Oncology

Complete remission of metastatic renal cell carcinoma to the bone with sunitinib

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ABSTRACT

Target agents such as tyrosine kinase inhibitors have improved renal cell carcinoma (RCC) patient outcomes. However, complete remission (CR) with target agents is rare. Furthermore, CR of bone metastasis is much less common. We report a case of CR in bone and lung metastatic RCC. Radical nephrectomy was performed first, and clear cell RCC was diagnosed. Thereafter, sunitinib was started, and bone and lung metastases resolved entirely after 8 months of treatment. Sunitinib therapy was discontinued after 2 years because of the adverse event of proteinuria. However, the patient has remained in CR for over 1 year after sunitinib cessation.

Introduction

Recently, immuno-oncology drugs (I-O drugs) have made dramatic advances in clinical practice. However, tyrosine kinase inhibitors (TKIs) including sunitinib are still widely used as first-line treatment for patients at good risk as identified by the International Metastatic RCC Database Consortium (IMDC) criteria for metastatic renal cell carcinoma (RCC), and they have been shown to prolong patient survival. Nevertheless, complete remission is rare with sunitinib, and complete remission of bone metastasis with sunitinib therapy is much less reported, even though bone is the second most common metastatic site in RCC. We report a patient with bone and lung metastases who achieved complete remission with nephrectomy and sunitinib treatment. The patient remains without evidence of recurrence for over 1 year after sunitinib therapy was discontinued because of an adverse event.

Case presentation

A 56-year-old Japanese man presented with right shoulder pain in March 2017. A computed tomography (CT) scan revealed a 5.8-cm tumor of the left kidney, multiple pulmonary nodules, and a 5.0-cm expansile lytic lesion of the left scapula (Fig. 1A–C). These findings suggested that the tumor was RCC with bone and lung metastases. He first underwent laparoscopic right radical nephrectomy. The pathological examination indicated Fuhrman nuclear grade 3 clear cell RCC concomitant with a few papillary RCCs. The patient was considered to

be at intermediate risk according to the Memorial Sloan-Kettering Cancer Center (MSKCC) criteria (same risk level as with IMDC criteria), and sunitinib treatment was started at 50 mg daily for two of every three weeks. Although this dosing method does not follow the global standards schedule, it is often used in Japan.

At the 1-month staging visit, the lung metastases were diminished, and the left scapula lesion had significantly decreased. After 5 months of treatment, proteinuria as side effect of sunitinib occurred, and sunitinib therapy was discontinued. At the 8-month staging visit, despite interruption of the sunitinib, the scapula metastasis had entirely disappeared, and complete remission was determined (Fig. 2A and B). Although sunitinib was restarted at 37.5 mg daily for two of every three weeks at 1 year after the first treatment, proteinuria appeared again, and sunitinib was definitively stopped after a total of 2 years of treatment. The patient has remained in complete remission for over 12 months after sunitinib cessation.

Discussion

To our knowledge, there are few cases of the complete remission of a bone metastasis treated only with sunitinib without the combination of radiation therapy or metastasectomy. Beuselinck et al. found that RCC patients with bone metastases have shorter overall survival and progression-free survival following treatment with sunitinib than patients without bone metastases.¹ Of 76 RCC patients with bone metastasis, there were no cases of complete remission in their review. Badalian

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Fig. 1. Contrast-enhanced CT images of the chest and abdomen. (A) A 5.8-cm primary tumor in the right kidney (arrow). (B) An 8.0-cm expansile lytic lesion in the left scapula (arrow). (C) Multiple nodules in the lungs.

Fig. 2. After 8 months of sunitinib treatment, CT showed complete remission. (A) Left scapula and (B) lungs.

et al. reported that in their examination of 20 bone metastasectomy or biopsy samples, VEGF-receptor-2 protein expression fell from 35% in the primary tumor to 10% in the bone metastasis, which could explain the lower efficacy of TKI therapy.² It is not clear why sunitinib was so effective in our patient. It is expected that further studies will be needed to identify patients in whom TKI is highly effective.

Our patient remains in complete remission after the cessation of sunitinib therapy. There is no consensus regarding whether sunitinib therapy can be safely discontinued in patients achieving complete remission. In a recent retrospective analysis of 64 patients achieving CR with first-line TKI therapy, the relapse rate was significantly different between the patients who stopped (52%) and continued (18%) TKI therapy.³ This report suggested that continuing TKI therapy could prevent relapse and might be desirable even after achieving CR. However, Buchler et al. reported that there were no significant differences in post-CR survival between patients discontinuing and continuing TKIs.⁴ Our case suggested that discontinuation of TKI therapy is possible in some patients.

The efficacy of I-O drugs for bone metastasis is still uncertain. In the CheckMate 214 trial, which demonstrated the efficacy of combination therapy with ipilimumab and nivolumab as a first-line treatment, subgroup analysis of overall survival according to metastatic sites showed that the nivolumab and ipilimumab group had a better overall survival than the sunitinib group for patients with lung and liver metastases but

not for those with bone metastases.⁵ Even with the emergence of I-O drugs, patients with bone metastases may still have a poor prognosis. Currently, therapy with a combination of I-O drugs and TKIs has also begun, and it is expected that such treatment will improve the prognosis of patients with bone metastasis.

Conclusion

We report a patient with metastatic RCC who had bone and lungs metastases and achieved complete remission by nephrectomy and sunitinib therapy. The patient has not relapsed for more than 3 years despite the discontinuation of sunitinib. To our knowledge, this is a rare case of complete response of RCC bone metastasis to sunitinib therapy alone. It is unclear in which cases sunitinib is effective, and further studies are needed. Our case suggests that TKIs are still useful in some patients even as I-O drugs are emerging.

Consent for publication

Informed consent was obtained from the patient for this publication.

Declaration of competing interest

None.

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