Outcomes after radioembolization involving the phrenic artery: Case series and literature review

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Abstract

Purpose:
To evaluate outcomes after radioembolization of the phrenic artery, versus particle or coil embolization of the phrenic artery followed by radioembolization of the hepatic artery.

Methods:
An IRB-approved retrospective review was performed of 611 radioembolization mapping and treatment angiograms in 248 patients with primary or secondary liver cancer. In 10 of 248 (4%) patients, the phrenic artery was either included in the radioembolization treatment (*n*=1), or was embolized using coils (*n*=4), particles (*n*=4), or both (*n*=1) at the time of mapping or treatment. Complications were analyzed, as well as response by RECIST at 2-3 months after treatment.

Results:
In 1 patient, a pericardiophrenic artery arising from the left hepatic artery was included in the radioembolization treatment. This patient developed dyspnea and transient elevation of the left hemidiaphragm, which resolved 5 weeks after treatment. In 5 patients, particle embolization of phrenic artery supplying tumor was performed prior to radioembolization of the hepatic artery. These patients had no complications. Particle embolization of tumor supplied by phrenic artery resulted in a similar response rate, compared to radioembolization of tumor supplied by the hepatic artery. In 3 patients, coil embolization of phrenic artery not supplying tumor was performed to prevent non-target embolization. These patients had no complications. In 1 patent, coil embolization of phrenic artery supplying tumor was not successful at redistributing flow to the hepatic artery.

Conclusion:
Phrenic artery supplying tumor can be safely and effectively treated with particle embolization prior to radioembolization.

Key points

- Radioembolization of the phrenic artery can result in diaphragm paralysis
- Coil embolization of the phrenic artery does not redistribute flow to the hepatic artery
- Particle embolization of tumors supplied by the phrenic artery is safe and effective

Introduction

Radioembolization can be used to treat hepatocellular carcinoma [1-3], as well as liver metastases from colorectal cancer [4], neuroendocrine tumor [5, 6], and other primaries. Radioembolization is usually performed from a branch of the hepatic artery, and coil embolization of extrahepatic vessels is sometimes necessary to prevent nontarget embolization to the stomach, duodenum, or pancreas. However, sometimes the liver tumors are supplied by an extrahepatic vessel, most commonly the right inferior phrenic artery [7].

Radioembolization of the phrenic artery could potentially result in complications from nontarget embolization. In addition to supplying the diaphragm, branches of the phrenic artery can supply stomach, esophagus, adrenal gland, pericardium, and skin; and shunts from the phrenic artery can connect to the portal vein or pulmonary artery [8-10].

Here, we retrospectively evaluated outcomes after three different techniques for managing the phrenic artery during radioembolization procedures: 1. Radioembolization of the phrenic artery, 2. Particle embolization of tumor supplied by the phrenic artery, followed by radioembolization of the hepatic artery, and 3. Coil embolization of the phrenic artery to redirect flow to an intrahepatic artery.

Methods

An IRB-approved retrospective review (protocol 16-402) was performed of 611 radioembolization mapping and treatment angiograms in 248 patients with primary or secondary liver cancer who were treated with radioembolization between January 2009 and July 2018. In 10 of 248 (4%) patients, a phrenic or accessory phrenic artery was either included in the radioembolization treatment (*n*=1), or was embolized using coils (*n*=4), particles (*n*=4), or both (*n*=1) at the time of mapping or treatment. Complications were classified according to the SIR system [11]. Response of the largest target liver tumor by RECIST was evaluated at 2-3 months after treatment (of tumors supplied by phrenic artery versus tumors supplied by hepatic artery).

For the 10 patients in which the phrenic artery was embolized during radioembolization mapping or treatment, pathology was: hepatocellular carcinoma (HCC; *n*=4), neuroendocrine tumor (NET; *n*=2), colorectal cancer (*n*=1), breast cancer (*n*=1), sarcoma (*n*=1), and ampullary mucinous adenocarcinoma (*n*=1). Average age was 63, and 40% of patients were male. Radioembolization was performed by a board-certified, fellowship-trained interventional radiologist. 6 patients were treated with Therasphere (Boston Scientific, Marlborough, MA), and 4 patients were treated with SIR-Spheres (Sirtex Medical, Woburn, MA). The prescribed activity for SIR-Spheres was calculated using the BSA method, and the prescribed activity for Therasphere was calculated to achieve a dose of 120 Gy.

Results

Radioembolization of the phrenic artery

In 1 patient, a pericardiophrenic artery arising from the left hepatic artery was included in the radioembolization treatment (Figure 1). This patient developed dyspnea and transient elevation of the left hemidiaphragm (presumably due to phrenic nerve injury), which resolved 5 weeks after treatment (mild adverse event). 4 months after radioembolization, the patient developed bacteremia and infected bilomas in the left liver that required aspiration, hospital admission, and long term antibiotics (severe adverse event). This patient had a history of Whipple for ampullary mucinous adenocarcinoma, and was therefore prescribed a 5 day course of oral ciprofloxacin and metronidazole after radioembolization.

