



Clear Cell Renal Carcinoma in a 58-year-old Single-Kidney Patient: A Case Report

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Abstract

The clear cell renal carcinoma is the most common malignant neoplasm in the kidney. We present the clinical case of a 58-year-old patient with a history of weight loss of 10 kg in six months and fatigue. Her medical history highlights a left total nephrectomy due to a benign tumor. Currently, she is admitted to our service for a right partial nephrectomy due to suspicion of clear cell renal carcinoma. We consider this case report relevant due to the bilateral presentation of a tumor, both of which underwent nephrectomy.

Keywords: Clear Cell Renal Carcinoma; Partial Nephrectomy; Endothelial Growth Factor; Radiotherapy and Case Report

Introduction

Renal cell carcinoma (RCC) stands as one of the most common cancer entities, boasting a global prevalence of 2% among all diagnosed cancer types. In the United States alone, it is estimated that over 80,000 new cases will be diagnosed this year, leading to more than 14,000 deaths [1]. There are three primary histological categories: clear cell or conventional RCC (ccRCC), papillary RCC, and chromophobe RCC. Of these, 80% will be of the ccRCC type [2]. The most widely accepted histological classification for RCC is the Fuhrman nuclear grade, which consists of 4 grades. These grades are also used as an independent prognostic factor, especially in ccRCC [3].

Due to the often poor clinical presentation, patients are generally diagnosed incidentally through imaging studies such as computed tomography (CT), ultrasound, or magnetic resonance imaging [4]. However, a classical triad occurs in up to 10% of patients, consisting of flank pain, a palpable mass, and hematuria. Other less specific symptoms include leukocytosis, fever, weight loss, and asthenia. They can also lead to paraneoplastic syndromes such as anemia, hypertension, polycythemia, hypercalcemia, Cushing's disease, and alterations in liver function [5].

The treatment will depend on the patient's characteristics and the tumor. For localized tumors, the treatment of choice is nephrec-

tomy, either partial or total depending on each case. Meanwhile, for metastatic or advanced tumors, the standard treatment is cytoreductive nephrectomy followed by systemic therapy [2].

Case Report

A 58-year-old female was admitted to our institution with a history of significant weight loss of 10 kg in less than 6 months and moderate fatigue. Her weight loss began in April 2023, and simultaneously, she experienced uncontrolled glucose levels peaking at 400 mg/dl.

There is no relevant family history for this case report. Her medical record highlights Type 2 Diabetes treated with Empagliflozin/Linagliptin and a left nephrectomy 18 years ago associated with a benign tumor; however, she does not recall the type of tumor.

For the initial evaluation, laboratory and imaging studies were required. The CT showed a kidney tumor (Figure 1). As part of the presurgical study, laboratory studies were requested where the alterations that occurred were an elevation of BUN of 24.76 mg/

dL and a urea of 53 mg/dL without any other alteration (Tables 1 and 2). Considering the left kidney tumor antecedent and the new tumor, a renal carcinoma was suspected.



Figure 1: Abdominopelvic computed tomography. Tumor in the right lower renal pole, measuring up to 6.5 cm with a heterogeneous appearance and loss of interface with the second portion of the duodenum. It shares the proximal ureter without invading vascular structures. No lymphadenopathy was found. Right pelvicalyceal ectasia, Bosniak 5 right renal cyst, aortoiliac atherosclerosis, and osteodegenerative changes.

Test/date	11/09/23	15/09/23	16/09/23	17/09/23	18/09/23	19/09/23
Leukocytes	8.73 10 ³ /uL	16 10 ³ /uL ↑	9.15 10 ³ /uL	8.1 10 ³ /uL	8.7 10 ³ /uL	9.4 10 ³ /uL
Hemoglobin	11.84 g/dl	9.29 g/dl ↓	9.2 g/dl ↓	9.92 g/dl ↓	10.09 g/dl ↓	11.48 g/dl
Hematocrit	38.44 %	31 % ↓	28.54 % ↓	28.79 % ↓	32.22 % ↓	36.8 % ↓
Platelets	352.1 10 ³ /uL	356 10 ³ /uL	219.5 10 ³ /uL	213.20 10 ³ /uL	272 10 ³ /uL	234 10 ³ /uL
Neutrophils	5.02 10 ³ /uL	13.03 10 ³ /uL ↑	6.88 10 ³ /uL ↑	6.06 10 ³ /uL	5.17 10 ³ /uL	5.41 10 ³ /uL
Lymphocytes	2.87 10 ³ /uL	2.19 10 ³ /uL	1.48 10 ³ /uL	1.07 10 ³ /uL	2.61 10 ³ /uL	2.9 10 ³ /uL

Upon admission, optimal hemoglobin levels for age and gender were noted. Post-procedure, Grade I anemia was observed, which recovered by the day of discharge. During hospitalization, post-surgical leukocytosis associated with surgical trauma was present, with subsequent improvement after intervention. No lymphocytosis was observed during the hospital stay.

