Delayed bronchobiliary fistula and cholangiolithiasis following percutaneous radio frequency ablation for hepatocellular carcinoma

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Abstract

Although percutaneous radio frequency ablation for hepatocellular carcinoma is a minimally invasive therapy, there are some complications reported; major complications include hemorrhage (0.477%), hepatic injuries (1.690%), and extrahepatic organ injuries (0.691%). We, for the first time, described a rare complication of delayed bronchobiliary fistula and cholangiolithiasis in common bile duct following radio frequency ablation and the salvage treatment in a patient with chronic hepatitis B virus infection. Surgeons should be aware of severe and rare complications before deciding the ablation area and when performing radio frequency ablation, and should be aware of the relevant salvage treatment.

Keywords: Radio frequency ablation, hepatocellular carcinoma, delayed bronchobiliary fistula, cholangiolithiasis, salvage treatment

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Introduction

Hepatocellular carcinoma (HCC) is considered as the fifth most common cancer-related death and is estimated to cause half a million deaths per year; its incidence continues to increase.^{1,2} Surgical resection is a major treatment for HCC while local ablation therapy, such as radio frequency ablation (RFA), is regarded as an alternative option. RFA was originally reserved for HCC that was unsuitable for surgical resection, but it is now proving its worth in small operable HCC as well,^{3,4} even in medium and large HCC.⁵ It was reported that three-year and five-year survival rates of RFA for HCC were 33–45%^{6,7} and 33–55.4%,^{8,9} respectively.

RFA for HCC is a minimally invasive therapy, which can be performed percutaneously, intraoperatively, or endoscopically under the guidance of ultrasonography (US) or computed tomography (CT). Although RFA is minimally invasive, there are some complications reported: according to a recent multicenter study in Japan,¹⁰ of the complications of RFA for HCC, the mortality rate of RFA was 0.038%, the rate of complications was 3.54%, and the major complications include hemorrhage (0.477%), hepatic injuries (1.690%), and extrahepatic organ injuries (0.691%). To our knowledge, there were two reported cases of rare complication of bronchobiliary fistula within 30 days following RFA for HCC; however, no subsequent salvage treatment was

reported.¹¹ Here, we, for the first time, report a case with rare complication of delayed bronchobiliary fistula and cholangiolithiasis about 16 months after RFA for HCC resulted from chronic hepatitis B virus (HBV) infection and propose the relevant salvage treatment.

Case presentation

Abdominal US examination of a 58-year-old Chinese man with chronic HBV infection showed a liver tumor in segment 8; the tumor was close to cavo-hepatic intersection and with a diameter of 4 cm, which was then identified as HCC by contrast-enhanced US (Figure 1(a)). The tumor was subsequently confirmed by magnetic resonance imaging (MRI), which was shown to compress middle hepatic vein and the anterior branch of right portal vein (Figure 1(b) and (c)). The result of liver function test showed Child-pugh A, result of liver enzyme test showed alanine aminotransferase 64 U/L, the concentration of serum α -fetoprotein was 10.27 ng/mL, and serum HBV DNA load was 1.4×10^4 IU/mL. The patient also had diabetes and was receiving insulin injection therapy.

The patient subsequently received percutaneous RFA under guidance of real-time sonography. The patient was on left lateral position, after general inhalation anesthesia; an internally cool-tip single electrode with a 200-W

generator (Cool-tip, Valleylab, MA, USA) was percutaneously and intercostally inserted into the bottom of the tumor under guidance of real-time sonography. The electrode was inserted for 12 times from different angles to cover and ablate the entire tumor, and each ablation following each insertion of electrode persisted for 12 min. Complete ablation was confirmed by subsequent contrast-enhanced US (Figure 2). The patient was then discharged uneventfully, and there was no evidence of residual or recurrence of tumor according to US and MRI imaging during follow-up.

The patient gradually presented a series symptoms of mild jaundice and fever 14 months after RFA, and was once misdiagnosed; however, the patient at last presented expectoration with biliary sputum, and delayed bronchobiliary fistula was diagnosed with evidence of CT imaging (Figure 3).

Percutaneous transhepatic cholangiography (PTC) and percutaneous transhepatic cholangial drainage (PTCD) were then performed. The result of PTC showed that there were filling defects (Figure 4) in dilated common

bile duct, which was considered as calculus and not confirmed by MRI and US imaging before RFA; the anterior right hepatic duct was damaged. After PTCD for one week, the patient received salvage right hemihepatectomy and lithotomy of common bile duct. There were no residual tumor foci or recurrent tumor foci according to the result of pathology of the right liver. The patient is uneventful till now during follow-up for 18 months after salvage operation.

