Use of an Inhibitor of Tyrosine Kinase as a Targeted Therapy in a Case of Inoperable RCC

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Abstract

Renal cell carcinoma (RCC) falls within the range of 2-3% of all oncology disorders in adults. Given the pathogenic mechanisms of RCC growth and dissemination, the disease is now actively treated by means of various types of the targeted therapy. One of the medicines available and widely used is Pazopanib which affects cancer cells in the form of inhibition of tyrosine kinase receptors. This article describes a case study of Pazopanib use in the course of treatment of inoperable RCC.

Keywords: Clear cell renal cell carcinoma (ccRCC); Targeted therapy; Metastasis

Introduction

RCC falls within the range of 2-3% of all oncology disorders in adults. Every year RCC kills more than eight thousand people in Russia. The standardized incidence rate of malignant kidney tumors is 8.09 per 100,000.00 of the Russian population [1,2]. Currently, up to 40% of RCC cases are detected accidentally during routine examinations.

Given the pathogenic mechanisms of RCC growth and dissemination, various types of targeted therapy are actively being used.

Pazopanib is a tableted-tyrosine kinase inhibitor that affects all known types of receptors for Platelet-Derived Growth Factor (PDGF) and Vascular Endothelial Growth Factor (VEGF), such as Vascular Endothelial Growth Factor Receptors (VEGFRs), PDGF receptors (PDGFR-a, PDGFR-b), mast/stem cell growth factor receptor (SCFR), also known as c-KIT and FMS-like tyrosine kinase 3 (FLT-3) participating in the process of tumor growth, pathologic angiogenesis and metastasis.

The above medicine was approved in the U.S. and Europe as the means of the first and second-line treatment of advanced RCC and it is recommended and widely used in common medical practice during the course of treatment of patients with favorable and intermediate prognosis of the disease, according to Memorial Sloan Kettering Cancer Center (MSKCC) criteria [3-8].

Side effects and complications caused by Pazopanib often require a dose adjustment or discontinuation of the use of the medicine, which naturally affects the effectiveness of anticancer therapy. Most frequent side effects caused by the usage of Pazopanib are general weakness, hypertension, complications of gastrointestinal (nausea, vomiting, diarrhea), skin manifestations, as well as changes in blood indices (increased transaminases, bilirubin, leucopenia and thrombocytopenia) [9,10].

Case Presentation

Clinical case of the effective use of Pazopanib in a case of inoperable RCC.

Patient A: male, born-1946; December 2010-detection of RCC located in the right kidney, T3NoMo.

The examination by ultrasound and helical computed tomography revealed a tumor located in the lower half of the right kidney, grown out of the kidney contour and accumulating the contrast agent (Figure 1). No evidence of distant metastasis was revealed.

Static renoscintigraphy showed severe impairment of renal excretory function of both kidneys.

Co-morbidity-severe hypertension, st. 3; obesity, st 3.

The patient was consulted by a primary care physician and an anesthesiologist and given the presence of co-morbidity it was decided to conduct a renotropic infusion therapy in terms of preoperative preparation. The above therapy had no effect, and it was decided to abstain from the surgical treatment for the reason of high risks of possible complications that may be caused by anesthesia and surgery.

April 11, 2012-biopsy of the right kidney (local anesthesia); histological results: clear cell RCC (ccRCC)

April 19, 2013-palliative radiofrequency ablation of ccRCC located in the right kidney, followed by a drug therapy by Pazopanib administered in the dose of 600 mg per day.

Subsequent outpatient treatment, including: computed tomography of the chest, abdomen and pelvis, renal function, and complete blood

Figure 1: Computed Tomography (CT)-Before treatment.

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Figure 2: CT During the treatment.

Figure 3: CT During the treatment.

and urine tests—every three months; electrocardiogram (ECG)—once in three months. The patient was interviewed about the presence of adverse events.

Spiral computed tomography (CT) of the abdomen showed the stabilization of the process (Figure 2).

CcRCC dimensions ranged within the same limits as before the treatment.

Study of September 2013—ccRCC: location—right kidney

Renoscintigraphy showed no change in indicators of renal excretory function. The patient was consulted by a primary care physician and a cardiologist, surgery—recommended only in an emergency situation. Given the effectiveness of the therapy and the absence of adverse effects above 1-2 tbsp it was decided to continue the treatment by Pazopanib in the dose of 600 mg (Figure 3).

The analysis of the adverse events during the first week of treatment by Pazopanib showed an increase of blood pressure up to 160/100 mmHg. The said complication was jugulated by antihypertensive therapy. During week 4 of the treatment the discoloration of hair was noted. Apart from the above, the remaining adverse events were limited to weakness not exceeding the 1st degree. The most recent examination of the patient showed the stabilization of the process, the patient continues the drug therapy earlier prescribed.

Discussions

In the course of the therapy with Pazopanib we registered

the stabilization of the disease which allows us to refrain from recommending a surgical treatment at the present.

During the course of treatment with Pazopanib the following main adverse effects were registered: weakness, hypertension (not exceeding st. 1-2). During the treatment regular monitoring of blood pressure was conducted; in cases of blood pressure increase the respective antihypertensive therapy was conducted (prescribed by a cardiologist), no discontinuation of the targeted therapy was required.

Conclusions

The targeted therapy is currently widely used, the results show the increase of progression-free survival, which allows to recommend the said therapy as a possible treatment for patients even in cases of inoperable ccRCC.

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