Drug-Eluting Bead Transarterial Chemoembolization as Bridge Therapy for Hepatocellular Carcinoma Before Living-Donor Liver Transplantation

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ABSTRACT

Background. The majority of hepatocellular carcinoma (HCC) patients is diagnosed in late stages and therefore becomes ineligible for potentially curative treatment such as resection or liver transplantation. Transarterial chemoembolization (TACE) with drug-eluting beads (DC beads, Biocompatibles, Farnham, United Kingdom) has been proven with less side effects and better efficacy than conventional TACE, especially among patients with poor liver function.

Purpose. The aim of this study is to evaluate outcomes of HCC patients who received TACE with DC beads, which resulted to eligibility for liver transplantation.

Methods and Materials. From January 2012 to June 2015, 60 patients with HCC received pre–liver transplantation evaluation whose cases were managed with TACE using DC beads at Kaohsiung Chang Gung Memorial Hospital were included in the study. DC beads loaded with doxorubicin were used.

Results. Forty percent of the patients had complete tumor response. Thirty-three percent of the patients had partial tumor response, of which 15% showed stable disease, 11.7% exhibited disease progression including 3 with portal vein thrombosis, 1 with both hepatic vein and portal vein thrombosis, and 3 with increase in tumor size. Twenty-three patients were beyond University of California, San Francisco (UCSF) criteria initially. The successful downstage rate was 73.9% (17 of 23). Thirty-seven patients fit the USCF criteria initially. The 3-, 6- and 12-month drop rates of these patients were 0%, 3.9%, and 16.8%, respectively. Twenty-four (40%) patients successfully underwent liver transplantation. Three patients (12.5%) demonstrated recurrent HCC after liver transplantation.

Conclusion. TACE with DC bead can effectively induce tumor necrosis and appears to be a successful approach as bridge therapy for patients with advanced HCC and poor liver function.

HEPATOCELLULAR carcinoma (HCC) is the leading malignant tumor in Taiwan. Liver transplantation (LT) is an important treatment option in the management of end-stage liver disease with HCC because this procedure is able to cure not only the tumor but also the underlying cirrhosis. The most frequently used selection criteria for LT, such as Milan or University of California San Francisco (UCSF) criteria, focus on tumor size and number, which are

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considered predictors of tumor recurrence [1,2]. The majority of HCC patients is diagnosed in late stages and therefore not eligible for potentially curative treatment such as resection or LT.

Locoregional therapy plays a significant role in the management of patients who otherwise cannot undergo surgical resection or transplantation. Percutaneous treatment such as transarterial chemoembolization (TACE) is used for patients with localized HCC while awaiting LT and for downstaging tumor size and number to satisfy the criteria. Drug-eluting beads (DC beads, Biocompatibles, Farnham, United Kingdom), which can be loaded with cytotoxic drugs, have recently been developed for chemoembolization of hypervascular tumors. They allow a slow release of the cytotoxic drug in a controlled fashion into the tumor, inflicting local ischemia while reducing systemic drug concentrations [3]. It can potentially shrink the tumor, limit its progression, and eventually allow HCC patients to meet the selection criteria for transplantation [4]. The aim of this study is to evaluate outcomes of HCC patients who received TACE with DC beads before fulfilling eligibility for LT.

PATIENTS AND METHODS

Patients with histologically proven HCC or with radiological diagnosis of HCC were considered for the protocol. All were deemed unresectable, either because of anatomic considerations or inadequacy of hepatic reserve. Demographic and clinical data were collected prospectively and analyzed retrospectively. By imaging methods, the UCSF criteria was used in selecting our patients undergoing LT. HCC patients without signs of metastatic disease or vascular invasion, as documented by computed tomography of the chest, abdomen, and pelvis, underwent TACE with DC beads. DC beads loaded with doxorubicin were used.

