Cholangiocarcinoma in a 21-year-old male with pancreaticobiliary malunion and choledochal cyst: A case report

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Abstract

Significance: Choledochal cysts and pancreaticobiliary malunion are rare conditions. Both are highly correlated with biliary tract cancer. Its predisposition to malignant transformation is due to chronic pancreaticobiliary reflux and inflammation leading to dysplasia and carcinoma. *Clinical Presentation:* A 21-year-old male presented with three months' duration of epigastric pain and no known risk factors. Initial ultrasound imaging noted an ill-defined lesion at the left hepatic lobe and concomitant dilated intrahepatic and biliary ducts. *Management:* Considering a liver abscess, ultrasound-guided drainage of abscess was done along with complete antibiotic regimen. Repeat imaging showed a Type IVa choledochal cyst and persistent left hepatic lobe lesion. CA 19-9 was markedly elevated. ERCP confirmed presence of choledochal cyst and a concomitant pancreaticobiliary malunion with high insertion of pancreatic duct about 1.6 cm away from the ampulla. Biliary stenting was done. Highly suspecting malignant transformation associated with choledochal cysts, diagnostic laparoscopy was done revealing whitish peritoneal implants. Final histopathological diagnosis was conclusive of metastatic cholangiocarcinoma. Thereafter he was then referred to oncology service. Unfortunately, after three months, the patient expired. *Recommendations:* In a young patient with recurring and worsening abdominal pain associated with presence of choledochal cyst and evidence of biliary tract anatomical malunion, a possible biliary tract malignancy should be highly suspected. Reporting this anomaly when discovered at imaging is important for close follow-up of patients at risk.

Keywords: case report, choledochal cyst, pancreaticobiliary malunion, cholangiocarcinoma, malignant transformation

Introduction

Pancreaticobiliary malunion, also known as pancreaticobiliary maljunction (PBM), and choledochal cysts are important risk factors for biliary cancer. Studies of incidence in Japan showed that in those with pancreaticobiliary malunion, biliary tract cancer develops 15-20 years sooner than in individuals without PBM.[1]

Choledochal cyst, otherwise known as congenital biliary dilatation, first described by Vater and Ezler in 1723, is a rare congenital cystic dilation of the biliary tract.[2] The first well-documented case was described by Douglas in 1852 of a biliary cyst in a 17-year-old girl.[3] This condition presents primarily in female infants and young children and are more prevalent among East Asians, with a reported incidence of one in 1,000; and about two-thirds of which occurring in Japan.[4] In western countries, it is reported that this occurs in one of every 50,000 to 150,000 individuals, and in one neonate in two million births.[5] At present, no prevalence data exists in the Philippines.

PBM is a congenital malformation in which a common channel for bile and pancreatic fluid is formed owing to the absence of a septum between the ducts. This abnormal union occurs outside the duodenal walls;

thus, the influence of sphincter of Oddi is lost, allowing reflux of pancreatic exocrine secretions into the biliary system and bile into the pancreatic duct.[5] This was first noted by Arnold in 1804, while Kozumi and Kodama then reported in detail the abnormal union of the pancreatic and bile ducts in 1916 in an autopsy report.[6] The frequency of PBM varies from 1.5-3.2%.[7]

Case Presentation

A 21-year-old male student, single, with no known co-morbidities or history of high-risk behavior and with unremarkable family history, was admitted due to epigastric pain. Three months prior to admission, there was onset of intermittent crampy upper abdominal pain, fluctuating at 5-8/10 pain score, associated with postprandial vomiting. There was no associated fever or changes in bowel and urinary patterns. Ultrasound of the whole abdomen showed a suspicious ill-defined echogenic focal lesion seen at the lateral segment of the left lobe of liver measuring 4.2 cm x 3.6 cm x 3.9 cm (LWH). Liver abscess was highly considered, for which he was admitted and subsequently treated. CT scan was suggestive of abscess formation (2.6 cm x 2.7 cm x 2.2 cm) and showed dilated common bile duct and intrahepatic duct, as well as multiple enlarged mesenteric, periaortic, interaortocaval, and periportal lymph nodes. Ultrasound-guided aspiration of the hepatic abscess yielded *Enterobacter sakazakii* susceptible to ciprofloxacin and metronidazole, and were therefore administered.

Magnetic resonance cholangiopancreatography (MRCP) showed dilated intra- and extrahepatic bile ducts (see **Figure 1**) compatible with choledochal cyst Type IVa of the Todani Classification (see **Figure 2** and **Table 1**), and multiple small cholecystolithiasis. He was consequently discharged on antibiotics.

