Gut and Gastroenterology

CASE REPORT

Complete Response to the Combination of Sorafenib and Bronchial Artery Infusion of Cisplatin for Hepatocellular Carcinoma with Multiple Lung Metastasis

Toru Ishikawa*, Yuichi Kojima, Saori Endo, Michitaka Imai, Motoi Azumi, Yujiro Nozawa, Tomoe Sano, Akito Iwanaga, Terasu Honma, Toshiaki Yoshida

Department of Gastroenterology and Hepatology, Saiseikai Niigata Hospital, Japan

Abstract

We herein report a complete response case of hepatocellular carcinoma (HCC) with lung metastasis that was successfully treated with bronchial arterial infusion chemotherapy and sorafenib administration. A 67-year-old male diagnosed with HCC in March 2013 was treated with transcatheter arterial chemoembolization and radiofrequency ablation. Lung metastasis was noted in October 2015. We administered sorafenib and IA-call®, a fine powder formulation of cisplatin, via the bronchial arteries. This therapy resulted in the disappearance of the lung metastases. The patient had complete response and remained alive for 4 years more after developing lung metastasis.

Keywords: Hepatocellular Carcinoma, Lung Metastasis, Bronchial Arterial Infusion Chemotherapy, Sorafenib, Hemoptysis

Abbreviations: HCC: Hepatocellular Carcinoma; CR: Complete Response; BAI: Bronchial Artery Infusion; CT: Computed Tomography; TACE: Transcatheter Arterial Chemoembolization; RFA: Radiofrequency Ablation; DCP: Des-γ-Carboxy Prothrombin

Introduction

Standard treatment for advanced hepatocellular carcinoma with distant metastasis, including lung metastasis, is a molecular targeted drug [1].

However, evidence for multidisciplinary treatment of other combination therapies in extending prognosis is poor. At present, various molecular targeted drugs are covered by insurance, and treatment options are increasing, but there are currently few cases of complete response (CR) in clinical practice. We herein report a CR case of hepatocellular carcinoma with lung metastasis that was successfully treated with bronchial artery infusion (BAI) of cisplatin and sorafenib administration. Bronchial artery infusion was applied to hepatocellular carcinoma with lung metastasis, for which sorafenib was initially ineffective, and sorafenib was dosed and continued, showing significant antitumor effects.

Case Description

Our patient, a 67-year old male with a history of type 2 diabetes mellitus, dyslipidemia and alcoholic liver disease, was referred to our department for treatment. He was diagnosed contrast-enhanced computed tomography (CT) showed a 50-mm-sized hepatocellular carcinoma in the lateral lobe in March 2013. Firstly, he was treated with transcatheter arterial chemoembolization (TACE) and radiofrequency ablation (RFA). He had been without recurrence since then, but chest CT showed multiple bilateral pulmonary nodules in October 2015. He was hospitalized for the introduction of sorafenib (Nexavar®, Bayer Yakuhin, Ltd., Osaka, and Japan) 400mg for multiple lung metastases. However, there is progressive disease after 1 month administration of sorafenib.

The first BAI of CDDP (IA-call®; Nippon Kayaku, Tokyo, Japan, a fine-powder formulation of cisplatin) was held in November 2015 (Figure 1). Additional CDDP was infused from the bronchial artery as the second BAI in February 2016. Multiple lung metastases remained almost unchanged, and increased des-γ-carboxy prothrombin (DCP) was observed. The dose of sorafenib was increased to 600 mg from March 2016. The dose was increased to sorafenib 800mg more gradually. In July 2016, CDDP was infused from the bilateral bronchial arteries as the third BAI. After that, sorafenib 800 mg has been continued for 4 years or more, with the normalization of DCP, multiple lung metastases became CR, no intrahepatic recurrence was observed, and a marked antitumor effect was obtained (Figures 2 & 3).

***Correspondence to:** Toru Ishikawa MD PhD, Department of Gastroenterology and Hepatology, Saiseikai Niigata Hospital, Teraji 280-7, Niigata 950-1104, Japan, Tel: 81-25-233-6161; Fax: 81-25-233-8880, Email: toruishi[AT]ngt[DOT]saiseikai[DOT]or[DOT]jp

Received: March 19, 2020; **Accepted:** March 23, 2020; **Published:** March 27, 2020

