Clinical Case Report

Medicine®

OPEN

The radiosensitive effect of apatinib for hepatocellular carcinoma patient with big paraspinal metastasis

A case report

Hong Zhu, MD, Yaqin Zhao, MD, Xin Wang, MD*

Abstract

Rationale: Hepatocellular carcinoma (HCC) is a highly invasive cancer associated with great mortality rates. The prognosis of advanced HCC is very poor.

Patient concerns: Here, we report a HCC patient with a big paraspinal metastasis with 10 cm in diameter who failed the treatment of sorafenib.

Diagnoses: Sorafenib refractory HCC with big paraspinal metastasis.

Interventions: The concurrent treatment of apatinib with stereotactic body radiotherapy (SBRT).

Outcomes: The paraspinal metastasis with 10 cm in diameter showed nearly complete response.

Lessons: We think that the apatinib may be a good choice for HCC and it may function as a radiosensitizer of HCC. However, it warrants further investigation in the future prospective clinical studies.

Abbreviations: AFP = alpha fetoprotein, BCLC = Barcelona Clinic Liver Cancer stage, CR = complete remission, HBV = hepatitis B virus, HCC = hepatocellular carcinoma, HCV = hepatitis C virus, PD = disease progression, SBRT = stereotactic body radiotherapy, SD = stable disease, TKI = tyrosine kinase inhibitor, VEGFR-2 = vascular endothelial growth factor receptor-2.

Keywords: apatinib, hepatocellular carcinoma (HCC), radiosensitizer, radiotherapy

1. Introduction

Hepatocellular carcinoma (HCC) is the third most common cause of cancer mortality worldwide.[1] More than 75% of cases occur in the Asia-Pacific region, largely in association with chronic hepatitis B virus (HBV) infection.[2,3] HCC is known to be highly refractory to conventional systemic chemotherapy. Although sorafenib- and oxaliplatin-based chemotherapy are now recommended as standard treatment for advanced HCC in Asian areas,[1,2,4] the treatment efficacy was still limited. A large proportion of Asian patients with HCC present with locally advanced or metastatic disease, at which point they are ineligible for curative treatments.[4]

Apatinib is a small molecule tyrosine kinase inhibitor targeting vascular endothelial growth factor receptor-2 (VEGFR-2), which functions as antiangiogenesis and has been recommended as a third-line treatment for metastatic gastric cancer patients.[5,6] However, there is no report to evaluate its efficacy and safety in patient with HCC. Herein, we report a case of advanced HCC with a big spinal metastasis treated with concurrent apatinib and stereotactic body radiotherapy (SBRT) in our hospital. The report was approved by the West China Hospital institutional review board, and the patient provided written informed consent.

2. Case presentation

A 44-year-old man was brought 3 years ago to our hospital because he was found with a tumor mass in his liver by ultrasonic examination in local hospital. The patient had a history of hepatitis B infection and liver cirrhosis for more than 5 years and without any treatment. The examination in our hospital found that there was a mass about 4.7 cm × 3.6 cm in right lobe of the liver with typical HCC radiological characteristics (Fig. 1A). The alpha fetoprotein (AFP) was higher than 1210 ng/mL.

The patient was then subjected to right hemihepatectomy, repair of portal vein, repair of vena cava, and cholecystectomy on November 19, 2014. The intraoperative ultrasound found there was only one tumor mass about 7 cm × 6 cm with complete capsule. The pathological examination found that the tumor was about 5.5 cm × 4.6 cm × 4 cm, middle differentiated HCC. The tumor invaded the capsule of liver. The Ishak score was 5. The Barcelona Clinic Liver Cancer (BCLC) stage was stage A. The gallbladder was not invaded. The AFP was decreased to 45.90 ng/mL after the surgery.

Four months later, the AFP of this patient was increased to 985.00 ng/mL. The contrast-enhanced ultrasound found there

Editor: N/A.

The authors have no conflicts of interest to disclose.

Department of Medical Oncology, West China Hospital, Sichuan University, Chengdu, Sichuan, P.R. China.

* Correspondence: Xin Wang, Department of Medical Oncology, West China Hospital, Sichuan University, Chengdu, 610041, Sichuan, P.R. China (e-mail: wangxin213@sina.com).

