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A Patient with a Large Hepatocellular Carcinoma Alive 13 Years after Repeated Transcatheter Arterial Chemoembolization and Hepatectomy

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ABSTRACT

We describe a rare case of a large hepatocellular carcinoma (HCC) in a patient who survived 13 years after repeated transcatheter arterial chemoembolization (TAE) and hepatectomy. The patient was a 41-year-old woman found in March 1985 to have a large HCC, measuring 14 × 12 cm in diameter and associated with obstruction of the main portal trunk. She underwent TAE 8 times over a period of 1 year. The serum alpha-fetoprotein level decreased from 18342 to 1871 ng/ml. The patient subsequently underwent left hepatectomy on October 9, 1986. Thirteen years after hepatectomy, the patient is being followed up on an outpatient basis and has had no evidence of recurrence.

Key words: *Hepatocellular carcinoma, Hepatectomy, Repeated transcatheter arterial chemoembolization*

The incidence of hepatocellular carcinoma (HCC), caused by hepatitis virus infection, is increasing in Japan. Despite the development of new techniques for diagnosis and hepatectomy, the outcome of treatment for HCC remains poor, and very few patients survive for long periods. The analysis of factors related to outcome may contribute to the improved survival of patients with HCC. We report on a patient who survived 13 years after repeated transcatheter arterial chemoembolization (TAE) and hepatectomy.

CASE REPORT

A 41-year-old woman with epigastric discomfort was referred to the Department of Surgery II, Hiroshima University School of Medicine in May 1985. The results of physical examination were normal, except for a swelling of the liver in the epigastric region. The laboratory data on admission revealed hepatic dysfunction: the GOT was 208 IU/liter, the GPT 345 IU/liter, the ALP 313 IU/liter, the LAP 314 IU/liter, the γ-GTP 738 IU/liter, and the indocyanin green retention rate at 15 min (ICG R15) was 15%. Alpha-fetoprotein (AFP), a tumor marker of HCC, was abnormally high (18,342 ng/ml) and hepatitis B surface antigen (HBsAg) was positive. However, no anemia or renal dysfunction was present (Table 1).

Table 1. Laboratory data on admission

T. Bill	1.0 mg/dl	WBC	5200
D. Bill	0.2 mg/dl	RBC	391×10^4
GOT	208 IU/liter	Hb	12.1 g/dl
GPT	345 IU/liter	Platelet	20.7×10^4
LDH	282 IU/liter	PT	84%
Ch-E	166 IU/liter	APTT	33.3 sec
ALP	313 IU/liter	FDP	2.5 μg/ml
LAP	314 IU/liter	FBS	79 mg/dl
γ-GTP	738 IU/liter	ICG R15	15%
T.P.	6.5 g/dl	K ICG	0.124
Albumin	3.9 g/dl	HPT	100%
Chol.	233 ml/dl	AFP	18342 ng/ml
NH3	77 ng/dl	CEA	1.7 ng/ml
		HBsAg	(+)

Abdominal computed tomography (CT): An abdominal CT scan revealed a low density area (14 × 12 cm) in the medial segment. The area extended to the left and right lobes on enhancement with contrast medium (Fig. 1).

Abdominal angiography: Hepatic arteriography showed a 12.5 × 12.0 cm area of tumor stain. This area was fed primarily by the middle hepatic artery and partially by the right hepatic artery in the medial segment (Fig. 2). Portography (via the superior mesenteric artery) showed no left portal vein and main portal trunk; a cavernous formation

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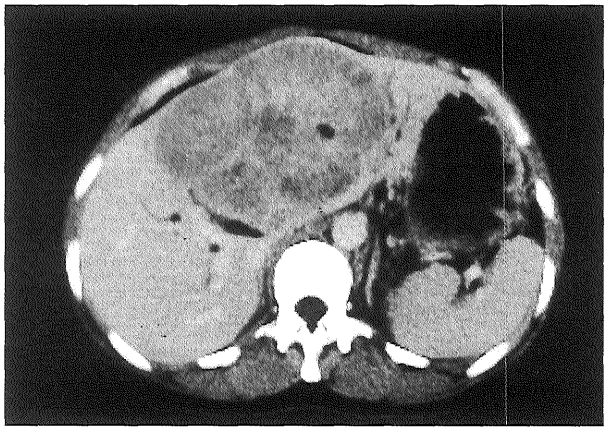

Fig. 1. Abdominal CT scan revealed a large low density area (14 × 12 cm) in segment IV of the liver.

