Case Report of Prolonged Stable Disease with Modified Schedule Sunitinib in Metastatic Renal Cell Carcinoma

Shyam Aggarwal1* and Sachin Minhas1

1Department of Medical Oncology, Sir Ganga Ram Hospital, New Delhi, India.

Authors’ contributions

This work was carried out in collaboration between both authors. Author SA designed the treatment regimen and prepared the manuscript. Author SM collected the patient data and managed the literature searches. Both authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JCTI/2017/31424

Received 5th January 2017
Accepted 2nd March 2017
Published 23rd March 2017

ABSTRACT

Background: New targeted therapies have revolutionized the treatment landscape of metastatic renal cell carcinoma over the last decade. Sunitinib has demonstrated high activity in renal cell carcinoma (RCC), still complete remission is not a common occurrence in patients. In patient achieving complete response, continuation of therapy beyond complete response is debatable. Cytoreductive nephrectomy has shown to be beneficial in metastatic renal cell carcinoma in patients treated with interferon. However, its role is not established in the targeted therapy era. 

Case Presentation: A patient was diagnosed with renal clear cell carcinoma with multiple pulmonary metastases. He underwent cytoreductive nephrectomy and was started Sunitinib post-operatively. He experienced toxicities which were manageable with dose adjustments. He showed significant improvement on sunitinib therapy demonstrating complete response after total 22 months of therapy. After careful consideration and discussion with patient, sunitinib was stopped. The patient continues to be in an excellent condition after having stopped Sunitinib 5 years ago.

Conclusions: This case highlights that complete response can be achieved by sunitinib post cytoreductive nephrectomy with good quality of life and manageable toxicities. The case also highlights that discontinuation of therapy can be an option for some patients.

*Corresponding author: Email: dshyam_aggarwal@yahoo.com;
Keywords: Complete response; Sunitinib; renal cell cancer; cytoreductive nephrectomy.

1. BACKGROUND

Cytoreductive nephrectomy followed by immunotherapy has shown to be beneficial in the treatment of metastatic renal cancer [1,2]. However, these studies had evaluated interferon based immunotherapy. Current therapy for metastatic renal cell carcinoma (mRCC) mainly includes use of the targeted agents [3] and, thus, the role of cytoreductive nephrectomy needs to be re-evaluated (in conjunction with targeted agents).

Sunitinib is an orally administered multitarget tyrosine kinase inhibitor (TKI) used as a first line therapy for mRCC, which has demonstrated longer progression-free survival (PFS), higher response rates and longer overall survival than interferon alfa. Partial response is reported in about 31-44% of patients treated with sunitinib but complete response is reported in only about 3% of cases [4,5]. Upon attaining complete response, continuation or discontinuation of sunitinib is debatable.

2. CASE PRESENTATION

A 68 year old, diabetic patient with history of past coronary artery bypass grafting presented in July 2008 with complaints of low grade fever & weight loss since one month. The computed tomography (CT) scans showed left sided renal mass with metastatic spread to pleura and lungs (Fig. 1). His echocardiograph was normal for the left ventricular ejection fraction and his baseline performance score was two.

The patient was subjected to pleural tap in July 2008, which confirmed malignant cells. Left radical nephrectomy was done with the pathological diagnosis of moderately differentiated renal clear cell carcinoma extending to renal pelvis and peripelvic adipose tissue and revealing tumor emboli in many lymphovascular spaces.

Post-operatively, in July 2008, patient was started on Sunitinib 50 mg daily for 4 weeks of treatment followed by 2-weeks-off (Schedule 4/2). In September 2008, patient reported shortness of breath, and hence the dose was reduced to 37.5 mg in 4/2 schedule. In November 2008, patient developed dyspnea at rest. CECT Thorax revealed irregular nodular soft tissue deposits in the left pleura, increased left pleural effusion & persistent enlarged left hilar lymph nodes & tiny nodular lesions in bilateral lungs. Sunitinib was thus stopped.

CECT done in January 2009, showed regression of pleural disease, left hilar lymph nodes and left pleural effusion. Sunitinib was restarted at dose of 25 mg (schedule 4/2). Patient reported improvement in his symptoms on dose reduction.

After receiving therapy for another 16 months, patients stopped Sunitinib in May 2011. Follow up PET scan in September 2011, revealed complete response (Fig. 2).

Patient is still maintaining complete remission, excellent overall health and 0 performance status.

