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Pancreaticobiliary malunion and incomplete pancreas divisum: an unusual cause of common bile duct obstruction

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ABSTRACT

Purpose: Pancreaticobiliary malunion (PBM) is a distinct disease entity of the pancreatic and biliary ductal system defined as a condition in which the junction of the pancreatic and biliary ducts occurs above the duodenal wall. PBM may be combined with a stenosis of the distal common bile duct and pathological changes in the common bile duct wall (congenital cyst of bile duct), being a potentially malignant condition. Pancreas divisum, resulting from a fusion failure of the ventral and dorsal pancreatic buds, and characterized by a dominant Santorine duct, is considered to be a predisposing factor to recurrent attacks of acute pancreatitis. In incomplete pancreas divisum, the ventral and dorsal pancreas are connected by a segmental branch.
Material and Methods: We report a case of a 33-year-old female patient with PBM associated with incomplete pancreas divisum, who had presented episodes of acute cholangitis due to a benign distal common bile duct stricture.
Results: Treatment with choledochoduodenostomy and cholecystectomy provided thorough relief and resolution of symptoms.
Conclusion: This is the first report of coexistent PBM and incomplete pancreas divisum in a Caucasian patient with unusually late clinical manifestation.

Key words: bile ducts/abnormalities, pancreatic ducts/abnormalities, adult

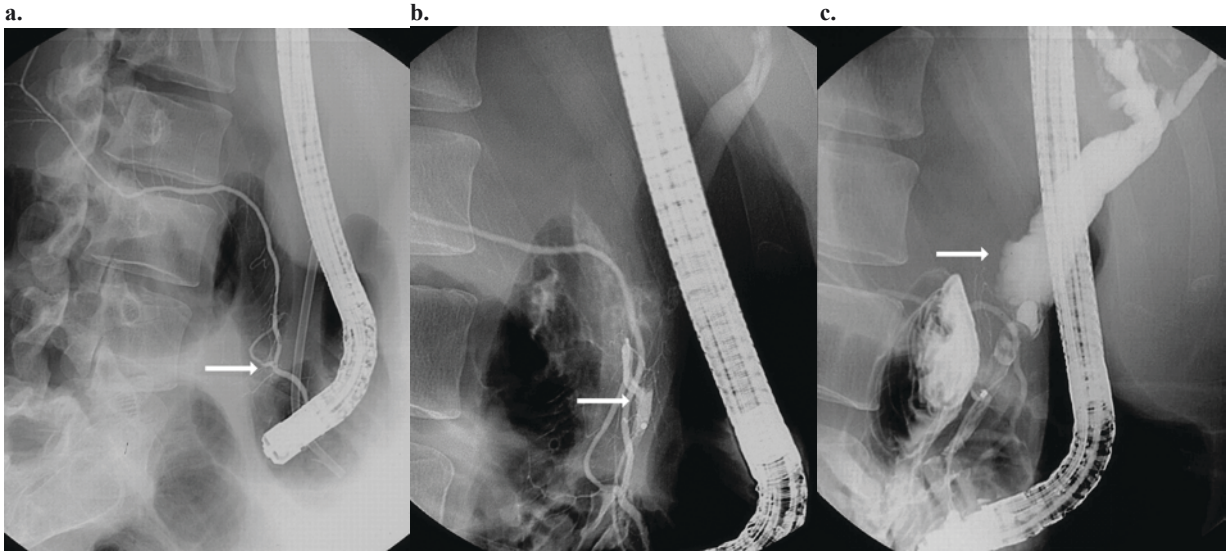
INTRODUCTION

Pancreaticobiliary malunion (PBM), first described by Babbitt in 1969 [1], is recognized as an anomalous arrangement of the pancreaticobiliary ductal system, commonly associated with congenital cyst of the bile duct (CCBD) [2]. A majority of cases have been reported from Asia, approaching a frequency of 1:1000, compared with an estimated prevalence of 1:100 000 in Europe [3]. Some series have documented CCBD in up to 90% patients with PBM, 10% having the ductal malunion alone [2,4]. Almost a half of cases are diagnosed in children younger than 15 years [5].

Suda [6] defined this anomaly as a junction of the pancreatic and biliary ducts located outside the duodenal wall, giving rise to a long common pancreatobilary channel [7]. The distance between the ductal junction and the orifice of the Vater´s papilla ranges from 0.5 to 5 cm on cholangiograms, whereas 0.5 cm is the upper reference limit of the normal common pancreatobiliary duct length [8]. The pancreaticobiliary malunion and CCBD are thought to arise following an arrest of normal migration of the pancreatobiliary union towards the duodenal wall [9].

