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Three Indonesian Cases of Intraperitoneal Development of Metastatic Hepatocellular Carcinoma, Possibly Disseminated by Spontaneous Tumor Rupture

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Abstract: We report 3 Indonesian patients with intraperitonial tumor development possibly caused by spontaneous rupture of hepatocellular carcinoma (HCC). Each case presented with expansively growing nodular metastatic tumors and all nodules were surgically removed in each case. The first case underwent lateral segmentectomy in Shanghai, while the second and third cases underwent liver resection for primary HCC in YMU hospital. Although the first case had seven intraperitoneal tumors, ranging from approximately 1 to 6 cm in maximal diameter, together with skin metastasis, the other two cases had a large solitary tumor, covered by the greater omentum; the tumors measured 6.5 cm and 13 cm in maximal diameter, respectively. In the third case, there were no intrahepatic metastases detected. Since this kind of recurrence pattern is very rare among Japanese HCC patients, we report these 3 cases and discuss the present findings on the distribution of HCC recurrence patterns in Japan.

Key words: Hepatocellular carcinoma, Spontaneous rupture, Indonesian, Intraperitoneal metastasis

INTRODUCTION

Peritoneal dissemination of hepatocellular carcinoma (HCC) is not a common type of recurrence. The Liver Cancer Study Group of Japan has reported the prevalence of peritoneal metastasis as about 16.3%[1)], but in most cases disseminated tumors were multiple, either diffuse or sporadic, and not resectable. In this paper, we report three cases of intraperitoneal and extrahepatic development of resectable HCC tumor nodules which had developed beneath the greater omentum; one in each of two patients and 7 in one patient. Coincidentally, all 3 cases were Indonesians who underwent surgical removal of these tumors in Yamanashi Medical University (YMU) Hospital. This pattern of recurrence has not been seen among 150 Japanese HCC patients who underwent liver resection in YMU Hospital during the past 10 years. We report these cases and possible causes of this recurrence pattern are discussed in the present study.

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CASE REPORTS

Case 1: A 33-year-old male, Chinese Indonesian, living in Surabaya, Java, 174 cm in height and 70 kg in weight. Blood type A, Rh positive. His father was a successful businessman and the patient had been educated in the U.S.A.

Liver dysfunction was first noted at the age of 24 years while in the U.S.A. and he was diagnosed as a carrier of hepatitis B virus (HBV). His mother was also an HBV carrier.

In January 1990, he developed sudden pain in the abdomen and underwent emergency laparotomy in Shanghai, China. At surgery, hemoperitoneum was found and about one liter of blood was suctioned. Under the diagnosis of spontaneous rupture of HCC in the lateral segment, he underwent lateral segmentectomy, but another large tumor was detected in the right lobe during surgery and was not resected. His family sought suitable treatment for the remnant liver in Shanghai, the U.S.A. and Indonesia, but everywhere additional liver resection was not recommended. In May, one subcutaneous tumor appeared at the lower presternal region and the patient decided to come to YMU Hospital in August, for examination and possible tumor removal. In July, selective angiography of the liver (SAG) performed in Surabaya revealed more than 2 large tumors in the right lobe and transcatheter hepatic arteial infusion (TAI) with 10 mg mitomycin (MMC) and 20 mg doxorubicin (adriamycin-ADR) with lipiodol was performed selectively to the right lobe.

On admission to YMU Hospital, there was no jaundice, vascular spider, or palmar erythema, but gynecomastia was observed. At the upper end of the upper median abdominal surgical scar a protruding tumor, 6.5 × 6.0 × 3.5 cm, was seen (Fig. 1). The tumor was solid and fixed to the rectus abdominal muscle. The abdomen was flat and soft and there was no tenderness. The liver was not palpable.

Blood examination on admission did not reveal anemia, but there were slight increases in GOT (88 U/*l*) and GPT (59 U/*l*). The Clinical Stage[2] of accompanying liver cirrhosis was Stage I: Alb, 4.3 g/d*l*; T. Bil, 1.2 mg/d*l*; PT, 93.1%; $ICGR_{15}$, 5.6%; no ascites. Virus marker analysis was positive for HBsAg, anti-HBe, anti-HBc, and anti-HCV. Tumor marker analysis detected higher levels of AFP (103 *n*g/m*l*) and PIVKA-II (8.3 AU/m*l*).

Abdominal CT revealed low density areas with lipiodol deposits in the right lobe (Fig. 1), suggesting a large HCC with central necrosis.

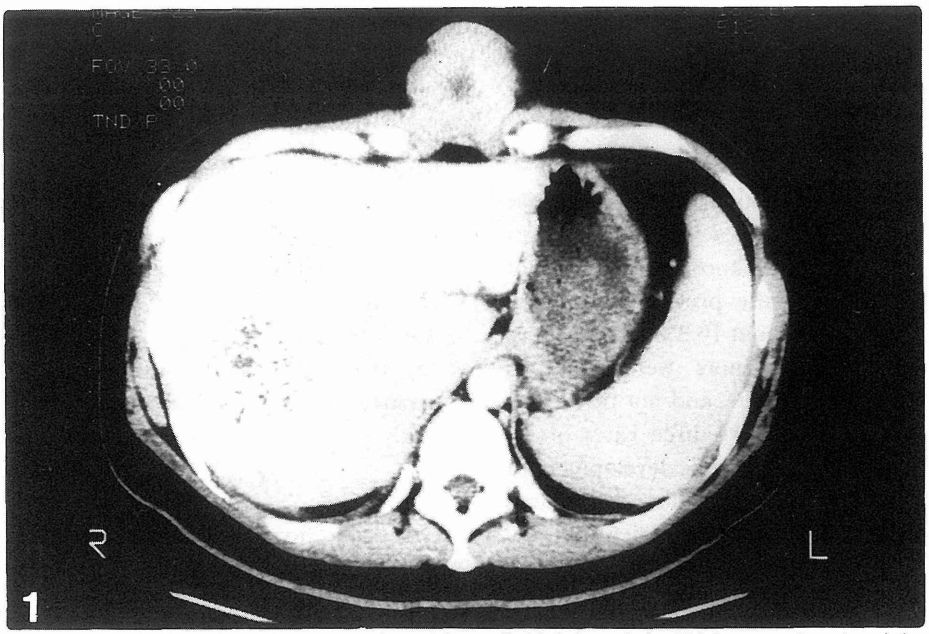


Fig. 1. CT indicated a skin metastasis and large lipidol deposit in HCC occupying the right lobe.

Splenomegaly and gallstones were also observed. US revealed at least 3 hyperechoic masses, 6.0 × 7.0 cm, 6.5 × 6.1 cm, 8.7 × 7.4 cm, in the right lobe but no echogenic mass in the left lobe. Many gallstones were also detected.

After examination, physicians in the First Department of Medicine persuaded the patient and his family to return to Indonesia to continue receiving TAI treatment in Indonesia as he had before coming to Japan, since there was no indication that tumor removal would extend his survival period. However, the family was eager for him to be treated in Japan and the doctors then referred him to our Surgical Department. Since his liver dysfunction was not severe and no liver tumor was found in the remnant region of the left lobe, resection of the tumor in the right lobe as well as the metastatic tumor to the skin was possible, although it was not certain whether these treatment would extend his survival period.

