Mixed Liver Cancer with Both Hepatocellular and Cholangiocellular Carcinoma Showing a High CEA Level — A Case Report —

Ryosuke YAMAMOTO, Kenji YOSHIDA, Kenichiro YATA, Tsuyoshi TOMIYAMA, Yutaka KASAI, Wataru FUJITA, Katsuhiko OHASHI and Shinichiro YAMAMATO*

Department of Family Practice,
**Division of Gastroenterology I, Department of Medicine,*
Kawasaki Medical School, Kurashiki 701-01, Japan

Accepted for publication on November 29, 1995

ABSTRACT. Among malignant neoplasma of the liver, mixed type of cancer which is histologically composed of both hepatocellular and cholangiocellular carcinoma, is rare in frequency (1～3%). Serum CEA levels of these cases are within 10 ng/ml at the maximum. We encountered a case of mixed liver cancer with an extremely high CEA level (1500 ng/ml). The details of the case and a review of the literatures are presented.

Key words: hepatocellular carcinoma (HCC)— cholangiocellular carcinoma (CCC)

We experienced a case of mixed liver cancer composed of both hepatocellular carcinoma (HCC) and cholangiocellular carcinoma (CCC). The serum carcinoembryonal antigen (CEA) level of the case was extremely high. In this report, we described his clinical features, discussed the CEA level, and reviewed the literature of such cases.

CASE REPORT

CASE: A 62-year-old male consulted his family doctor in May, 1991, complaining of anorexia and paralysis in his left lower limb. A few days later, the patient experienced right chest pain radiating to the right shoulder. He was admitted to the Gastroenterology ward of Kawasaki Medical School Hospital on May 27.

Physical examination revealed a thumb-sized lymph node in the right axillary region and hepatomegaly (5 cm in size by MSL and 4 cm by MCL) with an irregular surface. There were paralysis and sensory disturbance in his left lower extremity.

Laboratory data showed liver dysfunction and thrombocytepenia (5.6×10^4/mm^3). The HCV antibody was proved to be positive. Among various tumor markers, CEA level was found to be extremely high (Table 1). An abdominal ultrasonography revealed a hypoechoic lesion with a tumorous hyperechoic area in the right lobe of his liver (Seg 4-6), and a small amount of ascites (Fig 1). An abdominal CT scan extensively revealed a low density area with

山本亮輔, 吉田謙治, 矢田健一郎, 富山 毅, 笠井 裕, 藤田 渉, 大橋勝彦, 山本晋一郎

TABLE 1. Laboratory data on admission

WBC	5900/ul	Na	135mEq/l
RBC	322×10^4/ul	K	3.5mEq/l
Hb	11.1g/dl	Cl	98mEq/l
Ht	37.2%	P	1.6mEq/l
Platelet	5.6×10^4/ul	Ca	3.8mEq/l
SP	5.8g/dl	Mg	1.9mEq/l
BS	126mg/dl	PT	13.3sec
T-Bil	1.5mg/dl	APTT	33.3sec
D-Bil	67%	fibri.	297mg/dl
AlP	78IU/l	HPT	82%
Cho	97mg/dl	HB_s-Ag	(−)
γ-GTP	80IU/l	HB_s-Ab	(−)
LDH	1365IU/l (LDH2.3↑)	HCV-Ab	(+)
Alb	2.8g/dl	AFP	3ng/ml
Glb	3.0g/dl	CEA	1500ng/ml
γ-Glb	27.7%	CA19-9	39U/ml
ChE	86IU/dl	PIVKA-2	0.06AU/ml
GPT	53IU/l		
GOT	54IU/l		
Crn	1.2mg/dl		
BUN	17mg/dl		
Amy	141IU/l		

