

Transcatheter arterial chemoembolization as an examination method for hepatocellular carcinoma undetected by B-mode ultrasound, computed tomography and digital subtraction angiography: A case report

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Abstract. Transcatheter arterial chemoembolization (TACE) is the conventional treatment for patients with unresectable hepatocellular carcinoma (HCC), but few studies to date have demonstrated the use of TACE as an examination method for uneasily detected HCC. The present study describes an unusual case of HCC with TACE as an examination method. A 41-year-old male presented with an elevated α -fetoprotein level (AFP) of 3,635 ng/ml, however, no tumor lesions were detected by B-mode ultrasound, computed tomography (CT) or digital subtraction angiography. During TACE treatment, two tumor lesions of ~0.5 and 0.8 cm were revealed in the right liver lobe, with no tumors in the left liver lobe. A month after TACE, a liver CT scan found 11 lesions (8 in the right liver lobe and 3 in the left liver lobe). The HCC patient's AFP levels decreased to an almost normal level following the TACE treatment. This study provokes consideration of the application of TACE in the diagnosis and treatment of HCC patients with liver lesions that are hard to detect by conventional means.

Introduction

Primary hepatocellular carcinoma (HCC) is a highly malignant tumor with the characteristics of rapid progression and a poor prognosis. It is one of the most commonly observed malignant tumors in China, with ~130,000 associated mortalities annually, accounting for ~40% of liver cancer-associated mortality (1,2). The physical symptoms of HCC are largely dependent on the stage of disease. Early stage HCC is often asymptomatic, whereas patients with advanced stage HCC often present with symptoms such as, weakness, malaise, anorexia, upper abdominal pain

and weight loss. In addition, hepatomegaly is identified in the majority of HCC patients (3). A number of treatment modalities exist for HCC, including hepatic resection, liver transplantation, percutaneous ethanol injection (PEI), radiofrequency ablation (RFA), and transcatheter arterial chemoembolization (TACE) (4-7). Treatment choice is dependent on various factors, which include tumor stage, liver function reserve and patient performance status [Barcelona Clinic Liver Cancer stage (8)] and thus, a multidisciplinary approach is required for optimal treatment. Hepatic resection (5,9,10) and liver transplantation (11-13) are the only curative options for patients with early stage HCC. However, recently, there have been significant advances in local ablative and transarterial therapies (14-16). For patients with small HCC (nodular diameters <2 cm), RFA has been shown to exhibit the same efficacy as surgical resection, with five-year survival rates ranging between 40 and 70% (17) and has replaced PEI as the locoregional therapy of choice. Previous studies have demonstrated that RFA treatment provides better local control and survival outcomes when compared with PEI (18-20). TACE is considered as the conventional treatment method for patients with unresectable HCC (21,22). The majority of hepatic lesions are identified by B-mode ultrasound, computed tomography (CT), magnetic resonance imaging (MRI) or digital subtraction angiography (DSA). However, such examinations are often unable to detect smaller lesions, particularly those in the liver. Thus, a number of issues must be overcome to enable the early detection and treatment of liver cancer. The present study reports the case of an HCC patient with an elevated α -fetoprotein (AFP) level, with lesions that went undetected by B-mode ultrasound, CT and DSA, but were finally detected by TACE. The diagnosis and treatment through TACE for such an HCC patient provides novel insights into clinical and basic research. To the best of our knowledge, the current study is the first to report the use of TACE as an examination technique in any disease. In the majority of cases, TACE was considered to be an appropriate treatment method for HCC in which the lesions are clearly detected.

Case report

A 41-year-old male presented to the Jiangxi Province Cancer Hospital (Nanchang, Jiangxi, China) in December 2013 with

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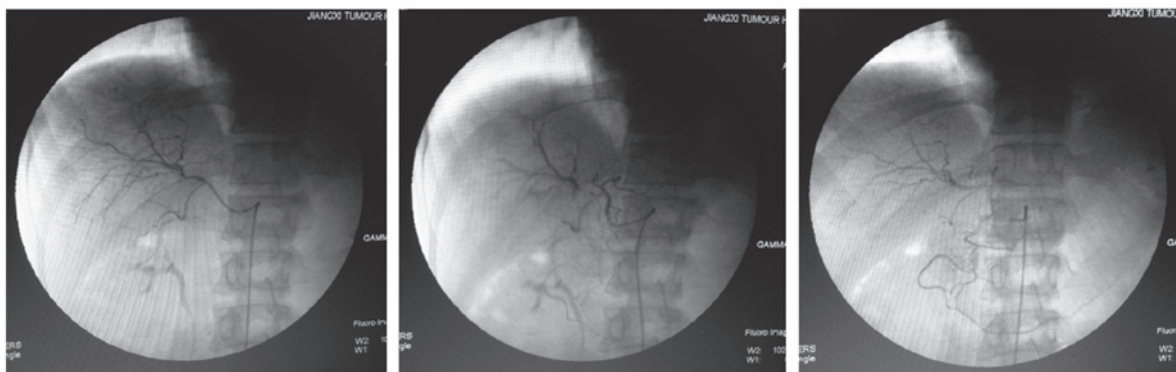


Figure 1. Tumor lesions were not found in the liver during digital subtraction angiography examination.

