

Transcatheter Hepatic Arterial Embolization Followed by Microwave Ablation for Hemobilia from Hepatocellular Carcinoma

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Abstract

Bile duct invasion is rare in patients with hepatocellular carcinoma (HCC). We show the usefulness of selective transcatheter hepatic arterial embolization (TAE) followed by microwave coagulation therapy (MCT) in a case of HCC with portal and biliary tumor thrombi that ruptured into the biliary system. A 70-year-old man with HCC was admitted because of melena and postprandial abdominal pain. Four years earlier, he had undergone posterior segmentectomy of the liver for HCC. Portal venous thrombus was detected on computed tomography (CT) 3 months earlier. On admission laboratory tests revealed the following values: serum alkaline phosphatase, 760 IU/L; total serum bilirubin, 11.9 mg/dL; direct bilirubin, 9.8 mg/dL; serum hemoglobin, 7.7 g/dL; alpha-fetoprotein 103.9 ng/mL; and PIVKA-2, 52,655 mAU/mL. Serum examinations were positive for anti-hepatitis C virus antibody but negative for hepatitis B surface antigens. Ultrasonography revealed a hypoechoic mass in the right branch of the bile duct at the hepatic hilum. Doppler ultrasonography showed blood flow in the mass. CT showed diffuse tumor involvement throughout the liver parenchyma and the presence of a high-density substance in the right intrahepatic bile duct. The diagnosis was hemobilia secondary to HCC in the right hepatic lobe. The symptoms recurred, and emergency TAE was performed 5 days after the onset of hemobilia. The symptoms subsided, and liver function improved. Endoscopic retrograde cholangiography revealed obstruction of the right intrahepatic bile duct. Surgery was performed 15 days after TAE, and MCT of the right hepatic hilum was performed. After MCT, CT revealed necrosis of the right hepatic hilum. Seven months after TAE, the patient died of liver failure with no recurrence of hemobilia.

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Key words: hepatocellular carcinoma, transcatheter hepatic arterial embolization, microwave ablation, hemobilia, rupture, biliary tumor thrombus

Introduction

Invasion of blood vessels, particularly the portal

vein, is a common feature of hepatocellular carcinoma (HCC), whereas bile duct invasion is rare¹. Biliary tumor thrombi are found in 2% to 9% of patients with HCC²⁻⁵. Lin et al. have clinically

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classified such cases as icteric-type HCC¹. HCC with invasion of the biliary tree is characterized by obstructive jaundice and hemobilia due to rupture of the tumor into the biliary system. Hemobilia secondary to ruptured HCC is considered a terminal event, rapidly leading to death². However, effective treatments for hemobilia have not been established. Hepatectomy is an effective treatment, but most patients are not candidates for surgery because they have advanced HCC with a high risk of bleeding^{2,3,6}. Transcatheter hepatic arterial embolization (TAE) is a useful treatment for intraperitoneal hemorrhage secondary to ruptured HCC⁷. We have previously reported that TAE followed by hepatectomy is an effective treatment for ruptured HCC^{8,9}. However, hemobilia occasionally recurs after TAE alone^{10,11}.

Microwave coagulation therapy (MCT) is a treatment for HCC that has several advantages shared by thermal ablation techniques, such as a flexible treatment approach, good tolerability, and the ability to consistently create reproducible and predictable areas of necrosis¹².

We show usefulness of selective TAE followed by MCT in a case of HCC with portal and biliary tumor thrombi that ruptured into the biliary system.

Case

A 70-year-old man with HCC was admitted because of melena and postprandial abdominal pain. Four years earlier, he had undergone posterior segmentectomy of the liver to treat a 14-cm-diameter HCC. During the past 2 years, TAE or percutaneous transhepatic MCT were performed several to treat recurrent HCC. Three months earlier, portal venous thrombus was detected with computed tomography (CT). Laboratory tests revealed the following values 1 month earlier and on admission, respectively: glutamic oxaloacetic transaminase, 90 and 585 IU/L (normal, <31 IU/L); serum glutamic pyruvic transaminase, 101 and 257 IU/L (normal, <33 IU/L); serum alkaline phosphatase, 349 and 760 IU/L (normal, 66 to 220 IU/L); serum gamma glutamic transpeptidase, 81 and 229 IU/L (normal, 8 to 39 IU/L); total serum bilirubin, 1.1 and 11.9 mg/dL (normal, <1.2 mg/dL);

