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Case Report

Extended Progression-Free Survival of Renal Cell Carcinoma with Axitinib: Case Report

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Abstract

Axitinib is a selective inhibitor of vascular endothelial growth factor receptors approved for second line treatment of advanced renal cell carcinoma. The case report concerns an 85-year-old man with renal cell carcinoma of clear cells initially treated by left nephrectomy who presented with pulmonary progression 7 years later. Systemic treatment with pazopanib was initiated but disease progression and gastrointestinal toxicity were observed after 4 months. A second line treatment implemented with axitinib (5 mg twice daily, later reduced to 5 mg once daily due to gastrointestinal toxicity) led to favorable outcome and control of pulmonary progression. This case report demonstrates that axitinib in reduced dose can improve progression free survival (34 months at present) and surpass data published in Phase III clinical trials on patients with localized renal cell carcinoma of clear cells. It further contributes to the limited information currently available on axitinib in Latin-American populations.

Keywords: Kidney Cancer; Metastatic Renal Carcinoma; Tyrosine Kinase Inhibitors

Abbreviations

CT	:	Computer Tomography
ECOG	:	Eastern Cooperative Oncology Group
NCCN	:	National Comprehensive Cancer Network
OS	:	Overall Survival
PFS	:	Progression Free Survival
RCC	:	Renal Cell Carcinoma
RECIST 1.1	:	Response Evaluation Criteria in Solid Tumors
VEGFR	:	Vascular Endothelial Growth Factor Receptors

Introduction

Renal cancer varies greatly from region to region worldwide with an average incidence of 4.4 per 100,000 and a mortality of 1.8 per 100,000 for both genders [1]. In Central and Latin-American countries incidence rates of Renal Cell Carcinoma (RCC) range between 3.0 and 6.8 per 100,000 for men and between 2.5 and 6.4 per 100,000 for women [2]. In Ecuador, the estimated incidence of RCC is 4.2 per 100,000 for men and 3.0 per 100,000 for women [1,2]. Axitinib is a potent anti-angiogenic tyrosine kinase inhibitor approved for the second-line treatment setting in patients with metastatic RCC [3-5]. Two meta-analyses have evidenced a better objective response rate, disease control, progression-free survival (PFS: median 6.7 months) and overall survival (OS: median 20.1 months) after axitinib administration in comparison to sorafenib [6,7]. There is currently very limited information available on the

use of axitinib in Latin-American populations compared to other regions. The present case report describes a patient with RCC and distant metastases to the lung, first treated with radical nephrectomy and pazopanib and thereafter, at time of progression, successfully controlled by axitinib in reduced dose with an extended PFS.

Case Report

In November 2006, a 75-year-old man underwent a radical left nephrectomy consecutive to RCC incidentally detected by Computer Tomography (CT) scan. The patient had a medical history of splenectomy, due to a left renal retroperitoneal tumor, and pulmonary hypertension with bi-auricular severe dilatation for unknown reasons. No significant family history was reported. The patient had only routine clinical follow-up until December 2013 when he presented fever. Physical examination and laboratory data were normal, but an 11.5 cm left lung mass in the inferior left lobe was evidenced by CT scan. The RCC-related pulmonary metastasis was confirmed by biopsy some days later. Systemic treatment was initiated immediately with oral pazopanib at a daily dose of 400 mg until March 2014 when the drug was suspended due to diarrheic stools grade IV that compromised his life. Six months later, the patient started a second line therapy with axitinib at an oral dose of 5 mg twice a day, dose adjustments based on individual safety and tolerability. Axitinib was swallowed whole with a glass of water. The treatment was carried out according to the National Comprehensive Cancer Network (NCCN) recommendations and National Health Service policies. However, after one month the dose had to be reduced to a single daily dose of 5 mg due to gastrointestinal toxicity grade II (4-6 diarrheic stools per day). Moreover, in October 2014, the patient was transferred to our oncology clinic where medical imaging examinations, laboratory and histopathology tests were performed for a comprehensive management and control. Laboratory data were normal, but the physical examination showed hypophonetic heart sounds with systolic murmur grade 2 in aortic focus, significant edema in both lower extremities and signs compatible with pulmonary effusion. CT evidenced a large amount of left pleural effusion, right metastatic pulmonary nodules in segments II (2.2 cm of diameter) and IX (0.7 cm of diameter) plus left lower lobar atelectasis by occupational mass of 13 x 13.3 x 14 cm of diameter compatible with soft tissue (Figure 1).

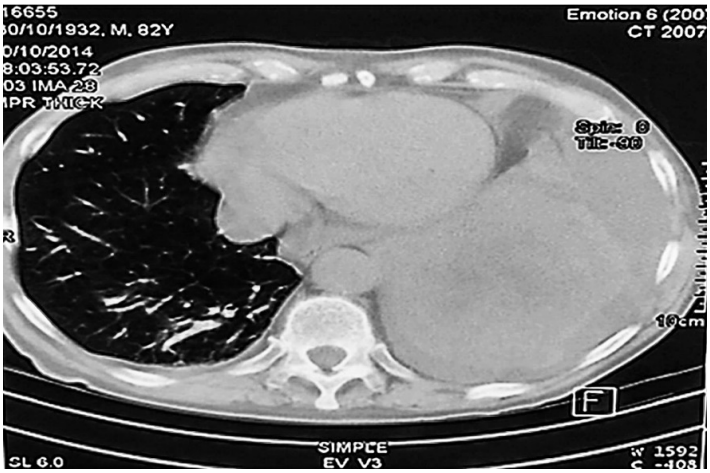

Figure 1: CT of October 2014 reported a large amount of left pleural effusion with an occupational mass of 13 x 13.3 x 14 cm of diameter compatible with soft tissue.

