

Biliary Cystadenocarcinoma — Report of 2 Cases —

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The clinical and pathologic features of two patients with biliary cystadenocarcinoma were presented and the previous literatures were reviewed. Case 1: A 52-year-old man complained of heart burn and weight loss. Abdominal ultrasound and CT offered suspicions of biliary cystadenocarcinoma of the left hepatic lobe. Left hepatic lobectomy was performed, but the tumor invaded to adjacent viscera. The resected tumor (26 × 21 × 5.5 cm) was multilocular cystadenocarcinoma with mucin production. He survived for one year and 8 months after surgery. Case 2: A 60-year-old man suffering from sudden-onset frost and high fever underwent left lateral segmentectomy of the liver with a diagnosis of cystadenocarcinoma defined by biopsy specimen in previous operation. The tumor (6.0 × 4.5 × 3.5 cm) was multilocular cyst with mucin-producing papillary adenocarcinoma. He died of recurrent cancer 2 years and one month after surgery. The histogenesis of cystadenocarcinoma is still unclear because of its rare disease. The presence of benign epithelium in our cases may support their origin from cystadenoma.

Introduction

Biliary cystadenocarcinoma of the liver is extremely uncommon among the primary liver cancer, although the benign hepatic cyst is not a rare disease. In 1990, the 26th Meeting of Liver Cancer Study Group of Japan provided a main theme of cystadenocarcinoma and the clinical and pathological features of 26 report cases were discussed¹⁾. The purpose of this paper is to review an experience of 2 patients with cystadenocarcinoma with particular reference to clinical features and pathological factors which might affect the patient's survival.

Patients

Case 1: A 52-year-old man admitted to the 1st Department of Surgery, Nagasaki University Hospital on October

29, 1986 with a one-week history of heart burn and weight loss. From 1965 until 1985 the patient experienced five episodes of recurrent duodenal ulcer accompanied by upper abdominal pain and vomiting. His symptoms disappeared following treatment for a duodenal ulcer. Family history and past medical history were not contributory. Laboratory tests were as follows: SGOT, 12 mU/ml; SGPT, 11 mU/ml; alkaline phosphatase, 178 mU/ml; total protein, 6.4 g/dl; albumin, 3.8 g/ml; BUN, 12 mg/dl; CEA, 1.2 ng/ml; AFP, 4.3 ng/ml; CA 19-9, 12.9 U/ml. A physical examination on admission did not reveal jaundice, ascites or anemia. His liver, spleen and an abnormal mass in the abdomen were not palpable. An upper GI series and endoscopy revealed the open ulcers of the prepyloric area and the duodenum. Ultrasonography and abdominal computed tomography revealed a multilocular cystic mass with irregular internal septa and solid portions, which replaced nearly the entire left lobe (Fig. 1 and 2). The peripheral portion and internal solid area of the mass were enhanced by contrast media. On 21 October 1986, the patient underwent a left lobectomy of the liver and a distal gastrectomy for peptic ulcer under the suspicions of cystadenocarcinoma of the liver and peptic ulcer with pyloric stenosis. However, the tumor tissues infiltrating the aorta and inferior caval vein were left in place. The remaining liver tissue was not cirrhotic, and neither cholestasis nor tumor emboli were demonstrated.

The resected specimen was largely replaced by a huge tumor mass measuring 26 × 21 × 5.5 cm. On section, the tumor was multilobulated and almost totally cystic, containing a dark reddish brown colored, muddy necrotic material. The tumor was well encapsulated by thick fibrocollagenous tissue which was connected with fibrous septa between the tumor nodules. There were several foci of tumor invasion into the fibrous septa and capsule. Microscopically, the predominant histologic pattern was a papillary configuration of cystadenocarcinoma supported by delicate cores of vascularized fibrous tissue (Fig. 3).



Fig. 1. Ultrasonogram in the left lobe of the liver showing a cystic pattern with internal septa (Case 1).