On September 20, 1990, he underwent surgery. The skin tumor, about 7 cm in diameter with a clear border, was resected. It was hard and infiltrated the anterior sheath of the rectus abdominal muscle. At laparotomy, a small quantity of serous ascites was observed. In addition, 7 tumor nodules were found in the abdominal cavity; 2 (6.0 × 4.3 × 4.0 cm, 1.8 × 1.7 × 1.1 cm) (Figs. 2 and 3a) covered by the greater omentum, one (3.7 × 3.3 × 3.0 cm) adhered to the ascending colon, one (2.8 × 2.5 × 1.8 cm) to the transverse colon, one (1.4 × 1.2 × 1.2 cm) to the ileum, one (1.6 × 1.4 × 1.4 cm) to the jejunum, and one to the parietal peritoneum (1.2 × 1.2 × 1.2 cm). There were no other small and diffuse peritoneal disseminations as seen in adenocarcinoma. All of the tumors adhered to the greater omentum. They seemed to be due to peritoneal dissemination during tumor rupture. All were excised surgically. Macroscopically, all intraperitoneal tumors were yellowish and compact, and the borders were clearly demarcated. The intrahepatic tumor (12 × 7 cm by perioperative US) was not removed but wedge resection of a small piece of the liver including a small metastatic nodule was performed. For subsequent TAI, cannulation to the hepatic artery

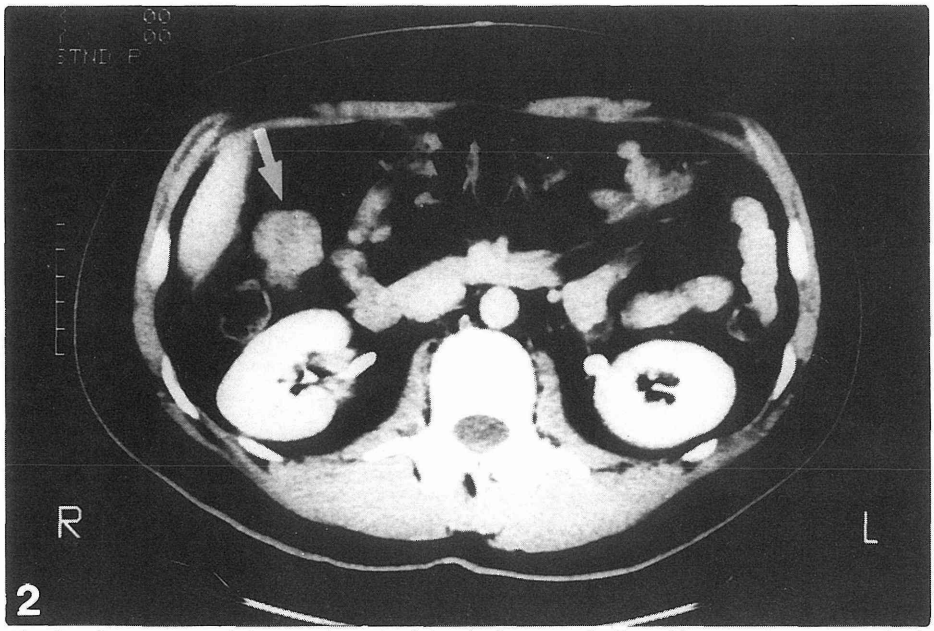
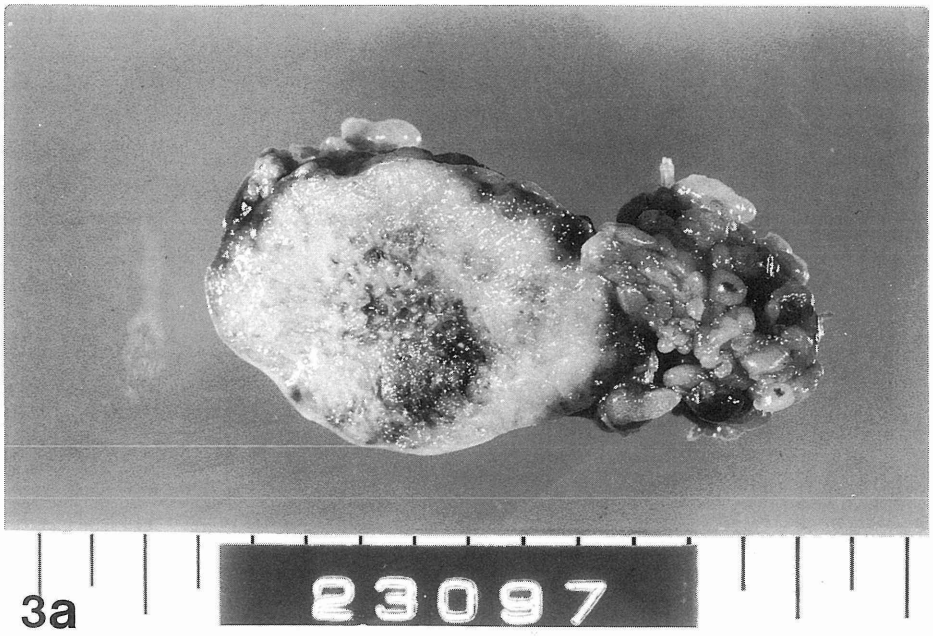


Fig. 2. Case 1: One of the extrahepatic abdominal tumors (indicated by arrow) was recognized on the preoperative CT, retrospectively.



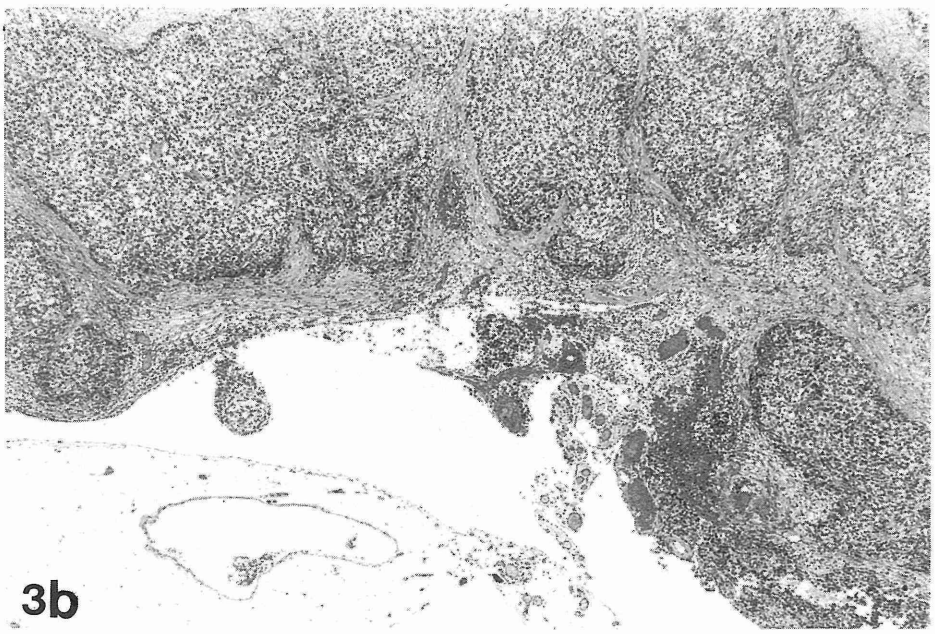


Fig. 3. Case 1: Macroscopic (a) and microscopic (b) findings of the largest extrahepatic abdominal tumor. Histologically the tumor was moderately differentiated hepatocellular carcinoma, covered by thin capsule (HE, original magnification ×40).

through the gastroduodenal artery and its connection to a subcutaneous port in the abdominal wall were performed together with cholecystectomy. None of the lymph nodes along the gastroduodenal ligament suggested metastasis.

Microscopically, all tumors were composed of thick trabecular-type and solid-type tumor cells, accompanied by giant cells and clear cells; moderately differentiated HCC (Edmondson Grade III) (Fig. 3b). One of the seven tumor nodules was located at the subserosal layer of the jejunum and was the only tumor where hematogenic metastasis may have been possible. All the other tumors were considered disseminated tumors.

After his return to Indonesia, although TAI was performed, he died in December 1990.

Case 2: A 68-year-old male, a retired businessman, 156.5 cm in height and 57.5 kg in weight, Indonesian living in Jakarta, Java. Blood type B, Rh positive.

He had a history of blood infusion many years ago, but the details were obscure. He underwent appendectomy at the age of 33 years. Since 1973, he had been followed for liver dysfunction. In January 1990, AFP increased to 649 ng/ml and on March 26, CT performed in Indonesia revealed a low density area in the anterior-superior region (S8) of the liver. He had only slight discomfort in the upper abdomen.

