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A Further Study of Advanced Hepatocellular Carcinoma (HCC) with the Chemotherapy and Traditional Medicine: Report of 12 Cases

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ABSTRACT

In this study, the objective response was obtained in 12 cases of hepatocellular carcinoma (HCC) following chemotherapy and traditional medicine. Among them, the clinical data for ten patients with HCC were previously described, and 2 cases were continuous to be present here. During the schedule of drug administration, 12 cases of HCCs were treated using the different protocol of chemotherapy in conjunction with traditional medicine. One HCC accompanied with colon polyps obtained complete remission via hepatectomy and targeting oncogenic receptor tyrosine kinase inhibitor sorafenib. And, an approach to hepatic artery intervention chemotherapy plus cantharidin was carried out in another advanced HCC. All 12 patients with disease-free survival were 2, 2, 8, 6, 1.6, 1.8, 10, 15, 20, 20, 5 years, respectively. In discussion, the incidence of HCC is on the rise due to the impact of HBV and HCV, an additional recent data implicate hepatocyte growth factor (HGF)and HGF receptor oncogenic signaling (also HGFR/met oncogenic receptor),which act as a trigger for liver regeneration even in (hepatocellular) carcinogenesis.

Keywords: HCC, HBV, HCV, HGF/met or met oncogenic receptor 5-fluorouracial, Traditional herbal medicine

INTRODUCTION

In clinical situation only 5.3% of patients who were belonged to the indication of hepatectomy whereas 90% of them were conclusively the protocol of chemotherapy. One of this approaches, traditional medicine occupied its important role in the field of hepatocellular carcinoma treatment. In search for the effective approach of PHC [1-6], we had summarized the retrospective study of HCC under remission, with the combined protocol of chemotherapy and traditional medicine.

METHODS AND RESULTS

The clinical data from case 1 to case 10 have been previously reported [7,8]. The detail results of ten patients described in **Table 1**.

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Table 1. Patients characteristics.

Cases	Sex	Ages	History of diseases	Diagnosis	Protocol	Response following therapy	Duration of remission
1	M	52	2 months	PHC (AFP 7500 ng/ml)	5-Fu (500 mg, once a week), VCR, Toyomycin, TCM	CR	2 years
2	M	55	2 months	PHC (AFP+)	5-Fu (1000 mg, once a week), TCM	CR	8 years
3	M	60	2 months	PHC (AFP 200 ng/ml)	Demethylcantharidine	CR	6 years
4	F	37	40 days	PHC	5-Fu (1500 mg, once a week), TCM	CR	10 years
5	M	26	3+ months	MHC (6 × 4 cm)	5-Fu (1000-1500 mg/day), VCR, CTX, MMC	CR	20+ years
6	M	30	3+ months	PHC (11.1 × 6.2 cm)	5-Fu (1500 mg/day), VCR, CTX, MMC	CR	20+ years
7	M	39	3+ months	Earlier PHC (AFP i.9 ng/ml in 1996, 8.7 ng in 2002, 2.05 ng after therapy)	Cantharidine, TCM	CR	15+ years
8	M	47	20 days	PHC (AFP+, 3.2 × 3.0 cm)	Dex, TCM	Short CR	18+ months
9	M	31	15 days	MHC (7 × 4.5 cm)	Retinoic acid, TCM	Short CR	20+ months
10	F	47	10 days	MHC (3 × 2.7 cm)	5-Fu, Tegafur (600#)	PR	2 years
11	M	63	1+ months	PHC	Hepatectomy, Sorafenib	CR	5 years
12	M	41	1+ months	PHC (AFP: 40.59 ng/ml)	Local chemotherapy, Cantharidin	Stable disease	3+ months

Note: PHC: Primary Hepatocellular Carcinoma; MHC: Metastatic Hepatocellular Carcinoma; 5-Fu: 5- Fluorouracil; VCR: Vincristine; CTX: Cyclophosphamide; MMC: Mitomycin; TCM: Traditional Medicine; M: Male; F: Female

CASE REPORTS

Case 11: A 63 year old man was diagnosed as his hepatic tumor due to his occasional colon polyp examination (**Figure 1**). At CT examination on August 23, 2012 and September 1, 2012 respectively showed 2.0 × 2.4 cm tumor in the right anterior lobe of his liver. Moreover, on B ultrasound on September 3, 2012 and December 13, 2012 respectively also consistently showed 26 × 17 mm mass in the right anterior lobe of his liver. Histologically, primary hepatocellular carcinoma (PHC) was further diagnosed after biopsy of liver tumor tissue on April 26, 2013 **(Figure 2)**. The remainder of liver enzyme performed serum AFP 1.74 ng/ml (control 0-7.0 ng/ml). He had a past history of viral hepatitis B (HBV) infection. The patient was once undergoing radio-frequency ablation of HCC on September 4, 2012; and repeat CT examination the tumor size was increased to 33 × 31 mm on April 15, 2013 and 33 × 37 mm liver nodule on June 17, 2013, respectively. In May, 2014 he was therefore given his hepatectomy (at right lobe), with the combination treatment of Sorafenib tablets (initial dosage 2#/day × 5 months, then 1#/day intermittent until to 1.5

years) and antivirus Entecavir despensible tablets. In the follow up, he was remained well with over 5 year's survivor.

