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Case Report

Histological assessment of the efficacy of drug-eluting beads in portal tumor thrombosis of hepatocellular carcinoma

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ABSTRACT

A 58-year-old man was diagnosed with advanced hepatocellular carcinoma with portal vein tumor thrombosis (PVTT). The tumors were multiple and existed in both lobes. Drug-eluting beads transcatheter arterial chemoembolization (DEB-TACE) was performed for the tumors in the left lobe. Embosphere and Hepasphere were selected for embolization of the arterioportal shunt, followed by loaded epirubicin infusion into the left hepatic artery. Computed tomography showed reduction of PVTT. However, liver failure progressed, and the patient died 67 days after DEB-TACE. Autopsy showed that the beads reached the tumor thrombosis in the portal vein. The prognosis of hepatocellular carcinoma with PVTT is poor. Although there are no established treatments for unresectable PVTT, DEB-TACE might be a useful option for such cases.

Introduction

Portal vein tumor thrombosis (PVTT) often occurs in cases of advanced hepatocellular carcinoma (HCC). The prognosis of HCC with PVTT is poor because of metastasis and portal hypertension associated with arterioportal shunting [1,2]. Unresectable cases with PVTT are treated with radiation therapy, continuous hepatic arterial infusion chemotherapy, or transcatheter arterial chemoembolization (TACE). However, the response to treatment, particularly to conventional

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Ethical standard: All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008 (5). Informed consent was obtained from the patient.

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TACE (cTACE), remains poor [3]. Various drug-eluting beads (DEB) have been developed as new embolus materials for TACE; these include Hepasphere (BioSphere Medical, Roissy-en-France, France); Embosphere (BioSphere Medical, Roissy-en-France, France); and DC beads (Biocompatibles UK, Ltd, London, United Kingdom). DEBs have several features that vary from cTACE, which uses ethiodized oil and gelatin sponge. DEB can carry and slowly release anticancer agents. Furthermore, compared with cTACE, DEB-TACE can embolize vessels that are more peripheral because the DEBs are highly deformable and vary in diameter [4]. These features may be more effective for PVTT cases and can improve the response to TACE. We conducted an autopsy on a patient with advanced HCC with PVTT and severe arterioportal shunt and who had undergone treatment with DEB-TACE to evaluate the efficacy of DEB for such cases.

Case report

A 58-year-old man was diagnosed with hepatitis B virus infection at the age of 30 years but was lost to follow-up. He visited another hospital due to abdominal pain, and contrast-enhanced computed tomography (CT) was performed. He was diagnosed with liver cirrhosis due to hepatitis B virus and multiple HCC. He was referred to our hospital for treatment.

At the time of hospital admission, ascites was seen on ultrasonography, and blood test showed prolonged prothrombin time. Therefore, we assessed his hepatic functional reserve as Child-Pugh class B. Tumor marker levels were notably increased, the protein induced by vitamin K absence or antagonists (PIVKA-II) level was 5750 mAU/mL, the α-fetoprotein (AFP) level was 3614 ng/mL, and the AFP-L3 measurement was 16.15% (Table 1).

Angiography was performed on the day after hospital admission. CT during arteriography showed that the left lobe was replaced with heterogeneously enhancing tumors with indistinct boundaries and that multifocal HCCs were present in the right lobe. The CT during arterial portography showed tumor thrombosis in the main portal vein and left portal vein (Fig. 1). The posterior branch of the right portal vein was intact, but the anterior branch was invaded by tumor. Angiography showed that blood flow in the hepatic artery was superior to that in the portal vein because of portal thrombosis. Poorly marginated stains mixed with tumors and liver parenchyma, as well as enhanced thorough arterioportal shunts, were seen in the left and right lobes (Fig. 2). The risk of HCC rupture was thought to be high because the patient complained of abdominal pain.

DEB-TACE was performed after obtaining the patient's consent. Treatment of the tumors in the left lobe was prioritized because those were the main lesions. Treatment of the right lobe was postponed to a later date to maintain hepatic reserve. To embolize arterioportal shunts, 10 mL of Embosphere (500–700 μm), which was diluted two times with the contrast medium, was infused from the left hepatic artery before chemoembolization. After infusing Embosphere, the enhancement of arterioportal shunts decreased (Fig. 3A). Following embolization by Embosphere, Hepasphere was infused from the same branch. The volume of Hepasphere (50–100 μM) was increased 4 times (200–400 μm) by addition of 25 mg of epirubicin dissolved in the contrast medium, resulting to 8–10 mL of mixed Hepasphere for infusion. After infusing Hepasphere, tumor staining decreased and the enhancement of the arterioportal shunts nearly disappeared (Fig. 3B). After the treatment, the hepatic functional reserve of the patient was maintained as Child-Pugh class B (9 points). Systemic chemotherapy was not administered after DEB-TACE.

Six days after, contrast-enhanced CT was performed to assess the effect of the treatment. Enhancement of the lateral segment disappeared because of tumor necrosis by DEB-TACE. However, enhancement of the medial segment remained. Invasion of the tumor to the inferior vena cava was shown and suggested rapid progression of the tumor.

The patient was discharged 37 days after treatment but was readmitted at 47 days after treatment because of fatigue and abdominal fullness. Ascites had increased markedly, and jaundice was noted. The level of hepatic functional reserve was Child-Pugh class C (10 points). Tumor markers were

Table 1 – Laboratory data on admission.

Blood cells		**Biochemistry**		**Coagulation factor**	
RBC	$4.15 \times 10^6/\mu L$	AST	163 U/L	PT	61.6%
Hemoglobin	13.7 g/dL	ALT	122 U/L	PT (INR)	1.25
Hematocrit	39.7%	ALP	779 U/L	**Virus markers**	
WBC	$4.3 \times 10^3/\mu L$	γ-GTP	448 U/L	HBs-Ag	175 IU/mL
Neutrophils	67.4%	LDH	264 U/L	HBe-Ag	(–)
Lymphocytes	19.2%	Cholinesterase	138 U/L	Anti HBe-Ab	(–)
Monocytes	7.5%	T-Bil	1.5 mg/dL	HBV-DNA	6.0 Log copies/mL
Eosinophils	4.5%	D-Bil	0.5 mg/dL	**Tumor markers**	
Basophils	1.4%	BUN	12 mg/dL	DCP	5750 mAU/mL
Platelets	$11.5 \times 10^4/\mu L$	Creatinine	0.7 mg/dL	AFP	3614 ng/mL
		Total protein	7.2 g/dL	AFP-L3	16.1%
		Albumin	3.3 g/dL		
		NH_3	48 μg/dL		
		CRP	2.53 mg/dL		

RBC, red blood cell; WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine aminotransferase; ALP, alkali phosphatase; γ-GTP, γ-glutamyl transpeptidase; LDH, lactate dehydrogenase; Bil, bilirubin; BUN, blood urea nitrogen; PT, prothrombin time; INR, internationalized normalized ratio; DCP, des-γ-carboxy prothrombin; AFP, α-fetoprotein; CRP, C-reactive protein; HBV-DNA, hepatitis B virus-DNA.