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# A Case of Recurrent Hepatocellular Carcinoma Acquiring Complete Remission of Target Lesion With Treatment With Traditional Chinese Medicine

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**Abstract**

Hepatocellular carcinoma (HCC) is one of the most prevalent malignancies worldwide. Although surgery is known as the most promising radical treatment, a high recurrent or metastatic rate after surgery has limited its clinical efficacy. Sorafenib, a target agent, has seemed to be the only option for metastatic HCC patients to date, but none of clinical trials showed it could prolong the overall survival (OS) of advanced HCC to 1 year. How to prolong the OS and improve cure rate of HCC patients is still beset with difficulties. This report presents a rare case of recurrent HCC patient with complete regression of target lesion with 2 years of Chinese herbal treatment. A 64-year-old Chinese man with hepatitis B virus–associated chronic hepatitis presented HCC has been clinically diagnosed tumor relapse and omentum metastasis with computed tomography and α-fetoprotein blood test 4 months after surgery. It was decided the patient would receive traditional Chinese medicine treatment because of poor prognosis. After approximately 2 years of treatment, recurrent hepatic tumor and omentum metastasis have been found in complete regression. The patient remains alive over 31 months after relapse.

**Keywords**

recurrent hepatocellular carcinoma, complete remission, traditional Chinese medicine, spontaneous regression, activities

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Hepatocellular carcinoma (HCC) is the most frequent histological type of primary liver cancer and the second most common cause of cancer-related mortality in males worldwide.[1] Although many treatments including transarterial chemoembolization, chemotherapy, radiotherapy, and target agents such as sorafenib are exploited, the prognosis of patients with advanced HCC still remains so poor that the majority of them survive less than 12 months.[2] Traditional Chinese medicine (TCM), an alternative usually applied to the control of side effects caused by chemical and radiotherapy, has been rarely reported to have reputable efficacy when used for advanced HCC alone. The present study presents a case of omentum metastasis of recurrent HCC with complete regression of target lesion after treatment with TCM, as revealed by image studies and blood test. The patient provided written informed consent.

## Case Report

A 64-year-old Chinese man came to our hospital with right upper quadrant abdominal pain that had lasted 10 days. His medical history included chronic viral hepatitis B infection. Physical examination revealed mild tenderness and percussion pain on the hepatic region. Ultrasound evaluation showed an enlarged solid mass in the right lobe of the liver. Computed tomography (CT) scan of the whole abdomen confirmed a single low-density mass measuring 9.2 × 7.5 cm with central necrosis (Figure 1A), and absence of abdominal lymph node enlargement or any distant metastasis. Blood tests showed α-fetoprotein 24627.50 ng/mL (normal range = 0-13.4 ng/mL). The preoperative liver function was evaluated as Child A. Hepatic resection was performed for a hepatic tumor measuring 9.5 × 8.5 × 5.0 cm (Figure 1B). Pathologic examination (1302269) confirmed HCC with intravascular cancer emboli

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**Figure 1.** Computed tomography findings before and after surgery. (A) An enlarged solid mass in right lobe of liver on February 11, 2013. (B) CT scan after tumor resection on March 18, 2013.

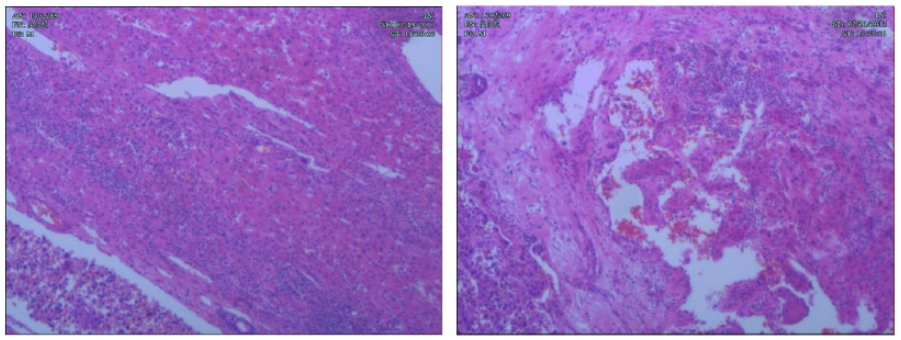


**Figure 2.** Pathological findings of tumor by hepatic resection. (A) Hepatocellular carcinoma cells with HE staining. (B) Intravascular cancer emboli.

