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J C N JOURNAL OF CLINICAL NEPHROLOGY
ISSN 2576-9529

Letter to Editor

Renal Adverse Reaction Secondary to Check-point Inhibitors in Metastatic Renal Cancer

Marta Guerra Lacambra*, Miguel Angel Gonzalez Martinez, Vanesa García Chumillas and Francisco Gutierrez Tejero

San Cecilio Clinical University Hospital, Knowledge Avenue, s/n, 18016 Granada, Spain

Abstract

Immune Checkpoint Inhibitors (PCIs,) are monoclonal antibodies directed against immune checkpoint regulatory molecules. These antibodies inhibit T-cell activation and prolong survival in patients with different types of cancer. However, they can produce adverse effects related to the immune response such as renal damage.

We present the clinical case of a 75-year-old man with a personal history of Chronic Kidney Disease (CKD) and metastatic renal cancer with lung, bone, and mediastinal involvement. He started treatment with immunotherapy with Nivolumab-Ipilimumab. Then, after 4 cycles of immunotherapy, the patient was admitted to the Urology Department for an adverse reaction to immunotherapy with the development of nephritis and toxic hepatitis. Despite treatment with methylprednisolone, he evolved poorly, and a palliative approach was finally decided.

The incidence of acute renal failure attributed to PCIs is estimated at 2% - 3%, being grade I-II in most cases. Among the renal complications associated with PCIs, acute interstitial nephritis is the most predominant with an incidence of 80% - 90% of cases. In addition, an increased risk is observed in patients with intermediate or poor risk metastatic renal cancer.

Despite their fundamental role in metastatic renal cancer, we must take into account the potential for renal failure as an adverse effect of PCIs, especially in patients with previous CKD.

More Information

***Address for correspondence:**
Marta Guerra Lacambra, San Cecilio Clinical University Hospital, Knowledge Avenue, s/n, 18016 Granada, Spain, Email: martaguela@gmail.com

Submitted: May 06, 2024
Approved: May 16, 2024
Published: May 17, 2024

How to cite this article: Lacambra MG, Martinez MAG, Chumillas VG, Tejero FG. Renal Adverse Reaction Secondary to Check-point Inhibitors in Metastatic Renal Cancer. J Clini Nephrol. 2024; 8: 076-077.

DOI: 10.29328/journal.jcn.1001130

Keywords: Immune checkpoint regulation; Immunotherapy; Renal failure; Nephritis

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Immune Checkpoint Inhibitors (ICPs) are monoclonal antibodies directed against immune checkpoint regulatory molecules that inhibit T-cell activation. These drugs can prolong overall survival in patients with different types of cancer, including clear cell Renal Cell Carcinoma (RCC) [1]. PCIs are drugs that act against PD1, PDL1, and CTLA4 by blocking the lymphocyte receptor or tumour ligand. However, these drugs can cause adverse effects related to the immune response [2].

We present the clinical case of a patient diagnosed with metastatic RCC with nephropathy and toxic liver disease secondary to immunotherapy with Nivolumab-Ipilimumab.

The patient was a 75-year-old man with a personal history of hypertension, type 2 diabetes mellitus, and CKD grade 3A2 (baseline creatinine 2 mg/dl) diagnosed with metastatic RCC with intermediate-risk pulmonary, bone, and mediastinal involvement. After presenting the clinical case to the Uro-Oncology Committee, it was decided to start treatment with analgesic radiotherapy on sacral metastases and immunotherapy with Nivolumab-Ipilimumab. Given the progressive worsening of renal function (creatinine 3.6 mg/dl), it was decided to suspend the third dose of Nivolumab-Ipilimumab.

One month after the last cycle of Nivolumab-Ipilimumab, the patient came to the emergency department for progressive oedematisation of the lower limbs associated with a decrease in the rate of diuresis until it progressed to anuria. In the laboratory tests requested in the ED, a resurgence of his CKD was observed (creatinine 7.51 mg/dl, U 194 mg/dl, Na 124 mEq/L, K 6 mEq/L) together with data suggestive of acute hepatitis (PT 55%, total bilirubin 4.05 mg/dl, GOT 3832 mg/dl, GPT 2222 mg/dl, GGT 385 mg/dl, FA 503 mg/dl). Serology for hepatotropic viruses (HAV, HBV, HCV, HEV, EBV, CMV, and HSV) and urine culture were negative. After ruling out a vascular-biliary obstructive cause or new metastases with imaging tests unchanged from previous ones, a definitive diagnosis of an adverse reaction to immunotherapy with the development of nephritis and toxic hepatitis was agreed upon.

It was decided to admit the patient to the urology department and start treatment with methylprednisolone at 1-2 mg/kg. However, given the persistence of anuria despite medical treatment and the worsening of ion levels (K 6.5 mEq/l), despite presenting haemodynamic instability, it was decided to place a femoral catheter and start an acute haemodialysis session. Despite this, during hospital admission, the patient evolved unfavourably with events typical of disease progression such as respiratory distress with tugging. For this reason, palliative care and subsequent death were agreed with the patient and relatives.

As a consequence of increasing the activity of the immune system, PCIs can have inflammatory side effects (59% - 85%) [3] and can affect multiple organs, the most common being the skin, gastrointestinal tract, and lungs, but also thyroid, adrenal, and kidney, among others.

The incidence of Acute Renal Failure (ARF) attributed to PCI is estimated at 2% - 3% and may reach 5% in the case of combining two PCIs. In most cases the associated ARF is mild, being grade I-II. Among the renal complications associated with PCI, Acute Interstitial Nephritis (AIN) is the most predominant with an incidence of 80% - 90% of cases, appearing 12 weeks - 14 weeks from the start of treatment [3]. Corticosteroids are the mainstay of treatment, and their early introduction is essential. On the other hand, the known risk factors for the development of acute renal failure secondary to PCIs are baseline renal function, the use of proton pump inhibitors, and the use of two or more PCIs, as well as age [4]. In addition, an increased risk is observed in those patients with intermediate or poor risk metastatic renal cancer according to the Memorial Sloan Kettering Cancer Center (MSKCC) risk classification [5].

After witnessing the aforementioned clinical case, we had some doubts about the risk-benefit in certain patients undergoing PCI treatment. Our patient had all the previously mentioned risk factors for the development of acute renal failure secondary to PCIs. Despite the indisputable role of PCIs in metastatic renal cancer, we must individualise the treatment of each patient in order to provide the best response in terms of both survival and quality of life. In the case of a patient with moderate-severe CKD, some options to consider in the future to reduce the risk of acute renal failure are the use of a single PCI or the use of a tyrosine kinase inhibitor.

The relevance of this clinical case resides in the low incidence of acute renal failure secondary to immunotherapy treatment which, in addition to presenting a mild evolution on most occasions, in our clinical case presented a torpid evolution, with a poor response to corticosteroid treatment. Therefore, despite the low prevalence of this complication, we must bear it in mind in our daily clinical practice, especially in patients with previous CKD, given the current boom with new immunotherapy drugs.

Ethical aspects

The authors declare that the protocols established in their workplace have been followed to access the data of the patient's medical history in order to be able to make this publication for the purpose of dissemination to the scientific community.

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