



Obstructive Jaundice Following Transarterial Chemoembolization for Hepatocellular Carcinoma with Bile Duct Invasion

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Abstract

Keywords

- ▶ hepatocellular carcinoma
- ▶ bile duct invasion
- ▶ transarterial chemoembolization

Hepatocellular carcinoma (HCC) with bile duct invasion is considered rare. A case in which a fragment of intraductal tumor dropped into the common bile duct after transarterial chemoembolization (TACE) and caused abdominal pain, and obstructive jaundice secondary to biliary obstruction is presented. This case was successfully managed by emergent endoscopic sphincterotomy. Physicians should recognize one of the complications due to TACE for HCC with intraductal tumor invasion.

Introduction

Hepatocellular carcinoma (HCC) often invades into blood vessels, particularly the portal vein. Biliary invasion of HCC has been considered relatively rare.¹ Transarterial chemoembolization (TACE) is one of the effective treatments for unresectable HCC. TACE may be considered as one of the treatment options for HCC with bile duct invasion if surgical or curative options are unavailable.^{2,3} TACE occasionally causes biliary complications, including intrahepatic biloma, bile duct necrosis, acute cholecystitis, and a hepatic abscess.²⁻⁵ Though rare, acute biliary obstruction due to the migration of necrotic tumor in bile duct may happen after TACE. A case of symptomatic acute biliary obstruction secondary to biliary migration of necrotic HCC is reported.

Case Report

Written informed consent was obtained from the patient for publication of this case report. A 64-year-old male with liver cirrhosis secondary to chronic hepatitis C infection was admitted to our department for TACE of primary HCC. He was not a suitable candidate for surgical resection and transplant due to poor general condition and no suitable donor, respectively. On admission, his serum bilirubin level was 0.9 mg/dL. Contrast-enhanced computed tomography (CT) showed a hypervascular tumor, 4 cm in diameter, with bile duct tumor invasion in segment IV of the liver and dilatation of the left intrahepatic bile duct (▶**Fig. 1**). Digital subtraction angiography showed tumor stain supplied by the middle hepatic artery, and CT during hepatic arteriography showed the

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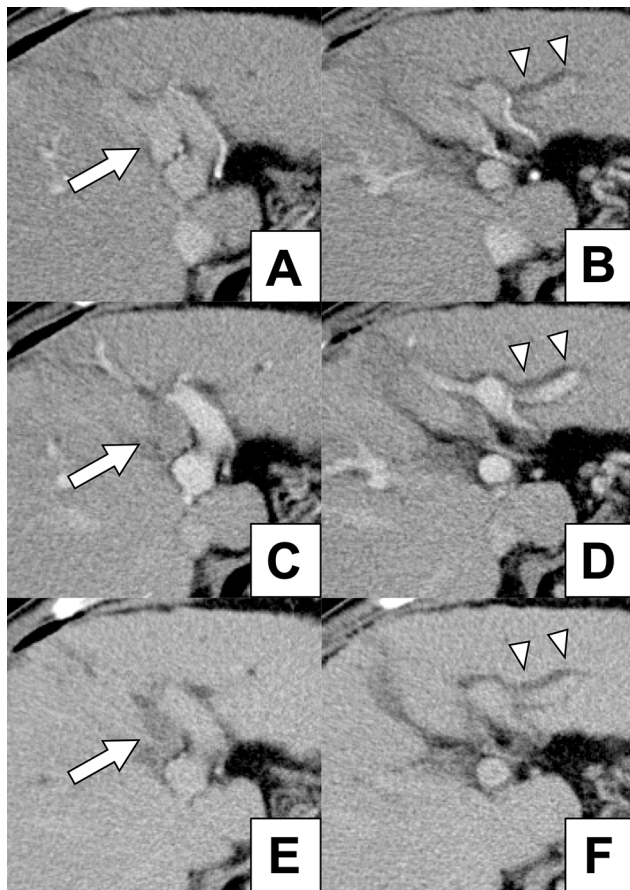


