

Hepatocellular carcinoma with extension into the right atrium : report of a successful liver resection by hepatic vascular exclusion using cardiopulmonary bypass

Shiro Yogita^{*}, Seiki Tashiro^{*}, Masamitsu Harada^{*}, Tetsuya Kitagawa^{**}, and Itsuo Kato^{**}

^{*} First Department of Surgery, and ^{**} Cardiovascular Surgery, The University of Tokushima School of Medicine, Tokushima, Japan

Abstract: We report a successful liver resection using cardiopulmonary bypass with, total hepatic vascular exclusion (THVE) for hepatocellular carcinoma (HCC), with extension into the right atrium. A 61-year-old man with a cirrhotic liver was referred to our department with HCC in the medial segment of the left lobe of the liver, and tumor thrombus extending into the right atrium. During surgery, a left lobe and caudate lobe of the liver were transected leaving the left lobe of the liver connected to the inferior vena cava (IVC) by only the left and middle hepatic trunks, and then the intracaval tumor thrombus and the left lobe of the liver were removed *en bloc* using cardiopulmonary bypass with total hepatic vascular exclusion (THVE). Cardiac arrest was not performed during THVE, and the patient had an uneventful postoperative course and was discharged from the hospital 2 months following surgery. He died of multiple pulmonary metastases 4 years and 8 months after surgery ; however, imaging showed no evidence of recurrence in the remnant liver during that period.

In conclusion, by performing dissection of the hepatic parenchyma to the hepatic vein prior to removal of the tumor thrombus, the period of extracorporeal circulation, duration of warm ischemic time to the liver, and intraoperative blood loss were all reduced and a radical operation could be performed safely without scattering tumor cells during extirpation of the tumor. *J. Med. Invest.* 47 : 155-160, 2000

Key words : hepatocellular carcinoma, extension into the right atrium, total hepatic vascular exclusion, cardiopulmonary bypass

INTRODUCTION

Hepatocellular carcinoma with extension into the right atrium has been regarded as beyond the realm of surgical resection. Most patients have died within a short period of pulmonary embolism, heart failure (1), or cancer progression.

In recent years, impressive progress has been made in liver surgery, and with the development of

liver transplantation and the introduction of vascular surgical techniques (2), successful surgery has been performed for hepatic malignancies with tumor thrombus to IVC and right atrium (3, 4). However, appropriate indications and surgical procedures for them are controversial. We report a patient with HCC with tumor thrombus extending into the right atrium through the middle hepatic vein and IVC. Using cardiopulmonary bypass with total hepatic vascular exclusion (THVE), we successfully performed a left lobectomy with the simultaneous removal of the tumor thrombus.

Received for publication June 9, 2000 ; accepted July 18, 2000.

Address correspondence and reprint requests to Shiro Yogita, M.D., First Department of Surgery, The University of Tokushima School of Medicine, Kuramoto-cho, Tokushima 770-8503, Japan and Fax : +81-88-631-9698.

Case report :

A 61-year-old man was referred to our department on February 16, 1994, with the diagnosis of a liver tumor which was detected on abdominal computed tomography (CT) during a periodic medical examination for chronic HCV hepatitis. At physical examination on admission, the liver was palpable 4 cm below the right costal margin with a firm consistency and round border. There was no evidence of ascites. Patient laboratory findings included a platelet count of $13.0 \times 10^4/\text{mm}^3$, serum bilirubin 0.6 mg/dl, glutamic oxaloacetic transaminase (GOT) 50 IU/L, glutamic pyruvic transaminase (GPT) 62 IU/L, γ -glutamyl transpeptidase (γ GTP) 65 IU/L, albumin 3.6 g/dl, prothrombin time (PT) 11.3 seconds, hepaplastin test (HPT) 76.7%, retention rate of indocyanine green 15 minutes after injection 8.7% (normal 10%), hepatitis B surface antigen (HBsAg) negative, hepatitis C virus antibody (HCV-Ab) positive, α -fetoprotein (AFP) 3 ng/ml, and PIVKA-II (protein induced by vitamin K absence of antagonist-II) 0.28 AU/ml (normal 0.07 AU/ml). Contrast CT showed a low-density mass with unclear borders (3.0 cm in diameter) between the middle hepatic vein (MHV) and left hepatic vein (LHV), which did not enhance with contrast, and the tumor thrombus extending from the main tumor to the inferior vena cava (IVC) (Fig. 1). In addition, a transesophageal echocardiogram revealed that the tumor thrombus extended into the right atrium (Fig. 2). On the basis of these findings, a diagnosis of hepatocellular carcinoma in the medial segment of the left lobe of the liver with growth into the right atrium was made. Surgery was performed on March 21, 1994 using cardiopulmonary bypass with total hepatic vascular