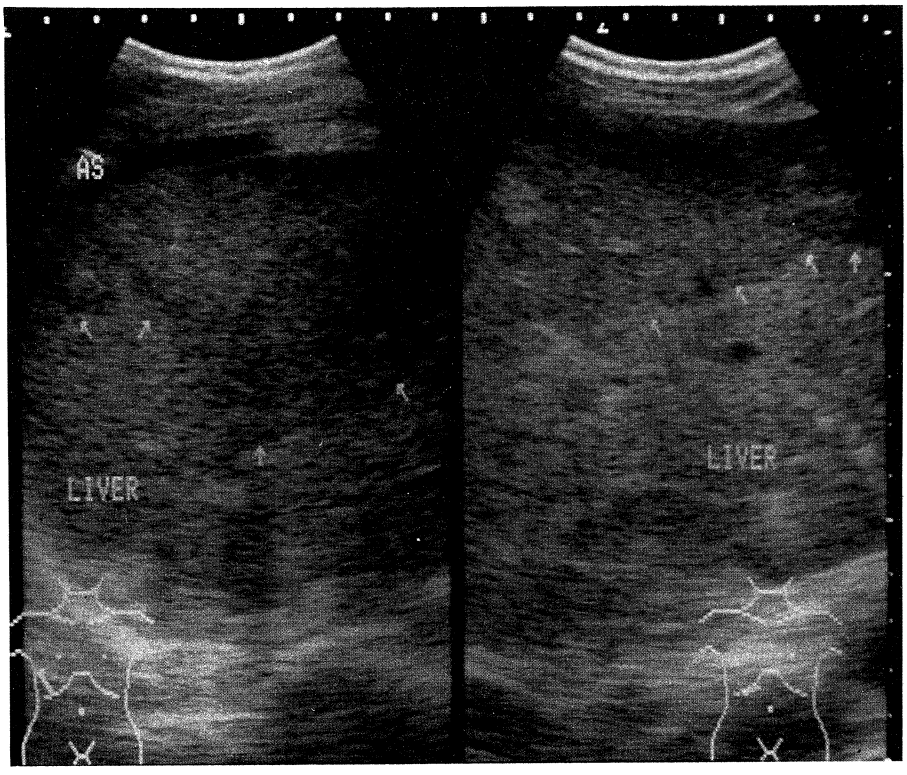

Fig 1. An abdominal ultrasonography on admission

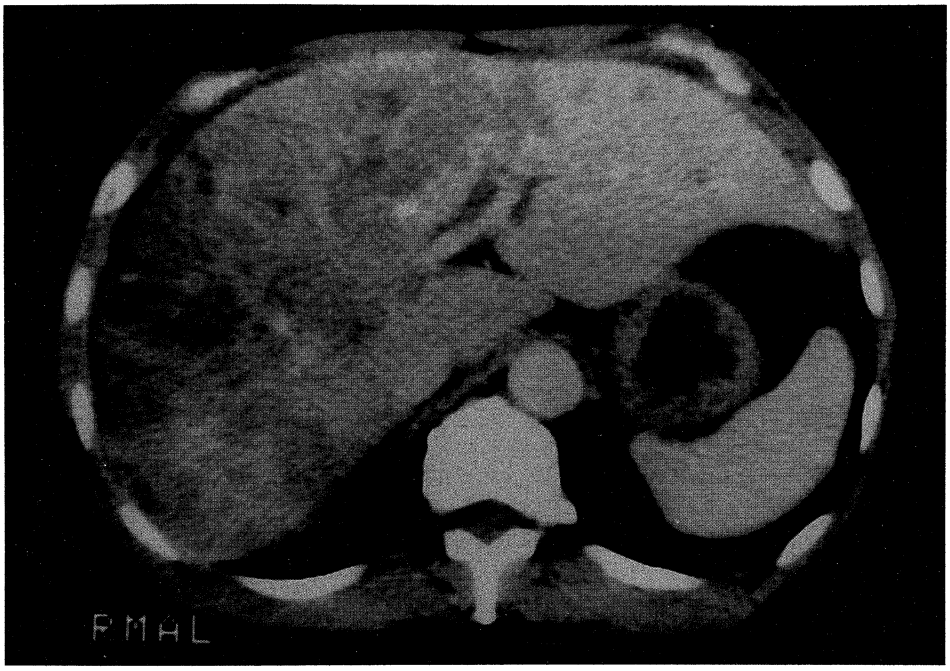

Fig 2. An abdominal CT-scan on admission

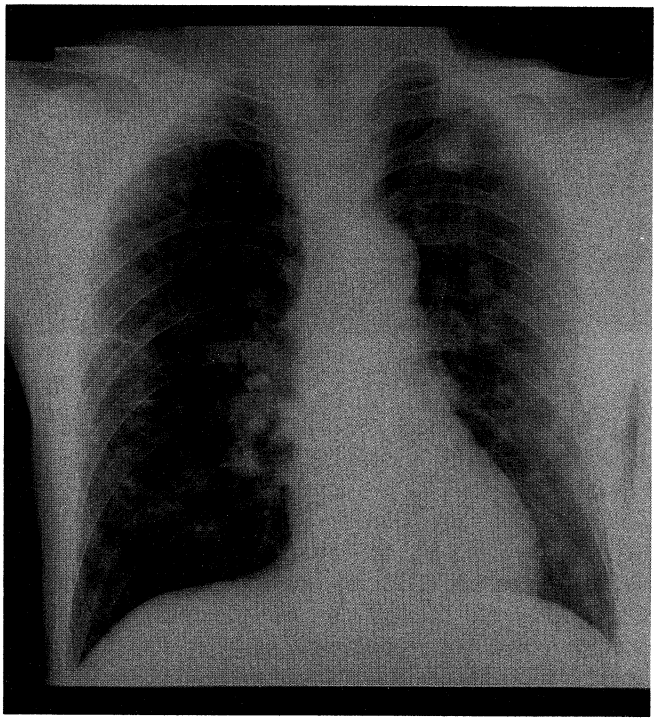

Fig 3. Chest X-ray Film on admission

inconspicuous margin in the right lobe of his liver (Fig 2). A chest X-ray film disclosed multiple coin lesions of various sizes and configrations (Fig 3). A diagnosis of primary liver cancer accompanied by pulmonary metastasis was suggested. Despite medical treatment, he repeatedly manifested convulsions. Brain CT scan revealed three masses (4 cm at large) which were suggestive of metastatic brain tumors (Fig 4). The patient died on June 21, 1991.