Fig. 1 Contrast-enhanced computed tomography prior to transarterial chemoembolization: (A, B) arterial phase, (C, D) portal phase, and (D, E) equilibrium phase. Left panels show intraductal tumor invasion (white arrows). The intraductal tumor has a typical contrast-enhancement pattern of hepatocellular carcinoma, which shows arterial enhancement in the arterial phase and washout in the equilibrium phase. Right panels show dilatation of the left intrahepatic bile duct (white arrowheads).

enhanced lesion same as previous contrast-enhanced CT prior to TACE (►Fig. 2A, B). Selective TACE using epirubicin and lipiodol was performed for the lesion in segment IV of the liver. He had undergone two sessions of TACE for the same lesion over 3 months. The second TACE was performed because we judged the first TACE was inadequate embolization. Retention of lipiodol in intraductal tumor in segment IV

was confirmed on CT just after the second TACE (►Fig. 2C). He had low-grade fever as a transient postembolization syndrome in the two sessions of TACE, and recovered from this symptom in a few days.

In total, 8 weeks after TACE, the patient presented with fever, epigastric pain, and jaundice. His serum bilirubin level increased to 10.2 mg/dL, and alkaline phosphatase and gamma-glutamyl transpeptidase levels also increased to 428 and 98 IU/L, respectively. CT showed disappearance of the intraductal tumor and a high-density mass in the lower part of the common bile duct (►Fig. 3A, B). There was neither a calcified bile duct stone nor a gallbladder stone on the previous CT scans; therefore, it was suspected that a necrotic biliary tumor of HCC containing lipiodol had spontaneously sloughed off and caused his symptoms. Emergent endoscopic retrograde cholangiopancreatography (ERCP) showed a yellowish black mass stuck at the ampulla of Vater (►Fig. 4A). The mass was completely removed by endoscopic sphincterotomy (EST), and his symptoms disappeared (►Fig. 4B).

Discussion

Although tumor thrombus in the portal vein is well known in advanced HCC, HCC with bile duct invasion is considered rare.^{1,2} Obstructive jaundice is an uncommon symptom in patients with HCC, except in advanced-stage HCC.^{3,4} Previous reports described that a tumor fragment detached from the bile duct wall after TACE and resulted in the symptoms of acute obstruction of the common bile duct (►Table 1). Kim et al and Miyayama et al reported that the incidence of migration of intraductal necrotic tumor in HCC patients with bile duct invasion after TACE was 10.4 and 10.8%, respectively.^{6,7} These studies included even asymptomatic patients due to a migrated tumor fragment into the common bile duct.

Symptomatic migrated tumors from previous reports were reviewed, and the detailed data available for each case are summarized in a table to understand the characteristics and background (►Table 1). To the best of our knowledge, a total of 14 cases including the present case have been reported in literature to cause obstructive jaundice by migrated tumor fragments from HCC after TACE (►Table 1). The patients ranged in age from 57 to 82 years and consisted of 11 males and 3 females. The tumors were mainly located in segment IV or near the hilum. Most patients showed bile



Fig. 2 (A) A digital subtraction angiography image obtained during TACE. Tumor is stained through the middle hepatic artery. (B) CT during hepatic arteriography of the first TACE shows the enhanced tumor in the left bile duct. (C) On nonenhanced CT after the second TACE, the tumor with the biliary invasion shows high density due to lipiodol. CT, computed tomography; TACE, transarterial chemoembolization.

Table 1 Summary of reported cases of symptomatic migrated tumors after transarterial chemoembolization for hepatocellular carcinoma