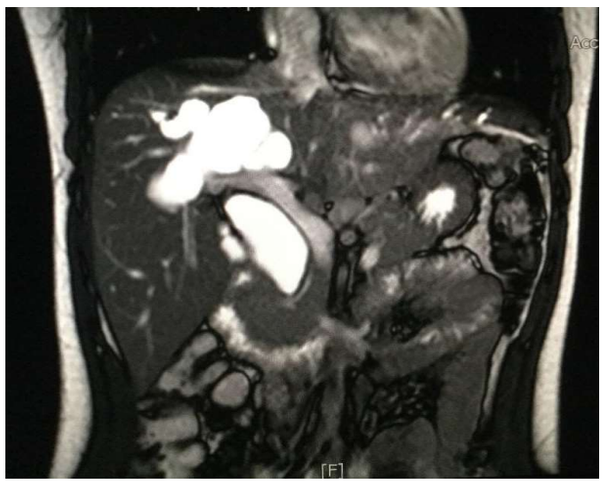

Figure 1. MRCP showing dilated intrahepatic (46 mm) and extrahepatic (28 mm) bile ducts compatible with choledochal cysts Type IVa of the Todani classification.

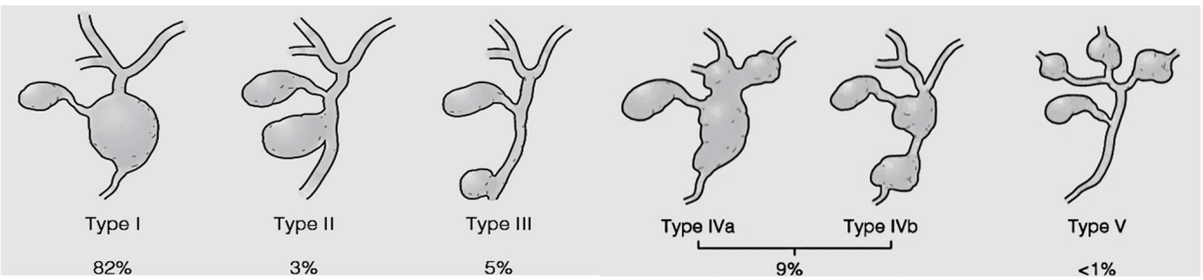

Figure 2. The Todani classification for biliary dilatation choledochal cysts and corresponding percentage incidence.[8]

Table 1. Classification of choledochal cysts and features.

Type	Features
I	Most common variety (80-90%) involving saccular or fusiform dilatation of a portion or entire common bile duct (CBD) with normal intrahepatic duct
II	Isolated diverticulum protruding from the CBD
III	Also called choledochocele: Arises from dilatation of duodenal portion of CBD
IVa	Characterized by multiple dilatations of the intrahepatic and extrahepatic biliary tree
IVb	Multiple dilatations involving only the extrahepatic bile ducts
V	Cystic dilatation of intrahepatic biliary ducts without extrahepatic duct disease. The presence of multiple saccular or cystic dilations of the intrahepatic ducts is known as Caroli's disease

Two months later, he was re-admitted due to recurrent severe abdominal pain, this time with accompanying anorexia and weight loss. Complete blood count and bilirubin levels were within normal range; alkaline phosphatase was 159 U/L, and SGPT was 77 U/L. Whole abdominal ultrasound showed dilated gallbladder, common duct, and left intrahepatic duct. Serum CA 19-9 was markedly elevated at 87,832.16 u/ml (lab reference: 0-37 u/ml) and CEA was 359.58 (lab reference: 0-5 ng/ml). Nucleic acid screening tests were negative for HIV, HBV and HCV. The patient underwent endoscopic retrograde cholangiopancreatography (ERCP), which showed a dilated common bile duct (2.6 cm) with no filling defect, and narrowing noted at the common hepatic duct (**Figure 3**). The pancreatic duct was normal in size but had a high pancreatic duct insertion of about 1.6 cm from the ampulla (**Figure 4**).