exclusion (THVE).

Bilateral subcostal incisions were made and, to gain better exposure, a small upper midline incision from the xyphoid process to the bilateral subcostal incision was added (inverted Y-incision). No adhesions, ascites or peritoneal dissemination were seen in the peritoneal cavity. There were no suspicious lymph nodes in the vicinity of the hepatoduodenal ligament. The liver was firm with a micronodular surface consistent with liver cirrhosis. The tumor was located at the surface of the medial segment of the left lobe of the liver. Intraoperative ultrasonography revealed a well-defined hyperechoic mass (3.4×4.0 cm) in the medial segment which was adherent to the MHV near the confluence of the MHV and IVC. There was no evidence of metastases or portal vein thrombosis. Despite concern that a tumor fragment might embolize distally, the hepatic parenchymal resection was performed initially leaving the left lobe connected by only the trunks of the MHV and LHV because heparin would be used during extracorporeal circulation.

After performing a cholecystectomy, the hepatoduodenal ligament was dissected. The left hepatic artery, left portal vein and left hepatic duct were ligated and divided separately. The entire liver was mobilized from its attachments. The suprahepatic and infrahepatic IVC were exposed and taped. The tumor thrombus was palpable in the suprahepatic IVC as an elastic, hard, mass arising from the left lobe of the liver. A demarcation line on the surface of the liver was created. Transection of the liver parenchyma was performed along this line with an ultrasonic scalpel (Cavitron Ultrasonic Surgical Aspirator : CUSA). The left lobe of the liver and the caudate lobe were resected leaving the left lobe connected to the IVC



Fig. 1. Contrast computed tomography. A ill defined solitary low density mass (arrow), approximately 3.0 cm in diameter was found in the medial segment of the left lobe of the liver with a filling defect extending into the IVC (arrow head).

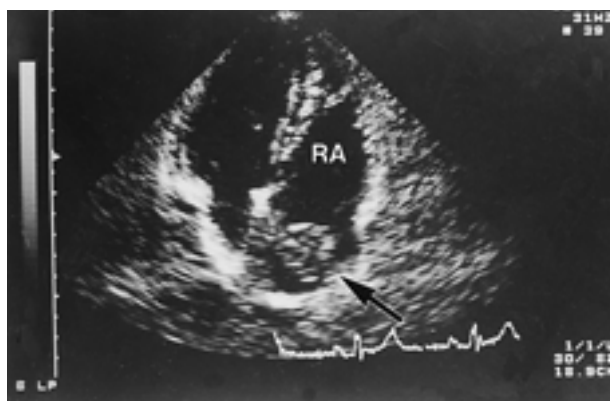


Fig. 2. A transesophageal echocardiogram demonstrated a mass indicating tumor thrombus (black arrow) in the right atrium. RA : right atrium

