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Synchronous Triple Primary Cancers – Liver, Gallbladder and Pancreas.

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We report here on a case of synchronous triple primary cancers that occurred in the liver, gall bladder and pancreas. A 69-year-old man who presented with symptoms of diarrhea, poor oral intake and dyspepsia was referred to our hospital. The diagnostic images showed a gall bladder mass (about 2cm in size), a pancreas head mass (2.7cm in size) and a liver mass (about 4cm in size) in segment 7. On positron emission tomography, the liver mass did not show a hypermetabolic uptake. We could not confirm a liver mass between the metastatic lesion and the hepatocellular carcinoma, and so we performed liver biopsy, which revealed hepatocellular carcinoma. Pylorus-preserving pancreaticoduodenectomy, extended cholecystectomy and liver wedge resection of segment 7 were performed. The biopsy showed gall bladder adenocarcinoma, pancreas ductal adenocarcinoma and hepatocellular carcinoma. Many multiple primary malignant neoplasms have previously been reported on, however, reports in the medical literature on synchronous multiple primary cancers occurring in the hepatobiliary and pancreas systems are very rare.

Key Words : Multiple Primary cancers, Synchronous

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INTRODUCTION

Numerous studies and reports have been published on multiple primary malignant neoplasm since Billroth first described this malady in 1988.[1] These lesions generally fall into two categories: synchronous, in which the cancers occur at the same time or within two months, and metachronous, in which the cancers follow in sequence (more than two months apart).[2] Triple primary cancers were detected in 0.14-0.28% of autopsy cases and in 0.03-0.28% cases in clinical practice.[3] Greg et al said that most multiple primary malignant neoplasms involve the respiratory, gastrointestinal and genitourinary systems.[4]

Most of the previously reported cases of triple primary cancer were metachronous and they involved the genitourinary or gastrointestinal system.[1, 3, 4] We could not find any previous reports of triple primary cancers occurring in the hepatobiliary and pancreatic system, so we present this case of synchronous triple primary cancers involving the liver, gallbladder (GB) and pancreas.

CASE REPORT

A 69-year-old man was referred to our hospital with a complaint of diarrhea for 1 month. He also complained of poor oral intake and dyspepsia. The physical examination revealed no significant findings. His medical histories included diabetes mellitus and hypertension, which were being regulated with medication. He had undergone appendectomy 40 years previously. His social and family histories were unremarkable. The laboratory investigations did not show any significant abnormalities except a HbA1c of 12.0%. The tumor markers such as alpha-fetoprotein, carcinoembryonic antigen, carbohydrate antigen 19-9 and CA 125 were 3.4 ng/ml, 17.6 ng/ml, 26.2 U/ml and 1325 U/ml, respectively. His viral markers for hepatitis were all negative. The colonofiberoscopic findings revealed a small polyp with mucosal ulceration around the polyp at 10 cm above the anal verge. The biopsy showed s hyperplastic polyp and lymphocytic infiltration. CT scanning and MR cholangiography showed a mass in the GB with regional lymph node enlargement, a pancreas head mass (2.7 cm in diameter) with mild pancreatic duct and common bile duct dilatation, and another mass (2.8 cm) in the right liver (Fig. 1). But it was not definite that 1) the liver mass was primary or metastatic, 2) which lesion the liver mass came from if it was metastatic and 3) if those masses in the GB and pancreas head were related or not. Positron emission tomography showed focal intense increased fluorodeoxyglucose (FDG) uptake in the GB mass (peak standard uptake value (pSUV) = 11.8) and in the pancreatic head region (pSUV = 8.4), suggesting malignancy. There was faint heterogenous FDG uptake in the liver mass. Liver biopsy was performed because it was essential to determine the nature of the mass in the liver for making a therapeutic plan. The biopsy revealed hepatocellular carcinoma.