Table 1: Hematic biometry.

Test/date	11/09/23	15/09/23	16/09/23	17/09/23	18/09/23	19/09/23
Glucose	106.24 mg/dL ↑	73 mg/dL	114.7 mg/dL ↑	116.67 mg/dl ↑	111 mg/dL↑	111.28 mg/dL ↑
BUN	24.76 mg/dL ↑	18 mg/dL	8.37 mg/dL	7.83 mg/dl	9.99 mg/dL	9.81 mg/dL
Urea	53 mg/dL ↑	39.6 mg/dL	17.9 mg/dL	16.8 mg/dl	21.4 mg/dL	21 mg/dL
Creatinine	0.98 mg/dL	0.90 mg/dL	0.56 mg/dL	0.56 mg/dL	0.61 mg/dL	0.63 mg/dL
Alkaline Phosphatase	92.49 U/L	75.49 U/L	114.38 U/L ↑		126 U/L ↑	136 U/L ↑
Lactate Dehydrogenase	120.05 U/L	316.12 U/L ↑	141.79 U/L		157.71 U/L	205.38 U/L
Sodium	137 mmol/L		134.44 mmol/L	135.47 mmol/L	140 mmol/L	139.4 mmol/L
Potassium	4.2 mmol/L		3.46 mmol/L	3.74 mmol/L	4.91 mmol/L	3.88 mmol/L
Chloride	106 mmol/L		102.58 mmol/L	105.61 mmol/L	108 mmol/L	107.52 mmol/L
C- reactive protein			135.05 mg/L ↑		73.09 mg/L ↑	

Renal function was monitored and showed no alterations despite the surgical intervention. Only an elevation in inflammatory markers (LDH, alkaline phosphatase, C-reactive protein) was observed post-intervention, with a subsequent decrease in levels following in-hospital management.

Table 2: Blood chemistry.

Therefore, it was decided to proceed to the operating room on 15/09/23 for a partial nephrectomy. The postoperative report indicated a tumor on the right pole and anterior surface of the right kidney, accompanied by bleeding of 350 cc with no other associated complications (figure 2). The excised tissue was sent for histopathological study. The histopathological study revealed a “conventional clear cell renal carcinoma with 20% necrosis, Fuhrman Histological Grade 3, with microscopic extension of the tumor focally towards the capsule and in contact with the surgical resection Edge”.