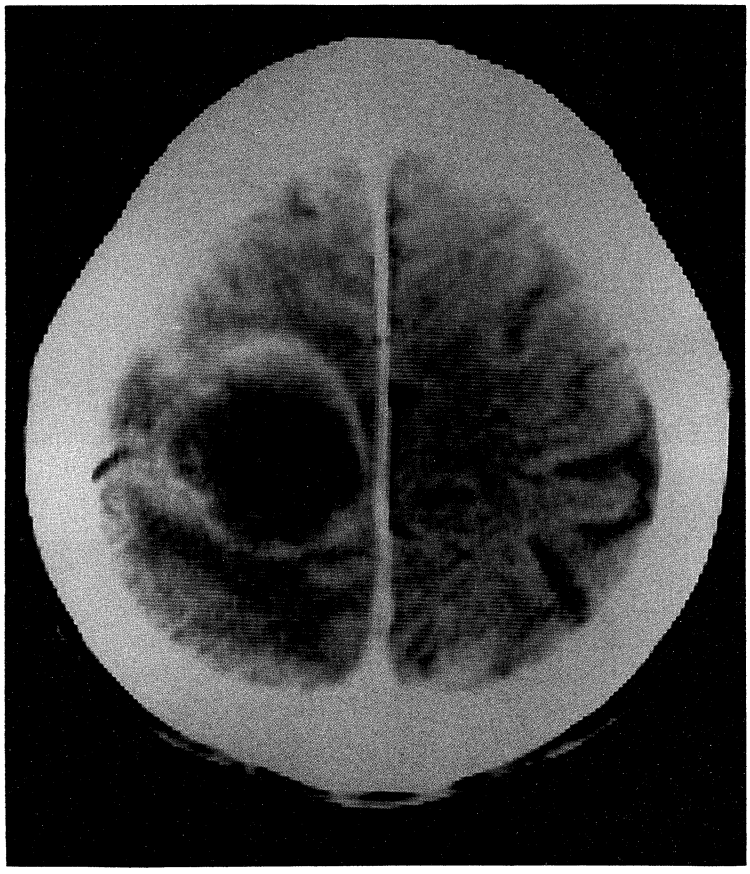

Fig 4. A brain CT-scan on June 3

AUTOPSY REPORT : The autopsy revealed hepatomegaly of 2970 g in weight. A tumor with severe necrosis occupying 70% to 80% of the cut surface was found in the liver (Table 2). Macroscopically the necrosis was located in the right lobe wiht map-like appearance. Nodule-like whitish stickiness were scattered in the left lobe (Fig 5). Histopathological examination disclosed that the tumor was composed of HCC in the trabecular pattern and CCC with mucin or intracytoplasmic lumina in the glandular pattern. These two carcinomatous components were coexistent without demarcation in the hepatic tumor and the metastatic lesion (Fig 6). Immunohistochemical staining of the tumor was positive for CEA, while it was negative for α-Fetoprotein (AFP) in both primary and metastatic tumors.

TABLE 2. The autopsy report

I	PRIMARY
	A. Liver cancer, mixed type, hepatocellular and cholangiocellular.
	B. Metastasis, lung, brain, thyroid gland, left kidney, pleura, peritonium, adrenal gland.
II	SECONDERY
	A. Ascites, bloody, 1400 ml
	B. Acute pancreatitis
	C. Status jaundice
	D. Bleeding teudency

