A case of advanced renal cell carcinoma with peritoneal carcinomatosis responding to sorafenib therapy

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Abstract Peritoneal carcinomatosis is a relatively rare presentation of renal cell carcinoma. We report the case of an advanced renal cell carcinoma patient with peritoneal carcinomatosis who received sorafenib and achieved a dramatic and ongoing response in the metastatic lesion. After 6 months of sorafenib administration, despite a CT scan showing a stable left renal mass, the patient had marked shrinkage of the peritoneal nodules and ascites had disappeared. To our knowledge, this is the first report showing therapeutic activity of sorafenib against peritoneal carcinomatosis in a patient with renal cell carcinoma.

Keywords Renal cancer · Peritoneal carcinomatosis · Sorafenib

Introduction

Renal cell carcinoma (RCC), which accounts for 2–3 % of all adult malignant neoplasm, has a tendency to metastasize. The frequent sites of metastases are the lung, lymph nodes, liver, and bone. Intraperitoneal metastatic spread of RCC involving mesentery and omentum is very uncommon [1].

Sorafenib is an orally available inhibitor of multiple receptor tyrosine kinases, including vascular endothelial growth factor receptor (VEGF), platelet-derived growth factor receptor (PDGF), and others, with direct antitumor

and antiangiogenic activity. On the basis of impressive outcomes in several clinical trials, sorafenib has been approved worldwide for treatment of RCC, and such tyrosine kinase inhibitors induce a high partial response rate at metastatic sites [2]. Herein, we report the case of an advanced RCC patient with peritoneal carcinomatosis who received sorafenib and achieved a dramatic and ongoing response in the metastatic lesion.

Case report

In March 2010, a 73-year-old man with a 5.5-cm left renal mass was referred to our institution. The CT scan also showed innumerable soft tissue implants throughout the peritoneum, a large amount of ascites, and renal hilar lymph nodes (Fig. 1). Karnofsky performance score was judged to be 80 %. The laboratory test results were hemoglobin 10.1 g/dl, lactate dehydrogenase 215 U/l, corrected calcium 5.1 mg/dl, and Memorial Sloan-Kettering Cancer Center classification was an intermediate risk. Although serum liver-associated enzymes, creatinine, and blood urea nitrogen were within normal limits, laboratory evaluation included total protein 7.8 mg/dl and albumin 1.7 g/dl. Diagnostic paracentesis was performed, which revealed visibly bloody peritoneal fluid. The differential cell count was 400/mm³: neutrophils 63 %, monocytes 31 %, and lymphocytes 6 %, with a specific gravity of 1.028, a total protein of 4.4 g/dl, an albumin of 0.7 g/dl, giving a serum–ascites albumin gradient (SAAG) of 1.0 g/l, which was suggestive of non-portal hypertension ascites. However, as this paracentesis was negative for malignant cells by cytologic evaluation, we performed a percutaneous, CT-guided biopsy of the left renal mass which revealed the histology of clear cell renal cell carcinoma (RCC).

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Fig. 1 Pretreatment CT scan showed **a** a 5.5-cm left renal mass (*black arrow*) and a large amount of ascites and **b** soft tissue implants throughout the peritoneum (*white arrows*)

Fig. 2 After 3 months of sorafenib therapy, a CT scan showed **a** a stable left renal mass (*black arrow*) and **b** the peritoneal nodules (*white arrows*); however, the ascites had disappeared

Fig. 3 After 6 months of sorafenib therapy, a CT scan showed **a** a stable left renal mass (*black arrow*), disappearance of the ascites, and **b** 95 % reduction in the peritoneal nodules (*white arrows*)

At that time, the patient seemed not to be a candidate for cytoreductive nephrectomy because of the possible diagnosis of peritoneal carcinomatosis and his poor general condition. We treated the patient with sorafenib (Nexavar®) 800 mg daily. After 4 weeks of treatment with sorafenib, grade 3 thrombocytopenia (according to the National Cancer Institute/Common Toxicity Criteria for Adverse Events version 3.0) was observed, which improved after reduction of the sorafenib dose to 400 mg. After 3 months of treatment with sorafenib, a CT scan showed a stable left renal mass and the peritoneal nodules; however, the ascites had disappeared (Fig. 2). Therefore, confidence in the diagnosis of peritoneal carcinomatosis was clinically obtained. After 6 months of treatment with sorafenib, the therapy was withdrawn owing to acute pancreatitis because of a pancreatic duct stone and grade 3 renal dysfunction. A follow-up CT scan after 3 months of

no sorafenib therapy showed a stable renal mass and no ascites with 95 % reduction in the peritoneal nodules (Fig. 3). After 6 months of no sorafenib therapy, the patient's acute pancreatitis was improved after the placement of a pancreatic duct stent, and renal dysfunction recovered to the grade 1 level. Repeat imaging still showed stable left renal mass and peritoneal nodules. Concerns about his quality of life on dialysis led the patient to avoid nephrectomy. Sorafenib treatment was resumed at a dose of 400 mg every other day.

Discussion

The treatment for metastatic renal cell carcinoma (mRCC) has changed dramatically since the introduction of molecular-targeted therapies including tyrosine kinase

inhibitors. These tyrosine kinase inhibitors have been shown to reduce tumors and prolong survival of patients with mRCC when compared with cytokine therapy [3, 4]. They also induce a high partial response rate at metastatic sites, with the most common sites of response being the lungs and lymph nodes. Peritoneal carcinomatosis is a relatively rare presentation of RCC. RCC accounts for only 2 % of primary neoplasms that metastasize to the peritoneum [1]. Although the ascitic fluid cytology exam was negative in this case, we nevertheless suspected a malignant etiology from the characteristics of the ascitic fluid because the vast majority (82.8 %) of patients have a SAAG of less than 1.1, and cytological examination of ascitic fluid is highly specific and its diagnostic sensitivity is only about 40–60 % [5].

VEGF-targeted molecular therapy has been reported to inhibit angiogenesis and tumor growth. VEGF is also known as a tumor-secreted permeability factor, and has been reported in ascitic fluid accumulation [6]. Blockade of VEGF using monoclonal antibodies or low molecular weight inhibitors has been shown previously to dramatically reduce ascites formation and tumor burden in peritoneal tumor models [7, 8]. Therefore, tyrosine kinase inhibitors should be chosen as a first-line therapy in advanced RCC patients with peritoneal carcinomatosis with ascites.

This is the first reported case of a therapeutic response to sorafenib by an advanced RCC patient with peritoneal carcinomatosis. This patient has had longer than 15 months of control of the mRCC with an unresected renal primary tumor following the target therapy. Relatively few data are available to indicate which patients might benefit from cytoreductive nephrectomy. However, the ongoing

improvement in this patient's peritoneal nodules and ascites and the stability of the renal mass have encouraged us to continue treatment for patients who are not candidates for cytoreductive nephrectomy because of their poor general condition and renal insufficiency.

Conflict of interest There is no financial or commercial interest in the paper.

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