by only the common trunk of the MHV and LHV. After obtaining hemostasis along the raw surface of the liver, cardiovascular surgeons performed a median sternotomy. The pericardium and diaphragm were divided at the level of the IVC hiatus in the diaphragm. The superior vena cava (SVC), trunk of the pulmonary artery, and the ascending aorta were exposed and taped. Three catheters were inserted into the SVC, IVC via the right femoral vein and the ascending aorta. Heparin (0.3 mg/kg) was administered intravenously. After satisfactory extracorporeal cardiopulmonary bypass was established, THVE was induced by clamping the SVC, the IVC just below the liver, and the hilar tributaries (Pringle's maneuver) (Fig. 3). The trunk of the pulmonary artery was also clamped to prevent the tumor thrombus from embolizing distally. A longitudinal incision was made in the center of the suprahepatic IVC from the right atrium to the trunk of the MHV and LHV. Then the common trunk was resected confluent with the IVC. A left lobectomy with resection of the caudate lobe and removal of the tumor thrombus

were performed *en bloc*. Although a cardiac arrest was not performed, bleeding from the IVC was easily controlled with a pump sucker. The tumor thrombus was covered with a thin, fibrous membrane, and there was no invasion into the wall of the right atrium or IVC. The suprahepatic IVC was closed with a running suture longitudinally. Heparin was neutralized with protamine sulfate. After confirmation of a normal activated clotting time (ACT), the extracorporeal bypass was removed. Total bypass time and total hepatic ischemic time were 25 minutes and 10 minutes, respectively. Operating time was 11 hours 22 minutes. Total blood loss during the operation was 2,910 ml. The resected specimen weighed 190 g. The main tumor, 4.0×5.0 cm was located in the medial segment of the left lobe of the liver and invaded the MHV (Fig. 4). Histologically, the tumor thrombus appeared to be partially covered with a thin, fibrous endothelial membrane where it extended into the IVC. Other regions of the tumor were exposed to the blood. Microscopic findings showed moderately differentiated HCC, trabecular type, with