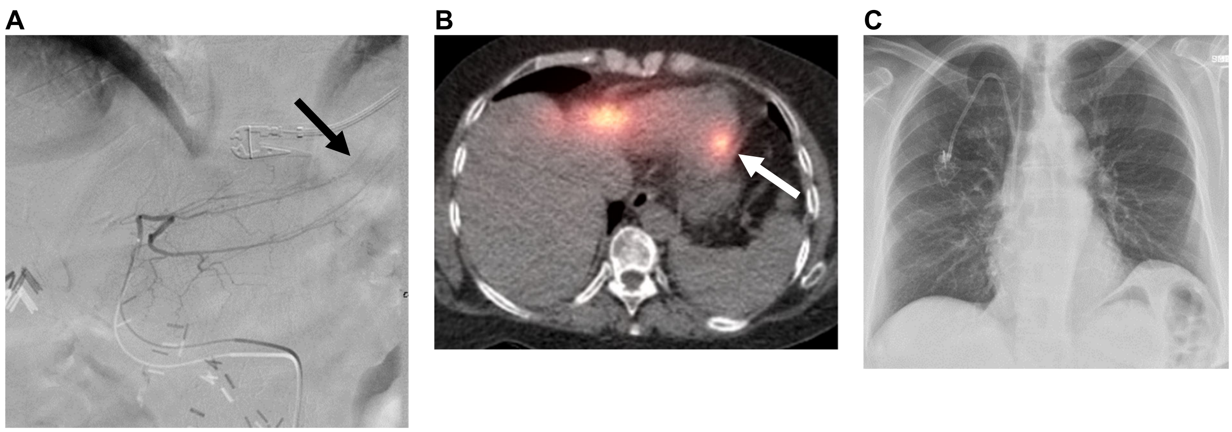

Figure 1. Radioembolization of the phrenic artery can cause transient diaphragm paralysis. **A**. Angiogram shows paired pericardiophrenic arteries (arrow) arising from the left hepatic artery, in a 63 year old woman with liver metastases from ampullary mucinous adenocarcinoma. This was not recognized at the time. **B**. Post-radioembolization bremsstrahlung SPECT/CT shows ^{90}Y deposition in the pericardium (arrow), along the expected location of the phrenic nerve. **C**. 3 weeks after radioembolization, the patient came to urgent care with dyspnea, and chest X-ray showed new elevation of the left hemidiaphragm. 5 weeks after radioembolization, patient reported resolution of dyspnea, and chest X-ray 1 week later showed resolution of the elevated hemidiaphragm.

Coil embolization of the phrenic artery

In 3 patients, coil embolization of phrenic artery not supplying tumor was performed to prevent non-target embolization. These patients had no complications after treatment.

In 1 patent, coil embolization of phrenic artery supplying tumor was performed in an attempt to redistribute flow to tumor via the hepatic artery (Figure 2). No flow redistribution was seen angiographically.