Medicine (2018) 97:2(e9598)

Received: 26 November 2017 / Accepted: 20 December 2017

http://dx.doi.org/10.1097/MD.0000000000009598

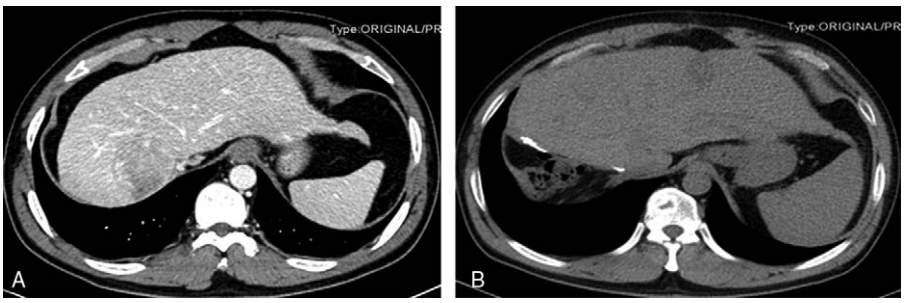

Figure 1. (A) The primary tumor in the right lobe of the liver. (B) The liver after radiofrequency ablation.

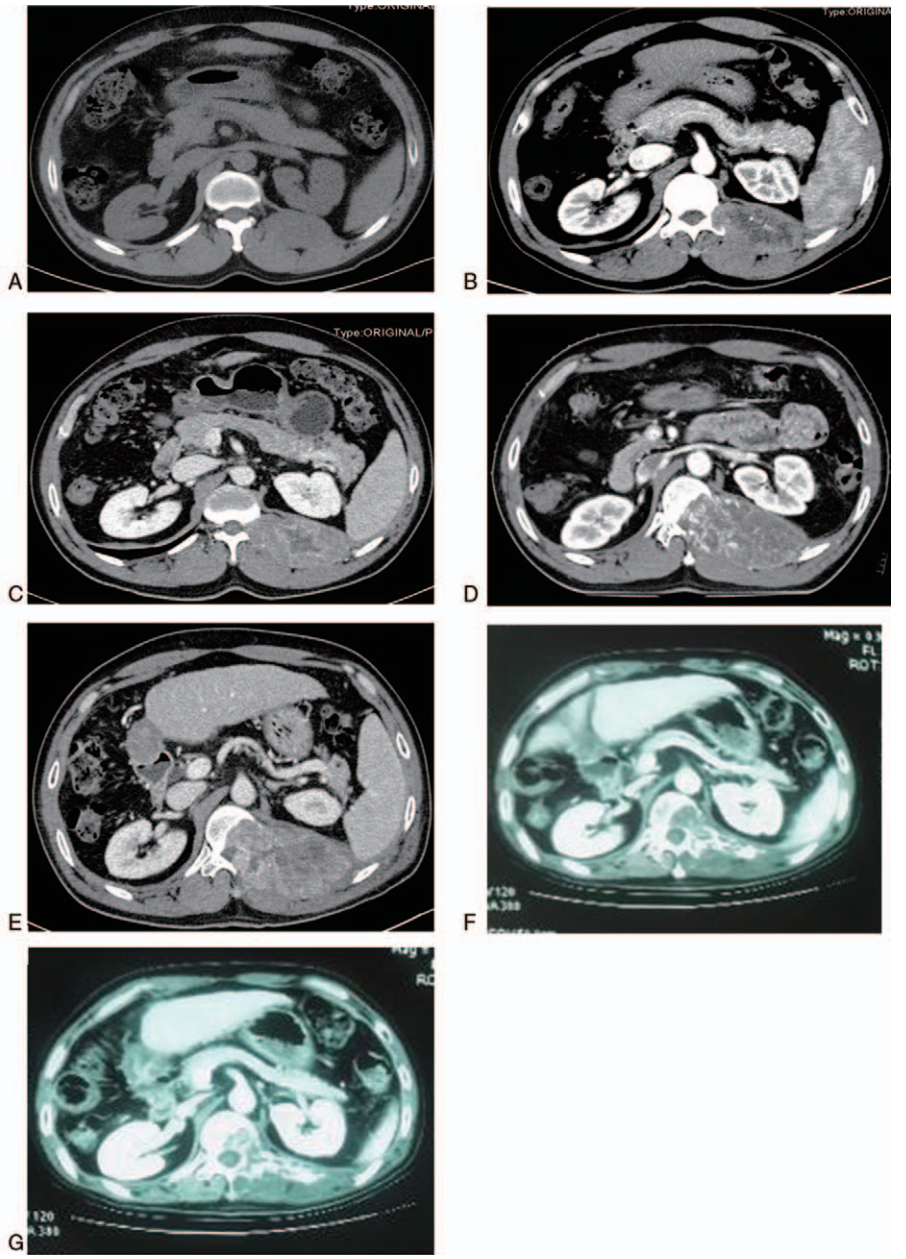

Figure 2. (A) The paraspinal metastasis first found (2015.6.22). (B and C) The paraspinal metastasis 3 months after sorafenib treatment (2015.9.16). (D and E) The paraspinal metastasis 8 months after sorafenib treatment (2016.3.3). (F and G) The paraspinal metastasis 8 months after apatinib treatment (2016.11.16).

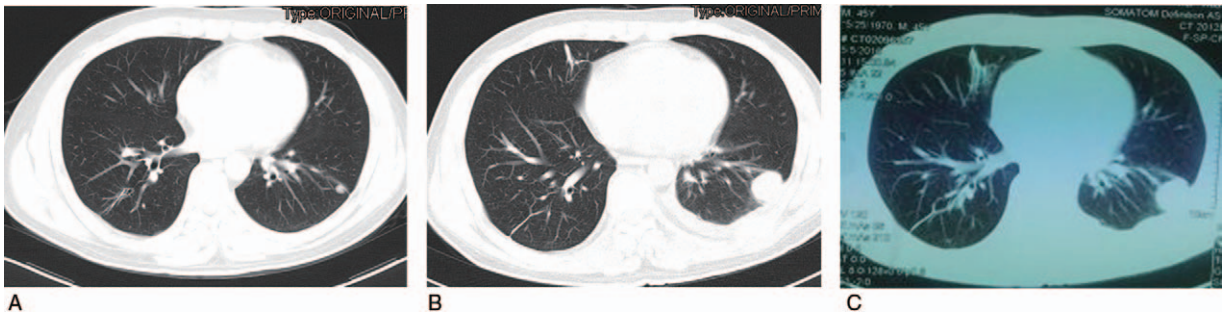

Figure 3. (A) The lung metastasis first found 3 months after sorafenib treatment (2015.9.16). (B) The lung metastasis 8 months after sorafenib treatment (2016.3.3). (C) The lung metastasis 8 months after apatinib treatment (2016.11.16).

was one nodule about 1 cm in the left lobe of liver. We considered this nodule as recurrence. The radiofrequency ablation was conducted on March 26, 2015 (Fig. 1B).

The patient was then under regular examination. However, the AFP was not decreased. On June 11, 2015, the computed tomography (CT) revealed that there was a paraspinal metastasis of the T12 vertebra (Fig. 2A). There was no other metastasis. The BCLC stage was stage C. Then, the patient was suggested to take sorafenib (400 mg, po, twice daily). Nevertheless, the patient developed lung metastasis 3 months later (Fig. 3A) and the paraspinal metastasis grew gradually (Fig. 2B and C). On March 3, 2016, the patient was brought to our hospital again complained with numbness of left lower limb and inability to walk. The CT scan found