(Figure 2). After 4 months, CT reexamination revealed recurrent hepatic carcinoma in the right lobe of the liver with omentum metastasis measuring 7.4 × 7.2 cm (Figure 3). Blood tests showed α-fetoprotein elevating from 458.54 ng/mL to 9021.55 ng/mL. Clinical diagnosis of stage IVB recurrent HCC with omentum metastasis was made. The patient was categorized as having a poor prognosis because of the cancer relapse with potential metastasis. With the consideration of the poor prognosis of recurrent HCC and financial difficulties of the patient himself, conservative therapy with TCM was finally chosen. The composition of the formula with doses of herbs listed in Table 1 was used for 1 day. The solution was mixed equitably after being boiled twice, then taken at 9:00 to 10:00 AM and 15:00 to 16:00 PM each day. During the TCM treatment, herbs were supplied every 2 weeks in our hospital. α-Fetoprotein variations were detected every 6 months while image examination was recommended every 6 to 12 months. During 2 years of treatment with Chinese herbs and antiviral treatment without any other therapy, the changes of recurrent hepatic carcinoma and omentum mass by CT scans and ultrasonography presented (Figures 4-6) with few toxicities of the herbal formula observed. The variations of the tumor measurements with the reports of ultrasonography and CT scans are listed in Table 2. Blood surveillance showed α-fetoprotein level range of 2766.67 to 3869.90 ng/mL (Table 3). The patient has been alive over 31 months since HCC relapse.

## Discussion

Hepatocarcinoma, one of the most common solid tumors, is a minimally curable disease even with surgery, target therapy, locoregional therapy, stereotactic body radiation therapy, and chemotherapy. Clinical studies evaluating the use of cytotoxic chemotherapy in the treatment of patients with

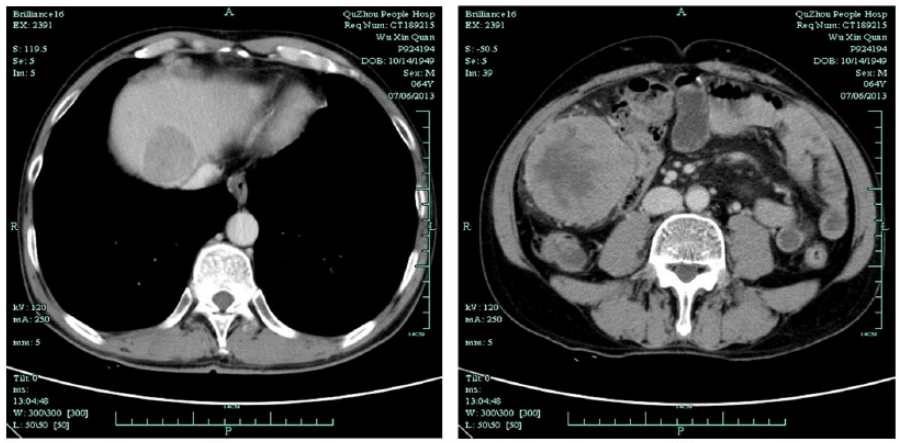


**Figure 3.** Computed tomography scan of recurrent liver tumor and omentum metastasis on July 5, 2013. (A) Recurrent tumor in right lobe of liver. (B) Omentum metastasis in right abdomen.

**Table 1.** Herbs and Dose in the Formula Used in the Case.

| Herbs | Dose (g) | Herbs | Dose (g) |
|---|---|---|---|
| Radix Bupleuri | 6 | Radix Paeoniae Alba | 15 |
| Angelica Sinensis | 10 | Radix Curcumae | 10 |
| Radix Salviae Miltiorrhizae | 20 | Ligusticum Wallichii | 15 |
| Actinidia valvata Dunn | 30 | Melia Toosendan | 10 |
| Fructus Aurantii | 10 | Artemisia carvifolia | 10 |
| Caulis Spatholobi | 20 | Chinese Lobelia | 15 |
| Sedum Sarmentosum Bunge | 30 | Squama Manis | 3 |
| Radix Ranunculi Ternati | 10 | Salvia Chinensis | 30 |
| Hedyotis Diffusa | 20 | Liquidambar Formosana Hance | 15 |
| Centipede | 3 | | |


