Long-term disease-free survival achieved by anti-angiogenic therapy plus surgery in a hepatocellular carcinoma patient with extensive liver involvement and lung metastases

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Sorafenib is the current standard treatment for patients with metastatic or advanced hepatocellular carcinoma (HCC) that cannot be treated by loco-regional therapy. However, its objective response rate is only 2–3% and the median time-to-progression is around 2.8 months in the Asian population. Other anti-angiogenic agents, such as bevacizumab, have been reported to have similar efficacy. The long-term disease-free or cure of advanced HCC by anti-angiogenic therapy alone is extremely rare.

A 24-year-old woman with no history of chronic hepatitis B or C virus infection was diagnosed with HCC in June 2005 by liver tumor biopsy. Computed tomography scans revealed multiple large intra-hepatic tumors extending into the subhepatic area (Fig. 1A) and bilateral lung metastasis (Fig. 1B). Serum alpha-fetoprotein (AFP) level exceeded 87,500 ng/mL. She was enrolled into a Phase II clinical trial using bevacizumab (7.5 mg/kg, on day 1, triweekly) and capecitabine (800 mg/m², twice daily, days 1–14, triweekly) as the first-line therapy. Partial response was achieved (Fig. 1C), and all the metastatic lung tumors disappeared (Fig. 1D). She was treated with the same regimen for a total of 2 years, and the disease was controlled in partial response status. The lowest AFP level was 76,636 ng/mL.

However, a follow-up computed tomography scan in April 2007 revealed spleen metastasis. Positron emission tomography with 18-fluorodeoxyglucose confirmed the involvement of liver and spleen, but not the lungs. Due to her young age, good performance status and there being no proven effective therapy at that time, right hepatectomy, segmentectomy of the second hepatic segment and splenectomy were performed in June 2007. Pathology reports showed a Grade III HCC with clear resection margins. Serum AFP level normalized afterwards. The patient then received regular follow-up by imaging exams every 3 months. In June 2012, 7 years after the diagnosis of advanced HCC and 5
years after the surgery, she remained disease-free and her serum AFP level remained normal.

A few case reports have previously described how good outcomes can be achieved with aggressive surgery of metastatic disease. However, these reported cases had either limited or solitary metastasis. Our patient had very extensive disease involvement at diagnosis, so direct surgery was not feasible. To our best knowledge, this is the first reported case describing how an effective systemic therapy converted an initially metastatic and unresectable HCC to resectable status.

A previous case report demonstrated that a complete pathological response was achieved in a locally-advanced HCC patient treated with sorafenib. Our current case demonstration, together with prior case reports, indicates that although advanced HCC is notoriously refractory to most systemic treatment and rapid in progression, multimodality treatment in carefully selected patients might lead to a surprisingly good outcome.

References