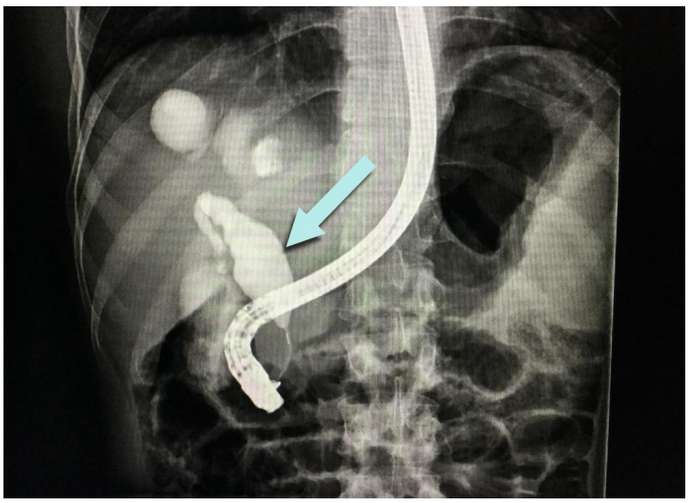

Figure 3. ERCP showing a dilated common bile duct (2.6 cm) (arrow) consistent with a choledochal cyst.

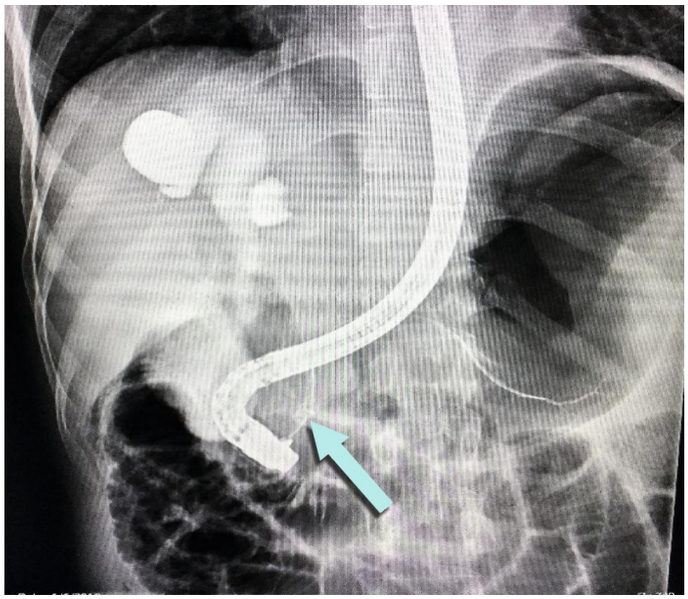

Figure 4. ERCP showing high pancreatic duct insertion about 1.6 cm from the ampulla (arrow)

There was obstruction in the left hepatic duct. Sphincterotomy was done. Stent placement to the right hepatic duct was done but attempt to visualize beyond the left hepatic duct stricture failed.

Upper abdominal pain still persisted. Malignancy was then entertained. Two days after initial procedure he underwent a diagnostic laparoscopy which showed multiple whitish peritoneal implants near the falciform ligament and lesser curvature, and whitish/caseous material at the left lobe of the liver (**Figure 5**).

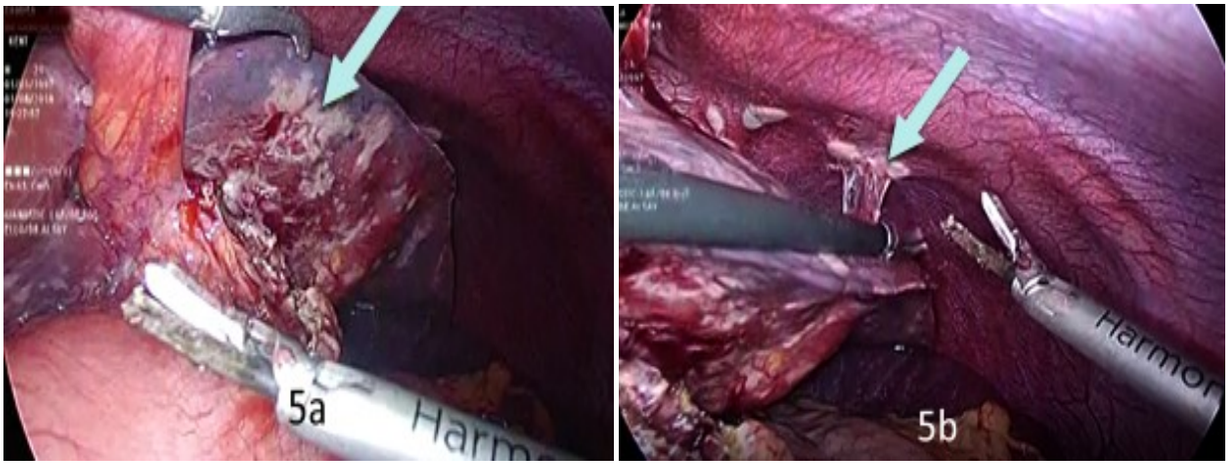

Figure 5. Diagnostic laparotomy showing multiple whitish peritoneal implants adherent to liver (5a), and peritoneum (5b).

