Skin Necrosis Resulting from Nontarget Embolization of the Falciform Artery during Transarterial Chemoembolization with Drug-Eluting Beads

Mitchell T. Smith, MD¹ David Thor Johnson, MD, PhD¹ Matthew G. Gipson, MD¹

¹Department of Radiology, University of Colorado, Aurora, Colorado

Semin Intervent Radiol 2015;32:22–25

Address for correspondence Mitchell T. Smith, MD, Stop L954, Leprino, 12401 East 17th Avenue, Room 540 Aurora, CO 80045 (e-mail: mitchell.smith@ucdenver.edu).

Abstract

Keywords

- chemoembolization
- complication
- nontarget embolization
- embolization
- interventional radiology

Intra-arterial embolic therapies are a mainstay of liver-directed therapies to palliate symptoms, improve survival, and bridge patients to transplantation. Vascular anatomy and type of embolic used can lead to complications of nontarget embolization with varying clinical consequences. This case report describes a rare, nontarget embolization of the falciform artery leading to supraumbilical skin necrosis.

Objectives: Upon completion of this article, the reader will be able to describe the importance of nontarget embolization involving the falciform artery, as well as preventative measures and management of such complications.

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: Tufts University School of Medicine 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.

Hepatocellular carcinoma is the third leading cause of cancer deaths worldwide with an estimated worldwide incidence of 500,000. Intra-arterial embolic therapies are a mainstay of liver-directed therapies used to palliate symptoms, improve survival, and bridge patients to transplantation.

Vascular anatomy and the type of embolic agent used can lead to complications of nontarget embolization with varying clinical consequences. This case report describes a rare, nontarget embolization of the falciform artery leading to supraumbilical skin necrosis.

Case

A 66-year-old man with history of cirrhosis secondary to hepatitis B virus presented to a multidisciplinary liver cancer clinic with a chief complaint of increased fatigue and weakness. An abdominal magnetic resonance imaging was performed during the initial evaluation, which demonstrated two right-sided hepatic lobe hemangiomas and an indeterminate lesion in the left hepatic lobe measuring approximately 5 cm (► **Fig. 1**). Serum α fetal protein at that time was 355 ng/mL. A biopsy was performed at an outside hospital that demonstrated a grade 2 moderately differentiated hepatocellular carcinoma with extensive tumor necrosis, as well as background liver that showed changes of chronic hepatitis with stage 4 fibrosis. The patient was referred to the interventional radiology clinic for consideration of liver-directed therapy in

Fig. 1 (a, b) Axial dynamic MRI images demonstrate two hemangiomas in the right hepatic lobe and a stellate lesion spanning segments 2, 3, and 4A corresponding to the patient's known HCC (arrows).

anticipation of either downstaging for possible transplant or volume reduction for surgical resection.

Transarterial chemoembolization with drug-eluting beads (DEB-TACE) was performed in standard fashion. Using ultrasound guidance and micropuncture technique, the right common femoral artery was accessed with placement of a 5-french vascular sheath. The celiac trunk was accessed using an SOS omni catheter (Cook, Inc., Bloomington, IN), and celiac arteriography was performed demonstrating two right hepatic hemangiomas and an early enhancing lesion in the left hepatic lobe spanning segments 2, 3, and 4A. A Renegade STC microcatheter (Boston Scientific Corp., Marlborough, MA) was advanced into the left hepatic artery, and angiography was performed demonstrating peripheral tumoral enhancement and areas of contrast pooling (►Fig. 2). There was no significant arteriovenous shunting visible on angiography. Chemoembolization was performed from the left hepatic artery near the bifurcation of segments 2, 3, and 4A using one vial of 70 to 150 μ m M1 LC beads and one vial of 100 to 300 μ m LC beads (BTG International Inc., West Conshohocken, PA), each loaded with 75 mg of doxorubicin. Completion arteriograms were performed from the left and common hepatic arteries, each demonstrating decreased flow to the left hepatic lobe.

The patient tolerated the procedure well and was monitored overnight for complications including postembolization syndrome, bleeding, infection, and hepatic encephalopathy. The patient was discharged the morning after his procedure;

Fig. 2 Angiogram via a coaxial microcatheter in the left hepatic artery demonstrating peripheral tumoral enhancement and contrast pooling, compatible with HCC-related neovascularity.

he was tolerating oral intake with mild postprocedural abdominal pain that was managed by oral narcotics.

Two weeks after the procedure, the patient complained of a small area of "red welts" that developed 24 hours post-procedure that overtime became purplish in color and were associated with skin peeling. The welts were lumpy and associated with pain that the patient described as "achy." The patient was evaluated in the Interventional Radiology clinic, and physical examination demonstrated multiple, small ovoid red and mildly indurated bumps above the umbilicus which now were not itchy or painful (►Fig. 3). Review of the patient's angiograms and CT scans when combined with the symptoms indicated that these physical exam findings represented nontarget embolization of drug-eluting beads to the falciform artery (►Figs. 4 and 5).