Fujii et al. [10] reported a significant bile flow disturbance in PBM patients by hepatobiliary scintigraphy, showing its close correlation with clinical symptoms. Babbitt [11] was the first to propose that the absence of sphincter at the pancreaticobiliary junction allows regurgitation of pancreatic juice into the bile duct and, reciprocally, of the bile to the pancreatic ductal system. This might be an etiological factor of choledocholithiasis, inflammatory ductal epithelial changes, distal common bile duct strictures and recurrent bouts of acute cholangitis. Furthermore, the pancreaticobiliary malunion resulting in the chronic bile duct inflammation is generally considered to be frequently associated with malignancy of the biliary tract.

Figure 1. **Endoscopic retrograde cholangiopancreatography (ERCP) showing the pancreatobiliary malunion: a. connection of both pancreatic ducts, b. common bile duct stenosis and c. suprastenotic dilatation (arrows).**



In pancreas divisum, resulting from a failure of the ducts of the embryological dorsal and ventral pancreas to fuse, the pancreatic exocrine secretion is drained preferentially via the Santorine duct and minor papilla, with only the uncinate process and part of the pancreatic body emptying through the duct of Wirsung and ampulla of Vater. Association of the pancreas divisum and recurrent pancreatitis may be attributed to a relative obstruction of the pancreatic juice flow through a relatively narrow minor papilla, causing increased intraductal pressure. This hypothesis is indirectly supported by cessation of recurrent pancreatitis attacks after endoscopic treatment in some patients. In incomplete pancreas divisum, considered merely an anatomic variant of pancreas divisum [12], a segmental branch connects the ventral and dorsal pancreas.

We report a case of a patient with PBM, distal common bile duct stricture and incomplete pancreas divisum, where the malunion of the pancreatic and biliary system causing cholangitis was treated by cholecystectomy and choledochoduodenostomy.

CASE REPORT

A 33-year-old woman of Caucasian descent was admitted to the hospital due to a sudden onset of abdominal pain, vomiting, jaundice and fever. The patient had been in excellent health until three days before admission, when fever, chills, and colicky right upper abdominal pain with dorsal propagation appeared. On physical examination, the patient was jaundiced, with high fever and mild tenderness in the right upper abdominal quadrant. The results of a complete blood count and the serum levels of glucose, electrolytes, pancreatic amylase and transaminases were within the normal range, as were the results of renal-function and coagulation tests. The level of total billirubin was 3.2 mg/dL (normal: 0.1–1 mg/dL), alkaline phosphatase 480 IU/L (normal: 35–132 IU/L) and C-reactive protein 83 mg/L (normal 0–6.5 mg/L). Tumor markers were not elevated. Abdominal ultrasonography revealed two concrements in the gallbladder and a slight dilation of the common bile duct. Antibiotic treatment for acute cholangitis was initiated.

Endoscopic retrograde cholangiopancreatography *(ERCP, Fig. 1)* examination showed a tight stenosis of the distal common bile duct with a suprastenotic dilatation. Above the stenosis, the short and relatively subtle pancreatic duct was filled. Through a segmental branch, the dominant Santorine duct was opacified up to the pancreatic tail, which was also visualized by cannulation through the minor papilla. Magnetic resonance and computed tomography did not show any lesion in the liver hilum and pancreas. Endoscopic ultrasonography revealed sludge and multiple stones in the common bile duct above the stricture and thickening of the distal common bile duct wall. Endoscopic sphincterotomy was performed and a plastic stent (Amsterdam, 10 F, 7 cm) was inserted with immediate relief of symptoms and alleviation of cholestasis. However, the patient developed two episodes of acute cholangitis within the following 6 weeks due to obstructed biliary stent, requiring stent replacement. The issue, particularly the risk of malignancy, was discussed with the patient in full detail and surgical treatment was offered. The patient, herself being a physician, decided to undergo surgery in her regional hospital. Ten weeks after the initial symptoms, cholecystectomy and choledochoduodenostomy were performed. No complications occurred in the postoperative period, and the patient is currently maintaining good health and is entirely symptom-free.

Table 1. **Clinical hallmarks and complications for patients with pancreaticobiliary malunion (PBM) in combination with congenital bile duct cyst or PBM alone [5].**

Clinical presentation:	*Complications:*
Intermittent abdominal pain (79%)	Gallstone (27%)
Jaundice (18%)	Secondary sclerosing cholangitis (15%)
Fever (17%)	Acute pancreatitis (14%)
Vomiting (15%)	Acute cholangitis (11%)
	Pancreatic stone (4%)
	Chronic pancreatitis (2%)

DISCUSSION

Pancreaticobiliary malunion and congenital cyst of the bile duct (CCBD) are thought to have different embryonic etiologies. In the normal course of prenatal development, the main pancreatic duct joins with the common bile duct in week 4 of gestational age to form a common channel (i.e. the ampulla of Vater) that moves inside the proper muscle layer of the duodenum. Subsequently, primordial bile duct luminization is initiated and completed 6 weeks afterwards. Accordingly, the evidence suggests that formation of the PBM anomaly occurs earlier than formation of the CCBD [9]. Hence their simultaneous appearance is not an absolute rule. However, pre-existence of PBM may disturb the recanalization of the primitive bile duct [13]. This may in part support the high ratio of both PBM and CCBD occurrence. From the nomenclature standpoint, the long common channel found in patients with PBM should not be regarded as either the pancreatic duct or the bile duct, but rather as the "common channel". However, the common channel presumably belongs to the ventral pancreatic ductal system [14].

