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Radiofrequency Ablation of the Main Lesion of Hepatocellular Carcinoma and Bile Duct Tumor Thrombus as a Radical Therapeutic Alternative

Two Case Reports

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Abstract: Hepatocellular carcinoma (HCC) with bile duct tumor thrombus (BDTT) formation is a rare entity found microscopically in 1% to 9.2% of resected specimens. The ideal treatment for HCC is surgical resection. However, because of poor hepatic functional reserve in patients with HCC, most tumors are unresectable. Here, we report 2 cases of HCC with BDTT type III accompanied by hepatic dysfunction that were successfully treated with radiofrequency (RF) ablation. We used RF ablation as both a radical therapeutic method and an efficient way to control bleeding from the origin of BDTT after BDTT removal. At the time of writing, the 2 patients have been disease-free for 16 and 12 months, respectively.

Our results show that RF ablation may be used as a radical therapeutic alternative for HCC with BDTT in patients with liver cirrhosis and obstructive jaundice.

(*Medicine* 94(27):e1122)

Abbreviations: BDTT = bile duct tumor thrombus, CA = carbohydrate antigen, CBD = common bile duct, CT = computed tomography, ERCP = endoscopic retrograde cholangiopancreatography, GGT = γ-glutamyl transpeptidase, HCC = hepatocellular carcinoma, INR = international normalized ratio, RF = radiofrequency, TACE = transarterial chemoembolization.

INTRODUCTION

Hepatocellular carcinoma (HCC) is the third most common global cause of cancer-related death.[1] Based on the previous reports, 1% to 9.2% of HCC cases have a coincident

bile duct tumor thrombus (BDTT).[2–8] Once a BDTT is formed, it can extend distally to obstruct the extrahepatic duct. Subsequently, the patient's condition can deteriorate quickly, and the prognosis is usually poor unless the disease is treated promptly.[2–8]

Radical resection or hepatectomy is the most effective treatment for HCC with BDTT.[2,3,8] However, obstructive jaundice, cholangitis, and hepatic dysfunction are obstacles for surgical treatment. Many nonsurgical treatments, including transarterial chemoembolization (TACE), endoscopic retrograde cholangiopancreatography (ERCP), intrabiliary duct stenting, radiation, and ethanol injection, can be used for patients who cannot tolerate surgery because of poor hepatic function. However, the effectiveness of these nonsurgical therapies is often unsatisfactory.[3]

Radiofrequency (RF) ablation is a widely used, safe, and effective treatment modality for HCC.[9–12] The minimally invasive nature of the treatment has led to it becoming the first-line treatment for small HCC in patients with compromised hepatic function or associated medical comorbidity.[12] As RF ablation has a prominent thermal coagulation effect, we successfully applied it in 2 cases of HCC with BDTT as both a radical therapeutic method and an efficient way to control bleeding from the origin of BDTT after BDTT removal. The 2 patients gave written informed consent before treatment, which was approved by the investigation and ethics committee of Chao-yang Hospital, Capital Medical University, according to the standards of the Declaration of Helsinki. To the best of our knowledge, no such report exists in the English language literature.

CASE 1

A 61-year-old man was admitted to our department for treatment of a 3.0-cm HCC lesion in segment VI of the liver with BDTT. The patient had severe liver cirrhosis caused by a hepatitis B viral infection. HCC involving BDTT was diagnosed with abdominal computed tomography (CT) (Figure 1A and B). Magnetic resonance cholangiopancreatography confirmed that the BDTT extended to the common bile duct (CBD) (Figure 1C). Laboratory test values were as follows: serum bilirubin, 296.8 μmol/L; alkaline phosphatase, 218.7 IU/L; γ-glutamyl transpeptidase (GGT), 527.3 IU/L; international normalized ratio (INR), 1.0; albumin, 28.0 g/L; α-fetoprotein, 9.6 ng/mL; and carbohydrate antigen (CA) 199, 88.2 IU/mL.

