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CASE REPORT

Advanced hepatocellular carcinoma treated by a combination of sorafenib and radiotherapy

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Summary Advanced hepatocellular carcinoma has a poor therapeutic outcome and treatment options are limited. Sorafenib, an orally active multikinase inhibitor, is the only systemic drug that has been shown to provide survival benefits in randomized control studies. However, the gains in survival are modest and new treatment strategies are needed. We report here the case of a patient with advanced hepatocellular carcinoma who had an impressive response to a combination of sorafenib and radiotherapy. The treatment was well tolerated with no unexpected toxicities. Post-treatment imaging showed a satisfactory partial response with regression of the tumor by more than 50%.

Introduction

Hepatocellular carcinoma (HCC) is the fifth most common cancer and the third cause of cancer-related death in the world (responsible for one million deaths per year) [1]. In Taiwan, HCC is the leading cause of cancer death, with approximately 8000 new cases diagnosed and 7000 deaths occurring annually. The 5-year survival rate of patients with HCC is less than 10%, even with aggressive conventional treatment. The treatment options for HCC are either curative or palliative. Curative treatments, which achieve the best outcomes, include liver resection and transplantation, whereas palliative treatments include tumor ablation, embolization, radiotherapy, and chemotherapy [2]. When aggressive treatments fail, there is currently no effective salvage treatment available. Clinical trials of

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multikinase inhibitors, such as sorafenib, have given impressive results, with a moderate improvement in survival for advanced HCC in patients with Child—Pugh grade A cirrhosis [3]. However, there are limited options for the management of HCC in patients with Child—Pugh grade B cirrhosis. We report here the case of a 68-year-old man with advanced HCC related to hepatitis C and Child—Pugh grade B cirrhosis. This patient was successfully treated with sorafenib combined with radiotherapy.

Case report

A 63-year-old Chinese man with a history of chronic hepatitis C without regular follow up presented to our emergency department with right upper quadrant abdominal pain and general weakness. A physical examination showed hepatosplenomegaly with abdominal tenderness and an abdominal ultrasound scan showed liver cirrhosis with suspected liver tumors. He was admitted to our gastrointestinal ward on November 3, 2010 for further management. His α-fetoprotein level was elevated (1032 ng/ml); however, his liver profile was Child—Pugh grade B. Imaging studies (abdominal magnetic resonance imaging) showed multiple T1W1-low and T2W1-high intensity lesions of variable sizes with early contrast enhancement over the whole liver except for segments 1 and 5, and extensive tumor thrombus involving the portal venous system, both hepatic veins, and extending into the inferior vena cava. HCC was diagnosed on the basis of his hepatitis C status with typical radiological findings and raised serum α-fetoprotein level. He had a European Cooperative Oncology Group performance status 1, a Barcelona Clinic Liver Cancer (BCLC) [4] classification stage C, and Cancer of the Liver Italian Program score 2. He was given Duragesic (fentanyl transdermal) for a short period to control his pain. Chemoembolization was not offered due to the extensive macrovascular involvement.

Palliative radiation therapy (three-dimensional conformal radiotherapy) was given 5 days per week at 1.8 Gy per day to the portal vein and tumor of the right lobe for 28 fractions to a total dose of 50.4 Gy; treatment with sorafenib (400 mg per day) was started on December 10, 2010. Fig. 1 A1,B1 and A2,B2 shows the dose distribution for the tumor, portal vein, and surrounding organs and tissues.

The patient's symptoms improved gradually with no abdominal pain and his appetite improved. The follow-up examination 6 months later indicated an early response, with a dramatic reduction in the size of the liver masses (8 cm to 3 cm) and a decrease in the α-fetoprotein level. He experienced manageable side-effects of mild diarrhea, itching of the skin with red papules over his scalp, Grade 2—3 hand and foot skin reactions, lesser control of hypertension, and some hair loss. On completion of 16 months of treatment he had ongoing marked clinical, radiological, and biochemical responses (Figs. 2—4).

Discussion

Sorafenib is an orally active multikinase inhibitor that has been shown to affect tumor cell proliferation and tumor angiogenesis. It inhibits molecular components of the Raf—MEK—ERK signaling pathway, abrogating tumor growth and vascular endothelial growth factor receptors (VEGFR) 1, 2 and 3, and endothelial growth factor receptors PDGFR-β, thus inhibiting neoangiogenesis [5]. Sorafenib emerged

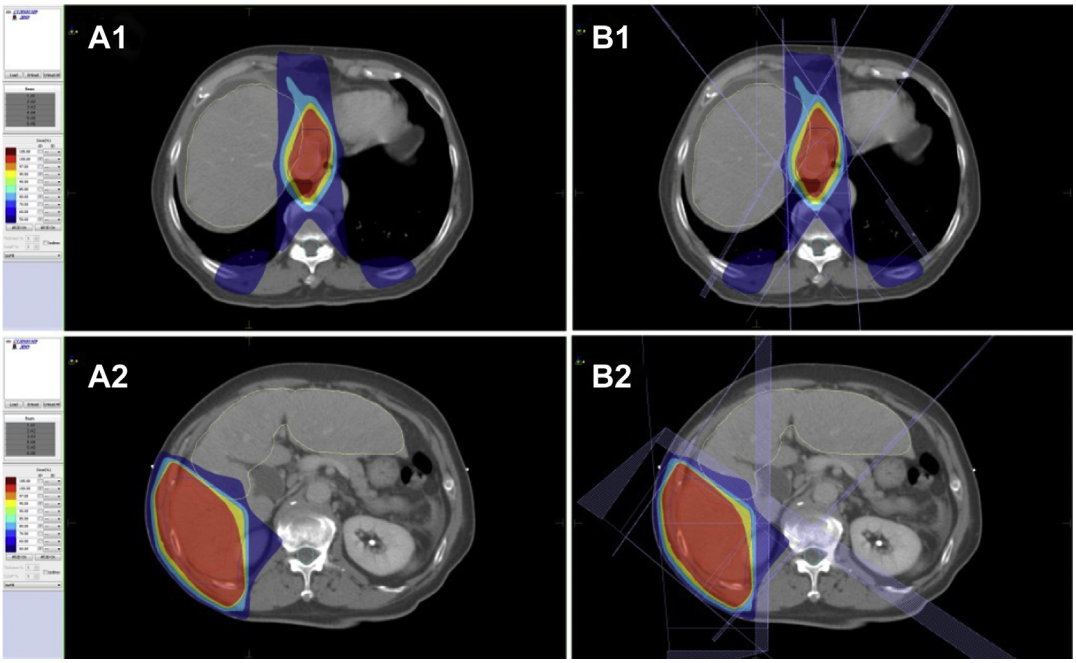

Figure 1 Computed tomography scans of our patient with hepatocellular carcinoma showing dose distribution of radiation from proton beam therapy (A) and that from standard X-rays using the same beam arrangement (B). The 100%, 95%, 80%, and 50% isodose lines are represented in red, yellow, light blue, and dark blue, respectively. The planning target volume (PTV) is represented in pink. The protocol required the PTV to be encompassed by the 95% dose envelope. (A1), (B1) On liver tumor. (A2), (B2) On portal vein. GTV = gross tumor volume.