direct bilirubin, 0.6 and 9.8 mg/dL (normal, <0.4 mg/dL); white blood cell count, 3,900 and 6,600 / μ L (normal, 4,000 to 8,000 / μ L); red blood cell count, 370×10^4 and 241×10^4 / μ L (normal, 410 to 550×10^4 / μ L); and serum hemoglobin, 12.0 and 7.7 g/dL (normal, 14 to 18 g/dL). Liver function deteriorated from Child class B to C. The initial serum concentration of alpha-fetoprotein was 103.9 ng/mL (<20 ng/mL), and that of PIVKA-2 was 52,655 mAU/mL (<40 mAU/mL). Serum examinations were positive for anti-hepatitis C virus antibody but negative for hepatitis B surface antigens.

Ultrasonography revealed a hypoechoic mass in the right branch of the bile duct at the hepatic hilum. Doppler ultrasonography showed blood flow in the mass, which was considered to be biliary tumor thrombi (**Fig. 1**). CT showed diffuse tumor involvement throughout the liver parenchyma and the presence of a high-density substance in the right intrahepatic bile duct which was considered to represent bleeding (**Fig. 2a**). Bone scintigraphy revealed a metastatic bone tumor of the 10th thoracic vertebra. The diagnosis was hemobilia secondary to HCC in the right hepatic lobe. The symptoms recurred, and emergency TAE was performed 5 days after the recurrence of hemobilia. Although hepatic arteriography revealed no extravasation of contrast medium, TAE was selectively performed in the tumor stain of the right hepatic artery without severe complications (**Fig. 3**). The symptoms subsided, and the liver profile improved. The red blood cell count, serum hemoglobin concentration, and total serum bilirubin level returned to their normal ranges.

After TAE, endoscopic retrograde cholangiography (ERC) revealed obstruction of the right intrahepatic bile duct by what was thought to be thrombus or debris (**Fig. 4**). Right hepatectomy was attempted 15 days after TAE, but could not be performed because of severe invasion of the diaphragm by HCC; therefore, MCT of the right hepatic hilum was performed via laparotomy. The postoperative course was uneventful. CT revealed necrosis of the right hepatic hilum (**Fig. 2b**). The patient was discharged on postoperative day 11. Seven months after TAE, the patient died of liver