Study (Year)	Age(y)/Sex	Location	Bile duct	Time to onset after the last TACE (d)	Treatment modality	Pathological finding	Outcome
Spahr et al (2000) ⁸	78/M	Segment IV	Rt HBD	50	EST	Necrosis	Resolved
Hiraki et al (2006) ¹	69/M	Segment II, III, IV	Lt HBD	18	EST	NA	Resolved
Choi et al (2009) ⁴	62/M	Segment III, IV	Proximal CHD and Lt HBD	14	PTBD	Necrosis	Resolved
Okuda et al (2010) ²	61/F	Segment IV	Lt HBD	7	ERCP	NA	Resolved
Okuda et al (2010) ²	82/F	Hilum	Rt HBD	10	ERCP	NA	Resolved
Okuda et al (2010) ²	71/F	Multiple	Rt HBD and CBD	7	ERCP	NA	Resolved
Ridtitid et al (2010) ⁹	63/M	NA	NA	NA	EST	NA	Resolved
Ridtitid et al (2010) ⁹	63/M	NA	NA	<21	Spontaneous	NA	Resolved
Sasaki et al (2012) ¹⁰	57/M	Segment VIII	NA	5	EPBD	HCC	Resolved
Matsumoto et al (2014) ¹¹	69/M	Segment V	NA	9	EPBD	Necrosis	Resolved
Park et al (2014) ³	71/M	Segment IV	Lt HBD	45	EST	Necrosis	Resolved
Miyayama et al (2017) ⁷	78/M	Hilum	NA	1,036	ERCP	NA	Resolved
Hyo et al (2018) ⁵	67/M	Segment VI, VII	Rt HBD	14	EST	Necrosis	Resolved
Present case	64/M	Segment IV	Lt HBD	64	EST	NA	Resolved

Abbreviations: CBD, common bile duct; CHD, common hepatic duct; EPBD, endoscopic papillary balloon dilation; ERCP, endoscopic retrograde cholangiopancreatography; EST, endoscopic sphincterotomy; F, female; HBD, hepatic bile duct; HCC, hepatocellular carcinoma; Lt, left; M, male; NA, not available; PTBD, percutaneous transhepatic bile drainage; Rt, right; TACE, transcatheter arterial chemoembolization.

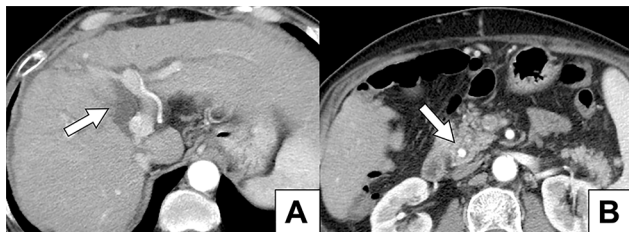


Fig. 3 (A) The tumor that had existed in the left bile duct disappeared when the patient's symptoms appeared. (B) The intraductal tumor migrated to the distal bile duct and dilated the biliary duct.

duct dilatation and bile duct invasion on CT prior to TACE. The number of days to biliary obstruction due to tumor migration after TACE ranged from 7 to 1,036. Although no clear findings from a statistical perspective can be presented, we should be aware that lesions of the hilum tend to have a high risk of causing obstructive jaundice by migration of tumor fragments after TACE. Ghosn et al reported a similar complication with Yttrium-90 transarterial radioembolization which was also managed with ERCP.¹²

A high-density lesion in the common bile duct can be misidentified as a biliary stone because its CT density is similar to that of a typical biliary stone. The present case was accurately diagnosed by CT and successfully managed by emergent EST. Most patients were treated successfully by endoscopic treatments or percutaneous transhepatic biliary drainage, except for one case that improved spontaneously (► **Table 1**). Biliary treatment improved clinical symptoms along with

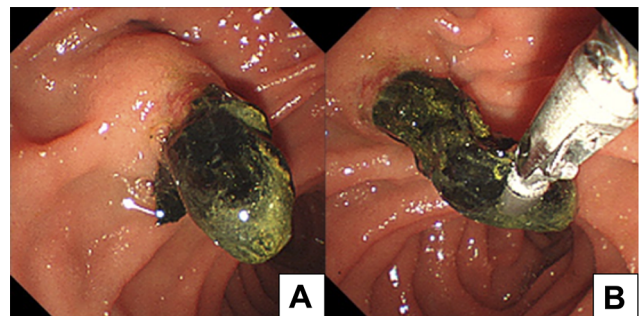


Fig. 4 Endoscopic images obtained during endoscopic retrograde cholangiography. (B) A yellowish black mass is extracted through the ampulla and completely removed by endoscopic sphincterotomy.

protecting liver condition and allowed additional treatments for HCC.³ The clinical symptoms and management of dropped intraductal tumors into the common bile duct were similar to those of biliary obstruction. Therefore, we should develop a treatment plan for migrated tumor fragment after TACE based on the typical treatments for biliary obstruction. Park et al investigated whether there is any need for preprocedural biliary drainage prior to TACE for HCC with bile duct invasion. They concluded that biliary drainage may not be mandatory prior to TACE in the patients with HCC invading the bile duct.¹³

