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CASE REPORT

Resolution of Refractory Hypertension Following Radical Nephrectomy for Renal Cell Carcinoma: A Case Report from Somalia in Resource Limit Setting

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Introduction: Renal cell carcinoma (RCC) is among the most prevalent kidney malignancies and is characterized by a variety of histological subtypes, with clear cell RCC being the most common subtype. Hypertension may occur as a paraneoplastic manifestation, although the resolution of refractory hypertension following radical nephrectomy remains an uncommon event. To our knowledge, this is the first documented case from a resource-limited setting in which refractory hypertension resolved completely following radical nephrectomy for RCC, underscoring unique diagnostic and therapeutic challenges in such environments.

Case Presentation: A 56-year-old male presented with severe uncontrolled hypertension accompanied by persistent headaches and palpitations and was unresponsive to standard anti-hypertensive therapy. Clinical examination revealed a palpable mass in the right flank. Abdominal computed tomography revealed a large, heterogeneous mass (approximately 10 cm) occupying the hepatorenal space, which was initially suggestive of pheochromocytoma. Due to limited diagnostic resources, confirmatory biochemical testing was unavailable. The patient underwent radical nephrectomy and histopathology confirmed clear cell RCC (WHO/ISUP grade 2). The patient's hypertension resolved completely postoperatively, with subsequent follow-ups demonstrating stable blood pressure and no metastatic disease.

Conclusion: This case emphasizes an uncommon presentation of refractory hypertension linked directly to RCC that resolved after radical nephrectomy. This case underscores the importance of considering RCC as a differential diagnosis for refractory hypertension, particularly in resource-limited settings where advanced diagnostics and recent surgical are unavailable.

Keywords: renal cell carcinoma, refractory hypertension, radical nephrectomy, paraneoplastic syndrome, case report, Somalia

Introduction

Renal cell carcinoma (RCC) is one of the top ten most prevalent cancers in the world and includes a diverse collection of tumors originating from renal tubular epithelial cells.[1] Renal cell carcinoma (RCC) accounts for 2.4% of all cancer diagnoses globally, with over 400,000 new cases and 180,000 deaths annually, driven largely by modifiable risk factors such as smoking, obesity, and hypertension, especially in high-income countries.[2] RCC accounts for 90% of kidney-derived tumors, with a median age of 64 years, it is prevalent in the sixth and seventh decades of life and largely affects the elderly, with a two-fold male predominance.[3]

Africa had the lowest rate of RCC mortality and incidence, with a cumulative risk of less than 0.2% for both sexes. With cumulative mortality risks ranging from 0.17% to 0.27%, the highest death rates were found in Egypt (2.4), Libya (2.3), Mali (1.8), and Tunisia (1.7).[4]

The disorder typically manifests as one or more of the following symptoms palpable flank mass, weight loss, or macroscopic hematuria. While RCC is a collection of tumors with a wide variety of histopathologic features, the most prevalent histologic subtype is clear cell RCC (ccRCC). It frequently spreads to the lungs, regional lymph nodes, bone, liver, adrenal glands, contralateral kidney, and the brain.[5]

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Paraneoplastic syndrome is a collection of symptoms that occur subsequent to cancer but do not directly result from tumor extension or metastasis. According to estimates, 10–40% of people with RCC will experience paraneoplastic syndrome at diagnosis.[6]

Paraneoplastic syndromes linked to renal cell carcinoma include those that cause particular metabolic and biochemical abnormalities (such as hypercalcemia, non-metastatic hepatic dysfunction, amyloidosis, etc), as well as those that present with constitutional symptoms (such as fever, cachexia, and weight loss). In patients with renal cell carcinoma, the existence of paraneoplastic syndrome is not always a sign of poor prognosis or a predictor of metastatic illness.[7] Hypertension occurs in approximately 15.8% of patients with renal cell carcinoma and is considered one of its most common paraneoplastic syndromes, it arises through multiple tumor-driven mechanisms, including ectopic renin secretion, arteriovenous fistulas within the mass, and erythrocytosis-induced hyperviscosity.[8]

