

## Surgical Treatment of a Patient with Diaphragmatic Invasion by a Ruptured Hepatocellular Carcinoma with Biliary and Portal Venous Tumor Thrombi

Hiroshi Maruyama<sup>1,2</sup>, Hiroshi Yoshida<sup>1,2</sup>, Atsushi Hirakata<sup>1,2</sup>, Takeshi Matsutani<sup>1,2</sup>,  
Tadashi Yokoyama<sup>1,2</sup>, Seiji Suzuki<sup>1,2</sup>, Akira Matsushita<sup>1,2</sup>, Koji Sasajima<sup>1,2</sup>,  
Yuta Kikuchi<sup>1</sup> and Eiji Uchida<sup>1</sup>

<sup>1</sup>Surgery for Organ Function and Biological Regulation, Graduate School of Medicine, Nippon Medical School

<sup>2</sup>Department of Surgery, Nippon Medical School Tama Nagayama Hospital

### Abstract

We describe the surgical treatment of a patient with diaphragmatic invasion by a ruptured hepatocellular carcinoma (HCC) associated with biliary and portal venous tumor thrombi. A 67-year-old man was admitted because of jaundice (total serum bilirubin, 6.6 mg/dL). The serum concentration of alpha-fetoprotein was 236.1 ng/mL. The anti-hepatitis C virus antibodies were present in the serum. Computed tomography showed a large hypervascular mass in the right subphrenic region, surrounded by local effusion. Endoscopic retrograde cholangiography revealed dilatation of the left intrahepatic bile duct caused by biliary tumor thrombi extending from the right hepatic duct to the common bile duct. Endoscopic nasobiliary drainage was performed, and the total serum bilirubin level returned to the normal range. Angiography revealed a hypervascular tumor without extravasation of contrast medium in the right lobe and obstruction of the right anterior branch of the portal vein. Right hepatectomy was attempted 15 days after drainage. Severe invasion of the diaphragm by the ruptured HCC was detected. Bleeding of the ruptured HCC stopped spontaneously. Partial resection of the diaphragm was performed, followed by primary suture, without an artificial patch. Tumor thrombectomy was performed from the common bile duct. Macroscopic examination revealed that the ruptured HCC had invaded the diaphragm. Biliary and portal venous tumor thrombi were present. Histopathological examination showed a moderately differentiated HCC with biliary and portal venous tumor thrombi. The postoperative course was uneventful. The patient was discharged on postoperative day 14. Five months after the operation, local and intrahepatic recurrences of HCC were detected. Six months after operation, the patient died of liver failure. In conclusion, the outcome of a patient with diaphragmatic invasion by a ruptured HCC with biliary tumor thrombi was poor, even after curative hepatic resection.

(J Nippon Med Sch 2012; 79: 147–152)

**Key words:** hepatocellular carcinoma, obstructive jaundice, hemobilia, rupture, biliary tumor thrombi

---

Correspondence to Hiroshi Yoshida, MD, Department of Surgery, Nippon Medical School Tama Nagayama Hospital, 1-7-1 Nagayama, Tama, Tokyo 206-8512, Japan

E-mail: [hiroshiy@nms.ac.jp](mailto:hiroshiy@nms.ac.jp)

Journal Website (<http://www.nms.ac.jp/jnms/>)

## Introduction

Invasion of blood vessels, particularly the portal vein, is a common feature of hepatocellular carcinoma (HCC), whereas bile duct invasion is rare<sup>1</sup>. Biliary tumor thrombi are found in 2% to 9% of patients with HCC<sup>2-5</sup>. Lin et al. have clinically designated such cases as icteric-type HCC<sup>1</sup>. HCC with biliary tree invasion is characterized by obstructive jaundice and hemobilia due to rupture of the tumor into the biliary system.

Spontaneous rupture of HCC is potentially life-threatening<sup>6</sup>. Accurate diagnosis and proper management by such procedures as transarterial chemoembolization (TACE) or operation are urgent priorities. However, operative mortality rates of emergency hepatectomy (28.5%–54.5%)<sup>7-9</sup> remain high. TACE followed by elective hepatectomy is an effective treatment for ruptured HCC<sup>9,10</sup>. HCC with biliary tumor thrombi is associated with increased rates of tumor rupture and vascular invasion<sup>11</sup>.

We describe the surgical treatment of a patient with diaphragmatic invasion by a ruptured HCC associated with biliary and portal venous tumor thrombi.

