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**ORIGINAL ARTICLE**

# Simultaneous gallbladder and bile duct cancers: revisiting the pathological possibilities

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**Abstract**
The pathogenesis of gallbladder cancer presenting synchronously with malignancy of the bile duct has not been clearly understood. The possible causes for the simultaneous presence of these tumors could be due to local spread, metastases, de novo multifocal origin, or as part of a field change in the extrahepatic biliary apparatus. In this article, we discuss the cases of four patients with simultaneous gallbladder and bile duct malignancies and analyze their individual pathologies to provide an explanation into the mechanisms that may play a role in such conditions.

**Key Words:** *Cancer, cholangiocarcinoma, field cancerization, gall bladder, synchronous*

## Introduction

Synchronous malignancies within the extrahepatic biliary tree are a rare cause for and there may be the simultaneous presence of gallbladder cancer coexisting with bile duct cholangiocarcinoma. The possible explanations for such an occurrence could range from the rare synchronous malignancies to local spread, to metastasis.

The majority of cases of synchronous malignancies reported are from Japan [1–4], where malignancies are usually associated with anomalous pancreatic bile duct junction (APBDJ). This association with APBDJ is not an absolute necessity, as shown by Kurosaki et al. [5] in a series of seven patients. An often confused clinical scenario has been that of local metastasis from a primary in the biliary tree leading to the misdiagnosis of synchronous malignancy. Warren et al. [6] and Gertsch et al. [7] have attempted to describe criteria for differentiation of the two conditions.

Over the past few decades, the reasons for labeling extrahepatic biliary cancers as synchronous have been based on multifocal origin [8]. The criteria for differentiating between synchronous primaries and metastasis are still being developed [9]. Gallbladder cancer, in patients without APBDJ, does not follow the adenoma-carcinoma but rather the dysplasia in situ invasive carcinoma sequence [10,11].

The field cancerization theory was first introduced in 1953 by Slaughter when describing the concept in the aerodigestive tract [12]. This concept has been used to explain the possibility of distant related primary tumors in the upper aerodigestive tract [13].

The p53 gene mutations have been closely associated with determination of clonality [13]. Allelic loss or deletions at the TP53 locus (17p13) have been reported ranging from 58% to 92% in gallbladder cancer [14,15]. These deletions have been noted at histologically normally appearing epithelium near gallbladder cancer [14].

In discussing the cases of four random patients with simultaneous gallbladder and bile duct malignancies who presented to us, our aim was to describe the various pathological possibilities in which gallbladder cancer may occur synchronously with a malignancy of the extra-hepatic bile duct.

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## Case reports

*Case 1*

A 49-year-old male referred to us with obstructive jaundice and pruritis that had developed over 2 months. He had undergone endoscopic retrograde cholangiopancreatography (ERCP) with papillotomy and stenting with a 10Fr plastic stent in view of a stricture of the lower common bile duct (CBD). On examination, the patient was icteric and generally well preserved. His blood examination revealed direct hyperbilirubinemia (serum bilirubin = 2.80 mg/dl) with a CA19-9 level of 0 units/ml. A targeted endoscopic ultrasound (EUS) was performed which showed a hypoechoic tumor in the lower CBD extending to the pancreas (uT4N0) (Figure 1a). A contrast-enhanced computed tomography (CT) scan of the abdomen (Figure 1b) showed a mild thickening of the fundus of the gall bladder with altered attenuation extending into segment IVB of the liver. There was intrahepatic biliary dilatation with evidence of CBD stent in situ. The patient was taken for surgery, where the findings were a neoplastic mass in the fundus of the gall bladder infiltrating the liver with pericholedochal lymphadenopathy. There was another separate neoplastic mass in the lower CBD. An extended cholecystectomy with extrahepatic CBD excision with a pancreaticoduodenectomy with radical lymphadenectomy was performed (Figure 1c, d). Intra-operative ultrasonography was done to rule out other lesions in the pancreas as well as metastasis in the liver. A frozen section confirmed the negative proximal margin of the CBD. Postoperative histopathology revealed a poorly differentiated adenocarcinoma of the gallbladder (T3N1) along with a poorly differentiated adenocarcinoma of the lower CBD (T3N1) with no anatomical continuity between the two tumors with a solitary lymph node metastasis. The patient is disease-free at 5 months' follow-up.