**Figure 4.** Ultrasonography of liver and omentum metastasis with TCM treatment on July 30, 2014. (A) Recurrent tumor in liver disappeared. (B) Omentum metastasis measuring 6.2 cm × 4.5 cm.

advanced HCC have typically reported low response rates, and evidence for a favorable impact of chemotherapy on overall survival in patients with HCC is lacking.[3-5] For target therapy, there have been 2 randomized, placebo-controlled, phase III trials for assessment of sorafenib in the treatment of patients with advanced or metastatic HCC so far (SHARP


**Figure 5.** Ultrasonography of liver and omentum metastasis with TCM treatment on December 28, 2014. (A) Recurrent tumor in liver disappeared. (B) Omentum metastasis measuring 4.5 cm × 3.7 cm.

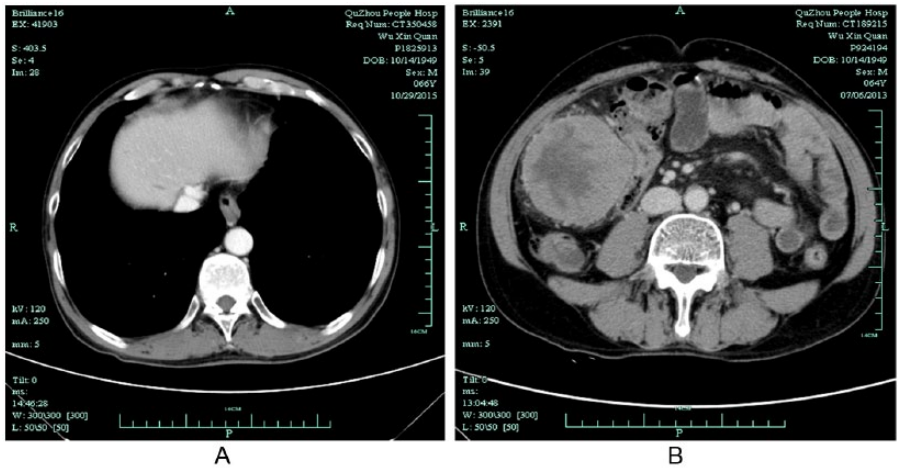


**Figure 6.** Computed tomography scan of liver and abdomen with 2 years of TCM treatment on October 29, 2015. (A) CT showed tumor in the liver disappeared. (B) Omentum metastasis in the abdomen vanished.

**Table 2.** Progress of the Disappearance of Recurrent Hepatic Carcinoma and Omentum Metastasis.

| | Measurements of the Tumor With Imaging | |
|---|---|---|
| Date | Liver (LD × SD) | Omentum (LD × SD) |
| February 11, 2013 | 9.2 cm × 7.5 cm | N/A |
| July 5, 2013 | 3.9 cm × 3.7 cm | 7.4 cm × 7.2 cm |
| July 30, 2014 | N/A | 6.2 cm × 4.5 cm |
| December 28, 2014 | N/A | 4.5 cm × 3.7 cm |
| October 29, 2015 | N/A | N/A |

Abbreviations: LD, longest diameter; SD, shortest diameter.

**Table 3.** Progress of α-Fetoprotein (AFP) Throughout the Course of the Case.

| Date | AFP (0-13.4 ng/mL) |
|---|---|
| February 11, 2013 | 24627.50 |
| February 19, 2013 | 20076.10 |
| February 21, 2013 | 8794.96 |
| March 4, 2013 | 2627.80 |
| March 18, 2013 | 458.54 |
| July 2, 2013 | 9021.55 |
| December 19, 2013 | 2515.58 |
| July 30, 2014 | 3485.91 |
| December 29, 2014 | 2766.67 |
| May 24, 2015 | 3294.28 |
| October 28, 2015 | 3869.90 |

and Asian-Pacific trial), neither of which has shown sorafenib to prolong overall survival of patients with

