Reduction of Arteriohepatovenous Shunting by Temporary Balloon Occlusion in Patients Undergoing Radioembolization

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Radioembolization with yttrium-90 resin microspheres is a treatment option that selectively targets hepatic tumors. One of the primary limiting factors for this therapy is the degree of arteriohepatovenous shunting, as excessive radiation to the lungs may cause radiation pneumonitis. To safeguard patients against this, a technetium Tc 99m macroaggregated albumin scan is performed before treatment to assess the degree of arteriohepatovenous shunting. As lung shunt fraction increases, activity reductions are mandated, with a 20% shunt sufficient to prohibit treatment. Temporary occlusion of shunts may be achieved by placement of balloon catheters in the hepatic veins. This endovascular technique used to reduce arteriohepatovenous shunting allows otherwise untreatable patients to undergo radioembolization.

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Abbreviations: MAA = macroaggregated albumin, SPECT = single-photon emission computed tomography

RADIOEMBOLIZATION, or selective internal radiation therapy, is a technique that is gaining prominence as an effective treatment modality for patients with unresectable hepatic neoplasms (1). This technique uses the dual hepatic blood supply to deliver a therapeutic radiation dose greater than 200 Gy to tumors while delivering less than 10 Gy to the normal liver parenchyma (2).

Although it has shown to be a promising technique for cases of disease refractory to standard treatment patterns, radioembolization has some limitations to its use. The most common complications consist of nontarget radiation delivered to the gastrointestinal tract and lungs (3). The use of coils and other embolic agents is an established technique that is frequently used to limit nontarget flow of microspheres to the gastrointestinal tract. However, the same technique cannot be used to prevent radioactive microspheres lodging in the lungs via arteriovenous shunts that bypass the hepatic capillary bed.

Current practice in limiting nontarget flow to the lungs consists of the use of intraarterially injected technetium Tc 99m macroaggregated albumin (MAA) to measure lung shunting fraction and assess the degree of pulmonary shunting. As the degree of pulmonary shunting increases, the activity of yttrium-90 resin microspheres (SIR-Spheres; Sirtex Medical, Sydney, Australia) that may be administered decreases, with a pulmonary shunting fraction of 20% sufficient to prevent implantation altogether (4). Effective use of this workup procedure to modify the administered dose of ^{90}Y microspheres has limited the radiation exposure of the lungs to a tolerable 30 Gy in a single implantation, ensuring that radiation pneumonitis is a very rare occurrence (5,6). These large shunts are predominantly invisible on digital subtraction and computed tomographic (CT) hepatic angiography.

Increased pulmonary shunting is most frequently encountered in patients with hepatocellular carcinoma and metastatic disease with larger tumor burden (6). Our experience in more than 500 patients evaluated for treatment has indicated that as many as 5% of patients, depending on disease type, require an activity reduction or are prohibited from receiving treatment as a result of high lung shunt fraction.

The standard technique used to treat hepatocellular carcinoma is transcatheter arterial chemoembolization (7). Like radioembolization, this treatment cannot be used for patients with a high degree of pulmonary lung shunting as a result of the effects of the chemoembolic products and/or particles on the lungs (8). However, a novel technique involving the placement of balloon catheters to temporarily reduce hepatic arteriovenous shunts has been reported as a method to allow conventional chemoembolization treatment to be used effectively (9). Endo-

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vascular occlusion has not only allowed treatment of hepatic lesions by an immediate reduction in the degree of pulmonary shunting, but it has been shown that this technique may result in a permanent reduction of pulmonary shunts.

This report documents the use of this temporary balloon occlusion technique to sufficiently reduce the flow through the arteriohepatovenous shunts, thereby permitting radioembolization in patients who might otherwise be precluded from treatment.

PATIENTS AND METHODS

Patients

Five patients with increased lung shunting fractions were detected between April 2005 and June 2006 at two institutions. After an explanation of the planned approach to reduce the lung shunting fraction to allow implantation to go ahead, three of the five patients signed a consent form allowing treatment to proceed. Institutional review board approval was not required at the treating locations for retrospective reports. The outcomes of treatment on all three patients who consented to treatment are documented in this report.

