Transarterial chemoembolization of hepatocellular carcinoma using antireflux catheter

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Abstract
Transarterial chemoembolization is an effective treatment option for patients with intermediate and advanced hepatocellular carcinoma. There are several complications that can occur with this procedure, most of which are the result of nontarget embolization. One such complication is acute cholecystitis following nontarget embolization of the cystic or accessory cystic arteries, which usually occurs secondary to reflux of the embolic agent. Our case demonstrates utilization of the Surefire Infusion System to prevent this complication. This antireflux catheter was very effective in a case where vessel anatomy created a substantial risk for a clinically significant nontarget embolization of the cystic artery.

Keywords
Transarterial chemoembolization, Hepatocellular carcinoma, Antireflux catheter, Cystic artery

1 Introduction
Hepatocellular carcinoma (HCC) is currently the fifth most common malignant primary neoplasm in the world and is increasing in incidence. There are several therapies available for this tumor that is either curative or palliative. Curative therapies include surgical resection, percutaneous ablation and liver transplantation. Transarterial chemoembolization (TACE) is an effective alternative for patients with advanced HCC. HCC tumors receive essentially all of their vascular supply from the hepatic artery. TACE exploits this fact by eliminating the vascular supply to the tumor, while attempting to preserve the vascular supply to the normal hepatic parenchyma via the portal venous system [1-3].

The TACE procedure is not without risk, however. A frequent complication of this procedure is nontarget embolization of tissues supplied by the hepatic arteries and their branches. One observed complication is cholecystitis and subsequent gallbladder infarction, which can occur secondary to reflux of embolic agents into the cystic or accessory cystic arteries [4]. The Surefire Infusion System (SIS) antireflux catheter is a new device with the intended purpose of reducing nontarget embolization, as well as improving tumor penetration by the embolic therapy. This catheter has been used to optimize several interventional procedures, especially Yttrium-90 radioembolization of hepatic tumors. This case demonstrates a novel utilization of this device for a complicated TACE.
2 Case report

Preparation of this retrospective case report received institutional acknowledgement from the office of research administration. A 69-year-old African-American female with past medical history of hepatitis C was referred to the interventional radiology department for management of advanced hepatocellular carcinoma. A liver biopsy 2 years prior to presentation demonstrated chronic active hepatitis, grade 3, and stage 3. She reported a 15-pound unintentional weight loss over the 3 prior months. Family and social histories were unremarkable. On physical exam, the patient was afebrile and normotensive. She was anicteric without abdominal tenderness. She had strong bilateral femoral and distal pulses.

A screening sonogram (see Figure 1) at the outside facility demonstrated a right hepatic lobe mass. Per the medical record, her alpha-fetoprotein levels had recently been trending up. A diagnostic contrast-enhanced MR further demonstrated a hypervascular, heterogeneously enhancing mass in segment 8 measuring 7.5 cm × 6.8 cm with numerous adjacent satellite lesions (see Figure 2), consistent with hepatoma. TACE was offered to the patient, as other treatment options were suboptimal.

The right common femoral artery was accessed for transarterial chemoembolization. Selective superior mesenteric arteriogram demonstrated a replaced right hepatic artery (see Figure 3a). Celiac arteriogram demonstrated left and middle hepatic arteries arising from the proper hepatic artery. A selective replaced right hepatic arteriogram demonstrated a cystic artery originating very near the branching point of the right hepatic artery (see Figure 3b). The Surefire device was advanced just beyond the origin of the cystic artery, the expandable tip was deployed, and the right hepatic artery branches were embolized with 50 mg of doxorubicin-containing QuadraSphere® drug-eluting beads (see Figure 3c). A post embolization replaced right hepatic arteriogram demonstrated pruning of the vascularity supplying the tumor, as well as patency of the cystic artery without evidence of nontarget embolization (see Figure 3d).

A follow-up CTA/CTV of the abdomen demonstrated a significant response to therapy (see Figure 4).

