Radioembolization Complicated by Nontarget Embolization to the Falciform Artery

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ABSTRACT

The most common application of radioembolization is in the treatment of primary and secondary liver tumors, and the most common radioisotope is Yttrium-90. This form of treatment has proven to be successful in achieving reduction of tumor size and ultimately improving survival. Fatigue and nausea/vomiting are the most common side effects related to radioembolization and are usually self-limiting. This report describes a case of abdominal pain caused by shunting of yttrium-90 microspheres to the anterior abdominal wall via a patent hepatic falciform artery. This case highlights the need for vigilant angiography and awareness of the falciform artery with prophylactic embolization when necessary/warranted.

KEYWORDS: Radioembolization, yttrium-90, falciform artery

CASE REPORT

The patient is a 57-year-old woman diagnosed with stage II colorectal cancer in December 2004. She underwent a left hemicolectomy and was subsequently treated with FOLFOX and Avastin. In January 2007, she was diagnosed with liver metastases and her regimen was changed to Erbitux and Irinotecan (CPT-11). Secondary to progressive hepatic metastases, she was referred to the interventional oncology service for liver-directed therapy. Given her progressive hepatic metastases and failure on systemic chemotherapy, preserved performance status and hepatic functions, the patient was deemed a good candidate for radioembolization.

Planning angiography revealed nonvariant hepatic anatomy. The right gastric artery, which arose from the proximal left hepatic artery, was coil embolized. Technetium (Tc) 99-labeled macroaggregated albumin was delivered into the right hepatic artery. Planar and tomographic imaging was performed to calculate the

degree of hepatopulmonary shunting. The relative pulmonary uptake was estimated from geometric mean data to be 10%, a shunt magnitude acceptable for radioembolization.

Radioembolization was initially performed to the right hepatic lobe. The patient tolerated the procedure well and returned for treatment of the left hepatic lobe 2 months later. A microcatheter was advanced into the left hepatic artery, beyond the previously coil embolized right gastric artery, and angiography demonstrated hypervascular tumors in hepatic segments II, III, and IV. Radioembolization to the left hepatic lobe was performed.

Imaging follow-up revealed a decrease in the size and enhancement of multiple hepatic tumors and no evidence of extrahepatic metastatic disease. However, the patient's CEA levels remained slightly elevated and there was a focal tumor in segment 4 that demonstrated increased uptake on a positron emission tomography

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Figure 1 (A) A 57-year-old woman with metastatic colorectal cancer described in the case presentation. Superselective angiogram of the segment 4 branch of the left hepatic artery, arterial phase. A diminutive hepatic falciform artery (arrows) is seen arising from the left hepatic artery. Although the artery was identified, its diminutive size and tortuosity prevented coil embolization. After radioembolization, the patient subsequently experienced supraumbilical pain, which is theorized to be secondary to nontarget administration of yttrium-90 to the patent hepatic falciform artery. (B) Initial planning angiography from the same patient in (A). Selective angiogram of the proper hepatic artery, arterial phase. Retrospective analysis of the planning angiography from the patient described in the case presentation demonstrates questionable visualization of the falciform artery (arrow). This emphasizes the need for superselective angiography when identifying the falciform artery.

(PET) scan. Therefore, it was decided to repeat selective radioembolization to segment IVA and IVB. During the final treatment, the microcatheter was advanced selectively into the segment IV branch of the left hepatic artery. Angiography revealed a hypervascular tumor and the falciform artery (Fig. 1A). Secondary to its diminutive appearance and tortuous course, this artery could not be coil embolized. Radioembolization was performed with a 5 GBq vial of yttrium-90 glass microspheres.

Unlike the previous radioembolization procedures, the patient experienced severe pinpoint pain cephalad to the umbilicus, just right of the midline. The pain was eased with nonsteroidal antiinflammatory drugs, but required narcotics for abatement. The abdominal pain eventually resolved after several months.

DISCUSSION

The liver is the most common site of distant metastatic spread from colorectal cancer. Approximately 25% of

patients present with synchronous disease and an additional 30% to 40% develop hepatic metastases during their course of the disease.¹ According to Iñárraigui et al, elderly patients with colorectal carcinoma metastatic to the liver have a median overall survival of 10 months (95% CI, 5.2–14.7) and younger patients have 13 months (95% CI, 7.0–18.9; $p = .3$).²

Over the last 2 decades, hepatic resection has been established as the standard therapy for resectable metastases, and many studies have shown that resection offers the only chance of long-term survival and cure.^{3,4} Despite good long-term survival and improving modern chemotherapy, most patients will experience recurrence of disease after hepatic resection. The challenge remains to reduce the burden of liver disease to enable greater patient eligibility for resection, lengthen survival for those who remain unsuitable for surgery, or provide an alternative therapy to completely eradicate the metastatic lesions. Therefore, much effort has been placed on the integration of radioembolization into the treatment paradigm.

