

# Successful Interventional Treatment for Arterioportal Fistula Caused by Radiofrequency Ablation for Hepatocellular Carcinoma

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## Key Words

Hepatocellular carcinoma · Radiofrequency ablation · Arterioportal fistula · Transarterial embolization

## Abstract

Radiofrequency ablation (RFA) is commonly used as a treatment for small hepatocellular carcinoma (HCC). Although several complications such as intraperitoneal bleeding are often observed after RFA, hepatic arterioportal fistula (APF) is a less frequently occurring complication. In this study, we describe two cases of APF caused by RFA, which was successfully occluded by an interventional approach. Case 1 involved a 68-year-old man with solitary HCC in segment VIII of the liver. Both contrast-enhanced computed tomography and color Doppler sonography indicated an APF between the anterosuperior branch of the right hepatic artery (A8) and the portal branch (P8). Concordant with these findings, digital subtraction angiography (DSA) revealed an APF in segment VIII of the liver. Subsequently, the APF was successfully occluded by transarterial embolization (TAE) using gelatin sponge particles. Case 2 involved a 67-year-old man with solitary HCC in segment VII of the liver. Although he developed obstructive jaundice because of hemobilia after RFA, it was improved by endoscopic nasobiliary drainage and the systemic administration of antibiotics. In addition, color Doppler

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sonography revealed a disturbed flow of the right branch of the portal vein. Similar to case 1, DSA showed an APF between A8 and P8. The APF was successfully embolized by TAE using microcoils. In conclusion, it appears that the formation of APF should be checked after RFA. It is preferable to treat RFA-induced APF promptly by an interventional approach to avoid secondary complications such as portal hypertension and liver dysfunction. © 2014 S. Karger AG, Basel

## Introduction

Hepatocellular carcinoma (HCC) is the sixth most common malignancy in the world and the third most common cause of cancer-related death [1]. Chronic infection with hepatitis B virus or hepatitis C virus (HCV), alcoholic abuse and nonalcoholic fatty liver disease are major risk factors for hepatocarcinogenesis [2]. Recent progress in new therapeutic approaches contributes to the improvement in the survival and prognosis of patients with HCC. Among them, radiofrequency ablation (RFA) has been widely applied to the local treatment of HCC. The overall survival in patients treated with RFA was shown to be nearly equal to that in patients receiving surgical resection [3, 4]. Although RFA appears minimally invasive and comparatively safe, it often causes complications such as intraperitoneal bleeding [5, 6]. Arterioportal fistula (APF) commonly occurs either secondary to iatrogenic causes, such as liver biopsy, transhepatic biliary drainage, transhepatic cholangiogram, and surgery, or following mechanical insult, such as blunt or penetrating trauma [7–11]. APF usually remains clinically asymptomatic at the outset of the formation. However, it causes portal hypertension and deterioration of liver function in some cases [12, 13]. The frequency of APF caused by RFA was estimated in only 0.4% of all patients treated with RFA [14]. The clinical condition and therapeutic approach remains to be elucidated. In this case study, we report two cases complicated by APF caused by RFA, which was successfully occluded by an interventional approach.

## Case Reports

### Case 1

A 68-year-old man was referred to our hospital for the treatment of a liver tumor. He had been followed for liver cirrhosis because of alcohol abuse and diabetes mellitus. However, he had never received any treatments against HCC. On admission, physical examination revealed mild splenomegaly. Blood examination showed that serum hepatobiliary enzyme levels and markers for renal function such as blood urea nitrogen and creatinine were normal. The serum ammonia level was modestly increased (69 µg/dl). The blood count tests showed thrombocytopenia ( $9.6 \times 10^4/\mu\text{l}$ ). His Child-Pugh score was 5 (class A). Neither anti-HCV antibody nor hepatitis B surface antigen (HBsAg) was positive. The  $\alpha$ -fetoprotein level was slightly increased to 11.0 ng/ml, although that of des-gamma-carboxy prothrombin (DCP) remained normal. Contrast-enhanced computed tomography (CT) demonstrated an encapsulated hypervascular tumor, approximately 20 mm in diameter, in segment VIII of the right hepatic lobe. The tumor was diagnosed as HCC, and the patient was successfully treated with RFA (fig. 1a). Although he had no clinical symptoms the day after RFA, contrast-enhanced CT and color Doppler sonography demonstrated an APF between the anterosuperior branch of the right hepatic artery (A8) and the portal vein (P8) (fig. 1b, c). In addition, the right branch of the portal vein showed diminished blood flow signals (fig. 1c). Concordant with the findings of Doppler sonography, digital subtraction angiography (DSA) revealed

an APF in segment VIII of the liver (fig. 1e). Subsequently, the APF was successfully occluded by transarterial embolization (TAE) using gelatin sponge particles (fig. 1d, f). The postoperative course was uneventful, and the patient was discharged 21 days after admission.

