Hepatocellular Carcinoma Rupture Following Transarterial Chemoembolization

Nimarta Singh Bhinder, MD, MPH¹ Steven M. Zangan, MD¹

¹ Department of Radiology, Section of Interventional Radiology, University of Chicago, Chicago, Illinois

Semin Intervent Radiol 2015;32:49–53

Address for correspondence Nimarta Singh Bhinder, MD, MPH, Department of Radiology, University of Chicago Medicine, 5841 S. Maryland Avenue, MC 2026, Chicago, IL 60637 (e-mail: Nimarta.Singh@uchospitals.edu).

Abstract

Keywords

- hepatocellular carcinoma
- transarterial chemoembolization
- spontaneous rupture
- intraperitoneal hemorrhage
- interventional radiology

As the incidence of primary and metastatic liver cancer increases, minimally invasive treatment methods such as transarterial chemoembolization (TACE) have gained momentum as their efficacy and safety profile have been validated. Complications of TACE are rare and typically well tolerated. A unique complication is tumor rupture with hemorrhage. Reports of hepatocellular carcinoma (HCC) rupture after TACE are limited. It is critical to recognize this complication and understand the treatment options, which range from conservative to surgical management. This report describes a case of HCC rupture following TACE successfully managed with coil embolization.

Objectives: On completion of this article, the reader will be able to identify the types of complications associated with transarterial chemoembolization (TACE) and treatment options for hepatocellular carcinoma rupture following TACE.

Accreditation: This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint providership of Tufts University School of Medicine (TUSM) and Thieme Medical Publishers, New York. TUSM is accredited by the ACCME to provide continuing medical education for physicians.

Credit: TUSM designates this journal-based CME activity for a maximum of **1 AMA PRA Category 1 Credit™**. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Transarterial chemoembolization (TACE) is an established treatment option for primary and secondary hepatic tumors. The safety profile of TACE is relatively good with a risk of major complication in approximately 5%, and as a fatal complication in 1%. Vascular complications can be related to the puncture site, hepatic artery injury, and nontarget embolization. Nonvascular complications include postembolization syndrome, infection such as hepatic abscess, biloma,

bacteremia, sepsis, and extrahepatic abscess, biliary strictures, hepatic failure, renal failure, and variceal bleeding.^{1,2} The authors describe a case of post-TACE hepatocellular carcinoma (HCC) rupture with intraperitoneal hemorrhage treated by coil embolization.

Case Report

A 67-year-old man with the medical history of hepatitis C, alcoholic cirrhosis, and pancytopenia underwent HCC screening because of an elevated serum α fetoprotein level. A triphasic computed tomographic (CT) scan revealed cirrhotic liver morphology with an enhancing segment VII lesion with subsequent washout, compatible with HCC (**► Fig. 1**). Interventional radiology was consulted and the patient was thought to be a good candidate for TACE. Via a 5F right common femoral artery access, an abdominal aortogram was performed that demonstrated a patent visualized aorta and mesenteric vessels. Selective celiac and superior mesenteric angiograms with portal phase demonstrated conventional anatomy. Using a Renegade Hi-Flo microcatheter (Boston Scientific, Natick, MA), a right hepatic angiogram showed a patent right hepatic artery and segmental branches. A large tumor blush was

Issue Theme Morbidity and Mortality in Interventional Radiology: Case Series; Guest Editors, Brian Funaki, MD, FSIR, and Charles E. Ray, Jr., MD, PhD, FSIR

Copyright © 2015 by Thieme Medical Publishers, Inc., 333 Seventh Avenue, New York, NY 10001, USA. Tel: +1(212) 584-4662.

DOI <http://dx.doi.org/10.1055/s-0034-1396964>. ISSN 0739-9529.

Fig. 1 Enhanced computed tomography in arterial phase demonstrates an enhancing 4 cm mass within segment VII of the liver (arrow) consistent with hepatoma.

identified arising from the segmental hepatic artery supplying segment VII; this segmental hepatic artery was selected and selective arteriography showed tumor blush with no significant shunting (►Fig. 2). This vessel was chemoembolized with drug-eluting beads (50 mg of epirubicin and 2 vials of Quadraspheres; Merit, South Jordan, UT). The particles were 50 to 100 μm in diameter when dry, which correlates to 200 to 400 μm in diameter when hydrated. Approximately, 75% of the prepared chemotherapy dose was administered. Postembolization angiography revealed near stasis in the segment VII vessel with sparing of the remaining right hepatic vessels. An additional segmental artery was subselected to evaluate for tumoral supply, and an angiogram was performed that revealed a patent segmental artery with branches supplying the inferior segments of the right lobe with no evidence of tumoral blush or extravasation (►Fig. 3). The sheath was removed

Fig. 2 Selective right hepatic angiogram identifies a large tumoral blush in segment VII (arrows).