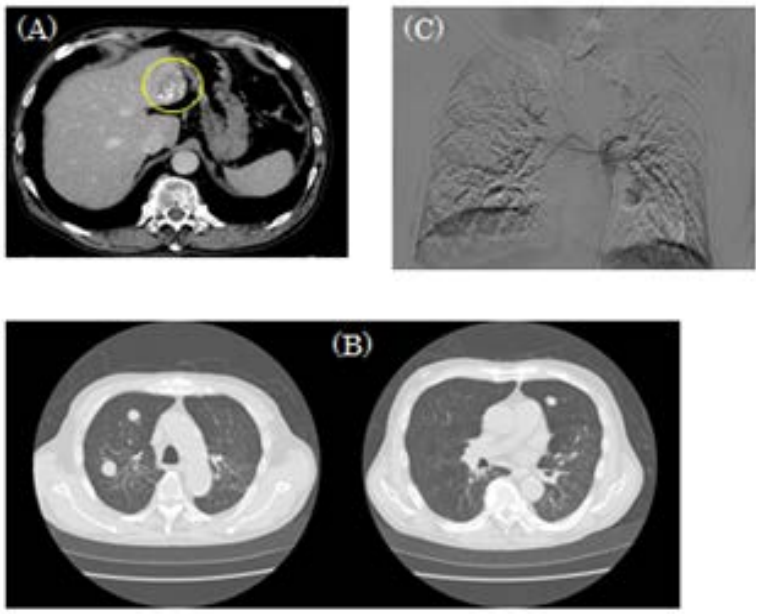

Figure 1:
(A) Angio-CT did not indicate recurrence after lateral segment treatment.
(B) Chest CT showed multiple lung metastases.
(C) Bronchial arteriography: feeding artery for lung metastasis were confirmed, and CDDP infusion were performed.

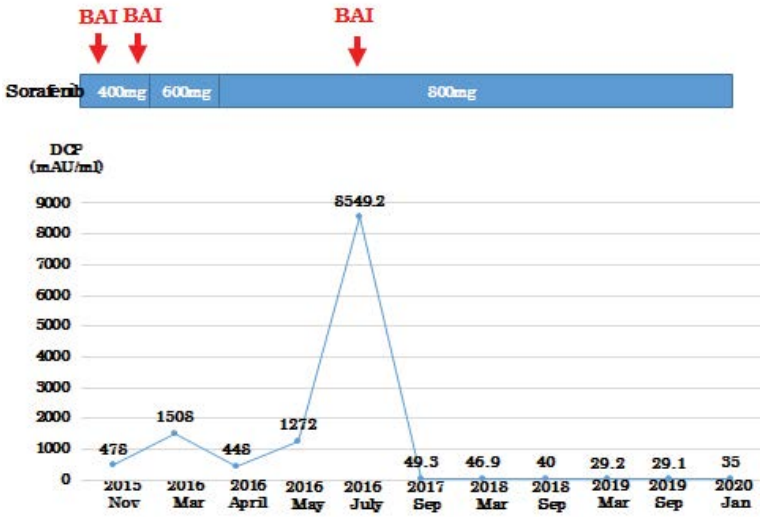

Figure 2: Clinical course of the patient after lung metastasis. The panel shows the levels of DCP as tumor markers.

Discussion

Extrahepatic metastasis of hepatocellular carcinoma occurs in the order of lung, lymph node, bone, adrenal gland, peritoneum, and brain, with the highest frequency of lung metastasis reported [2, 3]. The standard treatment for hepatocellular carcinoma with distant metastasis, including lung metastasis, is a molecular targeted drug. However, most patients treated with a molecular targeted drug including sorafenib achieve only stable disease, with a median gain in overall survival of less than 3 months [4, 5].

In patients with good hepatic reserve and pulmonary metastasis as a prognostic factor, additional treatment should be considered if the efficacy of the targeted drug is insufficient.

Therefore, additional management strategies need to be identified and optimized to improve therapeutic benefits. Treatments for lung metastases include surgery, stereotactic radiation therapy, and radiofrequency ablation. However, since lung metastases are often found to be synchronous or multiple, any treatment is indicated for multiple lesions. On the other hand, bronchial arterial infusion therapy can treat multiple lesions. BAI is often used to treat metastatic lung cancer, with dramatic effects [6].

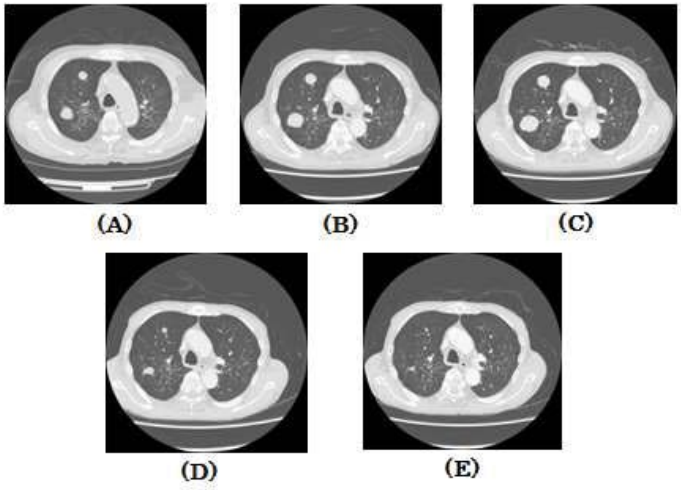

Figure 3: Chest CT showing multiple lung metastasis at baseline in October 2015 (A), 1 Month after sorafenib in November 2015 (B), Third BAI in July 2016 (C), Decreased DCP in September 2017 (D), No nodules found in January 2020 continuing administration of sorafenib.(E).