He was admitted to the First Department of Medicine on April 6. There was no anemia or jaundice and no vascular spider or palmar erythema. An elastic hard liver was palpable for 9 cm on the median line and 5 cm on the right middle clavicular line. The edge of the liver was dull and the surface was irregular. The spleen was palpable to a two-finger width. Besides HCC accompanied by liver cirrhosis and gallstones, he had hypertension, asthma bronchialis, a slight glucose intolerance and esophageal varices. Biochemical examination indicated liver dysfunction, such as high GOT (128 U/*l*) and GPT (141 U/*l*), but the accompanying liver cirrhosis was Clinical Stage I; Alb, 3.6 g/d*l*; T. Bil, 1.1 mg/d*l*; PT%, 114.8%; $ICGR_{15}$, 17.6%; no ascites. Virus marker

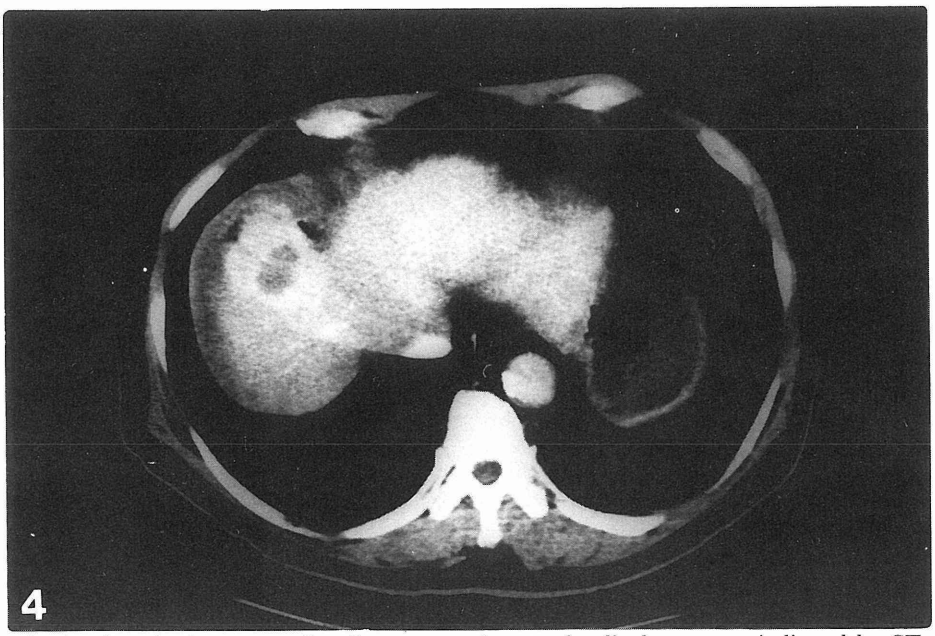


Fig. 4. Case 2: One protruding liver tumor close to the diaphragm was indicated by CT.

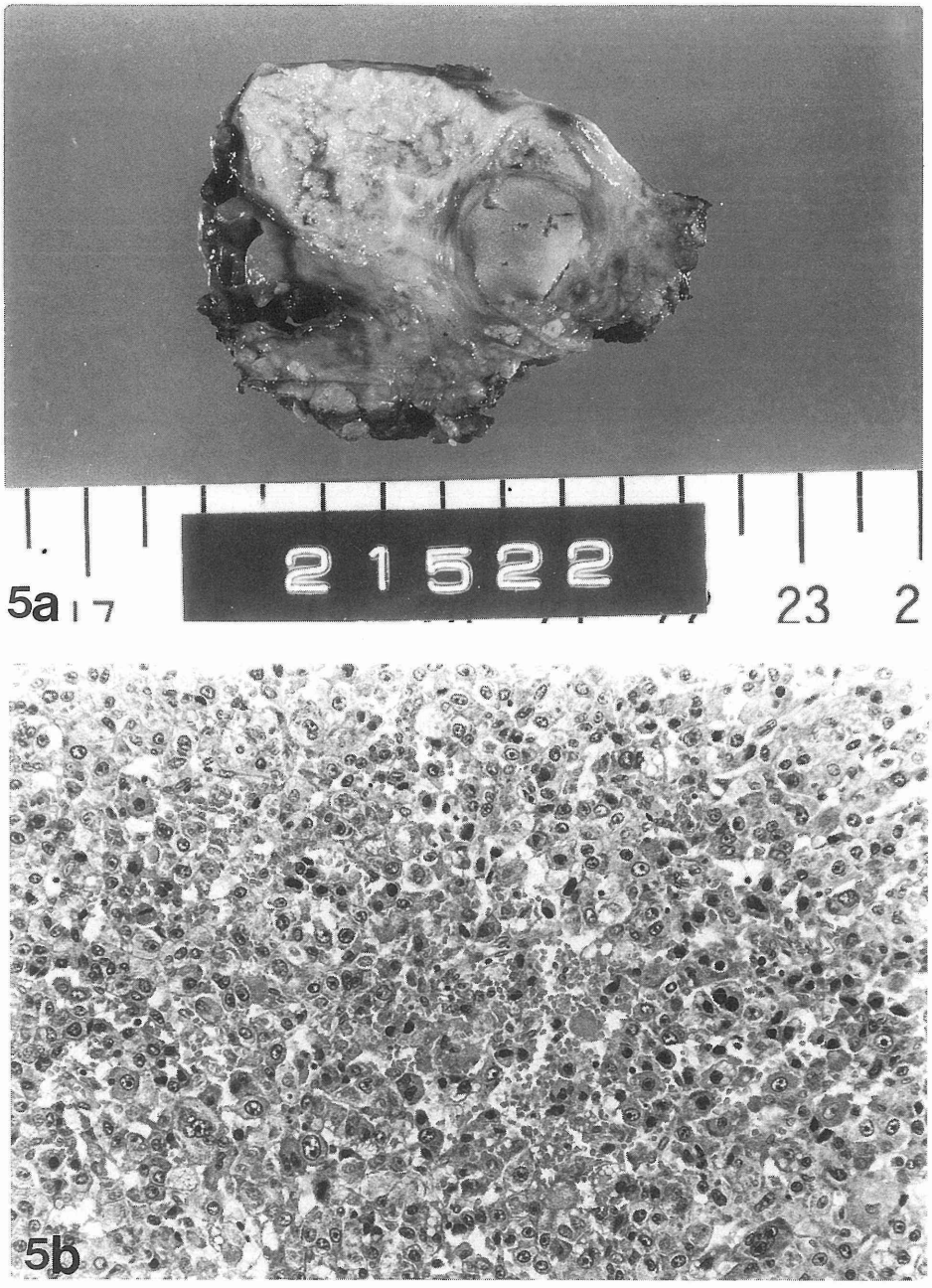


Fig. 5. Case 2: Macroscopic (a) and microscopic (b) findings of the primary tumor. The tumor was almost necrotized. Viable portions found at the subcapsular region were composed of moderately differentiated hepatocellular carcinoma with a thick trabecular pattern and poorly differentiated carcinoma with irregular and large nuclei (HE, original magnification ×200).

analysis was negative for HBsAg, HBeAg, and anti-HCV. AFP was 1318 *ng*/m*l* and PIVKA-II was less than 0.06 AU/m*l*.

On SAG performed on April 16, a S8 tumor irrigated by the anterior-superior branch of the right hepatic artery was recognized. Vascular invasion was negative. From the right hepatic artery, the transcatheter arterial embolization (TAE) was performed using 40 mg ADR, 10 m*l* lipiodol and Spongel®. Then, he was transferred to the First Department of Surgery on May 1.

On May 15, 1990, after his general condition and liver function had improved following TAE, he underwent partial liver resection of the S8 tumor (Fig. 4) and cholecystectomy. The cirrhotic liver surface of the right lobe adhered tightly to the diaphragm, but the greater omentum gathered between the tumor and the diaphragm. Cautious dissection of the strongly fibrous adhesion gave access to the tumor, but the protruding tumor adhered tightly to the diaphragm suggesting a post-rupture state. In the surgical specimen, the 3.0 × 2.0 × 3.5 cm tumor was a single nodular type with infiltration of the surrounding tissue, and without capsule formation. Serosal infiltration was positive. The macroscopic Stage (TNM)[2] was II. Microscopically, most of the tumor was necrotic probably due to preoperative TAE. The viable portion was moderately to poorly differentiated HCC (Fig. 5). Microscopic invasion of the vasculature was positive, and tumor infiltration of the connective tissue adhering to the diaphragm was positive. According to surgical findings and macro- and microscopic analysis, the tumor was apparently in a status after tumor rupture.

After liver resection, AFP decreased to 14 *ng*/m*l* on May 28 and 10 *ng*/m*l* on June 11. TAI with 60 mg epirubicin and 8 m*l* lipiodol was performed on June 25. Lipiodol CT did not indicate lipiodol deposits in the remnant liver.

