outlined amorphous material obstructing the lower part of the CBD. Sphincterotomy was performed and a plastic biliary stent was inserted to treat the bile duct obstruction. Two additional endoscopic procedures were required because of failure to obtain effective CBD drainage due to stent migration and obstruction. Eventually a large covered biliary metallic stent was positioned to treat recurrent bile duct obstruction (**Figure 1c**) and to exclude the PB fistula (**Figure 1d**); combined with prolonged antibiotherapy these manoeuvres allowed biliary sepsis control, but jaundice still persisted. A surgical approach was then decided to treat both persistent obstructive jaundice and the IPMN; intraoperative exploration revealed hard-texture pancreatic parenchyma, and a large cystic lesion in the head of the pancreas (**Figure 2a**). Due to the diffuse involvement of the pancreas by IPMN total pancreatectomy was undertaken (**Figure 2b, c**). Transection of the bile duct revealed thick mucin within the lumen of the metallic duodenal stent. Frozen-section examination of the biliary

resection margin revealed no evidence of malignant involvement. Macroscopic examination of the specimen revealed thick mucus protruding from the pancreas via a large PB fistula with a diameter >15 mm which connected the intrapancreatic portion of the CBD and the MPD (**Figure 2d**). Pathological examination of the operative specimen revealed intestinal-type IPMN and high-grade dysplasia with focal in-situ invasive carcinoma (pTis N0 M0). Malignancy was not recorded at the site of the PB fistula. The postoperative course was uneventful, and the patient was discharged from hospital on POD 19.

DISCUSSION

In the present case, the main difficulty was the control of sepsis and jaundice related to the PB fistula. Several endoscopic procedures were necessary to treat obstructive cholangitis but did not allow complete regression of jaundice due to stent migration and obstruction by thick mucus. Eventually these complications were successfully managed by total pancreatectomy.

In the literature, fistula formation was reported in 6.6% of the IPMN patients, of whom 94% had intestinal-type IPMN [2]. Most of the PB fistula associated with

