First Case of SMARCB1-deficiency Renal Medullary Carcinoma in Kingdom of Bahrain: A Case Report

Lina Fadhulalla[1*], Noor Alnajem[2] and Aalaa S. Majed[3]

[1]General Practitioner

[2]General Practitioner, Royal College of Surgeons, Ireland

[3]Department of Histopathology, Salmaniya Medical Complex, Bahrain

Received: 23 April 2025

Accepted: 22 June 2025

*Corresponding author:linamiralj88@gmail.com

DOI 10.5001/omj.2028.33

Abstract

This study presents a case not previously reported in the Kingdom of Bahrain or the Middle Eastern region. Renal medullary carcinoma SMARCB1-deficiency (SWI/SNF‐related matrix‐associated actin‐dependent regulator of chromatin subfamily B member 1) is an invasive type of cancer strongly associated with hemoglobinopathies (specifically sickle cell trait). We present a case of SMARCB1-deficient Renal Medullary Carcinoma (RMC) in a Bahraini patient with a two-year history of chronic kidney disease, who experienced sudden flank pain and subsequently underwent radical nephrectomy because of abnormal radiological findings. Hematological investigation confirmed the sickle cell trait. The patient was of Asian descent and deviated from the typically reported and observed lineages. Histopathological analysis revealed papillary and focal cribriform neoplastic cells with mitosis. Immunohistochemistry demonstrated positive uptake of CK7 and PAX8 stains and loss of expression of the INI1 (integrase interactor 1) protein expression. The patient received palliative care. The rare presentation and late identification of cancer emphasizes the importance of a deep understanding of the condition and the need for further research to address this topic.

Keywords: Renal Medullary Carcinoma; SMARCB1; Pathology; Oncology; Nephrology.

Introduction

Renal medullary carcinoma (RMC) is a rare and highly aggressive neoplasm, representing fewer than 0.5% of all renal malignancies, with approximately 600 cases reported worldwide to date.[1,2] It primarily affects young individuals of African descent and is strongly associated with sickle cell trait or disease and, less frequently, with other hemoglobinopathies.[3,4] Characteristic symptoms include flank pain, gross hematuria, and signs related to metastases. Prognosis remains poor, with a median survival of less than 12 months and a mortality rate exceeding 90% due to limited effective treatment options.[2,3]

RMC is now classified under the 2022 World Health Organization (WHO) Classification of Urinary and Male Genital Tumors, Fifth Edition, as a molecularly defined renal epithelial tumor distinguished by a loss of SMARCB1 (INI1) protein expression.[5] SMARCB1, a tumor suppressor gene located at chromosome 22q11.23, encodes a core component of the SWI/SNF chromatin remodeling complex. Functional loss of this gene—commonly through deletion or rearrangement—results in deregulation of epigenetic pathways and uncontrolled proliferation, partially via dysregulated EZH2 activity.[6]

Although RMC has been historically described as the "seventh sickle cell nephropathy" due to its association with hemoglobinopathies, emerging reports have documented RMC cases in patients without sickle cell trait or disease, suggesting a broader etiopathogenesis.[7] The 2022 WHO classification now includes “unclassified renal cell carcinoma with medullary phenotype,” encompassing such variants.[5,7]

In this report, we present a case of SMARCB1-deficient RMC in a male patient of Bahraini origin with confirmed sickle cell trait, highlighting diagnostic nuances and regional relevance in an individual of non-African ancestry.

Case Report

A male patient in his early 60s, of Bahraini origin with West Asian ancestry, presented with right-sided flank pain persisting for several months. His medical history was notable for hypertension, diabetes mellitus, asthma, dyslipidemia, and chronic kidney disease. He denied urinary symptoms. Laboratory tests showed persistently elevated serum creatinine over the past year.

Non-contrast computed tomography (NCCT) revealed a right upper pole renal mass measuring 8 × 9 × 6 cm. Subsequent positron emission tomography-computed tomography (PET-CT) showed hypermetabolic activity in the renal mass with retroperitoneal lymphadenopathy and pulmonary lesions suggestive of metastasis. No prior surgical history was reported. The patient was diagnosed with a right renal mass with lymph node and pulmonary metastases. Therefore, open radical right nephrectomy was performed.

Macroscopic analysis revealed that the right kidney specimen measured 12.3 × 9.2 × 3.4 cm with attached perinephric fat that was 5.6 cm in thickness. The total weight was 616.5 g, and the outer surface was nodular. A small nodule was identified at the hilum measuring 4.2 × 2.2 × 0.7 cm. An ill-defined non-encapsulated mass with a whitish-tan heterogeneous cut section was identified in the upper pole of the kidney measuring 8.3 cm (superior to inferior) × 7.2 cm (anterior to posterior) × 3.5 cm (medial to lateral). The mass grossly invaded the renal sinus fat, abutting the renal capsule, and invading the perinephric fat (1 cm at maximum invasion). The remainder of the kidney parenchyma was unremarkable, and no adrenal gland was identified.