We decided to perform an operation. The hepatoma in the right liver seemed to be resectable and the masses in the GB and pancreas head also seemed to be resectable. At laparotomy, there were no other lesions in the liver and peritoneum, and the three separate lesions were resectable. We performed pylorus-preserving pancreaticoduodenectomy, extended

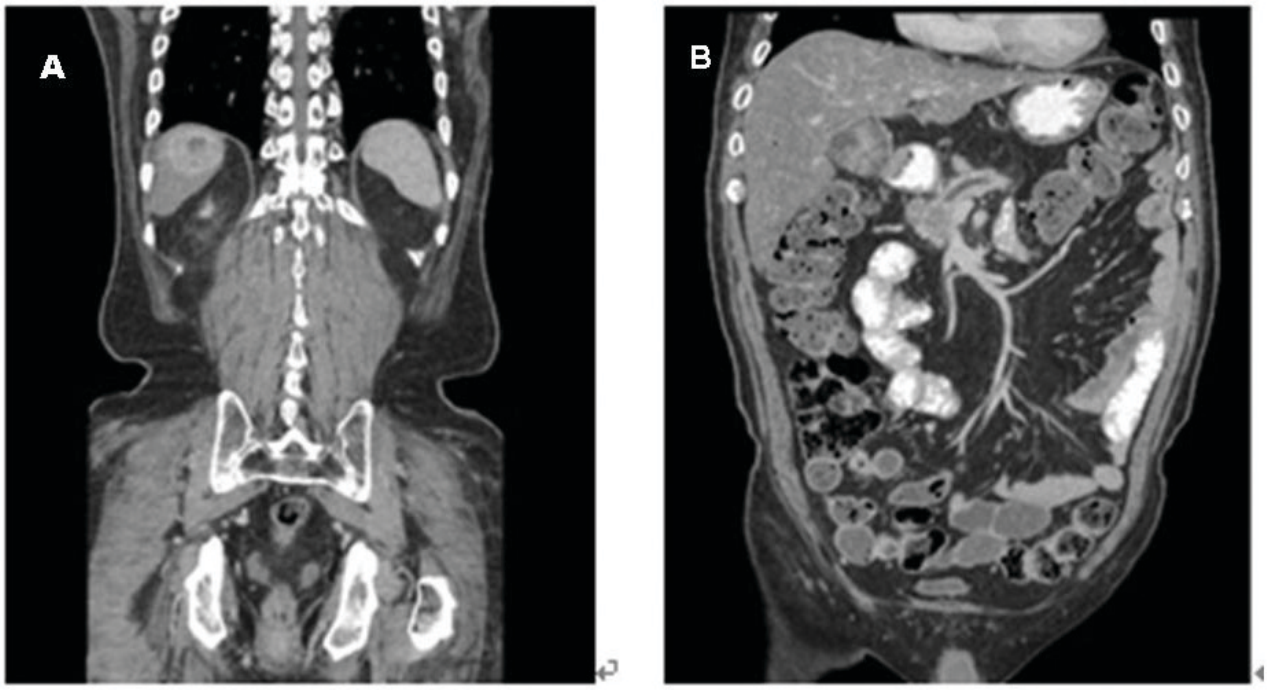

Fig. 1. The preoperative CT findings. A. A liver mass (2.8cm) in the right lobe segment 7. B. GB cancer and pancreas head cancer (2.7cm) with pancreatic duct dilatation.

cholecystectomy and wedge resection of the right liver segment 7 in December, 2007. The surgery was performed with a curative intention. The patient was discharged after recovering from pseudomembranous colitis. We checked the p53 gene and looked for K-ras gene mutation by performing polymerase chain reaction (PCR) -directed sequencing, but no mutation was found.

PATHOLOGIC FINDINGS

The pancreas mass was 3.3×2.2 ×2.5cm in size, ill-defined whitish, partly myxoid, solid and firm. The tumor extended in to the peripancreatic soft tissue and common bile duct. On opening the common bile duct, the segment near the ampulla of Vater is markedly narrowed with an irregular mucosal lesion. On microscopic examination, it showed well differentiated ductal adenocarcinoma.