**Table 4.** Reported Potential Antitumor Activities of Herbs Involved in the Formula.

| Activities | Source | Antitumor Spectrum | References |
|---|---|---|---|
| Saikosaponin | Radix Bupleuri | Breast, lung | 22, 23 |
| Paeoniflorin | Radix Paeoniae Alba | Gastric, lung, cervical, breast | 24-27 |
| Angelica | Angelica Sinensis | Colorectal | 28 |
| Curcumin | Radix Curcumae | Colorectal, breast, ovarian, lung, pancreatic, cervical, hepatocellular | 20, 29-34 |
| Curcumol | Radix Curcumae | Colorectal | 35 |
| Beta-Elemene | Radix Curcumae | Esophageal, ovarian, hepatocellular, kidney, lung | 21, 36-39 |
| Ligustrazine | Ligusticum Wallichii | Lung, breast | 40, 41 |
| Saponin | Actinidia valvata Dunn | Hepatocellular | 18 |
| Toosendanin | Melia Toosendan | Hepatocellular | 19 |
| Limonoids | Fructus Aurantii | Colon, breast, cervical | 42-44 |
| Artemisinin | Artemisia Carvifolia | Cervical, gastric, breast | 45-47 |
| Artesunate | Artemisia Carvifolia | Breast, hepatocellular, ovarian, gastric, esophageal, bladder, colorectal | 48-54 |
| Spatholobus suberectus | Caulis Spatholobi | Breast, lung | 55, 56 |
| Lobeline | Chinese Lobelia | Colon | 57 |
| Polysaccharides, Saponins | Radix Ranunculi Ternati | Gastric | 58 |
| Ursolic acid | Salvia Chinensis | Pancreatic, ovarian, gastric, lung, breast, prostate | 59-64 |
| Hedyotis diffusa water extract | Hedyotis diffusa | Breast, prostate, colorectal, bladder | 65-68 |
| Centipede extract | Centipede | Cervical | 69 |

advanced HCC to 1 year.[5,6] Therefore, most patients with advanced or metastatic HCC are not eligible for potential curative therapies.

Spontaneous regression of cancer was defined as partial or complete disappearance of malignant tumor without any anticancer therapy.[7] Kinds of malignant tumors including colon cancer, breast cancer, renal cell carcinoma, neuroblastoma, and choriocarcinoma have been reported to convert to spontaneous regression in a PubMed search.[8-12] However, spontaneous regression of HCC still remains a rare event.[13] Because of the antitumor treatment with Chinese herbs for 2 years in this case, spontaneous regression of HCC has not been taken into consideration.

Traditional Chinese medicine, which has been observed to be effective and used in China for more than a thousand years, was widely exploited in diseases including malignancy. According to recent research, traditional Chinese herbal extracts seem to be emerging as a novel antitumor selection in the treatment of cancers including nasopharyngeal carcinoma, bladder carcinoma, and HCC.[14-17] The formula in the case, made in our hospital, boiled by the patient himself, mainly contains crude of 19 herbs listed with doses in Table 1. The patient denied any changes in lifestyle or diet that he started along with the Chinese herbs.

All herbs in the formula have been searched for the possible antitumor activities with PubMed. According to the result, the antitumor activities of herbs in the formula have been identified (Table 4), some of which including *Actinidia valvata* Dunn, Toosendanin, Radix Curcumae, and *Artemisia carvifolia* involved in the formula have been verified for antitumor activity on HCC. Saponin extracted from the root of *Actinidia valvata* has been reported to have anti-HCC activity in vitro with HCC cells in cell lines BEL-7402, HepG2, PLC, SMMC-7721, MHCC-97-H, and MHCC-97-L.[18] The extract could restrain adhesion, invasion, mobility, and migration abilities of BEL-7402 and MHCC-97-H cells in vitro.[18] Toosendanin extract has potent anti-HCC effects via suppressing proliferation and inducing apoptosis of cancer cells in vitro with HCC cell lines SMMC-7721 and Hep3B and in vivo with BALB/c mice. The mechanism of apoptosis involves the mitochondrial pathway and death receptor pathway.[19] Curcumin extracted from Radix Curcumae has demonstrated a synergistic effect with bevacizumab on the inhibition of the effects of the VEGF signaling pathways in HCC progression.[20] Beta-elemene, well known for its antitumor activity, capable of sensitizing HCC cells to oxaliplatin, could also be extracted from Radix Curcumae.[21] Despite all these findings, changes caused by chemical reactions when herbs are mixed and boiled together still remain unknown. Therefore, more research on the possible activities of herbs might be indeed necessary to lead to the discovery of new antitumor drugs.

In conclusion, complete regression of target lesion in recurrent HCC by TCM is an interesting phenomenon, the

mechanism of which still remains unknown. Further discussion and deeper research on the anti-HCC activity of TCM will help in understanding this phenomenon and in curing malignancies.

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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