Fig. 1. CT scans showing left sided renal mass with bilateral lung involvement
3. DISCUSSION

Our case demonstrates achievement of complete response with Sunitinib and prolonged sustained complete response even after stopping Sunitinib. Although complete remission (CR) is uncommon during treatment for mRCC with tyrosine kinase inhibitors (TKIs), it may occur in few patients (<3%) [5]. In a multicentric, retrospective analysis of 64 patients with mRCC who achieved CR during treatment with TKI either Sunitinib or Sorafenib, 36 patients had received TKI treatment alone and 28 had also received local treatment. Most of the patients were of favorable or intermediate risk. Though total number of patients treated with either TKI is not available, at the main center only 1.7% (6 out of 353) of patients achieved CR [6].

In our case, the dilemma was about the continuation or discontinuation of Sunitinib after attaining complete response. In the pivotal phase III studies of sunitinib in metastatic renal cell carcinoma (mRCC), treatment was continued until the occurrence of disease progression or unacceptable adverse effects (or death) [4,5]. The possibility of having residual cancer cells left behind even after attainment of CR where discontinuation may allow the cells to proliferate and lead to disease recurrence, can be an argument for continuation. Continued therapy can maintain therapeutic pressure on the residual cancer cells. Authors have also mentioned rebound effect, with rapid regrowth and development of metastases observed after treatment discontinuation with TKIs which has been observed in preclinical models.

Discontinuation of therapy could be argued to avoid toxicity and to avoid development of resistance [6,7].

Another report evaluated the outcome of 5 renal cancer patients achieving CR with sunitinib and later discontinued sunitinib. After one year of stopping, 2 patients were still in CR, 3 patients had relapsed at 3, 12 and 15 months [7].

Another case report discussed attainment of complete response with sunitinib, given for renal cell cancer recurrence in native kidney after renal transplantation. Eight cycles of preoperative Sunitinib lead to 33% tumor size reduction. Post-surgery, Sunitinib was given for total of 11 months. Complete response was attained in 9 months. Authors had given Sunitinib for additional one course before discontinuation. Complete response was maintained for 2 years during follow up [8].

Cytoreductive nephrectomy has shown to be beneficial in mRCC. Studies by Flanigan RC, et al. [1] & Mickisch GH, et al. [2] showed benefit of cytoreductive nephrectomy in mRCC. Flanigan et al. [1] studied in 331 patients, cytoreductive nephrectomy plus interferon α compared with interferon α alone with resectable primary tumor and reported a median survival of 13.6 months for nephrectomy plus interferon versus 7.8 months for interferon alone. Mickisch GH, et al. [2] reported that radical nephrectomy done before interferon therapy improved overall survival compared with interferon alone (17 vs 7 months). Both studies demonstrated benefits mainly in patients with good performance status.
and lung metastasis. Since both trials were published in immunotherapy era, similar question needs to be answered with respect to targeted agents [3].

In 2014, Genitourinary Cancers Symposium, Heng DYC, et al. [9] presented data of mRCC patients undergone cytoreductive nephrectomy versus no nephrectomy. Median overall survival in the former group was 20.6 months as compared to 9.5 months observed in later group (p<0.0001). A retrospective analysis conducted by Choueiri TK, et al. [10] suggests that the efficacy of TKIs is greater in nephrectomised mRCC. The cytoreductive nephrectomy was associated with a median overall survival of 19.8 months compared to 9.4 months for patients who did not undergo cytoreductive nephrectomy.

Currently there are two largely awaited randomized trials in mRCC patients to address the question. CARMENA (NCT00930033) will compare nephrectomy followed by sunitinib versus sunitinib alone whereas EORTC 30073 trial (NCT01099423) will compare upfront or delayed nephrectomy with sunitinib [11].

4. CONCLUSIONS

We report here a case of cytoreductive nephrectomy followed by sunitinib treatment. In this case Sunitinib led to CR and the patient stopped Sunitinib upon achieving CR and still continues to be in CR (60 months since sunitinib is stopped). Both the options based on the existing data were explained to patient. Patient favored discontinuation for lack of recommendations for continuation and lack of negative data for discontinuation. Sunitinib shows acceptable tolerability and manageable side effects. Such prolonged CR has not been reported after discontinuation of Sunitinib. Therapeutic efficacy of TKIs after cytoreductive nephrectomy needs to be studied in a wider population. Results of CARMENA and EORTC 30073 will help address the role of cytoreductive nephrectomy in the era of targeted therapy in mRCC.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES