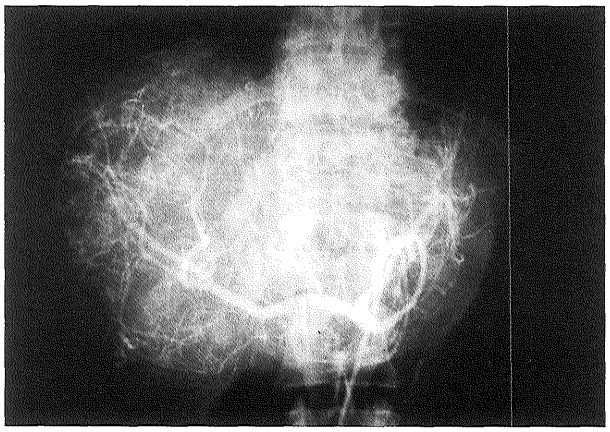

Fig. 2. An hepatic arteriogram showed a tumor stain (14.5 × 120. cm) fed by the middle and right hepatic arteries in the medial segment.

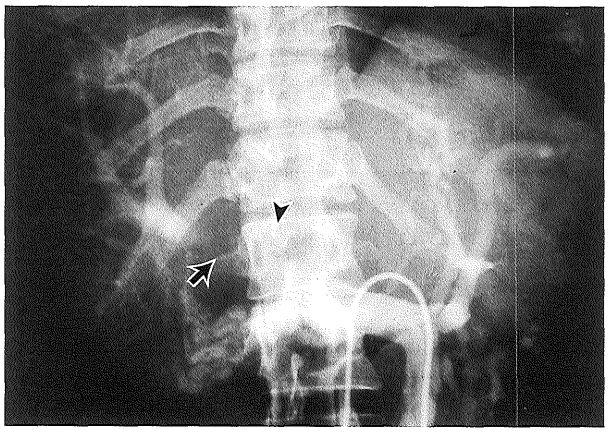

Fig. 3. Main portal trunk (arrow) and left portal vein (arrow head) were not demonstrated in portography.

fed the right side of the liver (Fig. 3).

Histologic examination of a liver biopsy specimen obtained under ultrasonographic guidance verified that the tumor was HCC.

HCC due to hepatitis B virus infection was diagnosed, and treatment was started. Resection of the liver was considered dangerous because of obstruction of the portal main trunk. We first administered transarterial infusion chemotherapy (TAI) with 30 mg of doxorubicin and 3 ml of Lipiodol via the proper hepatic artery by Seldinger's maneuver. Then we repeated TAI by combining embolization with Spongel to 8 times over a period of 1 year. Figure 4 shows an abdominal CT scan obtained after 1 session of TAI, showing a substantial amount of Lipiodol in the tumor. After 4 sessions of TAI with Lipiodol or Spongel (or both), the size of the tumor decreased to 13.3 × 10.5 cm on an abdominal CT scan (Fig. 5), and the obstructed portal trunk became patent on portography. The patient underwent TAI with Lipiodol 8 times over a period of a year, and the serum AFP level decreased from 18342 to 1871 ng/ml. An arteriogram taken 11 months after starting TAI showed no tumor staining in the liver and no partial irregularity of the middle hepatic artery (Fig. 6). Portography showed no tumor thrombus; however, the left portal branch was not visualized (Fig. 7). An abdominal CT scan showed a remarkable decrease in the size of the tumor, located in the medial segment of the liver (Fig. 8). The patient was followed up on an outpatient basis, and the

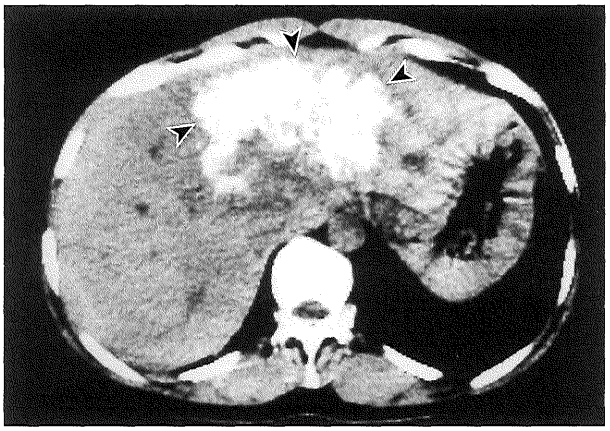

Fig. 4. Lipiodol accumulation of the tumor (arrow head) located in segment IV was found after a session of chemolipiodolization.

