



Traditional Chinese Medicine is Useful Treatment for Hepatocellular Carcinoma with Severe Liver Cirrhosis: A Case Report

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Abstract

Background: There are several treatments for Hepatocellular Carcinoma (HCC) such as surgery, internal medical treatment, and radiation therapy. Sometimes further HCC treatments are difficult to implement in those with severe liver complications such as decompensated cirrhosis. However, Traditional Chinese Medicine (TCM) can be used to treat HCC even in cases of advanced liver damage.

Case Summary: We describe here a case involving successful treatment of HCC with advanced liver cirrhosis using TCM, including representative herbal medicines well known for their anti-tumor components.

A 71-year-old male visited our hospital with an HCC diagnosis, and TACE was performed several times for a few years. Finally, when the liver function reached Child-Pugh C class, we stopped performing TACE; however, the patient wanted to try another therapy. Hence, we treated him using TCM (including *H. diffusa* Willd 60 g and *S. barbata* D. DON 30 g, *Prunella vulgaris* L 10 g).

After TCM administration, the HCC was not detected in a computed tomography scan and serum alfa fetoprotein and Des-gamma-Carboxy Prothrombin (DCP) levels decreased to almost normal levels for two years; however, the patient died from encephalopathy and pneumonia due to an influenza infection.

Conclusion: In the treatment of advanced liver cancer, prognosis and treatment are greatly influenced by liver function. The usage of TCM, especially including *H. diffusa* Willd, *S. barbata* D. DON and *Prunella vulgaris* L is one of the methods of HCC treatment in advanced cirrhosis, when anticancer drugs in Western medicine are not available.

Keywords: Traditional Chinese medicine; Hepatocellular carcinoma; Severe liver cirrhosis

Abbreviations

TCM: Traditional Chinese Medicine; HCC: Hepatocellular Carcinoma

Introduction

There are several treatments for Hepatocellular Carcinoma (HCC) such as surgery, radiofrequency ablation, molecular targeted drugs, arterial embolization and hepatic arterial infusion chemotherapy, and proton and heavy particle beam radiation therapy. Prognosis of local therapy with Radiofrequency Ablation (RFA) and surgical resection is relatively good but HCC has a characteristic pattern of multicentric recurrence, and the recurrence rate is higher than that for other organ cancers. Sometimes, further treatments are difficult in severe liver disease such as cirrhosis. BCLC classification for the advanced stage allows for only conservative treatment and molecular targeted drugs such as sorafenib and lenvatinib. However, these are not preferred in those with Child-Turcotte-Pugh class B cirrhosis due to worsening liver failure prognosis. Artery embolization treatment is also not considered for advanced liver damage in those with a Child-Turcotte-Pugh C score of more than 10. Herbal medicine is actively used for treating severe liver cirrhosis and HCC. Even in those with extremely poor liver function such as those in the non-compensatory phase, herbal medicines can be used although their effectiveness is not so strong. Herein, we report a case involving successful use of Traditional Chinese Medicine (TCM) for HCC treatment with advanced liver damage, in the absence of Western medical treatments.

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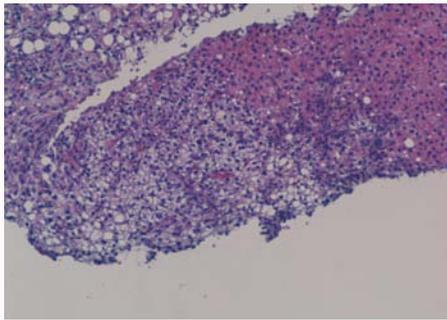


Figure 1: Needle biopsy was performed at the S8 lesion. A well to moderate differentiated hepatocellular carcinoma was found in this mass lesion.

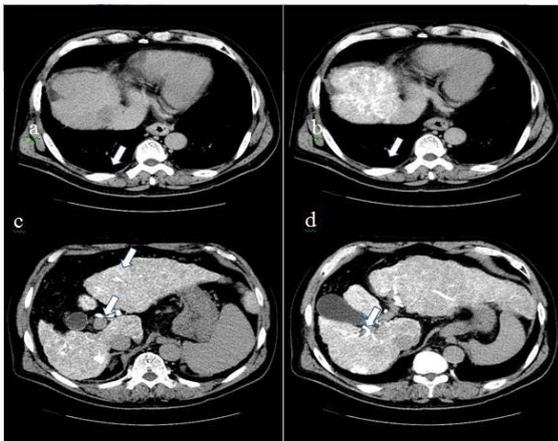


Figure 2: CTA, CTAP. Low density area in CTAP (a) and slight enhancement in CTA (b) were observed in S8 near the IVC, and there were multiple enhancement lesions near S3, S6, and S7 (c,d).