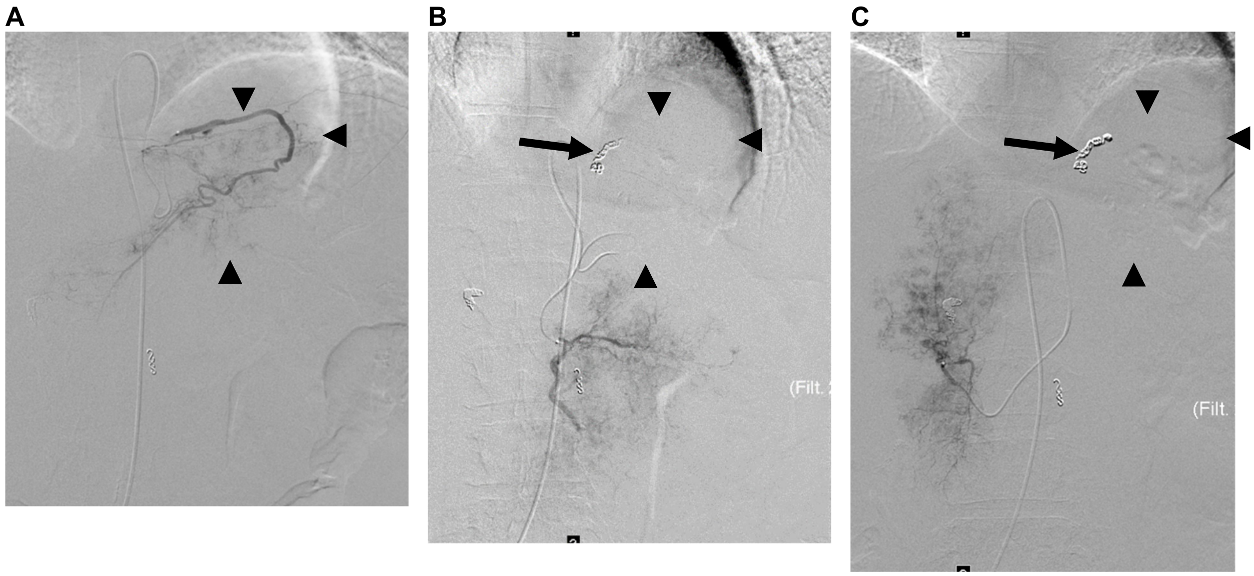

Figure 2. Coil embolization of tumor supplied by the phrenic artery does not redistribute flow to the hepatic artery. **A**. Left inferior phrenic arteriogram shows supply to segment 2 liver tumors (arrowheads) in a 67 year old man with cirrhosis from hepatitis C virus, and multifocal HCC, which did not respond to prior bland embolization. **B**. After coil embolization of the phrenic artery (arrow), the segment 2 tumor (arrowheads) is not supplied by the hepatic artery. The replaced left hepatic artery (arising from the gastrohepatic trunk) supplies tumor in segment 3. **C**. Middle hepatic arteriogram shows supply to segment 4 tumor. The arrow points to the embolization coils in the phrenic artery, and the arrowheads show tumor that was supplied by the phrenic artery.

Particle embolization of the phrenic artery

In 5 patients, particle embolization of phrenic artery supplying tumor was performed prior to radioembolization of the hepatic artery, using either 100–300 micron Embospheres (*n*=4) or 40–120 micron Embospheres (*n*=1). These patients had no complications after treatment. In 4 of 5 patients, the phrenic artery and hepatic artery supplied different tumors, and the response and disease control rates were similar in tumors treated by bland embolization of the phrenic artery (25% PR, 75% PR+SD) versus radioembolization of the hepatic artery (25% PR, 75% PR+SD).

In 1 of the 5 patients, the phrenic artery supplied tumor in the right atrium. This tumor grew after bland embolization, but responded to external beam radiation.

Discussion

There are several different strategies for dealing with the phrenic artery during radioembolization procedures. Here, we review our single-center experience, combined with several other case series from other institutions.

Radioembolization of tumor supplied by the phrenic artery can be safely performed in some patients, with several caveats. Phrenic artery to pulmonary artery shunts are common, and should be embolized prior to radioembolization [8]. Patients with extrahepatic perfusion from the phrenic artery to the stomach or esophagus, arterioportal shunting, or only a small amount of tumor supplied by the phrenic artery, are not good candidates for phrenic artery radioembolization [9]. Catheter CT angiography or cone beam CT are necessary to evaluate for subtle extrahepatic perfusion [9]. In our case series, radioembolization of a pericardiophrenic artery resulted in phrenic nerve injury, transient diaphragm paralysis, and dyspnea (Figure 1). Thus, phrenic artery that does not supply tumor should be coil embolized to prevent complications from extrahepatic perfusion.

Coil embolization of the phrenic artery does not redistribute flow to the hepatic artery: see Figure 2 and reference [7]. This is presumably due to the fact that the diaphragm is supplied by a rich network of arteries (superior phrenic, inferior phrenic, intercostal, pericardiophrenic, musculophrenic), so coil embolization of one of these arteries will redistribute flow to a different phrenic artery. In contrast, coil embolization of a hepatic artery usually results in flow redistribution via intra-hepatic collaterals, thus allowing the coil-embolized territory to be treated with radioembolization via an adjacent branch of the hepatic artery [12, 13]. Interestingly, embolization of the phrenic artery using particles larger than 500 micron, followed by coils, can restore intrahepatic supply in 94% of patients [7]. Presumably, these particles enter the liver (thus blocking supply from a phrenic artery), but are larger than intrahepatic collaterals (thus allowing supply from the hepatic artery). However, flow redistribution doesn't always work, and treating via small collateral arteries could result in suboptimal outcomes [13].

Bland embolization of tumor supplied by the phrenic artery can be safely performed using 100-300 micron Embospheres [14]. Bland embolization is an effective treatment for HCC (including hypovascular tumors), as well as metastases from NET, sarcoma [14], and colorectal cancer [15]. In this series, 4 patients had separate tumors treated via bland embolization of the phrenic artery, and radioembolization of the hepatic artery. This provided a controlled experiment, where the same pathology in the same patient was treated using two different treatment modalities. The same response rate was seen in tumors treated using bland embolization versus radioembolization.

In conclusion, phrenic artery supplying tumor can be safely and effectively treated using 100-300 micron Embospheres prior to radioembolization. Radioembolization of tumor supplied by the phrenic artery can sometimes be safely performed, but this requires catheter CT angiography or cone beam CT to detect subtle extrahepatic perfusion or shunting. Finally, particle embolization of the phrenic artery using >500 micron particles can redistribute flow to the hepatic artery.

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