Radioembolization is a therapeutic procedure that involves the delivery of a radiation source directly to the microvasculature of hepatic tumors via the arterial route as a form of brachytherapy. The most common use of radioembolization is in the treatment of primary and secondary liver tumors. The carriers of the radioactive isotope are microspheres; usually made up of either glass or resin (TheraSphere[®], MDS Nordion, Kanata, ON, Canada; or SIR-Spheres[®], Sirtex Medical, Lane Cove, Australia, respectively). The most common radioisotope used is yttrium-90. This form of therapy has proven to be successful in improving the quality of life and prolonging survival.⁵ Fever and

nausea/vomiting are the most common side effects related to radioembolization and are usually self-limiting.⁶ However, a few uncommon complications have also been reported in the literature: radiation hepatitis, cholecystitis, peptic ulceration, radiation pneumonitis, radiation dermatitis/supraumbilical skin rash, and abdominal pain.^{6,7}

Nontarget administration of radioactive yttrium-90 microspheres into a patent hepatic falciform artery has been postulated to cause a localized midabdominal burning sensation and pain. The hepatic falciform artery most commonly arises as a small terminal branch off the proper or left hepatic artery, runs through the hepatic

Figure 2 An 83-year-old woman with hepatocellular cancer. (A) Selective angiogram of the left hepatic artery, arterial phase. The hepatic falciform artery (arrows) arises from the left hepatic artery and follows a characteristic caudal and medial L-shaped course. (B) Superselective angiogram of the falciform artery demonstrates tortuosity along the proximal aspect of the vessel (arrows). (C) Postcoil embolization of the hepatic falciform artery. Radioembolization therapy was performed successfully without supraumbilical abdominal pain.

falciform ligament, distributes itself around the umbilicus, and communicates with branches of the superior and inferior epigastric arteries.^{8,9} On angiography, the hepatic falciform artery is seen following a characteristic L-shaped caudal and medial course on the posterior surface of the anterior abdominal wall from its origin off the proper or left hepatic artery⁸ (Fig. 2A). Furthermore, the localized tortuosity of the artery serves as an important landmark in its identification (Fig. 2B).¹⁰ Given the anatomic distribution of the artery, shunting of the radioactive microspheres into the artery can lead to supraumbilical abdominal pain and possibly other skin-related complications.

Transcatheter arterial chemoembolization has also been widely used to treat advanced hepatocellular carcinoma that cannot be treated with systemic chemotherapy or surgical resection. Many studies have also reported complications of supraumbilical skin rash and pain associated with chemoembolization.¹¹ Similarly, it has been hypothesized that these side effects might be caused by the distribution of chemotherapeutic agents through the hepatic falciform artery.¹¹

The presence of an angiographically identifiable falciform artery varies, and is reportedly found in ~25% of cases.¹⁰ However, a patent falciform artery has been identified in as many as 67% of postmortem dissections.¹² This high degree of variation in identification may be due to the slow velocity of the small terminal

branches of the falciform artery, which prevents the vessel from being visualized during the early arterial angiographic phases. According to Gibo et al, the hepatic falciform artery is more easily recognized in the capillary or venous phase of angiography because the contrast medium remains within this small vessel (Fig. 3).¹⁰ Other factors such as the need for adequate superselective catheterization of the left hepatic artery, previous abdominal surgery, and variable contrast agent bolus delivery also contribute to the wide discrepancy in identification of the falciform artery angiographically. In addition, the left hepatic artery forms an anastomotic network with the superior epigastric artery, which flows toward the falciform artery, which may washout the contrast within the falciform artery.¹³ As a result of this competing blood flow, the contrast agent may not be seen in the falciform artery. Therefore, a higher flow rate and prolonged imaging may be required to identify the falciform artery. Conversely, patients who have developed adhesions around the hepatic falciform ligament after laparotomy or have a stenosis or occlusion of the hepatic artery, the hepatic falciform artery may become enlarged and easily demonstrated on angiography.¹⁰