Recent advances in robotic platforms such as single port systems, three dimensional modeling, and artificial intelligence have significantly improved precision and safety in urologic oncology surgery in developed countries.[9]

When compared to partial nephrectomy, radical nephrectomy was linked to a greater risk of both new-onset and exacerbated hypertension, even in patients who were old or had adequate kidney function.[10] Here, we present a rare case of refractory hypertension that resolves following radical nephrectomy for RCC, underscoring the importance of recognizing and managing RCC as a potential underlying cause in cases of persistent and unexplained hypertension, particularly in resource-limited settings.

Case Presentation

A 56-year-old male, previously in good health with no history of hypertension or diabetes, presented with a month-long history of severe headaches, palpitations, and uncontrolled high blood pressure, despite starting anti-hypertensive medications at a local clinic. Due to his persistent hypertension, his physician referred him to the hospital for further evaluation.

The patient had no past surgical history or similar condition, no history of weight loss and he did not smoke or drink alcohol or other bad habits. The patient stated that his headache persisted throughout the day and was not relieved by medication.

On physical examination, the patient appeared thin body built, alert, and oriented. His body mass index (BMI) was 19 kg/m². However, abdominal palpation revealed an immobile, non-tender mass in the right flank. This unexpected discovery prompted further investigation using an abdominal computer tomography (CT) scan. Vitals on admission were as follows: blood pressure (BP)=164/104, pulse=73, spo2=99%; Temperature, 36.3 °C; blood glucose, 109 mg/dl.

The initial laboratory results are shown (Table 1). An abdominal CT scan revealed a massive, well-defined heterogeneous enhancing mass at the hepatorenal space, measuring 9.5×9.8x10.3 cm, with the right kidney displaced downward (Figure 1). Pheochromocytoma was initially suspected as the cause of severe hypertension in the patient. However, limited resources in

Table 1 The Laboratory Investigations Results

Tests	Reference Range	On Admission	On Operation	On Discharge
White cell count (WBC, $*10^9$ /L)	4.00–10.00	10.2	7.4	8.6
Hemoglobin (HB, g/dl)	12.0–16.0	14.2	14.4	12.5
Platelet (PLT, $*10^9$ /L)	100–300	200	240	198
C-reactive protein (CRP, mg/L)	2.5–10	<2.5	8.4	4.2
Aspartate transaminase (AST-U/L)	6–38	36.2	29	31
Alanine transaminase (ALT, U/L)	6–40	35	19.6	25.2
Creatinine (Creatinine, mg/dl)	0.4–1.4	1.15	0.95	1.2
Blood urea (Blood urea, mg/dl)	10–50	33.6	27.3	23.4
Sodium (Na+, mmol/l)	135.0–145.0	140.3	142.2	139.6

(*Continued*)

Table 1 (Continued).

Tests	Reference Range	On Admission	On Operation	On Discharge
Potassium (K+, mmol/l)	3.5–5.5	4.3	3.6	3.9
Calcium (Ca+, mmol/l)	2.12–2.62	2.01	2.26	2.24
Prothrombin time (PT, sec)	10–14	12.6	13.8	13.2
Activated partial Thromboplastin time (APTT, sec)	11–45	38.6	28	32.8
INR (International Normalized Ratio)	0.8–1.1	1.05	1.15	1.1
D-Dimer (ng/mL)	50–500	589.34	347.31	652

Note: *Multiplication Sign.

the country have prevented confirmatory testing for this hormone-secreting tumor. Despite this uncertainty, the team initiated aggressive blood pressure management, aiming to stabilize the patient before surgery. The patient was admitted to the ward and was immediately started on a doxazosin regimen. The dose was progressively increased daily from 2 to reach a maximum of 18 mg. Intravenous fluids were administered to support the patient's circulatory system.

