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## Hepatocellular Carcinoma with Hemobilia and Obstructive Jaundice

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**Abstract** A case with hemobilia and obstructive jaundice caused by hepatocellular carcinoma was presented. A 57 year-old woman who was suffered from liver cirrhosis was transferred to ambulatory clinic in our hospital, because of the sudden onset of severe abdominal pain. She had operation of acute cholecystitis diagnosed by surgeons. During the operation, the hemobilia was observed in the gall bladder and the common bile duct. At about 3.5 months after the operation, she died of remarkable anemia and jaundice. Autopsy revealed the hemobilia due to hepatocellular carcinoma invasion into the bile duct. A few report of hepatocellular carcinoma accompanied with hemobilia are reviewed, so it might be worthy to describe that severe abdominal pain caused by hemobilia in this case gave an occasion of diagnosis to hepatocellular carcinoma. Concerning the diagnosis of hemobilia, retrospective analysis suggested that the ultrasonography was an important study among the examinations performed.

*Key Words* : Hepatocellular carcinoma, Hemobilia, Obstructive jaundice

### Introduction

When the patient with hepatocellular carcinoma (HCC) showed severe anemia abruptly, gastrointestinal bleeding or rupture of the tumor should be considered at first. In addition to a cause of anemia in the patient with HCC, hemobilia produced by the invasion of HCC into bile duct has been noted. The patient was 57 year-old woman suffered from liver cirrhosis and cholelithiasis. She complained right hypochondralgia urgently and was transferred to the surgery in the diagnosis of acute cholelithiasis. Examinations aimed at HCC using radiopaque medium

could not be performed, because of her hypersensitivity for iodized materials. On the occasion of cholecystectomy, hemobilia was observed and after the operation HCC was suspected by the histological study of the coagulated material collected from gall bladder. At about 3.5 months after operation, she was died of remarkable anemia and obstructive jaundice. Bleeding into bile duct caused by invasion of HCC was confirmed by the autopsy examination. In this case, the ultrasonic examination for the liver and biliary tract was performed just one day before and after the biliary hemorrhage. Retrospective study on the diagnosis of hemobilia revealed

that the ultrasonography gave the most valuable information among the examinations performed.

### Case report

A 57 year-old woman had been received medication for her liver cirrhosis in an ambulatory clinic of Yamaguchi University Hospital. One of her brother was died of HCC. She had no personal history of blood transfusion and no habit of drinking alcohol. Although repeated examinations of ultrasonography and serum level of alpha-fetoprotein (AFP) were performed periodically, the diagnosis of HCC was not established in her clinical course. Only single gall stone was observed sonographically. One day before the admission, she visited our outpatient clinic with a 4 day history of slight epigastralgia. By the ultrasonic examination, one gall stone with no debris in the gall bladder was detected (Fig.1), but some focal lesions with very low echoic pattern located in the right lobe of the liver were not drawn any attention (Fig.2). On the early morning of the following day, the right upper abdominal pain was suddenly aggravated. She came over again and admitted to our hospital. Ultrasonography was taken immediately to examine the hepato-biliary tract and pancreas. Echographically the gall bladder was filled with high echoic materials (Fig.3) and the very low echoic lesions shown in the right love of the liver had changed to high echoic pattern as compared with the ultrasonography on one day before (Fig.4). But, she had no signs such as fever, nausea, vomiting and jaun-

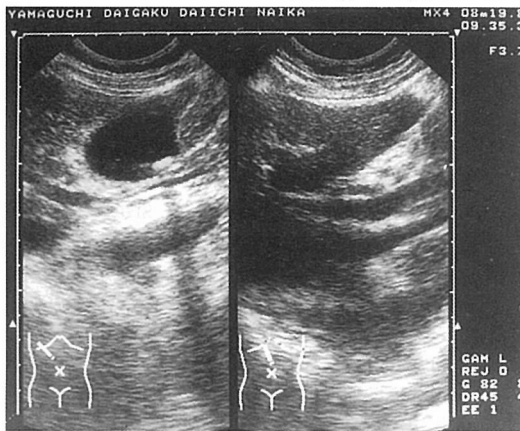


Fig.1 Ultrasonography on one day before admission. One gall stone was shown in the gall bladder.

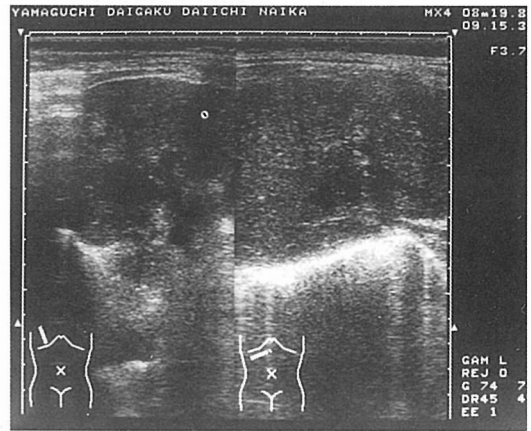


Fig.2 Ultrasonography on one day before admission. Some focal lesions with very low echoic pattern located in the right lobe of the liver.