Fig. 3 An additional segmental artery was injected revealing no feeding arteries and near stasis in segment VII. Note, there was no evidence of contrast extravasation/hemorrhage.

and hemostasis was achieved with a 6F Angio-Seal device (St. Jude Medical, St. Paul, MN).

The patient was admitted to the medical service for overnight observation. He had an abrupt drop in hemoglobin from 9.3 to 7.5 g/dL the following day, with an appropriate response in hemoglobin level following a 2 unit packed red blood cell transfusion. An unenhanced CT examination of the abdomen was performed demonstrating heterogeneous attenuation of the segment VII lesion with a focus of gas, consistent with recent TACE, and a large perihepatic/intra-abdominal hemorrhage (►Figs. 4 and 5).

The patient returned to interventional radiology for angiography and possible embolization.

Fig. 4 Nonenhanced computed tomography demonstrates heterogeneous attenuation of the segment VII lesion (arrow) with a focus of gas, consistent with recent transarterial chemoembolization, and heterogeneous predominantly high density perihepatic fluid (F), consistent with hemorrhage.

Fig. 5 Nonenhanced computed tomography demonstrates heterogeneous perihepatic fluid (arrows), consistent with hemorrhage.

Via a 5F left common femoral artery access, an RC1 catheter (Cook, Bloomington, IN) and Renegade STC microcatheter (Boston Scientific, Natick, MA) were used to access the right hepatic artery. A selective right hepatic angiogram demonstrated a patent vessel with active extravasation originating from a small branch supplying the previously embolized tumor (►Fig. 6). The microcatheter was advanced as distally as possible within the segmental artery, and several 2 and 3 mm microcoils were deployed. Postembolization angiography revealed successful occlusion (►Fig. 7). Following the procedure, there was no

Fig. 7 Post coil-embolization selective right hepatic angiogram reveals successful occlusion of the previous small branch extravasation.

clinical evidence of further bleeding and the patient had an uneventful recovery.

A CT examination in liver protocol approximately 1 month (►Fig. 8) and 7 months (►Fig. 9), as well as a magnetic resonance imaging examination approximately 11 months (►Fig. 10) after the TACE, demonstrated no evidence of residual or recurrent disease or evidence of further hemorrhage.

Fig. 6 Selective segmental right hepatic angiogram demonstrates a patent vessel with active extravasation (arrow) originating from a small branch supplying the previously chemoembolized tumor in segment VII.

Fig. 8 Enhanced computed tomography in portal venous phase 1 month after transarterial chemoembolization (TACE) demonstrates post-TACE defect (arrow) without evidence of residual or recurrent disease.

Fig. 9 Enhanced computed tomography in portal venous phase 7 months after transarterial chemoembolization (TACE) demonstrates a smaller post-TACE defect (arrow) without evidence of residual or recurrent disease.

Fig. 10 Enhanced magnetic resonance imaging 11 months after transarterial chemoembolization (TACE) demonstrates a post-TACE defect (arrow) without evidence of residual or recurrent disease.

Discussion

Spontaneous intraperitoneal hemorrhage is uncommon and has a broad differential diagnosis. Besides trauma and iatrogenic causes, gynecologic disorders (ectopic pregnancy, ruptured ovarian cysts, and tumors); solid organ malignancies including renal, hepatic and splenic tumors; vascular disorders including vasculitis and aneurysms; and coagulation disorders may all be implicated in peritoneal hemorrhage.^{3–5} Rupture of HCC following TACE is a rare etiology of intraperitoneal hemorrhage.

Pathophysiologic mechanisms leading to spontaneous HCC rupture and HCC rupture following TACE are not fully known. Zhu et al proposed several mechanisms that may be involved in spontaneous rupture of HCC. One proposed mechanism suggests that poor macrophage phagocytosis function results in vascular injury in patients with HCC.⁶

Another proposed mechanism suggests abnormal proliferation of elastin and degradation of collagen fibrils in the small arteries of HCC in patients with ruptured HCC when compared with nonruptured HCC.^{7–9} An additional mechanism proposes that there are fewer cell junctions and larger fenestrae in vascular endothelial cells in patients with ruptured HCC versus nonruptured HCC.⁸ Overall, vascular injury renders the vasculature stiff and weak, making it more prone to rupture. Reactive tissue edema causes rapid tumoral expansion, which precedes rupture.¹⁰ The combination of factors including reactive tissue edema associated with TACE in conjunction with the local vasculopathy associated with malignancy theoretically increases the risk of rupture after TACE.