Grossly, the GB was 9cm in length and 6cm in circumference, and it was removed along with a rectangular lump of the liver segment. A 2.3×2.2×2.0cm sized, ill-defined whitish gray friable polypoid mass was found in the GB 1.5cm away from the cystic duct resection margin. The mass extended into the perimuscular soft tissue, but it did not invade the liver. Microscopically, it revealed well differentiated papillary adenocarcinoma with focal areas of clear cell features.

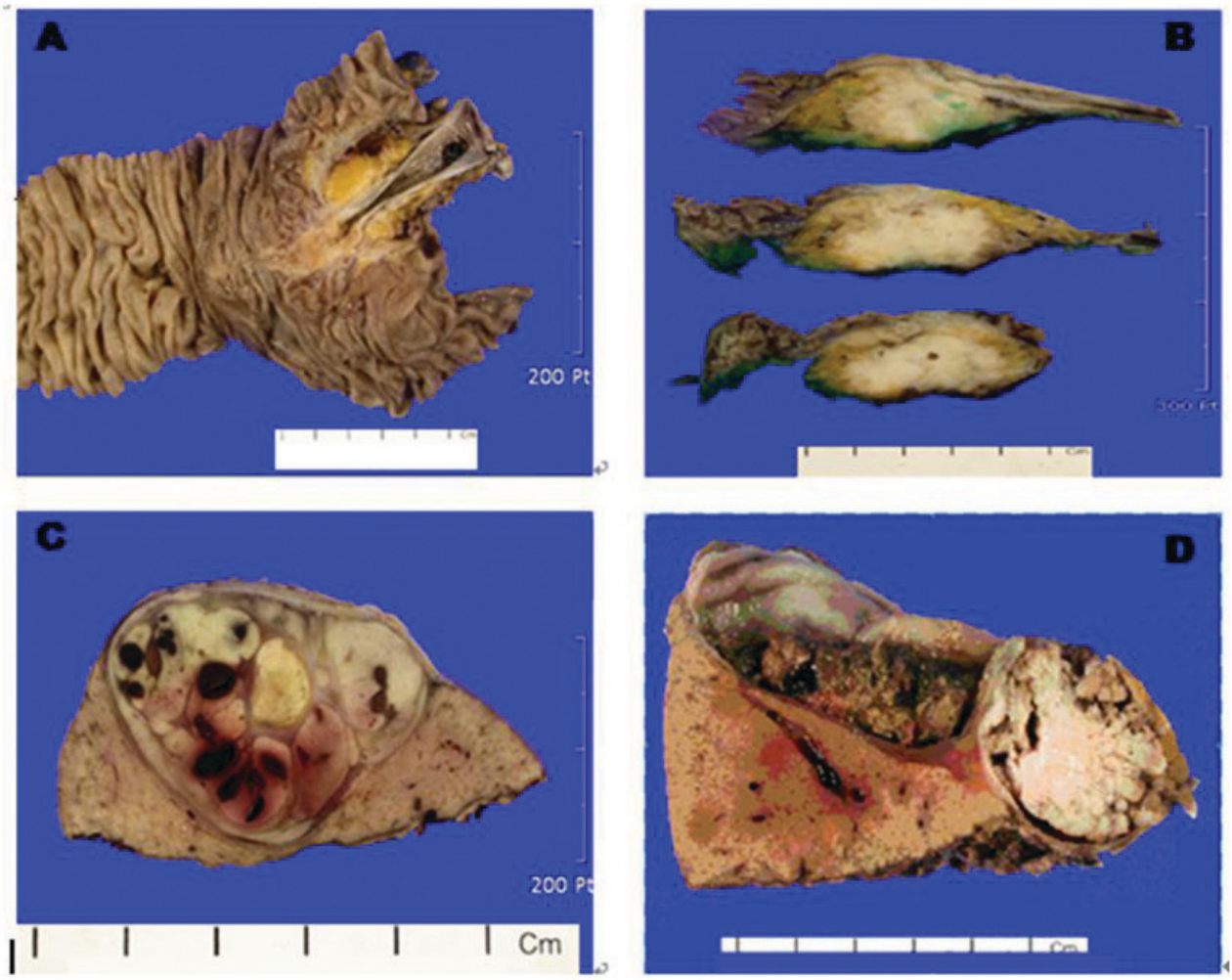

Fig. 2. The gross findings. A. The segment near the ampulla of Vater is markedly narrowed with an irregular mucosal lesion. The remaining distal mucosa is relatively unremarkable. B. An ill-defined, whitish, partly myxoid and firm mass 3.3×2.2×2.5cm in diameter in the pancreatic parenchyma with extension to the proximal portion of the common bile duct and the peripancreatic soft tissue. C. The liver showed a well demarcated multilobulated whitish, greenish and orange-yellow solid mass that was 4.2×3.5×2.8cm in diameter. D. An ill defined whitish gray friable polypoid mass at the neck of the gall bladder, and the mass was 2.3×2.2×2.0cm in diameter.

The liver mass was a well demarcated multilobulated whitish, greenish and orange-yellowish solid mass. Its size was 4.2×3.5×2.8cm. Microscopically, it showed hepatocellular carcinoma (Edmonson grade I). The tumor included 15% tumor necrosis, 20% hemorrhage and 20% fatty change. There was no capsular, serosal, or micro-vessel invasion. The non-tumor bearing liver parenchyme showed non-alcoholic steatohepatitis, but there was no evidence of cirrhosis (Fig. 2).

There was lymphovascular invasion, but no definite evidence of perineural invasion. All 15 lymph nodes were free from tumor cells. All the resection margins were clear.

DISCUSSION

Multicentric cancers occurring in same organ or system usually develop after a carcinogenic stimulus to that organ or system. For example, skin tumors often develop in the patients who have history of exposure to sunlight or ionizing radiation. Stomach cancers often develop in patients with anaplastic anemia, colorectal cancers develop in patients with ulcerative colitis or multiple familiar polyposis, and oral cavity cancers develop in smokers.