All patients underwent angiography with complete celiac and superior mesenteric artery injection for localization of tumor(s) in the liver before embolization. The lobar/segmental hepatic artery supplying the tumor was selectively cannulated with a microcatheter. The diameter of the beads chosen was based on the size of the lesion, feeders' diameter, and vascularity [5]. In all patients, two different sizes of DC beads were used: 100 μm to 300 μm and/or 300 μm to 500 μm. Each vial (2 mL of DC beads) was loaded with 75 mg of doxorubicin. Slow injection of this chemotherapeutic agent followed until the intended complete dose was administered or until intratumoral vascularity was completely obliterated and slow flow was observed. Individual treatment sessions were limited to unilobar or segmental therapy to minimize the risk of TACE-induced hepatic failure.

The results of embolization were evaluated by computed tomography in all patients 4 weeks after the procedure. Treatment response was evaluated by using the modified Response Evaluation Criteria in Solid Tumors (mRECIST). A complete response (CR) was defined as disappearance of any intratumoral arterial enhancement in all lesions; partial response (PR) was considered as at least 30% decrease in the sum of diameters of viable lesions compared to the preprocedural sum of diameters of lesions. Progressive disease (PD) included increase of at least 20% in the sum of the diameters of viable lesions; and stable disease (SD) was defined as any case that did not qualify as either PR or PD [6].

All cases with PR and SD received second embolization 3 to 4 weeks after liver function had improved. Following radiological restaging after TACE, the patients were then able to undergo liver transplantation after fitting the criteria and with a graft available. Patients were excluded for LT if there was extra hepatic tumor, tumor progression beyond UCSF criteria, or tumor thrombosis of the portal vein or hepatic vein.

The patient drop rate was estimated by the Kaplan-Meier method and was analyzed using statistics computer software STATA (STATA Corporation, College Station, Texas, United States).

RESULTS

From January 2012 to June 2015, 60 patients with HCC received pre-LT evaluation and underwent drug-eluting bead TACE at Kaohsiung Chang Gung Memorial Hospital. There were 56 males and 4 females. The overall mean age was 56.6 ± 8.9 years (range, 31 years to 72 years) at the time of transplantation evaluation. The mean size of the largest tumor was 2.3 ± 1.6 cm (range, 0.56 cm to 12.2 cm). The overall mean total bilirubin level was 1.1 ± 0.7 mg/dL (range, 0.2 mg/dL to 4 mg/dL), the mean glutamate oxaloacetate transaminase level was 50.7 ± 27 U/L (range, 21 U/L to 129 U/L), and the mean glutamate pyruvate transaminase level was 48.4 ± 30.6 U/L (range, 10 U/L to 136 U/L). The mean alpha-fetoprotein level was 235.9 ± 775.6 ng/mL (range, 2 ng/mL to 4550 ng/mL).

After initial DC bead TACE treatment, 40% (n = 24) had complete tumor response, whereas 33.3% (n = 20) had partial tumor response. Among the latter, 15% (n = 9) had SD and 11.7% (n = 7) showed progression of HCC (3 with portal vein thrombosis, 1 with both hepatic vein and portal vein thrombosis, and 3 with increase tumor size). No major complications or hepatic failure was noted after the procedure.

Twenty-three patients were beyond UCSF criteria initially, then 17 patients were successfully downstaged to fit the criteria for LT. The successful downstage rate was 73.9%. The tumor size, number, and outcome of downstaging are shown in Fig 1. Thirty-seven patients (61.7%) fit the USCF criteria initially. The 3-, 6-, and 12-month drop rates of these patients were 0%, 3.85%, and 16.8%, respectively.

Twenty-four patients (including 11 downstaging patients and 13 fit-criteria patients) successfully underwent LT and the other received further treatment such as continued DC bead TACE, radiofrequency ablation, local liver resection, or conventional TACE. Up to date, no patient was lost after LT. Three patients (12.5%) demonstrated recurrent HCC after LT. The mean interval to HCC recurrence was 10.8 months.

DISCUSSION

The primary treatment of HCC is surgical resection whenever possible. However, half of the patients have advanced disease at the time of diagnosis with a dismal prognosis. LT has been successful in treating limited-stage HCC providing