Five days after admission, metoprolol was added to the treatment plan. The dose of metoprolol was also gradually increased from 25 mg/day to 75 mg/day, achieving a dual-regimen approach to control persistent hypertension and reflex

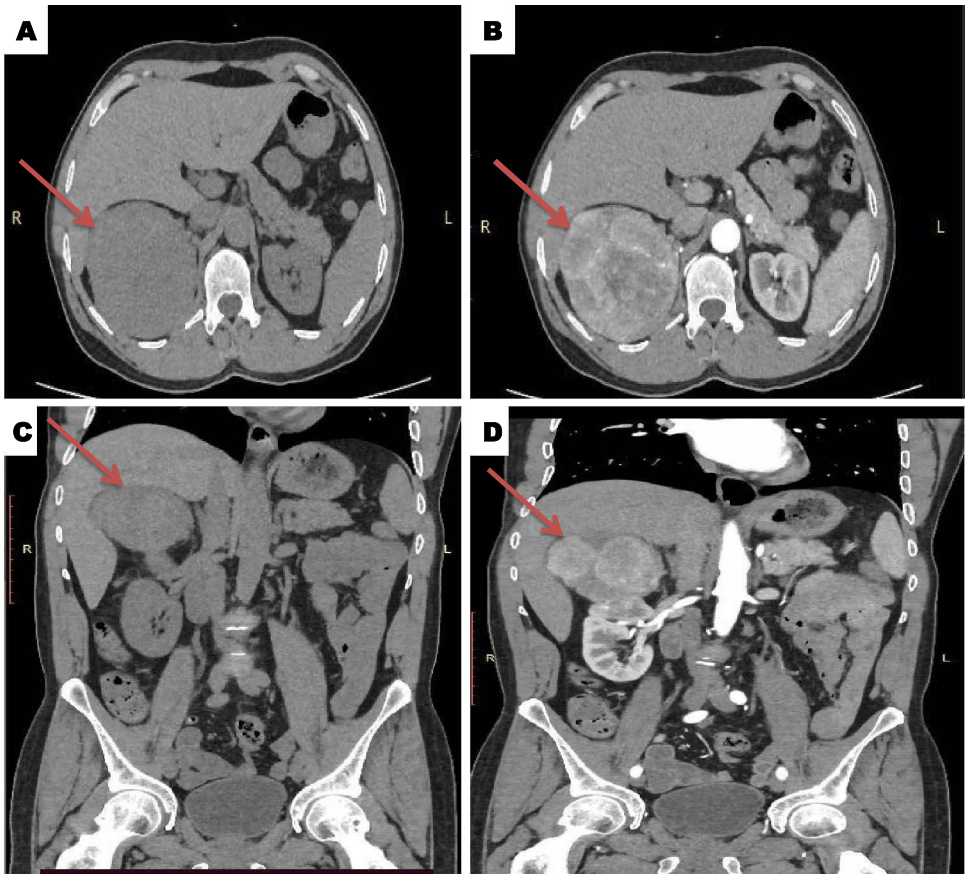

Figure 1 Contrast-enhanced computed tomography (CT) images of the abdomen demonstrating a large heterogeneous mass in the hepatorenal space causing downward displacement of the right kidney. (**A**) Axial pre-contrast CT image shows a large well-defined heterogeneous mass (red arrow) occupying the hepatorenal recess. (**B**) Axial post-contrast CT image clearly illustrates heterogenous enhancement of the mass (red arrow) with displacement of the adjacent right kidney inferiorly. (**C**) Coronal pre-contrast CT reconstruction highlighting the mass (red arrow) and its anatomical relation to the right kidney. (**D**) Coronal post-contrast CT reconstruction demonstrating enhancement and clear delineation of the mass (red arrow), with significant displacement of the right kidney downward. R indicates right side; L indicates left side.

