A Simple Method to Avoid Bile Duct Injury during Percutaneous Radiofrequency Ablation Therapy for Hepatocellular Carcinoma

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Keywords
Pericutaenous radiofrequency ablation · Hepatocellular carcinoma · Percutaneous transhepatic cholangiodrainage · Intraductal chilled saline perfusion

Abstract
Hepatocellular carcinoma represents a major global health burden. Its treatment is often complicated by the anatomical location of tumors, which can lead to adverse outcomes. Radiofrequency ablation has recently gained attention as a safe method for treating hepatocellular carcinoma, but only in tumors that are not adjacent to bile ducts. Here, we report a new method for cooling the bile duct during radiofrequency ablation therapy, in which the outer jacket of an elastro needle was fixed and flash-cooled with chilled saline. This method was applied in a patient with hepatocellular carcinoma tumors near the main bile duct. The patient underwent successful radiofrequency ablation with bile duct cooling. The advantages of this method include low medical cost, simpler securing of nonexpanded bile ducts, and simultaneous removal upon termination of the radiofrequency ablation therapy. Bile duct complications associated with radiofrequency ablation typically have delayed onset. Computed tomography examination 2 months after treatment showed no bile duct injury in this case.
Introduction

Hepatocellular carcinoma (HCC) is the second-leading cause of cancer-related death [1]. The major risk factors for HCC in contemporary clinical practice include post-sustained virological response hepatitis C, treatment-suppressed hepatitis B virus, alcoholic and nonalcoholic fatty liver disease, and dietary exposure to aflatoxins B1 in developing countries. Radiofrequency ablation (RFA) is frequently used for the local treatment of HCC [2–6]. RFA is the best treatment alternative in patients with early-stage HCC who are not eligible for surgical resection. RFA was shown to extend survival by >60 months in patients with HCC [6]. HCC is often anatomically complex, leading to difficulty with treatment. Glisson’s capsule extends into the liver as sheaths around the hepatic bile ducts, hepatic arteries, and portal veins. HCC lesions adjacent to Glisson’s capsule may be affected by RFA, thus increasing the risk of complications, such as intrahepatic bile duct dilatation, hepatic arterioportal fistula, and hepatic infarction. Most of these complications are irreversible and may negatively affect liver function and prognosis. Wakamatsu et al. [6] reported that arterioportal fistula, intrahepatic bile duct dilatation, and hepatic infarction caused by RFA developed in 10.0, 8.2, and 1.2% of patients, respectively.

Because bile duct damage is very serious in the hilar region, central liver tumors are considered to be a contraindication for RFA [7–9]. Various mitigating measures have been reported, such as cooling the tissue by infusing chilled saline through the endoscopic nasobiliary drainage (ENBD) tube or percutaneous transhepatic cholangiography (PTCD) tube [7, 10–12]. Acute pancreatitis occasionally occurs, which may be a critical complication [10, 11]. Here, we report a safer and more effective new method of cooling the bile duct during RFA therapy for HCC.

Case Report

In April 2020, an 86-year-old man visited the Department of Gastroenterology due to an intrahepatic lesion. He was a long-time drinker but had normal liver function (Table 1). His liver function was sufficient for RFA therapy, with a Child-Pugh classification of A and ALBI grade 2, but the tumor was located near the main bile duct. We obtained informed consent

Table 1. Patient laboratory data on admission

| Parameter | Value |
|-----------|-------|
| WBC       | 8,200/μL |
| RBC       | 30.6×10⁶/μL |
| Hb        | 10.8 g/dL |
| Ht        | 31.7% |
| PLT       | 18.6×10⁴/μL |
| PT        | 76% |
| TP        | 6.2 g/dL |
| ALB       | 3.7 g/dL |
| AST       | 20 IU/L |
| ALT       | 10 IU/L |
| LDH       | 236 IU/L |
| ALP       | 308 IU/L |
| γGTP      | 37 IU/L |
| T-Bil     | 0.7 mg/dL |
| ChE       | 158 IU/L |
| BUN       | 24 mg/dL |
| Cre       | 0.90 mg/dL |
| eGFR      | 60.8 mL/min/1.73 m² |
| Na        | 131 mEq/L |
| K         | 5.0 mEq/L |
| Cl        | 96 mEq/L |
| T-chol    | 151 mg/dL |
| TG        | 57 mg/dL |
| HDL-C     | 76 mg/dL |
| LDL-C     | 53 mg/dL |
| GLU       | 72 mg/dL |
| S-AMY     | 74 IU/L |
| HbA1c     | 5.3% |
| CRP       | 0.67 mg/dL |
| AFP       | 3.9 ng/mL |
| PIVKAII   | 52 mAU/mL |
| HBs-Ag    | (-) |
| HBs-Ab    | (-) |
| HCV-Ab    | (-) |
from the patient regarding the treatment method. Therefore, we chose a method that can achieve sufficient ablation and avoid bile duct damage.