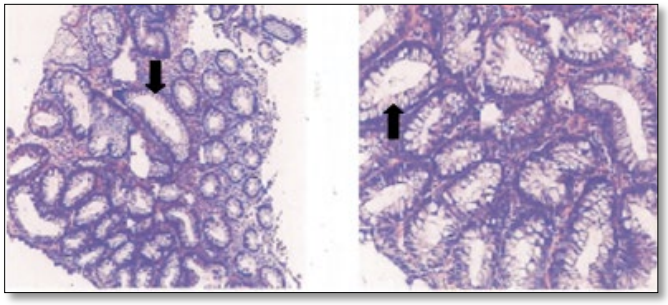

Figure 1. Adenomatous polyp of descending colon (case 11).

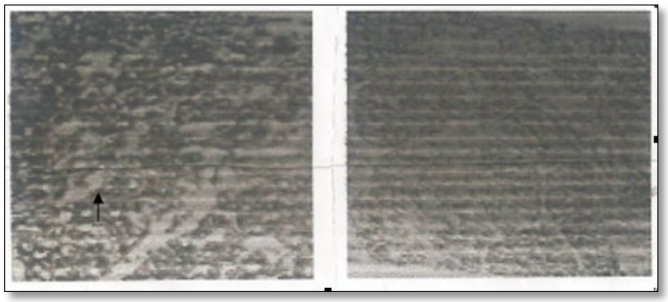

Figure 2. Primary hepatocellular carcinoma (HCC) (case 11).

Case 12: A 41 year old man stated that he was disgusted with taste of greasy, accompanied with nausea and vomiting for one month, and chief complaint of abdominal mass one day ago. At physical examination showed 6 × 5 cm harden mass in his hepatic lesion, and an enlarged liver was felt 7 cm below the right costal margin. Laboratory data included serum AFP 40.59 ng/ml (control 0-7 ng/ml), CEA 5.86 (control<5.0 mg/L), CA-125 63.0 (control<35.0 u/ml), CA-159 91.31 (control<35.0 ku/L), serum HBsAg (-), serum HBsAb 53.3 (+), serum HBeAg (-), serum HBeAb 1.29 (+), serum HBcAb 1.45 (+). He was diagnosed as advanced HCC. Treatment consisted of hepatic artery intervention chemotherapy (Lobaplatin plus camptothecin injection, **Figure 3**) in another provincial tumor hospital and demethylcantharidin tablets. He was in stable disease for 3 months and now being treated in other hospital.

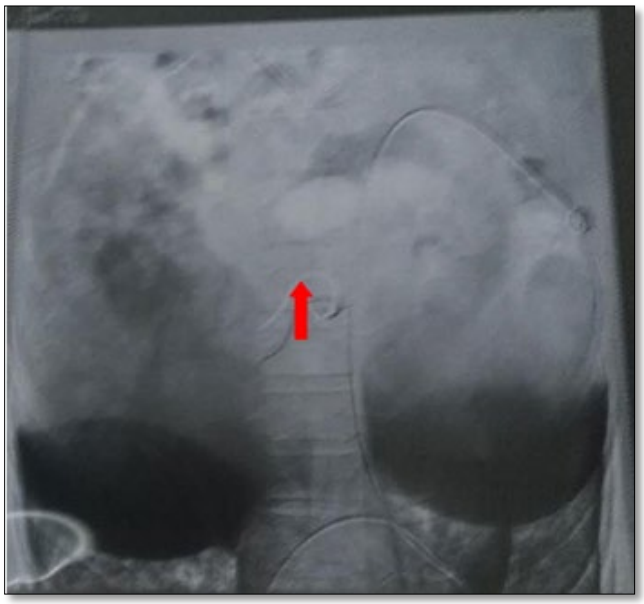

Figure 3. Hepatic artery intervention chemotherapy (Lobaplatin plus camptothecin local injection around hepatic tumor) (case 12).

DISCUSSION

Sorafenib is an oral inhibitor of oncogenic receptor tyrosine kinases, including VEGFR, PDGFR, KIT, FLT3 and also its activity against c-Raf and b-Raf [9-22]. There were several clinical trials of sorafenib evaluated in HCC in European centers [23], in Asian and Pacific centers [24] and in Hong Kong [25]. Subgroup analysis indicated a benefit for sorafenib in stable disease. Compared with those HCC with hepatitis B, those HCC with hepatitis C had longer time to progression [26-32]. Moreover, in those with HBV, the HCC without extrahepatic metastasis, particularly the absence of lung metastasis, predicted clinical benefit [33]. At present, a durable complete remission of an earlier HCC with the combination of hepatectomy and sorafenib in a third-line setting, in the follow up, that has offered a progression-free survival of 5 years.

Steroid androgen is another environmental revelance factor of breast tumors and hepatoma. Up to now, the development of at least 22 hepatic tumors had been well documented in patients receiving androgenic steroid (oxymetholone, methyl testosterone) therapy, and promotion of murine hepatocarcinogenesis by testostertone is androgen receptor-dependent [34,35]. Regression of the hepatic tumor has been reported in four cases after cessation of therapy. Bone marrow transplantation from a histocompatible sibling was advocated by successful hematopoietic and immunological reconstitution and associated with regression of the hepatic masses in a 13 year old boy with aplastic anemia. In clinical study, Zhu [36] previously reported that androgen methyl testosterone can induce breast tumors in one patient with severe aplastic anemia, which implicate that androgen via its oncogenic androgen receptor (AR) signaling had oncogenic potential.

More recent, HGF-HGF receptor (met oncogenic receptor) oncogenic signaling might play an important role in HCC, which implicate its target therapy. Foretinib, the first multi-target c-met TKI to under investigation, produced a promising benefit in HCC patients [37]. The chemically-modified monovalent antibody DN30 was found to inhibit ligand-independent activation of the met oncogenic receptor, providing another target therapy [38,39]. This is testable.

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The authors confirm that this article content has no conflict of interest.

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