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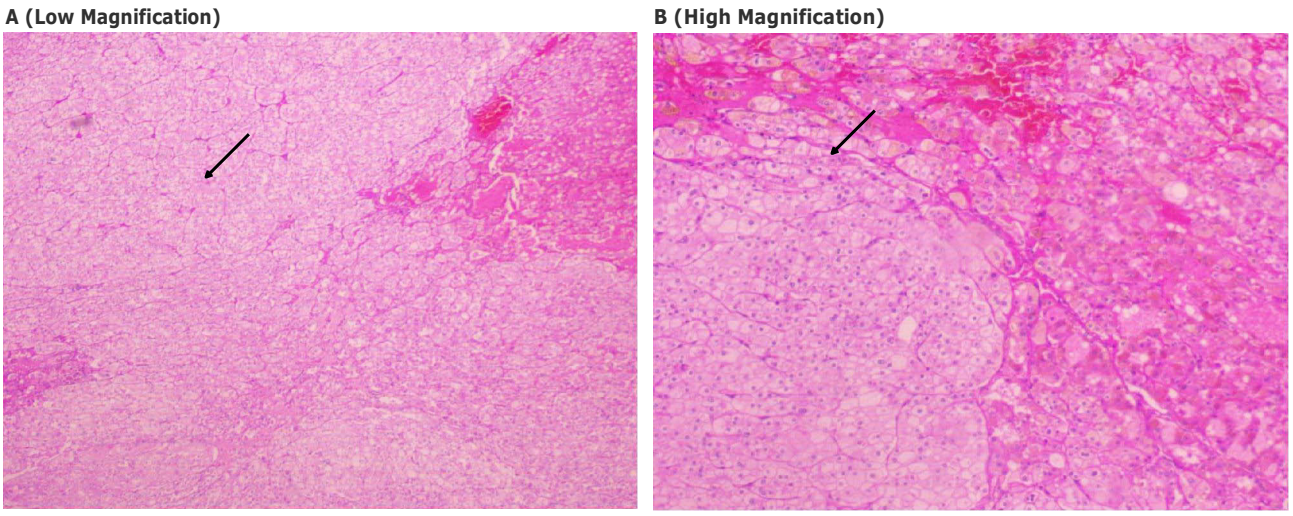

Figure 2 Clear cell renal cell carcinoma. (**A**) Low magnification demonstrating diffuse growth and clear cell morphology with delicate vascular network (Black arrow highlights area of necrosis). (**B**) High magnification illustrating compact tumor nests with clear cytoplasm and thin-walled vascular structures characteristic of WHO/ISUP Grade 2 (Black arrow indicates hemorrhagic area). Hematoxylin and eosin stain.

tachycardia. Even with combined Doxazosin and Metoprolol therapy, the patient's blood pressure remained uncontrolled. Therefore, amlodipine 10mg was added to the regimen.

The patient's blood pressure was monitored closely in various positions, such as sitting, supine, and standing, to assess orthostatic changes and ensure stability. After two weeks of intensive blood pressure management, the patient's blood pressure normalized. The surgical team then scheduled an exploratory.

Intraoperative findings revealed a highly vascularized tumor originating from the upper pole of the right kidney, occupying the hepatorenal space. The tumor was approximately 10 cm in size. No regional lymph nodes, venous thrombosis, or distant metastases were noted. Radical nephrectomy was performed, and a biopsy was taken from the tumor to confirm and revealed Renal Cell Carcinoma (RCC), WHO/ISUP grade 2 and pT2aNxMx (Figure 2). Postoperatively, the patient was admitted to the intensive care unit (ICU) for close monitoring. He remained in the ICU for a few days before being transferred to a regular ward and subsequently discharged home.

At the time of discharge, all investigations, including blood pressure, were within the normal range. He was scheduled for a follow-up appointment three weeks later. His blood pressure remained stable at follow-up and there were no signs of metastasis, suggesting successful removal of the tumor.

