Excessive Hepatic Arterial-portal Venous Shunting May Predict Failure of Microparticle Localization in Hepatocellular Carcinomas

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Abstract

Locoregional treatment of hepatocellular carcinomas using yttrium-90 (Y-90) microspheres is an emerging modality, and involves the administration of such radioactive particles directly into the hepatic arterial vasculature. We present the case of a 58-year-old gentleman undergoing evaluation for Y-90 microsphere therapy for hepatocellular carcinoma, in which our findings suggest that significant hepatic arterial portal venous shunting detected during the angiogram maybe a predictor of poor localization of microspheres in the turmor, and that centers that utilize body surface area (BSA) approaches for dosimetry should take note of such findings.

Keywords: Hepatocellular carcinoma, Y-90 microsphere therapy, arteria-portal venous shunting

Introduction

Selective internal radiation therapy (SIRT) is an emerging therapy that uses yttrium-90 (Y-90) microspheres to deliver tumoricidal doses to the tumor while sparing the normal hepatic parenchyma, with the preferential localization of such particles within the tumor based on the principle that hypervascular tumors in the liver are predominantly perfused by the hepatic artery, as compared with normal liver parenchyma which is largely supplied by the portal venous system.[1,2] Microparticles injected into the hepatic artery will preferentially flow to the hypervascular lesion, where the particles will be implanted in the tumor vasculature as they are too large to pass through the end arterioles of the hepatic sinusoids (diameter size: 8-10 microns).

SIR-Spheres® (Sirtex Medical Limited) is one of such approved devices of the United States Food and Drug Administration (FDA) approved for SIRT, and consists of biocompatible microparticles containing Y-90, measuring between 20 and 30 microns in diameter.

Most centers adopt the body surface area (BSA) dosimetry model, which is an empirical method for calculation of the dose. However, the presence of tumoral hepatic arterial portal venous shunting may imply poor localization of microparticles in the tumor, due to the injected particles transiting through the capillary bed without stasis, reducing the therapeutic tumoricidal dose.

We present a case in which hepatic angiographic computed tomography (CT) demonstrated good tumoral contrast enhancement but due to prominent hepatic arterial portal venous shunting, subsequent technetium 99m-labeled macroaggregated albumin (Tc-99m MAA) SPECT/CT (SPECT: Single photon emission CT) imaging demonstrated poor localization of microparticles within the tumor and poor tumor-to-normal liver ratio (TNR).

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Case Report

A 58-year-old gentleman with a history of hepatitis C was detected to have an asymptomatic arterial enhancing right liver lobe mass on CT imaging, measuring approximately

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6 × 8 cm in the longest cross-sectional diameter in liver segments 7/8, with evidence of branch portal vein thrombosis. His alpha fetoprotein levels were elevated as well. The results were in keeping with a hepatocellular carcinoma. He was subsequently referred for consideration of Y-90 SIRT using SIR-Spheres®. Biochemical evidence of underlying liver dysfunction was noted [albumin: 29 G/L, bilirubin: 26 umol/L, aspartate aminotransferase (AST): 164 U/L, alanine transaminase (ALT): 57 U/L, and prothrombin time (PT): 12.1 seconds], but values were still within acceptable limits for Y-90 SIRT.

A hepatic angiogram was performed. A 5F Cobra catheter was advanced into the hepatic artery proper, and selective angiogram followed by an intra-arterial catheter CT angiogram was performed. The CT angiogram demonstrated good vascular blush in liver segments 7/8, corresponding to the tumor seen on prior CT imaging. However, subsequent portal venous enhancement was noted, indicating hepatic arterial-portal venous shunting [Figure 1].

Five millicuries of Tc-99m-MAA was subsequently administered slowly under manual hand control, and the patient underwent SPECT/CT imaging of the liver within one hour of administration of MAA.

SPECT/CT imaging revealed minimal accumulation of MAA in the tumor in liver segment 7/8, with conversely more intense tracer localization in the surrounding liver parenchyma, resulting in an 'inverse'-type localization of microspheres within the liver [Figure 2].

Based on the findings of the Tc99m-MAA SPECT/CT, the calculated TNR by partition dosimetry model was 0.18 with a liver lung shunting value of 19%. With a calculated dose limit to the normal liver parenchyma of 70 Gy, the radiation dose to the tumor was 36 Gy and to the lung was 15Gy. Based on assessment by partition modeling, the patient was deemed not a suitable candidate for Y-90 SIRT.