In addition to assessing lung shunting, hepatic arterial scintigraphy with technetium (Tc) 99m macroaggregated albumin (MAA) can also demonstrate the presence of extrahepatic deposition. The extrahepatic deposition of the radiotracer in the anterior abdominal

Figure 3 38-year-old woman with history of metastatic cervical cancer. (A) Digital subtraction proper hepatic angiogram, arterial phase. A diminutive hepatic falciform artery (arrows) is faintly seen arising from the left hepatic artery in the arterial phase. (B) Digital subtraction common hepatic angiogram, venous phase. On the more delayed images, the hepatic falciform artery arising from the left hepatic artery (arrows) is more conspicuous because the contrast medium remains in the vessel until the venous phase.

wall is highly indicative of a patent hepatic falciform artery (Fig. 4). Williams et al presented a case in which a postprocedural Bremsstrahlung scan confirmed the presence of increased uptake in the liver as well as in the anterior abdominal wall. Upon further scrutiny of the corresponding hepatic angiogram, a dilated falciform artery arising from the left hepatic artery was identified and explained the increased activity in the anterior abdominal wall.⁸

Figure 4 58-year-old man with progressive metastatic neuroendocrine disease on standard care therapy presented for radioembolization planning. Tc-99m macroaggregated albumin single photon emission computed tomography (MAA SPECT) fused with computed tomography, axial (A) and sagittal (B) views. There is increased activity in the anterior abdominal wall (arrows). Comparison with the planning angiography demonstrated a falciform artery originating from a variant segment 4 branch, which arose directly off the right hepatic artery. The patent falciform artery was coil embolized prior to the patient receiving radioembolization to the right hepatic lobe. The patient underwent successful radioembolization without postprocedural supraumbilical abdominal pain.

Advances in catheter and guidewire technology, as well as in embolic agents, have enabled interventionalists to perform safe and effective procedures on small vessels such as the falciform artery. When the targeted hepatic lesions lie within the left hepatic lobe, a patent hepatic falciform artery is identified, and the microcatheter cannot be placed distal to the falciform artery for infusion, embolization is recommended to prevent postprocedural supraumbilical abdominal pain. Antegrade embolization via the left or middle hepatic artery is the most effective method (Figs. 2C and 5B). Using superselective catheterization, microcoils are the most effective means to occlude this artery.

With the growing popularity of liver-directed therapies such as chemoembolization and radioembolization for primary and secondary hepatic tumors, the understanding of possible toxicities and establishing standard treatment protocols have become increasingly important. This case report serves to highlight a potential risk of nontarget administration of radioactive yttrium-90 microspheres into a patent falciform artery, and it emphasizes the need to carefully evaluate the preinfusion angiogram and embolize any nonhepatic artery. Although the falciform artery was not identified on this patient's preinfusion angiogram or the first 2 radioembolization therapies, a selective angiogram of the segment 4 branch of the left hepatic artery during the final treatment demonstrated a patent hepatic falciform artery (Fig. 1). This further confirms the need for superselective angiogram when trying to identify the falciform artery. Due to the tortuosity and diminutive caliber, the hepatic falciform artery in our patient was not embolized and she inevitably developed midabdominal pain, which is felt to be secondary to unintentional shunting of the radioactive microspheres into the patent vessel. However, in cases similar to this scenario in which the falciform artery is identified but difficult to embolize it is still recommended to proceed with the liver-directed therapy. Given the self-limiting complications associated with liver-directed treatment through a patent falciform artery, the benefits of treating the hepatic lesions certainly outweigh the risks. Patients who experience abdominal pain due to a nonembolized patent hepatic falciform artery, as in this case, can be treated expectantly. Although this is an infrequent complication of therapy, recognition of the symptoms and proper palliative therapies enable effective therapy.

In summary, meticulous effort made in identifying and embolizing any nonhepatic artery arising from the hepatic artery, such as the falciform artery, will avoid potential adverse risks related to inadvertent nontarget administration of yttrium-90 and ideally improve the safety profile of these therapies.

Figure 5 A 61-year-old male with unresectable multifocal hepatocellular carcinoma. (A) Digital subtraction superselective angiogram of the left hepatic artery, arterial phase. Partial tortuosity and distal branching of the hepatic falciform artery (white arrows) arising from the left hepatic artery is visualized. A tumor stain is also seen in the left hepatic lobe (black arrows). (B) Superselective angiogram of the left hepatic artery, arterial phase. Coil embolization of the proximal hepatic falciform artery prevents opacification of the vessel. The patient underwent successful radioembolization without postprocedural supraumbilical abdominal pain.

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