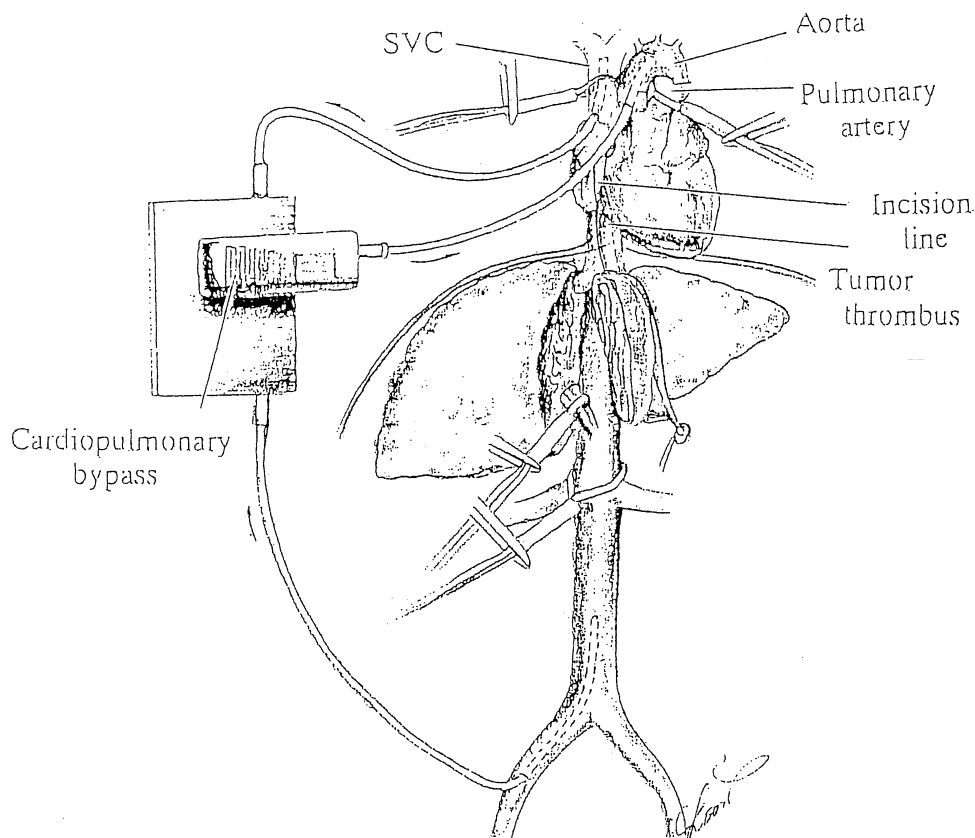


Fig. 3. Cannulation for cardiopulmonary bypass

The superior vena cava, the pulmonary trunk, and the ascending aorta were exposed and taped. Two venous catheters were inserted into the SVC and IVC via the right femoral vein, one arterial catheter was inserted into the ascending aorta. The pulmonary artery was clamped to prevent air embolism, backflow of blood into the IVC and the tumor thrombus from embolizing distally during extracorporeal circulation without cardiac arrest.



Fig. 4. Surgically resected specimen (posterior view). Tumor thrombus (white arrow) had extended from the main tumor via the middle hepatic vein.

capsule formation and liver cirrhosis.

The patient recovered uneventfully. He was discharged from the hospital after a prophylactic hepatic arterial injection of styrene maleic acid neocarzinostatin (SMANCS, 3 mg). Unfortunately, multiple lung metastases in both lungs were recognized in follow-up chest radiography in June, 1995. However, the patient obtained only a partial response (PR) from the administration of Carboplatin (CBDCA) intravenously and 5'-dexy-5-fluorouridine (5'-DFUR) orally. Although the patient had a cancer bearing condition, his dialy life was without restrictions.

In August, 1996, 2 years and 5 months after surgery, the patient experienced hemoptysis due to a metastatic lesion in the hilum of the left lung that increased and invaded the bronchus directly. Radiotherapy (total dose 50 Gy) was administered for this lesion. Afterwards, he was administered CBDCA (50 mg) intravenously once a week in the out-patients clinic, and the right lung metastatic lesions disappeared. However, that of the left lung gradually increased, and he experienced hemoptysis again. The patient died of cancer in November, 1998 (4 years and 8 months after initial surgery). However, there was no evidence of tumor in the remnant liver on computed tomography (CT), ultrasonography (US) or magnetic resonance imaging (MRI) during that period.

DISCUSSION

Tumor extension into the right atrium in HCC is rare. The incidence is reported as 0.6% in autopsy cases (5). However, HCC with tumor invasion into the IVC is reported to occur in 2.9% of patients by imaging techniques, 0.7% at operation, and 18.2% at autopsy in Japan (6). Since most of these patients

have accompanying intrahepatic metastases or distant metastases, they have been deemed to be beyond conventional surgical resection. Liver transplantation is also contraindicated for such patients (7); therefore, extended surgery such as total hepatic vascular exclusion (THVE) using various bypasses has been introduced to treat patients with advanced tumors (2). However, these methods including a "bench procedure" have yet to be established, and many issues must be resolved including (8): 1) indications, 2) the hepatic tolerance to liver ischemia of THVE, especially in the impaired liver, 3) surgical technique, 4) hemodynamic and metabolic consequences of THVE, and 5) tumor recurrence following surgery.

With regard to the indications for extended surgery, Pichlmayr *et al.* (9) have reported that these approaches are necessary only in selected patients and defined three categories of indications for the "bench procedure": 1) preferable, 2) optional, and 3) necessary. The present patient was classified in category 3 due to conventional unresectability and contraindications for liver transplantation. Furthermore, the right atrial tumor may obstruct the orifice of the tricuspid valve with resultant sudden cardiac death (ball valve syndrome) (1). Goth *et al.* reported a patient with acute cardiac insufficiency treated successfully by operative removal of a tumor thrombus (10). Nimura *et al.* also reported a patient who survived 4 years following surgery (11). Accordingly, patients with advanced HCC extending into the right atrium may be candidates for surgery in the emergency or elective setting. The present patient had good hepatic reserve function (Child-Pugh A classification). The main tumor lay within the medial segment of the left lobe of the liver, and intrahepatic or distant metastases were not evident. Therefore, this suggest this patient was a good candidate for surgery.