Discussion

This case report presents a patient with refractory hypertension, initially suspected to be due to pheochromocytoma but ultimately diagnosed as a manifestation of renal cell carcinoma (RCC). The patient's hypertension and associated symptoms resolved following radical nephrectomy, which highlights the complex relationship between RCC and its paraneoplastic manifestations.

The range of relationships between hypertension and renal cell carcinoma includes secondary hypertension as a paraneoplastic phenomenon and essential hypertension as a risk factor for renal cell carcinoma.[8,11] The patient in this case did not have any of the known independent risk factors for renal cell carcinoma (RCC), including essential hypertension, obesity and cigarette smoking but he is appeared thin body built. This implies that additional variables may have been contributed to RCC development in this case. Both genetic and environmental factors may have contributed to RCC in this patient. A key hereditary pathway involves mutation or inactivation of the von Hippel-Lindau (VHL) tumor suppressor gene, central to clear cell RCC (ccRCC) pathogenesis through deregulation of hypoxia-inducible factors (HIFs), leading to increased angiogenesis and tumor proliferation.[11–13] VHL disease, a rare autosomal dominant syndrome (~1 in 36,000 births), predisposes individuals to multiple neoplasms including ccRCC and pheochromocytomas, which occur in 10–20% of VHL cases, often before age 30.[14] In addition, environmental exposures such as

chlorinated solvents and cadmium have been strongly linked to RCC risk.[15,16] Although genetic testing and biochemical screening were not feasible in our setting, these mechanisms are plausible contributors to tumor development in this case.

The patient's presentation with refractory hypertension prompted a consideration of pheochromocytoma, a rare adrenal tumor known to cause significant fluctuations in blood pressure due to excessive catecholamine secretion.[17] The classic symptoms of pheochromocytoma include headaches, palpitations, and sweating, which can overlap with other conditions.[17] However, the lack of access to blood and urine tests that measure catecholamines and their metabolites, which are crucial diagnostic tools for pheochromocytoma, limited the diagnostic process in this case. Histologically, clear cell renal cell carcinoma (ccRCC) presents with clear cells arranged in nests surrounded by a rich vascular network, whereas pheochromocytoma displays a zellballen pattern with granular cytoplasm.[18] Although immunohistochemistry, cytokeratin positivity for ccRCC and chromogranin A for pheochromocytoma, is typically used to differentiate the two, this was not available in our setting; thus, diagnosis relied on classical morphological features.[19]

Numerous studies have not been able to establish a direct link between the prognosis and the occurrence of hypertension in RCC patients. Increased renin secretion, ureteral or parenchymal compression, arteriovenous fistula, and polycythemia are possible causes of hypertension in these patients.[7,8] In a retrospective cohort study from Lagos State University Teaching Hospital, hypertension was observed in 16 of 101 patients with RCC, often linked to low-grade clear cell tumors.[8]

Renin-producing tumors, including renin-secreting RCCs and juxtaglomerular cell tumors, can activate the renin-angiotensin-aldosterone system (RAAS), and RCC may also exert a local mass effect that impairs renal perfusion and indirectly stimulates RAAS, while rare tumors containing adrenal-like tissue may secrete hormones that exacerbate hypertension. Given this spectrum of mechanisms, renal tumors should be considered in cases of secondary hypertension, especially when hypertension is resistant to standard therapy.[20]

Renin secretion in RCC may result from autonomous production by tumor cells or secondary activation of the renin angiotensin aldosterone system (RAAS) due to tumor-induced renal compression, both of which have been reported to contribute to paraneoplastic hypertension.[18] A 87% of patients with Wilms' tumor and 37% of patients with RCC have elevated serum renin levels.[11] Even while renin has been investigated as a possible tumor marker in RCC and its levels usually drop following nephrectomy. In our case, although direct renin measurement was not feasible in our country, the clinical profile of severe hypertension unresponsive to therapy and radiological evidence of a renal mass suggested a renin-mediated mechanism.

