

Synchronous gallbladder carcinoma in a patient with distal bile duct cholangiocarcinoma: a histopathological surprise

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Introduction

Double malignancies of the biliary tract are rare. They could be either metachronous or synchronous, and much of the knowledge on synchronous biliary tract malignancies come from Japanese literature [1, 2].

The simultaneous presence of malignancies could be due to synchronous primary or metastasis. The majority of synchronous carcinomas identified in Japanese literature are linked to an abnormal pancreatic biliary duct junction [APBDJ]. However, this is not a requirement for the development of synchronous extrahepatic biliary tract cancers [1]. A few Indian studies have hypothesized the possible aetiopathogenesis, diagnosis and the best way to treat them [5]. Here we report a case of synchronous primary gallbladder carcinoma in a patient with distal cholangiocarcinoma.

Case presentation

A 55-year-old female presented with complaints of right-sided abdominal pain, back pain for 4 months, loss of appetite for 3 months and obstructive jaundice for two weeks. She was referred from a local hospital due to progressively elevated liver enzymes and gallbladder calculi in an ultrasound scan.

On examination she was icteric and a tender globular mass was palpable in the right hypochondrium. A clinical diagnosis of obstructive jaundice due to malignant obstruction distal to the insertion of cystic duct was made.

Ultrasound scan of the abdomen found more than 20 mobile calculi measuring 5 - 10 mm in the gallbladder without evidence of acute cholecystitis. The common hepatic duct was dilated up to 10mm without intrahepatic duct dilatation. The liver was grossly enlarged with grade 2 fatty liver.

MRI/MRCP showed an irregular stricture with shouldering in the common bile duct [CBD] immediately above the pancreatic head with proximal CBD [diameter 14mm] and intrahepatic duct dilatation. No calculi were seen in the CBD. Dilated biliary ducts showed a beaded outline. The gallbladder was distended and contained multiple calculi. The gallbladder wall was not thickened. No definite masses were seen in the pancreatic head.

The patient was discussed at the multi-disciplinary team meeting [MDT] and was concluded to have a tumour in the distal CBD with intact common hepatic duct and the biliary confluence. Since there was no evidence of vascular invasion and distant metastasis, Pancreaticoduodenectomy [Whipple's procedure] was planned after optimization.

The patient underwent a Whipple's procedure. The specimen showed an irregular circumferential growth of the distal CBD. At surgery, the gall bladder was noted to be a mildly distended with stones in situ without significant wall thickening [Figure 1]. The post-operative period and recovery was uneventful.

Histopathological examination showed synchronous malignant tumours arising in the distal CBD and fundus of the gallbladder [Figure 2]. Microscopic sections revealed extrahepatic cholangiocarcinoma of pancreaticobiliary type involving the distal CBD with clear resection margins, regional lymph nodes and adenocarcinoma of the gallbladder involving the muscularis propria without invasion of the serosa.

Pathological staging of pT3pN1pMx [Stage III or higher] for distal CBD cholangiocarcinoma and pT2aNxMx [stage IIB] for adenocarcinoma of gallbladder were made. Post-surgery, the patient was referred to an oncologist for adjuvant chemotherapy and further radiotherapy to the gallbladder to be discussed. The repeat MRI in three months showed a normal gallbladder bed and liver.

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Table 1. Biochemical profile of the patient at presentation

Investigation	Value	Unit
Hb [haemoglobin]	11.4	g/dL
AST [aspartate aminotransferase]	119	IU/L
GGT [gamma-glutamyltransferase]	901	IU/L
ALT [alanine aminotransferase]	322	IU/L
ALP [alkaline phosphatase]	813	IU/L
Protein, total	73.9	g/L
Bilirubin, total	4.66	mg/dL

Discussion

Synchronous gallbladder and bile duct malignancies are rare. Approximately 5 -7.4% of patients with bile duct carcinoma had synchronous carcinoma of the gallbladder [1]. The reported incidence of multiple tumours of the extrahepatic biliary tract and the association with unsuspected gallbladder cancers are higher[3], probably due to inadequate sampling of the gallbladder when performing the extrahepatic bile duct malignancy resection.

The simultaneous presence of two malignant tumours is frequently mistaken for metastasis from a primary tumour elsewhere in the biliary tree. To distinguish these two entities, the following characteristics are used: 1] There is no direct continuity between the two tumours. 2] The growth patterns are typical of primary tumours. 3] There is a clear histologic distinction between the two tumours. [3]. All three criteria were fulfilled in our patient; the adenocarcinoma of the gallbladder was at an early stage [pT2aNxMx- stage IIa] whereas the cholangiocarcinoma of distal CBD was more advanced [pT3pN1Mx- stage III or higher]. Both were accounted for as primary adenocarcinoma by the pathologist as they had the primary growth patterns. Anyway, these measures may not be adequate to affirm the synchronicity of extrahepatic biliary malignancies, subsequently, Kurosawa et al have indeed encouraged a mapping method to affirm the uniqueness of the two lesions[1].

The aetiopathogenesis of synchronous extrahepatic biliary cancers has not been properly understood. Anomalous pancreaticobiliary duct junction [APBDJ] is an important aetiology as it is thought to be due to the effects of pancreatic juice reflux on the mucosa of the biliary tract [4]. In our case the normal pancreatic biliary duct junction was demonstrated in MRCP imaging, supporting that synchronous extrahepatic malignancy can occur even with a normal pancreatic biliary duct system [5].

Field cancerization is explained by the biliary tree being exposed to concentrated bile, bile salts and bile acids for a long term, affecting lining epithelium and consequently on

carcinogenesis. Adenocarcinoma of the gallbladder generally arises due to the metaplasia dysplasia-carcinoma sequence and chronic inflammation increase the frequency of expression of intestinal goblet cells and p53 mutation [6]. Intraepithelial spread may also contribute as an aetiology, especially in patients with papillary adenocarcinomas [7].

The presence of the gallbladder carcinoma was a histopathological surprise; as we were unable to diagnose gallbladder malignancy preoperatively. Since the post-resection status of the cholangiocarcinoma was R0 with regional lymph nodes the patient had to undergo adjuvant chemo-radiotherapy and re-imagining in three months for two years. The repeat MRI liver was normal in this case. Although the gallbladder resection margins were negative with negative lymph nodes following classic cholecystectomy, MDT decided to follow up with regular imaging rather than offering resection of the gallbladder fossa and regional lymphadenectomy – considering the surgical morbidity. In case of evidence of probable recurrence, radiotherapy to gallbladder fossa was contemplated.

Conclusion

The finding of extrahepatic biliary tract malignancies is becoming more common than previously believed. The preoperative diagnosis of such cases is rarely made. Therefore aggressive resection and careful histopathological examination are essential for successful management and diagnosis of these special cases.

All authors disclose no conflict of interest. The study was conducted in accordance with the ethical standards of the relevant institutional or national ethics committee and the Helsinki Declaration of 1975, as revised in 2000.

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Learning Points:

- A careful preoperative assessment of the anatomy of the biliary tree as well as the gallbladder in patients going through pancreaticoduodenectomy should be done.
- Adequate sampling of the gallbladder might be significant in recognizing early lesions in patients with extrahepatic cholangiocarcinomas; We recommend that all gallbladders resected with the bile ducts for cholangiocarcinoma be inspected intraoperatively, and any suspicious lesions undergo frozen section examination.