Sorafenib in Metastatic Renal Cell Carcinoma With Sarcomatoid Differentiation

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Targeted therapy in the management of metastatic renal cell cancer has been recently introduced to urology practice. The drugs used for management are used in a very limited number of patients and only for clear cell histology. We present a case where we administered sorafenib, a multikinase inhibitor of tumor-cell proliferation and angiogenesis, to a patient with metastatic renal cell carcinoma of clear cell histology. We found that our results were different from those of previously reported studies, because sarcomatoid differentiation was evident in a histological examination of this case. There was an excellent response to sorafenib. This case report might provide evidence that antiangiogenic agents may be active in any histological type of renal cell carcinoma. However, there are no available data to demonstrate the duration of response and survival benefit. [*J Chin Med Assoc* 2010;73(5):262–264]

Key Words: metastasis, renal cell cancer, sarcomatoid differentiation, sorafenib

Introduction

Sorafenib and sunitinib, which are multikinase inhibitors of tumor-cell proliferation and angiogenesis, have been shown to have some activity in 2 double-blinded, placebo-controlled trials in patients with metastatic renal cell carcinoma (RCC).[1,2] All of the patients' histology results were clear cell cancer. There are currently no studies showing that sorafenib and sunitinib are also effective in metastatic RCC other than clear cell histologic components. We report a case where sorafenib was used in a patient with metastatic RCC with sarcomatoid differentiation.

Case Report

A 38-year-old male with metastatic RCC presented with developing progressive disease after standard interleukin (IL)-2 and interferon-α (IFN-α) therapy. A computed tomography (CT) scan of the abdomen demonstrated a 73 × 65-mm left-sided renal mass and a 15-mm mass with perifocal edema in the parietal lobe of the brain. We also observed multiple metastatic nodules in both lung parenchyma (Figures 1–3). Left radical nephrectomy had been performed in October 2005. Pathological examination revealed clear cell carcinoma with diffuse sarcomatoid differentiation. Fuhrman's grade was III. Pathological staging was T3 and the surgical margin was positive. The lymph nodes and adrenal glands were not invaded (Figures 4 and 5).

Postoperative radiotherapy for intracranial metastasis and edema was applied immediately. A total of 30 Gy radiotherapy in 10 fractions within each 3 Gy was given to whole brain sections. In January 2006, regression was observed in both intracranial diameters of the mass and edema. Thereafter, immunotherapy consisting of IL-2 and IFN-α was administered to the patient for 8 weeks (20 MU/day, 3–5 days per week IFN-α and 72,000 IU/kg IL-2). Unfortunately, during re-evaluation, no response was observed, but a new mass was detected in the left renal fossa.

We decided that targeted therapy with sorafenib was the last chance of treatment for this patient. In April 2006, the patient started treatment with sorafenib given orally at a dose of 400 mg twice a day as recommended by Kroog and Motzer.[3] At the 6-month follow-up, the patient was alive and a total body CT scan showed

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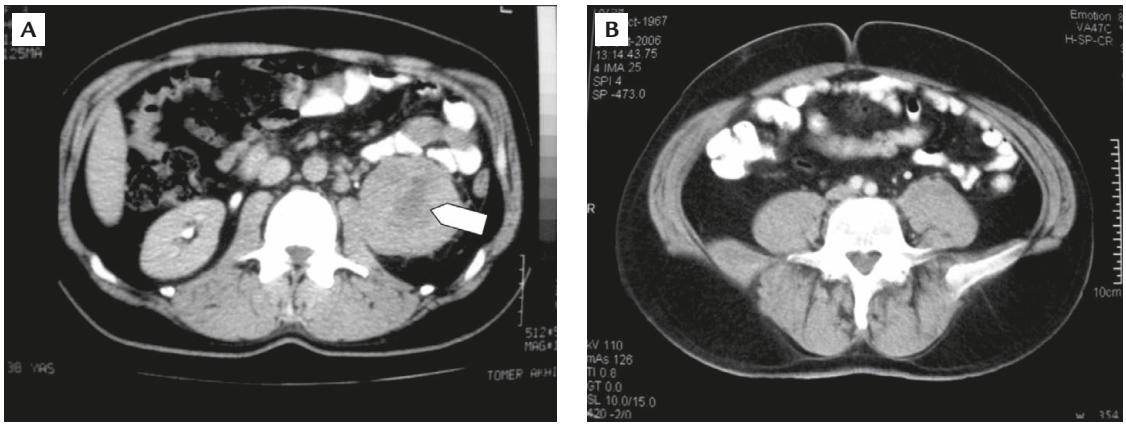

Figure 1. (A) Preoperative abdominal computed tomography shows a left-sided renal mass. (B) Postoperative abdominal computed tomography.