Immediate cause of the death : liver failure

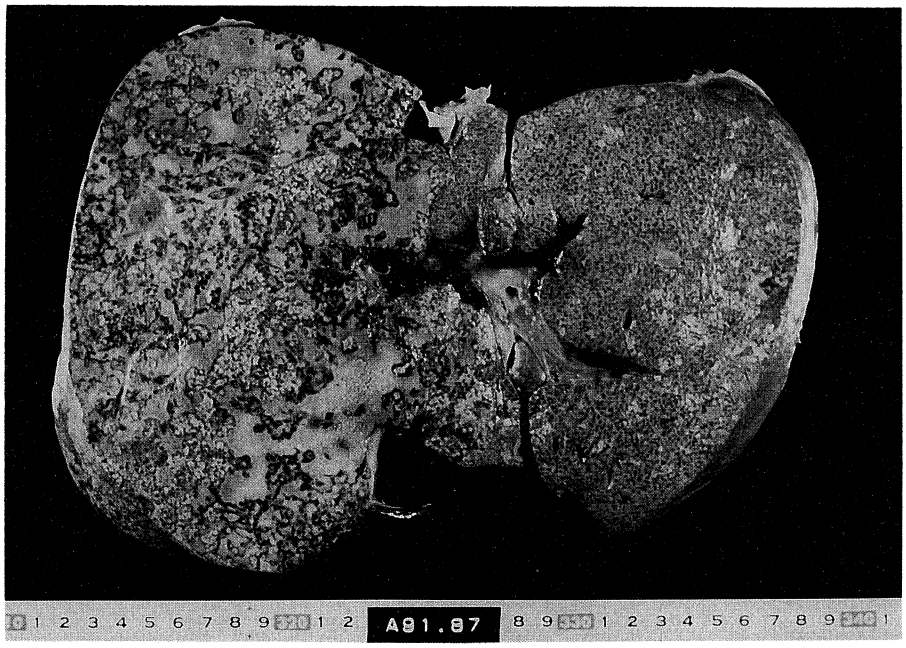

Fig 5. Cut surface of liver on autopsy

DISCUSSION

Whereas, 91.7% of primary liver cancer in Japan is hepatocellular carcinoma (HCC) on histology, cholangiocellular carcinomas (CCC) originating from the bile duct is loss in frequency, account for only 5.2%.[1] Mixed liver cancer histologically composed of both HCC and CCC is rarely identified (only 1-3% of all liver tumors[1-4]). The average age, sex ratio, clinical symptoms, and biochemical data have not significantly differed from those of HCC or mixed liver cancer. Serum AFP was positive in 60% of the cases, but its levels were relatively low, being within 10000 ng/ml at the maximum. Serum CEA was positive in 70~80% of the cases, but the levels was also relatively low, being within 10ng/ml at the maximum.[2-4] In our case, however, the CEA level was extremely high (1500 ng/ml), while his AFP level was

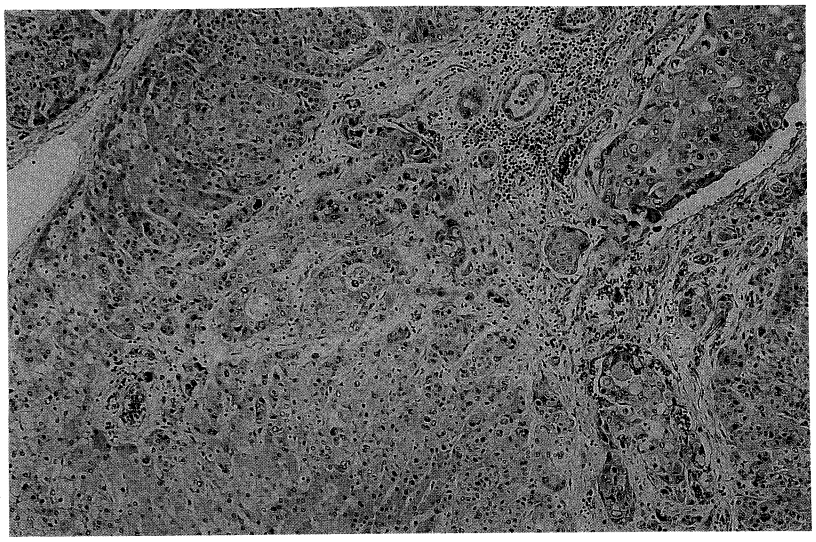

Fig 6. Pathological findings of the liver on autopsy

normal (3 ng/ml). These findings of tumor markers were different from those in usual HCC and may be diagnostic of mixed liver cancer. Of course, those levels seem to be affected by factors other than the histology, such as the size of primary lesion, the metastasis and the occupying ratio of HCC to CCC within the tumor. The General Rules for the Clinical and Pathological Study of Primary Liver Cancer[5] base the classification of mixed liver cancers on Allen's classification.[6] That classification divides mixed liver cancers into the following three types[2,4,7];

1) double type: HCC and CCC originating from different areas are coexistent separately. Each tumor is of the simple cellular type.
2) combined type: HCC and CCC are coexistent in close proximity. Although each tumor consists of a different cellular type in the beginning, HCC and CCC become mixed as the tumors grow large.
3) mixed type: A single type of tumor, in which HCC and CCC are closely mixed histologically, has been proven to originate in the same area.

According to Allen's classification,[6] most mixed liver cancers are classified into the double type or the combined type. HCC and CCC are found separately in those types. The mixed type is considered to be very rare. We considered that our case can be categorized into either combined type or mixed type. Previous reports demonstrated that the mixed type is characterized by high risk of metastasis with poor prognosis.[1-4] Although the mixed hepatic cancer is rare in frequency, it seems necessary to include this type as a differential diagnosis, especially those cases with positive CEA. This concept is inevitable in the start of treatment for patients suspected of having hepatic cancer.

CONCLUSION

We report the case of a 62-year-old male with mixed hepatocellular and cholangiocellular carcinoma. In this case, the CEA level was extremely high, while the AFP level was normal.

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