Two thoracenteses were performed with a drain of 1800 cc of pleural fluid. Pelvic echography reported a benign prostatism grade I treated with tamsolusin and prophylactic nitrofurantoin and a right renal nodule of 25 mm on the superior pole with a parapielic cyst without surgical criteria. Finally, the lamellae histopathological and immune-histochemical review revealed pulmonary metastases of RCC of clear cells with Fuhrman grade 2. With regards to baseline outcomes of axitinib therapy 34 months later the patient experienced a clinical benefit with stable disease according to RECIST 1.1 (Response evaluation criteria in solid tumors) based on CT scan [8] (Figure 2).

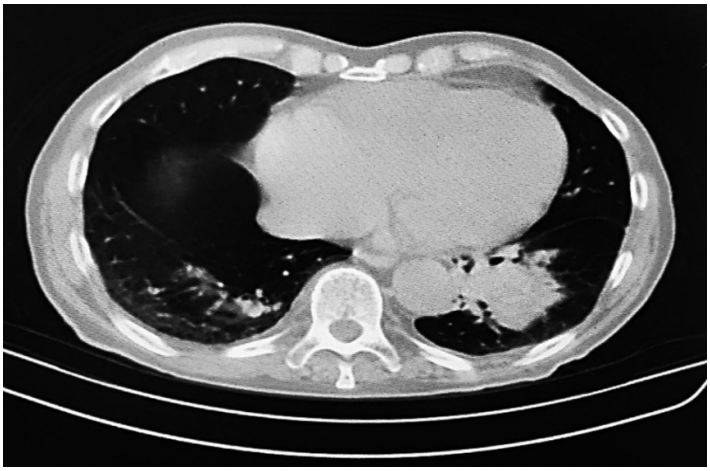

Figure 2: CT of May 2017 reported a tumor mass of heterogeneous density with multilobed contours, extends from the pulmonary hilum to the chest wall and measures 9.6 x 7.2 cm of diameter.

Nevertheless, the patient presented complications such as a deep venous thrombosis of the left safena vein treated with clinical treatment, fecal impaction and bladder balloon treated by enema and urinary catheter, respectively, and a multi-infarct disease in brain (bilateral white matter of the supratentorial area) without sequels controlled with levetiracetam. Additionally, he had subclinical asymptomatic hypothyroidism and reported asthenia, somnolence, dyspnea, periungual desquamation, need for supplemental oxygen for at least 16 hours a day, grade I retrolisthesis in C6, spondylosis and generalized osteopenia in the spine. At present, the 85-year-old patient continues with axitinib (dose of 5 mg orally daily) and has an OS of more than 10.5 years since RCC diagnosis and a PFS of 34 months with an ECOG (Eastern Cooperative Oncology Group) performance index equal to 1 and a Karnofsky score of 90%.

Discussion

Cancer of the kidney and renal pelvis represents the sixth most common cancer in men worldwide [2]. Although metastatic cancers are traditionally associated with an overall poor prognosis, axitinib is a potential therapeutic option to consider in advanced RCC [3]. In the latest clinical guidelines, systemic treatment with tyrosine kinase inhibitors, such as sunitinib, pazopanib and axitinib, has been approved as first line therapy for RCC [3-5]. Pazopanib in a phase III trial reported a PFS of 10.5 months and a better toxicity profile in comparison to sunitinib although in this case study the patient experienced toxicity after only 4 months of pazopanib treatment [9]. In turn axitinib is a potent and selective second-generation inhibitor of Vascular Endothelial Growth Factor Receptors (VEGFR) that bears a relative potency 50-450 times greater than the first-generation VEGFR inhibitors [10]. International guidelines recommend axitinib at doses of 5 mg twice a day for an anti-neoplastic activity but in our case the dose had to be reduced to 5 mg once a day [3-5]. Despite the dose reduction our patient showed a notable therapeutic response with an extended PFS. Axitinib demonstrated to be a well-tolerated drug, with positive clinical outcomes and no negative impact on quality of life. Our patient experienced the classical adverse events reported in clinical trials such as fatigue, hypothyroidism, decrease appetite, nausea and asthenia [7]. Concomitantly, he presented with a major episode of fecal impaction and bladder balloon due to unidentified reasons. This case report which adds to the limited knowledge currently available about the use of axitinib for RCC in Latin-American populations shows that a reduced dose treatment regimen with axitinib can be as effective as the recommended doses and may prolong survival in advanced RCC. This hypothesis requires confirmation in randomized trials.

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