

A Case of Double Primary Cancer (Gallbladder cancer and pancreatic cancer) in Patient with Anomalous Union of Pancreaticobiliary Duct

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Anomalous union of the pancreaticobiliary duct (AUPBD) has been shown to predispose to carcinomas of the biliary tract (bile duct and gallbladder) and pancreatic cancer because of chronic recurrent inflammatory reaction due to pancreatic or bile juice refluxes. However, pancreatic duct would be less affected by the bile because of the relatively higher intraductal pressure of the pancreatic duct. We report a case of metachronous pancreatic cancer in AUPBD patient without choledochal cyst who underwent cholecystectomy because of gallbladder cancer.

Key Words: AUPBD, Gallbladder cancer, Pancreatic cancer

INTRODUCTION

Anomalous union of the pancreaticobiliary duct (AUPBD) is a rare congenital anomaly in which the confluence of the common bile duct and pancreatic duct is outside the duodenal wall, usually forming a long common channel.^{1,2} Pancreatic juice refluxes into the common bile duct, or bile regurgitates into the pancreatic duct because the action of the sphincter muscle does not functionally affect the union.³ AUPBD has been shown to predispose to pancreaticobiliary disorders such as choledochal cyst, stone formation, cholangitis, pancreatitis, carcinomas of the biliary tract (bile duct and gallbladder) and pancreatic cancer.¹ AUPBD patients without choledochal cyst are generally recommended to undergo cholecystectomy. Reported cases of pancreatic cancer with AUPBD were rarer than biliary cancer.⁴ Pancreaticobiliary reflux occurs more commonly due to the relatively higher intraductal pressure of the pancreatic duct. Therefore, pancreatic duct would be less affected by the bile resulting in lower the incidence of malignancy.⁴ We report a case of double primary cancer (gallbladder and pancreatic cancer) at different time in patient with AUPBD.

CASE REPORT

A 56-year-old woman was admitted with epigastric pain. She had to epigastric discomfort in the past two months does not eat well, and recent 7 kg weight loss between two months. 2 years ago, she underwent simple cholecystectomy because of gallbladder mass associated with acute cholecystitis (Fig. 1). After surgery, in pathologic result showed adenocarcinoma which invaded perimuscular, but clear resection margin. She was observed in outpatient because of her refusal of additional surgery. WBC, hemoglobin, and platelet were 4,800/uL, 12.7 g/dL, and $171 \times 10^3/dL$, respectively. Liver panel including aminotransferase, alkaline phosphatase, and bilirubin was within normal range. Serum amylase level was 212.4 IU/L (reference range 36-128 IU/L), lipase level was 807.2 U/L (reference range 22-51 U/L), and CA19-9 level was 9.24 U/mL (reference range 0-39 U/mL). Ig G4 level was 429 mg/L (reference range 30-2,010 mg/L). She was performed computed tomography, resulting as 1.8 cm hypoechoic mass was

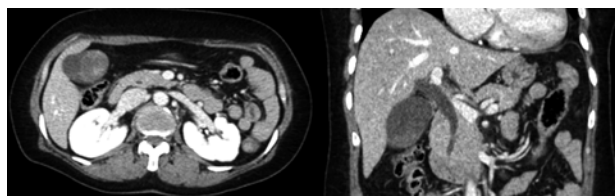


Fig. 1. Abdomen CT scan 2 years ago.

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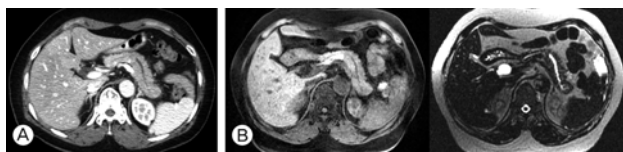


Fig. 2. (A) Finding of abdomen-pelvis CT, (B) Finding of MR pancreas.



Fig. 3. Finding of ERCP.

founded in pancreatic body, and pancreatic duct dilatation in pancreatic tail, parenchymal edema, and fat stranding (Fig. 2A). She was showed the same findings in abdominal MRI, another tumor was not found in the liver parenchyma (Fig. 2B). The patient was observed AUPBD in endoscopic retrograde cholangio-pancreatography (ERCP) finding, the length of the common channel is about 2.3 cm. And cut-off sign was observed in pancreatic body. Brush cytology in obstruction area during ERCP was performed resulting as ductal adenocarcinoma. Endoscopic retrograde pancreatic drainage (ERPD) was done during ERCP for resolving obstructive pancreatitis (Fig. 3). After drainage, patient's abdominal pain was improved. In laboratory finding, Serum amylase level was 98.1 IU/L (reference range 36-128 IU/L), lipase level was 197.2 U/L (reference range 22-51 U/L). He underwent distal pancreatectomy with splenectomy, and adjuvant 5-FU and cisplatin based concurrent chemoradiation therapy (CCRT). He was observed in outpatient in regularly.