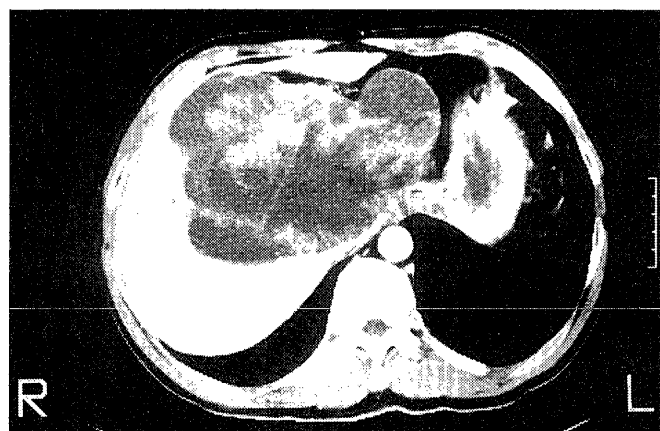


Fig. 2. Contrast-enhanced CT scan showing papillary projection with enhancing effect in the multilocular cyst (Case 1).

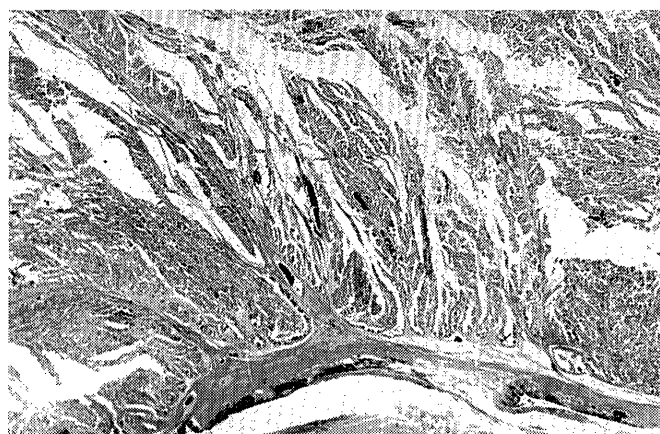


Fig. 3. Cystadenocarcinoma showing papillary epithelium supported by delicate cores of vascularized fibrous tissue (Case 1, H & E, $\times 40$).

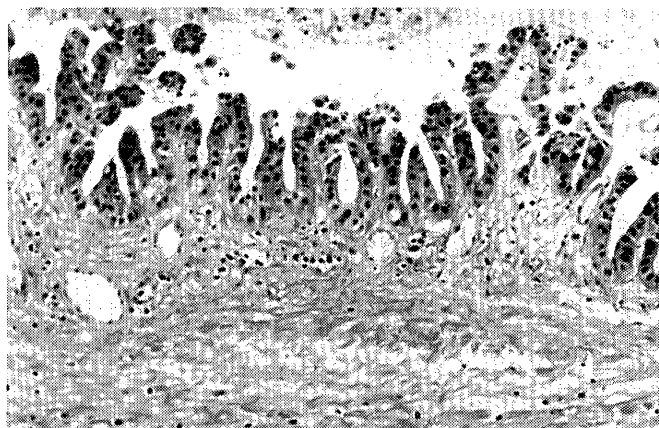


Fig. 4. Locule of low-grade cystadenocarcinoma showing multiple small papillary projections into lumen (Case 1, H & E, $\times 20$).

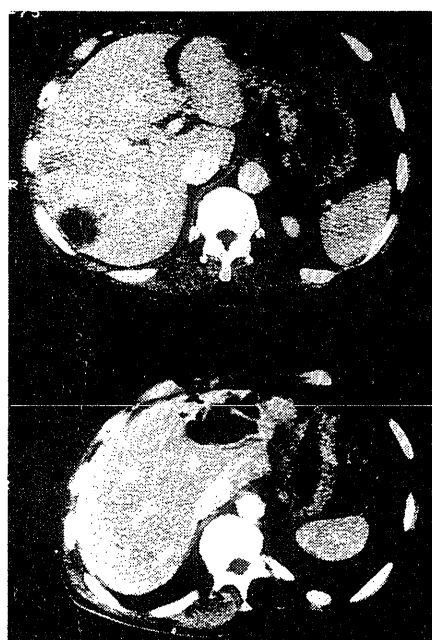


Fig. 5. Contrast-enhanced CT scan showing a multilocular cyst in the left lobe (above) and a unilocular cyst in the right lobe of the liver (below) (Case 2).

Adjacent locules of cystadenocarcinoma were lined by small papillary projections of low grade malignancy (Fig. 4) and/or a partially benign epithelium of cystadenoma. Tumor ploidy patterns on flow cytometric DNA analysis was aneuploidy (DI : 1.68). The patient underwent postoperative radiotherapy (50 Gy) and anticancer chemotherapy (5FU and mitomycin C). However, he died of hepatic failure due to progression of the remaining carcinoma in September 1988, one year and 8 months after surgery.