## Case

A 67-year-old man was admitted because of jaundice. The medical history was not relevant to the present disorder. Initial laboratory studies revealed the following values: serum aspartate aminotransferase, 107 IU/L (normal, <38 IU/L); serum alanine aminotransferase, 87 IU/L (normal, <44 IU/L); serum alkaline phosphatase, 685 IU/L (normal 104 to 338 IU/L); serum gamma glutamic transpeptidase, 519 IU/L (normal, 16 to 73 IU/L); total serum bilirubin, 6.6 mg/dL (normal, 0.2 to 1.2 mg/dL); direct serum bilirubin, 5.4 mg/dL (normal, <0.4 mg/dL); serum albumin, 3.6 g/dL (normal, 3.8 to 5.5 g/dL); serum C-reactive protein, 3.96 mg/dL (normal, <0.3 mg/dL); white blood cell count, 6,000/ $\mu$ L (normal, 4,000 to 9,000/ $\mu$ L); red blood cell count,  $363 \times 10^4$ / $\mu$ L (normal, 427 to  $570 \times 10^4$ / $\mu$ L); serum

hemoglobin concentration, 11.7 g/dL (normal, 14 to 18 g/dL); and serum platelet count,  $12.0 \times 10^4$ / $\mu$ L (normal, 20 to  $40 \times 10^4$ / $\mu$ L). The serum concentration of des-gamma-carboxyprothrombin (DCP) was 261,000 mAU/mL (normal, <40 mAU/mL), that of alpha-fetoprotein (AFP) was 236.1 ng/mL (normal, <6.92 ng/mL), and that of lectin-bound AFP (AFP-L3%) was 32.2% (normal, <10%). The serum surface antigen for hepatitis B was negative, and anti-hepatitis C virus antibody was positive.

Computed tomography showed a large hypervascular mass in the right subphrenic region, surrounded by local effusion. The right anterior branch of the portal vein was occluded by tumor thrombi. Biliary tumor thrombi were seen from the right hepatic duct to the common bile duct, and dilatation of the left intrahepatic duct was detected (**Fig. 1**). Upper gastrointestinal endoscopy revealed mild esophageal varices without gastric varices (Li, Cw, F<sub>1</sub>, RC<sub>0</sub>: according to the General Rules for Recording Endoscopic Findings of Esophagogastric Varices<sup>12</sup>). Endoscopic retrograde cholangiography revealed dilatation of the left intrahepatic bile duct caused by biliary tumor thrombi extending from the right hepatic duct to the common bile duct (**Fig. 2**). Endoscopic nasobiliary drainage was performed, and the total serum bilirubin level returned to the normal range. Angiography revealed a hypervascular tumor without extravasation of contrast medium in the right lobe, obstruction of the right anterior branch of the portal vein, and an arteriportal venous shunt of the left lateral section (Segment 3) (**Fig. 3**).

Right hepatectomy was attempted 15 days after drainage. Severe invasion of the diaphragm by the ruptured HCC was detected. Bleeding of the ruptured HCC stopped spontaneously. Partial resection of the diaphragm was performed, followed by primary suture, without an artificial patch. After the right hepatic duct was cut, tumor thrombectomy was performed from the common bile duct. The stump of the right hepatic duct was sutured, and the common bile duct was preserved. After right hepatectomy, a biliary leakage test was performed with an injection of saline and air, and several