Spontaneous rupture of HCC occurs in 3 to 26% of patients with HCC,¹¹ and mortality rates as high as 32% have been reported in the literature.^{11–16} Although there has been significant improvement in safety of chemoembolization of tumors, ruptured HCC is a rare but very serious complication following TACE.¹⁷ Several studies report the following risk factors associated with spontaneous rupture of HCC: large tumor size, capsular location of the tumor, contour protrusion and exophytic tumoral growth, thrombosis of the portal venous system, and occlusion of the feeding artery.¹³ The predisposing risk factors of HCC rupture following TACE are similar to those of spontaneous rupture of HCC.^{17–20}

Despite the high mortality rate associated with spontaneous rupture of HCC, the optimal management approach varies.^{9,11,12,15,21–26} While several studies conclude that embolization for spontaneously ruptured HCC is the treatment of choice, there is limited literature on the treatment of HCC rupture status post-chemoembolization. There is no consensus on which material to use for embolization, but the options include microcoils, particles, gelatin sponge, liquid embolics, and repeat chemoembolization. Irrespective of which agent is utilized, several complications can arise including rebleeding, worsening of liver failure, and postembolization syndrome. Conservative treatment is possible in hemodynamically stable patients without evidence of active bleeding. Emergency surgery was the treatment of choice for spontaneously ruptured hepatic tumors until the 1990s. However, with the advancements in minimally invasive treatments, surgery is limited to cases of critically unstable patients. These include emergent liver resections as well as hemostatic procedures, where the goal is hemostasis with packing and temporary hepatic pedicle clamping. Definitive surgery may be a consideration if the patient has rebleeding after embolization of the ruptured hepatic tumor.²⁷ It should be noted that difficulties in subsequent operations after bland or chemoembolization have been reported.²⁸

Although there is extensive literature on spontaneous rupture of HCC and subsequent arterial embolization as a mainstay of treatment, management of HCC rupture following TACE is less well described. Sun et al reported five patients who developed rupture of the tumor after TACE (in 1,005 HCC patients). Of the six patients, five patients underwent emergency selective arterial embolization for intractable hepatic capsular, perihepatic, and peritoneal hemorrhage that could

not be managed by conservative means. This review concluded that emergency arterial embolization is effective for hemostasis of ruptured HCC following TACE in patients who are hemodynamically unstable.²⁹

The case presented here demonstrates the effectiveness of transarterial embolization of HCC rupture after TACE. Additional studies are needed to determine the optimal treatment algorithm and identify patients who would most benefit from embolization.