At this point, primary consideration was biliary tract malignancy. Microscopic examination of the peritoneal implants showed fragments of malignant neoplasm composed of tumor cells with enlarged, pleomorphic, vesicular nuclei with conspicuous nucleoli and scant cytoplasm. There was noticeable presence of "signet ring" cells (**Figure 6**)**.**

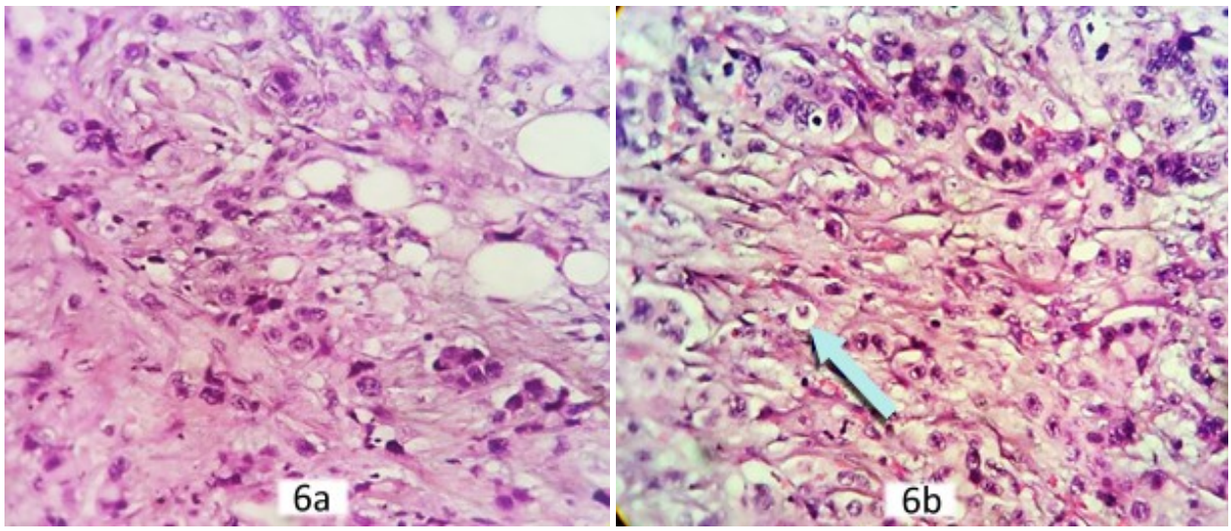

Figure 6. Microscopic examination of implants shows tumor cells with enlarged pleomorphic, vesicular nuclei with conspicuous nucleoli and scant cytoplasm (**6a**). Some cells show enlarged nuclei and abundant foamy vacuolated mucin-filled cytoplasm pushing nuclei to the periphery giving a "signet ring" appearance (**6b**).

Final histopathological diagnosis was consistent with a metastatic moderately poorly differentiated cholangiocarcinoma.

He was discharged with pain medications and referred to the oncology outpatient service. Unfortunately, however, three months after his discharge and prior to the initiation of chemotherapy, he succumbed to infection.

Discussion

Choledochal cysts and pancreaticobiliary malunion are rare conditions, one often known to be closely related to the other. Choledochal cysts are associated with different degrees of dilatation at various portions of the bile duct. The Todani classification identifies five types (**Figure 2** and **Table 1**). Incidence is common among Asians. Studies in Japan report a male-to-female ratio of 1:3.[8] Clinical manifestations include abdominal pain, vomiting, jaundice and fever.

The frequency of biliary tract cancer occurring in adults with choledochal cyst is extremely high at 21.6%, manifesting as gallbladder malignancy in 62.3% and bile duct cancer in 32.1%.[10]

It is reported that choledochal cyst patients are a high-risk group for developing biliary tract cancers, having an incidence of 21.6% compared to 42.4% for those without.[9] A study done in Japan showed that the age range in which they are predisposed to developing gallbladder cancer is 15-20 years earlier, at 60 ± 10 years compared to the population developing gallbladder cancer without choledochal cyst (75-79 years old).[9] Another group estimated early onset age at 50-65 years of age.[10] The uniqueness of our case is the presentation of advanced-stage cholangiocarcinoma in a very young male of 21 years.