Case Presentation

A 71-year-old male diagnosed with Hepatocellular carcinoma of medical history of Cirrhosis, esophageal varices, high blood pressure, diabetes, ventricular arrhythmias, and idiopathic atrial fibrillation. Medical conditions: At 2010, esophageal varices and cirrhosis were diagnosed at another hospital. The cause of liver cirrhosis was considered to be Non-Alcoholic Steatohepatitis (NASH). At his own request, since 2013, he has been undergoing treatment at our hospital. In April of 2014, a Space-Occupying Lesion (SOL) of 28 mm × 26 mm appeared in the S8 area, with using Computed Tomography (CT), and hepatocellular carcinoma (well to moderately differentiated) was diagnosed by needle biopsy (Figure 1). CT arteriography and CT during arterial portography (CTA/CTAP) were performed for detailed scanning of the liver. Multiple HCC lesions were detected in the S3, S6, S7 and S8 area (Figure 2). Transcatheter Arterial Chemoembolization (TACE) was performed; however, the patient could not have surgery due to his poor liver function and because of the multiple HCC lesions that occupied a large area. Table 1 shows the lab data results of the first therapy. At this time, the Child-Pugh score was 7 (Child B).

The following were all the TACE therapies implemented (Figure 3).

- 2014, Nov. TACE therapy and liver function Child-Pugh Class B
- 2015, Jun. TACE for multiple HCC recurrences
- 2015, Dec. TACE for multiple HCC recurrences

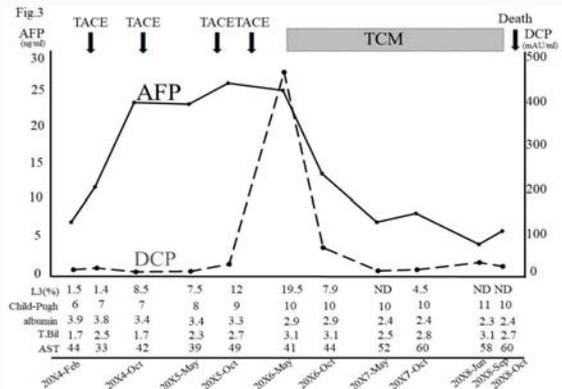


Figure 3: Both AFP and DCP levels decreased to almost normal ranges after administration of the TCM and no significant change was observed in the liver function. (ND: Not Detected).

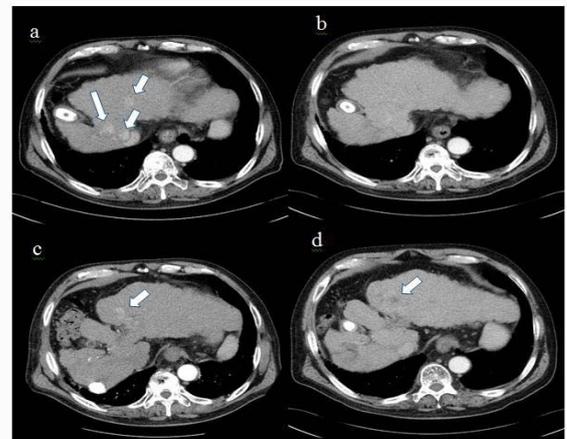


Figure 4: Early enhancements were found near S3, S5, and S8 (a,c) but one year later enhancement of lesions reduced in these areas and other areas (b). At some lesions, apparent necrosis appeared, the disappearance of lesion enhancement was also observed (d).

2016, May. Liver function became worse leading to a Child Pugh score of 10 (C) (Table 2)

2018, Oct. –Death (encephalopathy and pneumonia due to influenza in another hospital).

In May 2016, Alfa-Fetoprotein (AFP) and Des-Gamma-Carboxy Prothrombin (DCP) increased rapidly and the L3 fraction increased more than 10%. In addition, multiple HCCs developed according to the enhanced CT (Figure 4a, 4c). Because his liver function became worse, we decided to not perform more TACE procedures and advised the patient to undergo Best Supported Care (BSC). However, he wanted to try another treatment option for HCC.

Hence, we recommended treating HCC and liver cirrhosis using Traditional Chinese Medicine (TCM). TCM was started in 2016, 5/28 containing the following: *Hedyotis diffusa* Willd., 60 g, Panax ginseng C.A. Meyer 6 g, Poria cocos Wolf 6 g, *Atractylodes ovata* DC 6 g, *Glycyrrhiza uralensis* FISCH 2 g, *Paeonia lactiflora* PALL 6 g, *Artemisia capillaris* THUNB 3 g, *Astragalus membranaceus* BGE 15 g, Citrus tangerine HORT 6 g, *Scutellaria barbata* D. DON 30 g, *Prunella vulgaris* L 10 g. The method of oral administration is a general TCM method, and taking the above-mentioned herbal medicine as a recipe of chopped in 700 ml of water and boiled for 40 min, divided into 2

Table 1: Lab data results of the first therapy.

a)		
WBC	3900	/ μ l
RBC	480	10^4 / μ l
Hb	14.3	g/dl
Plt	5.6	10^4 / μ l

b)	
HBs antigen	negative
HBc antigen	negative
HCV antibody	negative
ANA	negative
AMA	negative

c)	
PT	60.30%
TP	7.4 g/dl
Alb	3.7 g/dl
AST	44 U/l
ALT	33 U/l
LDH	210 U/l
ALP	225 U/l
GTP	38 U/l
Cho-E	206 U/l
NH3	194 μ g/dl
T.Bil	1.7 mg/dl
D.Bil	0.3 mg/dl
DCP	11 mAU/ml
AFP	13.1 ng/ml
L3 fraction	1.40%

to 3 times a day to take total amount. After administration of TCM, no significant change was observed in the liver function and no severe side effects occurred. Additionally, serum AFP and DCP levels both decreased (Figure 3) to normal ranges and the L3 fraction decreased to undetected levels (ND). One year later, many lesions vanished in the follow-up CT scan (Figure 4b, 4d).

