RESEARCH ARTICLE

Percutaneous Radiofrequency Ablation Guided by Contrast-enhanced Ultrasound in Treatment of Metastatic Hepatocellular Carcinoma after Liver Transplantation

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Abstract

This study evaluated the advantages and applications of contrast-enhanced ultrasound (CEUS)-supported percutaneous radiofrequency ablation (RFA) in the treatment of metastatic hepatocellular carcinoma after liver transplantation, based on clinical details. CEUS-supported percutaneous RFA was adopted to treat 12 patients with hepatic metastatic carcinomas after liver transplantation. The diameters of the metastatic carcinomas varied from 1 cm to 5 cm, and the foci were discovered after 3 months to 12 months. Each focus was diagnosed and localised by CEUS for RFA once or twice. Curative effects were evaluated by CEUS or contrast-enhanced CT after the treatment. The re-examination results at 2 weeks post-treatment showed that the foci of 11 patients were ablated completely, whereas one patient with the largest focus required retreatment by RFA because of a partial residue. No local recurrence was found one month later in the re-examination. CEUS-supported percutaneous RFA in the treatment of hepatic metastatic carcinoma after liver transplantation has the advantages of accurate localisation, good efficacy, easy operation, and minimal invasion without any complications. Therefore, it can be recommended as the preferred therapy for hepatic metastatic carcinoma after liver transplantation.

Keywords: Contrast-enhanced ultrasound - radiofrequency ablation - liver transplantation - hepatic metastatic carcinoma

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Introduction

Metastases after liver transplantation for liver cancer are the main and challenging problem that disturbs the effects of long-term treatment of the disease. Given that deeply disappointed patients are reluctant to receive another highly invasive treatment, a minimally invasive treatment with sound effects is more likely to be accepted. Hence, selecting a convenient and effective treatment to control the status of a disease without bringing patients too much mental pressure is important. However, no effective clinical treatment is available until now, and only conservative therapies such as chemotherapy and radiotherapy are applied to metastases that occur in different areas. Radiofrequency ablation (RFA) under the guidance of ultrasound positioning is considered the best technique to treat liver metastases when the tumour is still small. However, the relatively low resolution of ordinary ultrasound cannot detect the accurate position of small tumours (<3 cm), making the patients miss the optimal time for treatment. Hence, the accurate detection of tumour location is the key to an effective treatment. For the past few years, the clinical application of contrast-enhanced ultrasound (CEUS) technology (Kudo, 2007; Moriyasu et al., 2009), which increased the diagnosis rate to 93.2% (Ryota, 2011), has greatly improved the diagnostic sensitivity of focal liver masses (Catalano et al., 2005). Only a few cases have been reported (Numata et al., 2008; Minami et al., 2010) in which RFA, guided by CEUS technology, was performed to treat liver metastases after liver transplantation to find inchoate focal liver masses and treat them promptly. Certain therapeutic effects have been achieved through tentative application; a preliminary summary and evaluation are in progress.

Materials and Methods

Objects

From February 2009, CEUS technology was adopted for a post-operation routine examination on patients having liver transplant because of hepatocellular carcinoma. It was conducted once every month during one year after the operations and once every three months after one year. To date, 12 patients were discovered with hepatic metastatic carcinomas, accounting for 9% of the total 124 patients who underwent liver transplants because of hepatocellular carcinoma. All 12 patients were male, aged between 39 and 57 years, with an average age of 51. The diameters of the foci ranged between 12 mm and 55 mm, with an average of 22 mm. The foci were discovered 3

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months to 12 months after the operations, with an average of 8 months. One patient had more than one focus (2 foci), whereas the others had only one focus. All patients were accompanied by an increase in AFP, which was more than 200 μg/L. An apparent focal enhancement was observed using CEUS. The general conditions of the patients were good, and they had no abnormal feelings. This study was conducted in accordance with the declaration of Helsinki and with the approval from the Ethics Committee of the 309th Hospital of Chinese PLA. Written informed consent was obtained from all participants.

Localisation by the examination under CEUS

The GELOQIC9ultrasonic diagnostic apparatus with a transducer frequency of 3.5 MHz was used in this study. Sono Vue manufactured by Braeeo in Italy was used as ultrasound contrast agent. Approximately 5 ml of 0.9% sodium chloride solution was injected for dilution before the agent was used. The solution was shaken sufficiently to become a turbid liquid, and 2.4 ml was then extracted for bolus injection through the patient's antecubital vein. Subsequently, 5 ml normal saline was used for flushing. Routine ultrasound was used for full liver scan before the contrast to determine the suspected area and set the position for centesis, which was usually the left lateral position. The contrast model was then switched on, and the mechanical index was adjusted to 0.09 to 0.12. Ultrasonic contrast examination was conducted, and the enhanced variations of the focus were recorded uninterruptedly in real time. The most suspicious focus was the object of observation for the arterial phase. Rapid scanning was conducted in relevant areas for the portal and delay phases. The dynamic images of ultrasonic contrast were saved during examination. More than two veteran ultrasound doctors conducted the analysis, diagnosis, and localisation after the examination.

