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Successful selective arterial embolizations for bone metastases in renal cell carcinoma integrated with systemic therapies: A case report

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ABSTRACT

Herein is described the case of a 64-year-old patient affected by metastatic clear-cell carcinoma, with exclusive bone disease, subjected after the initial cytoreductive nephrectomy to 3 successive lines of medical treatment (sunitinib, everolimus, and sorafenib) and multiple locoregional treatments (spinal surgery, radiation therapy, and selective arterial embolization), resulting in a surprisingly long survival of over 75 months. In the era of target therapy, integration strategies, including additional locoregional treatment to medical therapy, are essential to optimize the clinical benefit, to maximize treatment duration overcoming focal progressive disease, and to improve the quality of life. In this context, we would highlight that selective transcatheter embolization of bone metastases from renal cell carcinoma should be considered as an effective and safe option in the palliative setting for patients with bone metastasis, especially for pain relief.

Introduction

Renal cell carcinoma (RCC) represents 3% of all cancers, with the highest incidence occurring in western countries and representing the seventh most common cancer in men and the ninth most common cancer in women [1]. Approximately 30% of all patients with RCC have metastatic disease at presentation, and distant metastases occur most often in the lungs, the lymph nodes, the liver, the bones, and the brain. In particular, lung metastases affect 45%-50% of patients with advanced disease, followed by bone (30%) and liver (20%) metastases [2]. The estimated average 5-year survival in metastatic renal cancer is approximately 20% [3].

Bone metastases represent a crucial point in patient management because of the significant morbidity related to skeletal

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complications, such as pathologic fracture, spinal cord compression, and hypercalcemia, and correlate with a poor prognosis and a reduced overall survival [3,4].

The recent advances in our understanding of the pathogenesis and the molecular landscape of renal cancer, and in particular of clear-cell carcinoma, have led to the development of molecular therapies targeting the vascular endothelial growth factor and the mammalian target of rapamycin (mTOR) pathways, and of immunotherapy resulting in a significant improvement of treatment options, rates of survival, and quality of life [5]. The introduction of these new drugs revolutionized the clinical management of patients affected by RCC with more attention to the early clinical and imaging predictive factors of treatment efficacy, with a more accurate management of the side effects, and with a systematic and critical attitude on the treatment sequence [5–8].

In addition to these varied scenarios of systemic approach, the locoregional treatments should be placed, with the aim of controlling disease symptoms and optimizing systemic therapies, expanding the duration of each therapeutic line and improving the quality of life.

Preoperative and palliative transarterial selective embolization is a safe and effective minimally invasive, interventional treatment for pain relief and devascularization of primary and metastatic bone tumors by various primary cancers [9–15]. This treatment can also be repeated during the course of disease and can be combined with other treatment modalities such as radiotherapy and chemotherapy.

Here we present the case of a patient affected by metastatic RCC managed with a multimodality approach, consecutively treated, for over 6 years, with 3 tyrosine kinase inhibitors and several local treatments, including surgery, radiotherapy, and, in particular, with two superselective arterial embolizations of bone metastases, one in the right femur bone and one in the right pubic region.

Case presentation

In April 2008, a 63-year-old man with a smoking habit and hypertension, and overweight in personal medical history presented with cruralgia and an intermittent pain in the left lumbar region. The subject underwent a contrast-enhanced computed tomography (CT) scan study, which demonstrated a large infiltrative mass in the lower pole of the left kidney measuring $5.7 \times 5.6 \times 6.0$ cm, with vertebral metastasis (D9-L3) and with D12 and L1 cord compression and a right iliac crest metastasis. Admission laboratory tests revealed a normocytic anemia, a mildly elevated white cell count, and an elevated platelet count (Hg of 8.9 g/dL, MCV 87 fL, white blood cell count 12,000/μL, platelet count 573,000/μL). Chemistry laboratories revealed an elevated lactate dehydrogenase (584 U/L) with normal kidney and liver functions. A bone biopsy was performed, and the pathologic examination revealed a metastasis by clear-cell RCC.

The patient underwent, in the first instance, a left cytoreductive nephrectomy, followed by a surgical spinal decompression (D12 and L1) and stabilization (D9-L3) to avoid bone complications and a radiation treatment of the back-lumbar spine (D9-L3) with 20 Gy in 5 fractions for pain control.

After surgery, a first-line treatment with sunitinib as the first-line therapy at a dose of 50 mg/day in a 4/2 schedule and zoledronic acid was started. Under sunitinib treatment, which was well tolerated, the patient had a progression-free survival of approximately 41 months, higher than the median progression-free survival observed in clinical trials [16–18]. A CT scan performed after the sixth cycle of sunitinib documented an increase in the diameter of the metastatic lesion localized in the right iliac crest associated with osteolytic aspects and the new appearance of a right femoral osteolytic metastasis.

Radiotherapy of the right iliac crest (30 Gy in 10 fractions) was performed for pain control, and an mTOR inhibitor was started as a second-line therapy. Between April 2012 and November 2013, the patient was administered everolimus at a dose of 10 mg/day, obtaining a surprisingly stable disease for about 19 months. After 6 months of everolimus treatment, the patient experienced an interstitial pneumonitis, which required drug discontinuation for 20 days, therapy with supplemental oxygen, b-agonists, and prednisone 0.5 mg/kg.

In July 2013, during everolimus treatment, there was a significant clinical progression of the disease with worsening of the painful symptomatology in the right femur, with poor response to opioid analgesics. A fluorine-18 fluorodeoxyglucose-positron emission tomography scan showed hypermetabolic lesions in the right femoral neck (SUVmax = 4.5) and the omolateral pubic bone (SUVmax = 9) (Fig. 1).

With the aim of improving pain control and delaying the occurrence of local complications, such as pathologic fractures, an arterial embolization treatment was proposed. The angiography, realized by microcatheter insertion into the common femoral artery, showed the presence of 2 hypervascular metastases in these 2 regions. The femoral and pubic lesions, characterized by a rich and pathologic neovascularization (Fig. 2), were embolized using N-butyl-cyanoacrylate with palliative intent, obtaining a complete devascularization, with the postembolization angiography showing a complete occlusion of the pathologic feeding vessels (Fig. 3). Moreover, a significant reduction in the pain score and the need for analgesics were observed.

In June 2014, because of a further skeletal disease progression, a third-line therapy with sorafenib was started, at a standard dose of 800 mg/day. After a 2-cycle occurrence of G2 anemia, G2 thrombocytopenia, fatigue, and G2 hand-foot syndrome required a dose reduction to 400 mg/day. In December 2014, because of a severe deterioration of the performance status and disease progression, the cancer treatment was suspended, directing the patient only to supportive care.

Discussion

Before 2005, kidney cancer was considered a malignancy orphan of effective therapies, but in the past 10 years, the treatment options have been greatly expanded. The discovery of the crucial role of angiogenesis and the approval of sorafenib and sunitinib, respectively, in 2005 and 2006 dramatically changed the clinical outcome in these patients. In the following years, several other therapeutic options, characterized by a high rate of disease control, were approved, including vascular endothelial growth