References

- Clark TW. Complications of hepatic chemoembolization. *Semin Intervent Radiol* 2006;23(2):119–125
- Brown DB, Nikolic B, Covey AM, et al; Society of Interventional Radiology Standards of Practice Committee. Quality improvement guidelines for transhepatic arterial chemoembolization, embolization, and chemotherapeutic infusion for hepatic malignancy. *J Vasc Interv Radiol* 2012;23(3):287–294
- Kasotakis G. Spontaneous hemoperitoneum. *Surg Clin North Am* 2014;94(1):65–69
- Lucey BC, Varghese JC, Anderson SW, Soto JA. Spontaneous hemoperitoneum: a bloody mess. *Emerg Radiol* 2007;14(2):65–75
- Lucey BC, Varghese JC, Soto JA. Spontaneous hemoperitoneum: causes and significance. *Curr Probl Diagn Radiol* 2005;34(5):182–195
- Zhu LX, Geng XP, Fan SD. Mechanism of spontaneous rupture of hepatocellular carcinoma [in Chinese]. *Zhonghua Wai Ke Za Zhi* 2004;42(17):1036–1039
- Zhu LX, Meng XL, Fan ST. Elasticity of small artery in patient with spontaneous rupture of hepatocellular carcinoma. *Hepatol Res* 2004;29(1):13–17
- Zhu LX, Liu Y, Fan ST. Ultrastructural study of the vascular endothelium of patients with spontaneous rupture of hepatocellular carcinoma. *Asian J Surg* 2002;25(2):157–162
- Zhu LX, Geng XP, Fan ST. Spontaneous rupture of hepatocellular carcinoma and vascular injury. *Arch Surg* 2001;136(6):682–687
- Zhu LX, Wang GS, Fan ST. Spontaneous rupture of hepatocellular carcinoma. *Br J Surg* 1996;83(5):602–607
- Li J, Huang L, Liu CF, et al. Risk factors and surgical outcomes for spontaneous rupture of BCLC stages A and B hepatocellular carcinoma: a case-control study. *World J Gastroenterol* 2014;20(27):9121–9127
- Al-Mashat FM, Sibiany AM, Kashgari RH, et al. Spontaneous rupture of hepatocellular carcinoma. *Saudi Med J* 2002;23(7):866–870
- Kim HC, Yang DM, Jin W, Park SJ. The various manifestations of ruptured hepatocellular carcinoma: CT imaging findings. *Abdom Imaging* 2008;33(6):633–642
- Liu CL, Fan ST, Lo CM, et al. Management of spontaneous rupture of hepatocellular carcinoma: single-center experience. *J Clin Oncol* 2001;19(17):3725–3732
- Miyoshi A, Kitahara K, Kohya N, Noshiro H, Miyazaki K. Outcomes of patients with spontaneous rupture of hepatocellular carcinoma. *Hepatogastroenterology* 2011;58(105):99–102
- Tan FL, Tan YM, Chung AY, Cheow PC, Chow PK, Ooi LL. Factors affecting early mortality in spontaneous rupture of hepatocellular carcinoma. *ANZ J Surg* 2006;76(6):448–452
- Jia Z, Tian F, Jiang G. Ruptured hepatic carcinoma after transcatheter arterial chemoembolization. *Curr Ther Res Clin Exp* 2013;74:41–43
- Battula N, Srinivasan P, Madanur M, et al. Ruptured hepatocellular carcinoma following chemoembolization: a western experience. *Hepatobiliary Pancreat Dis Int* 2007;6(1):49–51
- Reso A, Ball CG, Sutherland FR, Bathe O, Dixon E. Rupture and intra-peritoneal bleeding of a hepatocellular carcinoma after a transarterial chemoembolization procedure: a case report. *Cases J* 2009;2(1):68
- Shin BS, Park MH, Jeon GS. Outcome and prognostic factors of spontaneous ruptured hepatocellular carcinoma treated with transarterial embolization. *Acta Radiol* 2011;52(3):331–335
- Buczkowski AK, Kim PT, Ho SG, et al. Multidisciplinary management of ruptured hepatocellular carcinoma. *J Gastrointest Surg* 2006;10(3):379–386
- Chen CY, Lin XZ, Shin JS, et al. Spontaneous rupture of hepatocellular carcinoma. A review of 141 Taiwanese cases and comparison with nonrupture cases. *J Clin Gastroenterol* 1995;21(3):238–242
- Hai L, Yong-Hong P, Yong F, Ren-Feng L. One-stage liver resection for spontaneous rupture of hepatocellular carcinoma. *World J Surg* 2005;29(10):1316–1318
- Rossetto A, Adani GL, Risaliti A, et al. Combined approach for spontaneous rupture of hepatocellular carcinoma. *World J Hepatol* 2010;2(1):49–51
- Tarantino L, Sordelli I, Calise F, Ripa C, Perrotta M, Sperlongano P. Prognosis of patients with spontaneous rupture of hepatocellular carcinoma in cirrhosis. *Updates Surg* 2011;63(1):25–30
- Yoshida H, Mamada Y, Tani N, et al. Long-term results of elective hepatectomy for the treatment of ruptured hepatocellular carcinoma. *J Hepatobiliary Pancreat Surg* 2008;15(2):178–182
- Darnis B, Rode A, Mohkam K, Ducerf C, Mabrut JY. Management of bleeding liver tumors. *J Vis Surg* 2014;7886(14):73
- Zhou WP, Lai EC, Li AJ, et al. A prospective, randomized, controlled trial of preoperative transarterial chemoembolization for resectable large hepatocellular carcinoma. *Ann Surg* 2009;249(2):195–202
- Sun JH, Wang LG, Bao HW, et al. Emergency embolization in the treatment of ruptured hepatocellular carcinoma following transcatheter arterial chemoembolization. *Hepatogastroenterology* 2010;57(99-100):616–619