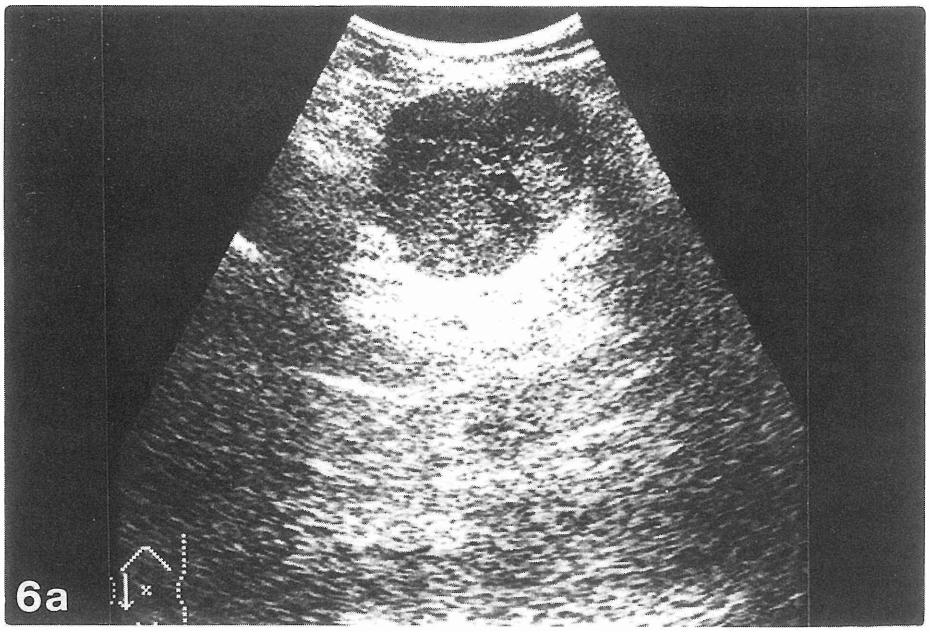
After discharge, he returned to Indonesia. In March 1991, AFP increased to more than 1,000 *ng*/m*l* and CT revealed a large mass in the right lobe. He was readmitted to the First Department of Medicine on May 20, 1991.

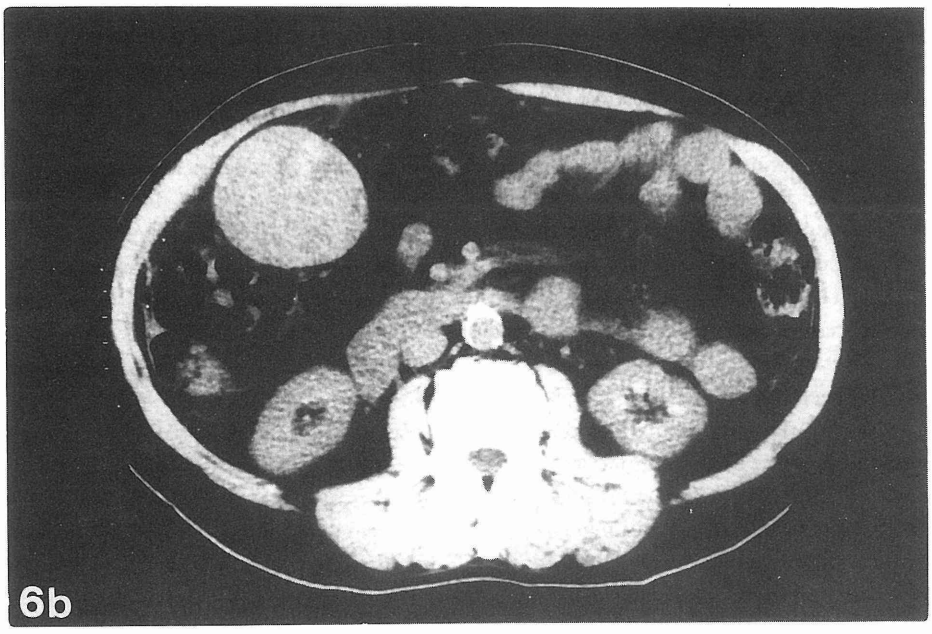
On admission his body weight was 56 kg. General condition was good. There was no anemia or jaundice. In the upper right abdominal region, a round tumor mass, about 5 cm in diameter, free from the liver, was palpable. It was elastic firm with tenderness.

On admission, accompanying liver cirrhosis was Clinical Stage II: Alb, 3.4 g/d*l*; T. Bil, 1.3 mg/d*l*; PT%, 85.1%; $ICGR_{15}$, 27.0 %; no ascites. Tumor marker analysis detected elevated AFP (May 27, 73,000 *ng*/m*l*) and PIVKA-II (May 27, 48.4 AU/m*l*).

US, CT and scintigraphy revealed one extrahepatic tumor in the abdominal cavity (Figs. 6-a, -b, -c), and a massive tumor occupying the anterior segment of the right lobe (Fig. 6-d). SAG on May 27 revealed a large tumor stain in the right lobe and small stains in the left lobe. One extrahepatic tumor stain, about 7 cm in diameter, fed by the gastroduodenal artery was also recognized. Portography did not indicate the right branch of the portal vein. To the right hepatic artery, 40 mg epirubicin and 6 m*l* lipiodol were infused. Endoscopy revealed that the blue esophageal varices had progressed, compared with those before the initial surgery.

He was transferred to the First Department of Surgery on June 10, 1991. From the above observations, the liver tumor was considered unresectable, but the rapidly growing abdominal tumor was removed to prevent rupture and also to allow subsequent TAI treatment to focus exclusively on the liver. On June 20, 1991, extirpation of the extrahepatic abdominal tumor and cannulation to the right hepatic artery for TAI were performed. Slight ascites was recognized. The abdominal tumor was covered by the greater omentum and had slight adhesion to the transverse colon. There were no other tumors or peritoneal dissemination detected. There was no lymph node metastasis observed. Macroscopic TNM Stage

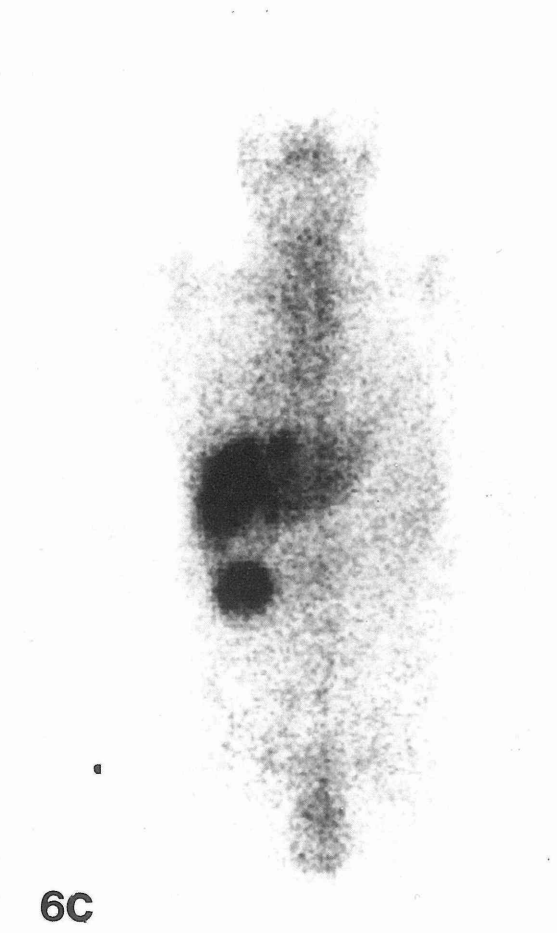




was Stage IV-B.

The tumor was 6.5 × 6.0 × 5.5 cm, round and elastic hard. Thick tumor capsule had not developed. Microscopically, the tumor was a metastatic nodule of HCC, containing abundant polynuclear giant cells (poorly differentiated HCC) (Fig. 7). Examination of ascites did not reveal any cancer cells.

Postoperative weekly TAI using 10 mg ADR and 1 m*l* lipiodol through the port, subcutaneously connected to the hepatic cannula, was started from the second week and continued after his return to Indonesia, but he died within 6 months.



Case 3: A 52-year-old male, medical doctor, 168 cm in height and 68 kg in weight, living in Sumatra. Blood type A, Rh positive. In July 1981, liver dysfunction was first diagnosed. Liver biopsy diagnosed fatty liver. In June 1992, he felt epigastric pain and distension in the abdomen. Acidic food exacerbated his pain. US examination in a local hospital diagnosed liver abscess and he was prescribed medicine, which sedated his complaint. However, CT (Fig. 8a) and MRI, taken in Jakarta, indicated HCC and he was referred to the First Department of Medicine at Yamanashi Medical University.