Discussion and conclusion

It was reported that only 10–30% of the affected patients are suitable for hepatic resection or transplantation.^{12,13} RFA is now proving its worth in small operable HCC,^{3,4} there are current RFA indication of being a size of 3 cm or smaller and no more than three lesions^{14,15}; however, there were some studies focusing on RFA for medium and large HCC. Khan *et al.*¹⁶ concluded that for medium HCC between 3 cm and 5 cm, the surgical approach seems to achieve better overall survival and may be a preferred option, while Yin *et al.*⁵

Figure 1 Preoperative imaging examination. (a) Contrast-enhanced ultrasonography showed a liver mass in segment 8 with a diameter of 4 cm, which was identified as hepatocellular carcinoma (white arrow); (b) T1 weighted image of magnetic resonance imaging (MRI) showed the segment 8 tumor located adjacent to middle hepatic vein (white arrow), (c) the tumor also located adjacently to and compressed the anterior branch of right portal vein (white arrow). (A color version of this figure is available in the online journal.)

reported that percutaneous thermal ablation was effective and safe in treating HCC between 3 cm and 7 cm, with acceptable local tumor control and long-term outcomes. Our patient with a 4-cm HCC achieved pathologically complete ablation following adequate times of ablation, which was in accordance with the conclusion of Yin *et al.*

Completeness of ablation remains a challenge for RFA, which is a major prognostic factor. We performed 12 continuous times of ablation in the current case for the sake of achieving complete ablation, which negatively resulted in subsequent biloma, delayed bronchobiliary fistula, and cholangiolithiasis. Complications of RFA for HCC include hemorrhage (0.477%), hepatic injuries (1.690%), and extra-hepatic organ injuries (0.691%),¹⁰ and bile duct injuries, including biloma, were usually found several months later; however, biloma is often considered to be of no

clinical significance. The anterior right hepatic duct of our patient was damaged and destroyed during RFA, which was the main cause of biloma; the surrounding adjacent diaphragm was also injured by heat, which provided a route for the delayed bronchobiliary fistula. The most interesting point was cholangiolithiasis in common bile duct, which was not shown in US or MRI imaging before RFA. We speculated that the possible reason of cholangiolithiasis in common bile duct was the necrotic tissue produced by RFA flowing into the bile duct and accumulating in common bile duct. Pressure of biloma gradually increased because of cholangiolithiasis in common bile duct, and then delayed bronchobiliary fistula happened at last.

Releasing the obstruction of bile duct was the key point for our patient. After PTCD for one week in our patient, symptoms of jaundice, fever, and expectoration with biliary

Figure 2 Contrast-enhanced ultrasonography after RFA. Complete ablation was confirmed by contrast-enhanced ultrasonography immediately after RFA (white arrow). (A color version of this figure is available in the online journal.)

Figure 4 Percutaneous transhepatic cholangiography imaging. Common bile duct was dilated, the diameter was about 1.8 cm, there were filling defects (black arrow) in the common bile duct, which was considered as calculus; the anterior right hepatic duct was damaged

Figure 3 Computed tomography imaging. Bronchobiliary fistula was confirmed by computed tomography imaging. (a) The fistula tract that communicated abdominal and pleural cavities was shown in left figure (white arrow). (b) The lower portion of the right lung showed inflammation and consolidation (white arrow)

sputum disappeared. Further salvage right hemihepatectomy and lithotomy of common bile duct were performed. There were no residual tumor foci or recurrent tumor foci according to the result of pathology of the right liver. The patient is uneventful till now during follow-up after the salvage operation.

Although RFA is considered to be effective and safe for HCC, and most complications of RFA are also regarded as minor and without clinical significance, some severe complications have been reported. Surgeons should be aware of the severe and rare complications before deciding the ablation area and when performing RFA. In conclusion, we reported a rare complication of delayed bronchobiliary fistula and cholangiolithiasis in common bile duct following RFA and the salvage treatment in a patient with chronic HBV infection. Surgeons should be aware of this kind of complication and the relevant salvage treatment.

Authors' contribution: The first two authors contributed equally to this work. YZ carried out the design of the report, drafted the manuscript and participated in the follow-up of the patient. MD helped to draft the manuscript and the follow-up of the patient, KL helped to revise the manuscript critically for RFA procedure and ultrasonography. RX participated in coordination and the follow-up of the patient. All authors read and approved the final manuscript.