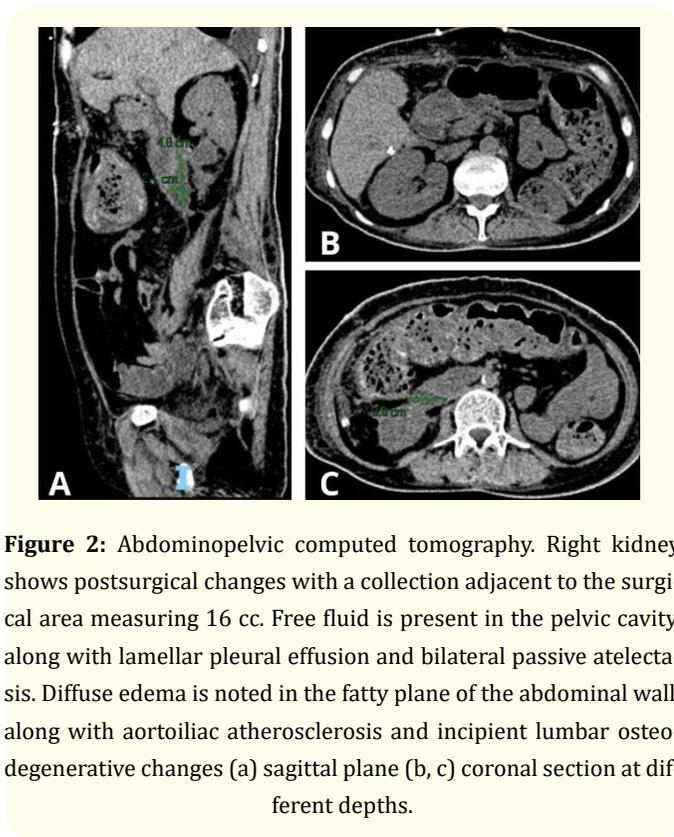


Figure 2: Abdominopelvic computed tomography. Right kidney shows postsurgical changes with a collection adjacent to the surgical area measuring 16 cc. Free fluid is present in the pelvic cavity, along with lamellar pleural effusion and bilateral passive atelectasis. Diffuse edema is noted in the fatty plane of the abdominal wall, along with aortoiliac atherosclerosis and incipient lumbar osteodegenerative changes (a) sagittal plane (b, c) coronal section at different depths.

The patient did not experience complications during the immediate or delayed postoperative period. No systemic treatment was required after the surgery due to the localized nature of the tumor and the absence of metastasis. Consequently, she was discharged from our institution with vital signs within normal parameters and renal function within the expected ranges for the patient. According to the histological subtype of this patient, five-year survival models dictate that clear cell carcinoma has a cancer-specific survival of 71% [6]. However, the literature does not report the specific prognosis for individuals who meet the characteristics outlined in the case report of our patient.

Discussion

RCC arises from nephritic epithelial cells and occurs in approximately 400,000 people worldwide. It exhibits a higher incidence in men compared to women, with a mean age of presentation of 60 years. This type of cancer is classified into three histological subtypes: Papillary RCC, chromophobe RCC and ccRCC, with CCRCC being the most prevalent variant, accounting for 70%-80% of cases, and a third of these patients presenting metastasis [7,8]. The ccRCC is characterized by the loss of part or all of chromosome 3p [7]. Other genes and proteins associated with chromosome 3p include BRCA-associated protein 1 (BAP1), SET2, and PBRM1. Another gene involved is the Von Hippel Lindau gene mutation, inherited in an autosomal dominant manner and associated with bilateral ccRCC, which can be diagnosed up to 20 years earlier [7,9].

The ccRCC typically originates in the tubular epithelium and renal stem cells found in the proximal nephron. Therefore, the most common metastasis pathway is the hematogenous route to other organs, with the lungs, lymph nodes, bones, and liver being the most affected sites [10].

More than 50% of ccRCC cases are diagnosed accidentally when renal masses are detected in imaging studies indicated for other pathologies [4]. Only 30% of cases are diagnosed by urinary symptoms and paraneoplastic syndromes [4,11]. Radiography may show the presence of calcification (14-24%) and lymphadenopathy (>1 cm in diameter) [11].

Early detection helps offer better treatment, a urine or blood test is used to identify 3p loss [7]. If urinary symptoms are present, a CT and urography should be performed; in the case of a paraneoplastic syndrome, thoracic and abdominal imaging studies are required [12].

Radiotherapy and chemotherapy are ineffective treatments for ccRCC. Some treatments are focused on vascular endothelial growth factor (VEGF) signaling, especially tyrosine kinase inhibitors (TKIs) such as Pazopanib and Sunitinib, considered first-line agents, and Sorafenib and Axitinib, considered second-line agents. New treatments are based on immunological inhibitors (PD1-PDL1/CTLA4) that act by inhibiting tumor cells from unfolding [13]. Vaccines with oncolytic viruses are currently being tested for positively regulating the exposure of tumor neoantigens to the immune system [14]. Surgical treatment consists of partial or total nephrectomy and is indicated when there is no metastasis; however, a large

percentage of patients at diagnosis already have metastasis [15]. The study conducted by Méjean et al. demonstrated that the use of sunitinib is not inferior to the results obtained by using cytoreductive nephrectomy with sunitinib. This opens the possibility of using systemic therapies without the need for surgery in metastatic RCC [16].

It is important to stage ccRCC patients in order to establish their specific prognosis; the most used way to do this is through the Fuhman histological classification and the Hemoxygenase 1 (HO-1) enzyme. The overexpression of HO-1 in tumors with high Fuhman grade (III or IV) suggests that HO-1 could be a good complementary marker of ccRCC aggressiveness [17]. RCC in advanced stages represents a 5-year survival of 11.7% and it presents a recurrence of up to 30% after a complete resection of the primary tumor [13].

