Short-Term Follow-Up of Radioembolization With Yttrium-90 Microspheres Before Liver Transplantation: New Perspectives in Advanced Hepatocellular Carcinoma

Liver transplantation is a well-established procedure in patients affected by hepatocellular carcinoma (HCC) within the Milan criteria (*1*) or the extended Milan criteria (*2*). However, orthotopic liver transplantation (OLT) is not considered for patients who exceed the extended Milan or Milan criteria (i.e., size of nodule >7 cm or vascular invasion) because of the high risk of recurrence. In these patients, OLT can only be planned after downstaging of the disease to within acceptable limits. Patients with HCC who are transplanted after downstaging have similar outcomes in terms of survival and recurrence-free survival as those who meet the accepted criteria at initial presentation (*3*). We report a case of advanced HCC with neoplastic portal vein thrombosis, which was downstaged after radioembolization with yttrium-90 (^{90}Y) microspheres and led to a successful liver transplantation.

In February 2007, a 62-year-old man with hepatitis C virus-related cirrhosis with a model for end-stage liver disease score of 10 was diagnosed with an unresectable advanced HCC in the right lobe (7.5-cm diameter) and an increased α-fetoprotein (AFP) level more than 70,000 ng/mL. Macrovascular invasion of the right branch of the portal vein was confirmed by spiral computed tomography (CT) (Fig. 1) imaging. The clinical case was discussed by a multidisciplinary panel, and it was concluded that the patient was unsuitable for OLT because of the size of the tumor and vascular invasion.

In May 2007, the patient received whole-liver treatment with an intraarterial infusion of ^{90}Y resin microspheres (SIR-Spheres; Sirtex Medical Ltd., Sydney, Australia). The radioembolization activity administered was 1702 MBq. The treatment was well tolerated. Follow-up 1 month later revealed a positive tumor response. AFP level at 2 months after treatment was 15 ng/mL. CT imaging at 3 months postradioembolisation documented a complete radiologic response with total regression of the primary lesion and portal thrombus.

The patient was then regularly seen in the outpatient clinic for 22 months after treatment, during which time, no other lesions developed in the liver. In February 2009, the patient was reassessed and considered to be a suitable candidate for OLT. Transplant assessment performed by positron emission tomography, CT, and bone scans did not reveal new HCC lesions within and outside the liver. In March 2009, the patient was placed on the transplant waiting list. While waiting for transplantation, a CT scan showed a suspected hypervascularized lesion at the site of the previously treated lesion, measuring less than 1 cm. In May 2009, a second segmental-liver treatment with ^{90}Y resin microspheres was performed (1665 MBq). The patient developed liver dysfunction (ascites and cholestasis with bilirubin that peaked at 7 mg/dL), which resolved after 2 months of conservative treatment. In November 2009, the patient was transplanted successfully by the piggy-back technique without veno-venous bypass. Transplant surgery was unexpectedly more difficult than normal because of the presence of fibrous tissue between the inferior vena cava and the caudate lobe where the HCC was located probably due to the radioembolization and resulting edema. The postoperative course was uneventful, and the patient was discharged on day 14 on tacrolimus (Prograf; Astellas Pharma, Europe, Staines, UK) and prednisone. Pathologic examination of the explanted liver showed two 5-mm HCC nodules surrounded by the fibrous tissue. The lymph nodes were negative, and no portal vein thrombus was found. Eight months after OLT, the patient has no signs of HCC recurrence as showed by a CT scan, and the last AFP level was 10 ng/mL.

In the past 10 years, different techniques for downstaging HCC have been evaluated with encouraging results. However, radioembolization using intraarterial ^{90}Y-labeled microspheres has proved to be one of the most effective techniques. Approved in Europe for the treatment of unresectable liver tumors, radioembolization seems to be a safe and possibly more effective technique than transarterial chemoembolization for the downstaging of HCC (*4*, *5*). The Y^{90}-bound microspheres remain confined to the vascular rim of the tumor, where they deliver a high (>120 Gy) but localized

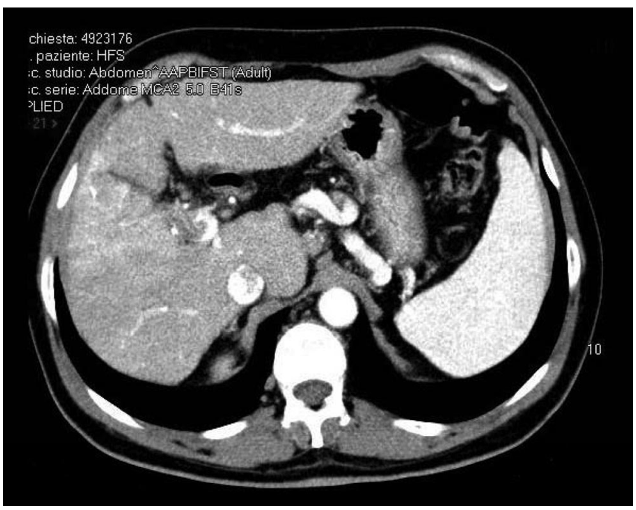

FIGURE 1. The computed tomography scan shows an hypervascular area corresponding to hepatocellular carcinoma with neoplastic right portal vein thrombosis before yttrium-90 microspheres treatment.

dose of β-radiation to the tumor compartment (*6*). The limited tissue penetration of β-radiation (mean 2.5 mm) (*6*) means that most of the normal liver tissue is spared (*7*, *8*). Radioembolization can be used in the liver transplant setting (a) as a bridge to transplant (controlling tumor progression for those on the waiting list) or (b) for the downstaging of tumors and resolution of vascular invasion, thereby enabling access to the organ waiting list for those outside the conventional criteria for organ transplant.

In conclusion, radioembolization is an effective treatment of patients with unresectable HCC, allowing downstaging to OLT in selected cases. Although the post-OLT follow-up period is still too short to draw any definitive conclusions, we would encourage liver and transplant surgeons to share our experience and consider radioembolization as an alternative treatment of unresectable advanced and intermediate stage HCC.

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