Metastatic HCC can be life-threatening [7], although the stage of intrahepatic HCC is a significant and independent prognostic factor [8]. Therefore, we added BAI of CDDP to the treatment regimen for lung metastasis in the present case because BAI has the advantage of delivering a high concentration of drugs to the bronchial arteries, which supply arterial blood to metastatic lesions.

Bronchial arterial infusion therapy has been reported to be effective not only for primary lung cancer but also for metastatic lung tumors in reducing tumor shrinkage, reducing symptoms such as hemoptysis, and maintaining QOL. Complications such as arterial dissection / obstruction and post-embolism syndrome (fever, chest pain, and dyspnea) have been reported, and careful procedures are required [9]. In Japan, bronchial arterial infusion therapy has been reported to be highly effective for pulmonary metastases of hepatocellular carcinoma [10].

In this case, sorafenib was initially diagnosed as ineffective, and a marked antitumor effect was obtained by gradually increasing and continuing sorafenib in combination with bronchial arterial infusion therapy. Intrahepatic control was also achieved, and treatment with sorafenib combined with bronchial arterial infusion of CDDP was considered as one of the treatment options for multiple lung metastases of hepatocellular carcinoma.

Sorafenib plus BAI of CDDP may present a new potential treatment option for the sub-population. However, its efficacy and safety need further investigation in a randomized study.

Conflicts of interest

There are no conflicts of interest in the manuscript.

Acknowledgement

None

Financial disclosure

The authors declare that they do not have any current financial arrangements or affiliations with any organization that may have a direct interest in their work.

References

1. Kokudo N, Takemura N, Hasegawa K, Takayama T, Kubo S, et al. (2019) Clinical practice guidelines for hepatocellular carcinoma: The Japan Society of Hepatology 2017 (4th JSH-HCC guidelines) 2019 update. *Hepatol Res* 49: 1109–1113. [View Article]
2. Kummar S, Shafi NQ (2003) Metastatic hepatocellular carcinoma. *Clin Oncol (R Coll Radiol)* 15: 288–294. [View Article]
3. Kudo M (2015) Surveillance, Diagnosis, Treatment, and Outcome of Liver Cancer in Japan. *Liver Cancer* 4: 39–50. [View Article]
4. Llovet JM, Ricci S, Mazzaferro V, Hilgard P, Gane E, et al. (2008) Sorafenib in Advanced Hepatocellular Carcinoma. *N Engl J Med* 359: 378–90. [View Article]
5. Cheng AL, Kang YK, Chen Z, Tsao CJ, et al. (2009) 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* 10: 25–34. [View Article]
6. Yonezawa M, Seki A, Numoto A, Kawada K, Eguchi K, et al. (1994) Successful treatment of metastatic pulmonary tumors by bronchial arterial infusion chemotherapy in two patients with locally well controlled uterine cancer. *Acta Med Okayama* 48: 109–112. [View Article]
7. Uka K, Aikata H, Takaki S, Shirakawa H, Jeong SC, et al. (2007) Clinical features and prognosis of patients with extrahepatic metastases from hepatocellular carcinoma. *World J Gastroenterol* 13: 414–420. [View Article]
8. Kawaoka T, Aikata H, Kan H, Fujino H, Fukuhara T, et al. (2014) Clinical outcome and prognostic factors of patients with hepatocellular carcinoma and extrahepatic metastasis treated with sorafenib. *Hepatol Res* 44: 1320–1328. [View Article]

9. Shao H, Wu J, Wu Q, Sun X, Xing Z, et al. (2015) Bronchial artery embolization for hemoptysis: a retrospective observational study of 344 patients. *Chin Med J (Engl)* 128: 58–62. [View Article]

10. Yoshida T, Kamada K, Miura K, Goto T, Ohshima S, et al. (2014) Successful treatment of hepatocellular carcinoma with lung metastasis using hepatic and bronchial artery infusion chemotherapy. *Intern Med* 53: 2493–2497. [View Article]

Citation: Ishikawa T, Kojima Y, Endo S, Imai M, Azumi M, et al. (2020) Complete Response to the Combination of Sorafenib and Bronchial Artery Infusion of Cisplatin for Hepatocellular Carcinoma with Multiple Lung Metastasis. Gut Gastroenterol 3: 001-004.