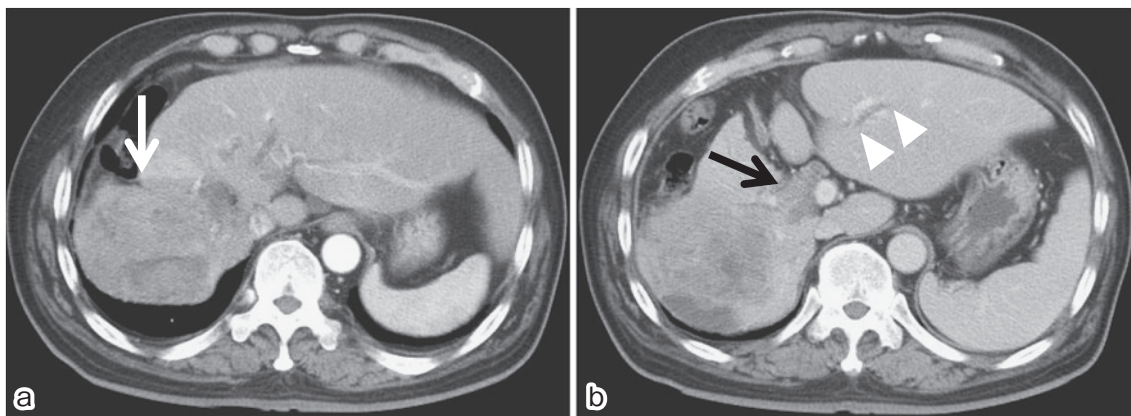


Fig. 1 Computed tomography showed a huge hypervascular mass in the right subphrenic area, surrounded by local effusion (**white arrow**) (a). The right anterior branch of the portal vein was occluded by tumor thrombi. Biliary tumor thrombi (**black arrow**) extended from the right hepatic duct to common bile duct, and dilatation of the left intrahepatic duct (**arrow heads**) was detected (b).

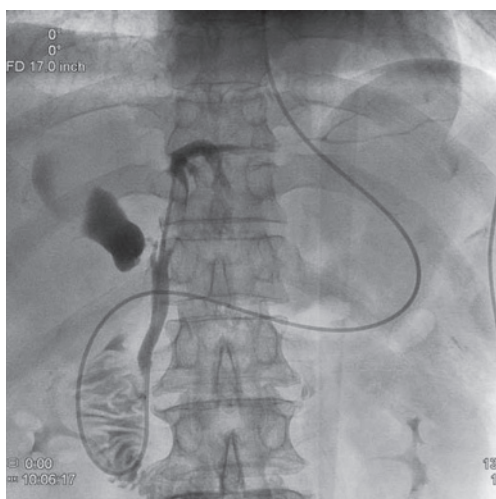


Fig. 2 Endoscopic retrograde cholangiography revealed dilatation of the left intrahepatic bile duct due to biliary thrombi extending from the right hepatic duct to the common bile duct.

leakage points were repaired with fine sutures. Hemostasis of the cut surface of the liver was achieved with ligation and the application of a fibrin glue spray (Bolheal; Chemo-Sero Therapeutic Research Institute, Kumamoto, Japan). An external drainage catheter (19 Fr. Blake Silicon Drain; Ethicon, Somerville, NJ, USA) was positioned in the space created by surgery.

Macroscopic examination revealed that the ruptured HCC had invaded the diaphragm (**Fig. 4**). Histopathological examination showed a moderately differentiated HCC with biliary and portal venous

tumor thrombi. There was no HCC at margin of resection.

The postoperative course was uneventful. The patient was discharged on postoperative day 14. The serum concentrations of DCP and AFP had decreased to 20 mAU/mL and 10.1 ng/mL, respectively. Five months after the operation, the serum concentrations of DCP and AFP had increased again to 57 mAU/mL and 114.9 ng/mL, respectively. Obstructive jaundice due to biliary invasion of recurrent tumor was detected. Biliary drainage was performed, and the jaundice was improved transiently. Stenosis of the portal vein due to invasion of recurrent tumor was detected. Refractory ascites rapidly increased. Local and intrahepatic recurrences of HCC were detected (**Fig. 5**). The biliary drainage catheter was exchanged because drainage was poor, but total serum bilirubin level rapidly increased. Six months after the operation, the patient died of liver failure.

### Discussion

Biliary tumor thrombi, portal venous thrombi, diaphragmatic invasion, and rupture are poor prognostic factors for HCC.

Icteric-type HCC is HCC with progressive obstructive jaundice due to bile duct invasion or hemobilia secondary to HCC<sup>13</sup>. The outcomes of patients with icteric-type HCC are poorer than those