Microscopic investigation of the H&E sections revealed neoplastic cells arranged in various architectural patterns (nests, sheets, papillary, and focal cribriform architecture). The cells were cuboidal with abundant eosinophilic cytoplasm, mild cytological atypia, and prominent nuclei [Figure 1]. Frequent mitotic figures were also identified. The tumor was observed invading the renal sinus and surrounding the renal vein [Figure 2 a and b]. No sarcomatous or rhabdoid features or necrosis were observed.

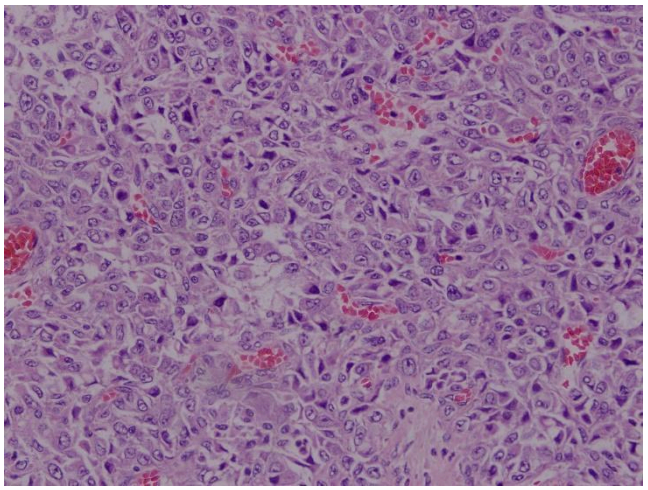

Figure 1: Histopathology slide of a cluster of the neoplastic cell arranged in a sheet manner. It exhibits pleomorphic cells with eosinophilic cytoplasm and prominent nucleoli. A predominance of cuboidal cells. H & E stained.

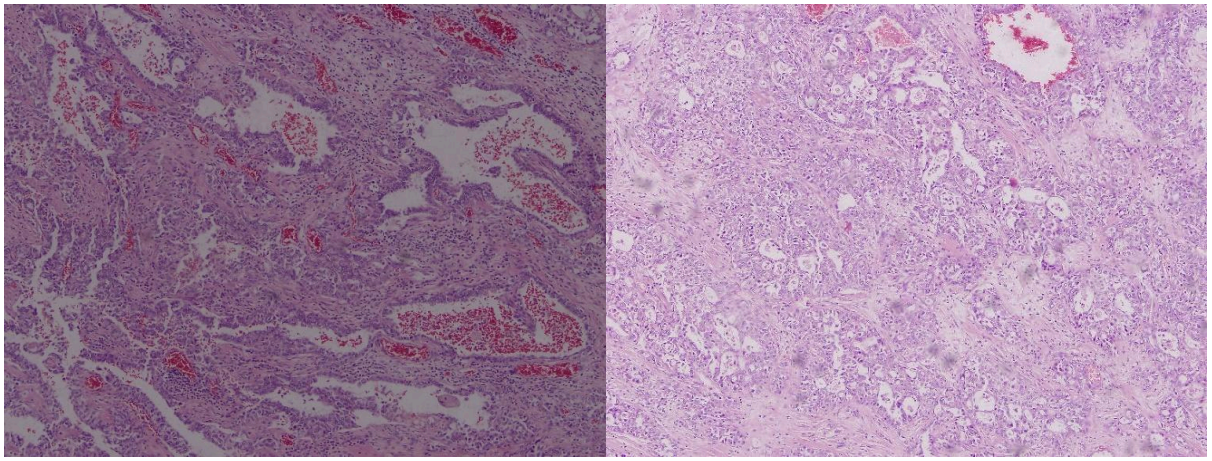

Figure 2: a&b. The slides show the variation of cells patterns and architecture range from papillary-shaped projections to cribriform and nested growth. H & E stained.

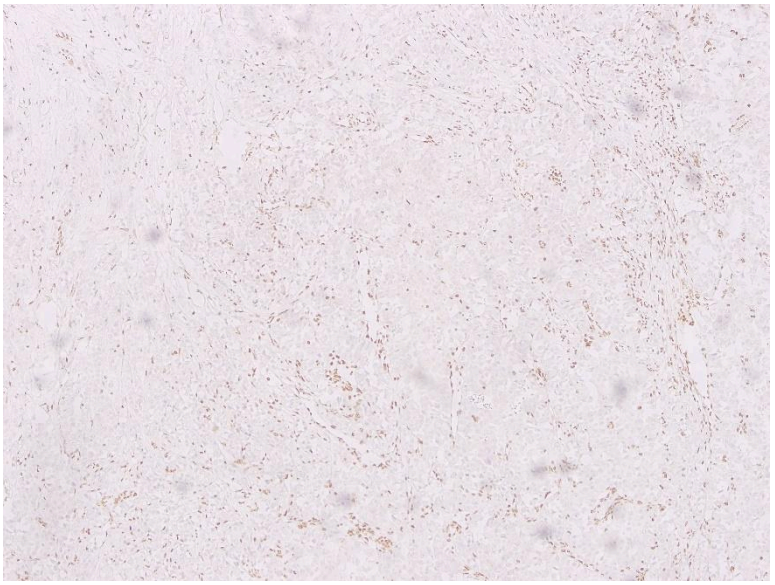

Figure 3: An immunohistochemistry of INI-1 stain is negative, supporting the diagnosis of RMC smarcb-1 deficient. At 20x magnification.