He was admitted on August 3, 1992. His general condition was good. There was no palmar erythema, vascular spider, anemia or jaundice. His liver was palpable at the right hypochondrial region to one finger width, and was elastic soft with a regular surface and a somewhat dull edge. On blood examination, there was no anemia or liver dysfunction detected (GOT 23 U/*l*, GPT 30 U/*l*), although ZTT was 11.3 KU and TTT 5.9 KU. He was in Clinical Stage I; Alb, 4.4 g/d*l*; T. Bil, 0.3 mg/d*l*; PT%, 127.7%; $ICGR_{15}$, 8.3%; no ascites. Virus marker analysis was negative for HBsAg, HBeAg, anti-HBc, and anti-HCV, but anti-HBe was positive. AFP (below 10 *n*g/m*l*) and CEA (1.4 *n*g/m*l*) were negative but PIVKA-II

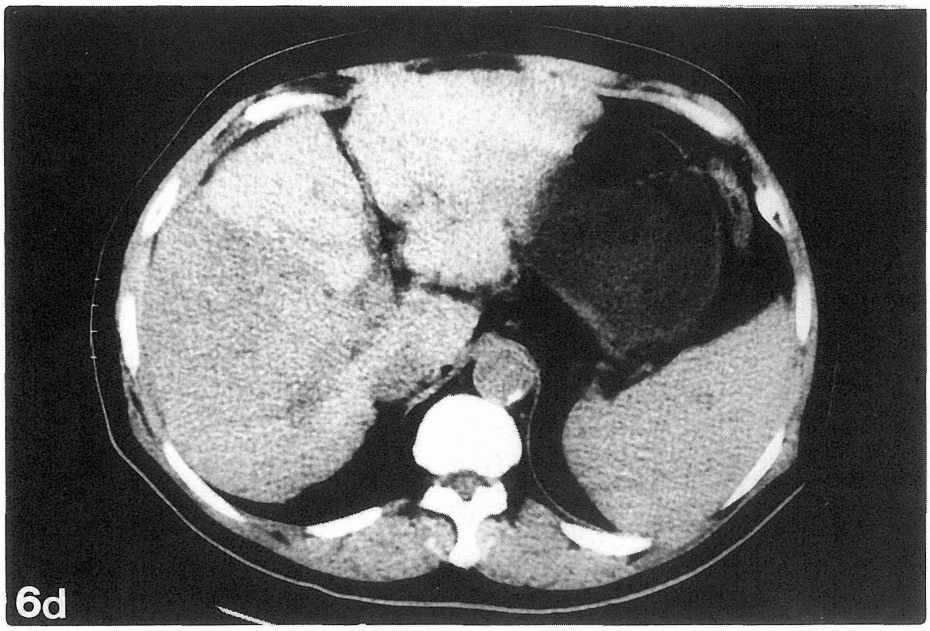


Fig. 6. Case 2: US (a), CT (b) and scintigraphy (c) revealed one extrahepatic tumor in the abdominal cavity and a massive tumor in the anterior liver segment (d).

(0.3 AU/m*l*) was positive.

US revealed an echogenic mass with a mosaic pattern, about 8 cm in diameter, in the right lobe. Adjacent to the main tumor hypoechoic lesion was found beneath the liver capsule (Fig. 8b). There was no splenomegaly or gallstone. On CT, similar findings were recognized; one protruding tumor in S5 was accompanied by a low density area. Tumor rupture beneath the liver capsule was suspected. SAG was performed on August 10. The tumor was fed by the right hepatic artery. Possible multiple small tumor stains in the right lobe and another possible tumor stain, 1.5 cm in diameter, in the left lobe were detected. In the right hepatic artery, a solution of 60 mg epirubicin, 6 m*l* lipiodol and Spongel® was infused for TAE, and after setting a metal coil at the right gastric artery to separate it from the left hepatic artery, a solution of 20 mg epirubicin and 2 m*l* lipidol was injected to the left hepatic artery. On lipiodol CT two weeks later, there were no lipiodol deposits in the right lobe except in the clearly detected tumor, but a faint lipiodol deposit was detected on the visceral surface of the lateral segment.

Therefore, the surgical plan included right lobectomy and a partial resection of the small lesion in the lateral segment, if confirmed at surgery. At surgery on September 4, the liver was dark red with small regenerative nodules but not hard, indicating fibrotic change due to chronic hepatitis. There was no peritoneal dissemination or lymph node swelling at the gastroduodenal ligament. On the visceral surface of the right lobe a soft mass, about 9 cm in diameter, was found. There was no tumor detected in the rest of the liver.

Macroscopically, the resected tumor was 10.5 × 9.7 × 6.3 cm with a thick capsule. Capsular invasion was positive; the single nodular tumor with infiltration to the surrounding tissue. Subcapsular (between the Glissonian capsule and the tumor capsule) accumulation of fluid was not recognized (Fig.

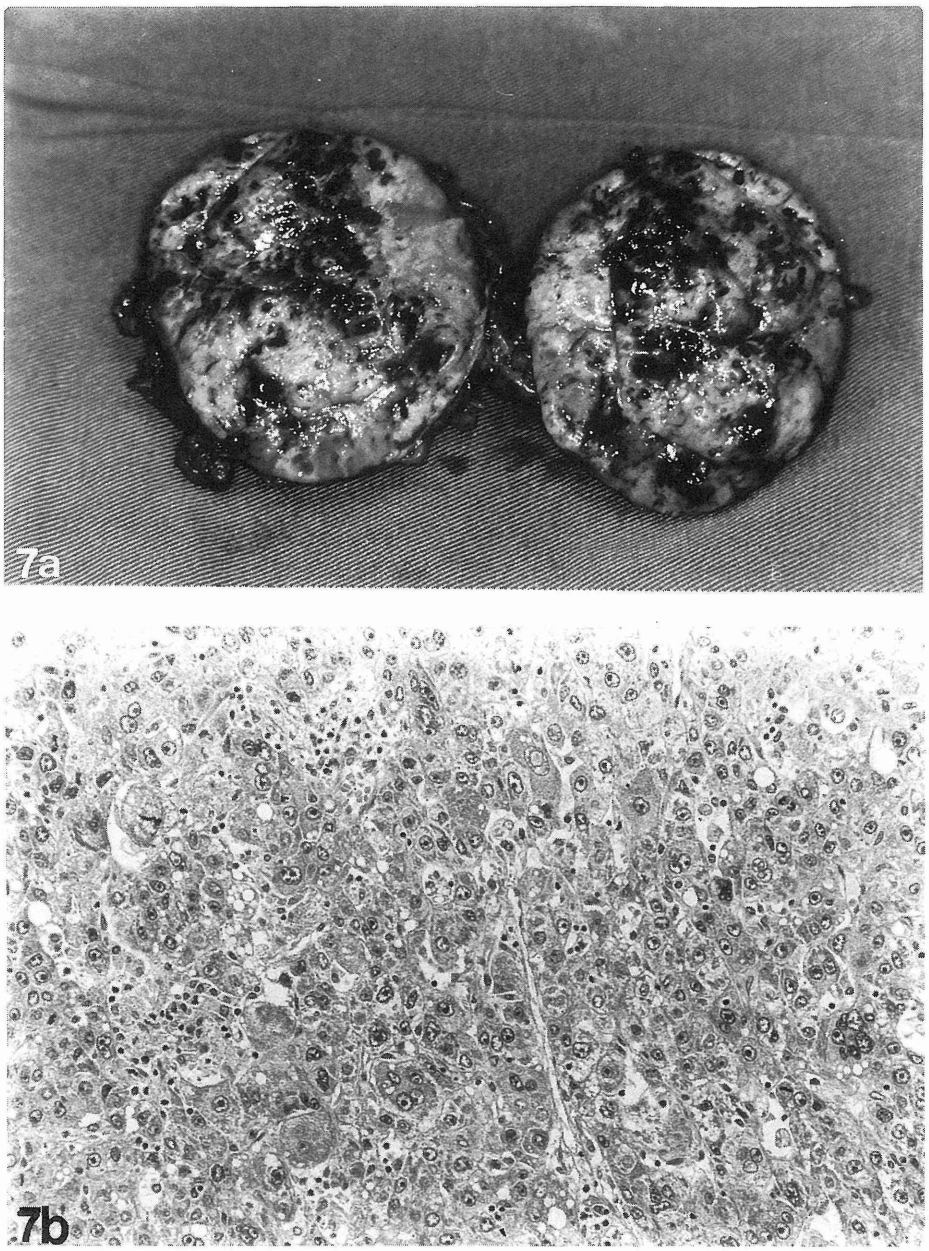


Fig. 7. Case 2: Macroscopic (a) and microscopic (b) findings of the metastatic tumor in the abdominal cavity. The tumor was poorly differentiated hepatocellular carcinoma including giant cells (HE, original magnification ×200).