Conclusion

CCR arises from nephritic epithelial cells, diagnosed more frequently in men than in women, with the most common variant being ccRCC in 70%-80% of cases. This report presents the case of a 58-year-old female patient diagnosed with ccRCC with 20% necrosis, Fuhrman Histological Grade 3, with microscopic extension of the tumor focally towards the capsule, successfully treated with partial nephrectomy at an oncology center in Mexico City. This tumor is diagnosed incidentally in over 50% of cases, highlighting the importance of early detection for providing better treatment. Radiotherapy and chemotherapy are ineffective treatments for ccRCC. Some treatments focus on VEGF and TKI signaling.

Conflict of Interest

The authors declare there are no conflicts of interest.

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Protection of People and Animals

The authors declare that no experiments were carried out on humans or animals for this research.

Data Confidentiality

The authors declare that they have followed the protocols of their work center regarding the publication of patient data.

Bibliography

1. Siegel Rebecca L., et al. "Cancer statistics, 2023". *CA: A Cancer Journal for Clinicians* 73.1 (2023): 17-48.
2. Blanc Julien and Beat Roth. "Clear cell renal cancer metastasis in the contralateral ureter: a case report". *Journal of Medical Case Reports* 15.1 (2021): 309.
3. Uscanga Yépez Jaime., et al. "Diferencias en los indicadores pronóstico de supervivencia en pacientes con cáncer de células renales entre el medio hospitalario público y privado". *Revista Mexicana de Urología* 77 2 (2017).
4. Bahadoram, Sara., et al. "Renal cell carcinoma: an overview of the epidemiology, diagnosis, and treatment". *Giornale Italiano Di Nefrologia : Organo Ufficiale Della Societa Italiana Di Nefrologia* 39.3 (2022).
5. Ikuero, S O., et al. "Paraneoplastic syndromes and oncological outcomes in renal cancer". *Nigerian Journal of Clinical Practice* 22.9 (2019): 1271-1275.
6. Hori Shunta., et al. "Impact of Radical Nephrectomy and Partial Nephrectomy on Actual Estimated Overall Survival Compared to Life Expectancy in Patients with Renal Cell Carcinoma". *Research and Reports in Urology* 13 (2021): 155-165.
7. Jonasch, Eric., et al. "Clear cell renal cell carcinoma ontogeny and mechanisms of lethality". *Nature Reviews. Nephrology* 17.4 (2021): 245-261.
8. Wolf, Melissa M., et al. "Modeling clear cell renal cell carcinoma and therapeutic implications". *Oncogene* 39.17 (2020): 3413-3426.
9. Padala Sandeep Anand., et al. "Epidemiology of Renal Cell Carcinoma". *World Journal of Oncology* 11,3 (2020): 79-87.
10. Dudani Shaan., et al. "Evaluation of Clear Cell, Papillary, and Chromophobe Renal Cell Carcinoma Metastasis Sites and Association With Survival". *JAMA Network Open* 4.1 (2021): e2021869.
11. Stolpa Weronika., et al. "Clear Cell Renal Cell Carcinoma, Diagnostic and Therapeutic Difficulties, Case Report and Literature Review". *Medicina (Kaunas, Lithuania)* 58.10 (2022): 1329.
12. Gray Richard E and Gabriel T Harris. "Renal Cell Carcinoma: Diagnosis and Management". *American family physician* 99.3 (2019): 179-184.

13. Makhov Peter, *et al.* "Resistance to Systemic Therapies in Clear Cell Renal Cell Carcinoma: Mechanisms and Management Strategies". *Molecular Cancer Therapeutics* 17.7 (2018): 1355-1364.
14. Deleuze Antoine., *et al.* "Immunotherapy in Renal Cell Carcinoma: The Future Is Now". *International Journal of Molecular Sciences* 21.7 (2020): 2532.
15. Grammatikaki, Stamatiki., *et al.* "An Overview of Epigenetics in Clear Cell Renal Cell Carcinoma". *In vivo (Athens, Greece)* 37.1 (2023): 1-10.
16. Méjean, Arnaud., *et al.* "Sunitinib Alone or after Nephrectomy in Metastatic Renal-Cell Carcinoma". *The New England Journal of Medicine* 379.5 (2018): 417-427.
17. Mingote Pablo A., *et al.* "Expresión de Hemo Oxigenasa-1 y agresividad del carcinoma renal de células claras" [Expression of Hemeoxygenase-1 and clear cell renal cell carcinoma aggressiveness.]. *Archivos espanoles de urologia* 73.9 (2020): 794-802.