Case 2 : The patient was a 60-year-old man who noticed frost and high fever in August 1981, and admitted to the Inoue Hospital, Nagasaki City. Endoscopic retrograde



Fig. 6. Surgical resected specimen showing the tumor composed of cavity and solid portion surrounded by prominent capsule (Case 2).

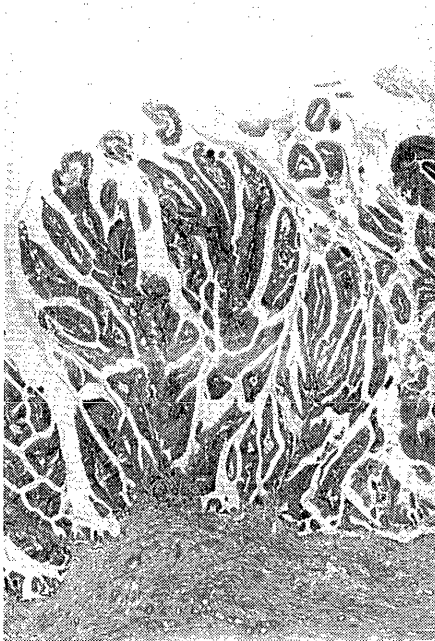


Fig. 7. Histology showing papillary proliferation of cystadenocarcinoma (Case 2, H & E. $\times 40$).

cholangiopancreatography (ERCP) showed dilatation of the common bile duct and the intrahepatic bile duct. Abdominal CT scan showed a well-defined multilocular low density area in the left lateral segment of the liver and a small low density area in the right lobe, in addition to dilatation of the intrahepatic bile ducts. With a diagnosis of liver abscess, he was given an antibiotic medication for 2 months and discharged. During January 1982, high fever with frost and a transient jaundice recurred, and he was admitted to the hospital. Contrast-enhanced CT scan revealed nearly the same lesions as previously described (Fig. 5). PTCO for the cystic lesion of the right lobe was emergently performed, with result of simple cyst. On April

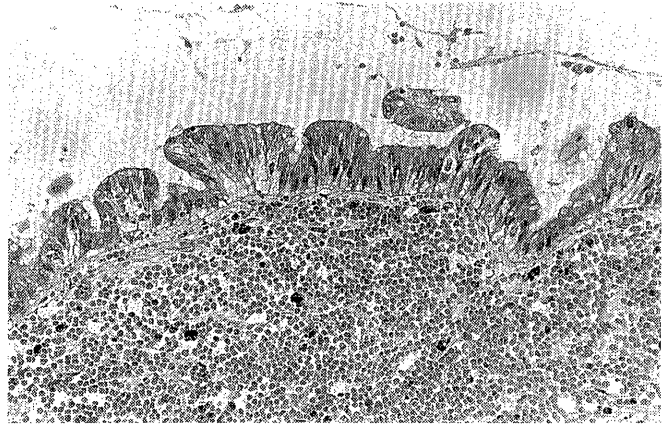


Fig. 8. A benign locule of cystadenoma showing single layer of columnar epithelium (Case 2, H & E. $\times 20$).

1982 exploratory laparotomy was done; cystic liver tumor of the left lateral segment was found, and cholecystectomy, choledochotomy with T-tube drainage in common bile duct and external drainage for the liver cyst was performed. A biopsy specimen of the cystic tumor revealed definite cystadenocarcinoma. The patient was transferred to the Nagasaki University Hospital in July 1982.

The laboratory tests were as follows: SGOT, 20 IU/l; SGPT, 25 IU/l; alkaline phosphatase, 318 IU/l; total protein, 6.8 g/dl; albumin, 3.8 g/dl. The alpha-fetoprotein was below 20 ng/ml, and the carcinoembryonic antigen was less than 2.0 ng/ml. The patient underwent a left lateral segmentectomy. The resected liver showed multilocular and almost totally cystic tumor measuring 6.0 \times 4.5 \times 3.5 cm. It was partly solid and partly cystic (Fig. 6). The cystic portion contained a mucinous substance, and its inner surface was covered by papillary projection. The histologic examination of the cyst revealed mucin-producing adenocarcinoma (Fig. 7). In some areas of the tumor, the locules of cystadenoma showing polypoid projection and/or single layer of low cuboidal to columnar epithelium was confirmed (Fig. 8). The remaining liver tissue was not cirrhotic, and neither cholestasis nor tumor emboli was demonstrated. Tumor ploidy pattern on flow cytometric DNA analysis was diploidy. The patient died of widespread recurrent cancer 2 years and one month after hepatectomy.