#### Case 2

A 67-year-old man with a liver tumor was admitted to our hospital. He had been treated with RFA against HCC three times previously. On admission, physical examination revealed no special signs. Although blood examination showed that the serum alkaline phosphatase (ALP) level was mildly elevated (434 U/l), the total bilirubin and aminotransferase levels were normal. Although the blood count tests showed thrombocytopenia ( $7.5 \times 10^4/\mu\text{l}$ ), the red and white blood cell counts were normal. His Child-Pugh score was 6 (class A). The patient was tested negative for anti-HCV antibody and HBsAg. The serum  $\alpha$ -fetoprotein level was markedly increased to 42.1 ng/ml, but that of DCP remained normal. Arterial dominant-phase images obtained by contrast-enhanced magnetic resonance imaging (MRI) showed a hypervascular tumor, approximately 25 mm in diameter, in segment VII of the right hepatic lobe (fig. 2a). We made a diagnosis of recurrent HCC, and the tumor was successfully treated with RFA (fig. 2b). However, the patient developed upper abdominal pain and jaundice the day after the treatment. Laboratory data exhibited increased total bilirubin (5.0 mg/dl) and ALP (880 U/l) levels. Non-contrast CT indicated hemobilia in the right anterior branch of the intrahepatic bile duct. Subsequently, an endoscopic nasobiliary drainage tube was placed in the anterior right hepatic duct, and antibiotics were systematically administered. Because his condition and laboratory data rapidly improved, the drainage tube was removed 5 days after the placement. In addition, color Doppler sonography revealed a disturbed flow of the right branch of the portal vein (fig. 2c), which indicated the formation of APF. As expected, DSA revealed an APF between A8 and P8 and an early filling of the anterior branch of the portal vein (fig. 2e). Eventually, the APF was successfully occluded by TAE using microcoils (fig. 2d, f). The postoperative course was uneventful, and the patient was discharged 30 days after admission.

#### Discussion

According to previous reports, most cases of APF are acquired. Vauthey et al. [15] found that the most common cause of APF was injury (28%), followed by iatrogenic causes (16%), congenital causes (15%), tumor (15%), and aneurysm (14%). Iatrogenic APF has often been reported to arise as a result of transhepatic puncture techniques such as liver biopsies and percutaneous transhepatic cholangiodrainage [16–18]. In recent years, RFA has become widely recognized as a useful local treatment for HCC and is becoming more widely adopted. In a multicenter study of RFA complications, Livraghi et al. [14] reported APF formation in 9 of 2,320 patients (0.4%). However, these were cases of asymptomatic APF that were detected with CT; therefore, the actual number could have been higher. Iatrogenic APF is usually diagnosed and targeted for intervention after the appearance of portal hypertension symptoms, including esophagogastric varix rupture and massive ascites [19]. However, even if an APF is asymptomatic when it initially forms, if left untreated, liver dysfunction and portal hypertension can progress as time passes [20–22]; therefore, caution is required. In the two cases presented in this study, a confirmation of the ablated area around the tumor and a check for complications was performed on the day after RFA using contrast-enhanced CT or MRI. Furthermore, the blood flow of the portal vein was evaluated with color Doppler sonography, which allowed for an early diagnosis of APF and a detailed evaluation of the shunt

blood flow. Considering that a disturbed flow of the right portal vein was observed in both cases, we concluded that an interventional closure of the APF should be conducted to prevent portal hypertension and liver dysfunction.

The therapeutic approaches used for APF are surgery and interventional radiology (IVR) techniques [21–23]. In the past, the majority of patients have required a surgical ligation of the artery supplying the APF or a simple resection of the vascular anomaly. Recently, embolization of APF using interventional procedures has been increasingly performed instead of surgery. Because of recent advances in IVR techniques and devices, IVR is safer and less invasive than surgery; therefore, it is now considered the first-line treatment for APF. IVR has a success rate of more than 90% for APF cases, although surgery is often performed when IVR is not indicated or when IVR fails [23]. Embolic agents are usually chosen according to the size of vascular communication, and a proper selection of the embolic materials is very important for a successful procedure. Among the treatments for APF, embolization using microcoils is usually performed [24, 25]. However, the diameter of the APF was comparatively small in case 1; therefore, embolization was performed with gelatin sponge particles instead. Although embolization with microcoils can be visually confirmed, the procedure causes artifacts on CT or MRI, which makes the observation of the area surrounding the coils a time-intensive and difficult task. Therefore, in some cases, it may be better to choose gelatin sponge particles over microcoils for TAE.