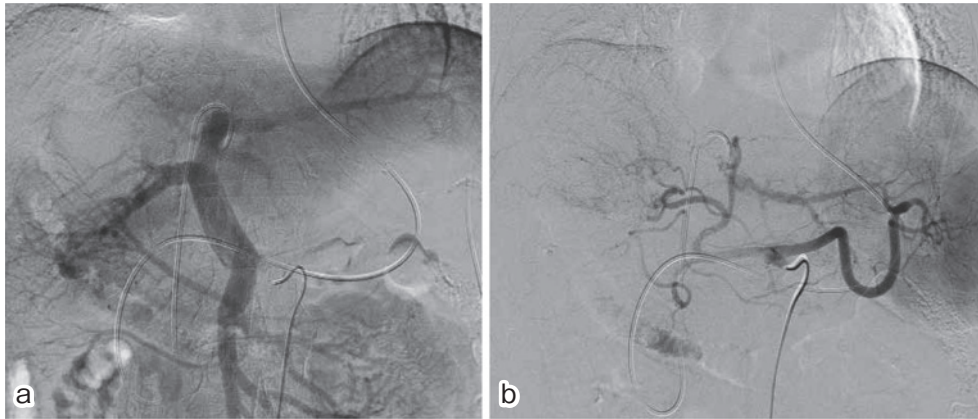


Fig. 3 Angiography revealed obstruction of the right anterior branch of the portal vein (a), a hypervascular tumor without extravasation of contrast medium in the right lobe, and an arterioportal venous shunt of the left lateral section (Segment 3) (b).

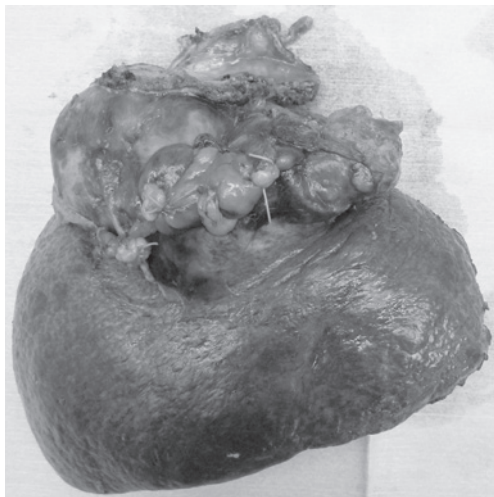


Fig. 4 Macroscopic examination revealed that the ruptured HCC had invaded the diaphragm.

of patients without biliary invasion<sup>2</sup>. Yeh et al.<sup>11</sup> have reported that HCC patients with biliary tumor thrombi after surgery have significantly poorer overall survival than those without thrombi (5-year survival, 6.7% vs. 33.0%, respectively). Ikenaga et al.<sup>14</sup> have reported that 53% of patients with bile duct thrombosis have recurrence in the remnant liver within 3 months after surgery. Satoh et al.<sup>15</sup> have found no significant difference in the survival rate between patients with and those without bile duct thrombi after hepatic resection. Surgical resection has been considered the preferred treatment for HCC with bile duct invasion; however, whether outcomes differ between HCC with and without bile duct invasion remains controversial.

Direct diaphragmatic involvement is found in 10% to 13% of patients with HCC<sup>16</sup>. Although, Lau et al.<sup>17</sup> have reported that there was no significant difference in survival, operative morbidity, or mortality rates after resection between HCC with and without diaphragmatic invasion, Leung et al.<sup>18</sup> have reported that a resection margin of 1 cm was the only significant prognostic factor for poor disease-free survival after en bloc resection. Spontaneous rupture is common in patients with HCC. The mechanism of spontaneous rupture of HCC in the peritoneum remains unclear, but rupture has been attributed to central necrosis in a rapidly growing HCC, hemorrhage and venous congestion inside a tumor, coagulopathy due to underlying cirrhosis, and minor trauma causing a sudden increase in pressure within a tumor<sup>19-23</sup>. In our patient, rupture of HCC occurred, but hemostasis was achieved spontaneously.

Staging of HCC is usually done according to the tumor-node-metastasis (TNM) classification system of the International Union Against Cancer (UICC)<sup>24</sup>, which is based on tumor extension and used worldwide. The General Rules for the Clinical and Pathological Study of Primary Liver Cancer, compiled by the Liver Cancer Study Group of Japan (LCSGJ), base their classifications on TNM staging<sup>25</sup>. Both the TNM staging system of the UICC and the LCSGJ rules classify HCC with perforation of the visceral peritoneum as T4, the most advanced stage (stage 4), even if the tumor is small and solitary.