The mechanism for biliary carcinogenesis in patients with PBM differs from those without PBM. Normally, the junction of the main pancreatic duct and the common bile duct lies within the duodenal wall; however, in patients with PBM it lies outside the duodenal wall. There is still no unified recognition about the normal length of the common duct and the literature varies according to the type of imaging modality used**.** The junction of the common bile duct and pancreatic duct is crucial for sphincteric control of bile and pancreatic juice drainage, with bidirectional regurgitation if the union is above Oddi's sphincter.[10] This would lead to persistent inflammation and regeneration of the biliary tract mucosa. A sequence of events called hyperplasia-dysplasia-carcinoma is assumed to take place in the gallbladder of patients with PBM (**Figure 7**)**.**

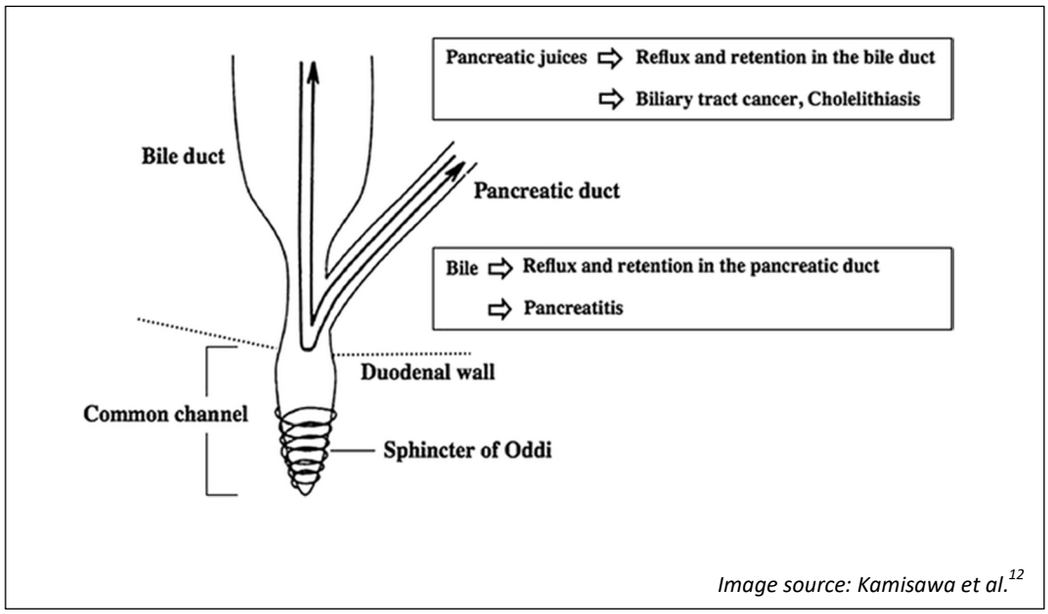

Figure 7. Proposed pathophysiology of pancreaticobiliary malunion and its association with biliary cancer.

Diagnosis can be done by x-ray (intra- and/or post-cholangiogram), helical CT scan, ultrasound and the new non-invasive modality called Magnetic Resonance Cholangiopancreatography (MRCP). ERCP remains indispensable in diagnosing PBM. Radiologic diagnosis of a PBM via ERCP is acceptable when it involves a long common channel (over 1.5 cm in length) and presence of a junction outside the duct.[11]

This patient was of the p-b (pancreatic duct to bile duct) type in which the pancreatic duct appears to join the bile duct with a length of 1.6 cm from the ampulla.

We suspect that the malignant transformation in this case was due to the presence of both PBM and choledochal cyst. In choledochal cysts, with the influence of the accompanying PBM, a thickening of the gallbladder wall can often be observed. In PBM, a mixture of pancreatic juices and bile is retained in the gallbladder, causing repeated inflammation and recovery of the gallbladder epithelial wall. The resulting enhanced cell proliferation in the gallbladder wall is thought to provoke hyperplasia and subsequent dysplasia, which is assumed to trigger carcinogenesis in the gallbladder.[12]

Conclusion

Cholangiocarcinoma in this young male probably occurred due to the consequence of the pancreaticobiliary malunion with choledochal cyst exerting chronic mucosal irritation due to recurring reflux, ultimately leading to malignancy.

When faced with a case of a young patient with recurring and worsening abdominal pain associated with presence of choledochal cyst and evidence of a biliary tract anatomical malunion one should have a high index of suspicion of possible malignancy in the biliary tract. Reporting this anomaly during imaging should be encouraged in order to identify patients at risk and to encourage close follow-up. Early diagnosis and appropriate surgical management is crucial for a favorable clinical outcome.

Conflicts of Interest

The authors declare no conflicts of interest.

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