Although radical resection or hepatectomy with removal of BDTT might have helped to achieve effective treatment, severe damage to liver function and increased risk of postoperative hepatic insufficiency, or even hepatic failure, might have
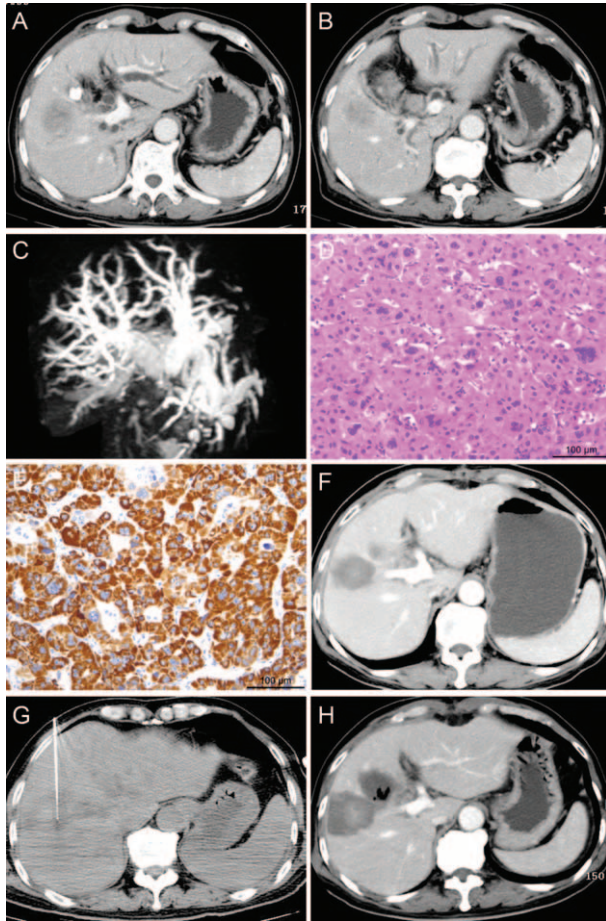
FIGURE 1. (A) A 61-year-old man with a 3.0-cm hepatocellular carcinoma (HCC) in segment VI of the liver on contrast-enhanced computed tomography (CT) scan. (B) CT showed a bile duct tumor thrombus (BDTT) with a clear margin in the bile duct accompanied by peripheral bile duct dilation. (C) Magnetic resonance c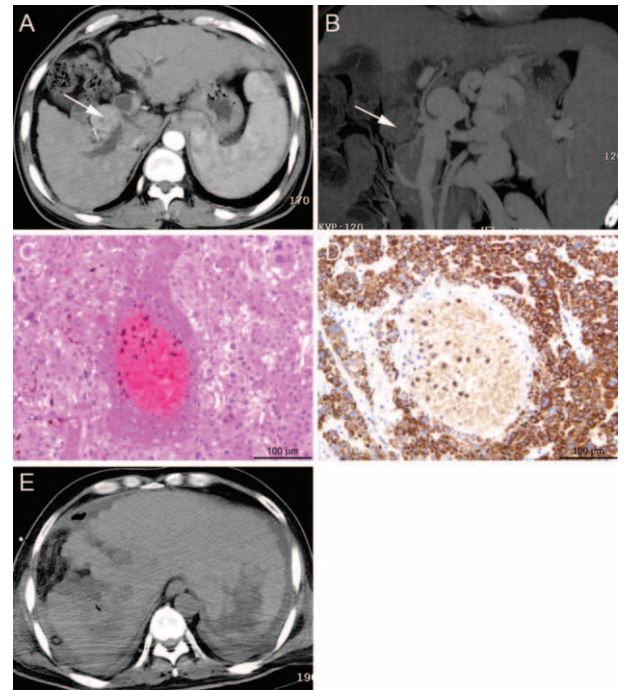holangiopancreatography indicated a bile duct lesion in the hepatic hilus. (D) The histological findings of the HCC cells in the BDTT (hematoxylin and eosin staining, original magnification 200×, scale bar 100 μm). (E) Positive staining of HepPar-1 was confirmed in the BDTT (original magnification 200×, scale bar 100 μm). (F) Abdominal CT 1 month postoperatively shows an ablative margin of <0.5 cm. (G) The patient received a second radiofrequency (RF) ablation session under CT guidance. (H) The ablative margin increased to ≥1.0 cm after the second RF ablation.