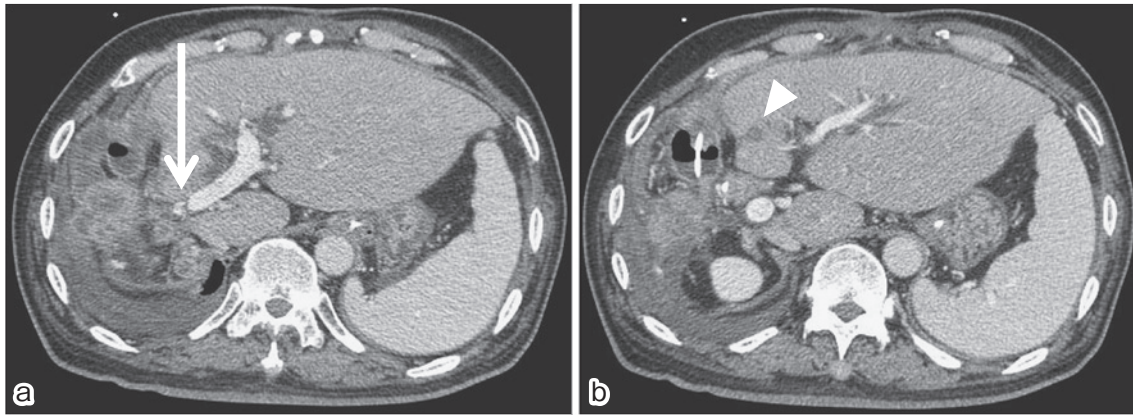


Fig. 5 Obstructive jaundice due to biliary invasion of recurrent tumor was detected. Stenosis of the portal vein due to invasion of recurrent tumor was detected (a: **white arrow**). Local and intrahepatic recurrences (b: **arrow head**) of HCC were detected.

The cumulative survival rate of patients with ruptured HCC is reported to be higher than that of patients with stage 4 disease who have nonruptured HCC and similar to that of patients with stage 2 or stage 3 disease. The cumulative disease-free survival rate of patients with ruptured HCC is similar to that of patients with stage 1, stage 2, or stage 3 disease who have nonruptured HCC<sup>10</sup>. Yeh et al. have demonstrated that elective hepatic resection in patients with ruptured HCC may achieve long-term survival comparable to that in patients with nonruptured HCC<sup>26</sup>.

Recurrence of HCC can rarely be caused by peritoneal dissemination in patients with ruptured HCC. Although surgical treatment of peritoneal dissemination of HCC is not curative, surgery may improve survival and provide a good quality of life in selected patients<sup>27</sup>. Our patient had recurrence 5 months after operation and died of liver failure 6 months after operation without peritoneal dissemination. We could not perform resection because both local and intrahepatic recurrence was detected.

In this case, diaphragmatic invasion by a ruptured HCC associated with biliary and portal venous tumor thrombi was detected. Because the prognosis was thought to be poor without treatment, right hepatectomy was attempted after biliary drainage. Although, curative hepatic resection succeeded, local and intrahepatic recurrence of HCC occurred 5 months after the operation. Intrahepatic recurrence

might have occurred owing to biliary tumor thrombi and portal venous thrombi. Local recurrence might have occurred due to diaphragmatic invasion and rupture. Surgical treatment might have been difficult in this advanced case.

In conclusion, the outcome of a patient with diaphragmatic invasion by a ruptured HCC with biliary tumor thrombi was poor, even after curative hepatic resection.

## References

1. Lin TY, Chen KM, Chen YR, Lin WS, Wang TH, Sung JL: Icteric type hepatoma. *Med Chir Dig* 1975; 4: 267-270.
2. Kojiro M, Kawabata K, Kawano Y, Shirai F, Takemoto N, Nakashima T: Hepatocellular carcinoma presenting as intrabiliary duct tumor growth: a clinicopathologic study of 24 cases. *Cancer* 1982; 49: 2144-2147.
3. Chen MF, Jan YY, Jeng LB, Hwang TL, Wang CS, Chen SC: Obstructive jaundice secondary to ruptured hepatocellular carcinoma into the common bile duct. Surgical experiences of 20 cases. *Cancer* 1994; 73: 1335-1340.
4. Nakashima T, Okuda K, Kojiro M, et al: Pathology of hepatocellular carcinoma in Japan. 232 Consecutive cases autopsied in ten years. *Cancer* 1983; 51: 863-877.
5. Ueda M, Takeuchi T, Takayasu T, et al: Classification and surgical treatment of hepatocellular carcinoma (HCC) with bile duct thrombi. *Hepatogastroenterology* 1994; 41: 349-354.
6. Chen CY, Lin XZ, Shin JS, Lin CY, Leow TC, Chang TT: Spontaneous rupture of hepatocellular carcinoma. A review of 141 Taiwanese cases and comparison with nonrupture cases. *J Clin Gastroenterol* 1995; 21: 238-242.
7. Lai EC, Wu KM, Choi TK, Fan ST, Wong J:

