Sunitinib Enables a Clinical and Pathological Complete Remission of Metastatic Renal Cell Carcinoma (mRCC)

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Abstract
Renal cell carcinoma (RCC) is the most common renal cancer, and has a poor prognosis in individuals with metastases (mRCC). In this report, we describe a 48-year-old woman with unresectable multiple liver metastases and a colonic metastasis of RCC who was treated with sunitinib in combination with hepatic microwave ablation and obtained a clinical and pathological complete remission. We consider that sunitinib combined with microwave ablation can prevent unresectable hepatic metastases of RCC from evolving, and that sunitinib alone can achieve clinical and pathological remission in patients with colonic metastasis of RCC.

Introduction
Sunitinib, a multi-tyrosine kinase inhibitor (TKI), is recommended as a first-line treatment for the treatment of metastatic renal cell carcinoma (mRCC) in preference to interferon (IFN)-α.1 Sunitinib has been shown to markedly prolong progression-free survival (PFS) and overall survival (OS) in patients with mRCC.2 Although it has been reported that some patients achieve a complete remission (CR) with sunitinib therapy, clinical and pathological remission has seldom been described. In this report, we describe a patient with unresectable multiple liver metastases and a colonic metastasis of RCC who obtained a clinical and pathological remission with sunitinib therapy administered in combination with hepatic microwave ablation.

Case report
A 48-year-old Chinese woman who was diagnosed with right RCC underwent a right radical nephrectomy in 2007. The pathological report indicated clear-cell carcinoma of the kidney. Three years later, she presented with recurrent upper abdominal pain and an abdominal ultrasound scan indicated cholecystitis and gall bladder stones. She was therefore referred to our hospital for treatment on 30 July, 2010. As a computed tomography (CT) scan and plain abdominal radiograph showed subdiaphragmatic free air as the aggravating abdominal symptom, she received an exploratory laparotomy. During this procedure, a hepatic flexure colonic mass adhering to the surrounding tissue was observed. This was considered to be a metastasis of RCC, and it resulted in intestinal perforation. This diagnosis was confirmed by a positron emission-computed tomography (PET-CT) scan (Fig. 1). As the lesion was too firm to be removed, an ileostomy was performed at right lower quadrant of abdomen. Subsequently, the patient was started on sunitinib therapy which was administered at the recommended dosage of 50 mg daily in a 4/2 schedule (4 weeks on therapy followed by 2 weeks off therapy). Five months later, the patient was admitted to our department because of fever. A CT scan showed multiple low-density shadows in the liver, and a percutaneous liver biopsy indicated metastases of RCC (Fig. 2).

As it was not possible to perform metastasectomy, the patient also received hepatic microwave ablation therapy in January and April 2011. No disease progression was noted in subsequent periodic reviews. However, the patient presented with several sunitinib-related adverse effects including hypertension, peripheral edema, skin discoloration, dry skin, and hypothyroidism.

In 2014, the patient was admitted to hospital due to a parasomal hernia and multiple myomas. Ileostomy reversal,
hysterectomy, right hemicolectomy, and partial ileostomy procedures were performed as PET-CT imaging indicated no local signs of relapse. All pathological results were benign (Fig. 3).

Discussion

On the basis of morphologic, cytogenetic, and molecular criteria, 5 types of RCC have been classified, the most common of which is the clear-cell subtype which comprises 60-80% of cases. RCC accounts for approximately 3% of adult malignant tumors and 85% of primary renal tumors. In China, renal cancer is expected to account for 1.5% of all new cancers during 2015, with a mortality rate of about 35%. The incidence of RCC tends to increase with increasing age, as does the rate of distant metastases. Approximately 25% of RCC patients suffer from metastases postoperatively, among which pulmonary metastases comprise 50% to 60% of cases, and hepatic metastases 12.9%. In comparison, colonic metastases are rare.

Patients with mRCC have a poor prognosis. Before the advent of TKIs, cytokine therapies such as interleukin (IL)-2 and IFN-α were considered first-line drugs in the treatment of mRCC, and a limited number of patients did obtain benefit from cytokine therapy. In 2006, sunitinib was approved as it was shown to significantly PFS in comparison with IFN-α in a randomized, phase III clinical trial. Although some mRCC patients have achieved CR with sunitinib in combination with surgical interventions, clinical and pathological remission has seldom been reported.

The patient described in this report presented with a colonic metastasis 3 years after undergoing a nephrectomy, and with liver metastases which were discovered during a later follow-up. The most common RCC metastasis sites are the lung, liver, and bone, while brain, skin, and colonic metastases are rare. Surgery is considered the first choice intervention for metastatic lesions, but in this patient, surgical removal of the colonic metastasis lesion was not possible as she presented with intestinal perforation which required emergency surgery. During surgery, a hepatic flexure colonic mass firmly adhering to the surrounding tissue that could not be radically resected was found. Consequently, an ileostomy was performed as palliative treatment. For the liver metastases, metastasectomy was not possible due to the presence of multiple liver metastases, we choose microwave ablation following a comprehensive evaluation. Microwave ablation for the treatment of liver metastases of gastrointestinal tumors has achieved good results, but there is currently little experience with microwave ablation in the treatment of liver metastasis of RCC.

The patient described in this report received sunitinib in a dosage of 50 mg daily administered in a 4/2 schedule. A follow-up CT scan showed reduction of the colonic metastasis with this treatment and PET-CT imaging indicated no local signs of relapse. Pathological analysis of a specimen indicated an inflammatory response but no evidence of a colonic metastasis. On the basis of the patient’s clinical features, imaging data, and pathology results, we concluded that sunitinib alone can achieve clinical and pathological remission of colonic metastases of mRCC.

Our findings in this patient indicated that: (1) RCC can metastasize throughout the body, including the colon, although the incidence of colonic metastasis is extremely low; (2) sunitinib therapy in combination with microwave ablation can prevent
unresectable hepatic metastases of RCC from evolving; and (3) sunitinib therapy alone can achieve clinical and pathological remission of colonic metastases of RCC.

**Conflict of interest statement**

We declare that we have no financial and personal relationships with other people or organizations that can inappropriately influence our work, there is no professional or other personal interest of any nature or kind in any product, service and/or company that could be construed as influencing the position presented in, or the review of, the manuscript entitled.

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