occurred. Instead, the patient selected a local therapeutic strategy, BDTT removal, together with RF ablation of the HCC lesion. During the operation, by choledochoscopy we found that the BDTT extended to the CBD via the right bile duct. The BDTT was dark green in color, and soft or slightly elastic, relatively friable, and extremely vascular, tending to bleed even with light touch. After removal of the BDTT, the bleeding from the origin of the BDTT was active, and we ablated the origin of the BDTT to achieve definitive hemostasis. The RF process was monitored by choledochoscopy. The RF ablation procedure was performed under direct visualization using a Cool-tip ACT 1520 electrode and an RF generator (Covidien Healthcare, Dublin, Ireland). A power of 30 W was delivered for approximately 3 minutes to avoid iatrogenic bile

duct injuries. The origin of the BDTT became a depressed lesion with a hard texture after the RF ablation session. Subsequently, the patient underwent RF ablation by ultrasound guidance for the HCC lesion in hepatic segment VI, followed by Roux-en-Y biliary-enteric anastomosis, because of a concern about relapse of BDTT and obstructive jaundice. The BDTT was confirmed by histopathological examination (Figure 1D and E). The patient was discharged on day 20 after surgery. Laboratory test results were as follows: serum bilirubin, 33.5 μmol/L; alkaline phosphatase, 67.5 IU/L; GGT, 57.4 IU/L; INR, 1.02; albumin, 33.0 g/L; and CA 199, 32.1 IU/mL.

Evaluation 1 month postoperatively was performed by contrast-enhanced CT. The HCC lesion was ablated completely; however, the ablative margin was <0.5 cm (Figure 1F). Therefore, CT-guided percutaneous consolidation RF ablation was performed to achieve an ablative margin of ≥1.0 cm (Figure 1G). The RF procedure was performed using a Cool-tip ACT 1530 electrode. At the follow-up visit 1 month after the second RF ablation session, the ablation area was evidently enlarged with an ablative margin of ≥1.0 cm (Figure 1H). The follow-up protocol mainly included routine physical examination and laboratory tests, as well as enhanced CT studies every 2 or 3 months. The patient remains in good condition without recurrence 16 months after the first RF ablation session.

FIGURE 2. (A) A 47-year-old man with an irregular bile duct tumor thrombus (BDTT) (arrow) in the right posterior hepatic duct, common hepatic duct, and common bile duct as confirmed by enhanced-control computed tomography (CT). (B) The BDTT (arrow) in a coronal oblique plane reformation CT image at portal phase and portal hypertension with esophageal varices. (C) The histological findings of the hepatocellular carcinoma (HCC) cells in the BDTT (hematoxylin and eosin staining, original magnification 200×, scale bar 100 μm). (D) Positive staining of HepPar-1 was confirmed in the BDTT (original magnification 200×, scale bar 100 μm). (E) Abdominal CT showed that the right posterior portion of the liver was ablated, the BDTT was removed, and the spleen was resected.

CASE 2

A 47-year-old man was admitted for obstructive jaundice and concomitant bleeding from esophageal varices. The patient had portal hypertension and severe liver cirrhosis caused by a hepatitis B viral infection and failed endoscopic treatment because the esophageal variceal bleeding relapsed after a course of sclerotherapy. Laboratory test results showed the following: serum bilirubin, 57.7 μmol/L; alkaline phosphatase, 95.8 IU/L; GGT, 54.4 IU/L; INR, 1.5; albumin, 28.0 g/L; hemoglobin, 51 g/L; platelets, 58×10^9/L; α-fetoprotein, 7.6 ng/mL; and CA 125, 141.9 IU/mL. Contrast-enhanced CT showed portal hypertension with esophageal varices, dilated bilateral intrahepatic ducts with an intraductal nodule obstructing the hilar bile duct and CBD, but no tumor thrombus in the portal vein or systemic vein and no obvious mass in the hepatic parenchyma (Figure 2A and B).

BDTT, evident hepatic cholestasis, and typical liver cirrhosis were found during surgery. No obvious primary lesion was detected by intraoperative ultrasonic exploration. We first made an incision anterior to the CBD and removed the BDTT. After removal of the BDTT, bleeding from the origin of the right BDTT was active and could not be controlled with gauze tamponade for >10 min. A right hepatectomy was not indicated because of poor liver function reserve; therefore, we elected for RF ablation for hemostasis of the origin of BDTT using a Cool-tip ACT 1520 electrode. The RF process was monitored by choledochoscope. Subsequently, the patient received RF ablation for the right posterior hepatic lobe, splenectomy, and pericardial devascularization. The pathological reports of BDTT revealed moderately differentiated HCC (Figure 2C and D). The patient had a good postoperative course and was discharged on day 16 after surgery. Laboratory test results were as follows: serum bilirubin, 23.7 μmol/L; alkaline phosphatase, 55.7 IU/L; GGT, 24.4 IU/L; INR, 1.1; albumin, 31.0 g/L; hemoglobin, 78 g/L; platelets, 301×10^9/L; and CA 125, 35.7 IU/mL. Evaluation 1 month postoperatively was performed by contrast-enhanced CT. Abdominal CT showed that the right posterior portion of the liver was ablated, the BDTT was removed, and the spleen was resected (Figure 2E). Because there was no detectable intrahepatic tumor in this case, it was unnecessary to evaluate the ablative margin in the hepatic parenchyma. The follow-up protocol mainly included routine physical examination and laboratory tests every month, as well as enhanced CT studies every 2 or 3 months. No signs of recurrence of BDTT and intrahepatic metastasis have been observed for 12 months since RF ablation.