The tumor cells were diffusely positive for CK7 and PAX8 and negative for CD10, RCC, ALK, AMACR, GATA3, and CKBetaE12. Additionally, the results were inconclusive for P63. Loss of expression in tumor cells of INI-1 [Figure 3] indicated a diagnosis of SMARCB1-deficient RMC with a pathological stage of pT3a pNx pMx.

Outcome: The patient was referred to the oncology center in the Kingdom of Bahrain for further management and started on chemotherapy following surgery. There is no conclusive protocol for treating RMC owing to its aggressiveness and low survival rate. Nevertheless, radical renal surgery in conjunction with a platinum-based regimen is the treatment of choice in the majority of cases.[4]

Discussion

Our case is that of a Bahraini male in his early 60s of Asian descent who differs from most cases reported regarding RMC. In 2019, the predominant ethnicities of RMC were reported to be 84% African-American (246/292) and 6% Caucasian (16/292), respectively.[3]

In this case, the tumor was localized to the right kidney, with metastasis observed on radiological scanning to the surrounding lymph nodes and possibly to the lungs. This is in agreement with recent studies regarding the RMC stages of metastasis, where it is commonly present in the regional lymph nodes (87%), lungs and liver (75%), adrenal glands, and peritoneum (placed in order of frequency).[3,4] It primarily appears in the right kidney (67%) and left kidney (33%) owing to microinfarctions resulting from the longer length of the right renal artery. Overall, the size of the tumor ranges from 4 to 12 cm,[3,4] which correlates with our case.

Histologically, the tumor exhibits variations in architectural arrangement. A study performed in 2019 stated that high grade RMC exhibits unique patterns, including reticular, cribriform, yolk sac tumor-like, adenoid cystic, and microcytic architectures. Other features such as cords, nests, glandular, and tubular sheet-like patterns can be observed in other types of kidney malignancies, such as fumarate (FH)-deficient renal carcinoma and collecting duct carcinoma. Immunohistochemical staining can discriminate RMC and rule out other differential malignancies.[7] INI-1 staining confirmed the diagnosis of SMARCB1-deficient RMC.

Conclusion

In conclusion, this case presents a male in his 60s diagnosed with a rare form of renal cancer known as SMARCB1-deficient renal medullary carcinoma. There is a lack of documented cases involving patients of Asian ethnicity, as observed in our case. Microscopic analysis revealed the organization of different patterns, with a predominance of cuboidal cells. The indistinguishable clinical presentation and poor survival rate emphasize the need for early discovery, screening of suspected individuals, and updating the existing literature through potential future studies.

Disclosure

The authors declare that there are no conflicts of interests. This study has not received any external funding.

Acknowledgments

We thank all the patients of renal medullary carcinoma.

References

1. Valeri M, Cieri M, Elefante GM, De Carlo C, Rudini N, Lughezzani G, Buffi NM, Terracciano LM, Colombo P. Case report: unclassified renal cell carcinoma with medullary phenotype and SMARCB1/INI1 deficiency, broadening the spectrum of medullary carcinoma. Frontiers in Medicine. 2022 Feb 7;9:835599.

2. Tsuzuki S, Kataoka TR, Ito H, Ueshima C, Asai S, Yokoo H, Haga H. A case of renal cell carcinoma unclassified with medullary phenotype without detectable gene deletion. Pathology International. 2019 Dec;69(12):710-4.

3. Lakshmy S, Vijayalekshmi N, K P Aravindan. Renal Medullary Carcinoma, A Rare But Aggressive Sickle Cell Nephropathy: A Case Report. 2023 Oct 19; DOI:10.21276/APALM.3268.

4. Su Y, Hong AL. Recent advances in renal medullary carcinoma. International Journal of Molecular Sciences. 2022 Jun 26;23(13):7097.

5. van der Beek JN, Uittenboogaard A, de Krijger RR, Duijkers FA, Meijs MJ, Baard J, Vermeulen MA, Liebrechts-Akkerman G, Janssens GO, van der Voorn JP, van den Heuvel-Eibrink MM. A pediatric and young adult case of unclassified renal cell carcinoma with medullary phenotype (RCCU-MP): Clinical course and treatment. Journal of Onco-Nephrology. 2024 May 8:23993693241248495.

6. Kanakaraj J, Chang J, Hampton LJ, Smith SC. The New WHO Category of "Molecularly Defined Renal Carcinomas": Clinical and Diagnostic Features and Management Implications. InUrologic Oncology: Seminars and Original Investigations 2024 Mar 21. Elsevier.

7. Blas L, Roberti J, Petroni J, Reniero L, Cicora F. Renal medullary carcinoma: a report of the current literature. Current Urology Reports. 2019 Jan;20:1-8.