The patient's symptoms gradually improved, and he underwent a second round of DEB-TACE following Gelfoam embolization of the proximal falciform artery. There was no worsening of periumbilical symptomatology following the second DEB-TACE procedure.

Discussion

Nontarget embolization is a recognized complication of transarterial liver-directed therapy and has been described

Fig. 3 Photograph of the patient's periumbilical region showing the small ovoid bumps with a small area of skin ulceration.

Fig. 4 Postembolization CT demonstrating good tumoral response with lack of enhancement in the central portion of the tumor with persistent contrast enhancement along the periphery compatible with viable tumor (arrowheads).

Fig. 5 Same image as Fig. 2, demonstrating diagonal vessel from the left hepatic artery corresponding to the falciform artery (arrowheads).

for the cystic, pancreaticoduodenal, right gastric, and falciform arteries.¹

The cystic artery has a variable anatomic origin, but usually arises from the right hepatic arterial supply. Chemical cholecystitis or more severe postembolization syndrome can be observed following intra-arterial treatments proximal to the origin of the cystic artery.² If possible, treatment distal to the origin is preferred, although proximal treatment is generally well tolerated with antibiotic prophylaxis prior to and after the procedure. In severe cases, chemical cholecystitis may require emergent cholecystectomy.

The pancreaticoduodenal arteries arise from the gastroduodenal artery 78% of the time, and provide a vascular bed that feeds the pancreas and duodenal bulb. Enteric vascular reflux of embolic can lead to duodenal ulceration and necrosis similar to right gastric arterial nontarget embolization.³ Asymptomatic elevation of serum pancreatic enzymes can be noted in up to 40% of patients treated with conventional, lobar TACE.⁴ Symptomatic acute pancreatitis is observed in fewer than 4% of patients, and typically resolves with medical management (although there are case reports of fatalities).⁵ Prophylactic embolization of the gastroduodenal artery and/

or selective placement of the microcatheter can help to avoid this complication.

The right gastric artery demonstrates a highly variable origin, arising from the proper or left hepatic arteries approximately 75% of the time. Nontarget embolization of the right gastric artery can lead to gastric ulcers, necrosis, and perforation.⁶ Prophylactic embolization is routinely used during selective internal radiation therapy (SIRT) if the treatment zone includes the origin of the right gastric artery or the right gastric artery is the first, most proximal run-off vessel from the treatment site.

The falciform artery was first described in 1753 by Albrecht von Haller and is visualized on celiac angiography less than 25% of the time. The classic anatomic position of the falciform artery has been described as running in an oblique orientation from the left intersegmental fissure to the anterior abdominal wall.¹ Anatomic studies have demonstrated the origin of the falciform artery to be either the middle hepatic artery or the left hepatic artery.¹ When visualized, prophylactic embolization of the falciform artery or placement of ice packs on the periumbilical area has been considered mandatory during SIRT to prevent nontarget embolization, which typically results in localized mid-abdominal pain that can last several weeks. Prophylactic embolization has not been routinely recommended for TACE, although there are case reports in the literature of nontarget embolization.

The hepatic falciform artery is present in up to 67% of autopsy specimens and is a small terminal branch of the middle or left hepatic arteries that course around the umbilicus to anastomose with branches of the superior and inferior epigastric arteries. Although present on postmortem evaluation in the majority of patients, its visibility on angiography varies from 2 to 24.5%.⁷⁻⁹ Given its relatively low incidence during angiography, reports of complications from embolization are rare and confined to case reports in the literature. A possible explanation for the limited number of case reports is that either flow in the falciform artery is limited during angiographic run timing and/or volume, or that particle size may influence nontarget embolization. Most of the case reports of nontarget embolization involve lipiodol emulsifications that show occlusion of vessels to <15 μ m in diameter, which are small enough to stain the portal venous track or smaller drug-eluting beads.¹⁰ When the falciform artery is visualized on angiography, preventive measures such as coil or large particle embolization coupled with ice packs on the upper abdomen may help to prevent this rare complication.