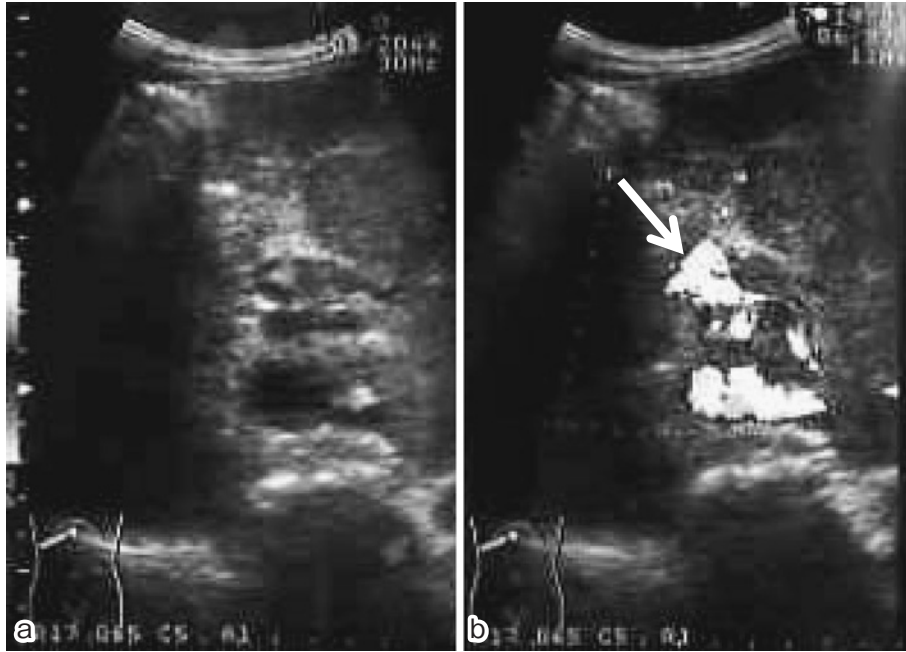


Fig. 1 Ultrasonography revealed a hypoechoic mass in the right branch of the bile duct at the hepatic hilum (a). Doppler ultrasonography showed blood flow in the mass, believed to be biliary tumor thrombi (**arrow**) (b).

failure with no recurrence of hemobilia.

Discussion

We have shown that Doppler ultrasonography, CT, and ERC are useful for both diagnosis and the localization of bleeding sites, although hepatic arteriography failed to demonstrate extravasation of contrast medium. Doppler ultrasonography revealed a hypoechoic mass with flow in the bile duct which was believed to be biliary tumor thrombi, at the hepatic hilum. CT studies demonstrated the presence of a high-density substance in the biliary system believed to represent bleeding¹³. ERC showed intraductal filling defects at bleeding sites which was believed to be thrombus or debris¹⁴.

Invasion of the portal vein by HCC is not rare; however, growth of HCC into the biliary tract is much less common. Icteric-type HCC is HCC with progressive obstructive jaundice due to bile duct invasion or hemobilia secondary to HCC. The outcomes of patients with icteric-type HCC are poorer than those of patients without biliary invasion². Several studies have focused on hemobilia secondary to HCC^{1-3,6}. Kojiro et al. have reported

hemobilia in 5 of 24 cases (21%) of icteric-type HCC on autopsy and examination of resected specimens; hemobilia was considered the immediate cause of death in 1 patient (4.2%)². Symptoms of hemobilia include acute abdominal pain, jaundice, and melena, as seen in our patient. Early diagnosis of hemobilia remains challenging. The rarity of this condition and the consequent failure to recognize its presence delayed the diagnosis. Because liver function deteriorates after the onset of hemobilia, early and accurate diagnosis is essential.

Although hepatectomy seems to be the treatment of choice, most patients are not candidates for surgery because they have far advanced HCC, as did our patient. Hepatic arterial ligation could not control the hemobilia, and the patient died 28 hours after the procedure⁶. TAE is one treatment for HCC. However, poor liver function, especially, the presence of hyperbilirubinemia, and a high frequency of portal vein invasion discourage the use of TAE. Kitagawa et al.¹⁰ have reported that selective TAE is effective for the treatment of advanced HCC that has ruptured into the biliary system and caused hemobilia. They attributed their good results to the following reasons: 1) the

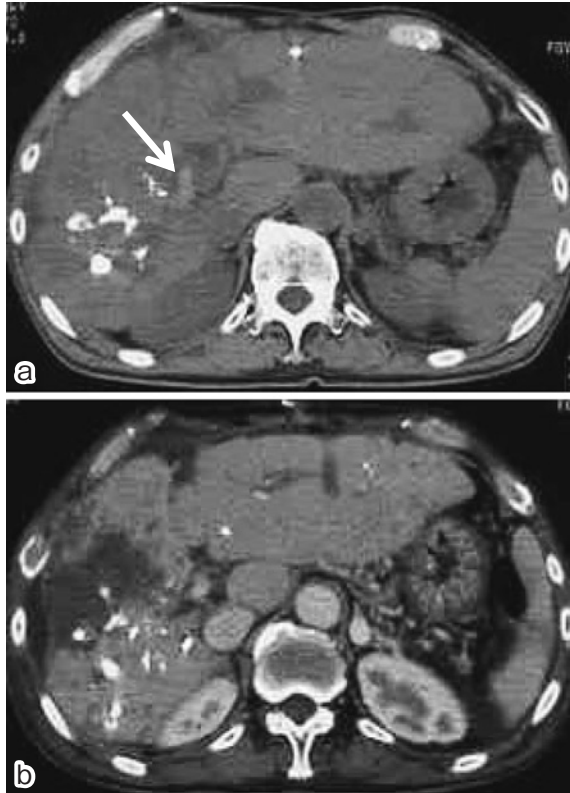


Fig. 2 Plain CT showed diffuse tumor involvement throughout the liver parenchyma and the presence of a high-density substance (**arrow**) in the right intrahepatic bile duct which was believed to represent bleeding (a). After treatment, enhanced CT revealed necrosis of the right hepatic hilum (b).