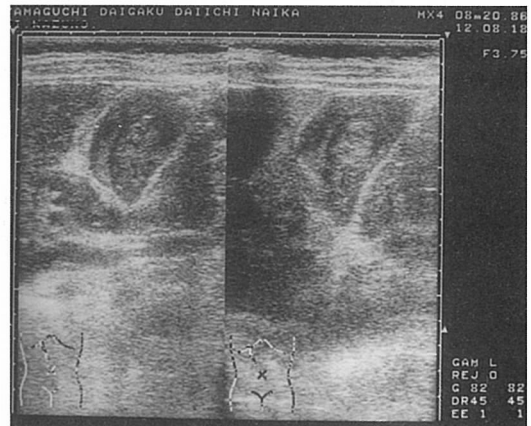


Fig.3 Ultrasonography on admission. The gall bladder was filled with high echoic materials.

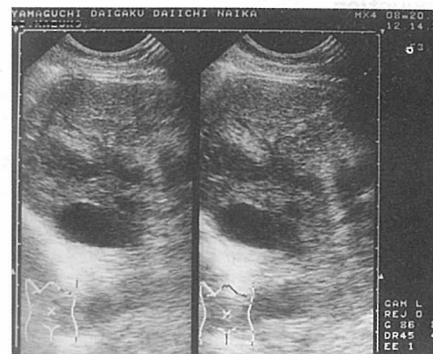


Fig.4 Ultrasonography on admission. Some focal high and low echoic lesions were shown in the right lobe of the liver.

dice. On the basis of findings of the echography of gall bladder and severe abdominal pain, she was diagnosed as an acute cholecystitis. Then, the surgical treatment was performed.

Laboratory data : Red blood cell count  $371 \times 10^4/\text{mm}^3$  ; hematocrit 34.5% ; hemoglobin 12.0 mg/dl ; white blood cell count  $2900/\text{mm}^3$  ; bilirubin (total/direct) 2.8/2.4 mg/dl ; albumin 2.7g/dl ; GOT 84 U/L ; GPT 33 U/L ; alkaline phosphatase 53 U/L ; prothrombin time 46.3% ; AFP 110.6 ng/ml ; HBs Ag(-), HBs Ab(-).

During the operation of biliary tract, large amounts of blood clot were observed in both gall bladder and common bile duct. The surface of the liver showed irregularity, but there was no finding of hepatic tumor on the surface of the liver. Cholecystectomy and T-tube insertion into common bile duct were performed. As the pathological examination revealed malignant cells in these blood clots (Fig.5), the cause of the hemobilia was presumed to be an invasion of hepatic cancer into the bile duct. After the operation, fresh blood oozed in the drained bile through T-tube. At the second week after the surgery, serum level of bilirubin (total/direct) began to increase to 4.7/3.3 mg/dl in accordance with the decrease of bile volume from T-tube. After that, she had a transient high fever with gram negative bacillus cultivated in the bile. Anemia and jaundice were both aggravated, and melena was continuously accompanied. Serum examination showed RBC  $169 \times 10^4/\text{mm}^3$  ; Ht 18% ; Hb 6.0 mg/dl and serum bilirubin (total/direct) 28.9/20.8 mg/dl during 10 weeks after the operation. HCC was doubtful by the evidence of serum level of AFP rising to 1877 ng/ml. Remarkable ascites appeared in her poor condition. On the fifteenth week,



Fig. 5 Microscopic findings of the blood clots collected from the operated gall bladder. Malignant cells were observed in it.

the patient expired with severe anemia and obstructive jaundice. The laboratory data was  $144 \times 10^4/\text{mm}^3$  of RBC, 16.5% of Ht, 5.7g/dl of Hb and 57.7/36.0mg/dl of bilirubin (total/direct).

Autopsy findings : Gross examination of the liver showed micronodular cirrhosis and massive liver tumor occupied half of the right lobe of the liver (Fig.6). Sagittal section of the tumor revealed the enlarged bile duct filled with blood clots (Fig.7). As the intrabiliary clots were adjacent to extrabiliary tumor masses, a direct communication was suspected. Microscopically, the tumor often showed necrosis and hepatocellular cancer with trabecular pattern was disclosed (Fig.8).

### Discussion

Among symptoms of the patient with HCC, hemobilia is rarely seen as a cause of gastro-

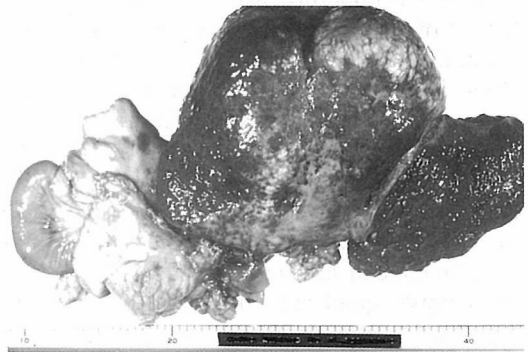


Fig. 6 Gross appearance of the autopsied liver. Massive tumor occupied half of the right lobe was shown.

