Complete response to sorafenib in a patient with recurrent hepatocellular carcinoma

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Abstract
Partial hepatectomy is still the treatment of choice aiming at a cure for patients with hepatocellular carcinoma (HCC), provided that the patient can tolerate the treatment. For patients with multiple recurrent HCC after partial hepatectomy which cannot be treated by re-hepatectomy or local ablative therapy, the prognosis is extremely poor. Sorafenib is a molecular-targeted agent which has been demonstrated in two global phase III randomized controlled trials to show survival benefit for advanced HCC. Here, we present a 56-year-old patient with HCC who showed complete clinical response after sorafenib was used for tumor recurrence which developed 3 mo after partial hepatectomy. There was no evidence of progression of disease for 60 mo till now after continuous treatment with sorafenib.

INTRODUCTION
Partial hepatectomy is still the treatment of choice aiming at a cure for patients with hepatocellular carcinoma (HCC), provided that the patient can tolerate the treatment. For patients with multiple recurrent HCC after partial hepatectomy which cannot be treated by re-hepatectomy or local ablative therapy, the prognosis is extremely poor[1][2]. Sorafenib is a molecular-targeted agent which has been demonstrated in two global phase III randomized controlled trials to show survival benefit for advanced HCC. It is an oral multi-kinase inhibitor that targets Raf kinases (Raf-1, wild-type B-Raf, and b-raf V600E), in addition to receptor tyrosine kinases associated with angiogenesis [vascular endothelial growth factor receptor (VEGFR)-2/-3, platelet-derived growth factor receptor (PDGFR)-β] or tumor progression (Flt-3, c-kit)[3].

Key words: Hepatocellular carcinoma; Partial hepatectomy; Sorafenib; Complete response

Core tip: For patients with multiple recurrent hepatocellular carcinoma (HCC) after partial hepatectomy which cannot be treated by re-hepatectomy or local ablative therapy, the prognosis is extremely poor. Our case showed that the patient with recurrent HCC treated with sorafenib can achieve a complete clinical response as it did in advanced HCC.

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However, in the SHARP (Sorafenib Hepatocellular Carcinoma Assessment Randomized Protocol) trial, only 7 sorafenib-treated patients had a partial response and no patient had a complete response[4]. In the Asia-Pacific trial, only 5 sorafenib-treated patients had a partial response and no patient had a complete response[5].

Here, we present a 56-year-old patient with HCC who showed a complete clinical response after sorafenib was used for tumor recurrence which developed 3 mo after partial hepatectomy. There was no evidence of progression of disease for 60 mo after continuous treatment with sorafenib.

CASE REPORT

In June 2008, a 56-year-old male was diagnosed with HCC on a background of hepatitis B virus (HBV)-related cirrhosis. Computed tomography (CT) showed a 4 cm × 4 cm mass in liver segment 6 with an adjacent metastatic satellite tumor nodule (Figure 1A). The a-fetoprotein (AFP) level was raised to 205 ng/mL. Resection of liver segments 5 and 6 together with cholecystectomy was performed for tumor recurrence which developed 3 mo after partial hepatectomy. There was no evidence of progression of disease for 60 mo after continuous treatment with sorafenib.

CASE REPORT

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DISCUSSION

Sorafenib acts on tumor cell proliferation and angiogenesis in patients with HCC\(^9\). It is therefore possible that HCC patients treated with sorafenib can achieve complete remission, although such a phenomenon is extremely rare. The effectiveness and safety of sorafenib have been confirmed in two multi-center clinical studies (the SHARP and the Asia-Pacific Studies)\(^4,5\). In the SHARP trial, 299 patients received sorafenib therapy. The survival rate at 1 year was 44% in the sorafenib group and 33% in the placebo group. However, only 7 patients (2%) developed a partial response and 211 (71%) showed stable disease (using the Response Evaluation Criteria in Solid Tumors). The disease-control rate was significantly higher in
the sorafenib group than in the placebo group. There was no complete response in the trial[9]. In the Asia-Pacific trial, 150 patients received sorafenib, most of whom had associated chronic HBV infection. The disease-control rate was significantly greater in the sorafenib group (53%) than the placebo group (12%). Only 5 patients (3.3%) developed a partial response in the sorafenib group and there was no complete response[9]. So et al[8] reported on the first patient with HCC who developed a complete response following sorafenib for six months. Irtan et al[3] reported on two patients who achieved complete regression using sorafenib which was followed by radical resection surgery. In addition, there have been a small number of patients with HCC who developed a complete response with sorafenib treatment.

Our case provides additional evidence to show that sorafenib is effective for patients with HCC, and it can achieve complete remission, long disease-free survival and provide patients with good quality of life. This case report is special because, first, there has not been any report of complete tumor remission with sorafenib for recurrent HCC after partial hepatectomy. In our patient, the sorafenib treatment was initiated for disease progression 3 mo after surgery and the patient had a long disease-free survival of 60 mo. Second, the patient had a long history of HBV-related chronic hepatitis. The high incidence of chronic HBV infection[9] makes the prevalence of HBV-related chronic hepatitis high in China largely reflects the high prevalence of chronic HBV infection[9]. To the best of our knowledge, this is the first report on a Chinese patient who had a complete response with sorafenib. Third, disease progression was observed within 3 wk of treatment with sorafenib. However, when its use was continued, remission of the disease was observed after 6 wk, which indicates that the patient had a delay in responses. The patient continued sorafenib for 6 mo, and a complete response was achieved. This suggests that tumor progression during treatment is not a sign to withdraw sorafenib. Moreover, a recent study demonstrated that sorafenib administration beyond the first radiological evidence showing progressive disease could later show suppression of HCC growth and survival benefit[9]. Fourth, our patient received surgery and TACE before sorafenib therapy. The combination therapy may be beneficial to patients. There have been reports which showed that sorafenib, in combination with other drugs, radiation therapy, or immunotherapy, promotes better clinical outcomes in HCC patients. Fifth, our patient developed thrombocytopenia and laryngeal foreign body sensation and pain. Complications usually occur within 1-3 wk after initiation of sorafenib. Effective control of complications can make patients accept the treatment better. In our case, sorafenib was continued and 6 mo later the patient achieved complete remission.

In conclusion, our patient shows the effectiveness of sorafenib on disease progression in patients with recurrent HCC after partial hepatectomy.

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