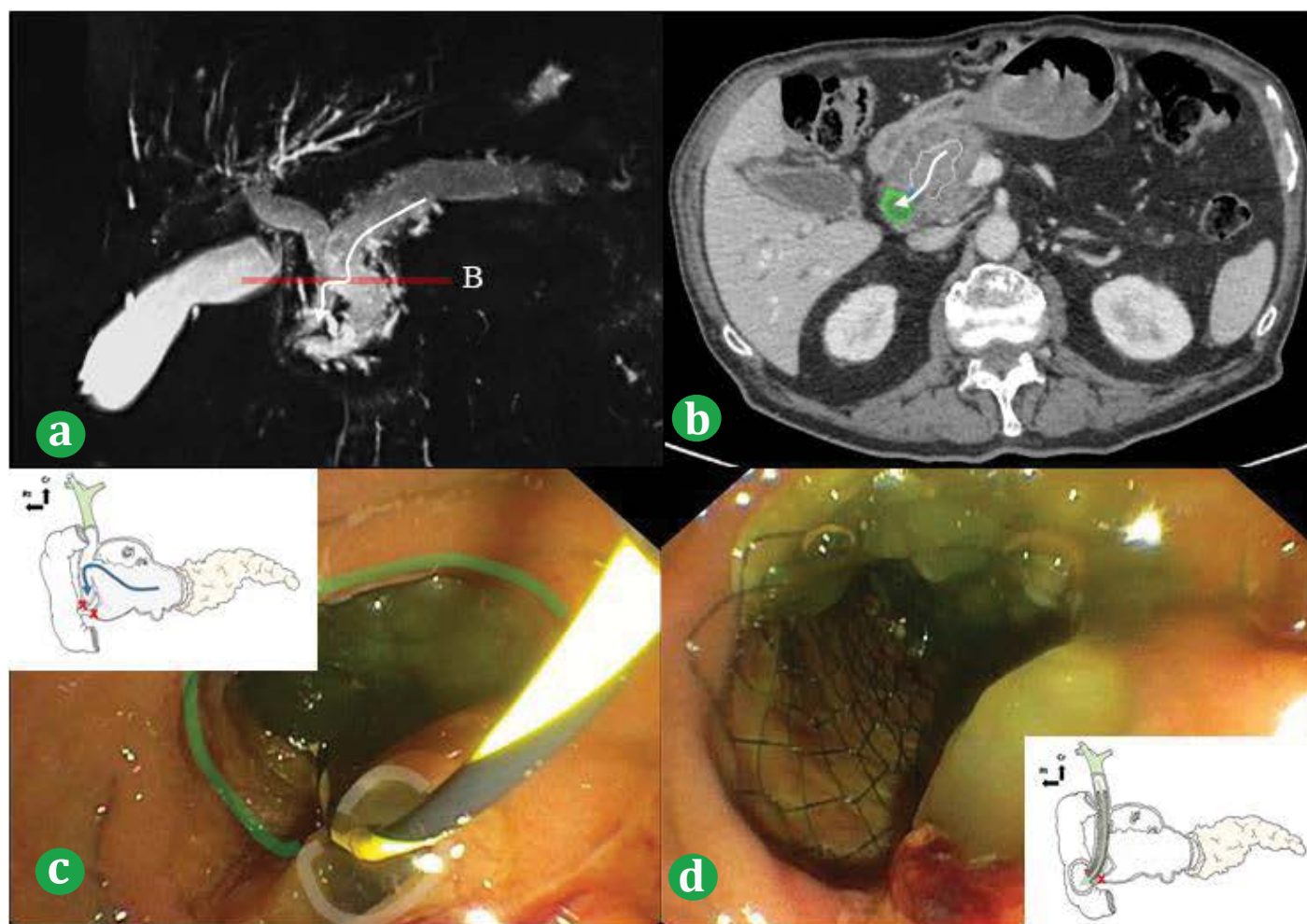


Figure 1. Preoperative assessment.

(a). Preoperative RMI showed dilatation of the common bile duct and the main pancreatic duct with a large pancreaticobiliary fistula (white arrow). **(b).** Preoperative abdominal CT scan at the level of the pancreaticobiliary fistula (blue), **(c).** third time endoscopic view of the duodenal papilla showed mucin secretion through a large common biliary duct (green) and pancreatic main duct (grey), **(d).** endoscopic view after biliary stenting procedure with metallic duodenal stent.