Technically, it is important for surgeons to confirm the degree of tumor thrombus extension. If tumor thrombus does not invade the IVC or right atrium, it may be possible to remove thrombus via the right atrium using conventional THVE by clamping the IVC just below the right atrium (11). However, when thrombus protrudes into the right atrium, it is necessary to use cardiopulmonary bypass. Transesophageal echocardiography is one of the most useful diagnostic tools in this setting. Chua *et al.* (12) advocated performing an echocardiographic examination by virtue of its versatility, safety and reliability in diagnosis of right atrial masses.

In 1987, Shimamura *et al.* (13) reported on two extremely instructive patients. In one patient, bleeding could not be controlled from the raw surface of the liver, and therefore removal of the tumor thrombus was performed using cardiopulmonary bypass with heparin prior to hepatectomy. The other patient had poor hemodynamic tolerance during THVE without bypass which led to incomplete removal of the tumor thrombus. Therefore, it was suggested that hepatectomy should be given priority over removal of the tumor thrombus. This method allows for control of bleeding from the raw surface of the liver prior to the administration of heparin and a radical operation may be performed without scattering tumor cells during extirpation of the tumor. One disadvantage of the present procedure is that no means could be taken to prevent distal embolization of the tumor thrombus during hepatectomy. However, the resected specimen showed that the tumor thrombus was covered with a thin, fibrous membrane and endothelium. Therefore, as long as these maneuvers are carefully performed, the tumor thrombi will seldom embolize distally during hepatectomy. Onitsuka *et al.* (14) reported a patient in whom removal of intracardiac tumor was performed prior to hepatectomy. By neutralizing heparin with protamine sulfate, bleeding from the raw surface of the liver was effectively controlled. However, during extirpation of the tumor thrombus, significant bleeding from the IVC prevented the complete removal of the tumor thrombus. With removal of the tumor thrombus prior to hepatectomy, bleeding from the IVC via the lumbar veins, phrenic veins, right adrenal vein and coronary vein may be a significant problem. With THVE, only clamping of the infrahepatic IVC just above the renal veins caused some bleeding (15) and made complete removal of tumor thrombus difficult. Houguet *et al.* (8) also noted that the effectiveness of THVE was strictly related to proper surgical technique.

We performed complete THVE with dissection of the posterior aspect of the retrohepatic IVC. After the tumor thrombus had been removed from the IVC and right atrium with the left lobe of the liver, the clamp of the portal triad at the hilum (Pringle's maneuver) was released, and the IVC was sutured. Bleeding from the IVC was well controlled with one pump sucker to examine the inside of the IVC sufficiently and shorten the period of warm liver ischemic time. Yamaoka *et al.* (16) have emphasized the importance of a period of warm liver ischemia with a time of less than 60 minutes under venoveous bypass in cirrhotic patients. Houguet *et al.* (17) applied THVE

to major hepatic resection in patients with normal liver function for 38 ± 5 minutes without any obvious detrimental effects. By performing dissection of the hepatic parenchyma prior to removal of the tumor thrombus, the period of extracorporeal circulation, duration of warm ischemic time and intraoperative blood loss were all reduced. Accordingly, removal of tumor thrombus prior to hepatic resection is only necessary in patients with cardiac insufficiency requiring emergency surgery.

Another technical consideration is whether cardiac arrest is necessary. We were able to remove the tumor thrombus with a beating heart. However, in patients with the tumor thrombus invading the wall of the right atrium or with extension into the right ventricle, removal of the tumor thrombus should be carried out with cardiac arrest.

Surgery is the only therapeutic modality for HCC with invasion of the IVC and/or right atrium. Therefore, every attempt should be made to establish an operative method that allows for surgical resection of HCC in an effort to prevent recurrence.