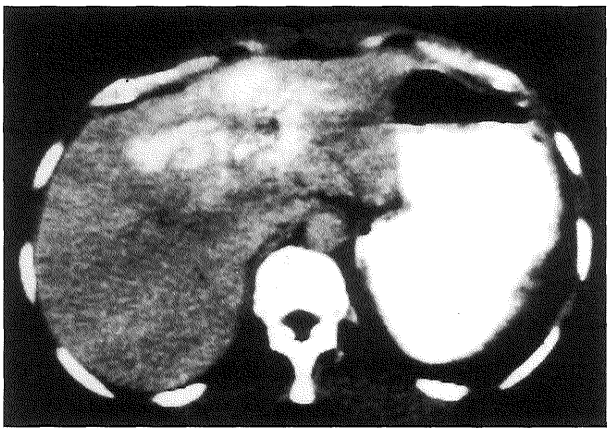

Fig. 5. The size of the tumor was reduced to 13.3 × 10.5 cm after performing 4 sessions of chemolipiodolization in abdominal computed tomography.

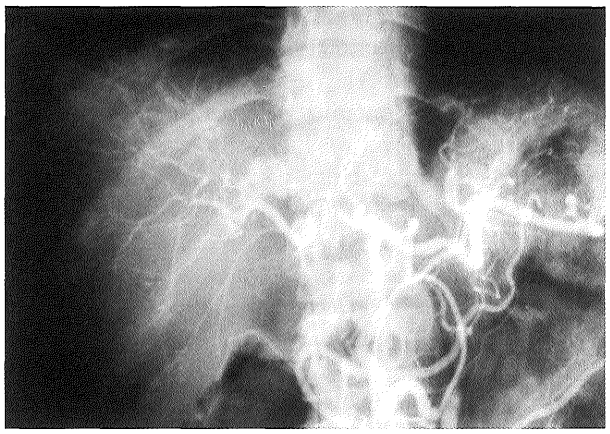

Fig. 6. An hepatic arteriogram showed partial irregularity of the middle hepatic artery and no tumor stain in the liver after 8 sessions of chemolipiodolization.

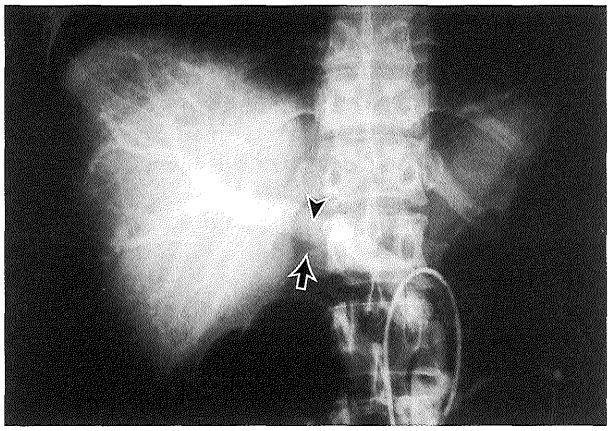

Fig. 7. Portography exhibiting good patency of the portal trunk (arrow), no visualization of the left portal vein (arrow head), and no tumor thrombi after 8 sessions of chemolipiodolization.

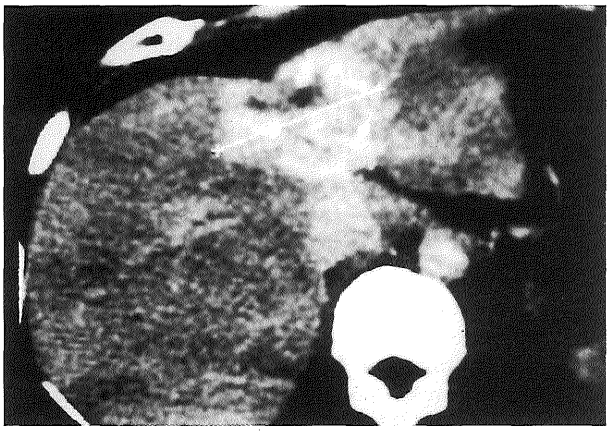

Fig. 8. Abdominal computed tomography showed a remrkable decrease in the size of the tumor after 8 sessions of chemolipiodolization.

serum AFP level increased 15 months after the start of TAI. We diagnosed regrowth of the tumor, and decided to perform hepatectomy.

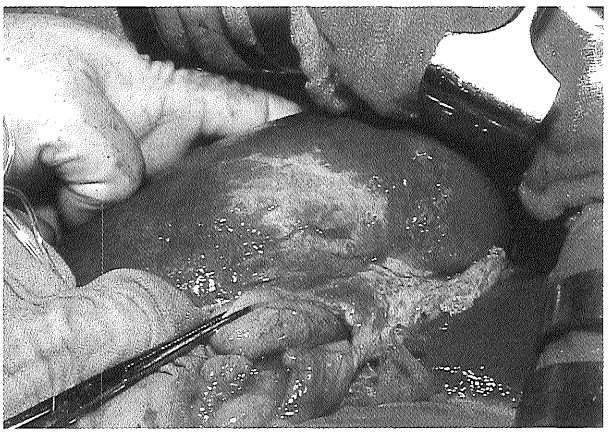

Fig. 9. Macroscopic findings revealed a small fibrous lesion on the surface of segment IV of the liver.