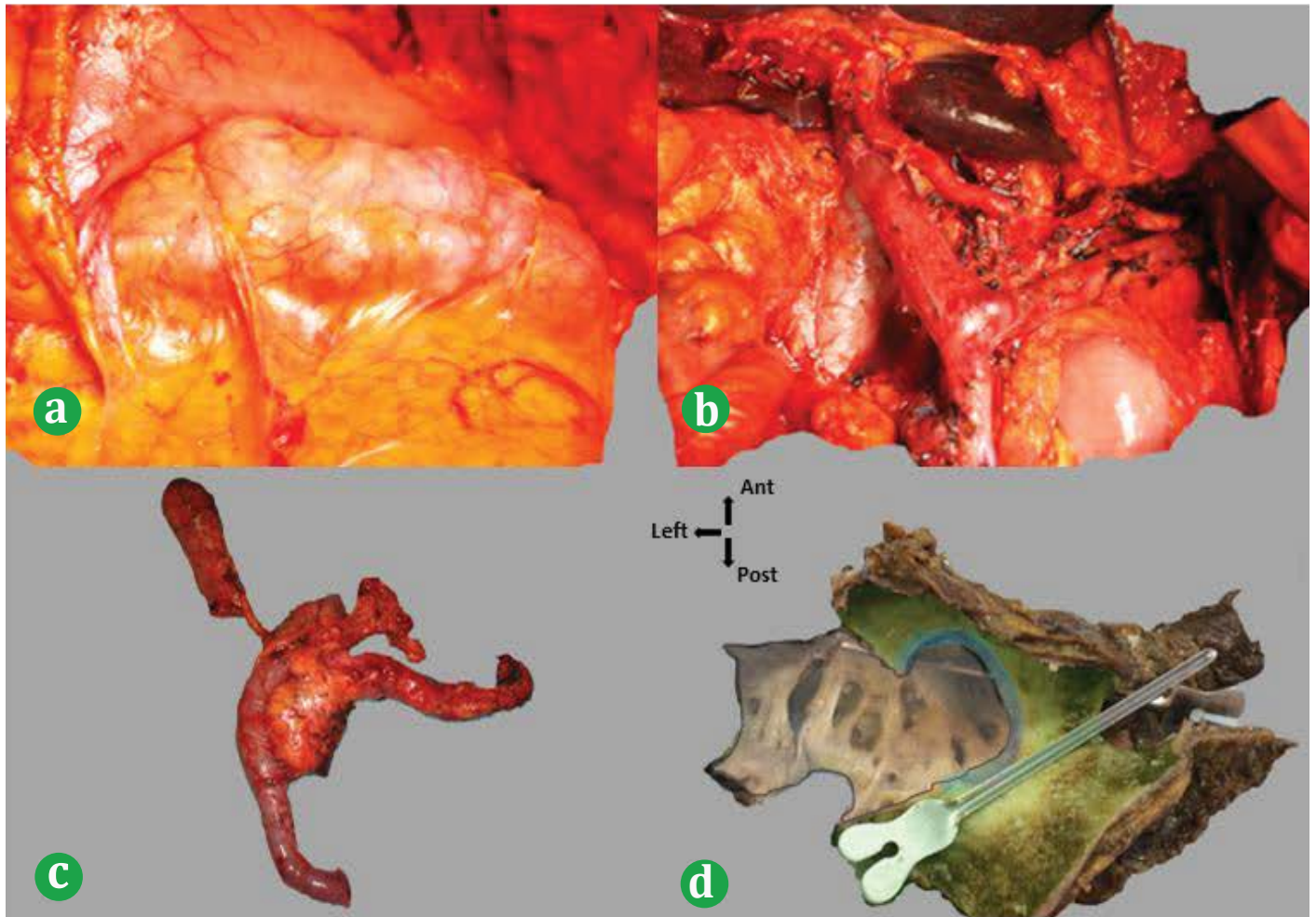


Figure 2. Operative and histopathological findings.

(a). intraoperative view showed a hard-pancreatic gland, diffuse dilatation of the main pancreatic duct and side branches from the head to the tail. **(b).** Resection area after total pancreaticoduodenectomy. **(c).** Total pancreaticoduodenectomy specimen before histopathological examination. **(d).** histopathological examination view after opening the common biliary duct (green) and the main pancreatic duct (grey), showed a large pancreaticobiliary fistula (blue).

IPMN has been identified by either ERCP, endoscopic ultrasonography or during surgery [2, 4]; our experience suggests that CT and MRI are also reliable in identifying large PB fistulas [3]. However it has been reported that, CT, MRI and ERCP are less performant for the diagnosis of small size PB fistulas [4, 6], due to thick mucus obstructing the CBD. In patients with IPMN, the resulting ERCP “pig-nose” appearance of the duodenal papilla, (dilation of both bile and pancreatic ducts due to thick mucus extrusion), may be suggestive of PB fistula [6]. Intraductal ultrasonography (IDUS) has proven the best diagnostic tool for IPMN relate PB fistulas in two specific settings: (1) after ERCP failure to detect the fistula; under these circumstances IDUS can be performed following ERCP; (2) in the presence of the “pig-nose” anomaly, because IDUS visualizes the CBD wall and its surrounding structures with higher resolution than CT and MRI [6].

PB fistula was not associated with malignant invasion in approximately half of the published cases; in the absence of malignancy PB fistula is probably secondary to mechanical compression by the cyst or/and mucin impaction within the lumen of the bile duct [1, 2, 4, 6]. Yamaguchi *et al.* [9] reported that mean survival times in patients with

PB fistula associated with IPMN who underwent surgical resection versus those who did not undergo surgical resection were 47.9 and 10.4 months, respectively.

The incidence of obstructive jaundice due to the mucinous material of PB fistula associated with IPMN was 97.1% [9]. When PB fistula associated with IPMN is revealed by obstructive jaundice, short term prognosis is conditioned by cholangitis. This situation is very rare and, in our knowledge, only 8 cases were reported in the literature [1, 4, 5, 6, 7, 8]. Management of this condition included ERCP drainage (n=6), percutaneous transhepatic drainage (n=1) and pancreatic resection (n=1) [4, 5, 6, 7, 8]. Similarly to our case, failure to obtain an effective biliary drainage required pancreatic resection (duodenopancreatectomy, n=5), and 2 patients died as a result of sudden worsening of cholangitis before surgery [4, 5, 6, 7, 8].