*Case 2*

A 49-year-old male presented to us with obstructive jaundice and pruritis that had developed over 1 month. On examination, the patient was icteric with a palpable gall bladder. His blood examination revealed direct hyperbilirubinemia (serum bilirubin = 27.19 mg/dl) with a CA19-9 level of 117322 units/ml. ERCP revealed a stricture extending from the proximal to the mid-CBD. In view of the suboptimal general condition of the patient with respect to surgical risk, the decision was taken to perform an ERCP with stenting with the relief of jaundice prior to surgery. Papillotomy was performed and a 10Fr plastic stent was placed. The patient developed post-ERCP pancreatitis, which was mild and settled with conservative management. Once the episode of acute pancreatitis subsided, a contrast-enhanced CT scan of the abdomen (post-ERCP) was performed which showed a distended gallbladder with dilatation of the intrahepatic biliary radicles in both lobes of the liver. The patient underwent surgical exploration, which revealed a neoplastic mass in the neck of the gall bladder contiguous with the hilar cholangiocarcinoma. An extended extrahepatic bile duct excision with cholecystectomy was performed. However, the entire biliary tree down to the intrapancreatic portion

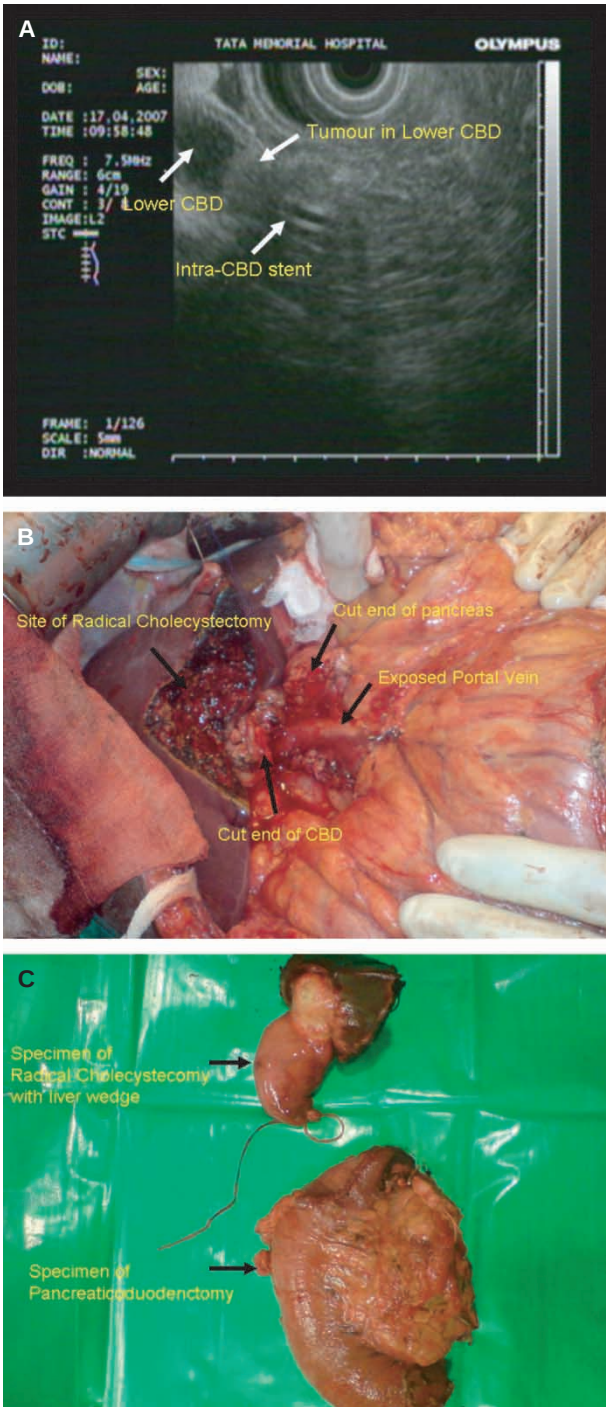


Figure 1. Images of Case 1. (a) Endoscopic ultrasonography image showing tumor in the lower CBD with a stent in situ. (b) Intra-operative photograph showing the excised gallbladder with wedge of liver, pancreas divided at the neck and the exposed portal vein following CBD resection. (c) Photograph showing resected specimens of radical cholecystectomy and pancreaticoduodenectomy