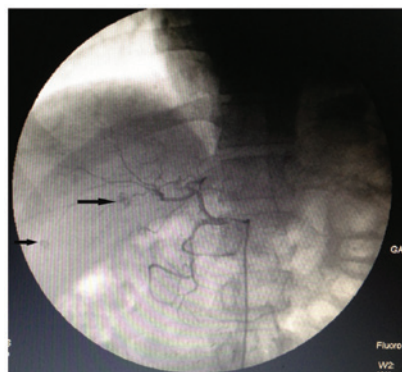


Figure 2. Two hepatocellular carcinoma lesions of ~0.5 and 0.8 cm (black arrows) were detected during the transcatheter arterial chemoembolization procedure.

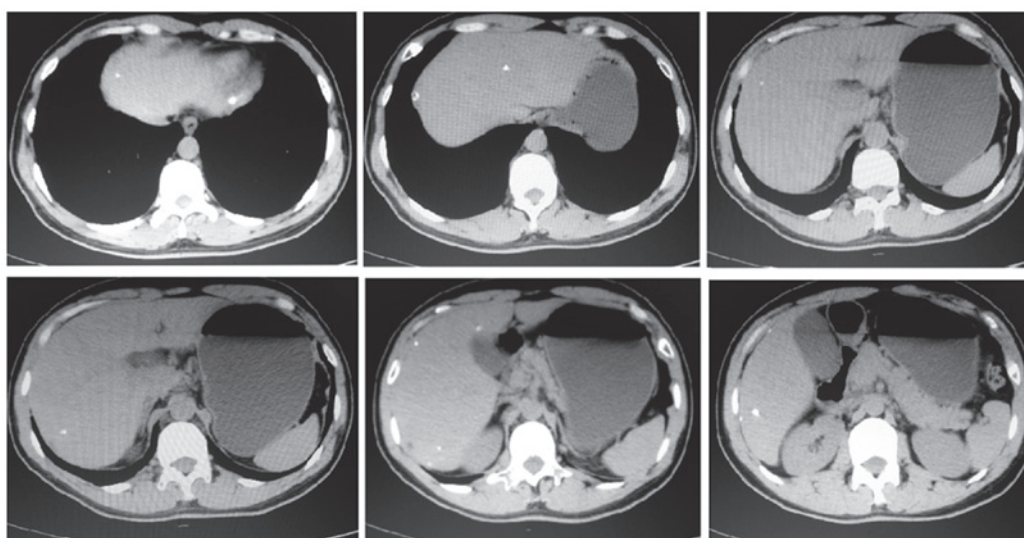


Figure 3. A month after transcatheter arterial chemoembolization, liver computed tomography found 11 lesions with Lipiodol deposition, including 2 lesions detected during the surgery. Among them, 8 lesions were located in the right liver lobe and 3 were located in the left liver lobe. The diameter of the majority of the lesions was <0.3 cm.

an elevated AFP level that was indicative of HCC. Upon admission, the patient was examined by B-mode ultrasound and CT, but no suspicious tumor lesions were found in the liver. The AFP level was 3,635 ng/ml (normal range, 0-7 ng/ml), and the patient was hepatitis B virus (HBV) surface antigen-positive, with an HBV DNA level of 246.2

upon quantitative examination (normal value, <100), and Child-Pugh grade A liver function (23). Other diseases were excluded and DSA was recommended for examination of the patient. However, DSA did not locate any suspicious lesions in the liver (Fig. 1). Next, TACE (10 mg Adriamycin + 5 ml Lipiodol) was performed upon the assumption that lesions

would be found during the procedure, due to the raised AFP level in this patient. Lipiodol was injected into the left and right hepatic arteries, respectively. During surgery, two lesions with Lipiodol deposition (~0.5 and 0.8 cm in diameter) were located in the right liver lobe, while no Lipiodol deposition was found in the left liver lobe (Fig. 2). A month after TACE, liver CT scanning found 11 lesions with Lipiodol deposition, including 2 lesions previously detected during the surgery (Fig. 3). Among them, 8 lesions were located in the right liver lobe and 3 were located in the left liver lobe, and the diameter of the majority of the lesions was <0.3 cm. A follow-up was conducted every 3 months and six months after surgery, the patient's AFP level had decreased to almost normal (20.32 ng/ml). Therefore, no further treatment was provided for the patient and thus far no tumor recurrence within the liver or distant metastasis have been observed.