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REFERENCES

1. Bosch FX, Ribes J, Díaz M, Cléries R. Primary liver cancer: worldwide incidence and trends. *Gastroenterology* 2004;**127**:S5-S16
2. Altekruse SF, McGlynn KA, Reichman ME. Hepatocellular carcinoma incidence, mortality, and survival trends in the United States from 1975 to 2005. *J Clin Oncol* 2009;**27**:1485-91
3. Ebara M, Okabe S, Kita K, Sugiura N, Fukuda H, Yoshikawa M, Kondo F, Saisho H. Percutaneous ethanol injection for small hepatocellular carcinoma: therapeutic efficacy based on 20-year observation. *J Hepatol* 2005;**43**:377-80
4. Huang GT, Lee PH, Tsang YM, Lai MY, Yang PM, Hu RH, Chen PJ, Kao JH, Sheu JC, Lee CZ, Chen DS. Percutaneous ethanol injection versus surgical resection for the treatment of small hepatocellular carcinoma: a prospective study. *Ann Surg* 2005;**242**:36-42
5. Yin, Xie, Lu MD, Xu HX, Xu ZF, Kuang M, Liu GJ, Liang JY, Lau WY. Percutaneous thermal ablation of medium and large hepatocellular carcinoma: long-term outcome and prognostic factors. *Cancer* 2009;**115**:1914-23
6. Vivarelli M, Guglielmi A, Ruzzenente A, Cucchetti A, Bellusci R, Cordiano C, Cavallari A. Surgical resection versus percutaneous radiofrequency ablation in the treatment of hepatocellular carcinoma on cirrhotic liver. *Ann Surg* 2004;**240**:102-7
7. Guglielmi A, Ruzzenente A, Battocchia A, Tonon A, Fracastoro G, Cordiano C. Radiofrequency ablation of hepatocellular carcinoma in cirrhotic patients. *Hepatogastroenterology* 2003;**50**:480-4
8. Buscarini L, Buscarini E, Di Stasi M, Vallisa D, Quaretti P, Rocca A. Percutaneous radiofrequency ablation of small hepatocellular carcinoma: long-term results. *Eur Radiol* 2001;**11**:914-21
9. Raut CP, Izzo F, Marra P, Ellis LM, Vauthey JN, Cremona F, Vallone P, Mastro A, Fornage BD, Curley SA. Significant long-term survival after radiofrequency ablation of unresectable hepatocellular carcinoma in patients with cirrhosis. *Ann Surg Oncol* 2005;**12**:616-28
10. Koda M, Murawaki Y, Hirooka Y, Kitamoto M, Ono M, Sakaeda H, Joko K, Sato S, Tamaki K, Yamasaki T, Shibata H, Shimoe T, Matsuda T, Toshikuni N, Fujioka S, Ohmoto K, Nakamura S, Kariyama K, Aikata H, Kobayashi Y, Tsutsui A. Complications of radiofrequency ablation for hepatocellular carcinoma in a multicenter study: an analysis of 16346 treated nodules in 13283 patients. *Hepatol Res* 2012;**42**:1058-64
11. Tateishi R, Shiina S, Teratani T, Obi S, Sato S, Koike Y, Fujishima T, Yoshida H, Kawabe T, Omata M. Percutaneous radiofrequency ablation for hepatocellular carcinoma. An analysis of 1000 cases. *Cancer* 2005;**103**:1201-9
12. Poon RT, Fan ST, Lo CM, Ng IO, Liu CL, Lam CM, Wong J. Improving survival results after resection of hepatocellular carcinoma: a prospective study of 377 patients over 10 years. *Ann Surg* 2001;**234**:63-70
13. Bismuth H, Majno PE, Adam R. Liver transplantation for hepatocellular carcinoma. *Semin Liver Dis* 1999;**19**:311-22
14. Bruix J, Sherman M. Management of hepatocellular carcinoma. *Hepatology* 2005;**42**:1208-36
15. Japan Society of Hepatology The. Clinical practice guidelines for hepatocellular carcinoma - The Japan Society of Hepatology 2009 update. *Hepatol Res* 2010;**40**(Suppl 1): 2-144
16. Khan MR, Poon RT, Ng KK, Chan AC, Yuen J, Tung H, Tsang J, Fan ST. Comparison of percutaneous and surgical approaches for radiofrequency ablation of small and medium hepatocellular carcinoma. *Arch Surg* 2007;**142**:1136-43; discussion 1143

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