Patient 1 was a 64-year-old man with a malignant insulinoma predominating in the right lobe of the liver and hypoglycemia refractory to standard therapy who was referred for radioembolization. The patient exhibited a poor response to octreotide, diazoxide, and carbohydrate loading even though all the lesions in the liver showed positive indium/octreotide–labeled uptake. The planning angiogram and CT hepatic angiogram demonstrated no evidence of visible arteriohepatovenous shunting. When single photon emission CT (SPECT) was performed in the nuclear medicine unit immediately after injection of ^{99m}Tc MAA, a shunting fraction of 28.7% was measured (**Fig 1**).

Patient 2 was a 62-year-old man with chemotherapy-refractory metastatic colorectal cancer in both lobes of the liver, increased serum carcinoembryonic antigen measurements, mildly increased liver function test results, and no clinical evidence of jaundice who was referred for radioembolization. The planning angiogram and CT hepatic angiogram showed no evidence of visible arteriohepatovenous shunting. SPECT images obtained immediately after injection of ^{99m}Tc MAA demonstrated a 27% lung shunting fraction.

Patient 3 was a 56-year-old woman with chemotherapy-refractory metastatic colorectal cancer in both lobes of the liver, increased serum carcinoembryonic antigen measurements, mildly increased liver function test results, and no evidence of jaundice who was referred for radioembolization. The planning angiogram and CT hepatic angiogram showed no evidence of visible arteriohepatovenous shunting. SPECT images obtained immediately after injection of ^{99m}Tc MAA demonstrated 25% lung shunting fraction.

Methods

As a part of pretreatment workup and assessment of the location of disease in each patient, an appropriate occlusion technique was determined. The right hepatic vein in the first patient and the right hepatic vein and middle hepatic vein in the second and third patients were identified by venography after direct right hepatic vein and middle hepatic vein catheterization via the left groin. The middle hepatic vein was not targeted in the first patient because the burden of disease was almost entirely on the right side of the liver, so it was viewed that the shunting would be predominantly via the right hepatic vein. Coil embolization of the aberrant gastroduodenal artery in the third patient was carried out at this time to prevent nontargeted flow. Coil embolization in the other two patients was not required because superselective catheter placement allowed the implantation to be performed distal to the gastroduodenal artery, which branched off from the common hepatic artery in these two cases. The workup procedures were carried out 1 week before implantation.

For all three patients, tandem punctures were performed in the left common femoral vein before balloon placement with use of the Seldinger technique. The veins identified during the workup procedure were targeted for balloon placement. The angiographic catheters were exchanged for noncompliant angioplasty balloon catheters (Cordis, Miami, Fla) in the first (**Fig 2**) and second patients and compliant flow-directed balloon catheters (Cook, Bloomington, Ind) in the third patient. A Seldinger puncture was performed, access was obtained to the right common femoral artery, and selective catheterization of the hepatic artery proper was performed in all three patients.

The balloon catheters in the hepatic veins were inflated to produce occlusion before infusion of ^{90}Y resin microspheres into the proper hepatic artery. Occlusion of the shunts was then confirmed by injection of contrast medium into the common hepatic artery, which revealed closure of the shunts and the opening of the collateral circulation. The hepatic veins remained occluded until 60 seconds after completion of implantation, at which time the balloons were deflated (**Fig 3**). Resin microspheres were infused over a period of 3–7 minutes. Heparinized saline solution (1000 U) in 1 liter of normal saline solution was infused into the patient during the procedure. No intravenous or intraarterial heparin was given during the procedure. A SPECT scan used to detect Bremsstrahlung radiation was carried out after the implantation in each patient. The Bremsstrahlung scan, which is used to detect the location of the ^{90}Y within the body after implantation, was performed immediately after implantation to assess the lung shunt fraction and nontarget flow. ^{99m}Tc MAA scans were not performed immediately after inflation of the balloons because this would have adversely influenced the microcirculation before implantation of the radiolabeled microspheres, as the size and density of the resin microspheres and MAA are similar.

RESULTS

Endovenous occlusion of the hepatic veins before radioembolization proved feasible and technically successful in all three patients. The Bremsstrahlung scans performed immediately after implantation showed reduction in pulmonary shunting to 5.8% in the first patient (**Fig 4**) and to less than 2% for the other two patients. This represented a significant reduction from the lung shunt fraction measurements on SPECT with ^{99m}Tc MAA.

Dosimetry used to treat patients was calculated according to the body