- Spontaneous ruptured hepatocellular carcinoma. An appraisal of surgical treatment. *Ann Surg* 1989; 210: 24-28.
8. Dewar GA, Griffin SM, Ku KW, Lau WY, Li AK: Management of bleeding liver tumours in Hong Kong. *Br J Surg* 1991; 78: 463-466.
  9. Yoshida H, Onda M, Tajiri T, et al: Treatment of spontaneous ruptured hepatocellular carcinoma. *Hepatogastroenterology* 1999; 46: 2451-2453.
  10. Yoshida H, Mamada Y, Taniai N, et al: Long-term results of elective hepatectomy for the treatment of ruptured hepatocellular carcinoma. *J Hepatobiliary Pancreat Surg* 2008; 15: 178-182.
  11. Yeh CN, Jan YY, Lee WC, Chen MF: Hepatic resection for hepatocellular carcinoma with obstructive jaundice due to biliary tumor thrombi. *World J Surg* 2004; 28: 471-475.
  12. Tajiri T, Yoshida H, Obara K, et al: General rules for recording endoscopic findings of esophagogastric varices (2nd edition). *Dig Endosc* 2010; 22: 1-9.
  13. Takao Y, Yoshida H, Mamada Y, Taniai N, Bando K, Tajiri T: Transcatheter hepatic arterial embolization followed by microwave ablation for hemobilia from hepatocellular carcinoma. *J Nippon Med Sch* 2008; 75: 284-288.
  14. Ikenaga N, Chijiwa K, Otani K, Ohuchida J, Uchiyama S, Kondo K: Clinicopathologic characteristics of hepatocellular carcinoma with bile duct invasion. *J Gastrointest Surg* 2009; 13: 492-497.
  15. Satoh S, Ikai I, Honda G, et al: Clinicopathologic evaluation of hepatocellular carcinoma with bile duct thrombi. *Surgery* 2000; 128: 779-783.
  16. Yuki K, Hirohashi S, Sakamoto M, Kanai T, Shimosato Y: Growth and spread of hepatocellular carcinoma. A review of 240 consecutive autopsy cases. *Cancer* 1990; 66: 2174-2179.
  17. Lau WY, Leung KL, Leung TW, Liew CT, Chan M, Li AK: Resection of hepatocellular carcinoma with diaphragmatic invasion. *Br J Surg* 1995; 82: 264-266.
  18. Leung KF, Chui AK, Leung KL, Lai PB, Liew CT, Lau WY: Clinicopathological study of hepatocellular carcinoma with diaphragmatic involvement. *Br J Surg* 2001; 88: 681-682.
  19. Zhu LX, Wang GS, Fan ST: Spontaneous rupture of hepatocellular carcinoma. *Br J Surg* 1996; 83: 602-607.
  20. Chen MF, Jan YY, Lee TY: Transcatheter hepatic arterial embolization followed by hepatic resection for the spontaneous rupture of hepatocellular carcinoma. *Cancer* 1986; 58: 332-335.
  21. Vivarelli M, Cavallari A, Bellusci R, De Raffe E, Nardo B, Gozzetti G: Ruptured hepatocellular carcinoma: an important cause of spontaneous haemoperitoneum in Italy. *Eur J Surg* 1995; 161: 881-886.
  22. Sato Y, Fujiwara K, Furui S, et al: Benefit of transcatheter arterial embolization for ruptured hepatocellular carcinoma complicating liver cirrhosis. *Gastroenterology* 1985; 89: 157-159.
  23. Yamagata M, Maeda T, Ikeda Y, Shirabe K, Nishizaki T, Koyanagi N: Surgical results of spontaneously ruptured hepatocellular carcinoma. *Hepatogastroenterology* 1995; 42: 461-464.
  24. Sobin LH: TNM, sixth edition: new developments in general concepts and rules. *Semin Surg Oncol* 2003; 21: 19-22.
  25. The general rules for the clinical and pathological study of primary liver cancer. Liver Cancer Study Group of Japan. *Jpn J Surg* 1989; 19: 98-129.
  26. Yeh CN, Lee WC, Jeng LB, Chen MF, Yu MC: Spontaneous tumour rupture and prognosis in patients with hepatocellular carcinoma. *Br J Surg* 2002; 89: 1125-1129.
  27. Yoshida H, Onda M, Tajiri T, et al: Successful surgical treatment of peritoneal dissemination of hepatocellular carcinoma. *Hepatogastroenterology* 2002; 49: 1663-1665.

(Received, March 15, 2011)

(Accepted, October 12, 2011)