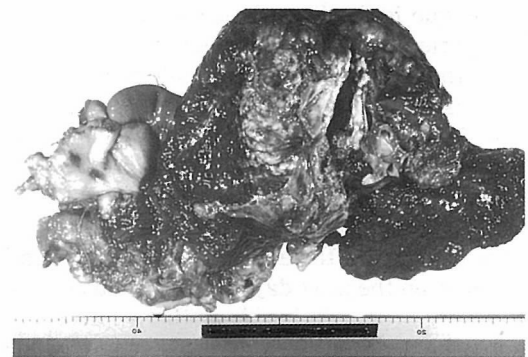


Fig. 7 Sagittal section of the tumor in the autopsied liver. Enlarged bile duct located in the tumor was shown.

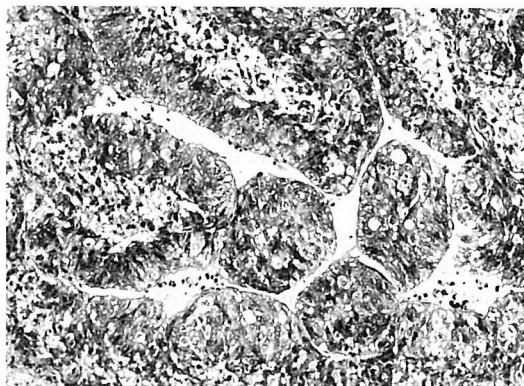


Fig. 8 Microscopic findings of the hepatic tumor. Hepatocellular carcinoma with trabecular pattern was shown.

intestinal bleeding. Liver trauma, either accidental or operative, is reported to be the most common cause of hemobilia.<sup>1)-3)</sup> Liver biopsy and needle puncture are also an iatrogenic factor of it.<sup>4)-6)</sup> On the other causes except trauma, HCC, metastatic liver cancer, gall stone and hepatic arterial aneurism are included.<sup>7)-10)</sup> In the hepatic tumors, HCC is known as commonly associated tumor with hemobilia. Clinical signs of the hemobilia complicated to HCC case were noted as follows, 1) jaundice—especially rising and falling one, 2) melena and/or hematoemesis and 3) right upper quadrant abdominal pain.<sup>11)</sup> The diagnosis could be based on angiography, endoscopic retrograde cholangio-pancreatography (ERCP), ultrasonography, computed tomography and Tc 99 m scan.<sup>2),12)-16)</sup> But, careful observation by ultrasonography has been more important, because this sensitive technique is the first choice examination for the patient with above symptoms.

In the present case, we should notice characteristic changes of ultrasonogram of the gall bladder and liver within only one day interval. The very low echoic lesions in the right lobe of the liver was not noticed to be HCC, because of unusual echogram for HCC. But, changes of the echoic pattern of the gall bladder on the next day may reflect a complication of hemobilia. And there presented focal high echoic lesions in the liver which was detected as the very low echoic lesions on one day before. These echogenic pattern has been also reported as the characteristic

ultrasonographic findings of the hemobilia.<sup>8),12),17)19)</sup> Yokoyama has shown that the echoic pattern of inner bloody materials of gall bladder is changeable day by day.<sup>17)</sup> The lesion which homogenous and high echoic at the beginning, changed to the mosaic pattern on one day after and finally to the more echogenic pattern with anechoic mirror image.

Direct cholangiography using both endoscopy and fine needle transhepatic puncture can reveal the tumor growth into the bile duct. Cholangiographic appearances are expressed as an intrabulky mass lesion. Endoscopically, the active bleeding from Vater's ampulla has been visualized in some cases.<sup>12)</sup> Hepatic angiography is also useful in the diagnosis of the hemobilia. That is, the leak of radiolucent material from artery to bile duct has been observed in the patient with HCC.<sup>18)</sup> Arterial embolization through the catheter is applied frequently to the hemobilia and sufficient therapeutic effect was detected.<sup>12)</sup> The hemobilia could be diagnosed by the computerized tomography demonstrating a gall bladder filled with bloody material by its density of the blood.<sup>13)</sup>

Cancer invasion into the blood vessels, particularly into the portal vein, is seen frequently in HCC, but its invasion into intra bile duct is rare. Kojiro has shown that the frequency of its intrabiliary invasion was about 9% among 259 Japanese patients with HCC.<sup>20)</sup> Histologically, they all were well to moderate differentiated HCC with trabecular pattern. Among his 24 patients with HCC accompanied with intra-biliary tumor growth, obstructive jaundice occurred in 11 patients (46%) and hemobilia developed in 5 patients (21%). In only one out of 5 patients, hemobilia was thought to be a direct cause of death. But, Yatagai reported that all 3 patients with HCC grew into the bile duct showed the hemobilia and the obstructive jaundice.<sup>11)</sup>

Although in the therapy of hemobilia due to HCC invasion the efficacy of transaortic embolization has been emphasized, it might be limited by the tumor size. Even in the patients who were transferred to surgery, their survival periods was within 4 months. In generally the prognosis of the patients with

HCC invaded into the bile duct is very poor.

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