that the paraspinal metastasis invaded the spinal cord (Fig. 2D and E). Besides, the lung metastasis grew bigger (Fig. 3B). Soon afterward, we conducted concurrent apatinib and SBRT to the paraspinal metastasis with dose of 7 Gy daily for 5 days. The sorafenib was stopped. Eight months later (November 16, 2016), the patient walked to our hospital without any symptoms. The adverse events were mild and tolerable, with grade I to grade II hand foot syndrome, alopecia, and diarrhea. The CT scans showed that the paraspinal metastasis was nearly disappeared (CR) (Fig. 2F and G). The lung metastases were stable (SD) (Fig. 3C). At last, this patient was died for the disease progression on May 25, 2017.

3. Discussion

Hepatocellular carcinoma (HCC) is the third most common cancer in Asia because of the high prevalence of its main etiologic agents: chronic hepatitis B virus (HBV) and hepatitis C virus (HCV) infections.[2,3] The annual incidence of HCC in China alone contributes to 55% of global HCC cases.[2] The prognosis of patients from the Asia-Pacific region is frequently worse than for those from other parts of the world, such as North America or Europe, with a median survival time of 3 to 4 months with supportive care.[2,4]

Sorafenib is now considered to be the standard treatment for advanced HCC worldwide since 2008.[1] However, the treatment efficacy was limited, especially in Asian population, only increased 2.3 months in median overall survival when used as first line treatment.[4] In this report, the patient used sorafenib for about 8 months. However, the patient developed progression disease (PD) only 3 months later. Besides, the tumor grew constantly during the following sorafenib treatment.