There have been at least four cases in the literature of post-TACE nontarget falciform artery embolization that resulted in patient symptomatology. Kim et al reported painless, epigastric subcutaneous nodules that had overlying skin pigmentation after DEB-TACE using 100 to 300 μ m particles loaded with 50 mg doxorubicin.¹¹ Excision of the lesion demonstrated fat necrosis and a drug-eluting bead in the sample.¹¹

Lin et al performed conventional TACE using 4 mL of lipiodol with 30 mg epirubicin and 6 mg of mitomycin-C injected into the left hepatic artery; devascularization was performed using gelatin sponge embolization.¹² On postoperative day 1, the patient exhibited supraumbilical skin

induration that was tender to the touch. The patient was treated with oral nonsteroidal anti-inflammatory medications and the symptoms gradually subsided. Using a similar regime of ethiodized oil mixed with chemotherapeutics and followed by Gelfoam embolization, Baysal et al observed nontarget embolization that resulted in skin thickening and discoloration that evolved into a sclerotic plaque with hyperpigmentation¹³; a punch biopsy performed showed dermal sclerosis and fat necrosis compatible with extravasation of chemotherapeutics. At 8 months, the lesion was still visible but no longer tender to palpation. Kanzaki et al reported immediate postoperative pain in the epigastric region followed 2 days later by a skin rash, after a segment 4 lesion was treated with lipiodol and epirubicin.¹⁴ Postprocedural steroids were given on postprocedure days 3 and 7, and 5 days later the pain resolved. Subcutaneous nodules were present on postoperative day 7, and it took 10 months for the skin rash to completely heal.

Nontarget embolization to the falciform artery, although rare, can cause significant complications. Careful evaluation for the filling of this artery and attempted preventative measures such as prophylactic embolization or placement of ice packs near the umbilicus may be helpful. Recognition of the complication, or the potential for the complication, is mandatory for any interventional radiologist performing these liver-directed transarterial therapies.

References

- 1 Liu DM, Salem R, Bui JT, et al. Angiographic considerations in patients undergoing liver-directed therapy. *J Vasc Interv Radiol* 2005;16(7):911–935
- 2 Goin J, Dancey J, Roberts C, Sickles C, Leung D, Soulen M. Comparison of post-embolization syndrome in the treatment of patients with unresectable hepatocellular carcinoma: trans-catheter arterial chemo-embolization versus yttrium-90 glass microspheres. *World J Nucl Med* 2004;3:49–56
- 3 Hirakawa M, Iida M, Aoyagi K, Matsui T, Akagi K, Fujishima M. Gastroduodenal lesions after transcatheter arterial chemo-embolization in patients with hepatocellular carcinoma. *Am J Gastroenterol* 1988;83(8):837–840
- 4 Khan KN, Nakata K, Shima M, et al. Pancreatic tissue damage by transcatheter arterial embolization for hepatoma. *Dig Dis Sci* 1993;38(1):65–70
- 5 Addario L, Di Costanzo GG, Tritto G, Cavaglià E, Angrisani B, Ascione A. Fatal ischemic acute pancreatitis complicating transcatheter arterial embolization of small hepatocellular carcinoma: do the risks outweigh the benefits? *J Hepatol* 2008;49(1):149–152
- 6 Murthy R, Brown DB, Salem R, et al. Gastrointestinal complications associated with hepatic arterial Yttrium-90 microsphere therapy. *J Vasc Interv Radiol* 2007;18(4):553–561, quiz 562
- 7 Baba Y, Miyazono N, Ueno K, et al. Hepatic falciform artery. Angiographic findings in 25 patients. *Acta Radiol* 2000;41(4):329–333
- 8 Gibo M, Hasuo K, Inoue A, Miura N, Murata S. Hepatic falciform artery: angiographic observations and significance. *Abdom Imaging* 2001;26(5):515–519
- 9 Williams DM, Cho KJ, Ensminger WD, Ziessman HA, Gyves JW. Hepatic falciform artery: anatomy, angiographic appearance, and clinical significance. *Radiology* 1985;156(2):339–340
- 10 Kruskal JB, Hlatky L, Hahnfeldt P, Teramoto K, Stokes KR, Clouse ME. In vivo and in vitro analysis of the effectiveness of doxorubicin combined with temporary arterial occlusion in liver tumors. *J Vasc Interv Radiol* 1993;4(6):741–747
- 11 Kim HY, Bae SH, Park CH, et al. Supraumbilical subcutaneous fat necrosis after transcatheter arterial chemoembolization with drug-eluting beads: case report and review of the literature. *Cardiovasc Intervent Radiol* 2013;36(1):276–279
- 12 Lin CC, Wu DK, Shih PMC, Liu GC, Chuang WL. Supraumbilical skin rash and fat necrosis after transcatheter arterial chemoembolization: a case report. *Kaohsiung J Med Sci* 2004;20(1):36–40
- 13 Baysal T, D'Agostino HB, Serra EE, Valji K, Rose SC, Kinney TB. Supraumbilical dermal sclerosis and fat necrosis from chemo-embolization of hepatocellular carcinoma. *J Vasc Interv Radiol* 1998;9(4):645–647
- 14 Kanzaki H, Nouse K, Miyahara K, et al. A case of hepatocellular carcinoma with skin injury of the upper abdominal wall after transcatheter arterial chemoembolization: a case report. *Cases J* 2009;2:7197