Pancreaticobiliary malunion is a congenital anomaly with a high risk of biliary tract carcinoma. Absence of a sphincter at the pancreaticobiliary junction allows regurgitation of pancreatic juice into the bile duct. Its mutagenicity in patients with PBM was examined by Matsubara et al. [15], and this issue was later considered further by Tschuchida [16], who observed different molecular patterns of cellular proliferative activity within the gallbladder mucosa in patients with PBM and in healthy controls. The carcinogenesis pathway has been shown to involve K-*ras* oncogene and *p53* tumor suppressor gene mutations [17], and further studies have emphasized the elevation of cellular proliferative activity of the gallbladder epithelium in children with PBM [18].

Pancreatic amylase would seem a plausible causative factor for the mucosal alterations in cases of pancreaticobiliary reflux in patients with PBM. It has been shown that high biliary amylase level is commonly observed in the biliary system in PBM patients [19]. The grade of biliary mucosal hyperplasia was related to the level of amylase in the bile, and the mean age of patients with gall bladder carcinoma has been shown to be significantly lower in patients with PBM than in the control group: about 40–50 years in the former compared with more than 65 years in the latter [20]. This proportional relationship, possibly attributable to the level of pancreatic amylase in the extrahepatic bile ducts and gallbladder, is in accordance with previous studies [21,22].

Table 2. **Prevalence of biliary cancer in patients with pancreaticobiliary malunion with and without congenital bile duct cyst, respectively [5].**

Pancreaticobiliary malunion without congenital bile duct cyst	*Pancreaticobiliary malunion with congenital bile duct cyst*
Cancer of extrahepatic biliary system including gallbladder cancer (33%)	Cancer of extrahepatic biliary system including gallbladder cancer (10%)
- Gallbladder (65%)	- Gallbladder (93%)
- Extrahepatic bile ducts (35%)	- Extrahepatic bile ducts (6%)

An important finding emerged from a Japanese retrospective study [5] involving several hundred patients with PBM alone and those with concurrent CCBD. The clinical presentation pattern and complications were similar for patients in both groups *(Tab. 1)*. As to the risk of cancer, a significant difference was observed between the groups *(Tab. 2)*. The pooled prevalence of gallbladder and extrahepatic bile duct cancer was 33% in the former group, gallbladder cancer constituting 65% of cancer cases, as compared to 10% in the latter group, where gallbladder cancer constituted 93% of cancer cases. The different prevalence of biliary cancer is consistent with the significantly higher amylase levels in the bile and gallbladder in patients with PBM alone [19]. However, the reason for the varying anatomical predilection sites of biliary cancer between the groups has not been elucidated.

The hypothesis of a significant reflux of pancreatic juice to the bile duct in PBM patients has arisen from both experimental and clinical studies [20,23]. A modified study of Kamisawa [24] aimed to investigate pancreatic juice reflux to the biliary tract in patients with PBM compared with patients where PBM was coincident with dorsal pancreatic ductal dominance, i.e. cases where the maximum diameter of the Santorine duct was equal to or greater than that of the Wirsung pancreatic duct. The authors proved that in patients with PBM with dorsal pancreatic duct dominance, most pancreatic juice was drained into the duodenum through the minor duodenal papilla. Thus the reflux of pancreatic juice to the biliary tract was diminished, potentially resulting in a reduced risk of associated biliary malignancies.

A comparison of cases with complete and incomplete pancreas divisum [12] indicated that the symptoms, clinical presentation and outcome of endoscopic treatment were similar in both groups. However, with regard to the dorsal pancreatic duct predominance described in the case report, we assume that the coexistence of incomplete pancreas divisum and PBM may reduce biliary cancer risk compared with patients with PBM alone.

CONCLUSIONS

The reported case exhibited several specific features. Firstly, association with pancreas divisum is very exceptional. Secondly, the manifestation of the disease appeared in adulthood, i.e. much later than in other reported cases [25]. Thirdly, due to the patient's strong desire to be operated on in a regional hospital with limited capacity for biliary tract surgery, choledochoduodenostomy was performed.

Cholecystectomy and bilio-enteral anastomosis remains the treatment of choice for all patients with proven pancreaticobiliary malunion. The choledochoduodenostomy performed in our patient can be regarded as a less suitable treatment for this premalignant condition. The benefit of mucosectomy of the bile duct below the stricture following the surgery needs to be further evaluated.

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