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Case Report

Metastatic Renal Cell Carcinoma: A Case Report of Multiple Treatment Options and a Review of the Literature

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Abstract

Renal cell carcinoma (RCC), the most common type of kidney cancer, may present in many different clinical forms. The treatment order to be given in cases of RCC, for which there are several alternative therapies, has become an important issue. A patient diagnosed with RCC in 2009 was treated with interferon, sorafenib, everolimus, nivolumab, and axitinib for 7 years. This patient was followed up for 4 years after the detection of hepatic metastasis; this patient was the first at this center to receive cytokine treatment, tyrosine kinase inhibitor, and immunotherapy with axitinib, consecutively.

Keywords: Cytokine treatment, immunotherapy, metastatic renal cell carcinoma, tyrosine kinase inhibitor

Renal cancers are defined as typical internist's cancers and a vast majority of such cancers (90%) are renal cell carcinoma. They are characterized by anemia, malaise and weight loss. The most common symptoms are abdominal pain, macroscobic hematuria and palpable abdominal mass; however, today only 10% of the patients present with this classic triad of symptoms. Only 2% of the cases also have hereditary syndromes. Smoking, obesity, hypertension and polycystic kidney disease are the most common etiological causes.[1] Several treatment options have been developed for metastatic RCC in recent years; therefore, the cascade of these treatment options is main focal point. We wanted to present our case who was followed up for 7 years with metastatic RCC and treated with multi-step treatment cascade since it was a rare entity.

Case Report

A 42-year old male patient presented to our center in 2009 with the complaints of right lateral pain and hematuria and a right renal mass was detected. His whole body computed tomography (CT) scan revealed that there was a right renal mass, tumor thrombus in vena cava superior, while the liver, spleen and pancreas were normal (Fig. 1). Right nephrectomy was reported as papillary renal cell carcinom, type 2, fuhrman grade 4. 3 million units of interferon alpha treatment for three days a week was planned for the patient, whereas it had to be discontinued in 3 weeks due to his intolerance and sorafenib 2x400 mg was initiated. The patient who was followed up under Sorafenib without progression for 2 years presented in 2012 with the complaint

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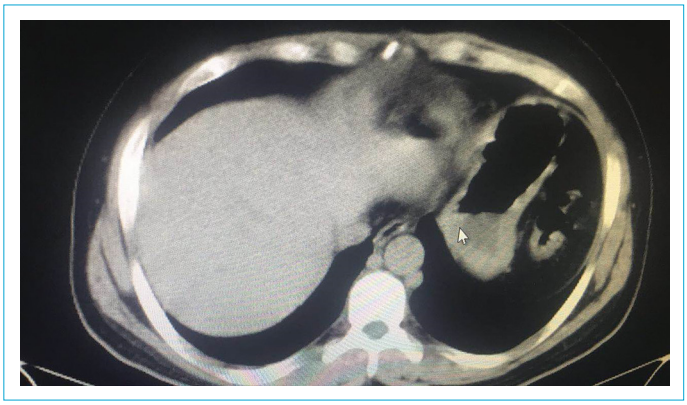

Figure 1. Computed tomography (CT) scan at the diagnosis time.

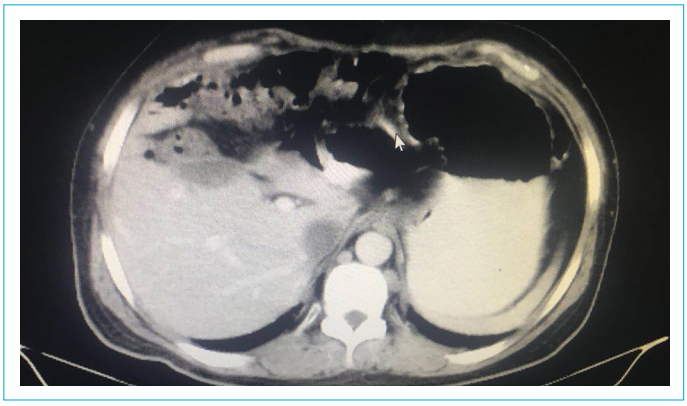

Figure 2. Computed tomography (CT) scan in 2012, multiple metastatic lesions in the liver parenchyma.