Then the patient received concurrent treatment of apatinib and SBRT of paraspinal metastasis immediately after it invaded the spinal cord. Eight months later, the paraspinal metastasis showed nearly complete response. We may argue that the paraspinal metastasis was cured by SBRT; nevertheless, the tumor with about 10 cm in diameter is very hard to be cured by SBRT, especially for HCC. Moreover, the radiotherapy dose was only 7 Gy × 5f for the tolerance of spinal cord. So we think that the apatinib plays an important role in the treatment of this HCC patient.

Apatinib is a small-molecule tyrosine kinase inhibitor (TKI) that highly selectively binds to and strongly inhibits vascular endothelial growth factor receptor 2 (VEGFR-2), with a decrease in VEGF-mediated endothelial cell migration, proliferation, and tumor microvascular density.[5,6] As we know, HCC is a kind of cancer that is rich in blood supply. Blockage of blood supply may exert strong antitumor effects of HCC. For advanced or metastatic gastric or gastroesophageal junction adenocarcinoma patients who failed at least 2 lines of chemotherapy, apatinib could increase the overall survival by nearly 2 months.[6] So the apatinib is now recommended as third-line treatment of advanced gastric cancer. However, the treatment efficacy of apatinib has not been reported in other cancers by clinical trials, except for some case reports.[7–9] In this report, we found that the concurrent treatment of apatinib and SBRT for a big paraspinal metastasis of HCC showed excellent efficacy. The tumor mass was nearly disappeared (CR). Although the patient died 6 months later, Apatinib extended the life expectancy significantly for this patient. So, we think that the apatinib may be a good choice for HCC and it may function as a radiosensitizer of HCC. However, it warrants further investigation in the future prospective clinical studies.

4. Conclusion

The concurrent treatment of apatinib and SBRT showed excellent treatment efficacy for a big paraspinal metastasis of HCC in this report. The tumor mass nearly showed complete response (CR). The apatinib may be a good choice for HCC and it may function as a radiosensitizer of HCC; however, it warrants further investigation in the future prospective clinical studies.

References

[1] Llovet JM, Ricci S, Mazzaferro V, et al. Sorafenib in advanced hepatocellular carcinoma. N Engl J Med 2008;359:378–90.

[2] Qin S, Bai Y, Lim HY, et al. Randomized, multicenter, open-label study of oxaliplatin plus fluorouracil/leucovorin versus doxorubicin as palliative chemotherapy in patients with advanced hepatocellular carcinoma from Asia. J Clin Oncol 2013;31:3501–8.
[3] Tsan YT, Lee CH, Wang JD, et al. Statins and the risk of hepatocellular carcinoma in patients with hepatitis B virus infection. J Clin Oncol 2012;30:623–30.
[4] Cheng AL, Kang YK, Chen Z, et al. Efficacy and safety of sorafenib in patients in the Asia-Pacific region with advanced hepatocellular carcinoma: a phase III randomised, double-blind, placebo-controlled trial. Lancet Oncol 2009;10:25–34.
[5] Li J, Qin S, Xu J, et al. Apatinib for chemotherapy-refractory advanced metastatic gastric cancer: results from a randomized, placebo-controlled, parallel-arm, phase II trial. J Clin Oncol 2013;31: 3219–25.
[6] Li J, Qin S, Xu J, et al. Randomized, double-blind, placebo-controlled phase iii trial of apatinib in patients with chemotherapy-refractory advanced or metastatic adenocarcinoma of the stomach or gastroesophageal junction. J Clin Oncol 2016;34:1448–54.
[7] Ding L, Li QJ, You KY, et al. The use of apatinib in treating nonsmall-cell lung cancer: case report and review of literature. Medicine (Baltimore) 2016;95:e3598.
[8] Kou P, Zhang Y, Shao W, et al. Significant efficacy and well safety of apatinib in an advanced liver cancer patient: a case report and literature review. Oncotarget 2017;18:14724.
[9] Lin Y, Wang C, Gao W, et al. Overwhelming rapid metabolic and structural response to apatinib in radioiodine refractory differentiated thyroid cancer. Oncotarget 2017;2:15036.