Discussion

Biliary cystadenocarcinoma is a rare tumor, and the clinical diagnosis is difficult to differentiate from the benign cyst during its preoperative course. The lesion usually represents the multilocular cystic tumors lined by columnar epithelium with mucin production, and papillary projection of the epithelial cells are common^{2,6)}. However, the histogenesis of this papillary cystic tumor of the liver

is not clear. Kawarada et al., in their 5 cases of cystic bile duct carcinoma of the liver and proposal of a new classification, reported that malignant cystic tumors of the liver should be divided into 3 groups⁶⁾: Group A is cystic adenocarcinoma, group B is bile duct carcinoma with primary or secondary intrahepatic bile duct, and group C is degenerative cyst formation by other types of malignant tumors; and cystic adenocarcinoma (Group A) can then be further subdivided into cystadenocarcinoma, cystadenocarcinoma with cystadenoma, and carcinoma in a simple cyst of the liver⁷⁾. According to Matsushita et al., a review of 106 Japanese cases of biliary cystadenocarcinoma of the liver revealed that 27 were from a simple cyst, 18 were from a cystadenoma and 24 occurred as biliary cystadenocarcinoma⁸⁾. In our two cases, the cyst wall was indeed partially covered by benign epithelium. It has also been suggested that the lesion may change from benign to malignant during the long clinical course (cystadenocarcinoma with cystadenoma).

Initial symptoms and physical findings were usually nonspecific. Although there were no relevant clinical features to the etiology of the biliary cystadenocarcinomas, main symptoms were abdominal pain, palpable mass and jaundice⁸⁻¹⁰⁾. In our cases, unusual presentations, such as intractable pain, frost and fever led to tumor detection. Serum CEA and CA 19-9 measurements have been frequently the useful screening test of cystadenocarcinoma to differentiate benign cyst⁹⁾. However, there was none of our 2 cases whose serum CEA and CA 19-9 measurements were the first diagnostic clue for cystadenocarcinoma. Therefore, initial and laboratory abnormalities seem to be generally minimal with this tumor, so that the role of imaging procedures for diagnosis of the tumor is important.

Currently accepted standard management of a cystadenocarcinoma of the liver first involves verification of the suspected diagnosis by imaging studies (sonography, CT or MRI). This tumor usually manifests the papillary protrusions in a cyst^{9,11)}. Recently, the useful information of MR imaging on cystadenocarcinoma have been published in several articles. Mashimo et al. indicated that on T1-weighted images of MRI, high-intensity signals were observed in the area suggestive of fluid retention, and on T2-weighted images a mixed pattern of high- and low-intensity signals was observed in the area suggestive of solid tissue¹²⁾. However, it is important that cystadenoma and solitary simple cyst have to be distinguished by histological examination of the cyst wall. Our case 2 was diagnosed by histologic examination at exploratory laparotomy, because there was no evidence of malignancy on US and CT.

The prognosis of biliary cystadenocarcinoma has not been evaluated because of its rare disease, but the prognosis generally seems to be much better than that for intrahepatic bile duct carcinoma^{4,13)}. Although the bio-

logical nature of biliary cystadenocarcinoma, regardless of their cause, seems to be potentially low-grade malignant as suggested in most reports^{2,3)}, several important pathologic features of this tumor affecting the prognosis have been pointed out. These include the invasive growth over the cyst wall, infiltration into surrounding organs, direct invasion to portal vein branches and/or nerves, lymphatic metastasis, and the presence of intrahepatic metastasis⁵⁾. In our cases, we confirmed histologically these factors by the analysis of the resected specimens with poor prognosis. This was attributed to advanced stage of the lesion due to delayed diagnosis. On the other hand, recently, many reports have suggested that the DNA content of the tumor was important for the prognosis¹⁴⁾, but a few have been studied on biliary cystadenocarcinoma. We could not evaluate prognostic significance of flow cytometric DNA analysis in our cases. The results of this report must be confirmed by additional data based on a large group of patients.

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