RFA method

The routes for centesis under CEUS were set according to the localisation and nature of the enhanced performance of the foci in different time phases. Under aseptic conditions, 2% lidocaine was injected for local anaesthesia. A single needle or clustered needles were used to puncture the focus, and the position of the focus full of blood vessels was selected for key treatment. The cold circulating pump was switched on after the position of the radiofrequency electrode was confirmed. The impedance model was then chosen to conduct the RFA treatment. The treatment time for each point was 12 min. The position of the electrode was adjusted according to the condition of the focus to add the treatment. The needle passages were ablated when the needles were pulled out.

Evaluation of the curative effect

A re-examination under CEUS was conducted for pre-treatment and post-treatment comparison after a month of treatment. Enhanced CT examination was performed to determine the condition of focus necrosis or residue to evaluate the curative effect as follows: (1) Complete necrosis: CEUS indicated a low-level echo without the signal of blood flow. Plain CT scanning indicated a low density, which was completely unintensified under enhanced CT scanning. (2) Incomplete necrosis or residual focus: CEUS indicated a strong echo with observable signal of blood flow in the partial focus. Enhanced CT scanning showed an intensified partial focus. A supplementary treatment should be conducted promptly for any residual focus.

Results

Curative Effect

All foci were discovered when they were less than 3 cm. Eleven patients had prompt RFA treatment, and their foci necrosed completely in the re-examination after a month. One patient who was not treated promptly because of objective factors had RFA treatment when the focus was up to 55 mm. In the re-examination after a month, about 10% residue was found. Repeated RFA treatment resulted in the completely necrosed focus. The patients' AFP evidently decreased after treatment. In addition, their lifetime lasted for over 6 months, during which, no hepatocellular metastasis reoccurred.

Adverse Effect

Slight thermal dilation and ache in the liver area and occasional nausea and chest distress were observed during the operation. The patients had low fever (temperature of 37 °C to 38 °C) during 2 d to 3 d post-operation. The patients basically returned to normal 3 d post-operation. All the patients did not have haemorrhea or implantation metastasis of needle passages. The liver functions were stable and no rejection occurred during treatment.

Discussion

Treatment of liver metastases after liver transplantation is a challenging problem that has beset surgeons. Another operation will bring great trauma to patients both physically and psychologically. Clinically, RFA achieved promising results in treating patients with small tumours in the liver because it is minimally invasive and convenient to perform. The following principle for the treatment is recommended to obtain certain therapeutic effects: early finding, early diagnosis, and early treatment. Considering that the treatment effect will be better when the tumour is small, RFA procedures were performed under CEUS guidance.

The metastasis of hepatocellular carcinoma after liver transplantation is a major problem influencing the long-term intractable curative effect. Given the heavy psychological burden of patients, adopting a simple and effective treatment that can control the progress their conditions effectively and will not bring about too much burden is important. Undoubtedly, RFA is the best choice to meet such requirement. However, the actual size of the tumour and the scope of the boundary should be determined. To achieve this goal, an importance principle is the "three early" phases, namely, early discovery, early diagnosis, and early treatment.

Previously, ultrasound was adopted as the major means of detection in the post-operation re-examination.

However, the naturally small foci were difficult to determine as the sound images were indicated differently. The indications on the colour Doppler for a deeply positioned and small-sized focus with a small blood supply were unsatisfactory. Thus, the etiologic diagnosis of the focus in routine ultrasonic re-examination had its limitations. With the emergence of CEUS, the rates of etiologic diagnosis and detection of small tumours in the liver can be enhanced by monitoring the perfusion changes in the blood flow of the normal and pathological tissues in different time phases (Chen et al., 2005; Guo et al., 2009). According to the report of Dietrich et al. (2006), the ultrasonic detection rate of metastatic hepatocellular carcinoma is 81.4%, whereas the detection rate under CEUS is 91.2% and that under CT is 89.2%. Moreover, the detection rate of small foci of less than 1.0 cm under CEUS is as good as or even better than that under the enhanced CT and MRI. According to Gultekin et al. (2006), CEUS can effectively monitor the metastases after adjuvant chemotherapy and sensitively indicate the foci approaching the liver surface and near the ligament. The identification of the tumour boundary using routine ultrasound is based on the different acoustic impedances of the neoplastic and normal tissues. The tumour boundary can be judged correctly when the hepatocellular carcinoma is in expansive growth and forms a fibrous envelope, indicating the complete aureole or clear boundary of the focus. The tumour size is easily underestimated under routine ultrasound when the carcinomatous tissue is in invasive growth or exists alternately with non-carcinomatous tissue, which usually indicates no envelope or ambiguous or incomplete envelopes (Chen et al., 2006). The signals around the hepatic metastasis and the inner blood flow are strengthened obviously and the actual tumour size and boundary can be confirmed more accurately under CEUS, providing accurate localisation for RFA treatment. Thus, the effect of RFA can be enhanced, and the opportunities for focus residues can be reduced. With the re-examination under CEUS, the patients' tumours were all discovered and diagnosed when they were less than 3 cm. Moreover, some tumours can be discovered and their nature can be determined when they were as small as 1 cm. The rate of discovery and diagnosis was 100%. In addition, the accurate boundary and vascular net of the focus were indicated. Supported by CEUS, they were localised accurately, and RFA treatment was performed. The treatment of the hepatic metastasis of hepatocellular carcinoma after liver transplantation is special, which is a palliative treatment and is important for the maintenance of transplanted liver and prolonging a patient's life. Moreover, it can obtain a good therapeutic effect because it can discover the small foci as early as possible. The more appropriate therapeutic method for a patient who had a transplantation operation should be considered carefully. The proposed method is simple, practical, effective, and minimally invasive with fewer complications. During recent years, the indications of RFA were expanded continuously, and its application range became increasingly more expansive. Thus, RFA has become one of the major therapeutic methods for hepatocellular carcinoma. The percutaneous RFA guided by B ultrasound is easily operated with small trauma. CEUS can enhance the detection rate of tumours and conduct the localisation more accurate. Using the clinical prospective study, Khan et al. (2007) found that the patient's survival rates after percutaneous RFA operation and open RFA operation have no significant difference, and that the complications of the percutaneous RFA are fewer, when a tumour is less than 3 cm. Currently, percutaneous RFA is recommended to treat small hepatocellular carcinomas. References showed the following values: HCC ≤ 3 cm: 80% to 100% ablation rate; HCC3 cm to 5 cm: 50% to 80% ablation rate; and HCC > 5 cm: 25% ablation rate (Livraghi et al., 1999; Livraghi et al., 2000; Lencioni et al., 2003; Lin et al., 2004; Lin et al., 2005; Shiina et al., 2005).