Relieving obstructive jaundice due to IPMN related is a challenging task. Of the 8 cases reported (including ours) biliary stenting was effective for the control of cholangitis in 6 patients and the control of jaundice in 3 patients [4, 5, 6, 7, 8]. In 4 of the 7 patients who underwent preoperative biliary drainage, several procedures were required to

allow sepsis control due to the small size of endoscopic biliary drain tube or stent migration, and a fully covered biliary metallic stent was inserted for fistula coverage and biliary drainage in 4 patients [4, 5, 6, 7, 8]. Reported cases and our experience, showed that several biliary drainage procedures are probably necessary to treat biliary obstruction associated with PB fistula, and that large metallic stent is required to allowed biliary sepsis control more than plastic stent [4, 5, 6, 7, 8]. Nevertheless, biliary stenting eventually failed in half of the patients because of the viscosity of the mucus in the bile; surgery is the most reliable treatment option under such circumstances [10].

CONCLUSION

In conclusion PB fistula presenting as jaundice and / or cholangitis is a rare condition and is associated with malignancy in half of the patients. Biliary stenting remains the first line treatment but fails to control symptoms in half of the cases. Under such circumstances resective surgery is a radical treatment that resolves both the symptoms and the cause of PB fistula and should not be delayed.

Conflict of Interest

There are no conflicts of interest or financial disclosure to declare.

References

1. Kurihara K, Nagai H, Kasahara K, Kanazawa K, Kanai N. Biliopancreatic fistula associated with intraductal papillary-mucinous pancreatic cancer: institutional experience and review of the literature. *Hepatogastroenterology* 2000; 47:1164-7.
2. Kobayashi G, Fujita N, Noda Y, Ito K, Horaguchi J, Obana T, et al. Intraductal papillary mucinous neoplasms of the pancreas showing fistula formation into other organs. *J Gastroenterol* 2010; 45:1080-1089. [PMID: 20549253]
3. Ravaud S, Laurent V, Jausset F, Cannard L, Mandry D, Oliver A, et al. CT and MR imaging features of fistulas from intraductal papillary mucinous neoplasms of the pancreas to adjacent organs: a retrospective study of 423 patients. *Eur J Radiol* 2015; 84:2080-8. [PMID: 26321495]
4. Okada KI, Furuuchi T, Tamada T, Sasaki T, Suwa T, Shatari T, et al. Pancreatobiliary fistula associated with an intraductal papillary-mucinous pancreatic neoplasm manifesting as obstructive jaundice: report of a case. *Surg Today* 2008; 38:371-6. [PMID: 18368332]
5. Bong JJ, Wang J, Spalding DR. Pancreatobiliary and pancreatoduodenal Fistulae in intraductal papillary mucinous neoplasm of the pancreas: report of a case. *Surg Today* 2011; 41: 281-4. [PMID: 21264770]
6. Koizumi M, Kumagi T, Kurado T, Azemoto N, Yamanishi H, Ohno Y, et al. Difficulty in management of intraductal papillary mucinous neoplasm-associated pancreatobiliary fistulas and the role of "pig-nose" appearance and intraductal ultrasonography in diagnosis. *Endosc Int Open* 2016; 4:e446-e450. [PMID: 27092326]
7. Komo T, Oishi K, Kohashi T, Hihara J, Kanou M, Nakashima A, et al. Pancreatobiliary fistula associated with intraductal papillary mucinous carcinoma accompanying obstructive jaundice: A case report. *Int J Surg Case Rep* 2018; 48:126-30. [PMID: 29890488]
8. Nagano H, Koneri K, Honda K, Murakami M, Hirono Y, Maeda H et al. Biliopancreatic fistula and abscess formation in the bursa omentalis associated with intraductal papillary mucinous cancer of the pancreas. *Int J Clin Oncol* 2009; 14: 460-4. [PMID: 19856058]
9. Yamaguchi T, Saitou F, Hori R, Yamashita I, Kiriya S, Sawada S, et al. A case of pancreatobiliary fistula associated with intraductal papillary mucinous neoplasm (IPMN) manifesting as obstructive jaundice and cholangitis. *J Jpn Biliary Assoc* 2011; 25:651-7.
10. Barnardo A, Fotiadis N, Meenan J, Wilkinson M, Wong T. Endoscopic management of intraductal papillary mucinous tumors fistulating into the common bile duct. *Gastrointest Endosc* 2007; 66:1060-62. [PMID: 17963895]