Since most RCC cases are now found incidentally through imaging, and only about 10% show the classic triad of symptoms, it is critical to consider RCC even when hypertension is the only presenting sign.[21] Significant blood pressure changes are linked to surgical treatment of renal tumors, with de novo hypertension developing in nearly 20% of patients.[22] This case underscores significant diagnostic challenges related to the non-specific clinical presentation of refractory hypertension combined with limited diagnostic tools, particularly biochemical renin testing, in a resource-limited setting. Diagnosis primarily relied on clinical assessment and imaging findings initially suggestive of pheochromocytoma rather than RCC. Additionally, the lack of long-term follow-up imaging represents a significant limitation; the patient's family returned to their rural area shortly after surgery, necessitating clinical follow-up as the only available method to monitor disease progression and blood pressure status.

The surgical treatment of renal masses, particularly in older or fragile patients, presents unique challenges, especially in low-resource settings. Management of metastatic RCC has advanced significantly, with cytoreductive nephrectomy and metastasectomy still valuable in select cases, though the ideal treatment regimen remains debated.[23] While radical nephrectomy remains the most feasible option in our setting, evidence suggests that partial nephrectomy should be considered when technically possible, as it better preserves renal function and is associated with favorable outcomes even in elderly populations. A recent review supports the role of minimally invasive nephron-sparing surgery in older patients, emphasizing that this approach, when available, reduces operative morbidity and protects long-term renal function, thereby enhancing overall recovery and quality of life.[24] Although our patient underwent radical nephrectomy due to tumor size and limited surgical alternatives, these insights underscore the need for tailored surgical planning and capacity-building to expand nephron-sparing options in similar settings.

The patient's hypertension resolved after undergoing radical nephrectomy, indicating that in some cases, the removal of the tumor itself can relieve this symptom. While we could not assess a direct prognostic correlation between hypertension and clinical outcomes in this case, existing literature reports no consistent link between hypertension and poor prognosis in RCC patients. Notably, hypertension often resolves following nephrectomy, supporting its role as a tumor-driven, reversible condition.

This is in contrast to studies that indicate that radical nephrectomy usually increases the risk of new or worsened hypertension, even in older people and those with healthy kidneys.[10] Therefore, clinicians should maintain a high index of suspicion for renal cell carcinoma in patients presenting with unexplained refractory hypertension, especially in settings with limited diagnostic resources and unavailability of recent advanced surgical management.

Conclusion

This case highlights the importance of considering RCC as a differential diagnosis in patients with unexplained refractory hypertension, especially in resource-limited settings where such associations may be overlooked. It also emphasizes the potential for blood pressure normalization following timely surgical intervention. To improve RCC outcomes in low-resource contexts, enhancing clinical awareness, expanding access to basic imaging modalities, and promoting training on paraneoplastic presentations are essential. Further research is needed to explore cost-effective diagnostic pathways, tailored management strategies that can be implemented even where advanced diagnostics and surgical are unavailable.

Abbreviations

RCC, renal cell carcinoma; ccRCC, clear cell renal cell carcinoma; CT, computed tomography; ICU, intensive care unit; WHO, World Health Organization; ISUP, International Society of Urological Pathology; pTNM, pathological tumor-node -metastasis; BP, blood pressure.

Ethics and Consent

Written informed consent was obtained from the patient for the publication of this case report and associated images. According to our institution's guidelines, ethical approval was not required for the publication of case reports.

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Author Contributions

All authors contributed substantially to this work, including its conceptualization, study design, data collection, analysis, and interpretation. Each author was actively involved in writing, revising, or critically reviewing the manuscript, approved the final version for publication, agreed to the journal selected for submission, and accepted responsibility for all aspects of the work.

Disclosure

The authors declare no conflicts of interest related to this work.

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