In this study, CEUS and RFA were combined to conduct percutaneous RFA monitored and guided by CEUS to treat hepatic metastatic carcinoma after liver transplantation in the principles of early discovery and early treatment. The detection rate and diagnostic accuracy were improved. The foci were treated promptly when they were less than 3 cm, which was convenient and efficient with good effects. This condition can meet the need of clinical treatment and can be easily accepted by the patients without bringing about unnecessary mental burdens. The 12 patients in the study accepted the examinations under CEUS regularly, and their foci were all discovered when the tumours were less than 3 cm. The patients were promptly treated by RFA. Eleven patients had ablated foci by one treatment, and one patient delayed the treatment because of his own objective reasons, which resulted in the enlargement of his focus and missing the best opportunity for treatment. Thus, the treatment cannot be completed in time, and the focus was ablated by the supplementary treatment. The subjective requirements were met, wherein the foci were discovered and treated at the best time, with satisfactory results. CEUS was used when RFA treatment was conducted to indicate the positions with abundant blood flow in the foci for key treatment. The foci were covered completely, and the treatment time was extended properly to damage the blood supply nets of the foci thoroughly. Thus, the therapeutic effect was further enhanced.

The adverse effects of RFA are fewer and usually slight. According to a domestic data, patients undergoing operation may have a hot feeling in the liver area, ache in the right shoulder, nausea, vomiting, and chest distress, which is usually remitted after the operation. The patients may commonly have a fever, aching right shoulder, abdominal distension, and temporary abnormal liver function after the operation. Severe complications, such as pneumothorax, haemopneumothorax, perforation of hollow organs, abdominal cavity bleeding, or hepatic abscess, showed a low rate of occurrence (Chen et al., 2000). The accurate guidance and localisation by CEUS guarantee a successful RFA. The adverse effects on the patients in this study included the slight burning pain in the liver area during the operation, and two patients had nausea and chest distress. The patients had a low fever for 2 d to 3 d after the operation; their temperatures were within 38 °C, which returned to normal after 3 d. In particular, all the patients' liver functions did not have any change or any rejection phenomenon during

treatment, which mainly resulted from the small foci and slight injuries. In addition, this phenomenon indicated that early discovery and early treatment are keys to ensure the curative effect and alleviate the adverse effect.

Given the particularity in the treatment of the hepatic metastasis of hepatocellular carcinoma after liver transplantation, attention should be paid to the patients' psychological endurance and reaction, as well as the influences on the human bodies in the immunosuppressive states when clinical issues are considered. Patients have difficulty in accepting treatments with large traumas and complicated operations. Based on the RFA treatment guided by B ultrasound, we made an improvement to use CEUS to monitor and accurately localise tumours to guide the RFA treatment to achieve the clinical goals of early discovery, early treatment, good effects, and small injuries. Thus, the functional durations of the transplanted organs have been enhanced, and the survival times of the transplant patients have been prolonged effectively.

In practice, RFA treatment was proven to be convenient and effective in treating liver metastases after liver transplantation for cancer under the guidance of CEUS, being a preferred treatment for this kind of disease.

At the same time, the small nodules at special sites, such as that beneath the diaphragm, cannot be visualised clearly even under CEUS. Therefore, physiological saline is often injected around the lesion area to improve resolution to visualise this kind of special nodules (Kondo et al., 2008). However, artificial abdominal effusion can help determine the tuberculum close to the gastrointestine (Kondo et al., 2006). Therefore, the proposed methods can strengthen and enhance the adaptation of CEUS.

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