Discussion

There are a number of examination methods for finding small HCC lesions, such as B-mode ultrasound, CT, C-arm CT, MRI, DSA and positron emission tomography-CT (24,25), however, each examination has its own advantages and disadvantages. HCC detection by B-mode ultrasound is considered to be relatively inaccurate, whereas CT and MRI have been used to establish a typical imaging profile for HCC (26). Previous studies have reported that iodinated-enhanced C-arm CT improved the detection rate of small HCC lesions during TACE (27,28), and the results also demonstrated that PET provided better accuracy in investigating patients with HCC compared with CT or MRI (29,30). However, the aforementioned examination methods are unable to detect all small hepatic tumor lesions. Previous studies have demonstrated that B-mode ultrasound, CT, C-arm CT and DSA are able to detect for hepatocellular carcinoma lesions 1-3 cm in diameter (31,32). In the majority of cases, TACE is considered as a treatment method for HCC where lesions have been clearly detected. The present study reports a case of HCC in which the lesions remained undetected by B-mode ultrasound, CT and DSA, and where 2 HCC lesions were revealed during the TACE procedure. Moreover, a month after TACE, liver CT scanning located 9 additional lesions in the liver. The majority of the lesions were <0.3 cm in diameter. These results suggested that TACE was a better examination method than DSA in the detection of small HCC lesions, and at the same time, that liver CT scans can identify more and smaller tumor lesions a month after TACE treatment; however, whether these lesions were newly identified because they were not present at the time of the original TACE procedure or because they were too small remains unclear. In view of its therapeutic role and the advantage in early detection, we believe that TACE should be a preferred inspection option for multiple and scattered microlesions that are difficult to find in HCC patients.

In general, the therapeutic effects of surgical resection, liver transplantation, percutaneous ethanol injection and radiofrequency ablation for primary liver carcinoma are better than those of TACE (20,33-38). However, in the present patient treated with TACE, liver CT scans found complete necrosis in all lesions and the AFP level had decreased to almost normal. Surgical resection, liver transplantation, percutaneous ethanol

injection and radiofrequency ablation are not suitable for such a patient with HCC. Therefore, it is promising that TACE may be used as a radical treatment method under certain conditions, particularly for primary liver cancer, such as in the present case. Nevertheless, further studies are required to support this.

In the present study, in order to avoid missing intrahepatic lesions, a catheter was inserted into the left and right hepatic arteries and Lipiodol was injected through each. However, during the surgery, only 2 suspicious lesions were located in the right liver lobe, with no other lesions found in the left liver lobe. Significantly, a month after TACE therapy 3 lesions were located in the left liver lobe and 8 were located in the right liver lobe. In fact, according to our previous treatment experience, when the anatomical orientation of HCC is clear, TACE treatment is performed only for a focal hepatic lobe lesion or for segments with detected hepatic lesions, while conventional TACE is rarely performed for focal hepatic lobe lesions or for segments where no small lesions have been found by B-mode ultrasound, CT and DSA. In conclusion, TACE therapy in the patient with HCC in the current study must be conducted with certain considerations: To prevent the omission of small hepatic tumor lesions, even when the anatomical orientation of HCC is clear, TACE treatment must be performed for focal hepatic lobe lesions or for segments in which no small lesions have been identified by B-mode ultrasound, CT and DSA, particularly on the initial treatment.

From the aforementioned clinical data, it can be observed that among the small hepatic lesions found by TACE examination, the majority are <0.5 cm, and can even be <0.3 cm. Following hepatic arterial embolization, Lipiodol is well deposited in these tumors. For this clinical phenomenon, there are two possible explanations. One explanation is that tumor lesions <0.5 or 0.3 cm have an arterial blood supply. Another explanation is that Lipiodol can diffuse into small intrahepatic tumors. In accordance with previous theories, tumors <0.3 cm rarely have been observed with an arterial blood supply. Therefore, we infer that Lipiodol can diffuse into small intrahepatic tumors. However, in the clinic, it was not difficult to find that certain hepatic tumors that lacked an arterial blood supply had no or poor Lipiodol deposition following TACE treatment. These paradoxical clinical findings do not support the aforementioned explanation that Lipiodol can diffuse into intrahepatic tumors. These results result in reconsideration of the association between tumor angiogenesis and tumor size, and the effect of tumor cell heterogeneity and the microenvironment of liver on the differences in biological behavior between HCC lesions with arterial an blood supply and those without.

In conclusion, the clinical data from the present unusual case not only provides another choice of technique for finding small hepatic tumor lesions that are difficult to detect by B-mode ultrasound, CT and DSA, but also raise new questions with regard to the basic theory behind liver cancer. These issues are worthy of further in-depth study.

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