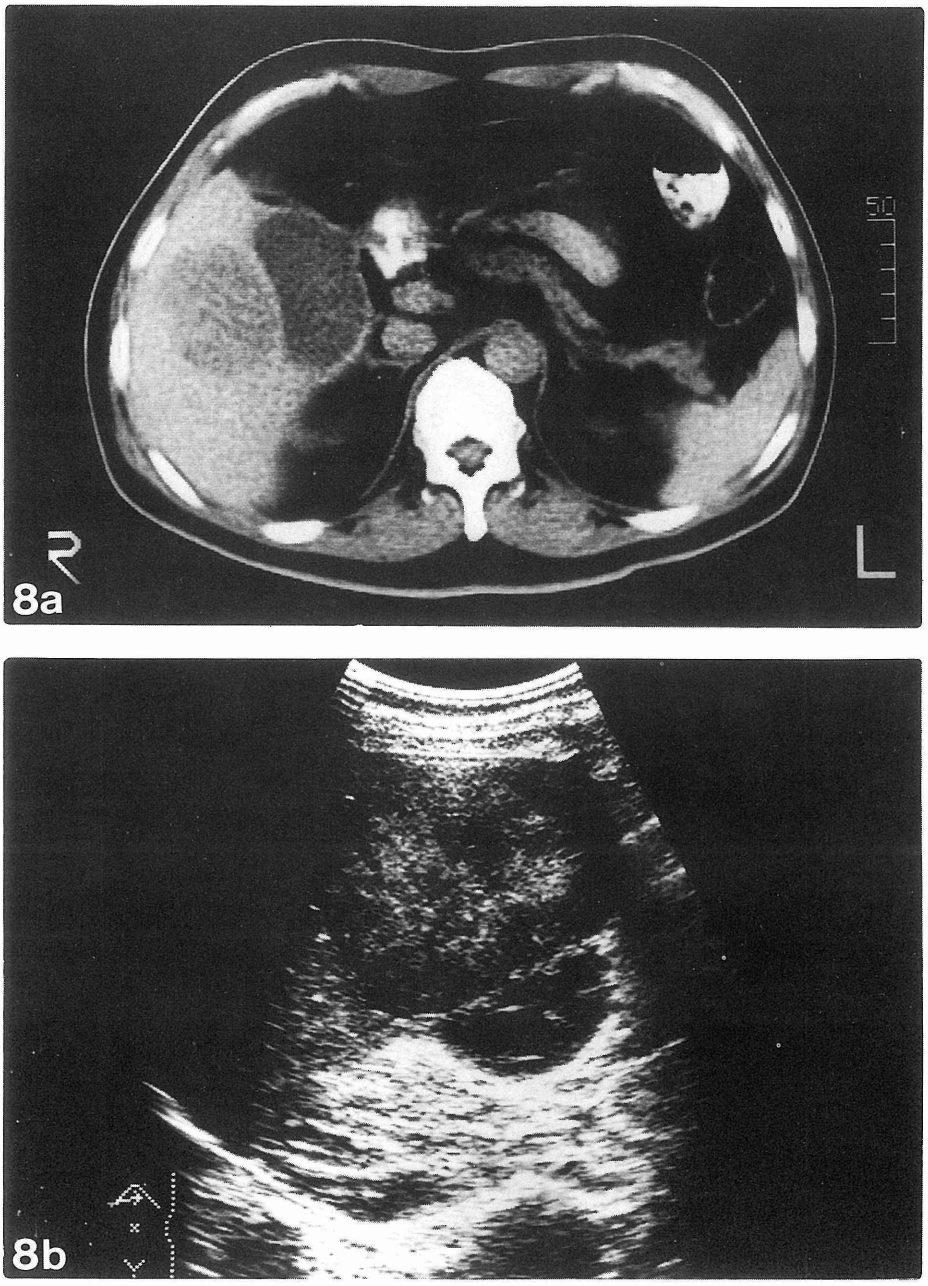


Fig. 8. Case 3: CT taken in Jakarta (a) indicated a protruding tumor in the liver. Subcapsular, beneath the Glissonian capsule, liquid accumulation was observed. US in Japan (b) showed an image similar to that on CT.

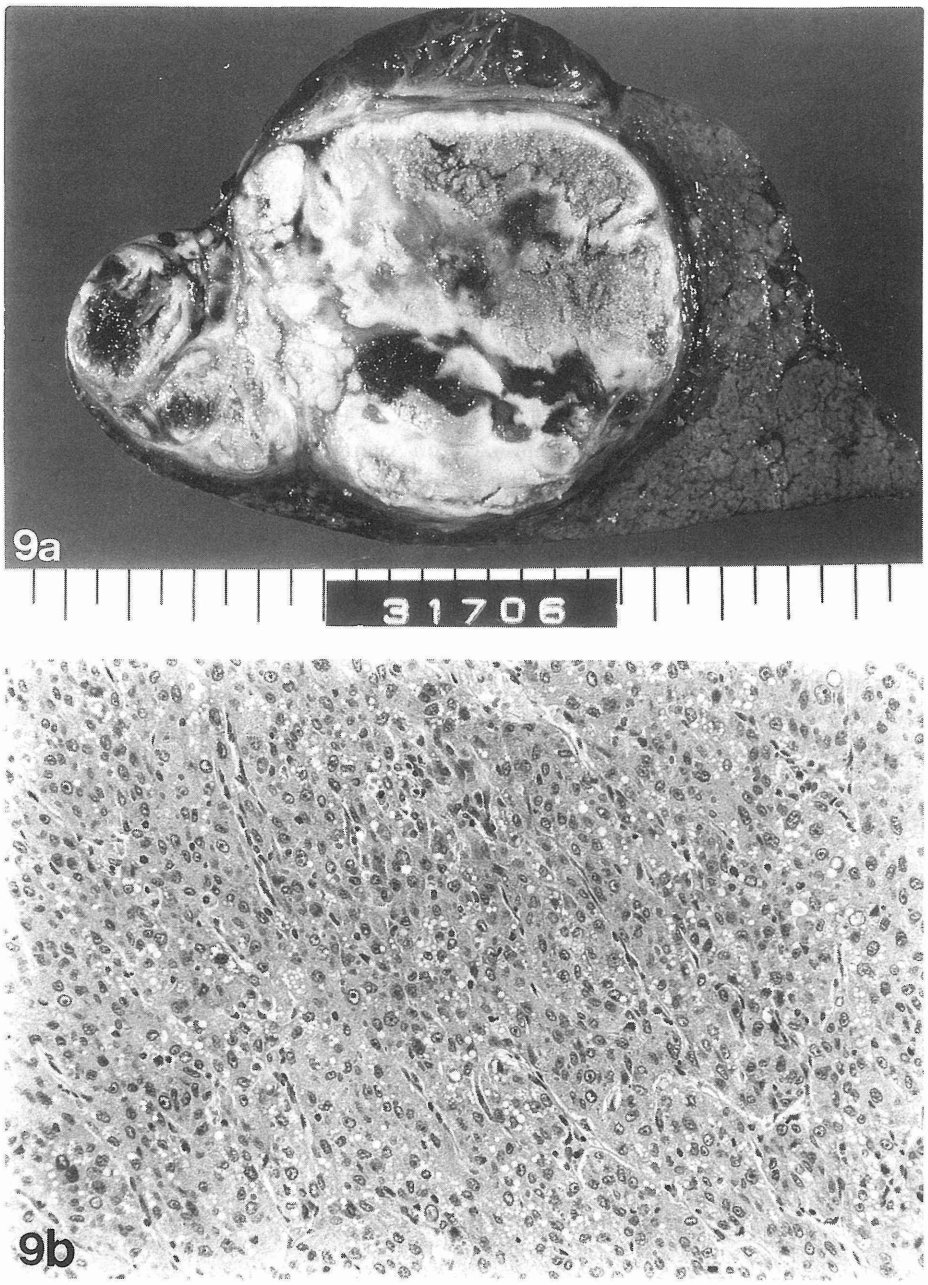


Fig. 9. Case 3: Macroscopic (a) and microscopic (b) findings of the primary tumor. The tumor was necrotized in most parts of the capsule, but an extracapsular viable portion demonstrated moderately differentiated hepatocellular carcinoma. There was no vascular infiltration (HE, original magnification ×200).