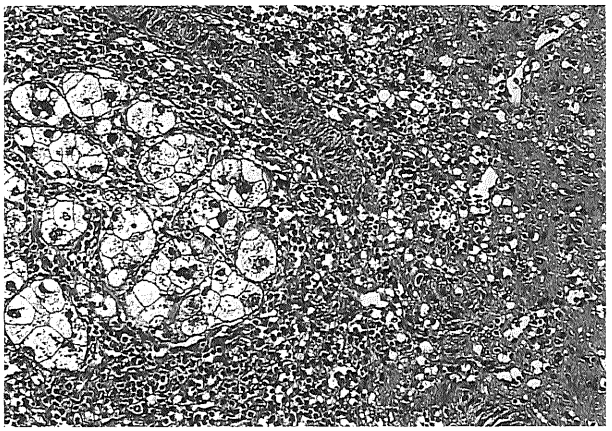

Fig. 10. A small viable tumor remained in the fibrous area.
The tumor was diagnosed as trabecular type of HCC, moderately differentiated, Edmondson's type II.

Operative findings: On October 9, 1986, laparotomy was performed via bilateral subcostal skin incisions with the patient under general anesthesia. We recognized atrophy of the left hepatic lobe and a fibrous lesion in the medial segment of the liver (Fig. 9). After ligation and transection of the left hepatic artery and portal vein at the hilar portion of the liver, a left hepatectomy was performed.

Pathological findings: The tumor was associated with a large fibrous lesion, probably caused by TAI. A small viable tumor remained in this fibrous area. The tumor was diagnosed as trabecular type HCC, moderately differentiated, Edmondson's type II (Fig. 10). The No. 12 lymph nodes had metastasis, and a centrilobular fatty change was found in non-tumor tissue that showed no evidence of chronic hepatitis or liver cirrhosis.

Postoperative course: The postoperative course was uneventful, and the patient was discharged on December 21, after having received TAI with 60 mg of doxorubicin 3 times prophylactically. She is now being followed up on an outpatient basis and has had no recurrence in the 13 years after operation.

DISCUSSION

The outcome of HCC is poor because the effect of treatment is restricted by the presence of multicentric tumors and by hepatic dysfunction due to liver cirrhosis. The cumulative 3- and 5-year survival rates were respectively 57.4 % and 34.3% among 349 patients who underwent hepatectomy at our department[1].

Recently, an increasing number of cases of early HCC are being detected because of improved diagnostic techniques, such as abdominal ultrasonography, CT, magnetic resonance imaging (MRI), and digital subtraction angiography (DSA). However, many patients have advanced HCC at the time of diagnosis, resulting in a poor prognosis. In a previous series of 17 patients with tumor thrombi of the main portal trunk, hepatic veins or both, who underwent hepatectomy, only 2 patients with tumor thrombi who received hepatectomy and had good hepatic function survived more than 3 years. Most patients whose tumor thrombi could not be resected or who did not undergo postoperative TAI died within 1 year. Shimamura[5] and Nishimine et al[4] reported that the outcome of HCC patients with tumor thrombi of the main portal trunk is poor. The prognoses of patients with large HCC is also poor. Nonsurgical treatment, percutaneous ethanol injection therapy (PEIT), and percutaneous microwave coagulation therapy (PMCT) are indicated for early HCC, but not for large HCCs because the effectiveness of these techniques is limited for large tumors. The effectiveness of transcatheter arterial embolization (TAE) is not established. Most large HCCs spread beyond the tumor capsule and metastatize to distant organs, the lung or bone via the portal or hepatic veins. Among 21 patients whose tumors were more than 10 cm in diameter, 10 who had tumor thrombi in the main portal trunk or intrahepatic metastases extending to 3 segments of the liver (or both) survived for less than 1 year because curative surgery was not feasible. In contrast, of the 11 patients who underwent curative hepatectomy, 7 survived more than 30 months, and 4 are still alive. Hepatectomy is thus more effective than other types of treatment for HCCs measuring more than 10 cm in diameter but is limited to patients who can undergo curative hepatectomy.

The reasons for the prolonged survival of our patients are: 1) good hepatic function, 2) a good response to preoperative TAI, 3) curative hepatectomy. Hara[2], Toyama[6], and Komori et al[3] also reported long-term survival in patients with HCC who responded to TAI.

It is rare that a patient who undergoes resection after many sessions of TAI survives for 13 years without recurrence. However, more cases must be critically evaluated to improve outcome in patients with HCC.

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