Gd-EOB-DTPA-enhanced MRI (EOB-MRI) revealed liver morphology consistent with chronic alcoholic liver injury. In the arterial phase, a hypervascular tumor of approximately 24 mm in diameter was visible. The hepatobiliary phase clearly demonstrates that the tumor was located near the main bile duct (Fig. 1a–d). Ultrasonography confirmed that the tumor was located near the hilar region (Fig. 1e, f, Fig. 2). A bile duct that could be punctured while avoiding the tumor was isolated and secured with a 21-G elastor needle in B8. Using a microguidewire, the outer needle was inserted into the right branch of the bile duct. The outer jacket of the needle was fixed and flash-cooled with saline. The tumor was ablated while refluxing cold saline into the bile duct. Computed tomography after RFA indicated that the tumor, despite being present near the main bile duct, was sufficiently ablated (Fig. 3).

Bile duct complications associated with RFA typically have delayed onset. Computed tomography examination 2 months after treatment showed no bile duct injury in this case.
Fig. 2. a A bile duct B8 was identified as a candidate to secure the tumor without puncturing it. b The red arrow is the puncture line for securing B8. c After puncturing B8 and confirming that it is a bile duct by imaging, a plastic mantle of an elastor needle was advanced to the hilum using a microguidewire. d The tumor was ablated from the plastic mantle, while slowly recirculating semi-thawed saline.

Fig. 3. After ablation of the tumor near the main bile duct, a sufficient safety margin was confirmed.
Discussion

In Japan, more than 60% of HCC cases are diagnosed at an early stage (Barcelona Clinic Liver Cancer stage 0 or A), which can be treated with curative therapies, such as surgical resection, local ablation, and liver transplantation [2]. RFA is considered the standard treatment for HCC worldwide for patients with <3 tumors that are <3 cm in diameter [13, 14]. Maeda et al. [15] reported that among 11,298 RFA procedures, only 330 complications (2.92%) were identified. Six patients (0.064%) died from RFA-related complications during the recent period (2011–2015), and according to quality improvement guidelines for RFA of liver tumors, RFA is contraindicated for the treatment of tumors located <1 cm from the main biliary duct or a bilioenteric anastomosis [9]. In Japan, the indications for RFA in patients with HCC tumors adjacent to the first or second branches of the bile duct have increased from 15 of 20 centers (75%) during the previous period (1999–2010) to 21 of 25 centers (84%) during the recent period. Indications have also increased for patients with a tumor near a bilioenteric anastomosis or papillary dysfunction from 5 of 20 centers (25%) during the previous period to 10 of 25 centers (40%) during the recent period, which has consequently increased performance of bile duct cooling via a nasobiliary drainage tube from 25 to 32% [15]. Ohnishi et al. [10] reported the utility of intraductal chilled saline perfusion (ICSP) to prevent bile duct injury during percutaneous RFA for HCC. Although there are similar subsequent reports, the complications of ENBD detention have been noted as a problem. The requirement for a longer hospital stay is an additional drawback. The method we present is simple and has very little impact on the medical economy. Although no large-scale studies have been done for this method, the therapeutic effect is considered to be equivalent to ENBD combination treatment.

Recently, Li et al. [12] reported that PTCD-ICSP appears to be a safe and effective technique for the management of larger HCC tumors (>3 cm) during microwave therapy. They reported that this method required 6- to 8.5-Fr tube insertion. Because of this, our method using the 21-G elastor needle has the potential to be safer and simpler, with shorter hospital stays and lower medical costs, which greatly benefits patients.

Statement of Ethics

This study was carried out in accordance with the Declaration of Helsinki. The patient had provided written informed consent to the cancer board of our institution before the procedure. Additionally, this patient provided written consent to publish this case (including publishing images).

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Funding Sources

The authors received no funding from any organization for this study.
Author Contributions

Hidetaka Takashima: formulation and execution of treatment methods; Michihisa Mori-guchi, Natsuko Hayashi, Kyohi Ikedu, Kiyoshi Ogiso, Chihiro Yokomizo, Hirokazu Uejima, Tadashi Itoh, Hideo Tomioka, Shigeto Mizuno, Seiji Shimizu, Kohichiroh Yasui, and Yoshito Itoh: advice on treatment strategies.

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