9a). Macroscopic TNM Stage was Stage II, since tumor rupture is not considered in this classification. Microscopically, the main tumor was almost necrotized but moderately differentiated HCC remained at the subcapsular region as well as at the extracapsular infiltration area (Fig. 9b).

On October 2, before discharge from the hospital, another TAI was performed using 30 mg ADR and 5 m*l* lipiodol to the remnant left lobe, although PIVKA-II had decreased after surgery to 0.06 on September 17.

Follow-up CT in June 1993 in Indonesia revealed an extrahepatic abdominal tumor, about 6 cm in diameter, but there was no recurrence in the liver. He was admitted to our Surgical Department on August 6, and extirpation of the tumor was performed on August 12 after an enlarged tumor, more than 10 cm in maximal diameter, was recognized in the right quadrant of the abdomen by CT (Fig. 10) and MRI. The tumor had a potato-like shape 13 cm in maximal diameter and was enlarged expansively, fed by an abundant blood supply from the greater omentum. The transverse colon was depressed down- and right-wards, but adhesion was not severe and there was no invasion. Frozen section of the connective tissue at points of adhesion showed microscopic inflammatory change. Macroscopically, the tumor was 13.5 × 11.0 × 10.5 cm, weighed 410 g and had a thin capsule (Fig. 11-a). The tumor was apparently HCC with no septal formation and central necrosis was partly recognized. Microscopic analysis revealed that this tumor was compatible with metastasis from the tumor resected previously (Fig. 11-b). The patient returned to Indonesia on August 22. AFP and PIVKA-II were within normal ranges before and after the second surgery.

Discussion

HCC spreads to extrahepatic organs through metastasis via the blood vessels or lymphatics, direct infiltration to the neighbouring organ, or dissemination after spontaneous rupture. In HCC, hematogenic metastasis is more common than lymphogenic

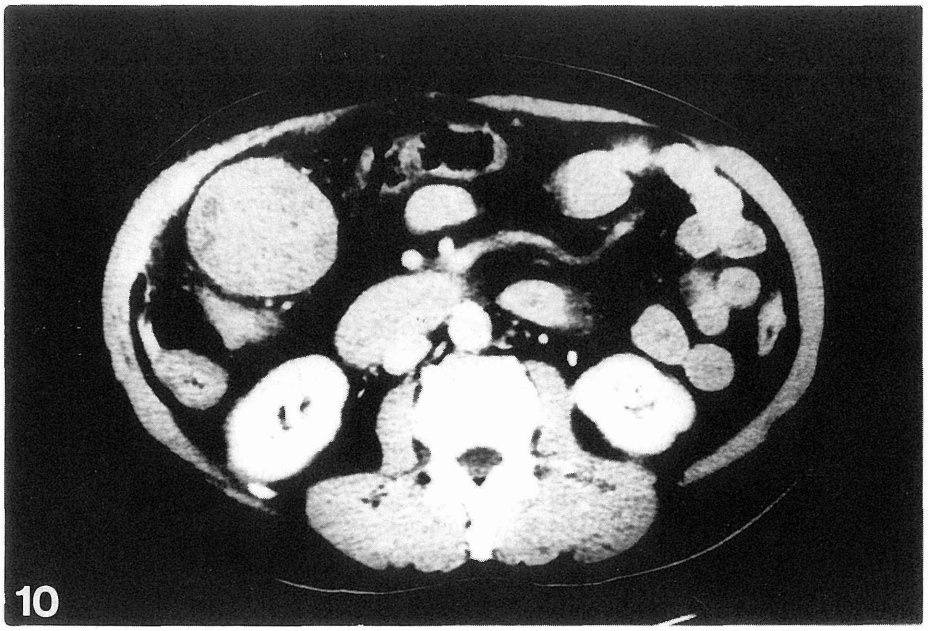
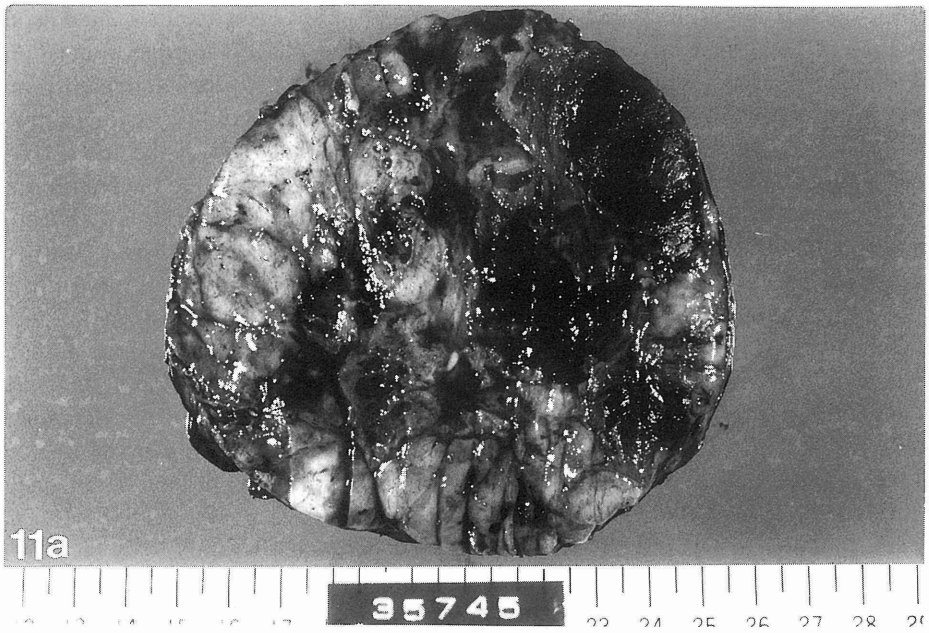


Fig. 10. Case 3: CT revealed a large intraperitoneal metastatic HCC.



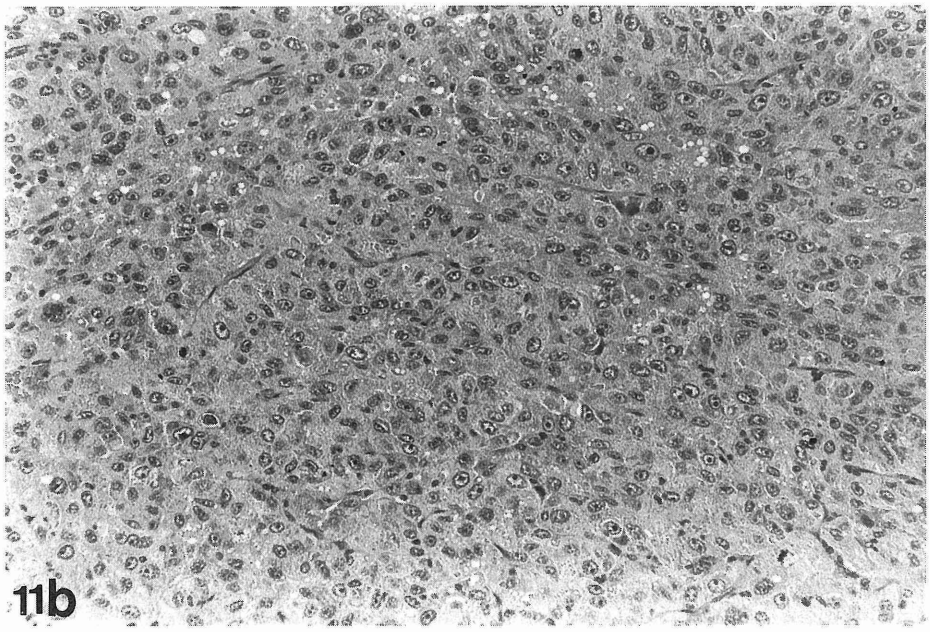


Fig. 11. Case 3: Macroscopic (a) and microscopic (b) findings of the metastatic tumor. Histologically, the metastatic tumor was similar to the primary tumor (HE, original magnification ×200).

metastasis. Vascular invasion, together with the size of the tumor, larger or smaller than 2 cm, and number of tumors, single or multiple, are factors in determining the macroscopic TNM Stage[2]. Clinically, lymph node metastasis is not common in the progession of HCC, although about 30 to 35% of autopsy cases showed lymph node metastasis[3]. Except for adjacent lymph node metastasis at the porta hepatis, lymph node metastasis is treated as a kind of distant organ metastasis (M factor) in the TNM classification system; lymph node metastasis in the hepatoduodenal ligament is registered as M1 (distant organ metastasis positive). The Liver Cancer Study Group of Japan (LCSG) reported that, among HCC patients who underwent laparotomy between 1988 and 1989, 2649 patients did not have lymph node metastasis while 76 patients had lymph node metastasis, and 349 patients were not reported[1]. In the metastatic cases, 52 metastasized lymph nodes were not adjacent and, therefore, considered M1.