DISCUSSION

AUPBD is a rare congenital condition reported to be found more commonly in Asians than in Westerners, particularly in women. AUPBD is defined that confluence of the common bile duct and pancreatic duct is outside the duodenal wall, usually forming a long common channel.^{1,2} In generally, AUPBD could be diagnosed by the length of the common channel,

more longer than 15 mm. However, some case was difficult to diagnose with short common channel.⁵ AUPBD was divided into type I (P-C union) and type II (C-P union) subtypes according to Kimura's classification. The main pancreatic duct joined the common bile duct (CBD) in P-C union, whereas CBD joined the main pancreatic duct in C-P union.⁶ AUPBD is commonly associated with choledochal cyst, bile duct stone, cholangitis, pancreatitis, and carcinomas of the biliary tract (bile duct and gallbladder).^{1,2,7} AUPBD results in mixing of bile and pancreatic juice, because the action of the sphincter muscle does not functionally affect the union.^{3,8,9} The biliary mucosa is repeatedly damaged and repaired, which causes an acceleration of cell proliferative activity and multiple gene mutations.⁹ Pancreaticobiliary reflux occurs more commonly due to the relatively higher intraductal pressure of the pancreatic duct.⁴ Therefore, pancreatic duct receives less affected by the bile will lower the incidence of malignancy. All of the pancreatic enzymes including amylase, lipase, trypsin, elastase-1, and phospholipaseA2 (PLA2) are detected at extremely high levels in the AUPBD bile, especially in gallbladder contents. 4 Activated PLA2, particularly powerful destructive action on the pancreatic duct and biliary epithelium converts the lecithin within the bile into lysolecithin and free fatty acids that have a strong damaging action on cell membranes.^{4,9} As well known, point mutations of K-ras oncogene and over-expression of p53 gene are suspicious as one of the cause of carcinogenesis.^{4,5,7}

As mentioned above, ABPUUD commonly associated with choledochal cyst. Many studies have demonstrated that it is generally perceived that the likelihood of the development of both bile duct cancer and gallbladder cancer increases in AUPBD patients with choledochal cyst, whereas there is a significant predilection for gallbladder cancer to occur in AUPBD patient without choledochal cyst.^{1,4,5} So, AUPBD patients without choledochal cyst are recommended to undergo cholecystectomy in generally., Total excision of the extrahepatic biliary tract is necessary in the cases with choledochal cyst.^{1-5,7}

Kim's study showed the proportion AUPBD patients with of bile duct cancer is similarly between with and without choledochal cyst, they recommend further surgical management including bile duct excision may be necessary in absence of choledochal cyst. They also recommended if physician think further surgical method such as total excision of the extrahepatic biliary tract is extreme measure, conceivable therapeutic strategy after cholecystectomy could be to resolve pancreaticobiliary reflux by performing endoscopic sphincterotomy (EST).¹

In this case, Metachronous pancreatic cancer was occurred in AUPBD patient without choledochal cyst who underwent

cholecystectomy because of gallbladder cancer. We think that remnant pancreaticobiliary reflux increased risk of carcinoma of pancreaticobiliary system. This finding suggest that vigilant surveillance is necessary if reflux is not resolved after cholecystectomy state in AUPBD without choledochal cyst.

REFERENCES

1. Kim YJ, Hyun JJ, Lee JM, Lee HS, Kim CD, Anomalous union of the pancreaticobiliary duct without choledochal cyst: is cholecystectomy alone sufficient?, *Langenbecks Arch Surg* 2014; 399:1071-1076
2. Yi SY, Gallbladder carcinoma associated with anomalous union of pancreatobiliary ductal system, *Open Journal of Gastroenterology* 2013;3:249-251
3. Song HK, Kim MH, Myung SJ, et al. Choledochal Cyst Associated the with Anomalous Union of Pancreaticobiliary Duct (AUP BD) Has a More Grave Clinical Course Than Choledochal Cyst Alone, *Korean J Intern Med* 1999;14(2)
4. Funabiki T, Matsubara T, Miyakawa S, Ishihara S, Pancreaticobiliary maljunction and carcinogenesis to biliary and pancreatic malignancy *Langenbecks Arch Surg* 2009;394:159-169
5. Hwang EJ, Dong SH, Congenital Pancreatobiliary Anomaly Associated with Pancreatobiliary Malignancy The Korean Society of Gastrointestinal Endoscopy 48th seminar
6. Kimura K, Ohto M, Ono T, et al. Congenital cystic dilatation of the common bile duct: relationship to anomalous pancreatobiliary ductal union. *AJR Am J Roentgenol* 1977;128(4): 571-577.
7. Kim SH, Kim HW, Kang DH, et al, A Case of Intrahepatic Cholangiocarcinoma Associated with Type IV Choledochal Cyst, *Korean J Gastroenterol* Vol. 60 No. 2, 123-127
8. Nomura T, Shirai Y, Sandoh N, Nagakura S, Hatakeyama K. Cholangiographic criteria for anomalous union of the pancreatic and biliary ducts, *Gastrointest Endosc* 2002;55(2): 204-8.
9. Tsuchida A, Itoi T. Carcinogenesis and chemoprevention of biliary tract cancer in pancreaticobiliary maljunction, *World J Gastrointest Oncol* 2010;15(3):130-135