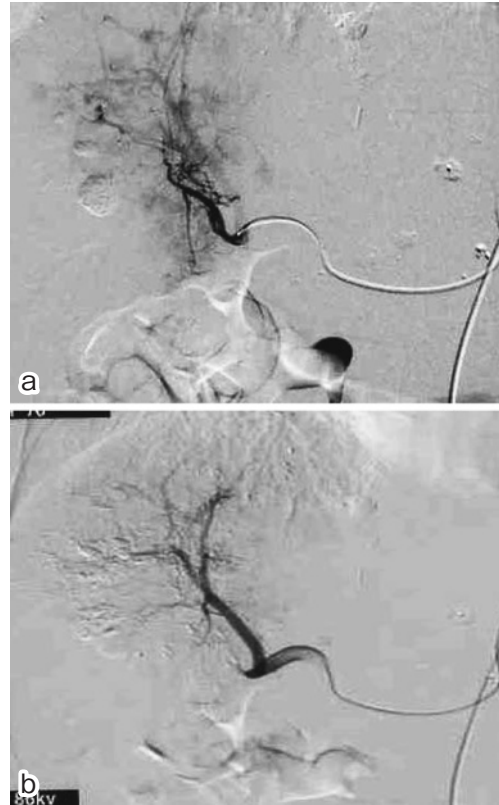


Fig. 3 Hepatic arteriography showed no extravasation of contrast medium (a: pre TAE). TAE was selectively performed in the tumor stain of the right hepatic artery with no severe complications (b: post TAE).

diagnosis of hemobilia was established soon after onset, 2) localization of the bleeding sites allowed selective TAE to be performed, and 3) the contralateral lobe was enlarged because of thrombus of the portal vein, and liver function was preserved. Kojiro et al. have reported that the frequency of associated portal vein invasion is as high as 88%.² We attributed the good outcome in our patient to the same reasons as those reported by Kitagawa et al.¹⁰

Kitagawa et al.¹⁰ reported that hemobilia recurred in 2 of 3 patients. The recurrent bleeding arose from the embolized tumor in 1 patient and from another tumor apart from the embolized liver segment in the other patient. Although selective chemoembolization with chemotherapeutic agents has a strong anticancer effect, it is sometimes difficult to achieve complete necrosis with large multiple tumors. Even

when the embolized tumor is well controlled, other tumors that are not embolized can cause hemobilia. Kitagawa et al. have reported that repeated selective TAE is useful for controlling recurrent hemobilia and contributes to prolonging survival in patients without rapid tumor progression.

Our patient underwent TAE followed by MCT, a treatment for HCC. Kim et al.¹⁵ have described a patient in whom hemobilia caused by HCC was successfully treated with percutaneous radiofrequency tumor ablation after several failed attempts at TAE. Ablation with MCT or radiofrequency current produces heat, causing coagulation and tissue necrosis. MCT shares several advantages with thermal ablation techniques, including a flexible treatment approach, good tolerability, and the ability to consistently create reproducible and predictable necrotic areas. The therapeutic efficacy of MCT can be augmented by other therapies. As with other thermal ablation



Fig. 4 ERC revealed obstruction of the right intrahepatic bile duct which was considered to be thrombus or debris.

techniques, coagulation diameters with MCT are influenced by perfusion-mediated cooling. Interruption of hepatic blood flow can significantly increase coagulation diameters^{16,17}. TAE effectively reduces the blood flow to HCC by blocking tumor arteries. Therefore, it was suggested that TAE followed by MCT successfully prevented the recurrence of hemobilia in our patient.

In conclusion, TAE followed by MCT is a useful treatment for HCC with portal and biliary tumor thrombi that rupture into the biliary system.

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