Direct infiltration to the neighbouring organ is more frequently observed to the diaphragm, especially after TAE to a large HCC near the diaphragm. Usually HCC has an expansive growing form and direct invasion to the duodenum or colon is rare. In Case 2 operative findings indicated that the previous spontaneous rupture and adhesion to the diaphragm occurred before TAE.

Peritoneal dissemination does not occur frequently in HCC, compared with that in adenocarcinoma of other intraperitoneal organs, and therefore, peritoneal dissemination or spontaneous rupture of HCC, its possible cause, is not an important factor in determining the TNM classification. Actually, distant organ metastasis of HCC is not rare. On autopsy analysis, the LCSG also reported that 435 of 918 cases (47.4%) had metastasis to the lungs, 151 of 881 cases (17.1%) to the intraperitoneal organs, 144 of 885 cases (16.3%) to the peritoneum, 119 of 893 cases (13.3%) to the adrenal glands, 108 of 853 cases (12.7%) to the bone, 7 of 884 cases (0.8%) to the skin, and 149 of 790 cases (18.9%) to other organs[1]. However, in 1803 HCC patients with recurrence after liver resection, 1448 (80.3%) had intrahepatic metastasis, 134 (7.4%) to the lungs, 105 (5.8%) to the bone, 39 (0.9%) to the lymph nodes, 23 (1.1%) to the peritoneum, 19 (1.1%) to the brain, 16 (0.9%) to the adrenal glands, and 19 (1.1%) to other organs. Peritoneal metastasis comprised 6.5% of extrahepatic metastases. Thus, in our clinical experience distant organ metastasis of HCC is rare. In particular, peritoneal metastasis usually demonstrates a disseminated form, diffuse or sporadic, or coexists with other distant organ metastases. Therefore, it is very rare for HCC patients with peritoneal metastasis to be referred to surgeons for resection of such tumors.

However, intraperitoneal metastatic tumors in this report were all round and expansively growing nodular types, most of which were covered by the omentum, free from other organs, and all were resectable. In Case 1, tumor cells were apparently scattered in the incisional wound during the surgical procedure and developed as skin metastases. The abdominal tumors in all 3 cases may also have been scattered to the abdominal cavity during tumor rupture and developed, fed by new vasculature from the omentum. Although in Cases 2 and 3 no hemoperitoneum or severe pain was experienced, their surgical and macroscopic findings persuade us that tumor rupture occurred. In Case 1, these multiple tumors may not be an unusual metastatic form of advanced HCC case after tumor rupture, but in Cases 2 and 3, the large extrahepatic recurrent tumor was solitary and covered by the greater omentum, from which nourishing arteries developed. How tumor cells delivered to the peritoneum after tumor rupture developed to a solitary large recurrent tumor remains unclear. Growth may be explained as the result of a decrease in the immune response of the host, but that does not explain why the tumor was solitary. Moreover, in Case

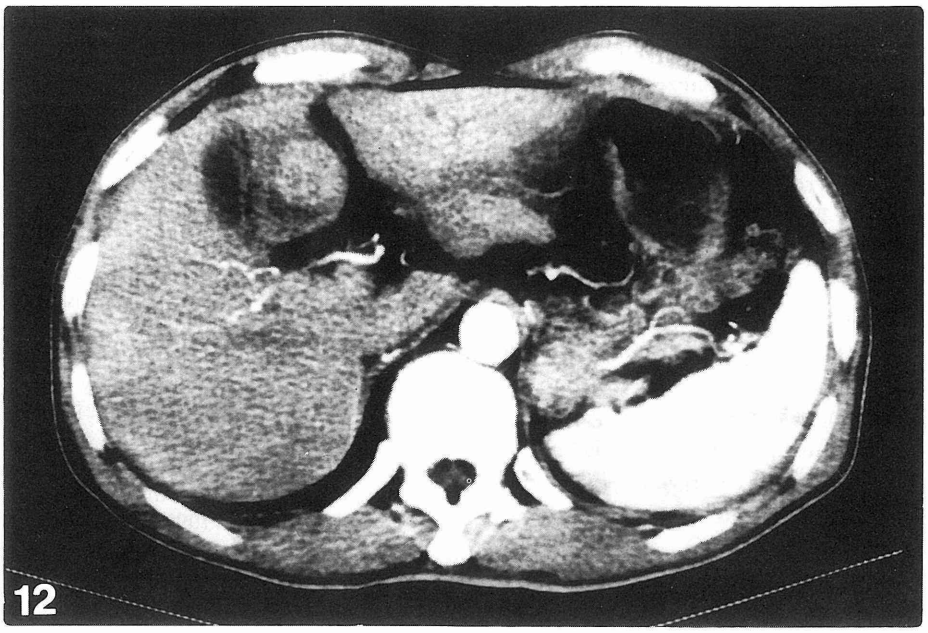


Fig. 12. CT of one Japanese case of spontaneous rupture of HCC. One nodular tumor accompanied by fluid accumulation in the medial segment, similar to that in Case 3, was detected. In this case, liquid accumulation also disappeared at surgery.

3, no intrahepatic metastasis was observed. In addition, this kind of recurrence, particularly that in Cases 2 and 3, has never been encountered among the more than 150 Japanese patients who underwent liver resection during the past ten years.

We have encountered one Japanese HCC patient with a history of tumor rupture (Fig. 12)[4] and thereafter his tumor was excised by left lobectomy. He had acute pain in the abdomen before rupture and hemoperitoneum soon after the symptom. However, he remains alive for 5 years without recurrence. We surgically treated 6 advanced HCC patients from Indonesia since 1988[5], including the present 3 cases. The remaining 3 cases underwent complete tumor resection by the excision of more than two segments. Two of the latter group were followed recurrence-free for 4 years, although minute lipiodol deposits, possible intrahepatic metastatic lesions, were recognized by follow-up lipiodol CT. Then distant organ metastasis was observed in the bilateral adrenal glands in one patient and in the rib in the other. It is unproductive and misleading to simply compare a small group of Indonesian cases to a large Japanese group, but it seems possible that the metastatic pattern of Indonesian HCC is different from that in Japan. Case 1 who was an HBV carrier and of Chinese origin seemed to have a background more similar to ours[6]. In personal communications with Indonesian surgeons, HCC is less common than colon cancer in Indonesia, and HCC is more common among Chinese Indonesian with HBV. The progress of HCC may be different in Indonesia. Further analysis is required before drawing a conclusion.

The clinical entity of non-fatal spontaneous rupture of HCC, such as that in the present cases has not been well elucidated in Japan or other countries[6–9], because the prognoses in most rupture cases are poor. In most cases, intraperitoneal hemorrhage is the first symptom and patients with accompanying liver cirrhosis easily fall into hemorrhagic shock and

die without sufficient resuscitation treatments or further surgical treatment, and very few cases are referred to specialized hospitals for surgery. Therefore, survival rates following resuscitation varied, and there are no clear reports on recurrence patterns after complete removal of the liver tumors. In the analysis of LCSG with respect to the cause of death in HCC patients, tumor rupture accounts for 9 to 11% of deaths. Similar or slightly highr rates were registered in other Asian[6),8–10)] and African[11)] countries, while a very low rate was reported among Caucasians[10,12)].

The present intraperitoneal nodular metastasis is not the same as peritoneal dissemination which often develops from adenocarcinoma in an abdominal organ. All tumors developed expansively in the abdominal cavity. The large tumor in Case 3 depressed the transverse colon but did not infiltrate to it. There was no microscopic metastasis detected in the surrounding tissue. Since extirpation of these tumors was not difficult and if Case 3 can survive longer, such intraperitoneal metastatic tumors should be resected. However at present, no data are available on the results of aggressive surgical maneuvers.

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