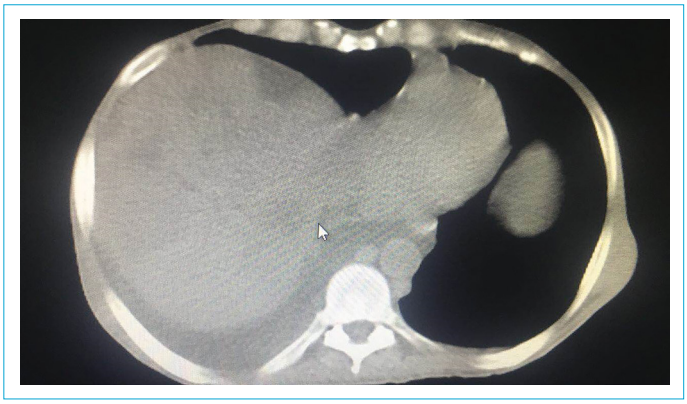

Figure 3. Computed tomography (CT) scan in 2016, the number of the lesions in the liver increased.

of pain in the right hip. His whole body CT scan revealed multiple metastatic lesions in the liver parenchyma with the largest having a diameter of around 1.4 cm at the level of dom, and metastatic lesions on the vertebra corpuses at T11-12 and posterior segment of the right iliac bone (Fig. 2). He received radiotherapy for 10 days to treat the bone lesions and then everolimus1x10 mg was given. He did not have any progression until February 2016 when his imaging (Fig. 3) revealed that the number of the lesions in the

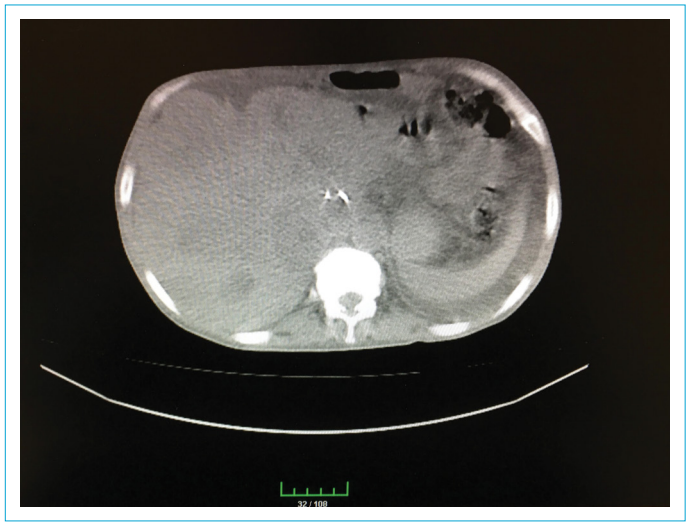

Figure 4. Computed tomography (CT) scan, he was found to have advanced pleural effusion and his liver lesions had a progression.

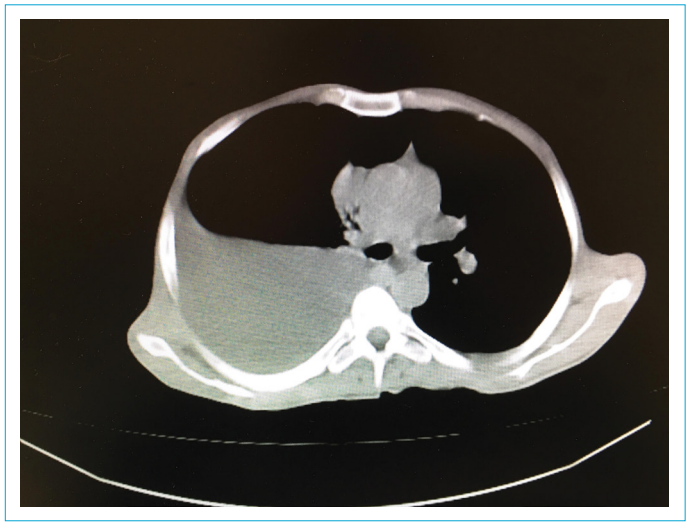

Figure 5. Computed tomography (CT) scan, he was found to have advanced pleural effusion and his liver lesions had a progression.