REFERENCES

1. Hahne OH, Climie ARH : Right atrial thrombi with ball-valve action. *Am J Med* 32 : 942-946, 1962
2. Ozawa K : Liver surgery approached through the mitochondria (in Japanese). *Medical Tribune*, Tokyo, 1992, pp. 127-160
3. Hwang YJ, Chang BH, Kim JW, Choi GS, Yun YK, Chui A, Kim YI : Successful resection of cecal hepatic metastasis extending into the right side of the heart under cardiopulmonary bypass. *J Hepatobiliary Pancreat Surg* 6 :320-323, 1999
4. Sano T, Kamiya J, Nagino M, Uesaka K, Yuasa N, Oda K, Kanai M, Yamamoto H, Hayakawa N, Nimura Y : Surgery for hepatocellular carcinoma with tumor thrombus into the inferior vena cava and the right atrium. *Gastroenterological Surgery* 22 : 1741-1751, 1999
5. Shimizu M, Okumura M, Masuda N : The death causes of patients with hepatocellular carcinoma. *Digestive Medicine (in Japanese with English abstract)* 8 : 227-233, 1988
6. The Liver Cancer Study Group of Japan : Follow-up investigation of primary liver cancer (in Japanese). 10th report. *Shinko Press*, Kyoto, 1992, pp. 51
7. Pichlmayr R, Weimann A, Lamesh P, Ringe B : Liver transplantation for hepatocellular carcinoma

- ma, with additional reference to bench surgery. *J Hep Bil Pancr Surg* 2 : 133-140, 1994
8. Houget C, Gavelli A, Sakai H : Vascular exclusion technique in liver resection for hepatocellular carcinoma. *J Hep Bil Pancr Surg* 2 : 123-127, 1994
 9. Pichlmayr R, Grosse H, Hauss J, Lamesh P, Bretschneider HJ : Technique and preliminary results of extra corporeal liver surgery (Bench procedure) and of surgery on the in situ perfused liver. *Br J Surg* 77 : 21-26, 1990
 10. Goto H, Kaneko Y, Utoh J, Nishimura K, Miyauchi Y, Iwanaga K : Surgery of hepatoma with intracavitary cardiac extension. *Heart and Vessels* 2 : 60-62, 1986
 11. Nimura Y : Surgery for Hepatocellular carcinoma with tumor in the inferior vena cava. *Syujyutu* (in Japanese) 48 : 257-263, 1994
 12. Chua SO, Chiang CW, Lee YS, Lin SH, Liaw YF : Moving right atrial mass associated with hepatectomy : Two cases detected by echocardiography. *Chest* 89 : 148-150, 1986
 13. Shimamura K, Takasaki K, Mutoh H, Tanaka S, Yamamoto M, Yamaguchi M, Nakagawa M, Kobayashi S : Removal of the tumor thrombus and hepatectomy for primary hepatocellular carcinoma with growth in the inferior vena cava and right atrium. *Jpn J Gastroenterol Surg* (abstract, in Japanese) 20 : 599, 1987
 14. Onitsuka A, Hirose H, Ozeki Y, Hino A, Mori Y, Murakawa S : Hepatoma with growth in right atrium : Report of successful resection. *Dig Surg* 7 : 57-60, 1990
 15. Fujisaki M, Kurihara E, Kikuchi K, Nishikawa K, Uematu Y : Hepatocellular carcinoma with tumor thrombus extending into the right atrium : Report of a successful resection with the use of cardiopulmonary bypass. *Surgery* 109 : 214-219, 1991
 16. Yamaoka Y, Ozawa K, Kumada K, Shimahara Y, Tanaka K, Mori K, Takayasu T, Okamoto R, Kobayashi N, Konishi Y, Egawa H : total vascular exclusion for hepatic resection in cirrhotic patients. *Arch Surg* 127 : 276-280, 1992
 17. Houguet C, Gavelli A, Chieco A, Bona S, Harb J, Joseph J, Jobard J, Gramaglia M, Lasserre M : Liver ischemia for hepatic resection : Where is the limit? . *Surgery* 111 : 251-259, 1992