![Figure 1. Initial surveillance sonogram demonstrating liver mass. Longitudinal image of the right hepatic lobe demonstrates a heterogeneous mass (white arrows) with cystic components.](image1)

![Figure 2. Initial diagnostic liver MRI prior to TACE. Coronal T1 LAVA post-contrast sequence of the abdomen demonstrates a well-circumscribed, heterogeneous mass (white arrowheads) in the right hepatic lobe measuring 7.5 cm × 6.8 cm with washout. There are numerous adjacent satellite nodules scattered throughout segment 5 and 6.](image2)
Figure 3. Transarterial chemoembolization of hepatocellular carcinoma. (a) The right superficial femoral artery was accessed and SMA was injected demonstrating a replaced right hepatic artery (black arrow). (b) Replaced right hepatic artery arteriogram demonstrates cystic artery (black arrows) originating near the branching point of the right hepatic artery. (c) Late injection of the right hepatic artery with deployed Surefire device just distal to the takeoff of the cystic artery (black arrow) demonstrates arterial blush of the HCC (black arrowheads). (d) Post embolization image demonstrates patency of the cystic artery (black arrow), as well as pruning of the arteries supplying the mass (black arrowheads).

Figure 4. Follow-up CTA/CTV of the abdomen 6 weeks after TACE. Coronal CTA/CTV of the abdomen demonstrates a well-circumscribed necrotic mass in the right hepatic lobe (white arrowheads), which has significantly decreased in size and vascularity.
3 Discussion

Hepatocellular carcinoma has an increased incidence in patients with cirrhosis or chronic inflammation, such as that seen in viral hepatitis or hepatic steatosis. HCC metastasizes via invasion into the portal and hepatic veins, biliary ducts, and tumor capsule. During hepatocarcinogenesis, venous supply evolves from hepatic to portal. Invasion of the portal sinusoids by tumor leads to intrahepatic satellite nodules. Early detection of hepatocellular carcinoma is therefore critical to improve survival. All current guidelines recommend ultrasound surveillance, and two advocate concurrent use of serum biomarkers (i.e. alpha fetoprotein). Once an abnormality is detected, diagnostic imaging is obtained with multiphasic CT and/or contrast enhanced MR \[1, 2\].

TACE is a continuously evolving procedure. The Society of Interventional Radiology (SIR) currently recognizes the conventional TACE as the standard of care for Barcelona Clinic Liver Cancer (BLCL) intermediate Child-Pugh class A disease. Conventional and drug-eluting bead (DEB) TACE have also shown benefit in advanced-stage HCC. In general, TACE has trended towards more selective embolization of tumors. In 2008, Irie et al. demonstrated better deposition of lipiodol with balloon-occluded TACE. A recent study by Prajapati, et al demonstrated lower toxicity and increased survival by utilizing smaller drug-eluting beads \[3, 5\]. Therefore, a more selective embolization with prevention of reflux would be in keeping with this trend and result in better outcomes.

Transarterial chemoembolization-related hepatic and biliary damage (TRHBD) can be a complication of TACE. TRHBD consists mainly of hepatic insufficiency, liver abscess, intrahepatic biloma formation and cholecystitis. These unintended side effects are mainly due to nontarget embolization of adjacent vessels supplying biliary structures or normal hepatic parenchyma. There are numerous reported cases of cholecystitis and gallbladder infarction following TACE \[4, 6\]. These occur due to nontarget embolization of the cystic and/or accessory cystic arteries. These arteries arise from the common, right or left hepatic arteries. Reflux of embolic agent into these arteries is often inevitable, especially if the origin of the cystic artery is near the site of embolization \[4, 6\].

The Surefire Infusion System (SIS) (Surefire Medical, Inc., Westminster, Colorado) is an antireflux catheter approved by the United States Food and Drug Administration. The SIS has been shown to prevent reflux, decrease blood pressure downstream, and increase antegrade flow by increasing hepatopetal flow in hepatocentric arteries \[7\]. The SIS has a funnel-shaped, pliant braided polymer self-expanding tip that partially collapses during systolic and diastolic forward flow of blood within the arterial lumen. During retrograde flow, the tip opens like an umbrella, occluding the lumen and preventing reflux of embolic agents. A porcine model study by Arepally et al. quantified the amount of reflux, demonstrating near-complete elimination of reflux with increased distal penetration of embolic substance \[8\]. Several recent studies comparing the SIS to traditional coil embolization during Yttrium-90 microsphere radioembolization procedures have demonstrated increased safety and efficiency with the SIS system \[9-11\].

In summary, TACE remains a staple procedure in the treatment of intermediate and advanced stage HCC, and continues to evolve and improve. This procedure can be technically difficult when tumor location or anatomy make hepatobiliary damage from nontarget embolization likely. The Surefire Infusion System is a new device that almost completely eliminates reflux of embolic agents and can be a useful tool in preventing nontarget embolization in difficult cases. In this case, the SIS facilitated a successful embolization without any signs of nontarget embolization in a case that would have required subselective embolization, and perhaps a much less favorable result, with traditional end hole microcatheter.

References

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