In conclusion, we report two cases demonstrating APF caused by RFA. The early diagnosis of APF and exhaustive evaluation of blood flow were made possible by contrast-enhanced CT or MRI, and color Doppler sonography performed on the day after RFA. Considering that patients with HCC are frequently complicated by cirrhosis, APF should be occluded early to prevent portal hypertension and deterioration of liver function. To ascertain the clinical condition and course in patients with APF caused by RFA, further analysis is necessary in a larger number of patients.

### Disclosure Statement

The authors have no conflicts of interest.

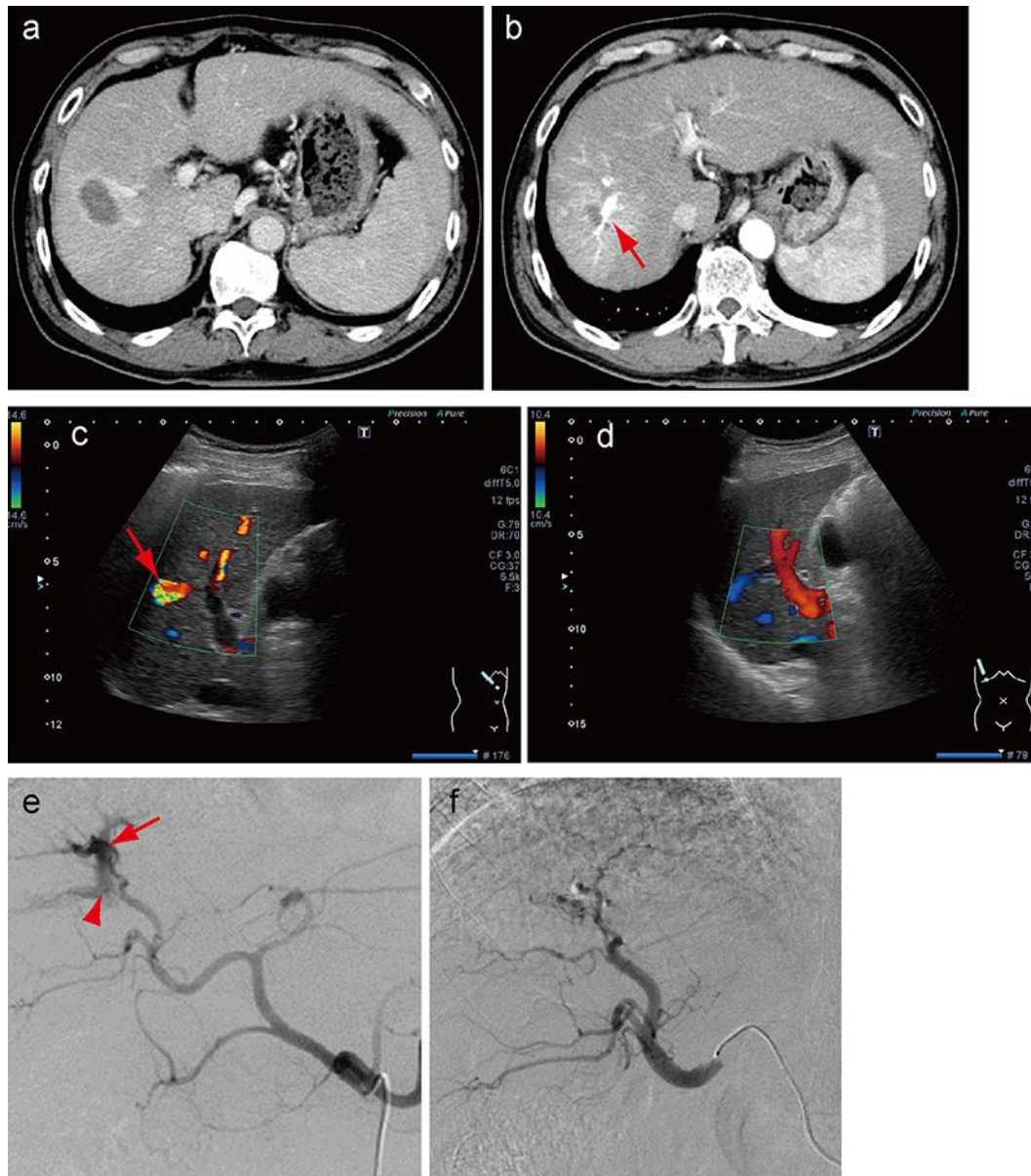
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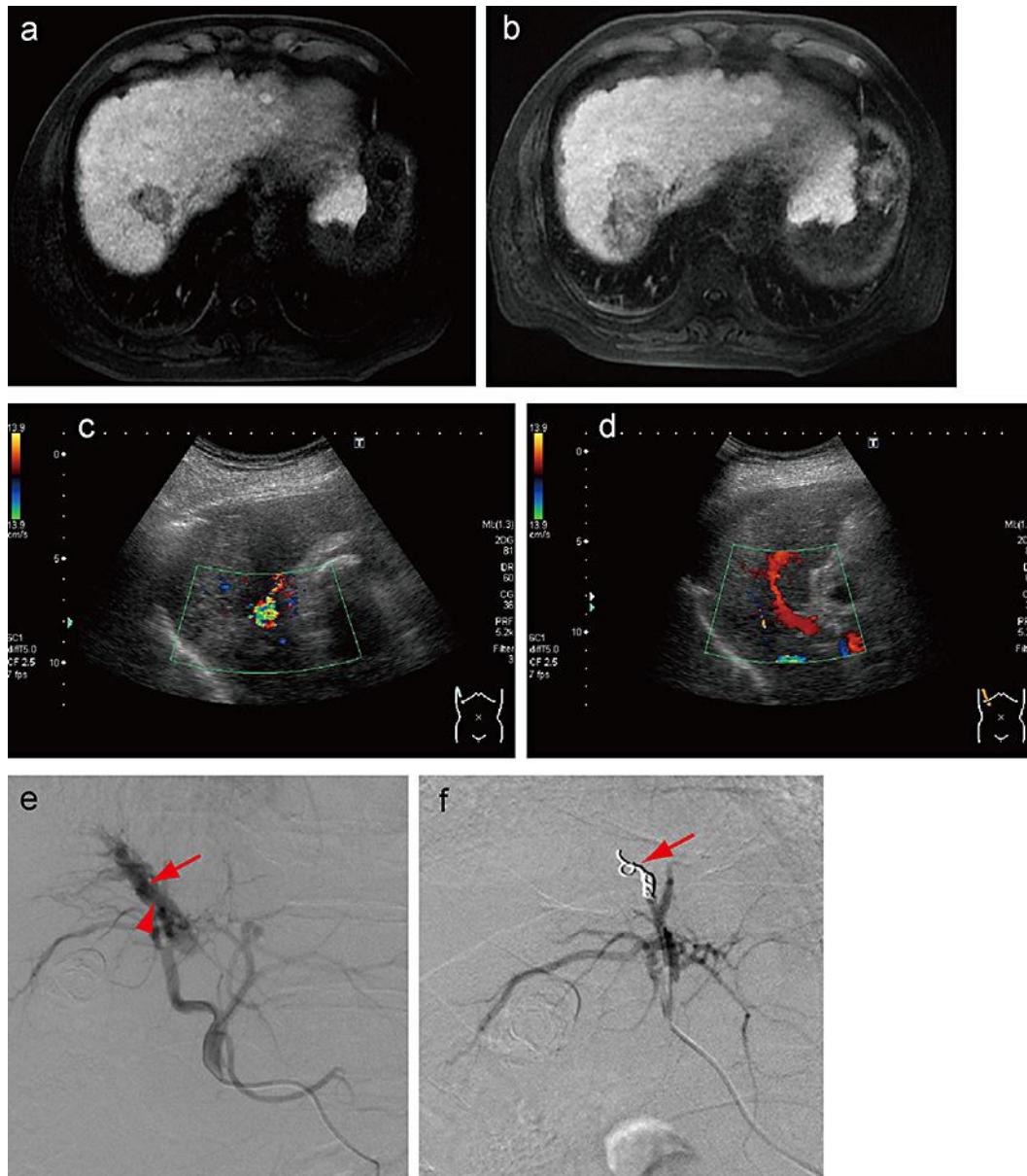
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**Fig. 1.** Findings of clinical imaging for case 1. **a** A CT image in the portal-dominant phase demonstrates an ablation region for HCC. **b** A CT image in the arterial-dominant phase detects a portal vein (P8, arrow). **c** Color Doppler sonography demonstrates APF (arrow) between the anterosuperior branch of the right hepatic artery (A8) and the portal vein (P8). Blood flow signals in the right branch of the portal vein disappear. **d** Color Doppler sonography demonstrates normal flow in the anterior branch of the portal vein after APF embolization. **e** Celiac arteriography reveals APF (arrow) and an early filling of the anterior branch of the portal vein (arrowhead). **f** Right hepatic arteriography after APF embolization with gelatin sponge particles shows the lack of right portal venous filling.

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**Fig. 2.** Findings of clinical imaging for case 2. **a** An MRI image in the portal-dominant phase demonstrates HCC in segment VIII. **b** An MRI image in the portal-dominant phase after RFA demonstrates successful ablation. **c** Color Doppler sonography shows a disturbed flow in the right branch of the portal vein. **d** Color Doppler sonography demonstrates normal flow in the right branch of the portal vein after APF embolization. **e** Proper hepatic arteriography reveals APF between A8 and P8 (arrow) and an early filling of the anterior branch of the portal vein (arrowhead). **f** Hepatic arteriography of the anterior branch after APF embolization with microcoils (arrow) shows the lack of right portal venous filling.