Discussion

Arterial-portal venous shunting during the hepatic angiogram is not uncommon, and approximately 10-15% of our cases demonstrate a visible shunting during the procedure itself. If the shunting appears prominent and rapid, it suggests that the underlying shunt maybe large, and nonembolic-type microparticles administered may not remain in stasis in the bed of the tumor. This was demonstrated in our case, where prominent arterial-portal venous shunting on the hepatic angiogram correlated with poor localization of MAA microparticles.

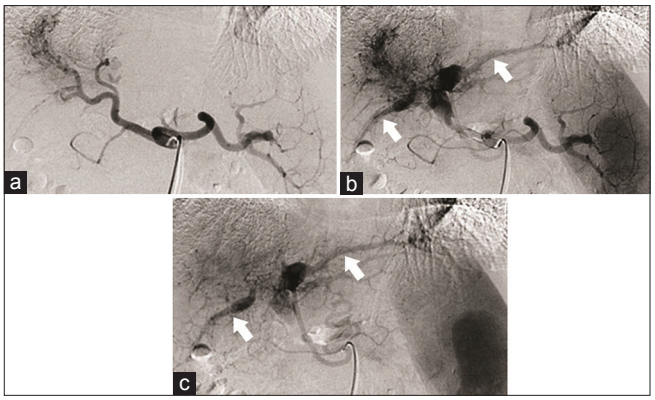

Figure 1: Anterioposterior digital subtraction angiogram of the celiac artery: (a) early arterial phase shows arterial feeders which supply the hypervascular tumor. (b) Mid-arterial phase, revealing marked coarse neovascularity and significant arterio-venous shunting, as demonstrated by early visualization of the left and right portal veins (arrows), typical for hepatocellular carcinoma. (c) Late arterial phase, tumor blush and delayed contrast washout with persistent opacification of the portal system (arrows)

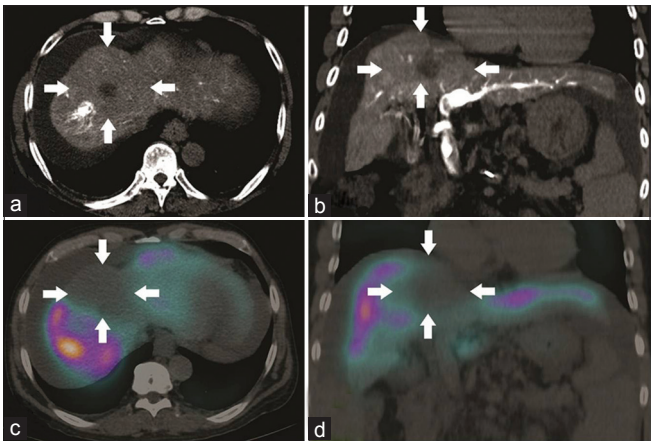

Figure 2: Computed tomography angiogram, axial and coronal images (a and b) indicating the site of the hepatocellular carcinoma in segments 7/8 (arrows). Corresponding axial and coronal SPECT/CT images (c and d). Note only minimal accumulation of MAA in segment 7/8 tumor, while more intense tracer uptake is noted in the surrounding normal hepatic parenchyma

The pretherapy evaluation of the patient before such therapy typically involves the evaluation of the hepatic vasculature and distribution patterns of administered microparticles using Tc-99m MAA as an adjunct to mimic the distribution of Y-90 microspheres.[3-10] Depending on the dosimetric approach used, specifically either the BSA or partition modeling, the uptake of microparticles between the tumor and normal liver compartments maybe assessed by calculating the TNR.

In centers utilizing the BSA method for dosimetric evaluation, only the BSA of the body of the patient, percentage tumor involvement of the liver, and lung breakthrough levels are taken into consideration, and TNR values are not evaluated. In comparison,

the partition model assumes that the distribution of Tc-99m MAA particles mimics the localization of Y-90 microspheres in the liver and tumor,[11] and can be used to determine doses to tumor, normal liver, and lung compartments.

The BSA approach is more widely practiced because of its easier application in clinical practice, and is recommended because this was the method utilized in trials upon which regulatory approval was granted.[12] However, in centers where calculations of dose are based on BSA approaches, the presence of significant arterial portal venous shunting during angiogram is a possible predictor of low TNR.

The issue of such shunting may not be so pertinent for larger implantable particles such as drug-eluting beads (100-700 microns), but at present we are unaware of any studies evaluating such localization of embolic particles in patients with prominent tumoral shunts.

In conclusion, the presence of such shunting may have implications on nonembolic locoregional therapy of the liver, as it may indicate subtherapeutic tumoricidal dosages, with increased morbidity risks to patients with limited or no clinical benefits from the therapy itself. In such cases, it maybe prudent to proceed with a partition model dosimetry for TNR calculations before initiating therapy.

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