[5] In the literature, most of the multiple primary cancers from the same system or organ have developed in the genitourinary system or gastrointestinal system.[1, 3, 5, 6] We could find only one case report in the medical literature of triple primary cancers from the GB, bile duct and pancreas.[7] But our case might to be the first reported case of triple primary cancers from the liver, GB and pancreas.

Some reports have suggested that there is no acceptable evidence that the patterns of occurrence of multiple primary malignant neoplasms of different organs or tissues are governed by anything more than coincidence.[5] On the other hand, several reports have suggested that genetic causes are important for multiple primary cancers. Kimura et al. also reported a germ-line p53 mutation in the patients with multiple primary cancers.[8] Yet our patient showed no mutation of the p53 and K-ras genes. Further, we could find no family history of cancer.

It is important to distinguish multiple primary lesions from metastatic lesions because the therapeutic plan can change as they carry a different prognosis according to the nature of the cancer. The liver is the most frequent metastatic site of the cancers from other intra-abdominal organs. In this case, after confirming that the hepatic mass was a primary hepatoma and not metastatic, we decided to perform surgery to resect the three lesions. Preoperatively, it was not definite that the mass in the pancreas head was primary tumor or if the metastatic tumor in the lymph nodes around the pancreas head was from the GB mass, but the lesions seemed to be resectable. At laparotomy, it was evident the pancreas head mass was both primary and resectable.

Cases of hepatoma often show no significant FDG uptake, so it is important to use all available diagnostic methods to confirm the nature of an uncertain lesion in the liver.

In conclusion, we experienced a case of synchronous triple primary cancers in the liver, GB and pancreas, and this may well be the first such case report in the medical literature. We were able to perform curative surgery for these lesions.

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