DISCUSSION

HCC has a high frequency of portal vein invasion, hepatic vein invasion, or both; however, bile duct invasion has been reported in only 1% to 9.2% of patients with primary HCC.[2–8] The size of primary HCC is not correlated with the occurrence of BDTT, and BDTT may exist in patients with primary HCC (≤3.0 cm) as well as in those without detectable primary HCC.[13–15]

The ideal treatment for HCC with BDTT is surgical resection. If the origin of the BDTT cannot be determined and no obvious tumor can be detected in the liver, the BDTT should be removed first. Then, examination of the nature of the bleeding from the bile duct may indicate the origin of the tumor thrombus, allowing removal of the corresponding hepatic lobe and bile duct.[2] Several studies have reported that HCC with macroscopic BDTT has a 5-year survival rate of 24% to 36.3% after surgical resection.[2–8] However, the low rate of surgical resection, which may be caused by fundamental liver diseases

and obstructive jaundice, appears to be responsible for the low rate of survival. Xiangji et al[2] retrospectively compared different therapy modalities in 184 patients with HCC complicated by BDTT. Of these 184 patients, only 48 (26.1%) received radical hepatic resection and BDTT removal (Group A). The remaining patients received palliative hepatectomy and BDTT removal (Group B, 13 cases), palliative hepatectomy and BDTT removal, along with unilateral hepatic artery ligation or postoperative TACE (Group C, 34 cases), TACE (Group D, 27 cases), drainage to relieve the jaundice by ERCP or percutaneous transhepatic cholangial drainage (Group E, 50 cases), and conservative treatment (Group F, 12 cases). The median survival times in Groups A, B, C, D, E, and F were 37, 6, 16, 11, 3, and 3 months, respectively. The 5-year survival rate in the Group A and Group C were 24.1% and 5.0%, respectively, and 0% in all the remaining treatment groups.

RF ablation is accepted as a potentially curative treatment for HCC at an early stage. RF ablation is less expensive and less invasive, and it is associated with lower complication rates and a shorter hospital stay than surgical resection.[9–12] The prevalence of major complications was evaluated to be <10% and procedure-related mortality is <1% in experienced hands. The complications of RF ablation mainly include pneumothorax, hemopneumothorax, visceral organ perforation, liver abscess, bile duct injury, intraperitoneal hemorrhage, and tumor seeding.[10] As RF ablation has a prominent thermal coagulation effect, we successfully applied RF ablation in the 2 cases of HCC with BDTT as both a radical therapeutic method and an efficient way to control bleeding from the origin of BDTT after BDTT removal. At the time of writing, patients 1 and 2 have been disease free for 16 and 12 months, respectively. The survival times in these 2 cases are much better than those for palliative hepatectomy and nonsurgical treatments groups reported previously.[2]

To the best of our knowledge, this report is the first to show the therapeutic efficacy of RF ablation of both the HCC main tumor and the BDTT as a radical treatment. Our results show that RF ablation is an effective, minimally invasive, and safe treatment method for the main lesion of HCC in patients with liver cirrhosis and obstructive jaundice. Moreover, RF ablation appears to be an effective radical therapy for macroscopic BDTT. The 2 BDTTs considered in this report were classified as type III (originating in the right hepatic duct and involving the hepatic confluence) according to the Ueda classification.[16] As the origin of the BDTT type III was large and had a rich arterial blood supply, control of the active hemorrhage from the origin of BDTT was difficult after BDTT removal through choledochotomy. Fortunately, with RF ablation under direct visualization, we efficiently controlled hemorrhaging from the origin of the BDTT, destroyed the origin of the BDTT to reduce the risk of recurrence, and avoided iatrogenic bile duct injuries.

In conclusion, RF ablation may be used as a radical therapeutic alternative for HCC with BDTT in patients with liver cirrhosis and obstructive jaundice.

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