Radioembolization for Hepatocellular Carcinoma Complicated by Biliary Stricture

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ABSTRACT

The authors present a case of radiation-induced biliary stricture following yttrium-90 (⁹⁰Y) radioembolization for hepatocellular carcinoma. Biliary complications (e.g., biliary stricture, biliary necrosis, biloma) following radioembolization and other locoregional therapies are uncommon and usually managed conservatively. In instances when biliary injury is refractory to medical management, as in the case presented herein, endoscopic, percutaneous, or surgical intervention may be required. Timely diagnosis of biliary complications with correlation to liver function permits optimal clinical management of patients undergoing ⁹⁰Y radioembolization.

KEYWORDS: Radioembolization, hepatocellular carcinoma, complications, biliary stricture

CASE REPORT

A 73-year-old man with a history of hepatitis C cirrhosis was found to have a 3.0-cm hepatocellular carcinoma (HCC) in hepatic segment IV on magnetic resonance (MR) imaging (Fig. 1). Given the patient's multiple comorbidities (e.g., coronary artery disease, hypertension, diabetes, and emphysema), he was considered high risk for surgical resection and liver transplantation at our institution's multidisciplinary HCC conference. A consensus decision was made to treat the patient with radioembolization using yttrium-90 (⁹⁰Y) glass microspheres.

Technical details of radioembolization using ⁹⁰Y have been previously described.¹ Briefly, using standard technique, a 5.5 French sheath was placed in the left common femoral artery. Celiac artery catheterization and angiography revealed standard anatomy. Middle hepatic artery catheterization and angiography revealed perfusion to the segment 4 tumor. Following the administration of nitroglycerin, radioembolization was per-

formed with a 5-GBq vial of ⁹⁰Y glass microspheres. There was the intended minimal embolic effect on completion angiography. There were no immediate complications following the procedure.

At routine follow-up 1 month after radioembolization, the patient complained of mild fatigue and anorexia postprocedure. Follow-up magnetic resonance imaging (MRI) at this time demonstrated an excellent response to therapy with complete necrosis of the segment 4 tumor (Fig. 2). In addition, the MRI study showed new mild biliary dilatation in the left hepatic lobe (Fig. 3). Because the patient's bilirubin levels were only mildly elevated, no further workup was initiated.

Over the next few weeks, the patient became progressively jaundiced and more fatigued. Repeat laboratory values revealed grade 3/4 bilirubin toxicity based on the Common Toxicity Criteria of the National Cancer Institute.² The patient was referred for endoscopic retrograde cholangiopancreatography (ERCP) that demonstrated an ischemic appearing stricture at

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Figure 1 Arterial phase postcontrast magnetic resonance image demonstrating a 3 cm tumor in hepatic segment 4 before radioembolization.

the takeoff of the left hepatic bile duct (Fig. 4). This was treated with balloon dilatation and placement of a 7-French 15-cm plastic biliary stent. After treatment, the patient's symptoms and laboratory values returned to baseline.

DISCUSSION

We present a case of radiation-induced biliary stricture following ^{90}Y radioembolization for HCC. Biliary complications following radioembolization with ^{90}Y have been described,^{3,4} although they are less common than other reported complications (e.g., nontarget organ radiation including gastrointestinal ulceration, pancreatitis, radiation pneumonitis, and radiation fibrosis).^{5,6} Atassi et al reported biliary sequelae in 33 of 327 (10.1%) patients based on imaging studies and serologic tests following ^{90}Y radioembolization for HCC or metastatic liver cancer.³

Figure 3 T2-weighted magnetic resonance image 1 month posttreatment showing new mild biliary dilatation in the left hepatic lobe.

Figure 2 Arterial phase postcontrast magnetic resonance image 1 month posttreatment demonstrating complete necrosis of the segment 4 tumor, consistent with an excellent response to radioembolization. The wedge-shaped enhancement surrounding the lesion is consistent with posttreatment changes.