liver increased, and there were two new lesions in the left surrenal gland; thus, nivolumab treatment was planned at the dose of 3mg/kg every 2 weeks. In total, 12 cycles of nivolumab were given to the patient with this regimen. No complication developed. His scans imaged in June 2016 showed that the liver lesions progressed and developed a diffusing pattern and there were new paraaortic metastatic lymphadenopathies. A comparative analysis of the scans in June 2016 and scans in February 2016 demonstrated that the mass lesions had a pronounced progression; therefore, he was considered to have no response to nivolumab treatment and the treatment was discontinued. After the nivolumab treatment, the axitinib that is a tyrosine kinase inhibitor was initiated at a dose of 2x5 mg. The dose was increased to 2x10 mg since he tolerated it well and the con-

trol CT performed 3 months later revealed stable findings. 2 months later, the patient presented with deterioration of overall state and shortness of breath, and he was found to have advanced pleural effusion and his liver lesions had a progression (Figs. 4, 5). He became exitus after his treatment in the intensive care unit for 3 days.

Discussion

The standard medication for RCC was interferon and IL-2 until 2006. When interferon is given, the overall response rate is usually around 10-20%. If the disease has a low volume, the best response rate may rise as high as 30%.[1] Sorafenib was developed as a c-RAF and BRAF inhibitor, however, it was later understood that it also inhibited the Vascular endothelial growth factor, Platelet-Derived Growth Factor, fms-like tyrosine kinase 3 and c-Kit receptors. In Phase III TARGET trial designed on the basis of a Phase II trial, placebo vs. sorafenib was given to the patients (cytokine refractory patients) and it was demonstrated that sorafenib contributed to the progression-free survival (PFS), therefore, it was approved for the second line treatment.[2] In RCC, mTOR (Mammalian Target of Rapamycin) pathway is usually activated; therefore, the drugs that inhibited mTOR pathway were used in the treatment. In a phase III trial with Everolimus, placebo vs everolimus was given to the patients who had previously taken sunitinib or sorafenib or both drugs and its contribution to PFS was demonstrated.[3] An immune control point inhibitor called nivolumab developed for programmed death-1 (PD-1) receptor in T lymphocytes have been recently used to treat advanced malign melanoma and RCC as well as non-small cell lung carcinoma.[4] Axis trial published in Lancet in 2011 shows that axitinib can be used as an alternative for the treatment of advanced RCC.[5] There is a limited set of data in the literature regarding the use of axitinib and other tyrosine kinase inhibitors after nivolumab and immunotherapy while the experience is mainly with clear RCC. Our case had papillary RCC and there are several aspects in the treatment of this sub-type yet to be clarified. The efficacy of the target therapies (sunitinib, sorafenib, everolimus) should be investigated in papillary RCC patients in phase III clinical experiments. Moreover, a systematic review and meta-analysis of several phase II and retrospective studies shows that these agents have limited efficacy for the treatment of patients with papillary RCC and the response rates are significantly lower than the response rate of clear RCC.[6] Similarly, the efficacy of immunotherapy in papillary RCC is also controversial. A case presentation reported that a patient with papillary RCC with sarcomatoid pattern responded very well to nivolumab.[7]

Conclusion

We are of the opinion that the efficacy of immunotherapy in papillary RCC should be investigated in well-designed studies. Our patient who was followed up with liver metastasis for 4 years and given nivolumab and axitinib that were among the available treatment options in recent years when multi-step treatment cascade was used was the first patient with papillary RCC at our center who received both of these options.

Disclosures

Informed Consent: Written informed consent was obtained from the patient who participated in this study.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Informed consent: Written informed consent was obtained from the patient for the publication of the case report and the accompanying images.

Authorship contributions: Concept – M.B., I.O.K.; Design – A.E.Y.; Supervision – C.M.; Materials – S.G.; Data collection &/or processing – A.O.; Analysis and/or interpretation – M.T.; Literature search – H.E.S.; Writing – K.B.; Critical review – I.O.K.

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