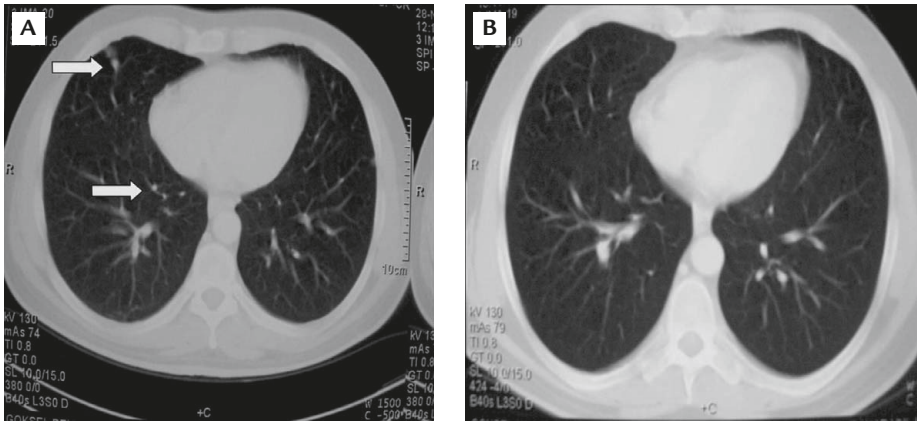

Figure 2. (A) Multiple lung metastases. (B) No metastasis after treatment.

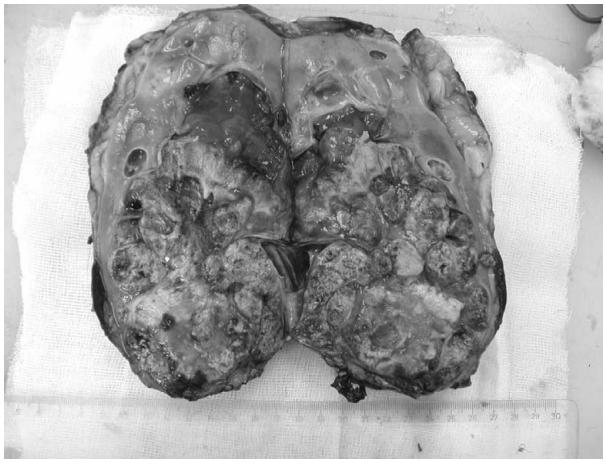

Figure 3. Radical nephrectomy specimen.

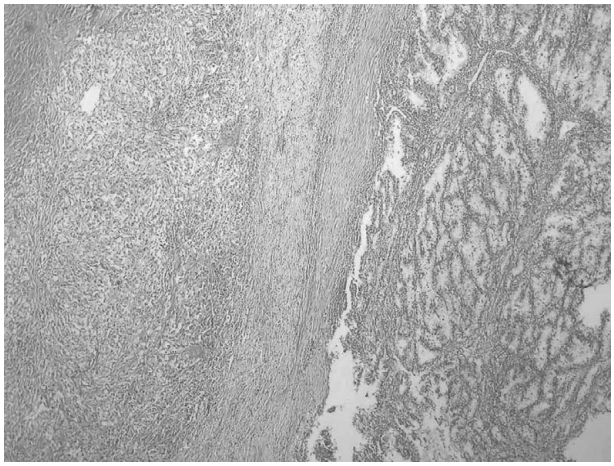

Figure 4. Clear cell carcinoma with sarcomatoid differentiation (hematoxylin & eosin, 100×).

no evidence of clinical progression. An abdomen and thorax CT revealed no metastatic focus in both the left renal fossa and lung parenchyma.

Unfortunately, the patient died because of disease progression, with multiple metastases 22 months from the first diagnosis, even though there was a complete response with disappearance of all tumoral deposits demonstrated at the 6-month follow-up after the first diagnosis. However, we obtained 22 months of survival advantage for this patient. The patient had a slight

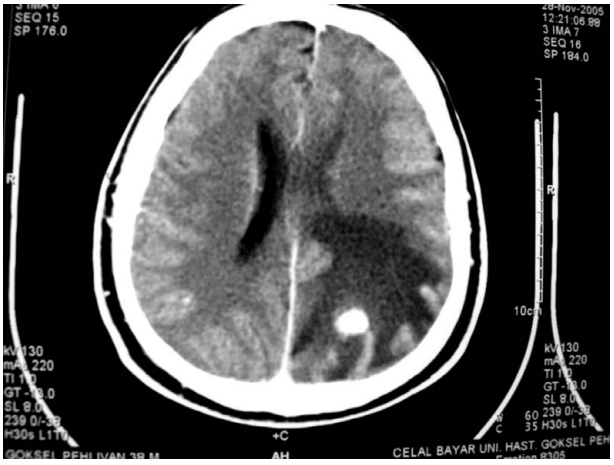

Figure 5. Left parietal mass and peripheral edema.

hand and foot syndrome due to toxicity of the drug. He needed no additional drugs for this complication.

Discussion

RCC is the most aggressive and lethal genitourinary cancer, with more than 40% of patients dying of cancer.[4] Unfortunately, no reliable treatment alternative has yet been developed for metastatic RCC. Recently, investigations in targeted therapy including multikinase inhibition and antiangiogenesis have been encouraging to clinicians in that they have some activity in the management of metastatic RCC. Overall, progression-free survival advantages with targeted therapy was demonstrated in 2 double-blinded, placebo-controlled studies in the treatment of metastatic disease.[1,2] Nevertheless, there are still many unanswered questions. The response rate in different histological types is not clear. We administered sorafenib in a patient with metastatic RCC with sarcomatoid differentiation and obtained an excellent result.

This case report provides evidence that certain antiangiogenic agents may be active in renal cancers of cell types other than those with clear cell histology. Additional data on the durability of the response may further clarify the complete response and survival benefit.

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