Surgical resection is considered the first option for patients with HCC with bile duct invasion, if feasible.^{2,4} However, most tumors with bile duct invasion are not resectable, and such patients usually have poor hepatic function because HCC

with biliary ductal invasion is generally large and located near the hepatic hilum.^{2,3} TACE may be considered as one of the treatment options if surgical or curative options are unavailable.^{2,3}

There is a limitation to this report. Histopathologic confirmation of the dropped tumor thrombus was not obtained because the mass was released from the common bile duct into the duodenum after removal.

In conclusion, physicians should recognize that TACE for HCC with intraductal tumor invasion can obstruct the common bile duct due to tumor sloughing. When the sloughed tumor results in symptomatic biliary obstruction, biliary treatment is required to improve clinical symptoms.

Conflict of Interest

None declared.

References

- Hiraki T, Sakurai J, Gobara H, et al. Sloughing of intraductal tumor thrombus of hepatocellular carcinoma after transcatheter chemoembolization causing obstructive jaundice and acute pancreatitis. *J Vasc Interv Radiol* 2006;17(3):583–585
- Okuda M, Miyayama S, Yamashiro M, et al. Sloughing of intraductal tumor thrombus of hepatocellular carcinoma after transcatheter arterial chemoembolization. *Cardiovasc Intervent Radiol* 2010;33(3):619–623
- Park HC, Park HB, Chung CY, et al. Acute obstructive cholangitis complicated by tumor migration after transarterial chemoembolization: a case report and literature review. *Korean J Gastroenterol* 2014;63(3):171–175
- Choi KH, Cho YK, An JK, Woo JJ, Kim HS, Choi YS. Acute obstructive cholangitis after transarterial chemoembolization: the effect of percutaneous transhepatic removal of tumor fragment. *Korean J Radiol* 2009;10(2):197–201
- Hyo JP, Ji HS. Intraductal migration of necrotic hepatocellular carcinoma: a possible cause of obstructive cholangitis after chemoembolization. *Gastrointest Interv*. 2018;7:29–33
- Kim GM, Kim HC, Hur S, Lee M, Jae HJ, Chung JW. Sloughing of biliary tumour ingrowth of hepatocellular carcinoma after chemoembolization. *Eur Radiol* 2016;26(6):1760–1765
- Miyayama S, Yamashiro M, Nagai K, et al. Excretion of necrotic hepatocellular carcinoma tissues into the biliary system after transcatheter arterial chemoembolization. *Hepatol Res* 2017;47(13):1390–1396
- Spahr L, Frossard JL, Felley C, Brundler MA, Majno PE, Hadengue A. Biliary migration of hepatocellular carcinoma fragment after transcatheter arterial chemoembolization therapy. *Eur J Gastroenterol Hepatol* 2000;12(2):243–244
- Ridtitid W, Chittmittrapap S, Kriengkirakul C, Kongkam P, Janchai A, Rerknimitr R. Lipiodol as a marker for hepatocellular carcinoma migrating into the bile duct. *Endoscopy* 2010;42(Suppl 2):E233–E234
- Sasaki T, Takahara N, Kawaguchi Y, et al. Biliary tumor thrombus of hepatocellular carcinoma containing lipiodol mimicking a calcified bile duct stone. *Endoscopy* 2012;44(Suppl 2 UCTN):E250–E251
- Matsumoto K, Osanai M, Maguchi H. Biliary tumor fragment of hepatocellular carcinoma containing lipiodol mimicking a bile duct stone. *Dig Endosc* 2014;26(2):295–296
- Ghosn M, Mulé S, Chalaye J, et al. Acute biliary obstruction after transarterial radioembolization with yttrium-90. *J Vasc Interv Radiol* 2019;30(12):2043–2045
- Park J, Kim HC, Lee JH, et al. Chemoembolisation for hepatocellular carcinoma with bile duct invasion: is preprocedural biliary drainage mandatory? *Eur Radiol* 2018;28(4):1540–1550