Case Report

A Case of Synchronous Combined Cholangiocellular and Hepatocellular Carcinoma Observed after Resection of Intraductal Papillary-mucinous Tumor

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A Japanese man with chronic hepatitis C underwent distal pancreatectomy because of intraductal papillary-mucinous tumor (IPMT) located in the pancreas tail. Seven years later, when the patient was 72, liver tumor was detected by computed tomography in the anterior superior segment. Eight months after angiography, CT-A and CT-AP showed a hypervascular tumor which was enlarging gradually and a small satellite tumor. Subsegmental hepatectomy was performed in August, 2005. The two tumors were different from each other immunopathologically. The main tumor was diagnosed as cholangiocellular carcinoma (CCC), and the satellite tumor as hepatocellular carcinoma (HCC). Both liver tumors differed from metastasis of IPMT which was previously resected. The patient is still alive without recurrence 17 months after resection of the liver.

Triple primary cancers with IPMT, CCC and HCC are very rare. No combination like this was found in a PubMed search.

Key Words: cholangiocellular carcinoma (CCC), hepatocellular carcinoma (HCC), intraductal papillary-mucinous tumor (IPMT), triple primary cancers

Introduction

In recent years, the number of multiple cancers has increased. However, the incidence of multiple cancers composed of three or more cancers is still rare. We encountered a case of triple cancer, where hepatic tumors developing after resection of intraductal papillary-mucinous tumor (IPMT) were resected and the pathologic examination demonstrated synchronous cholangiocellular carcinoma (CCC) and hepatocellular carcinoma (HCC).

Case Report

Patient: 72-year-old man.
Past history: Chronic hepatitis C.
Present history: In October 1997, the patient underwent resection of the body and tail of the pancreas and the spleen for mucus-producing pancreatic tumor in another hospital. The pathologic examination showed intraductal papillary-mucinous adenocarcinoma, 2.8 cm ly0, v0, and n0 (Fig. 1). Computed tomography (CT) in October 2004 showed a low-density area (LDA) in the antero-superior segment (S8) of the liver. In order to examine it in more detail, angiography, CT angiography (CT-A) and CT arterial portography (CT-AP) were carried out. Angiography showed a
tumor stain in S8 and CT-A and CT-AP revealed a tumor shadow showing early contrast enhancement and a satellite tumor. In August 2005, the patient was admitted for operation as metastasis from pancreatic carcinoma or primary hepatic cancer was suspected.

Physical examination on admission: anemia (−); jaundice (−); flat, soft abdomen without palpable tumor; and no blood vessel dilation in the abdominal wall.

Examination findings on admission: WBC count, 7,100/mm³; hemoglobin, 14.2 g/dl; platelet count, 24.2×10⁴/mm²; AST, 44 IU/l; ALT, 39 IU/l; total bilirubin, 0.7 mg/dl; and albumin, 4.0 g/dl. CEA, CA19-9, and PIVKAII were all within a normal range at 3.1 ng/ml, 18 U/ml, and 24 mAU/ml, respectively, but αFP was slightly high at 14.0 ng/ml.

MRI (Fig. 2): A mass lesion with a diameter of about 2 cm was observed in S8 of the liver as a light hyperintensity on T2-weighted image (T2-WI) and a hypointensity on T1-weighted image (T1-WI), because the satellite tumor near the lesion had light hyperintensity on T1-WI and hypointensity on T2-WI.

FDG-PET (Fig. 3): A hot spot was observed in the periphery of the right hepatic lobe. The SUVmax...
Fig. 3 Positron emission tomography revealed a hot spot in the S8 hepatic subsegment (arrow), where SUV max was elevated at 5.38. No other hot spots were found in the liver or other organs.

value was high at 5.38. The satellite lesion was not detected.

Angiography, CT-A and CT-AP (Fig. 4): Angiography revealed a tumor stain in S8 of the liver. A defect shadow was seen in the dorsal aspect of this lesion on CT-AP.

On the basis of those images, the larger lesion was a hypervascular tumor, which was diagnosed as probably an HCC, or possibly a metastatic tumor. The smaller lesion was diagnosed as well
Progress after admission: The patient underwent an S8 subsegmentectomy of the liver in August. The postoperative course was good and the patient was discharged in remission on postoperative Day 12.

Pathologic examination: A white solid tumor of $28 \times 18 \times 29$ mm showed nuclear enlargement and increased chromatin (Fig. 5). Immunohistochemical staining showed CK-7 positive, hepatocyte negative, AFP negative, and CAM5.2 positive (Fig. 6). From these results, the tumor was diagnosed as moderately to poorly differentiated CCC, Egs, Fc (-), Fc-inf (-), sf (-), S0, Vp0, Vv0, Va0, B0, IM0, and sm (-). A well-differentiated hepatocellular carcinoma [Fc (-), Fc-inf (-), sf (0), S0, Vp1 or Vv1, Va0, B0, IM0, sm (-)] was observed in the satellite lesion and histologically differed from the main lesion of CCC (Fig. 5C). The non-cancerous liver showed chronic hepatitis. We obtained a specimen of the pancreatic carcinoma that was previously resected to compare with our specimen, and ascertained that the two hepatic cancers were not metastases of pancreatic carcinoma.
Discussion

The incidence of multiple cancers composed of three or more cancers is not high. We encountered a case of triple cancer: CCC and HCC that developed in the same hepatic lobe after IPMT operation. We searched for reports on the combination of the above three diseases (IPMT, CCC and HCC) but found none.

It is said that IPMT had a better prognosis than the usual pancreatic carcinoma\(^{1-3}\). However, IPMT shows a tendency toward infiltration and can recur in the remaining pancreas or metastasize, and requires careful postoperative follow-up\(^{4,5}\). Furthermore, IPMT is said to be characterized by combined tumors in other organs\(^{6}\). The combination IPMT and HCC, however, is rare and there are only a few cases including one reported by Oka et al.\(^{6}\). Also, the combination of IPMT and cholangiocarcinoma arising from common bile duct has been reported in a few cases\(^{7-9}\). Our search also did not find any cases of combined IPMT and CCC arising in liver.

The combination of HCC and CCC is also rare and Allen and Lissa classify the cases of combined HCC and CCC into three categories\(^{10}\). The Liver Cancer Study Group of Japan reclassifies these three categories into double cancer, combined type, and mixed type\(^{11}\). Of these, double cancer, where each cancer forms separate masses, is very rare\(^{12,13}\). In this case, with the background liver of chronic hepatitis C, HCC and CCC with separate masses arose synchronously in the same hepatic lobe. After resection of IPMT, considering the size of each tumor, HCC was conjectured to have arisen in the liver after CCC.

The multiple cancer case like the combination of our case is very rare, and it is important that the liver is examined with metastasis in mind in the follow-up after the operation of IPMT.
References