We continued to administer TCM and no HCC appeared according to the CT scan; however, in 2018, October he suddenly died due to pneumonia and encephalopathy by influenza at another hospital.

Discussion

In the treatment of liver cancer, repeat TACE decreases basic hepatic function; hence, recently, it has been recommended that molecular targeted drugs be started in the early phase [1]. Molecular targeted drugs (sorafenib and lenvatinib) can be used for treating Child-Pugh Class A but are not recommended in advanced cirrhosis such as Child B and C [2,3] due to their severe adverse effects and poor prognosis. TACE treatment can be used for HCC treatment in those with cirrhosis in BCLC stage C without portal invasion or lymph node metastasis or other metastasis. However, Child-Pugh score can be increased more than 10 in advanced cirrhosis. In these cases, no more aggressive therapies are recommended [4].

Treatment of cirrhosis consists of two treatments: the goal in

Table 2: Child Pugh score.

PT	46.70%
TP	7.5 g/dl
Alb	2.9 g/dl
AST	41 U/l
ALT	25 U/l
LDH	219 U/l
ALP	560 U/l
GTP	25 U/l
Cho-E	97 U/l
NH3	186 μ g/dl
T.Bil	3.1 mg/dl
D.Bil	1.3 mg/dl
DCP	441 mAU/ml
AFP	24.1 ng/ml
L3 fraction	19.50%

the first stage of treatment is to eliminate the cause of cirrhosis and therefore consists of antiviral treatment, and the second stage of treatment consists of a compensated treatment for ailments such as hyperammonemia, ascites, and jaundice. TCM has also been used, such as shi-kunshi-to, ninjin-to, and inchinkou-to, which in the past were often used for those with cirrhosis and chronic liver disease.

For Western treatments of HCC, BSC (best supported care) is chosen for those with severe cirrhosis. While in TCM, basically all patients can use traditional herbal medicine for HCC treatment, including *S. barbata* D. DON [5,6], *Lobelia chinensis* LOUR [7], *H. diffusa* Willd [8], and *Prunella vulgaris* L [9].

S. barbata D. DON induced apoptosis in human hepatocarcinoma MHCC97-H cells and H22 cells via the mitochondrial pathway [6,10] and *S. barbata* D. DON also have an anti-angiogenic effect by regulating VEGF [11]. *H. diffusa* Willd suppresses proliferation of human hepatocellular carcinoma cell lines, HepG2 [8]. *Prunella vulgaris* L may have the therapeutic potential to inhibit the migration and invasion of hepatocellular carcinoma [9].

In clinical reports of cohort studies, TCM was associated with a significantly reduced HCC risk in patients with chronic hepatitis B. Their list of herbal medicines were *D. heyotis diffusa*, *S. barbata*, *Rehmannia glutinosa*, *Isatis tinctoria*, Yi Guan Jian, Xiao Chai Hu Tang Wu Ling San, and Gan Lu Yin [12].

For patients with chronic hepatitis, there are several therapies that can be performed in HCC because the liver function of the patient is still in good condition. However, in those with advanced liver damage, the therapy options are sorafenib and lenvatinib in those with Barcelona Clinic Liver Cancer (BCLC) stage C and best supported care in those with BCLC stage D [13].

However, TCM can be used in almost all the patients with severity ranging from that of acute hepatitis to severe liver damage (those with a Child-Pugh score of 10). In our case, after multiple treatments with TACE, liver function failed and we could not perform more TACE but the patient strongly wanted to continue some type of therapy to treat HCC. Therefore, we decided to administer TCM such as *H. diffusa* Willd, *S. barbata* D. DON and *Prunella vulgaris* L because these three herbal medicines are allowed to be used in Japan. Sometimes when we

use these herbal medicines, the amounts of both should be increased those with cirrhosis and other concomitant diseases. These amounts have been described in Chinese literature and often are used not only for cirrhosis and HCC treatment but also other malignant tumors [14].

Unfortunately, our patient died two years after beginning TCM treatment due to influenza related pneumonia and encephalopathy; however, for more than two years there were no apparent recurrences and no apparent worsening of his liver function.

Conclusion

In the treatment of advanced liver cancer, prognosis and treatment are greatly influenced by the patient's liver function. The usage of TCM such as *H. diffusa Willd.*, *S. barbata D.* DON and *Prunella vulgaris L* with anti-cancer action represent a potential candidate for effectively treating HCC in those with advanced cirrhosis, when anticancer drugs in Western medicine are not available.

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