In patients undergoing other locoregional therapies, such as transcatheter intraarterial chemoembolization and radiofrequency (RF) ablation, biliary complications have also been well documented.^{7–11} Sakamoto et al reported biloma development in 35 of 972 (3.6%) patients treated with chemoembolization for HCC or metastatic liver tumors.⁷ Similarly, Kim et al described biliary complications in 17 of 807 (2%) HCC patients treated with chemoembolization.⁸ Biliary sequelae following RF ablation are also uncommon and usually of no clinical significance. The most common type of bile duct injury in a series by Kim et al was mild dilatation of the upstream intrahepatic bile ducts surrounding the RF ablation zone in patients with HCC.¹¹ Overall, a higher incidence of biliary injury following locoregional therapies (including radioembolization) has been reported in patients with metastatic liver disease compared with primary HCC, possibly related to the well-known protective effect of the hypertrophied peribiliary vascular plexus in cases of cirrhosis and the significant chemotherapy history in patients with metastases.^{3,7}

Injuries to the biliary tree can manifest as bile duct strictures, biliary necrosis, bilomas, biliary cysts, cholangitis, cholecystitis, and gallbladder infarction.³ In patients treated with external beam radiotherapy to the hepatic parenchyma, bile duct strictures are thought to be the result of cellular and microvascular injuries leading to progressive microvasculitis and eventually to tissue hypoxia.^{12,13} Given the similarity in size of the peribiliary vascular plexus and the 20–60- μm ^{90}Y glass microspheres used for radioembolization, the radioactive microspheres may potentially embed within the arterioles of the peribiliary plexus causing a similar microvasculitis, postulated as the mechanism of biliary injury following radioembolization.⁵ A similar mechanism

Figure 4 (A) Fluoroscopic image from endoscopic retrograde cholangiopancreatography redemonstrating mild biliary dilatation in the left hepatic lobe due to an ischemic appearing stricture at the takeoff of the left hepatic bile duct. (B) This stricture was treated with balloon dilatation and placement of a plastic biliary stent.

(i.e., microvascular occlusion) has been proposed following transcatheter intraarterial chemoembolization,⁸ whereas bile duct injury after RF ablation is thought to be caused by direct thermal damage to the bile ducts.¹¹ Focal strictures of the biliary tree are thought to result from ischemia secondary to chronic inflammation and subsequent fibrosis as seen with RF ablation and repeated embolization.^{8,9} Bilomas are thought to result from bile duct leak caused by insult to the biliary tree and can be solitary or multiple.³

Diagnosis of biliary complications following radioembolization is usually based on imaging findings and/or liver function-based toxicities (grade 3/4) based on the Common Toxicity Criteria of the National Cancer Institute.^{2,3} On computed tomography (CT) or MRI, radiologists rely on the following imaging findings as evidence of biliary injury if not present before radioembolization: (1) biliary stricture in the form of peripheral or biliary ductal dilatation; (2) bilomas, i.e., large fluid-filled collection usually requiring drainage; (3) biliary necrosis in the form of multiple small, cystic-appearing structures not usually requiring drainage; (4) cholecystitis, i.e., gallbladder wall enhancement and/or disruption and/or pericholecystic fluid.³ The common liver-function based toxicities rely on aminotransferases, alkaline phosphatase, and bilirubin levels.²

Radiation-induced biliary complications usually occur without clinical consequences.³ In instances when biliary injury requires treatment, conservative measures usually suffice. In the event that a patient is refractory to medical management, endoscopic, percutaneous, or

surgical intervention may be required. As in the case presented above, endoscopic interventions include balloon dilation of strictures and placement of biliary stents. Percutaneous drainage of large bilomas has been described, as has cholecystectomy for radiation-induced cholecystitis.³

Although ⁹⁰Y radioembolization for HCC and metastatic liver cancer is safe,¹⁴ we discuss the most common biliary complications following radioembolization, most of which are clinically inconsequential. Although the published incidence of biliary complications following locoregional therapies such as radioembolization is low, timely diagnosis and recognition of these findings with correlation to liver function will permit optimal clinical management of patients undergoing ⁹⁰Y radioembolization.

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