

Hepatocellular Carcinoma after Transcatheter Arterial Chemoembolization: Difficulties on Imaging Follow-up

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Due to the narrow surgical indications for hepatocellular carcinoma (HCC) in the cirrhotic liver with decreased liver function, transcatheter arterial chemoembolization (TACE) has been generally performed in the worldwide institutions for the curative or palliative treatment of this tumor. In the majority of the cases, however, the tumors are not completely necrotized, and the recurrence rate after TACE is still high even for the patients who have received curative TACE for grossly uncomplicated localized lesions (1). Thus, on the follow-up imaging studies after TACE, accurate diagnosis of a residual or locally recurrent tumor is crucial and this can facilitate successful management at an early stage of the disease so as to avoid more complicated or advanced disease that has an unfavorable prognosis.

Multiphase dynamic CT, including the pre-contrast phase, the arterial phase and the more delayed phase imaging, is popularly used for evaluating the therapeutic effect of TACE because the degree of uptake and the distribution of the iodized oil within the tumor and the surrounding hepatic parenchyma can provide useful information on the degree of tumor necrosis, and so a strategy can be planned for the subsequent therapeutic approach (2–4). The article by Jang et al. (5) in this issue of the *Korean Journal of Radiology* is one of the studies that have assessed the diagnostic ability of multiphase dynamic CT to depict a viable tumor in HCC treated with TACE. In that study, a review of the previous serial CT images provided more accurate information for the determination of the viability of the lesion than did a review of the last CT alone in several cases that were roughly verified by subsequent pathological review of the resected specimens. The overall false positive interpretation rate for the totally necrotic tumors was just 3%; however, false negative interpretation for viable tumors was 22%, which was still too high to get reliable results with using the serial follow-up CT as the main diagnostic tool. In this editorial, I discuss the issues and difficulties for

the imaging follow-up of HCC after TACE.

Focal Iodized Oil Defect in the Lesion

A focal defect in the mass having iodized oil accumulation or focal washout of iodized oil during follow-up suggests the presence of a viable tumor within the corresponding area. However, the pre-existing tumor necrosis within the lesions before TACE also appears as an iodized oil defect after TACE. From this viewpoint, the pre-TACE initial CT should be reviewed along with the follow-up images in a side-by-side manner to determine the nature of the iodized oil defect. Multiple serial follow-up imaging studies are helpful to depict the interval change of the iodized oil defect area. A long-standing non-enhancing hypoattenuating area (longer than one year) within a HCC lesion is regarded as necrosis (5). Focal washout of the iodized oil from the tumor suggests the presence of collateral vessels. A careful search for the appropriate collateral vessels should be made during any subsequent TACE.

Partial Volume and/or Beam Hardening Artifact

Although grossly homogeneous and dense deposition of iodized oil within lesions would indicate massive necrosis of the tumors, the degree of iodized oil retention and the degree of necrotic areas sometimes differ (6). Although all of the false negative lesions in the study of Jang et al. (5) showed more than 90% or greater necrosis on pathologic examination, yet the high percentage of necrosis had no impact from the viewpoint of complete remission. The follow-up CT of patients treated with chemoembolization is generally affected by artifacts that are produced by high concentrations of iodized oil, and this makes it difficult to evaluate the enhancing characteristics of the lesion. Kubota et al. (7) documented the feasibility of dynamic MR imaging and power Doppler ultrasonography for the evaluation of viable tumor that is hidden in a high density of iodized oil on the CT scan taken at five to seven days

after TACE. Although highly concentrated iodized oil in the lesion shortens the T1-relaxation time, two to three months after TACE, iodized oil does not significantly affect the intra- and extralésional signal intensity and this has the advantage to find a hypervascular viable focus in the area of iodized oil accumulation (8).

Non-tumorous Arterioportal Shunt

After TACE, mechanical or chemical injury of the small hepatic arterial branches can cause non-tumorous small arterioportal fistula around or at a distance from the lesion (9). A typically wedge-shaped early enhancement pattern without any attenuation difference on the pre- and delayed phase images could be regarded as nontumorous lesion (5); however, structural distortion and/or inhomogeneous attenuation of the background parenchyma that consists of fibrosis and regeneration in the advanced cirrhotic liver can reduce the diagnostic confidence because some of the enhancing foci can show an irregular or nodular contour. MR imaging using Kupffer cell agent (superparamagnetic iron oxide particles) can be helpful to diagnose non-tumorous arterioportal shunt (10).

Perilesional Parenchymal Inflammation, Ischemic Injury or Infarct

The iodized oil and anticancer drug emulsion directly affects the perilesional hepatic parenchyma by causing chemical inflammation and ischemic injury of the portal track, and this is reversely correlated with the degree of cirrhosis (11, 12). Embolic materials also flow into the portal venules through the transplexal route, and this leads to obliteration of the portal venules. In the above conditions, the decreased arterial and portal venous perfusion results in parenchymal infarct. Reperfusion of previously infarcted parenchyma by collateralization of the hepatic arterioles can show inhomogeneous arterial phase enhancement, in addition to the low attenuation density of the affected area on the pre-contrast CT that mimics HCC. Although this area is seen as rather amorphous or irregular, the decreased Kupffer cell count that is due to the substantial parenchymal injury can be misdiagnosed as viable tumor even on MR imaging with using superparamagnetic iron oxide agent.

Making the correct diagnosis of viable tumor on follow-up CT after TACE for HCC is always challenging for the physician in their daily practice. Considering the various factors related to the tumor itself, the embolic agent, the perfusional variation and the adjacent parenchymal injury, I believe that meticulous observation of the serial follow-

up CT images along with the use of other imaging modalities, including MR imaging or ultrasonography with optimized imaging protocols, if indicated, can overcome the limitations of CT in many cases.

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